Dossier zur Nutzenbewertung gemäß § 35a SGB V

Isatuximab (SARCLISA®)

Sanofi-Aventis Deutschland GmbH

Anhang 4-G

Isatuximab in Kombination mit Carfilzomib und Dexamethason zur Behandlung des Multiplen Myeloms bei Erwachsenen, die mindestens eine vorausgegangene Therapie erhalten haben

Zusammenfassung der Aussagen
im Dossier

Stand: 07.05.2021

Studie IKEMA (EFC15246)

16.2.6.2 Secondary efficacy endpoints - Overall survival
16.2.6.2.1 ITT population
16.2.6.2.1.3 Subgroup analyses by age
16.2.6.2.1.3.1 Overall survival by treatment group according to age - ITT population

	<65 years		>=65 years		
	Kd (N=66)	**IKd (N=88)**	**Kd (N=57)**	**IKd (N=91)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of deaths	13 (19.7)	18 (20.5)	12 (21.1)	13 (14.3)	0.4615
Number (%) of patients censored	53 (80.3)	70 (79.5)	45 (78.9)	78 (85.7)	
Kaplan-Meier estimates of OS in months					
25% quantile (95% CI)	NC (13.240 to NC)	23.13 (15.639 to NC)	23.39 (17.117 to NC)	NC (21.552 to NC)	
Median (95% CI)	NC (NC to NC)	NC (23.129 to NC)	NC (23.392 to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.9254		0.3655	
Hazard ratio (95% CI) vs Kd	-	1.03 (0.51 to 2.11)		0.70 (0.32 to 1.53)	
P-value	-	0.9256		0.3680	
OS probability (95% CI)[b]					
12 Months	0.877 (0.768 to 0.936)	0.919 (0.838 to 0.961)	0.892 (0.775 to 0.950)	0.898 (0.813 to 0.946)	

OS: Overall survival, CI: Confidence interval
Cut-off date: 07FEB2020 HR<1 favors IKd arm
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] Two-sided significance level is 0.05.
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables and the treatment-by-subgroup interaction as covariates.
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16.2.6.2 Secondary efficacy endpoints - Overall survival
16.2.6.2.1 ITT population
16.2.6.2.1.4 Subgroup analyses by gender
16.2.6.2.1.4.1 Overall survival by treatment group according to gender - ITT population

	Male		Female		
	Kd (N=68)	**IKd (N=101)**	**Kd (N=55)**	**IKd (N=78)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of deaths	15 (22.1)	19 (18.8)	10 (18.2)	12 (15.4)	0.9435
Number (%) of patients censored	53 (77.9)	82 (81.2)	45 (81.8)	66 (84.6)	
Kaplan-Meier estimates of OS in months					
25% quantile (95% CI)	23.39 (11.368 to NC)	NC (15.113 to NC)	NC (17.117 to NC)	23.13 (21.552 to NC)	
Median (95% CI)	NC (23.392 to NC)	NC (NC to NC)	NC (NC to NC)	NC (23.129 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.6879		0.7022	
Hazard ratio (95% CI) vs Kd	-	0.87 (0.44 to 1.71)		0.85 (0.37 to 1.97)	
P-value	-	0.6881		0.7025	
OS probability (95% CI)[b]					
12 Months	0.851 (0.740 to 0.917)	0.888 (0.806 to 0.936)	0.925 (0.813 to 0.971)	0.935 (0.850 to 0.972)	

OS: Overall survival, CI: Confidence interval
Cut-off date: 07FEB2020 HR<1 favors IKd arm
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] Two-sided significance level is 0.05.
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables and the treatment-by-subgroup interaction as covariates.
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16.2.6.2 Secondary efficacy endpoints - Overall survival
16.2.6.2.1 ITT population
16.2.6.2.1.5 Subgroup analyses by ethnic origin
16.2.6.2.1.5.1 Overall survival by treatment group according to ethnic origin - ITT population

	White		Other		
	Kd (N=83)	**IKd (N=131)**	**Kd (N=28)**	**IKd (N=34)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of deaths	17 (20.5)	23 (17.6)	4 (14.3)	4 (11.8)	0.9996
Number (%) of patients censored	66 (79.5)	108 (82.4)	24 (85.7)	30 (88.2)	
Kaplan-Meier estimates of OS in months					
25% quantile (95% CI)	NC (17.117 to NC)	23.13 (21.552 to NC)	23.39 (8.444 to NC)	NC (11.860 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (23.392 to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.6529		0.8626	
Hazard ratio (95% CI) vs Kd	-	0.87 (0.46 to 1.62)		0.88 (0.22 to 3.57)	
P-value	-	0.6532		0.8623	
OS probability (95% CI)[b]					
12 Months	0.903 (0.816 to 0.950)	0.923 (0.862 to 0.958)	0.923 (0.726 to 0.980)	0.904 (0.731 to 0.968)	

OS: Overall survival, CI: Confidence interval
Cut-off date: 07FEB2020 HR<1 favors IKd arm
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] Two-sided significance level is 0.05.
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables and the treatment-by-subgroup interaction as covariates.
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16.2.6.2 Secondary efficacy endpoints - Overall survival
16.2.6.2.1 ITT population
16.2.6.2.1.6 Subgroup analyses by geographical region
16.2.6.2.1.6.1 Overall survival by treatment group according to geographical region - ITT population

	Europe		America		Asia		Other countries		
	Kd (N=60)	**IKd (N=85)**	**Kd (N=20)**	**IKd (N=24)**	**Kd (N=21)**	**IKd (N=25)**	**Kd (N=22)**	**IKd (N=45)**	**p-value of treatment-by-subgroup interaction[c]**
Number (%) of deaths	15 (25.0)	16 (18.8)	4 (20.0)	2 (8.3)	3 (14.3)	4 (16.0)	3 (13.6)	9 (20.0)	0.6645
Number (%) of patients censored	45 (75.0)	69 (81.2)	16 (80.0)	22 (91.7)	18 (85.7)	21 (84.0)	19 (86.4)	36 (80.0)	
Kaplan-Meier estimates of event in months									
25% quantile (95% CI)	21.65 (11.368 to NC)	NC (15.639 to NC)	NC (8.936 to NC)	NC (1.478 to NC)	NC (7.721 to NC)	NC (5.848 to NC)	23.39 (8.674 to NC)	23.13 (14.752 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	23.39 (23.392 to NC)	NC (23.129 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (23.392 to NC)	NC (NC to NC)	

OS: Overall survival, CI: Confidence interval
Cut-off date: 07FEB2020 HR<1 favors IKd arm
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] Two-sided significance level is 0.05.
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables and the treatment-by-subgroup interaction as covariates.
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16.2.6.2 Secondary efficacy endpoints - Overall survival
16.2.6.2.1 ITT population
16.2.6.2.1.6 Subgroup analyses by geographical region
16.2.6.2.1.6.1 Overall survival by treatment group according to geographical region - ITT population

	Europe		America		Asia		Other countries		
	Kd (N=60)	**IKd (N=85)**	**Kd (N=20)**	**IKd (N=24)**	**Kd (N=21)**	**IKd (N=25)**	**Kd (N=22)**	**IKd (N=45)**	**p-value of treatment-by-subgroup interaction[c]**
Comparison vs. Kd									
Log-Rank test p-value[a] vs Kd	-	0.3893		0.3985		0.9682		0.4709	
Hazard ratio (95% CI) vs Kd	-	0.73 (0.36 to 1.49)		0.49 (0.09 to 2.67)		1.03 (0.23 to 4.61)		1.61 (0.44 to 5.95)	
P-value	-	0.3912		0.4085		0.9683		0.4753	
OS probability (95% CI)[b]									
12 Months	0.833 (0.712 to 0.907)	0.905 (0.819 to 0.951)	0.950 (0.695 to 0.993)	0.957 (0.729 to 0.994)	0.895 (0.641 to 0.973)	0.871 (0.650 to 0.957)	0.952 (0.707 to 0.993)	0.910 (0.778 to 0.965)	
18 Months	0.800 (0.675 to 0.881)	0.834 (0.735 to 0.898)	0.800 (0.551 to 0.920)	0.906 (0.673 to 0.976)	0.835 (0.570 to 0.944)	0.825 (0.597 to 0.931)	0.952 (0.707 to 0.993)	0.840 (0.693 to 0.920)	

OS: Overall survival, CI: Confidence interval
Cut-off date: 07FEB2020 HR<1 favors IKd arm
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] Two-sided significance level is 0.05.
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables and the treatment-by-subgroup interaction as covariates.
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16.2.6.2 Secondary efficacy endpoints - Overall survival
16.2.6.2.1 ITT population
16.2.6.2.1.7 Subgroup analyses by regulatory region
16.2.6.2.1.7.1 Overall survival by treatment group according to regulatory region - ITT population

	Western countries		Other countries		
	Kd (N=55)	**IKd (N=97)**	**Kd (N=68)**	**IKd (N=82)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of deaths	12 (21.8)	15 (15.5)	13 (19.1)	16 (19.5)	0.5335
Number (%) of patients censored	43 (78.2)	82 (84.5)	55 (80.9)	66 (80.5)	
Kaplan-Meier estimates of OS in months					
25% quantile (95% CI)	23.39 (12.879 to NC)	NC (21.552 to NC)	NC (13.437 to NC)	23.13 (15.671 to NC)	
Median (95% CI)	NC (23.392 to NC)	NC (NC to NC)	NC (NC to NC)	NC (23.129 to NC)	
75% quantile (95% CI)	NC (23.392 to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.4074		0.9835	
Hazard ratio (95% CI) vs Kd	-	0.73 (0.34 to 1.55)		1.01 (0.48 to 2.10)	
P-value	-	0.4094		0.9835	
OS probability (95% CI)[b]					
12 Months	0.873 (0.751 to 0.937)	0.916 (0.840 to 0.957)	0.892 (0.786 to 0.947)	0.899 (0.809 to 0.948)	

OS: Overall survival, CI: Confidence interval
Cut-off date: 07FEB2020 HR<1 favors IKd arm
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] Two-sided significance level is 0.05.
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables and the treatment-by-subgroup interaction as covariates.
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16.2.6.2 Secondary efficacy endpoints - Overall survival
16.2.6.2.1 ITT population
16.2.6.2.1.8 Subgroup analyses by baseline ECOG PS
16.2.6.2.1.8.1 Overall survival by treatment group according to baseline ECOG PS - ITT population

	0 or 1		>1		
	Kd (N=118)	**IKd (N=168)**	**Kd (N=5)**	**IKd (N=11)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of deaths	22 (18.6)	28 (16.7)	3 (60.0)	3 (27.3)	0.3774
Number (%) of patients censored	96 (81.4)	140 (83.3)	2 (40.0)	8 (72.7)	
Kaplan-Meier estimates of OS in months					
25% quantile (95% CI)	23.39 (18.924 to NC)	NC (21.552 to NC)	12.88 (5.125 to NC)	16.56 (0.427 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	13.44 (5.125 to NC)	NC (0.427 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (5.125 to NC)	NC (NC to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.7134		0.2839	
Hazard ratio (95% CI) vs Kd	-	0.90 (0.52 to 1.57)		0.42 (0.08 to 2.13)	
P-value	-	0.7135		0.2981	
OS probability (95% CI)[b]					
12 Months	0.887 (0.814 to 0.933)	0.915 (0.861 to 0.949)	0.800 (0.204 to 0.969)	0.800 (0.409 to 0.946)	

OS: Overall survival, CI: Confidence interval
Cut-off date: 07FEB2020 HR<1 favors IKd arm
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] Two-sided significance level is 0.05.
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables and the treatment-by-subgroup interaction as covariates.
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16.2.6.2 Secondary efficacy endpoints - Overall survival
16.2.6.2.1 ITT population
16.2.6.2.1.9 Subgroup analyses by ISS staging at SE
16.2.6.2.1.9.1 Overall survival by treatment group according to ISS staging at SE - ITT population

	I		II		III		
	Kd (N=71)	**IKd (N=89)**	**Kd (N=31)**	**IKd (N=63)**	**Kd (N=20)**	**IKd (N=26)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of deaths	8 (11.3)	9 (10.1)	6 (19.4)	9 (14.3)	11 (55.0)	13 (50.0)	0.8087
Number (%) of patients censored	63 (88.7)	80 (89.9)	25 (80.6)	54 (85.7)	9 (45.0)	13 (50.0)	
Kaplan-Meier estimates of OS in months							
25% quantile (95% CI)	NC (21.651 to NC)	NC (21.782 to NC)	NC (8.674 to NC)	23.13 (23.129 to NC)	7.03 (0.526 to 15.836)	11.33 (0.427 to 14.226)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (23.129 to NC)	20.25 (5.125 to NC)	17.58 (11.335 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (23.392 to NC)	21.55 (21.552 to NC)	
Comparison vs. Kd							
Log-Rank test p-value[a] vs Kd	-	0.8806		0.5082		0.9066	
Hazard ratio (95% CI) vs Kd	-	0.93 (0.36 to 2.41)		0.71 (0.25 to 1.99)		1.05 (0.47 to 2.35)	
P-value	-	0.8803		0.5102		0.9068	

OS: Overall survival, CI: Confidence interval
Cut-off date: 07FEB2020 HR<1 favors IKd arm
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] Two-sided significance level is 0.05.
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables and the treatment-by-subgroup interaction as covariates.
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16.2.6.2 Secondary efficacy endpoints - Overall survival
16.2.6.2.1 ITT population
16.2.6.2.1.10 Subgroup analyses by R-ISS stage at SE
16.2.6.2.1.10.1 Overall survival by treatment group according to R-ISS stage at SE - ITT population

	I or II		III		Not classified		
	Kd (N=103)	**IKd (N=155)**	**Kd (N=8)**	**IKd (N=16)**	**Kd (N=12)**	**IKd (N=8)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of deaths	21 (20.4)	20 (12.9)	3 (37.5)	10 (62.5)	1 (8.3)	1 (12.5)	0.2079
Number (%) of patients censored	82 (79.6)	135 (87.1)	5 (62.5)	6 (37.5)	11 (91.7)	7 (87.5)	
Kaplan-Meier estimates of OS in months							
25% quantile (95% CI)	23.39 (17.117 to NC)	NC (23.129 to NC)	5.06 (0.986 to NC)	6.36 (0.427 to 14.226)	NC (18.924 to NC)	NC (6.932 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (0.986 to NC)	15.39 (4.928 to NC)	NC (NC to NC)	NC (6.932 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (5.125 to NC)	NC (14.226 to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Kd							
Log-Rank test p-value[a] vs Kd	-	0.1083		0.3727		0.5151	
Hazard ratio (95% CI) vs Kd	-	0.61 (0.33 to 1.12)		1.79 (0.49 to 6.50)		2.45 (0.15 to 39.71)	
P-value	-	0.1119		0.3793		0.5287	

OS: Overall survival, CI: Confidence interval
Cut-off date: 07FEB2020 HR<1 favors IKd arm
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] Two-sided significance level is 0.05.
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables and the treatment-by-subgroup interaction as covariates.
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16.2.6.2 Secondary efficacy endpoints - Overall survival
16.2.6.2.1 ITT population
16.2.6.2.1.11 Subgroup analyses by nb of prior lines
16.2.6.2.1.11.1 Overall survival by treatment group according to nb of prior lines - ITT population

	1		>1		
	Kd (N=55)	**IKd (N=79)**	**Kd (N=68)**	**IKd (N=100)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of deaths	6 (10.9)	9 (11.4)	19 (27.9)	22 (22.0)	0.5700
Number (%) of patients censored	49 (89.1)	70 (88.6)	49 (72.1)	78 (78.0)	
Kaplan-Meier estimates of OS in months					
25% quantile (95% CI)	NC (21.651 to NC)	NC (NC to NC)	18.92 (8.674 to NC)	21.78 (15.113 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (23.392 to NC)	NC (23.129 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.8687		0.4108	
Hazard ratio (95% CI) vs Kd	-	1.09 (0.39 to 3.07)		0.77 (0.42 to 1.43)	
P-value	-	0.8688		0.4121	
OS probability (95% CI)[b]					
12 Months	0.962 (0.857 to 0.990)	0.936 (0.852 to 0.973)	0.822 (0.708 to 0.895)	0.887 (0.805 to 0.936)	

OS: Overall survival, CI: Confidence interval
Cut-off date: 07FEB2020 HR<1 favors IKd arm
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] Two-sided significance level is 0.05.
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables and the treatment-by-subgroup interaction as covariates.
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16.2.6.2 Secondary efficacy endpoints - Overall survival
16.2.6.2.1 ITT population
16.2.6.2.1.12 Subgroup analyses by cytogenetic abnormality
16.2.6.2.1.12.1 Overall survival by treatment group according to cytogenetic abnormality - ITT population

	At least one		None		
	Kd (N=31)	**IKd (N=42)**	**Kd (N=77)**	**IKd (N=114)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of deaths	7 (22.6)	10 (23.8)	15 (19.5)	15 (13.2)	0.5156
Number (%) of patients censored	24 (77.4)	32 (76.2)	62 (80.5)	99 (86.8)	
Kaplan-Meier estimates of OS in months					
25% quantile (95% CI)	21.65 (8.444 to NC)	21.78 (8.608 to NC)	23.39 (15.836 to NC)	NC (21.552 to NC)	
Median (95% CI)	NC (21.651 to NC)	NC (NC to NC)	NC (23.392 to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.9522		0.2819	
Hazard ratio (95% CI) vs Kd	-	1.03 (0.39 to 2.71)		0.68 (0.33 to 1.38)	
P-value	-	0.9523		0.2850	
OS probability (95% CI)[b]					
12 Months	0.831 (0.639 to 0.926)	0.881 (0.737 to 0.949)	0.908 (0.817 to 0.955)	0.937 (0.873 to 0.970)	

OS: Overall survival, CI: Confidence interval
Cut-off date: 07FEB2020 HR<1 favors IKd arm
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] Two-sided significance level is 0.05.
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables and the treatment-by-subgroup interaction as covariates.
PGM=DEVOPS/SAR650984/EFC15246/CIR_RWE/REPORT/PGM/eff_km_subgp_sr_de_i_t.sas OUT=REPORT/OUTPUT/eff_km_os_cyto_de_i_t_x.rtf (19FEB2021 15:18)

16.2.6.2 Secondary efficacy endpoints - Overall survival
16.2.6.2.1 ITT population
16.2.6.2.1.13 Subgroup analyses by MM type at SE
16.2.6.2.1.13.1 Overall survival by treatment group according to MM type at SE - ITT population

	IgG		Non-IgG		
	Kd (N=85)	**IKd (N=126)**	**Kd (N=38)**	**IKd (N=53)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of deaths	15 (17.6)	19 (15.1)	10 (26.3)	12 (22.6)	0.9046
Number (%) of patients censored	70 (82.4)	107 (84.9)	28 (73.7)	41 (77.4)	
Kaplan-Meier estimates of OS in months					
25% quantile (95% CI)	23.39 (19.187 to NC)	NC (21.782 to NC)	18.92 (5.125 to NC)	23.13 (12.649 to NC)	
Median (95% CI)	NC (23.392 to NC)	NC (NC to NC)	NC (NC to NC)	NC (23.129 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (23.129 to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.7021		0.6475	
Hazard ratio (95% CI) vs Kd	-	0.88 (0.45 to 1.72)		0.82 (0.35 to 1.91)	
P-value	-	0.7024		0.6480	
OS probability (95% CI)[b]					
12 Months	0.916 (0.832 to 0.959)	0.919 (0.854 to 0.955)	0.811 (0.644 to 0.905)	0.883 (0.759 to 0.946)	

OS: Overall survival, CI: Confidence interval
Cut-off date: 07FEB2020 HR<1 favors IKd arm
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] Two-sided significance level is 0.05.
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables and the treatment-by-subgroup interaction as covariates.
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16.2.6.2 Secondary efficacy endpoints - Overall survival
16.2.6.2.1 ITT population
16.2.6.2.1.14 Subgroup analyses by previous autologous stem-cell
16.2.6.2.1.14.1 Overall survival by treatment group according to previous autologous stem-cell - ITT population

	Yes		No		
	Kd (N=69)	**IKd (N=116)**	**Kd (N=54)**	**IKd (N=63)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of deaths	13 (18.8)	22 (19.0)	12 (22.2)	9 (14.3)	0.4200
Number (%) of patients censored	56 (81.2)	94 (81.0)	42 (77.8)	54 (85.7)	
Kaplan-Meier estimates of OS in months					
25% quantile (95% CI)	23.39 (15.836 to NC)	23.13 (16.559 to NC)	NC (11.828 to NC)	NC (17.577 to NC)	
Median (95% CI)	NC (23.392 to NC)	NC (23.129 to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.9350		0.3198	
Hazard ratio (95% CI) vs Kd	-	1.03 (0.52 to 2.04)		0.65 (0.27 to 1.54)	
P-value	-	0.9352		0.3235	
OS probability (95% CI)[b]					
12 Months	0.896 (0.795 to 0.949)	0.913 (0.844 to 0.952)	0.868 (0.743 to 0.935)	0.900 (0.791 to 0.954)	

OS: Overall survival, CI: Confidence interval
Cut-off date: 07FEB2020 HR<1 favors IKd arm
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] Two-sided significance level is 0.05.
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables and the treatment-by-subgroup interaction as covariates.
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16.2.6.2 Secondary efficacy endpoints - Overall survival
16.2.6.2.1 ITT population
16.2.6.2.1.15 Subgroup analyses by baseline eGFR (MDRD)
16.2.6.2.1.15.1 Overall survival by treatment group according to baseline eGFR (MDRD) - ITT population

	>=60 mL/min/1.73m2		<60 mL/min/1.73m2		
	Kd (N=93)	**IKd (N=122)**	**Kd (N=18)**	**IKd (N=43)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of deaths	14 (15.1)	22 (18.0)	7 (38.9)	5 (11.6)	0.0124
Number (%) of patients censored	79 (84.9)	100 (82.0)	11 (61.1)	38 (88.4)	
Kaplan-Meier estimates of OS in months					
25% quantile (95% CI)	23.39 (21.651 to NC)	NC (17.577 to NC)	15.84 (0.526 to NC)	NC (21.552 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (7.326 to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.4622		0.0072	
Hazard ratio (95% CI) vs Kd	-	1.29 (0.66 to 2.51)		0.24 (0.07 to 0.74)	
P-value	-	0.4633		0.0136	
OS probability (95% CI)[b]					
12 Months	0.934 (0.859 to 0.970)	0.899 (0.830 to 0.942)	0.770 (0.497 to 0.907)	0.976 (0.843 to 0.997)	

OS: Overall survival, CI: Confidence interval
Cut-off date: 07FEB2020 HR<1 favors IKd arm
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] Two-sided significance level is 0.05.
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables and the treatment-by-subgroup interaction as covariates.
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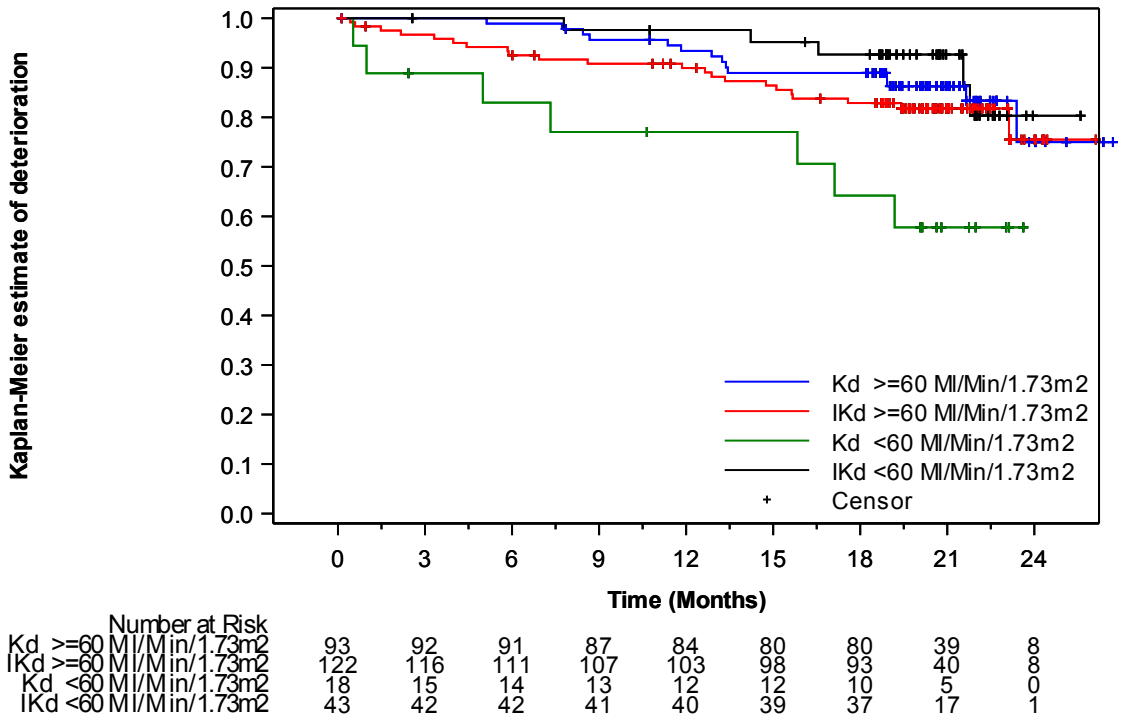
16.2.6.2 Secondary efficacy endpoints - Overall survival
16.2.6.2.1 ITT population
16.2.6.2.1.15 Subgroup analyses by baseline eGFR (MDRD)
16.2.6.2.1.15.2 Overall survival by treatment group according to baseline eGFR (MDRD) - Kaplan-Meier curve - ITT population



Number at Risk

Kd >=60 Ml/Min/1.73m2	93	92	91	87	84	80	80	39	8
IKd >=60 Ml/Min/1.73m2	122	116	111	107	103	98	93	40	8
Kd <60 Ml/Min/1.73m2	18	15	14	13	12	12	10	5	0
IKd <60 Ml/Min/1.73m2	43	42	42	41	40	39	37	17	1

16.2.6.2 Secondary efficacy endpoints - Overall survival
16.2.6.2.1 ITT population
16.2.6.2.1.16 Subgroup analyses by previous treatment with PI
16.2.6.2.1.16.1 Overall survival by treatment group according to previous treatment with PI - ITT population

	Yes		No		
	Kd (N=47)	**IKd (N=81)**	**Kd (N=76)**	**IKd (N=98)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of deaths	10 (21.3)	16 (19.8)	15 (19.7)	15 (15.3)	0.5777
Number (%) of patients censored	37 (78.7)	65 (80.2)	61 (80.3)	83 (84.7)	
Kaplan-Meier estimates of OS in months					
25% quantile (95% CI)	21.65 (13.240 to NC)	NC (14.752 to NC)	23.39 (13.372 to NC)	NC (21.782 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (23.392 to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.9557		0.3966	
Hazard ratio (95% CI) vs Kd	-	0.98 (0.44 to 2.16)		0.73 (0.36 to 1.50)	
P-value	-	0.9556		0.3984	
OS probability (95% CI)[b]					
12 Months	0.891 (0.757 to 0.953)	0.872 (0.776 to 0.929)	0.879 (0.781 to 0.935)	0.938 (0.867 to 0.972)	

OS: Overall survival, CI: Confidence interval
Cut-off date: 07FEB2020 HR<1 favors IKd arm
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] Two-sided significance level is 0.05.
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables and the treatment-by-subgroup interaction as covariates.
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16.2.6.2 Secondary efficacy endpoints - Overall survival
16.2.6.2.1 ITT population
16.2.6.2.1.17 Subgroup analyses by previous treatment with IMiD
16.2.6.2.1.17.1 Overall survival by treatment group according to previous treatment with IMiD - ITT population

	Yes		No		
	Kd (N=62)	**IKd (N=81)**	**Kd (N=61)**	**IKd (N=98)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of deaths	13 (21.0)	14 (17.3)	12 (19.7)	17 (17.3)	0.8515
Number (%) of patients censored	49 (79.0)	67 (82.7)	49 (80.3)	81 (82.7)	
Kaplan-Meier estimates of OS in months					
25% quantile (95% CI)	23.39 (12.879 to NC)	23.13 (14.752 to NC)	NC (13.372 to NC)	NC (19.417 to NC)	
Median (95% CI)	NC (23.392 to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.5907		0.7520	
Hazard ratio (95% CI) vs Kd	-	0.81 (0.38 to 1.73)		0.89 (0.42 to 1.86)	
P-value	-	0.5913		0.7521	
OS probability (95% CI)[b]					
12 Months	0.869 (0.755 to 0.932)	0.912 (0.824 to 0.957)	0.899 (0.790 to 0.954)	0.905 (0.826 to 0.950)	

OS: Overall survival, CI: Confidence interval
Cut-off date: 07FEB2020 HR<1 favors IKd arm
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] Two-sided significance level is 0.05.
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables and the treatment-by-subgroup interaction as covariates.
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16.2.6.2 Secondary efficacy endpoints - Overall survival
16.2.6.2.1 ITT population
16.2.6.2.1.18 Subgroup analyses by previous treatment with PI and IMiD
16.2.6.2.1.18.1 Overall survival by treatment group according to previous treatment with PI and IMiD - ITT population

	Yes		No		
	Kd (N=17)	**IKd (N=23)**	**Kd (N=106)**	**IKd (N=156)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of deaths	2 (11.8)	5 (21.7)	23 (21.7)	26 (16.7)	0.2842
Number (%) of patients censored	15 (88.2)	18 (78.3)	83 (78.3)	130 (83.3)	
Kaplan-Meier estimates of OS in months					
25% quantile (95% CI)	NC (0.526 to NC)	NC (1.478 to NC)	23.39 (13.437 to NC)	NC (21.552 to NC)	
Median (95% CI)	NC (21.651 to NC)	NC (NC to NC)	NC (23.392 to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.4406		0.3497	
Hazard ratio (95% CI) vs Kd	-	1.89 (0.37 to 9.73)		0.77 (0.44 to 1.34)	
P-value	-	0.4482		0.3511	
OS probability (95% CI)[b]					
12 Months	0.941 (0.650 to 0.991)	0.826 (0.601 to 0.931)	0.875 (0.795 to 0.926)	0.921 (0.865 to 0.954)	

OS: Overall survival, CI: Confidence interval
Cut-off date: 07FEB2020 HR<1 favors IKd arm
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] Two-sided significance level is 0.05.
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables and the treatment-by-subgroup interaction as covariates.
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16.2.6.1 Primary efficacy endpoint - Progression Free Survival
16.2.6.1.1 ITT population
16.2.6.1.1.3 Subgroup analyses by age
16.2.6.1.1.3.1 PFS - Primary analysis based on disease assessment by the IRC by treatment group according to age - ITT population

	<65 years		>=65 years		
	Kd (N=66)	**IKd (N=88)**	**Kd (N=57)**	**IKd (N=91)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	26 (39.4)	25 (28.4)	29 (50.9)	23 (25.3)	0.3663
Number (%) of patients censored	40 (60.6)	63 (71.6)	28 (49.1)	68 (74.7)	
Kaplan-Meier estimates of PFS in months					
25% quantile (95% CI)	9.36 (6.834 to 14.752)	13.63 (6.932 to NC)	11.14 (6.078 to 15.376)	16.92 (11.072 to NC)	
Median (95% CI)	NC (14.752 to NC)	NC (NC to NC)	17.18 (13.405 to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.1089		0.0019	
Hazard ratio (95% CI) vs Kd	-	0.64 (0.37 to 1.11)		0.43 (0.25 to 0.74)	
P-value	-	0.1118		0.0025	
PFS probability (95% CI)[b]					
6 Months	0.871 (0.759 to 0.934)	0.883 (0.793 to 0.935)	0.875 (0.756 to 0.938)	0.942 (0.866 to 0.975)	

PFS: Progression-free survival, CI: Confidence interval, HR: Hazard ratio, IRC: Independent Response Committee
Cut-off date: 07FEB2020 HR<1 favors IKd arm
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] Two-sided significance level is 0.05.
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables and the treatment-by-subgroup interaction as covariates.
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16.2.6.1 Primary efficacy endpoint - Progression Free Survival
16.2.6.1.1 ITT population
16.2.6.1.1.4 Subgroup analyses by gender
16.2.6.1.1.4.1 PFS - Primary analysis based on disease assessment by the IRC by treatment group according to gender - ITT population

	Male		Female		
	Kd (N=68)	**IKd (N=101)**	**Kd (N=55)**	**IKd (N=78)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	28 (41.2)	27 (26.7)	27 (49.1)	21 (26.9)	0.5131
Number (%) of patients censored	40 (58.8)	74 (73.3)	28 (50.9)	57 (73.1)	
Kaplan-Meier estimates of PFS in months					
25% quantile (95% CI)	9.43 (5.552 to 15.244)	14.92 (10.283 to NC)	9.92 (7.721 to 14.752)	16.16 (7.622 to NC)	
Median (95% CI)	NC (15.244 to NC)	NC (NC to NC)	16.99 (13.437 to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (20.271 to NC)	NC (NC to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.0473		0.0050	
Hazard ratio (95% CI) vs Kd	-	0.59 (0.35 to 1.00)		0.45 (0.25 to 0.80)	
P-value	-	0.0499		0.0063	
PFS probability (95% CI)[b]					
6 Months	0.859 (0.747 to 0.924)	0.915 (0.837 to 0.957)	0.889 (0.769 to 0.948)	0.909 (0.819 to 0.956)	

PFS: Progression-free survival, CI: Confidence interval, HR: Hazard ratio, IRC: Independent Response Committee
Cut-off date: 07FEB2020 HR<1 favors IKd arm
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] Two-sided significance level is 0.05.
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables and the treatment-by-subgroup interaction as covariates.
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16.2.6.1 Primary efficacy endpoint - Progression Free Survival
16.2.6.1.1 ITT population
16.2.6.1.1.5 Subgroup analyses by ethnic origin
16.2.6.1.1.5.1 PFS - Primary analysis based on disease assessment by the IRC by treatment group according to ethnic origin - ITT population

	White		Other		
	Kd (N=83)	**IKd (N=131)**	**Kd (N=28)**	**IKd (N=34)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	36 (43.4)	34 (26.0)	12 (42.9)	8 (23.5)	0.9528
Number (%) of patients censored	47 (56.6)	97 (74.0)	16 (57.1)	26 (76.5)	
Kaplan-Meier estimates of PFS in months					
25% quantile (95% CI)	10.18 (6.078 to 13.963)	14.95 (10.283 to NC)	13.24 (7.721 to 16.164)	17.08 (6.604 to NC)	
Median (95% CI)	19.45 (15.244 to NC)	NC (NC to NC)	18.99 (13.240 to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.0095		0.1371	
Hazard ratio (95% CI) vs Kd	-	0.54 (0.34 to 0.87)		0.51 (0.21 to 1.26)	
P-value	-	0.0107		0.1444	
PFS probability (95% CI)[b]					
6 Months	0.853 (0.756 to 0.914)	0.906 (0.840 to 0.945)	0.962 (0.757 to 0.994)	0.935 (0.766 to 0.983)	

PFS: Progression-free survival, CI: Confidence interval, HR: Hazard ratio, IRC: Independent Response Committee
Cut-off date: 07FEB2020 HR<1 favors IKd arm
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] Two-sided significance level is 0.05.
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables and the treatment-by-subgroup interaction as covariates.
PGM=DEVOPS/SAR650984/EFC15246/CIR_RWE/REPORT/PGM/eff_km_subgp_sr_de_i_t.sas OUT=REPORT/OUTPUT/eff_km_pfs_race_de_i_t_x.rtf (19FEB2021 15:18)

16.2.6.1 Primary efficacy endpoint - Progression Free Survival
16.2.6.1.1 ITT population
16.2.6.1.1.6 Subgroup analyses by geographical region
16.2.6.1.1.6.1 PFS - Primary analysis based on disease assessment by the IRC by treatment group according to geographical region - ITT population

	Europe		America		Asia		Other countries		
	Kd (N=60)	**IKd (N=85)**	**Kd (N=20)**	**IKd (N=24)**	**Kd (N=21)**	**IKd (N=25)**	**Kd (N=22)**	**IKd (N=45)**	**p-value of treatment-by-subgroup interaction[c]**
Comparison vs. Kd									
Log-Rank test p-value[a] vs Kd	-	0.0005		0.6857		0.3841		0.1136	
Hazard ratio (95% CI) vs Kd	-	0.37 (0.21 to 0.66)		1.24 (0.43 to 3.59)		0.64 (0.23 to 1.77)		0.54 (0.24 to 1.18)	
P-value	-	0.0008		0.6863		0.3880		0.1195	
PFS probability (95% CI)[b]									
6 Months	0.790 (0.659 to 0.875)	0.904 (0.817 to 0.951)	1.000 (1.000 to 1.000)	0.913 (0.695 to 0.978)	0.947 (0.681 to 0.992)	0.917 (0.706 to 0.978)	0.909 (0.683 to 0.976)	0.928 (0.791 to 0.976)	
12 Months	0.655 (0.512 to 0.764)	0.852 (0.753 to 0.913)	0.885 (0.614 to 0.970)	0.728 (0.490 to 0.868)	0.664 (0.399 to 0.833)	0.792 (0.570 to 0.908)	0.670 (0.429 to 0.827)	0.772 (0.607 to 0.875)	

PFS: Progression-free survival, CI: Confidence interval, HR: Hazard ratio, IRC: Independent Response Committee
Cut-off date: 07FEB2020 HR<1 favors IKd arm
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] Two-sided significance level is 0.05.
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables and the treatment-by-subgroup interaction as covariates.
PGM=DEVOPS/SAR650984/EFC15246/CIR_RWE/REPORT/PGM/eff_km_subgp_sr_de_i_t.sas OUT=REPORT/OUTPUT/eff_km_pfs_greg_de_i_t_x.rtf (19FEB2021 15:18)

16.2.6.1 Primary efficacy endpoint - Progression Free Survival
16.2.6.1.1 ITT population
16.2.6.1.1.7 Subgroup analyses by regulatory region
16.2.6.1.1.7.1 PFS - Primary analysis based on disease assessment by the IRC by treatment group according to regulatory region - ITT population

	Western countries		Other countries		
	Kd (N=55)	**IKd (N=97)**	**Kd (N=68)**	**IKd (N=82)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	29 (52.7)	25 (25.8)	26 (38.2)	23 (28.0)	0.2808
Number (%) of patients censored	26 (47.3)	72 (74.2)	42 (61.8)	59 (72.0)	
Kaplan-Meier estimates of PFS in months					
25% quantile (95% CI)	9.03 (2.793 to 13.240)	16.43 (10.283 to NC)	11.83 (8.312 to 14.752)	13.63 (6.932 to NC)	
Median (95% CI)	18.20 (13.240 to NC)	NC (NC to NC)	NC (15.770 to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (19.450 to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.0009		0.1341	
Hazard ratio (95% CI) vs Kd	-	0.42 (0.24 to 0.71)		0.65 (0.37 to 1.15)	
P-value	-	0.0013		0.1370	
PFS probability (95% CI)[b]					
6 Months	0.829 (0.698 to 0.907)	0.924 (0.847 to 0.963)	0.907 (0.805 to 0.957)	0.899 (0.807 to 0.948)	

PFS: Progression-free survival, CI: Confidence interval, HR: Hazard ratio, IRC: Independent Response Committee
Cut-off date: 07FEB2020 HR<1 favors IKd arm
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] Two-sided significance level is 0.05.
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables and the treatment-by-subgroup interaction as covariates.
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16.2.6.1 Primary efficacy endpoint - Progression Free Survival
16.2.6.1.1 ITT population
16.2.6.1.1.8 Subgroup analyses by baseline ECOG PS
16.2.6.1.1.8.1 PFS - Primary analysis based on disease assessment by the IRC by treatment group according to baseline ECOG PS - ITT population

	0 or 1		>1		
	Kd (N=118)	**IKd (N=168)**	**Kd (N=5)**	**IKd (N=11)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	51 (43.2)	42 (25.0)	4 (80.0)	6 (54.5)	0.4944
Number (%) of patients censored	67 (56.8)	126 (75.0)	1 (20.0)	5 (45.5)	
Kaplan-Meier estimates of PFS in months					
25% quantile (95% CI)	10.18 (8.312 to 13.963)	16.92 (11.893 to NC)	9.30 (2.793 to 17.183)	5.82 (0.427 to 13.372)	
Median (95% CI)	19.45 (16.099 to NC)	NC (NC to NC)	13.44 (2.793 to NC)	13.37 (0.427 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	17.18 (2.793 to NC)	NC (9.725 to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.0006		0.6874	
Hazard ratio (95% CI) vs Kd	-	0.49 (0.33 to 0.74)		0.77 (0.22 to 2.76)	
P-value	-	0.0007		0.6882	
PFS probability (95% CI)[b]					
6 Months	0.876 (0.800 to 0.925)	0.926 (0.873 to 0.957)	0.800 (0.204 to 0.969)	0.700 (0.329 to 0.892)	

PFS: Progression-free survival, CI: Confidence interval, HR: Hazard ratio, IRC: Independent Response Committee
Cut-off date: 07FEB2020 HR<1 favors IKd arm
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] Two-sided significance level is 0.05.
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables and the treatment-by-subgroup interaction as covariates.
PGM=DEVOPS/SAR650984/EFC15246/CIR_RWE/REPORT/PGM/eff_km_subgp_sr_de_i_t.sas OUT=REPORT/OUTPUT/eff_km_pfs_ecog_de_i_t_x.rtf (19FEB2021 15:18)

16.2.6.1 Primary efficacy endpoint - Progression Free Survival
16.2.6.1.1 ITT population
16.2.6.1.1.9 Subgroup analyses by ISS staging at SE
16.2.6.1.1.9.1 PFS - Primary analysis based on disease assessment by the IRC by treatment group according to ISS staging at SE - ITT population

	I		II		III		
	Kd (N=71)	**IKd (N=89)**	**Kd (N=31)**	**IKd (N=63)**	**Kd (N=20)**	**IKd (N=26)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	24 (33.8)	20 (22.5)	16 (51.6)	17 (27.0)	14 (70.0)	11 (42.3)	0.5952
Number (%) of patients censored	47 (66.2)	69 (77.5)	15 (48.4)	46 (73.0)	6 (30.0)	15 (57.7)	
Kaplan-Meier estimates of PFS in months							
25% quantile (95% CI)	13.96 (8.312 to 18.990)	20.34 (11.433 to NC)	11.14 (6.078 to 14.752)	16.92 (7.951 to NC)	5.91 (0.526 to 9.298)	6.93 (0.131 to 10.283)	
Median (95% CI)	NC (18.990 to NC)	NC (NC to NC)	18.20 (11.828 to 19.450)	NC (NC to NC)	9.36 (4.994 to 16.164)	12.88 (6.932 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (18.234 to NC)	NC (NC to NC)	16.16 (9.363 to NC)	NC (13.372 to NC)	
Comparison vs. Kd							
Log-Rank test p-value[a] vs Kd	-	0.0798		0.0038		0.2819	
Hazard ratio (95% CI) vs Kd	-	0.59 (0.33 to 1.07)		0.37 (0.19 to 0.75)		0.65 (0.29 to 1.43)	
P-value	-	0.0833		0.0054		0.2856	

PFS: Progression-free survival, CI: Confidence interval, HR: Hazard ratio, IRC: Independent Response Committee
Cut-off date: 07FEB2020 HR<1 favors IKd arm
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] Two-sided significance level is 0.05.
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables and the treatment-by-subgroup interaction as covariates.
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16.2.6.1 Primary efficacy endpoint - Progression Free Survival
16.2.6.1.1 ITT population
16.2.6.1.1.10 Subgroup analyses by R-ISS stage at SE
16.2.6.1.1.10.1 PFS - Primary analysis based on disease assessment by the IRC by treatment group according to R-ISS stage at SE - ITT population

	I or II		III		Not classified		
	Kd (N=103)	**IKd (N=155)**	**Kd (N=8)**	**IKd (N=16)**	**Kd (N=12)**	**IKd (N=8)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	45 (43.7)	38 (24.5)	6 (75.0)	9 (56.3)	4 (33.3)	1 (12.5)	0.3544
Number (%) of patients censored	58 (56.3)	117 (75.5)	2 (25.0)	7 (43.8)	8 (66.7)	7 (87.5)	
Kaplan-Meier estimates of PFS in months							
25% quantile (95% CI)	10.18 (8.312 to 14.752)	18.46 (13.076 to NC)	3.89 (0.986 to 9.429)	5.82 (0.131 to 9.725)	13.96 (5.552 to NC)	NC (6.932 to NC)	
Median (95% CI)	19.15 (15.770 to NC)	NC (NC to NC)	9.05 (0.986 to NC)	9.72 (5.815 to 13.372)	NC (11.992 to NC)	NC (6.932 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (4.994 to NC)	13.37 (9.232 to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Kd							
Log-Rank test p-value[a] vs Kd	-	0.0002		0.9438		0.5251	
Hazard ratio (95% CI) vs Kd	-	0.45 (0.29 to 0.70)		1.04 (0.37 to 2.95)		0.50 (0.06 to 4.47)	
P-value	-	0.0003		0.9440		0.5334	

PFS: Progression-free survival, CI: Confidence interval, HR: Hazard ratio, IRC: Independent Response Committee
Cut-off date: 07FEB2020 HR<1 favors IKd arm
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] Two-sided significance level is 0.05.
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables and the treatment-by-subgroup interaction as covariates.
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16.2.6.1 Primary efficacy endpoint - Progression Free Survival
16.2.6.1.1 ITT population
16.2.6.1.1.11 Subgroup analyses by nb of prior lines
16.2.6.1.1.11.1 PFS - Primary analysis based on disease assessment by the IRC by treatment group according to nb of prior lines - ITT population

	1		>1		
	Kd (N=55)	**IKd (N=79)**	**Kd (N=68)**	**IKd (N=100)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	20 (36.4)	18 (22.8)	35 (51.5)	30 (30.0)	0.8072
Number (%) of patients censored	35 (63.6)	61 (77.2)	33 (48.5)	70 (70.0)	
Kaplan-Meier estimates of PFS in months					
25% quantile (95% CI)	10.28 (8.312 to 16.164)	20.34 (9.561 to NC)	9.03 (4.994 to 13.437)	13.08 (9.232 to 18.760)	
Median (95% CI)	NC (15.376 to NC)	NC (NC to NC)	16.99 (13.437 to 20.271)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (19.450 to NC)	NC (NC to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.0724		0.0037	
Hazard ratio (95% CI) vs Kd	-	0.56 (0.30 to 1.06)		0.49 (0.30 to 0.80)	
P-value	-	0.0764		0.0045	
PFS probability (95% CI)[b]					
6 Months	0.906 (0.789 to 0.960)	0.947 (0.864 to 0.980)	0.846 (0.732 to 0.914)	0.885 (0.802 to 0.935)	

PFS: Progression-free survival, CI: Confidence interval, HR: Hazard ratio, IRC: Independent Response Committee
Cut-off date: 07FEB2020 HR<1 favors IKd arm
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] Two-sided significance level is 0.05.
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables and the treatment-by-subgroup interaction as covariates.
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16.2.6.1 Primary efficacy endpoint - Progression Free Survival
16.2.6.1.1 ITT population
16.2.6.1.1.12 Subgroup analyses by cytogenetic abnormality
16.2.6.1.1.12.1 PFS - Primary analysis based on disease assessment by the IRC by treatment group according to cytogenetic abnormality - ITT population

	At least one		None		
	Kd (N=31)	**IKd (N=42)**	**Kd (N=77)**	**IKd (N=114)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	15 (48.4)	17 (40.5)	35 (45.5)	27 (23.7)	0.2707
Number (%) of patients censored	16 (51.6)	25 (59.5)	42 (54.5)	87 (76.3)	
Kaplan-Meier estimates of PFS in months					
25% quantile (95% CI)	8.31 (2.891 to 17.183)	9.23 (5.848 to 14.949)	9.92 (8.411 to 14.752)	18.76 (12.879 to NC)	
Median (95% CI)	18.20 (8.674 to NC)	NC (13.076 to NC)	19.45 (15.376 to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (18.990 to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.3614		0.0010	
Hazard ratio (95% CI) vs Kd	-	0.72 (0.36 to 1.45)		0.44 (0.27 to 0.73)	
P-value	-	0.3634		0.0014	
PFS probability (95% CI)[b]					
6 Months	0.794 (0.598 to 0.902)	0.874 (0.723 to 0.945)	0.907 (0.815 to 0.955)	0.927 (0.859 to 0.963)	

PFS: Progression-free survival, CI: Confidence interval, HR: Hazard ratio, IRC: Independent Response Committee
Cut-off date: 07FEB2020 HR<1 favors IKd arm
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] Two-sided significance level is 0.05.
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables and the treatment-by-subgroup interaction as covariates.
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16.2.6.1 Primary efficacy endpoint - Progression Free Survival
16.2.6.1.1 ITT population
16.2.6.1.1.13 Subgroup analyses by MM type at SE
16.2.6.1.1.13.1 PFS - Primary analysis based on disease assessment by the IRC by treatment group according to MM type at SE - ITT population

	IgG		Non-IgG		
	Kd (N=85)	**IKd (N=126)**	**Kd (N=38)**	**IKd (N=53)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	37 (43.5)	32 (25.4)	18 (47.4)	16 (30.2)	0.9200
Number (%) of patients censored	48 (56.5)	94 (74.6)	20 (52.6)	37 (69.8)	
Kaplan-Meier estimates of PFS in months					
25% quantile (95% CI)	12.19 (8.936 to 15.770)	16.92 (10.283 to NC)	5.55 (2.793 to 9.922)	13.08 (6.932 to NC)	
Median (95% CI)	19.45 (16.164 to NC)	NC (NC to NC)	15.70 (8.312 to NC)	NC (18.464 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.0055		0.0474	
Hazard ratio (95% CI) vs Kd	-	0.52 (0.32 to 0.83)		0.51 (0.26 to 1.00)	
P-value	-	0.0064		0.0516	
PFS probability (95% CI)[b]					
6 Months	0.928 (0.847 to 0.967)	0.909 (0.842 to 0.949)	0.744 (0.566 to 0.858)	0.922 (0.805 to 0.970)	

PFS: Progression-free survival, CI: Confidence interval, HR: Hazard ratio, IRC: Independent Response Committee
Cut-off date: 07FEB2020 HR<1 favors IKd arm
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] Two-sided significance level is 0.05.
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables and the treatment-by-subgroup interaction as covariates.
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16.2.6.1 Primary efficacy endpoint - Progression Free Survival
16.2.6.1.1 ITT population
16.2.6.1.1.14 Subgroup analyses by previous autologous stem-cell
16.2.6.1.1.14.1 PFS - Primary analysis based on disease assessment by the IRC by treatment group according to previous autologous stem-cell - ITT population

	Yes		No		
	Kd (N=69)	**IKd (N=116)**	**Kd (N=54)**	**IKd (N=63)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	30 (43.5)	34 (29.3)	25 (46.3)	14 (22.2)	0.4501
Number (%) of patients censored	39 (56.5)	82 (70.7)	29 (53.7)	49 (77.8)	
Kaplan-Meier estimates of PFS in months					
25% quantile (95% CI)	9.92 (7.326 to 15.244)	14.92 (9.232 to 20.337)	9.30 (4.994 to 14.752)	16.16 (9.561 to NC)	
Median (95% CI)	19.15 (15.244 to NC)	NC (NC to NC)	18.99 (13.437 to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.0272		0.0090	
Hazard ratio (95% CI) vs Kd	-	0.58 (0.35 to 0.95)		0.43 (0.22 to 0.82)	
P-value	-	0.0291		0.0112	
PFS probability (95% CI)[b]					
6 Months	0.893 (0.788 to 0.947)	0.893 (0.820 to 0.938)	0.850 (0.722 to 0.922)	0.949 (0.849 to 0.983)	

PFS: Progression-free survival, CI: Confidence interval, HR: Hazard ratio, IRC: Independent Response Committee
Cut-off date: 07FEB2020 HR<1 favors IKd arm
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] Two-sided significance level is 0.05.
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables and the treatment-by-subgroup interaction as covariates.
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16.2.6.1 Primary efficacy endpoint - Progression Free Survival
16.2.6.1.1 ITT population
16.2.6.1.1.15 Subgroup analyses by baseline eGFR (MDRD)
16.2.6.1.1.15.1 PFS - Primary analysis based on disease assessment by the IRC by treatment group according to baseline eGFR (MDRD) - ITT population

	>=60 mL/min/1.73m2		<60 mL/min/1.73m2		
	Kd (N=93)	**IKd (N=122)**	**Kd (N=18)**	**IKd (N=43)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	38 (40.9)	32 (26.2)	10 (55.6)	10 (23.3)	0.1101
Number (%) of patients censored	55 (59.1)	90 (73.8)	8 (44.4)	33 (76.7)	
Kaplan-Meier estimates of PFS in months					
25% quantile (95% CI)	11.99 (9.035 to 15.376)	13.63 (8.575 to NC)	4.99 (0.526 to 13.405)	18.76 (11.893 to NC)	
Median (95% CI)	NC (16.164 to NC)	NC (NC to NC)	13.40 (4.830 to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (13.405 to NC)	NC (NC to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.0487		0.0021	
Hazard ratio (95% CI) vs Kd	-	0.63 (0.39 to 1.00)		0.27 (0.11 to 0.66)	
P-value	-	0.0508		0.0040	
PFS probability (95% CI)[b]					
6 Months	0.912 (0.831 to 0.955)	0.897 (0.826 to 0.940)	0.711 (0.438 to 0.869)	0.951 (0.817 to 0.987)	

PFS: Progression-free survival, CI: Confidence interval, HR: Hazard ratio, IRC: Independent Response Committee
Cut-off date: 07FEB2020 HR<1 favors IKd arm
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] Two-sided significance level is 0.05.
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables and the treatment-by-subgroup interaction as covariates.
PGM=DEVOPS/SAR650984/EFC15246/CIR_RWE/REPORT/PGM/eff_km_subgp_sr_de_i_t.sas OUT=REPORT/OUTPUT/eff_km_pfs_crcl_de_i_t_x.rtf (19FEB2021 15:18)

16.2.6.1 Primary efficacy endpoint - Progression Free Survival
16.2.6.1.1 ITT population
16.2.6.1.1.16 Subgroup analyses by previous treatment with PI
16.2.6.1.1.16.1 PFS - Primary analysis based on disease assessment by the IRC by treatment group according to previous treatment with PI - ITT population

	Yes		No		
	Kd (N=47)	**IKd (N=81)**	**Kd (N=76)**	**IKd (N=98)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	20 (42.6)	22 (27.2)	35 (46.1)	26 (26.5)	0.8391
Number (%) of patients censored	27 (57.4)	59 (72.8)	41 (53.9)	72 (73.5)	
Kaplan-Meier estimates of PFS in months					
25% quantile (95% CI)	8.41 (4.665 to 11.828)	14.29 (7.622 to NC)	13.24 (8.936 to 15.376)	16.99 (9.232 to NC)	
Median (95% CI)	NC (11.138 to NC)	NC (NC to NC)	19.15 (15.704 to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.0613		0.0054	
Hazard ratio (95% CI) vs Kd	-	0.56 (0.31 to 1.04)		0.49 (0.30 to 0.82)	
P-value	-	0.0649		0.0064	
PFS probability (95% CI)[b]					
6 Months	0.849 (0.708 to 0.925)	0.922 (0.834 to 0.964)	0.889 (0.789 to 0.943)	0.905 (0.825 to 0.949)	

PFS: Progression-free survival, CI: Confidence interval, HR: Hazard ratio, IRC: Independent Response Committee
Cut-off date: 07FEB2020 HR<1 favors IKd arm
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] Two-sided significance level is 0.05.
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables and the treatment-by-subgroup interaction as covariates.
PGM=DEVOPS/SAR650984/EFC15246/CIR_RWE/REPORT/PGM/eff_km_subgp_sr_de_i_t.sas OUT=REPORT/OUTPUT/eff_km_pfs_pi_de_i_t_x.rtf (19FEB2021 15:18)

16.2.6.1 Primary efficacy endpoint - Progression Free Survival
16.2.6.1.1 ITT population
16.2.6.1.1.17 Subgroup analyses by previous treatment with IMiD
16.2.6.1.1.17.1 PFS - Primary analysis based on disease assessment by the IRC by treatment group according to previous treatment with IMiD - ITT population

	Yes		No		
	Kd (N=62)	**IKd (N=81)**	**Kd (N=61)**	**IKd (N=98)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	29 (46.8)	22 (27.2)	26 (42.6)	26 (26.5)	0.8545
Number (%) of patients censored	33 (53.2)	59 (72.8)	35 (57.4)	72 (73.5)	
Kaplan-Meier estimates of PFS in months					
25% quantile (95% CI)	10.28 (8.411 to 15.244)	14.92 (7.951 to NC)	9.36 (4.830 to 13.437)	16.16 (10.283 to NC)	
Median (95% CI)	17.18 (15.244 to NC)	NC (NC to NC)	20.27 (13.437 to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.0123		0.0249	
Hazard ratio (95% CI) vs Kd	-	0.50 (0.29 to 0.87)		0.54 (0.31 to 0.93)	
P-value	-	0.0141		0.0273	
PFS probability (95% CI)[b]					
6 Months	0.898 (0.787 to 0.953)	0.910 (0.821 to 0.956)	0.849 (0.729 to 0.918)	0.914 (0.835 to 0.956)	

PFS: Progression-free survival, CI: Confidence interval, HR: Hazard ratio, IRC: Independent Response Committee
Cut-off date: 07FEB2020 HR<1 favors IKd arm
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] Two-sided significance level is 0.05.
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables and the treatment-by-subgroup interaction as covariates.
PGM=DEVOPS/SAR650984/EFC15246/CIR_RWE/REPORT/PGM/eff_km_subgp_sr_de_i_t.sas OUT=REPORT/OUTPUT/eff_km_pfs_imid_de_i_t_x.rtf (19FEB2021 15:18)

16.2.6.1 Primary efficacy endpoint - Progression Free Survival
16.2.6.1.1 ITT population
16.2.6.1.1.18 Subgroup analyses by previous treatment with PI and IMiD
16.2.6.1.1.18.1 PFS - Primary analysis based on disease assessment by the IRC by treatment group according to previous treatment with PI and IMiD - ITT population

	Yes		No		
	Kd (N=17)	**IKd (N=23)**	**Kd (N=106)**	**IKd (N=156)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	6 (35.3)	7 (30.4)	49 (46.2)	41 (26.3)	0.5148
Number (%) of patients censored	11 (64.7)	16 (69.6)	57 (53.8)	115 (73.7)	
Kaplan-Meier estimates of PFS in months					
25% quantile (95% CI)	9.92 (0.526 to NC)	14.29 (0.131 to NC)	9.43 (7.326 to 13.437)	16.16 (11.433 to NC)	
Median (95% CI)	NC (9.922 to NC)	NC (14.292 to NC)	18.99 (15.704 to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.6500		0.0007	
Hazard ratio (95% CI) vs Kd	-	0.78 (0.26 to 2.32)		0.49 (0.33 to 0.75)	
P-value	-	0.6509		0.0009	
PFS probability (95% CI)[b]					
6 Months	0.941 (0.650 to 0.991)	0.867 (0.643 to 0.955)	0.862 (0.779 to 0.916)	0.919 (0.862 to 0.953)	

PFS: Progression-free survival, CI: Confidence interval, HR: Hazard ratio, IRC: Independent Response Committee
Cut-off date: 07FEB2020 HR<1 favors IKd arm
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] Two-sided significance level is 0.05.
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables and the treatment-by-subgroup interaction as covariates.
PGM=DEVOPS/SAR650984/EFC15246/CIR_RWE/REPORT/PGM/eff_km_subgp_sr_de_i_t.sas OUT=REPORT/OUTPUT/eff_km_pfs_piimid_de_i_t_x.rtf (19FEB2021 15:18)

16.2.6.1 Primary efficacy endpoint - Progression Free Survival
16.2.6.1.1 ITT population
16.2.6.1.1.19 Subgroup analyses by refractory to lenalidomide status
16.2.6.1.1.19.1 PFS - Primary analysis based on disease assessment by the IRC by treatment group according to refractory to lenalidomide status - ITT population

	Yes		No		
	Kd (N=42)	**IKd (N=57)**	**Kd (N=81)**	**IKd (N=122)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	25 (59.5)	23 (40.4)	30 (37.0)	25 (20.5)	0.5568
Number (%) of patients censored	17 (40.5)	34 (59.6)	51 (63.0)	97 (79.5)	
Kaplan-Meier estimates of PFS in months					
25% quantile (95% CI)	8.67 (2.793 to 11.992)	9.23 (5.651 to 13.634)	11.83 (8.312 to 18.201)	NC (14.292 to NC)	
Median (95% CI)	15.70 (9.922 to 17.183)	NC (12.879 to NC)	NC (18.234 to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (16.164 to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.0737		0.0055	
Hazard ratio (95% CI) vs Kd	-	0.60 (0.34 to 1.06)		0.48 (0.28 to 0.82)	
P-value	-	0.0769		0.0067	
PFS probability (95% CI)[b]					
6 Months	0.793 (0.628 to 0.891)	0.854 (0.728 to 0.924)	0.912 (0.824 to 0.957)	0.940 (0.878 to 0.971)	

PFS: Progression-free survival, CI: Confidence interval, HR: Hazard ratio, IRC: Independent Response Committee
Cut-off date: 07FEB2020 HR<1 favors IKd arm
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] Two-sided significance level is 0.05.
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables and the treatment-by-subgroup interaction as covariates.
PGM=DEVOPS/SAR650984/EFC15246/CIR_RWE/REPORT/PGM/eff_km_subgp_sr_de_i_t.sas OUT=REPORT/OUTPUT/eff_km_pfs_refr2_de_i_t_x.rtf (19FEB2021 15:18)

16.2.6.6 Secondary efficacy endpoints - Overall response
16.2.6.6.1 ITT population
16.2.6.6.1.2 Subgroup analyses by age
16.2.6.6.1.2.1 Summary of overall response rate as per IRC - 2-sided p-value according to age - ITT population

	<65 years		>=65 years		
	Kd (N=66)	**IKd (N=88)**	**Kd (N=57)**	**IKd (N=91)**	**Treat.-by-subgroup[b]**
Best Overall Response					
Complete response	18 (27.3)	37 (42.0)	16 (28.1)	34 (37.4)	
Very good partial response	17 (25.8)	26 (29.5)	18 (31.6)	33 (36.3)	
Partial response	19 (28.8)	12 (13.6)	14 (24.6)	13 (14.3)	
Minimal response	3 (4.5)	2 (2.3)	2 (3.5)	2 (2.2)	
Stable disease	3 (4.5)	8 (9.1)	3 (5.3)	5 (5.5)	
Non Progressive disease	1 (1.5)	0	0	1 (1.1)	
Progressive disease	1 (1.5)	2 (2.3)	2 (3.5)	0	
Unconfirmed progressive disease	1 (1.5)	0	0	0	
Not evaluable	3 (4.5)	1 (1.1)	2 (3.5)	3 (3.3)	
Overall Response as per IRC (sCR, CR, VGPR or PR)					
Not responders	12 (18.2)	13 (14.8)	9 (15.8)	11 (12.1)	
95% CI[a]	(0.0976 to 0.2961)	(0.0811 to 0.2394)	(0.0748 to 0.2787)	(0.0619 to 0.2060)	
Responders (sCR, CR, VGPR or PR)	54 (81.8)	75 (85.2)	48 (84.2)	80 (87.9)	
95% CI[a]	(0.7039 to 0.9024)	(0.7606 to 0.9189)	(0.7213 to 0.9252)	(0.7940 to 0.9381)	
Risk ratio 95% CI vs Kd[b]	-	1.04 (0.902 to 1.203)	-	1.04 (0.911 to 1.196)	
P-value [b]	-	0.5767	-	0.5352	

CI: Confidence interval, IRC: Independent Response Committee, sCR: stringent Complete Response, CR : Complete Response, VGPR : Very Good Partial Response, PR : Partial Response
[a] Estimated using Clopper-Pearson method.
[b] Estimation, CI and P-value are calculated from PROC GLIMMIX procedure and a model with treatment, subgroup variables and the treatment-by-subgroup interaction as covariates.
PGM=DEVOPS/SAR650984/EFC15246/CIR_RWE/REPORT/PGM/eff_bestresp_subgp_sr_de_i_t.sas OUT=REPORT/OUTPUT/eff_bestresp_resp1fn_age_de_i_t_x.rtf (19FEB2021 15:21)

16.2.6.6 Secondary efficacy endpoints - Overall response
16.2.6.6.1 ITT population
16.2.6.6.1.2 Subgroup analyses by age
16.2.6.6.1.2.1 Summary of overall response rate as per IRC - 2-sided p-value according to age - ITT population

	<65 years		>=65 years		
	Kd (N=66)	**IKd (N=88)**	**Kd (N=57)**	**IKd (N=91)**	**Treat.-by-subgroup[b]**
P-value heterogeneity[b]					0.9826
Odds ratio 95% CI vs Kd[b]	-	1.28 (0.541 to 3.037)	-	1.36 (0.525 to 3.543)	
P-value [b]	-	0.5712	-	0.5231	
P-value heterogeneity[b]					0.9249
Percent difference 95% CI vs Kd(%)[b]	-	3.41 (-8.537 to 15.355)	-	3.70 (-7.942 to 15.345)	
P-value [b]	-	0.5748	-	0.5320	
P-value heterogeneity[b]					0.9725

CI: Confidence interval, IRC: Independent Response Committee, sCR: stringent Complete Response, CR : Complete Response, VGPR : Very Good Partial Response, PR : Partial Response
[a] Estimated using Clopper-Pearson method.
[b] Estimation, CI and P-value are calculated from PROC GLIMMIX procedure and a model with treatment, subgroup variables and the treatment-by-subgroup interaction as covariates.
PGM=DEVOPS/SAR650984/EFC15246/CIR_RWE/REPORT/PGM/eff_bestresp_subgp_sr_de_i_t.sas OUT=REPORT/OUTPUT/eff_bestresp_resp1fn_age_de_i_t_x.rtf (19FEB2021 15:21)

16.2.6.6 Secondary efficacy endpoints - Overall response
16.2.6.6.1 ITT population
16.2.6.6.1.3 Subgroup analyses by gender
16.2.6.6.1.3.1 Summary of overall response rate as per IRC - 2-sided p-value according to gender - ITT population

	Male		Female		
	Kd (N=68)	**IKd (N=101)**	**Kd (N=55)**	**IKd (N=78)**	**Treat.-by-subgroup[b]**
Best Overall Response					
Complete response	17 (25.0)	39 (38.6)	17 (30.9)	32 (41.0)	
Very good partial response	25 (36.8)	34 (33.7)	10 (18.2)	25 (32.1)	
Partial response	13 (19.1)	12 (11.9)	20 (36.4)	13 (16.7)	
Minimal response	3 (4.4)	3 (3.0)	2 (3.6)	1 (1.3)	
Stable disease	4 (5.9)	9 (8.9)	2 (3.6)	4 (5.1)	
Non Progressive disease	0	0	1 (1.8)	1 (1.3)	
Progressive disease	1 (1.5)	1 (1.0)	2 (3.6)	1 (1.3)	
Unconfirmed progressive disease	1 (1.5)	0	0	0	
Not evaluable	4 (5.9)	3 (3.0)	1 (1.8)	1 (1.3)	
Overall Response as per IRC (sCR, CR, VGPR or PR)					
Not responders	13 (19.1)	16 (15.8)	8 (14.5)	8 (10.3)	
95% CI[a]	(0.1059 to 0.3047)	(0.0933 to 0.2445)	(0.0650 to 0.2666)	(0.0453 to 0.1921)	
Responders (sCR, CR, VGPR or PR)	55 (80.9)	85 (84.2)	47 (85.5)	70 (89.7)	
95% CI[a]	(0.6953 to 0.8941)	(0.7555 to 0.9067)	(0.7334 to 0.9350)	(0.8079 to 0.9547)	
Risk ratio 95% CI vs Kd[b]	-	1.04 (0.901 to 1.201)	-	1.05 (0.920 to 1.199)	
P-value [b]	-	0.5873	-	0.4689	

CI: Confidence interval, IRC: Independent Response Committee, sCR: stringent Complete Response, CR : Complete Response, VGPR : Very Good Partial Response, PR : Partial Response
[a] Estimated using Clopper-Pearson method.
[b] Estimation, CI and P-value are calculated from PROC GLIMMIX procedure and a model with treatment, subgroup variables and the treatment-by-subgroup interaction as covariates.
PGM=DEVOPS/SAR650984/EFC15246/CIR_RWE/REPORT/PGM/eff_bestresp_subgp_sr_de_i_t.sas OUT=REPORT/OUTPUT/eff_bestresp_resp1fn_sex_de_i_t_x.rtf (19FEB2021 15:21)

16.2.6.6 Secondary efficacy endpoints - Overall response
16.2.6.6.1 ITT population
16.2.6.6.1.3 Subgroup analyses by gender
16.2.6.6.1.3.1 Summary of overall response rate as per IRC - 2-sided p-value according to gender - ITT population

	Male		Female		
	Kd (N=68)	**IKd (N=101)**	**Kd (N=55)**	**IKd (N=78)**	**Treat.-by-subgroup[b]**
P-value heterogeneity[b]					0.9259
Odds ratio 95% CI vs Kd[b]	-	1.26 (0.559 to 2.822)	-	1.49 (0.520 to 4.263)	
P-value [b]	-	0.5805	-	0.4566	
P-value heterogeneity[b]					0.8004
Percent difference 95% CI vs Kd(%)[b]	-	3.28 (-8.522 to 15.074)	-	4.29 (-7.253 to 15.831)	
P-value [b]	-	0.5852	-	0.4652	
P-value heterogeneity[b]					0.9039

CI: Confidence interval, IRC: Independent Response Committee, sCR: stringent Complete Response, CR : Complete Response, VGPR : Very Good Partial Response, PR : Partial Response
[a] Estimated using Clopper-Pearson method.
[b] Estimation, CI and P-value are calculated from PROC GLIMMIX procedure and a model with treatment, subgroup variables and the treatment-by-subgroup interaction as covariates.
PGM=DEVOPS/SAR650984/EFC15246/CIR_RWE/REPORT/PGM/eff_bestresp_subgp_sr_de_i_t.sas OUT=REPORT/OUTPUT/eff_bestresp_resp1fn_sex_de_i_t_x.rtf (19FEB2021 15:21)

16.2.6.6 Secondary efficacy endpoints - Overall response
16.2.6.6.1 ITT population
16.2.6.6.1.4 Subgroup analyses by ethnic origin
16.2.6.6.1.4.1 Summary of overall response rate as per IRC - 2-sided p-value according to ethnic origin - ITT population

	White		Other		
	Kd (N=83)	**IKd (N=131)**	**Kd (N=28)**	**IKd (N=34)**	**Treat.-by-subgroup[b]**
Best Overall Response					
Complete response	26 (31.3)	54 (41.2)	6 (21.4)	13 (38.2)	
Very good partial response	23 (27.7)	41 (31.3)	8 (28.6)	13 (38.2)	
Partial response	21 (25.3)	18 (13.7)	10 (35.7)	3 (8.8)	
Minimal response	3 (3.6)	2 (1.5)	2 (7.1)	1 (2.9)	
Stable disease	5 (6.0)	11 (8.4)	1 (3.6)	2 (5.9)	
Non Progressive disease	1 (1.2)	1 (0.8)	0	0	
Progressive disease	2 (2.4)	2 (1.5)	0	0	
Not evaluable	2 (2.4)	2 (1.5)	1 (3.6)	2 (5.9)	
Overall Response as per IRC (sCR, CR, VGPR or PR)					
Not responders	13 (15.7)	18 (13.7)	4 (14.3)	5 (14.7)	
95% CI[a]	(0.0861 to 0.2529)	(0.0835 to 0.2084)	(0.0403 to 0.3267)	(0.0495 to 0.3106)	
Responders (sCR, CR, VGPR or PR)	70 (84.3)	113 (86.3)	24 (85.7)	29 (85.3)	
95% CI[a]	(0.7471 to 0.9139)	(0.7916 to 0.9165)	(0.6733 to 0.9597)	(0.6894 to 0.9505)	
Risk ratio 95% CI vs Kd[b]	-	1.02 (0.911 to 1.148)	-	1.00 (0.809 to 1.224)	
P-value [b]	-	0.7017	-	0.9627	
P-value heterogeneity[b]					0.8197

CI: Confidence interval, IRC: Independent Response Committee, sCR: stringent Complete Response, CR : Complete Response, VGPR : Very Good Partial Response, PR : Partial Response
[a] Estimated using Clopper-Pearson method.
[b] Estimation, CI and P-value are calculated from PROC GLIMMIX procedure and a model with treatment, subgroup variables and the treatment-by-subgroup interaction as covariates.
PGM=DEVOPS/SAR650984/EFC15246/CIR_RWE/REPORT/PGM/eff_bestresp_subgp_sr_de_i_t.sas OUT=REPORT/OUTPUT/eff_bestresp_resp1fn_race_de_i_t_x.rtf (19FEB2021 15:21)

16.2.6.6 Secondary efficacy endpoints - Overall response
16.2.6.6.1 ITT population
16.2.6.6.1.4 Subgroup analyses by ethnic origin
16.2.6.6.1.4.1 Summary of overall response rate as per IRC - 2-sided p-value according to ethnic origin - ITT population

	White		Other		
	Kd (N=83)	**IKd (N=131)**	**Kd (N=28)**	**IKd (N=34)**	**Treat.-by-subgroup[b]**
Odds ratio 95% CI vs Kd[b]	-	1.17 (0.536 to 2.535)	-	0.97 (0.232 to 4.031)	
P-value [b]	-	0.6975	-	0.9628	
P-value heterogeneity[b]					0.8207
Percent difference 95% CI vs Kd(%)[b]	-	1.92 (-7.914 to 11.758)	-	-0.42 (-18.097 to 17.257)	
P-value [b]	-	0.7007	-	0.9627	
P-value heterogeneity[b]					0.8199

CI: Confidence interval, IRC: Independent Response Committee, sCR: stringent Complete Response, CR : Complete Response, VGPR : Very Good Partial Response, PR : Partial Response
[a] Estimated using Clopper-Pearson method.
[b] Estimation, CI and P-value are calculated from PROC GLIMMIX procedure and a model with treatment, subgroup variables and the treatment-by-subgroup interaction as covariates.
PGM=DEVOPS/SAR650984/EFC15246/CIR_RWE/REPORT/PGM/eff_bestresp_subgp_sr_de_i_t.sas OUT=REPORT/OUTPUT/eff_bestresp_resp1fn_race_de_i_t_x.rtf (19FEB2021 15:21)

16.2.6.6 Secondary efficacy endpoints - Overall response
16.2.6.6.1 ITT population
16.2.6.6.1.5 Subgroup analyses by geographical region
16.2.6.6.1.5.1 Summary of overall response rate as per IRC - 2-sided p-value according to geographical region - ITT population

	Europe		America		Asia		Other countries		
	Kd (N=60)	IKd (N=85)	Kd (N=20)	IKd (N=24)	Kd (N=21)	IKd (N=25)	Kd (N=22)	IKd (N=45)	Treat.-by-subgroup[b]
Best Overall Response									
Complete response	16 (26.7)	38 (44.7)	7 (35.0)	9 (37.5)	5 (23.8)	11 (44.0)	6 (27.3)	13 (28.9)	
Very good partial response	13 (21.7)	25 (29.4)	7 (35.0)	8 (33.3)	6 (28.6)	9 (36.0)	9 (40.9)	17 (37.8)	
Partial response	17 (28.3)	10 (11.8)	5 (25.0)	4 (16.7)	6 (28.6)	2 (8.0)	5 (22.7)	9 (20.0)	
Minimal response	2 (3.3)	1 (1.2)	0	1 (4.2)	2 (9.5)	1 (4.0)	1 (4.5)	1 (2.2)	
Stable disease	4 (6.7)	8 (9.4)	1 (5.0)	0	1 (4.8)	1 (4.0)	0	4 (8.9)	
Non Progressive disease	1 (1.7)	1 (1.2)	0	0	0	0	0	0	
Progressive disease	2 (3.3)	0	0	1 (4.2)	0	0	1 (4.5)	1 (2.2)	
Unconfirmed progressive disease	1 (1.7)	0	0	0	0	0	0	0	
Not evaluable	4 (6.7)	2 (2.4)	0	1 (4.2)	1 (4.8)	1 (4.0)	0	0	
Overall Response as per IRC (sCR, CR, VGPR or PR)									
Not responders	14 (23.3)	12 (14.1)	1 (5.0)	3 (12.5)	4 (19.0)	3 (12.0)	2 (9.1)	6 (13.3)	
95% CI[a]	(0.1338 to 0.3604)	(0.0751 to 0.2336)	(0.0013 to 0.2487)	(0.0266 to 0.3236)	(0.0545 to 0.4191)	(0.0255 to 0.3122)	(0.0112 to 0.2916)	(0.0505 to 0.2679)	
Responders (sCR, CR, VGPR or PR)	46 (76.7)	73 (85.9)	19 (95.0)	21 (87.5)	17 (81.0)	22 (88.0)	20 (90.9)	39 (86.7)	
95% CI[a]	(0.6396 to 0.8662)	(0.7664 to 0.9249)	(0.7513 to 0.9987)	(0.6764 to 0.9734)	(0.5809 to 0.9455)	(0.6878 to 0.9745)	(0.7084 to 0.9888)	(0.7321 to 0.9495)	

CI: Confidence interval, IRC: Independent Response Committee, sCR: stringent Complete Response, CR : Complete Response, VGPR : Very Good Partial Response, PR : Partial Response
[a] Estimated using Clopper-Pearson method.
[b] Estimation, CI and P-value are calculated from PROC GLIMMIX procedure and a model with treatment, subgroup variables and the treatment-by-subgroup interaction as covariates.
PGM=DEVOPS/SAR650984/EFC15246/CIR_RWE/REPORT/PGM/eff_bestresp_subgp_sr_de_i_t.sas OUT=REPORT/OUTPUT/eff_bestresp_resp1fn_greg_de_i_t_x.rtf (19FEB2021 15:21)

16.2.6.6 Secondary efficacy endpoints - Overall response
16.2.6.6.1 ITT population
16.2.6.6.1.5 Subgroup analyses by geographical region
16.2.6.6.1.5.1 Summary of overall response rate as per IRC - 2-sided p-value according to geographical region - ITT population

	Europe		America		Asia		Other countries		
	Kd (N=60)	**IKd (N=85)**	**Kd (N=20)**	**IKd (N=24)**	**Kd (N=21)**	**IKd (N=25)**	**Kd (N=22)**	**IKd (N=45)**	**Treat.-by-subgroup[b]**
Risk ratio 95% CI vs Kd[b]	-	1.12 (0.950 to 1.321)	-	0.92 (0.768 to 1.105)	-	1.09 (0.843 to 1.401)	-	0.95 (0.800 to 1.136)	
P-value [b]	-	0.1761	-	0.3755	-	0.5183	-	0.5927	
P-value heterogeneity[b]									0.3549
Odds ratio 95% CI vs Kd[b]	-	1.85 (0.785 to 4.368)	-	0.37 (0.035 to 3.888)	-	1.73 (0.337 to 8.824)	-	0.65 (0.119 to 3.543)	
P-value [b]	-	0.1589	-	0.4050	-	0.5111	-	0.6175	
P-value heterogeneity[b]									0.4753
Percent difference 95% CI vs Kd(%)[b]	-	9.22 (-3.851 to 22.282)	-	-7.50 (-23.886 to 8.886)	-	7.05 (-14.119 to 28.214)	-	-4.24 (-19.894 to 11.409)	
P-value [b]	-	0.1662	-	0.3684	-	0.5128	-	0.5941	
P-value heterogeneity[b]									0.3485

CI: Confidence interval, IRC: Independent Response Committee, sCR: stringent Complete Response, CR : Complete Response, VGPR : Very Good Partial Response, PR : Partial Response
[a] Estimated using Clopper-Pearson method.
[b] Estimation, CI and P-value are calculated from PROC GLIMMIX procedure and a model with treatment, subgroup variables and the treatment-by-subgroup interaction as covariates.
PGM=DEVOPS/SAR650984/EFC15246/CIR_RWE/REPORT/PGM/eff_bestresp_subgp_sr_de_i_t.sas OUT=REPORT/OUTPUT/eff_bestresp_resp1fn_greg_de_i_t_x.rtf (19FEB2021 15:21)

16.2.6.6 Secondary efficacy endpoints - Overall response
16.2.6.6.1 ITT population
16.2.6.6.1.6 Subgroup analyses by regulatory region
16.2.6.6.1.6.1 Summary of overall response rate as per IRC - 2-sided p-value according to regulatory region - ITT population

	Western countries		Other countries		
	Kd (N=55)	**IKd (N=97)**	**Kd (N=68)**	**IKd (N=82)**	**Treat.-by-subgroup[b]**
Best Overall Response					
Complete response	16 (29.1)	35 (36.1)	18 (26.5)	36 (43.9)	
Very good partial response	13 (23.6)	35 (36.1)	22 (32.4)	24 (29.3)	
Partial response	17 (30.9)	15 (15.5)	16 (23.5)	10 (12.2)	
Minimal response	1 (1.8)	2 (2.1)	4 (5.9)	2 (2.4)	
Stable disease	0	7 (7.2)	6 (8.8)	6 (7.3)	
Non Progressive disease	1 (1.8)	1 (1.0)	0	0	
Progressive disease	2 (3.6)	0	1 (1.5)	2 (2.4)	
Unconfirmed progressive disease	1 (1.8)	0	0	0	
Not evaluable	4 (7.3)	2 (2.1)	1 (1.5)	2 (2.4)	
Overall Response as per IRC (sCR, CR, VGPR or PR)					
Not responders	9 (16.4)	12 (12.4)	12 (17.6)	12 (14.6)	
95% CI[a]	(0.0777 to 0.2880)	(0.0656 to 0.2061)	(0.0947 to 0.2880)	(0.0780 to 0.2417)	
Responders (sCR, CR, VGPR or PR)	46 (83.6)	85 (87.6)	56 (82.4)	70 (85.4)	
95% CI[a]	(0.7120 to 0.9223)	(0.7939 to 0.9344)	(0.7120 to 0.9053)	(0.7583 to 0.9220)	
Risk ratio 95% CI vs Kd[b]	-	1.05 (0.911 to 1.204)	-	1.04 (0.899 to 1.195)	
P-value [b]	-	0.5106	-	0.6201	

CI: Confidence interval, IRC: Independent Response Committee, sCR: stringent Complete Response, CR : Complete Response, VGPR : Very Good Partial Response, PR : Partial Response
[a] Estimated using Clopper-Pearson method.
[b] Estimation, CI and P-value are calculated from PROC GLIMMIX procedure and a model with treatment, subgroup variables and the treatment-by-subgroup interaction as covariates.
PGM=DEVOPS/SAR650984/EFC15246/CIR_RWE/REPORT/PGM/eff_bestresp_subgp_sr_de_i_t.sas OUT=REPORT/OUTPUT/eff_bestresp_resp1fn_rreg_de_i_t_x.rtf (19FEB2021 15:21)

16.2.6.6 Secondary efficacy endpoints - Overall response
16.2.6.6.1 ITT population
16.2.6.6.1.6 Subgroup analyses by regulatory region
16.2.6.6.1.6.1 Summary of overall response rate as per IRC - 2-sided p-value according to regulatory region - ITT population

	Western countries		Other countries		
	Kd (N=55)	**IKd (N=97)**	**Kd (N=68)**	**IKd (N=82)**	**Treat.-by-subgroup[b]**
P-value heterogeneity[b]					0.9159
Odds ratio 95% CI vs Kd[b]	-	1.39 (0.542 to 3.546)	-	1.25 (0.520 to 3.006)	
P-value [b]	-	0.4948	-	0.6171	
P-value heterogeneity[b]					0.8746
Percent difference 95% CI vs Kd(%)[b]	-	3.99 (-7.825 to 15.810)	-	3.01 (-8.894 to 14.920)	
P-value [b]	-	0.5066	-	0.6189	
P-value heterogeneity[b]					0.9086

CI: Confidence interval, IRC: Independent Response Committee, sCR: stringent Complete Response, CR : Complete Response, VGPR : Very Good Partial Response, PR : Partial Response
[a] Estimated using Clopper-Pearson method.
[b] Estimation, CI and P-value are calculated from PROC GLIMMIX procedure and a model with treatment, subgroup variables and the treatment-by-subgroup interaction as covariates.
PGM=DEVOPS/SAR650984/EFC15246/CIR_RWE/REPORT/PGM/eff_bestresp_subgp_sr_de_i_t.sas OUT=REPORT/OUTPUT/eff_bestresp_resp1fn_rreg_de_i_t_x.rtf (19FEB2021 15:21)

16.2.6.6 Secondary efficacy endpoints - Overall response
16.2.6.6.1 ITT population
16.2.6.6.1.7 Subgroup analyses by baseline ECOG PS
16.2.6.6.1.7.1 Summary of overall response rate as per IRC - 2-sided p-value according to baseline ECOG PS - ITT population

	0 or 1		>1		
	Kd (N=118)	**IKd (N=168)**	**Kd (N=5)**	**IKd (N=11)**	**Treat.-by-subgroup[b]**
Best Overall Response					
Complete response	33 (28.0)	68 (40.5)	1 (20.0)	3 (27.3)	
Very good partial response	35 (29.7)	56 (33.3)	0	3 (27.3)	
Partial response	29 (24.6)	23 (13.7)	4 (80.0)	2 (18.2)	
Minimal response	5 (4.2)	4 (2.4)	0	0	
Stable disease	6 (5.1)	12 (7.1)	0	1 (9.1)	
Non Progressive disease	1 (0.8)	1 (0.6)	0	0	
Progressive disease	3 (2.5)	2 (1.2)	0	0	
Unconfirmed progressive disease	1 (0.8)	0	0	0	
Not evaluable	5 (4.2)	2 (1.2)	0	2 (18.2)	
Overall Response as per IRC (sCR, CR, VGPR or PR)					
Not responders	21 (17.8)	21 (12.5)		3 (27.3)	
95% CI[a]	(0.1137 to 0.2591)	(0.0791 to 0.1847)	5 (100.0)	(0.0602 to 0.6097)	
Responders (sCR, CR, VGPR or PR)	97 (82.2)	147 (87.5)	5 (100.0)	8 (72.7)	
95% CI[a]	(0.7409 to 0.8863)	(0.8153 to 0.9209)	(0.4782 to 1.0000)	(0.3903 to 0.9398)	
Risk ratio 95% CI vs Kd[b]	-	1.06 (0.956 to 1.168)	-	0.74 (0.672 to 0.821)	
P-value [b]	-	0.2769	-	<.0001	

CI: Confidence interval, IRC: Independent Response Committee, sCR: stringent Complete Response, CR : Complete Response, VGPR : Very Good Partial Response, PR : Partial Response
[a] Estimated using Clopper-Pearson method.
[b] Estimation, CI and P-value are calculated from PROC GLIMMIX procedure and a model with treatment, subgroup variables and the treatment-by-subgroup interaction as covariates.
PGM=DEVOPS/SAR650984/EFC15246/CIR_RWE/REPORT/PGM/eff_bestresp_subgp_sr_de_i_t.sas OUT=REPORT/OUTPUT/eff_bestresp_resp1fn_ecog_de_i_t_x.rtf (19FEB2021 15:21)

16.2.6.6 Secondary efficacy endpoints - Overall response
16.2.6.6.1 ITT population
16.2.6.6.1.7 Subgroup analyses by baseline ECOG PS
16.2.6.6.1.7.1 Summary of overall response rate as per IRC - 2-sided p-value according to baseline ECOG PS - ITT population

	0 or 1		>1		
	Kd (N=118)	**IKd (N=168)**	**Kd (N=5)**	**IKd (N=11)**	**Treat.-by-subgroup[b]**
P-value heterogeneity[b]					<.0001
Odds ratio 95% CI vs Kd[b]	-	1.52 (0.784 to 2.931)	-	0.00 (0.000 to .)	
P-value [b]	-	0.2159	-	0.9746	
P-value heterogeneity[b]					0.9738
Percent difference 95% CI vs Kd(%)[b]	-	5.30 (-3.261 to 13.854)	-	-27.27 (-35.830 to -18.715)	
P-value [b]	-	0.2242	-	<.0001	
P-value heterogeneity[b]					<.0001

CI: Confidence interval, IRC: Independent Response Committee, sCR: stringent Complete Response, CR : Complete Response, VGPR : Very Good Partial Response, PR : Partial Response
[a] Estimated using Clopper-Pearson method.
[b] Estimation, CI and P-value are calculated from PROC GLIMMIX procedure and a model with treatment, subgroup variables and the treatment-by-subgroup interaction as covariates.
PGM=DEVOPS/SAR650984/EFC15246/CIR_RWE/REPORT/PGM/eff_bestresp_subgp_sr_de_i_t.sas OUT=REPORT/OUTPUT/eff_bestresp_resp1fn_ecog_de_i_t_x.rtf (19FEB2021 15:21)

16.2.6.6 Secondary efficacy endpoints - Overall response
16.2.6.6.1 ITT population
16.2.6.6.1.8 Subgroup analyses by ISS staging at SE
16.2.6.6.1.8.1 Summary of overall response rate as per IRC - 2-sided p-value according to ISS staging at SE - ITT population

	I		II		III		
	Kd (N=71)	**IKd (N=89)**	**Kd (N=31)**	**IKd (N=63)**	**Kd (N=20)**	**IKd (N=26)**	**Treat.-by-subgroup[b]**
Best Overall Response							
Complete response	25 (35.2)	39 (43.8)	7 (22.6)	26 (41.3)	2 (10.0)	5 (19.2)	
Very good partial response	21 (29.6)	29 (32.6)	8 (25.8)	23 (36.5)	6 (30.0)	7 (26.9)	
Partial response	15 (21.1)	13 (14.6)	11 (35.5)	8 (12.7)	7 (35.0)	4 (15.4)	
Minimal response	1 (1.4)	2 (2.2)	1 (3.2)	1 (1.6)	2 (10.0)	1 (3.8)	
Stable disease	3 (4.2)	4 (4.5)	3 (9.7)	4 (6.3)	0	5 (19.2)	
Non Progressive disease	1 (1.4)	1 (1.1)	0	0	0	0	
Progressive disease	3 (4.2)	0	0	1 (1.6)	0	1 (3.8)	
Unconfirmed progressive disease	0	0	0	0	1 (5.0)	0	
Not evaluable	2 (2.8)	1 (1.1)	1 (3.2)	0	2 (10.0)	3 (11.5)	
Overall Response as per IRC (sCR, CR, VGPR or PR)							
Not responders	10 (14.1)	8 (9.0)	5 (16.1)	6 (9.5)	5 (25.0)	10 (38.5)	
95% CI[a]	(0.0697 to 0.2438)	(0.0396 to 0.1695)	(0.0545 to 0.3373)	(0.0358 to 0.1959)	(0.0866 to 0.4910)	(0.2023 to 0.5943)	
Responders (sCR, CR, VGPR or PR)	61 (85.9)	81 (91.0)	26 (83.9)	57 (90.5)	15 (75.0)	16 (61.5)	
95% CI[a]	(0.7562 to 0.9303)	(0.8305 to 0.9604)	(0.6627 to 0.9455)	(0.8041 to 0.9642)	(0.5090 to 0.9134)	(0.4057 to 0.7977)	

CI: Confidence interval, IRC: Independent Response Committee, sCR: stringent Complete Response, CR : Complete Response, VGPR : Very Good Partial Response, PR : Partial Response
[a] Estimated using Clopper-Pearson method.
[b] Estimation, CI and P-value are calculated from PROC GLIMMIX procedure and a model with treatment, subgroup variables and the treatment-by-subgroup interaction as covariates.
PGM=DEVOPS/SAR650984/EFC15246/CIR_RWE/REPORT/PGM/eff_bestresp_subgp_sr_de_i_t.sas OUT=REPORT/OUTPUT/eff_bestresp_resp1fn_seiss_de_i_t_x.rtf (19FEB2021 15:21)

16.2.6.6 Secondary efficacy endpoints - Overall response
16.2.6.6.1 ITT population
16.2.6.6.1.8 Subgroup analyses by ISS staging at SE
16.2.6.6.1.8.1 Summary of overall response rate as per IRC - 2-sided p-value according to ISS staging at SE - ITT population

	I		II		III		
	Kd (N=71)	**IKd (N=89)**	**Kd (N=31)**	**IKd (N=63)**	**Kd (N=20)**	**IKd (N=26)**	**Treat.-by-subgroup[b]**
Risk ratio 95% CI vs Kd[b]	-	1.06 (0.944 to 1.188)	-	1.08 (0.906 to 1.285)	-	0.82 (0.552 to 1.220)	
P-value [b]	-	0.3252	-	0.3936	-	0.3276	
P-value heterogeneity[b]							0.4482
Odds ratio 95% CI vs Kd[b]	-	1.66 (0.616 to 4.473)	-	1.83 (0.508 to 6.568)	-	0.53 (0.147 to 1.936)	
P-value [b]	-	0.3153	-	0.3547	-	0.3381	
P-value heterogeneity[b]							0.3106
Percent difference 95% CI vs Kd(%)[b]	-	5.10 (-4.985 to 15.176)	-	6.61 (-8.294 to 21.505)	-	-13.46 (-40.214 to 13.291)	
P-value [b]	-	0.3206	-	0.3837	-	0.3228	
P-value heterogeneity[b]							0.4050

CI: Confidence interval, IRC: Independent Response Committee, sCR: stringent Complete Response, CR : Complete Response, VGPR : Very Good Partial Response, PR : Partial Response
[a] Estimated using Clopper-Pearson method.
[b] Estimation, CI and P-value are calculated from PROC GLIMMIX procedure and a model with treatment, subgroup variables and the treatment-by-subgroup interaction as covariates.
PGM=DEVOPS/SAR650984/EFC15246/CIR_RWE/REPORT/PGM/eff_bestresp_subgp_sr_de_i_t.sas OUT=REPORT/OUTPUT/eff_bestresp_resp1fn_seiss_de_i_t_x.rtf (19FEB2021 15:21)

16.2.6.6 Secondary efficacy endpoints - Overall response
16.2.6.6.1 ITT population
16.2.6.6.1.9 Subgroup analyses by R-ISS stage at SE
16.2.6.6.1.9.1 Summary of overall response rate as per IRC - 2-sided p-value according to R-ISS stage at SE - ITT population

	I or II		III		Not classified		
	Kd (N=103)	IKd (N=155)	Kd (N=8)	IKd (N=16)	Kd (N=12)	IKd (N=8)	Treat.-by-subgroup[b]
Best Overall Response							
Complete response	26 (25.2)	67 (43.2)	1 (12.5)	1 (6.3)	7 (58.3)	3 (37.5)	
Very good partial response	31 (30.1)	53 (34.2)	1 (12.5)	4 (25.0)	3 (25.0)	2 (25.0)	
Partial response	29 (28.2)	21 (13.5)	3 (37.5)	4 (25.0)	1 (8.3)	0	
Minimal response	2 (1.9)	3 (1.9)	2 (25.0)	1 (6.3)	1 (8.3)	0	
Stable disease	6 (5.8)	9 (5.8)	0	3 (18.8)	0	1 (12.5)	
Non Progressive disease	1 (1.0)	1 (0.6)	0	0	0	0	
Progressive disease	3 (2.9)	1 (0.6)	0	1 (6.3)	0	0	
Unconfirmed progressive disease	1 (1.0)	0	0	0	0	0	
Not evaluable	4 (3.9)	0	1 (12.5)	2 (12.5)	0	2 (25.0)	
Overall Response as per IRC (sCR, CR, VGPR or PR)							
Not responders	17 (16.5)	14 (9.0)	3 (37.5)	7 (43.8)	1 (8.3)	3 (37.5)	
95% CI[a]	(0.0992 to 0.2511)	(0.0503 to 0.1469)	(0.0852 to 0.7551)	(0.1975 to 0.7012)	(0.0021 to 0.3848)	(0.0852 to 0.7551)	
Responders (sCR, CR, VGPR or PR)	86 (83.5)	141 (91.0)	5 (62.5)	9 (56.3)	11 (91.7)	5 (62.5)	
95% CI[a]	(0.7489 to 0.9008)	(0.8531 to 0.9497)	(0.2449 to 0.9148)	(0.2988 to 0.8025)	(0.6152 to 0.9979)	(0.2449 to 0.9148)	

CI: Confidence interval, IRC: Independent Response Committee, sCR: stringent Complete Response, CR : Complete Response, VGPR : Very Good Partial Response, PR : Partial Response
[a] Estimated using Clopper-Pearson method.
[b] Estimation, CI and P-value are calculated from PROC GLIMMIX procedure and a model with treatment, subgroup variables and the treatment-by-subgroup interaction as covariates.
PGM=DEVOPS/SAR650984/EFC15246/CIR_RWE/REPORT/PGM/eff_bestresp_subgp_sr_de_i_t.sas OUT=REPORT/OUTPUT/eff_bestresp_resp1fn_seriss_de_i_t_x.rtf (19FEB2021 15:21)

16.2.6.6 Secondary efficacy endpoints - Overall response
16.2.6.6.1 ITT population
16.2.6.6.1.9 Subgroup analyses by R-ISS stage at SE
16.2.6.6.1.9.1 Summary of overall response rate as per IRC - 2-sided p-value according to R-ISS stage at SE - ITT population

	I or II		III		Not classified		
	Kd (N=103)	**IKd (N=155)**	**Kd (N=8)**	**IKd (N=16)**	**Kd (N=12)**	**IKd (N=8)**	**Treat.-by-subgroup[b]**
Risk ratio 95% CI vs Kd[b]	-	1.09 (0.986 to 1.204)	-	0.90 (0.451 to 1.798)	-	0.68 (0.387 to 1.200)	
P-value [b]	-	0.0913	-	0.7646	-	0.1836	
P-value heterogeneity[b]							0.2447
Odds ratio 95% CI vs Kd[b]	-	1.99 (0.931 to 4.255)	-	0.77 (0.135 to 4.422)	-	0.15 (0.012 to 1.861)	
P-value [b]	-	0.0754	-	0.7701	-	0.1398	
P-value heterogeneity[b]							0.1171
Percent difference 95% CI vs Kd(%)[b]	-	7.47 (-1.033 to 15.978)	-	-6.25 (-47.848 to 35.348)	-	-29.17 (-66.332 to 7.998)	
P-value [b]	-	0.0849	-	0.7677	-	0.1235	
P-value heterogeneity[b]							0.1454

CI: Confidence interval, IRC: Independent Response Committee, sCR: stringent Complete Response, CR : Complete Response, VGPR : Very Good Partial Response, PR : Partial Response
[a] Estimated using Clopper-Pearson method.
[b] Estimation, CI and P-value are calculated from PROC GLIMMIX procedure and a model with treatment, subgroup variables and the treatment-by-subgroup interaction as covariates.
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16.2.6.6 Secondary efficacy endpoints - Overall response
16.2.6.6.1 ITT population
16.2.6.6.1.10 Subgroup analyses by nb of prior lines
16.2.6.6.1.10.1 Summary of overall response rate as per IRC - 2-sided p-value according to nb of prior lines - ITT population

	1		>1		
	Kd (N=55)	**IKd (N=79)**	**Kd (N=68)**	**IKd (N=100)**	**Treat.-by-subgroup[b]**
Best Overall Response					
Complete response	20 (36.4)	33 (41.8)	14 (20.6)	38 (38.0)	
Very good partial response	14 (25.5)	25 (31.6)	21 (30.9)	34 (34.0)	
Partial response	13 (23.6)	11 (13.9)	20 (29.4)	14 (14.0)	
Minimal response	0	3 (3.8)	5 (7.4)	1 (1.0)	
Stable disease	3 (5.5)	5 (6.3)	3 (4.4)	8 (8.0)	
Non Progressive disease	1 (1.8)	1 (1.3)	0	0	
Progressive disease	3 (5.5)	0	0	2 (2.0)	
Unconfirmed progressive disease	0	0	1 (1.5)	0	
Not evaluable	1 (1.8)	1 (1.3)	4 (5.9)	3 (3.0)	
Overall Response as per IRC (sCR, CR, VGPR or PR)					
Not responders	8 (14.5)	10 (12.7)	13 (19.1)	14 (14.0)	
95% CI[a]	(0.0650 to 0.2666)	(0.0624 to 0.2205)	(0.1059 to 0.3047)	(0.0787 to 0.2237)	
Responders (sCR, CR, VGPR or PR)	47 (85.5)	69 (87.3)	55 (80.9)	86 (86.0)	
95% CI[a]	(0.7334 to 0.9350)	(0.7795 to 0.9376)	(0.6953 to 0.8941)	(0.7763 to 0.9213)	
Risk ratio 95% CI vs Kd[b]	-	1.02 (0.890 to 1.174)	-	1.06 (0.924 to 1.224)	
P-value [b]	-	0.7559	-	0.3912	

CI: Confidence interval, IRC: Independent Response Committee, sCR: stringent Complete Response, CR : Complete Response, VGPR : Very Good Partial Response, PR : Partial Response
[a] Estimated using Clopper-Pearson method.
[b] Estimation, CI and P-value are calculated from PROC GLIMMIX procedure and a model with treatment, subgroup variables and the treatment-by-subgroup interaction as covariates.
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16.2.6.6 Secondary efficacy endpoints - Overall response
16.2.6.6.1 ITT population
16.2.6.6.1.10 Subgroup analyses by nb of prior lines
16.2.6.6.1.10.1 Summary of overall response rate as per IRC - 2-sided p-value according to nb of prior lines - ITT population

	1		>1		
	Kd (N=55)	**IKd (N=79)**	**Kd (N=68)**	**IKd (N=100)**	**Treat.-by-subgroup[b]**
P-value heterogeneity[b]					0.6936
Odds ratio 95% CI vs Kd[b]	-	1.17 (0.430 to 3.208)	-	1.45 (0.633 to 3.332)	
P-value [b]	-	0.7530	-	0.3777	
P-value heterogeneity[b]					0.7491
Percent difference 95% CI vs Kd(%)[b]	-	1.89 (-10.018 to 13.792)	-	5.12 (-6.488 to 16.723)	
P-value [b]	-	0.7553	-	0.3862	
P-value heterogeneity[b]					0.7025

CI: Confidence interval, IRC: Independent Response Committee, sCR: stringent Complete Response, CR : Complete Response, VGPR : Very Good Partial Response, PR : Partial Response
[a] Estimated using Clopper-Pearson method.
[b] Estimation, CI and P-value are calculated from PROC GLIMMIX procedure and a model with treatment, subgroup variables and the treatment-by-subgroup interaction as covariates.
PGM=DEVOPS/SAR650984/EFC15246/CIR_RWE/REPORT/PGM/eff_bestresp_subgp_sr_de_i_t.sas OUT=REPORT/OUTPUT/eff_bestresp_resp1fn_plne_de_i_t_x.rtf (19FEB2021 15:21)

16.2.6.6 Secondary efficacy endpoints - Overall response
16.2.6.6.1 ITT population
16.2.6.6.1.11 Subgroup analyses by cytogenetic abnormality
16.2.6.6.1.11.1 Summary of overall response rate as per IRC - 2-sided p-value according to cytogenetic abnormality - ITT population

	At least one		None		
	Kd (N=31)	IKd (N=42)	Kd (N=77)	IKd (N=114)	Treat.-by-subgroup[b]
Best Overall Response					
Complete response	7 (22.6)	10 (23.8)	20 (26.0)	53 (46.5)	
Very good partial response	10 (32.3)	14 (33.3)	22 (28.6)	37 (32.5)	
Partial response	7 (22.6)	9 (21.4)	24 (31.2)	14 (12.3)	
Minimal response	2 (6.5)	2 (4.8)	2 (2.6)	2 (1.8)	
Stable disease	1 (3.2)	7 (16.7)	4 (5.2)	5 (4.4)	
Non Progressive disease	1 (3.2)	0	0	0	
Progressive disease	2 (6.5)	0	1 (1.3)	1 (0.9)	
Unconfirmed progressive disease	0	0	1 (1.3)	0	
Not evaluable	1 (3.2)	0	3 (3.9)	2 (1.8)	
Overall Response as per IRC (sCR, CR, VGPR or PR)					
Not responders	7 (22.6)	9 (21.4)	11 (14.3)	10 (8.8)	
95% CI[a]	(0.0959 to 0.4110)	(0.1030 to 0.3681)	(0.0735 to 0.2413)	(0.0429 to 0.1554)	
Responders (sCR, CR, VGPR or PR)	24 (77.4)	33 (78.6)	66 (85.7)	104 (91.2)	
95% CI[a]	(0.5890 to 0.9041)	(0.6319 to 0.8970)	(0.7587 to 0.9265)	(0.8446 to 0.9571)	
Risk ratio 95% CI vs Kd[b]	-	1.01 (0.792 to 1.301)	-	1.06 (0.955 to 1.186)	
P-value [b]	-	0.9068	-	0.2567	

CI: Confidence interval, IRC: Independent Response Committee, sCR: stringent Complete Response, CR : Complete Response, VGPR : Very Good Partial Response, PR : Partial Response
[a] Estimated using Clopper-Pearson method.
[b] Estimation, CI and P-value are calculated from PROC GLIMMIX procedure and a model with treatment, subgroup variables and the treatment-by-subgroup interaction as covariates.
PGM=DEVOPS/SAR650984/EFC15246/CIR_RWE/REPORT/PGM/eff_bestresp_subgp_sr_de_i_t.sas OUT=REPORT/OUTPUT/eff_bestresp_resp1fn_cyto_de_i_t_x.rtf (19FEB2021 15:21)

16.2.6.6 Secondary efficacy endpoints - Overall response
16.2.6.6.1 ITT population
16.2.6.6.1.11 Subgroup analyses by cytogenetic abnormality
16.2.6.6.1.11.1 Summary of overall response rate as per IRC - 2-sided p-value according to cytogenetic abnormality - ITT population

	At least one		None		
	Kd (N=31)	**IKd (N=42)**	**Kd (N=77)**	**IKd (N=114)**	**Treat.-by-subgroup[b]**
P-value heterogeneity[b]					0.7297
Odds ratio 95% CI vs Kd[b]	-	1.07 (0.347 to 3.291)	-	1.73 (0.695 to 4.326)	
P-value [b]	-	0.9065	-	0.2373	
P-value heterogeneity[b]					0.5123
Percent difference 95% CI vs Kd(%)[b]	-	1.15 (-18.190 to 20.494)	-	5.51 (-3.914 to 14.941)	
P-value [b]	-	0.9067	-	0.2505	
P-value heterogeneity[b]					0.6901

CI: Confidence interval, IRC: Independent Response Committee, sCR: stringent Complete Response, CR : Complete Response, VGPR : Very Good Partial Response, PR : Partial Response
[a] Estimated using Clopper-Pearson method.
[b] Estimation, CI and P-value are calculated from PROC GLIMMIX procedure and a model with treatment, subgroup variables and the treatment-by-subgroup interaction as covariates.
PGM=DEVOPS/SAR650984/EFC15246/CIR_RWE/REPORT/PGM/eff_bestresp_subgp_sr_de_i_t.sas OUT=REPORT/OUTPUT/eff_bestresp_resp1fn_cyto_de_i_t_x.rtf (19FEB2021 15:21)

16.2.6.6 Secondary efficacy endpoints - Overall response
16.2.6.6.1 ITT population
16.2.6.6.1.12 Subgroup analyses by MM type at SE
16.2.6.6.1.12.1 Summary of overall response rate as per IRC - 2-sided p-value according to MM type at SE - ITT population

	IgG		Non-IgG		
	Kd (N=85)	**IKd (N=126)**	**Kd (N=38)**	**IKd (N=53)**	**Treat.-by-subgroup[b]**
Best Overall Response					
Complete response	23 (27.1)	42 (33.3)	11 (28.9)	29 (54.7)	
Very good partial response	22 (25.9)	45 (35.7)	13 (34.2)	14 (26.4)	
Partial response	27 (31.8)	22 (17.5)	6 (15.8)	3 (5.7)	
Minimal response	3 (3.5)	3 (2.4)	2 (5.3)	1 (1.9)	
Stable disease	4 (4.7)	8 (6.3)	2 (5.3)	5 (9.4)	
Non Progressive disease	1 (1.2)	1 (0.8)	0	0	
Progressive disease	2 (2.4)	1 (0.8)	1 (2.6)	1 (1.9)	
Unconfirmed progressive disease	1 (1.2)	0	0	0	
Not evaluable	2 (2.4)	4 (3.2)	3 (7.9)	0	
Overall Response as per IRC (sCR, CR, VGPR or PR)					
Not responders	13 (15.3)	17 (13.5)	8 (21.1)	7 (13.2)	
95% CI[a]	(0.0840 to 0.2473)	(0.0806 to 0.2072)	(0.0955 to 0.3732)	(0.0548 to 0.2534)	
Responders (sCR, CR, VGPR or PR)	72 (84.7)	109 (86.5)	30 (78.9)	46 (86.8)	
95% CI[a]	(0.7527 to 0.9160)	(0.7928 to 0.9194)	(0.6268 to 0.9045)	(0.7466 to 0.9452)	
Risk ratio 95% CI vs Kd[b]	-	1.02 (0.911 to 1.145)	-	1.10 (0.904 to 1.337)	
P-value [b]	-	0.7168	-	0.3415	

CI: Confidence interval, IRC: Independent Response Committee, sCR: stringent Complete Response, CR : Complete Response, VGPR : Very Good Partial Response, PR : Partial Response
[a] Estimated using Clopper-Pearson method.
[b] Estimation, CI and P-value are calculated from PROC GLIMMIX procedure and a model with treatment, subgroup variables and the treatment-by-subgroup interaction as covariates.
PGM=DEVOPS/SAR650984/EFC15246/CIR_RWE/REPORT/PGM/eff_bestresp_subgp_sr_de_i_t.sas OUT=REPORT/OUTPUT/eff_bestresp_resp1fn_semm_de_i_t_x.rtf (19FEB2021 15:21)

16.2.6.6 Secondary efficacy endpoints - Overall response
16.2.6.6.1 ITT population
16.2.6.6.1.12 Subgroup analyses by MM type at SE
16.2.6.6.1.12.1 Summary of overall response rate as per IRC - 2-sided p-value according to MM type at SE - ITT population

	IgG		Non-IgG		
	Kd (N=85)	**IKd (N=126)**	**Kd (N=38)**	**IKd (N=53)**	**Treat.-by-subgroup[b]**
P-value heterogeneity[b]					0.5226
Odds ratio 95% CI vs Kd[b]	-	1.16 (0.528 to 2.536)	-	1.75 (0.573 to 5.362)	
P-value [b]	-	0.7136	-	0.3244	
P-value heterogeneity[b]					0.5508
Percent difference 95% CI vs Kd(%)[b]	-	1.80 (-7.940 to 11.544)	-	7.85 (-8.066 to 23.756)	
P-value [b]	-	0.7161	-	0.3327	
P-value heterogeneity[b]					0.5243

CI: Confidence interval, IRC: Independent Response Committee, sCR: stringent Complete Response, CR : Complete Response, VGPR : Very Good Partial Response, PR : Partial Response
[a] Estimated using Clopper-Pearson method.
[b] Estimation, CI and P-value are calculated from PROC GLIMMIX procedure and a model with treatment, subgroup variables and the treatment-by-subgroup interaction as covariates.
PGM=DEVOPS/SAR650984/EFC15246/CIR_RWE/REPORT/PGM/eff_bestresp_subgp_sr_de_i_t.sas OUT=REPORT/OUTPUT/eff_bestresp_resp1fn_semm_de_i_t_x.rtf (19FEB2021 15:21)

16.2.6.6 Secondary efficacy endpoints - Overall response
16.2.6.6.1 ITT population
16.2.6.6.1.13 Subgroup analyses by previous autologous stem-cell
16.2.6.6.1.13.1 Summary of overall response rate as per IRC - 2-sided p-value according to previous autologous stem-cell - ITT population

	Yes		No		
	Kd (N=69)	**IKd (N=116)**	**Kd (N=54)**	**IKd (N=63)**	**Treat.-by-subgroup[b]**
Best Overall Response					
Complete response	20 (29.0)	50 (43.1)	14 (25.9)	21 (33.3)	
Very good partial response	18 (26.1)	34 (29.3)	17 (31.5)	25 (39.7)	
Partial response	21 (30.4)	18 (15.5)	12 (22.2)	7 (11.1)	
Minimal response	2 (2.9)	2 (1.7)	3 (5.6)	2 (3.2)	
Stable disease	2 (2.9)	9 (7.8)	4 (7.4)	4 (6.3)	
Non Progressive disease	1 (1.4)	0	0	1 (1.6)	
Progressive disease	1 (1.4)	2 (1.7)	2 (3.7)	0	
Unconfirmed progressive disease	1 (1.4)	0	0	0	
Not evaluable	3 (4.3)	1 (0.9)	2 (3.7)	3 (4.8)	
Overall Response as per IRC (sCR, CR, VGPR or PR)					
Not responders	10 (14.5)	14 (12.1)	11 (20.4)	10 (15.9)	
95% CI[a]	(0.0717 to 0.2504)	(0.0676 to 0.1942)	(0.1063 to 0.3353)	(0.0788 to 0.2726)	
Responders (sCR, CR, VGPR or PR)	59 (85.5)	102 (87.9)	43 (79.6)	53 (84.1)	
95% CI[a]	(0.7496 to 0.9283)	(0.8058 to 0.9324)	(0.6647 to 0.8937)	(0.7274 to 0.9212)	
Risk ratio 95% CI vs Kd[b]	-	1.03 (0.913 to 1.158)	-	1.06 (0.889 to 1.256)	
P-value [b]	-	0.6435	-	0.5326	

CI: Confidence interval, IRC: Independent Response Committee, sCR: stringent Complete Response, CR : Complete Response, VGPR : Very Good Partial Response, PR : Partial Response
[a] Estimated using Clopper-Pearson method.
[b] Estimation, CI and P-value are calculated from PROC GLIMMIX procedure and a model with treatment, subgroup variables and the treatment-by-subgroup interaction as covariates.
PGM=DEVOPS/SAR650984/EFC15246/CIR_RWE/REPORT/PGM/eff_bestresp_subgp_sr_de_i_t.sas OUT=REPORT/OUTPUT/eff_bestresp_resp1fn_auto_de_i_t_x.rtf (19FEB2021 15:21)

16.2.6.6 Secondary efficacy endpoints - Overall response
16.2.6.6.1 ITT population
16.2.6.6.1.13 Subgroup analyses by previous autologous stem-cell
16.2.6.6.1.13.1 Summary of overall response rate as per IRC - 2-sided p-value according to previous autologous stem-cell - ITT population

	Yes		No		
	Kd (N=69)	**IKd (N=116)**	**Kd (N=54)**	**IKd (N=63)**	**Treat.-by-subgroup[b]**
P-value heterogeneity[b]					0.8004
Odds ratio 95% CI vs Kd[b]	-	1.23 (0.514 to 2.966)	-	1.36 (0.524 to 3.506)	
P-value [b]	-	0.6359	-	0.5288	
P-value heterogeneity[b]					0.8869
Percent difference 95% CI vs Kd(%)[b]	-	2.42 (-7.823 to 12.670)	-	4.50 (-9.589 to 18.584)	
P-value [b]	-	0.6419	-	0.5303	
P-value heterogeneity[b]					0.8149

CI: Confidence interval, IRC: Independent Response Committee, sCR: stringent Complete Response, CR : Complete Response, VGPR : Very Good Partial Response, PR : Partial Response
[a] Estimated using Clopper-Pearson method.
[b] Estimation, CI and P-value are calculated from PROC GLIMMIX procedure and a model with treatment, subgroup variables and the treatment-by-subgroup interaction as covariates.
PGM=DEVOPS/SAR650984/EFC15246/CIR_RWE/REPORT/PGM/eff_bestresp_subgp_sr_de_i_t.sas OUT=REPORT/OUTPUT/eff_bestresp_resp1fn_auto_de_i_t_x.rtf (19FEB2021 15:21)

16.2.6.6 Secondary efficacy endpoints - Overall response
16.2.6.6.1 ITT population
16.2.6.6.1.14 Subgroup analyses by baseline eGFR (MDRD)
16.2.6.6.1.14.1 Summary of overall response rate as per IRC - 2-sided p-value according to baseline eGFR (MDRD) - ITT population

	>=60 mL/min/1.73m2		<60 mL/min/1.73m2		
	Kd (N=93)	IKd (N=122)	Kd (N=18)	IKd (N=43)	Treat.-by-subgroup[b]
Best Overall Response					
Complete response	28 (30.1)	49 (40.2)	4 (22.2)	18 (41.9)	
Very good partial response	27 (29.0)	38 (31.1)	4 (22.2)	16 (37.2)	
Partial response	28 (30.1)	15 (12.3)	3 (16.7)	6 (14.0)	
Minimal response	3 (3.2)	3 (2.5)	2 (11.1)	0	
Stable disease	4 (4.3)	10 (8.2)	2 (11.1)	3 (7.0)	
Non Progressive disease	1 (1.1)	1 (0.8)	0	0	
Progressive disease	1 (1.1)	2 (1.6)	1 (5.6)	0	
Not evaluable	1 (1.1)	4 (3.3)	2 (11.1)	0	
Overall Response as per IRC (sCR, CR, VGPR or PR)					
Not responders	10 (10.8)	20 (16.4)	7 (38.9)	3 (7.0)	
95% CI[a]	(0.0528 to 0.1889)	(0.1031 to 0.2418)	(0.1730 to 0.6425)	(0.0146 to 0.1906)	
Responders (sCR, CR, VGPR or PR)	83 (89.2)	102 (83.6)	11 (61.1)	40 (93.0)	
95% CI[a]	(0.8111 to 0.9472)	(0.7582 to 0.8969)	(0.3575 to 0.8270)	(0.8094 to 0.9854)	
Risk ratio 95% CI vs Kd[b]	-	0.94 (0.843 to 1.042)	-	1.52 (1.042 to 2.224)	
P-value [b]	-	0.2266	-	0.0300	
P-value heterogeneity[b]					0.0159

CI: Confidence interval, IRC: Independent Response Committee, sCR: stringent Complete Response, CR : Complete Response, VGPR : Very Good Partial Response, PR : Partial Response
[a] Estimated using Clopper-Pearson method.
[b] Estimation, CI and P-value are calculated from PROC GLIMMIX procedure and a model with treatment, subgroup variables and the treatment-by-subgroup interaction as covariates.
PGM=DEVOPS/SAR650984/EFC15246/CIR_RWE/REPORT/PGM/eff_bestresp_subgp_sr_de_i_t.sas OUT=REPORT/OUTPUT/eff_bestresp_resp1fn_crcl_de_i_t_x.rtf (19FEB2021 15:21)

16.2.6.6 Secondary efficacy endpoints - Overall response
16.2.6.6.1 ITT population
16.2.6.6.1.14 Subgroup analyses by baseline eGFR (MDRD)
16.2.6.6.1.14.1 Summary of overall response rate as per IRC - 2-sided p-value according to baseline eGFR (MDRD) - ITT population

	>=60 mL/min/1.73m2		<60 mL/min/1.73m2		
	Kd (N=93)	**IKd (N=122)**	**Kd (N=18)**	**IKd (N=43)**	**Treat.-by-subgroup[b]**
Odds ratio 95% CI vs Kd[b]	-	0.61 (0.272 to 1.390)	-	8.48 (1.865 to 38.597)	
P-value [b]	-	0.2411	-	0.0058	
P-value heterogeneity[b]					0.0029
Percent difference 95% CI vs Kd(%)[b]	-	-5.64 (-14.781 to 3.499)	-	31.91 (8.033 to 55.792)	
P-value [b]	-	0.2254	-	0.0090	
P-value heterogeneity[b]					0.0041

CI: Confidence interval, IRC: Independent Response Committee, sCR: stringent Complete Response, CR : Complete Response, VGPR : Very Good Partial Response, PR : Partial Response
[a] Estimated using Clopper-Pearson method.
[b] Estimation, CI and P-value are calculated from PROC GLIMMIX procedure and a model with treatment, subgroup variables and the treatment-by-subgroup interaction as covariates.
PGM=DEVOPS/SAR650984/EFC15246/CIR_RWE/REPORT/PGM/eff_bestresp_subgp_sr_de_i_t.sas OUT=REPORT/OUTPUT/eff_bestresp_resp1fn_crcl_de_i_t_x.rtf (19FEB2021 15:21)

16.2.6.6 Secondary efficacy endpoints - Overall response
16.2.6.6.1 ITT population
16.2.6.6.1.15 Subgroup analyses by previous treatment with PI
16.2.6.6.1.15.1 Summary of overall response rate as per IRC - 2-sided p-value according to previous treatment with PI - ITT population

	Yes		No		
	Kd (N=47)	**IKd (N=81)**	**Kd (N=76)**	**IKd (N=98)**	**Treat.-by-subgroup[b]**
Best Overall Response					
Complete response	13 (27.7)	26 (32.1)	21 (27.6)	45 (45.9)	
Very good partial response	13 (27.7)	31 (38.3)	22 (28.9)	28 (28.6)	
Partial response	11 (23.4)	12 (14.8)	22 (28.9)	13 (13.3)	
Minimal response	2 (4.3)	2 (2.5)	3 (3.9)	2 (2.0)	
Stable disease	4 (8.5)	6 (7.4)	2 (2.6)	7 (7.1)	
Non Progressive disease	1 (2.1)	1 (1.2)	0	0	
Progressive disease	2 (4.3)	1 (1.2)	1 (1.3)	1 (1.0)	
Unconfirmed progressive disease	0	0	1 (1.3)	0	
Not evaluable	1 (2.1)	2 (2.5)	4 (5.3)	2 (2.0)	
Overall Response as per IRC (sCR, CR, VGPR or PR)					
Not responders	10 (21.3)	12 (14.8)	11 (14.5)	12 (12.2)	
95% CI[a]	(0.1070 to 0.3566)	(0.0790 to 0.2445)	(0.0745 to 0.2442)	(0.0649 to 0.2041)	
Responders (sCR, CR, VGPR or PR)	37 (78.7)	69 (85.2)	65 (85.5)	86 (87.8)	
95% CI[a]	(0.6434 to 0.8930)	(0.7555 to 0.9210)	(0.7558 to 0.9255)	(0.7959 to 0.9351)	
Risk ratio 95% CI vs Kd[b]	-	1.08 (0.908 to 1.289)	-	1.03 (0.911 to 1.156)	
P-value [b]	-	0.3754	-	0.6706	

CI: Confidence interval, IRC: Independent Response Committee, sCR: stringent Complete Response, CR : Complete Response, VGPR : Very Good Partial Response, PR : Partial Response
[a] Estimated using Clopper-Pearson method.
[b] Estimation, CI and P-value are calculated from PROC GLIMMIX procedure and a model with treatment, subgroup variables and the treatment-by-subgroup interaction as covariates.
PGM=DEVOPS/SAR650984/EFC15246/CIR_RWE/REPORT/PGM/eff_bestresp_subgp_sr_de_i_t.sas OUT=REPORT/OUTPUT/eff_bestresp_resp1fn_pi_de_i_t_x.rtf (19FEB2021 15:21)

16.2.6.6 Secondary efficacy endpoints - Overall response
16.2.6.6.1 ITT population
16.2.6.6.1.15 Subgroup analyses by previous treatment with PI
16.2.6.6.1.15.1 Summary of overall response rate as per IRC - 2-sided p-value according to previous treatment with PI - ITT population

	Yes		No		
	Kd (N=47)	**IKd (N=81)**	**Kd (N=76)**	**IKd (N=98)**	**Treat.-by-subgroup[b]**
P-value heterogeneity[b]					0.6212
Odds ratio 95% CI vs Kd[b]	-	1.55 (0.611 to 3.951)	-	1.21 (0.502 to 2.932)	
P-value [b]	-	0.3533	-	0.6674	
P-value heterogeneity[b]					0.7044
Percent difference 95% CI vs Kd(%)[b]	-	6.46 (-7.622 to 20.546)	-	2.23 (-8.045 to 12.502)	
P-value [b]	-	0.3673	-	0.6697	
P-value heterogeneity[b]					0.6331

CI: Confidence interval, IRC: Independent Response Committee, sCR: stringent Complete Response, CR : Complete Response, VGPR : Very Good Partial Response, PR : Partial Response
[a] Estimated using Clopper-Pearson method.
[b] Estimation, CI and P-value are calculated from PROC GLIMMIX procedure and a model with treatment, subgroup variables and the treatment-by-subgroup interaction as covariates.
PGM=DEVOPS/SAR650984/EFC15246/CIR_RWE/REPORT/PGM/eff_bestresp_subgp_sr_de_i_t.sas OUT=REPORT/OUTPUT/eff_bestresp_resp1fn_pi_de_i_t_x.rtf (19FEB2021 15:21)

16.2.6.6 Secondary efficacy endpoints - Overall response
16.2.6.6.1 ITT population
16.2.6.6.1.16 Subgroup analyses by previous treatment with IMiD
16.2.6.6.1.16.1 Summary of overall response rate as per IRC - 2-sided p-value according to previous treatment with IMiD - ITT population

	Yes		No		
	Kd (N=62)	**IKd (N=81)**	**Kd (N=61)**	**IKd (N=98)**	**Treat.-by-subgroup[b]**
Best Overall Response					
Complete response	13 (21.0)	35 (43.2)	21 (34.4)	36 (36.7)	
Very good partial response	16 (25.8)	27 (33.3)	19 (31.1)	32 (32.7)	
Partial response	21 (33.9)	9 (11.1)	12 (19.7)	16 (16.3)	
Minimal response	2 (3.2)	2 (2.5)	3 (4.9)	2 (2.0)	
Stable disease	4 (6.5)	5 (6.2)	2 (3.3)	8 (8.2)	
Non Progressive disease	1 (1.6)	0	0	1 (1.0)	
Progressive disease	1 (1.6)	2 (2.5)	2 (3.3)	0	
Unconfirmed progressive disease	0	0	1 (1.6)	0	
Not evaluable	4 (6.5)	1 (1.2)	1 (1.6)	3 (3.1)	
Overall Response as per IRC (sCR, CR, VGPR or PR)					
Not responders	12 (19.4)	10 (12.3)	9 (14.8)	14 (14.3)	
95% CI[a]	(0.1042 to 0.3137)	(0.0608 to 0.2153)	(0.0698 to 0.2617)	(0.0804 to 0.2281)	
Responders (sCR, CR, VGPR or PR)	50 (80.6)	71 (87.7)	52 (85.2)	84 (85.7)	
95% CI[a]	(0.6863 to 0.8958)	(0.7847 to 0.9392)	(0.7383 to 0.9302)	(0.7719 to 0.9196)	
Risk ratio 95% CI vs Kd[b]	-	1.09 (0.938 to 1.260)	-	1.01 (0.881 to 1.148)	
P-value [b]	-	0.2667	-	0.9352	

CI: Confidence interval, IRC: Independent Response Committee, sCR: stringent Complete Response, CR : Complete Response, VGPR : Very Good Partial Response, PR : Partial Response
[a] Estimated using Clopper-Pearson method.
[b] Estimation, CI and P-value are calculated from PROC GLIMMIX procedure and a model with treatment, subgroup variables and the treatment-by-subgroup interaction as covariates.
PGM=DEVOPS/SAR650984/EFC15246/CIR_RWE/REPORT/PGM/eff_bestresp_subgp_sr_de_i_t.sas OUT=REPORT/OUTPUT/eff_bestresp_resp1fn_imid_de_i_t_x.rtf (19FEB2021 15:21)

16.2.6.6 Secondary efficacy endpoints - Overall response
16.2.6.6.1 ITT population
16.2.6.6.1.16 Subgroup analyses by previous treatment with IMiD
16.2.6.6.1.16.1 Summary of overall response rate as per IRC - 2-sided p-value according to previous treatment with IMiD - ITT population

	Yes		No		
	Kd (N=62)	**IKd (N=81)**	**Kd (N=61)**	**IKd (N=98)**	**Treat.-by-subgroup[b]**
P-value heterogeneity[b]					0.4402
Odds ratio 95% CI vs Kd[b]	-	1.70 (0.681 to 4.266)	-	1.04 (0.418 to 2.579)	
P-value [b]	-	0.2539	-	0.9350	
P-value heterogeneity[b]					0.4513
Percent difference 95% CI vs Kd(%)[b]	-	7.01 (-5.207 to 19.226)	-	0.47 (-10.856 to 11.793)	
P-value [b]	-	0.2598	-	0.9352	
P-value heterogeneity[b]					0.4403

CI: Confidence interval, IRC: Independent Response Committee, sCR: stringent Complete Response, CR : Complete Response, VGPR : Very Good Partial Response, PR : Partial Response
[a] Estimated using Clopper-Pearson method.
[b] Estimation, CI and P-value are calculated from PROC GLIMMIX procedure and a model with treatment, subgroup variables and the treatment-by-subgroup interaction as covariates.
PGM=DEVOPS/SAR650984/EFC15246/CIR_RWE/REPORT/PGM/eff_bestresp_subgp_sr_de_i_t.sas OUT=REPORT/OUTPUT/eff_bestresp_resp1fn_imid_de_i_t_x.rtf (19FEB2021 15:21)

16.2.6.6 Secondary efficacy endpoints - Overall response
16.2.6.6.1 ITT population
16.2.6.6.1.17 Subgroup analyses by previous treatment with PI and IMiD
16.2.6.6.1.17.1 Summary of overall response rate as per IRC - 2-sided p-value according to previous treatment with PI and IMiD - ITT population

	Yes		No		
	Kd (N=17)	**IKd (N=23)**	**Kd (N=106)**	**IKd (N=156)**	**Treat.-by-subgroup[b]**
Best Overall Response					
Complete response	3 (17.6)	10 (43.5)	31 (29.2)	61 (39.1)	
Very good partial response	5 (29.4)	6 (26.1)	30 (28.3)	53 (34.0)	
Partial response	5 (29.4)	3 (13.0)	28 (26.4)	22 (14.1)	
Minimal response	0	2 (8.7)	5 (4.7)	2 (1.3)	
Stable disease	2 (11.8)	1 (4.3)	4 (3.8)	12 (7.7)	
Non Progressive disease	1 (5.9)	0	0	1 (0.6)	
Progressive disease	0	1 (4.3)	3 (2.8)	1 (0.6)	
Unconfirmed progressive disease	0	0	1 (0.9)	0	
Not evaluable	1 (5.9)	0	4 (3.8)	4 (2.6)	
Overall Response as per IRC (sCR, CR, VGPR or PR)					
Not responders	4 (23.5)	4 (17.4)	17 (16.0)	20 (12.8)	
95% CI[a]	(0.0681 to 0.4990)	(0.0495 to 0.3878)	(0.0963 to 0.2443)	(0.0801 to 0.1910)	
Responders (sCR, CR, VGPR or PR)	13 (76.5)	19 (82.6)	89 (84.0)	136 (87.2)	
95% CI[a]	(0.5010 to 0.9319)	(0.6122 to 0.9505)	(0.7557 to 0.9037)	(0.8090 to 0.9199)	
Risk ratio 95% CI vs Kd[b]	-	1.08 (0.781 to 1.495)	-	1.04 (0.937 to 1.151)	
P-value [b]	-	0.6403	-	0.4735	

CI: Confidence interval, IRC: Independent Response Committee, sCR: stringent Complete Response, CR : Complete Response, VGPR : Very Good Partial Response, PR : Partial Response
[a] Estimated using Clopper-Pearson method.
[b] Estimation, CI and P-value are calculated from PROC GLIMMIX procedure and a model with treatment, subgroup variables and the treatment-by-subgroup interaction as covariates.
PGM=DEVOPS/SAR650984/EFC15246/CIR_RWE/REPORT/PGM/eff_bestresp_subgp_sr_de_i_t.sas OUT=REPORT/OUTPUT/eff_bestresp_resp1fn_piimid_de_i_t_x.rtf (19FEB2021 15:21)

16.2.6.6 Secondary efficacy endpoints - Overall response
16.2.6.6.1 ITT population
16.2.6.6.1.17 Subgroup analyses by previous treatment with PI and IMiD
16.2.6.6.1.17.1 Summary of overall response rate as per IRC - 2-sided p-value according to previous treatment with PI and IMiD - ITT population

	Yes		No		
	Kd (N=17)	**IKd (N=23)**	**Kd (N=106)**	**IKd (N=156)**	**Treat.-by-subgroup[b]**
P-value heterogeneity[b]					0.8193
Odds ratio 95% CI vs Kd[b]	-	1.46 (0.307 to 6.965)	-	1.30 (0.643 to 2.622)	
P-value [b]	-	0.6328	-	0.4644	
P-value heterogeneity[b]					0.8922
Percent difference 95% CI vs Kd(%)[b]	-	6.14 (-19.393 to 31.669)	-	3.22 (-5.555 to 11.989)	
P-value [b]	-	0.6365	-	0.4710	
P-value heterogeneity[b]					0.8315

CI: Confidence interval, IRC: Independent Response Committee, sCR: stringent Complete Response, CR : Complete Response, VGPR : Very Good Partial Response, PR : Partial Response
[a] Estimated using Clopper-Pearson method.
[b] Estimation, CI and P-value are calculated from PROC GLIMMIX procedure and a model with treatment, subgroup variables and the treatment-by-subgroup interaction as covariates.
PGM=DEVOPS/SAR650984/EFC15246/CIR_RWE/REPORT/PGM/eff_bestresp_subgp_sr_de_i_t.sas OUT=REPORT/OUTPUT/eff_bestresp_resp1fn_piimid_de_i_t_x.rtf (19FEB2021 15:21)

16.2.6.3 Secondary efficacy endpoints - Time to progression
16.2.6.3.1 ITT population
16.2.6.3.1.3 Subgroup analyses by age
16.2.6.3.1.3.1 Time to progression based on disease assessment by the IRC by treatment group according to age - ITT population

	<65 years		>=65 years		
	Kd (N=66)	**IKd (N=88)**	**Kd (N=57)**	**IKd (N=91)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	24 (36.4)	20 (22.7)	24 (42.1)	20 (22.0)	0.6577
Number (%) of patients censored	42 (63.6)	68 (77.3)	33 (57.9)	71 (78.0)	
Kaplan-Meier estimates of TTP in months					
25% quantile (95% CI)	9.43 (6.834 to 15.770)	18.46 (9.232 to NC)	13.24 (9.035 to 16.164)	18.76 (13.076 to NC)	
Median (95% CI)	NC (15.770 to NC)	NC (NC to NC)	19.15 (16.099 to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.0501		0.0048	
Hazard ratio (95% CI) vs Kd	-	0.56 (0.31 to 1.01)		0.44 (0.24 to 0.79)	
P-value	-	0.0534		0.0061	
TTP probability (95% CI)[b]					
6 Months	0.871 (0.759 to 0.934)	0.916 (0.831 to 0.959)	0.924 (0.809 to 0.971)	0.975 (0.905 to 0.994)	

TTP: Time To Progression, CI: Confidence interval, IRC: Independent Response Committee
Cut-off date: 07FEB2020 HR<1 favors IKd arm
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] Two-sided significance level is 0.05.
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables and the treatment-by-subgroup interaction as covariates.
PGM=DEVOPS/SAR650984/EFC15246/CIR_RWE/REPORT/PGM/eff_km_subgp_sr_de_i_t.sas OUT=REPORT/OUTPUT/eff_km_ttp_age_de_i_t_x.rtf (19FEB2021 15:18)

16.2.6.3 Secondary efficacy endpoints - Time to progression
16.2.6.3.1 ITT population
16.2.6.3.1.4 Subgroup analyses by gender
16.2.6.3.1.4.1 Time to progression based on disease assessment by the IRC by treatment group according to gender - ITT population

	Male		Female		
	Kd (N=68)	**IKd (N=101)**	**Kd (N=55)**	**IKd (N=78)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	24 (35.3)	22 (21.8)	24 (43.6)	18 (23.1)	0.5250
Number (%) of patients censored	44 (64.7)	79 (78.2)	31 (56.4)	60 (76.9)	
Kaplan-Meier estimates of TTP in months					
25% quantile (95% CI)	12.19 (7.326 to 17.183)	18.76 (12.550 to NC)	10.18 (8.411 to 15.704)	18.46 (9.725 to NC)	
Median (95% CI)	NC (16.164 to NC)	NC (NC to NC)	19.15 (15.376 to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (20.271 to NC)	NC (NC to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.0435		0.0044	
Hazard ratio (95% CI) vs Kd	-	0.56 (0.31 to 0.99)		0.42 (0.23 to 0.78)	
P-value	-	0.0466		0.0058	
TTP probability (95% CI)[b]					
6 Months	0.902 (0.795 to 0.955)	0.956 (0.888 to 0.983)	0.887 (0.766 to 0.948)	0.933 (0.847 to 0.972)	

TTP: Time To Progression, CI: Confidence interval, IRC: Independent Response Committee
Cut-off date: 07FEB2020 HR<1 favors IKd arm
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] Two-sided significance level is 0.05.
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables and the treatment-by-subgroup interaction as covariates.
PGM=DEVOPS/SAR650984/EFC15246/CIR_RWE/REPORT/PGM/eff_km_subgp_sr_de_i_t.sas OUT=REPORT/OUTPUT/eff_km_ttp_sex_de_i_t_x.rtf (19FEB2021 15:19)

16.2.6.3 Secondary efficacy endpoints - Time to progression
16.2.6.3.1 ITT population
16.2.6.3.1.5 Subgroup analyses by ethnic origin
16.2.6.3.1.5.1 Time to progression based on disease assessment by the IRC by treatment group according to ethnic origin - ITT population

	White		Other		
	Kd (N=83)	**IKd (N=131)**	**Kd (N=28)**	**IKd (N=34)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	31 (37.3)	27 (20.6)	11 (39.3)	7 (20.6)	0.9766
Number (%) of patients censored	52 (62.7)	104 (79.4)	17 (60.7)	27 (79.4)	
Kaplan-Meier estimates of TTP in months					
25% quantile (95% CI)	11.99 (7.326 to 15.704)	NC (12.550 to NC)	13.24 (8.674 to 16.986)	17.08 (6.637 to NC)	
Median (95% CI)	NC (16.099 to NC)	NC (NC to NC)	18.99 (15.376 to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.0058		0.1265	
Hazard ratio (95% CI) vs Kd	-	0.49 (0.29 to 0.82)		0.48 (0.19 to 1.25)	
P-value	-	0.0069		0.1347	
TTP probability (95% CI)[b]					
6 Months	0.885 (0.790 to 0.938)	0.943 (0.884 to 0.972)	0.962 (0.757 to 0.994)	0.967 (0.786 to 0.995)	

TTP: Time To Progression, CI: Confidence interval, IRC: Independent Response Committee
Cut-off date: 07FEB2020 HR<1 favors IKd arm
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] Two-sided significance level is 0.05.
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables and the treatment-by-subgroup interaction as covariates.
PGM=DEVOPS/SAR650984/EFC15246/CIR_RWE/REPORT/PGM/eff_km_subgp_sr_de_i_t.sas OUT=REPORT/OUTPUT/eff_km_ttp_race_de_i_t_x.rtf (19FEB2021 15:19)

16.2.6.3 Secondary efficacy endpoints - Time to progression
16.2.6.3.1 ITT population
16.2.6.3.1.6 Subgroup analyses by geographical region
16.2.6.3.1.6.1 Time to progression based on disease assessment by the IRC by treatment group according to geographical region - ITT population

	Europe		America		Asia		Other countries		
	Kd (N=60)	**IKd (N=85)**	**Kd (N=20)**	**IKd (N=24)**	**Kd (N=21)**	**IKd (N=25)**	**Kd (N=22)**	**IKd (N=45)**	**p-value of treatment-by-subgroup interaction[c]**
Number (%) of events	25 (41.7)	14 (16.5)	4 (20.0)	8 (33.3)	7 (33.3)	6 (24.0)	12 (54.5)	12 (26.7)	0.0630
Number (%) of patients censored	35 (58.3)	71 (83.5)	16 (80.0)	16 (66.7)	14 (66.7)	19 (76.0)	10 (45.5)	33 (73.3)	
Kaplan-Meier estimates of event in months									
25% quantile (95% CI)	9.92 (4.665 to 15.244)	NC (14.916 to NC)	15.77 (6.834 to NC)	11.89 (0.131 to NC)	11.14 (2.891 to NC)	17.08 (4.961 to NC)	10.18 (4.008 to 16.164)	14.95 (7.622 to NC)	
Median (95% CI)	18.99 (14.752 to NC)	NC (NC to NC)	NC (15.376 to NC)	NC (11.893 to NC)	NC (9.429 to NC)	NC (17.084 to NC)	19.15 (10.185 to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (19.154 to NC)	NC (NC to NC)	

TTP: Time To Progression, CI: Confidence interval, IRC: Independent Response Committee
Cut-off date: 07FEB2020 HR<1 favors IKd arm
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] Two-sided significance level is 0.05.
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables and the treatment-by-subgroup interaction as covariates.
PGM=DEVOPS/SAR650984/EFC15246/CIR_RWE/REPORT/PGM/eff_km_subgp_sr_de_i_t.sas OUT=REPORT/OUTPUT/eff_km_ttp_greg_de_i_t_x.rtf (19FEB2021 15:19)

16.2.6.3 Secondary efficacy endpoints - Time to progression
16.2.6.3.1 ITT population
16.2.6.3.1.6 Subgroup analyses by geographical region
16.2.6.3.1.6.1 Time to progression based on disease assessment by the IRC by treatment group according to geographical region - ITT population

	Europe		America		Asia		Other countries		
	Kd (N=60)	**IKd (N=85)**	**Kd (N=20)**	**IKd (N=24)**	**Kd (N=21)**	**IKd (N=25)**	**Kd (N=22)**	**IKd (N=45)**	**p-value of treatment-by-subgroup interaction[c]**
Comparison vs. Kd									
Log-Rank test p-value[a] vs Kd	-	<.0001		0.3162		0.3831		0.0800	
Hazard ratio (95% CI) vs Kd	-	0.29 (0.15 to 0.56)		1.83 (0.55 to 6.09)		0.62 (0.21 to 1.84)		0.50 (0.22 to 1.11)	
P-value	-	0.0002		0.3236		0.3877		0.0863	
TTP probability (95% CI)[b]									
6 Months	0.833 (0.704 to 0.910)	0.962 (0.886 to 0.987)	1.000 (1.000 to 1.000)	0.913 (0.695 to 0.978)	0.947 (0.681 to 0.992)	0.957 (0.729 to 0.994)	0.909 (0.683 to 0.976)	0.927 (0.789 to 0.976)	
12 Months	0.709 (0.563 to 0.814)	0.906 (0.813 to 0.954)	0.944 (0.666 to 0.992)	0.728 (0.490 to 0.868)	0.706 (0.429 to 0.866)	0.826 (0.601 to 0.931)	0.670 (0.429 to 0.827)	0.794 (0.628 to 0.891)	

TTP: Time To Progression, CI: Confidence interval, IRC: Independent Response Committee
Cut-off date: 07FEB2020 HR<1 favors IKd arm
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] Two-sided significance level is 0.05.
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables and the treatment-by-subgroup interaction as covariates.
PGM=DEVOPS/SAR650984/EFC15246/CIR_RWE/REPORT/PGM/eff_km_subgp_sr_de_i_t.sas OUT=REPORT/OUTPUT/eff_km_ttp_greg_de_i_t_x.rtf (19FEB2021 15:19)

16.2.6.3 Secondary efficacy endpoints - Time to progression
16.2.6.3.1 ITT population
16.2.6.3.1.7 Subgroup analyses by regulatory region
16.2.6.3.1.7.1 Time to progression based on disease assessment by the IRC by treatment group according to regulatory region - ITT population

	Western countries		Other countries		
	Kd (N=55)	**IKd (N=97)**	**Kd (N=68)**	**IKd (N=82)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	27 (49.1)	22 (22.7)	21 (30.9)	18 (22.0)	0.3103
Number (%) of patients censored	28 (50.9)	75 (77.3)	47 (69.1)	64 (78.0)	
Kaplan-Meier estimates of TTP in months					
25% quantile (95% CI)	9.30 (5.552 to 15.244)	16.99 (13.076 to NC)	13.96 (9.363 to 16.986)	18.76 (9.561 to NC)	
Median (95% CI)	18.23 (13.240 to NC)	NC (NC to NC)	NC (16.164 to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (20.271 to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.0006		0.1347	
Hazard ratio (95% CI) vs Kd	-	0.39 (0.22 to 0.68)		0.62 (0.33 to 1.17)	
P-value	-	0.0010		0.1384	
TTP probability (95% CI)[b]					
6 Months	0.862 (0.732 to 0.932)	0.955 (0.885 to 0.983)	0.921 (0.821 to 0.966)	0.934 (0.849 to 0.972)	

TTP: Time To Progression, CI: Confidence interval, IRC: Independent Response Committee
Cut-off date: 07FEB2020 HR<1 favors IKd arm
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] Two-sided significance level is 0.05.
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables and the treatment-by-subgroup interaction as covariates.
PGM=DEVOPS/SAR650984/EFC15246/CIR_RWE/REPORT/PGM/eff_km_subgp_sr_de_i_t.sas OUT=REPORT/OUTPUT/eff_km_ttp_rreg_de_i_t_x.rtf (19FEB2021 15:19)

16.2.6.3 Secondary efficacy endpoints - Time to progression
16.2.6.3.1 ITT population
16.2.6.3.1.8 Subgroup analyses by baseline ECOG PS
16.2.6.3.1.8.1 Time to progression based on disease assessment by the IRC by treatment group according to baseline ECOG PS - ITT population

	0 or 1		>1		
	Kd (N=118)	**IKd (N=168)**	**Kd (N=5)**	**IKd (N=11)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	45 (38.1)	35 (20.8)	3 (60.0)	5 (45.5)	0.4194
Number (%) of patients censored	73 (61.9)	133 (79.2)	2 (40.0)	6 (54.5)	
Kaplan-Meier estimates of TTP in months					
25% quantile (95% CI)	11.99 (8.674 to 15.704)	20.34 (14.916 to NC)	9.30 (2.793 to 17.183)	9.72 (4.961 to 18.760)	
Median (95% CI)	20.27 (16.164 to NC)	NC (NC to NC)	17.18 (2.793 to NC)	18.76 (4.961 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (2.793 to NC)	NC (13.372 to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.0004		0.7313	
Hazard ratio (95% CI) vs Kd	-	0.46 (0.29 to 0.71)		0.78 (0.18 to 3.29)	
P-value	-	0.0005		0.7320	
TTP probability (95% CI)[b]					
6 Months	0.900 (0.826 to 0.943)	0.956 (0.909 to 0.979)	0.800 (0.204 to 0.969)	0.778 (0.365 to 0.939)	

TTP: Time To Progression, CI: Confidence interval, IRC: Independent Response Committee
Cut-off date: 07FEB2020 HR<1 favors IKd arm
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] Two-sided significance level is 0.05.
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables and the treatment-by-subgroup interaction as covariates.
PGM=DEVOPS/SAR650984/EFC15246/CIR_RWE/REPORT/PGM/eff_km_subgp_sr_de_i_t.sas OUT=REPORT/OUTPUT/eff_km_ttp_ecog_de_i_t_x.rtf (19FEB2021 15:19)

16.2.6.3 Secondary efficacy endpoints - Time to progression
16.2.6.3.1 ITT population
16.2.6.3.1.9 Subgroup analyses by ISS staging at SE
16.2.6.3.1.9.1 Time to progression based on disease assessment by the IRC by treatment group according to ISS staging at SE - ITT population

	I		II		III		
	Kd (N=71)	**IKd (N=89)**	**Kd (N=31)**	**IKd (N=63)**	**Kd (N=20)**	**IKd (N=26)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	23 (32.4)	19 (21.3)	14 (45.2)	14 (22.2)	10 (50.0)	7 (26.9)	0.5703
Number (%) of patients censored	48 (67.6)	70 (78.7)	17 (54.8)	49 (77.8)	10 (50.0)	19 (73.1)	
Kaplan-Meier estimates of TTP in months							
25% quantile (95% CI)	13.96 (8.411 to 18.990)	20.34 (12.550 to NC)	11.14 (2.825 to 18.201)	18.76 (13.076 to NC)	9.30 (0.953 to 9.429)	9.72 (0.131 to NC)	
Median (95% CI)	NC (18.990 to NC)	NC (NC to NC)	18.23 (12.189 to NC)	NC (NC to NC)	13.40 (8.674 to NC)	NC (9.725 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (18.234 to NC)	NC (NC to NC)	NC (9.429 to NC)	NC (NC to NC)	
Comparison vs. Kd							
Log-Rank test p-value[a] vs Kd	-	0.0815		0.0027		0.2570	
Hazard ratio (95% CI) vs Kd	-	0.59 (0.32 to 1.08)		0.33 (0.16 to 0.71)		0.58 (0.22 to 1.52)	
P-value	-	0.0851		0.0042		0.2630	

TTP: Time To Progression, CI: Confidence interval, IRC: Independent Response Committee
Cut-off date: 07FEB2020 HR<1 favors IKd arm
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] Two-sided significance level is 0.05.
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables and the treatment-by-subgroup interaction as covariates.
PGM=DEVOPS/SAR650984/EFC15246/CIR_RWE/REPORT/PGM/eff_km_subgp_sr_de_i_t.sas OUT=REPORT/OUTPUT/eff_km_ttp_seiss_de_i_t_x.rtf (19FEB2021 15:19)

16.2.6.3 Secondary efficacy endpoints - Time to progression
16.2.6.3.1 ITT population
16.2.6.3.1.10 Subgroup analyses by R-ISS stage at SE
16.2.6.3.1.10.1 Time to progression based on disease assessment by the IRC by treatment group according to R-ISS stage at SE - ITT population

	I or II		III		Not classified		
	Kd (N=103)	**IKd (N=155)**	**Kd (N=8)**	**IKd (N=16)**	**Kd (N=12)**	**IKd (N=8)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	40 (38.8)	33 (21.3)	4 (50.0)	7 (43.8)	4 (33.3)	0 (0.0)	0.3163
Number (%) of patients censored	63 (61.2)	122 (78.7)	4 (50.0)	9 (56.3)	8 (66.7)	8 (100.0)	
Kaplan-Meier estimates of TTP in months							
25% quantile (95% CI)	11.14 (8.411 to 15.770)	20.34 (14.949 to NC)	8.67 (2.793 to 13.405)	6.64 (0.131 to 10.283)	13.96 (5.552 to NC)	NC (NC to NC)	
Median (95% CI)	20.27 (16.986 to NC)	NC (NC to NC)	13.40 (2.793 to NC)	9.72 (5.815 to NC)	NC (11.992 to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (8.674 to NC)	13.37 (9.232 to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Kd							
Log-Rank test p-value[a] vs Kd	-	0.0003		0.6813		0.1699	
Hazard ratio (95% CI) vs Kd	-	0.44 (0.27 to 0.69)		1.30 (0.37 to 4.49)			
P-value	-	0.0004		0.6821		0.9971	

TTP: Time To Progression, CI: Confidence interval, IRC: Independent Response Committee
Cut-off date: 07FEB2020 HR<1 favors IKd arm
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] Two-sided significance level is 0.05.
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables and the treatment-by-subgroup interaction as covariates.
PGM=DEVOPS/SAR650984/EFC15246/CIR_RWE/REPORT/PGM/eff_km_subgp_sr_de_i_t.sas OUT=REPORT/OUTPUT/eff_km_ttp_seriss_de_i_t_x.rtf (19FEB2021 15:19)

16.2.6.3 Secondary efficacy endpoints - Time to progression
16.2.6.3.1 ITT population
16.2.6.3.1.11 Subgroup analyses by nb of prior lines
16.2.6.3.1.11.1 Time to progression based on disease assessment by the IRC by treatment group according to nb of prior lines - ITT population

	1		>1		
	Kd (N=55)	**IKd (N=79)**	**Kd (N=68)**	**IKd (N=100)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	19 (34.5)	16 (20.3)	29 (42.6)	24 (24.0)	0.8857
Number (%) of patients censored	36 (65.5)	63 (79.7)	39 (57.4)	76 (76.0)	
Kaplan-Meier estimates of TTP in months					
25% quantile (95% CI)	10.28 (8.312 to 18.201)	NC (13.372 to NC)	11.99 (6.834 to 15.770)	16.92 (11.072 to NC)	
Median (95% CI)	NC (16.164 to NC)	NC (NC to NC)	18.99 (15.770 to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (20.271 to NC)	NC (NC to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.0482		0.0046	
Hazard ratio (95% CI) vs Kd	-	0.52 (0.27 to 1.01)		0.46 (0.27 to 0.80)	
P-value	-	0.0523		0.0056	
TTP probability (95% CI)[b]					
6 Months	0.905 (0.787 to 0.959)	0.973 (0.896 to 0.993)	0.888 (0.780 to 0.945)	0.923 (0.846 to 0.963)	

TTP: Time To Progression, CI: Confidence interval, IRC: Independent Response Committee
Cut-off date: 07FEB2020 HR<1 favors IKd arm
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] Two-sided significance level is 0.05.
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables and the treatment-by-subgroup interaction as covariates.
PGM=DEVOPS/SAR650984/EFC15246/CIR_RWE/REPORT/PGM/eff_km_subgp_sr_de_i_t.sas OUT=REPORT/OUTPUT/eff_km_ttp_plne_de_i_t_x.rtf (19FEB2021 15:19)

16.2.6.3 Secondary efficacy endpoints - Time to progression
16.2.6.3.1 ITT population
16.2.6.3.1.12 Subgroup analyses by cytogenetic abnormality
16.2.6.3.1.12.1 Time to progression based on disease assessment by the IRC by treatment group according to cytogenetic abnormality - ITT population

	At least one		None		
	Kd (N=31)	**IKd (N=42)**	**Kd (N=77)**	**IKd (N=114)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	14 (45.2)	15 (35.7)	30 (39.0)	23 (20.2)	0.3398
Number (%) of patients censored	17 (54.8)	27 (64.3)	47 (61.0)	91 (79.8)	
Kaplan-Meier estimates of TTP in months					
25% quantile (95% CI)	8.31 (2.891 to 17.183)	11.43 (6.012 to 16.164)	12.19 (9.035 to 15.770)	NC (14.916 to NC)	
Median (95% CI)	18.99 (8.674 to NC)	NC (14.292 to NC)	NC (15.770 to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (18.990 to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.3049		0.0017	
Hazard ratio (95% CI) vs Kd	-	0.68 (0.33 to 1.42)		0.43 (0.25 to 0.74)	
P-value	-	0.3078		0.0024	
TTP probability (95% CI)[b]					
6 Months	0.826 (0.631 to 0.924)	0.922 (0.778 to 0.974)	0.932 (0.844 to 0.971)	0.953 (0.891 to 0.980)	

TTP: Time To Progression, CI: Confidence interval, IRC: Independent Response Committee
Cut-off date: 07FEB2020 HR<1 favors IKd arm
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] Two-sided significance level is 0.05.
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables and the treatment-by-subgroup interaction as covariates.
PGM=DEVOPS/SAR650984/EFC15246/CIR_RWE/REPORT/PGM/eff_km_subgp_sr_de_i_t.sas OUT=REPORT/OUTPUT/eff_km_ttp_cyto_de_i_t_x.rtf (19FEB2021 15:19)

16.2.6.3 Secondary efficacy endpoints - Time to progression
16.2.6.3.1 ITT population
16.2.6.3.1.13 Subgroup analyses by MM type at SE
16.2.6.3.1.13.1 Time to progression based on disease assessment by the IRC by treatment group according to MM type at SE - ITT population

	IgG		Non-IgG		
	Kd (N=85)	**IKd (N=126)**	**Kd (N=38)**	**IKd (N=53)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	33 (38.8)	27 (21.4)	15 (39.5)	13 (24.5)	0.9944
Number (%) of patients censored	52 (61.2)	99 (78.6)	23 (60.5)	40 (75.5)	
Kaplan-Meier estimates of TTP in months					
25% quantile (95% CI)	13.96 (9.429 to 16.164)	20.34 (13.372 to NC)	6.83 (2.825 to 11.138)	16.43 (9.232 to NC)	
Median (95% CI)	20.27 (16.986 to NC)	NC (NC to NC)	NC (9.035 to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.0038		0.0578	
Hazard ratio (95% CI) vs Kd	-	0.48 (0.29 to 0.80)		0.49 (0.23 to 1.04)	
P-value	-	0.0046		0.0631	
TTP probability (95% CI)[b]					
6 Months	0.939 (0.859 to 0.974)	0.940 (0.878 to 0.971)	0.792 (0.612 to 0.895)	0.962 (0.856 to 0.990)	

TTP: Time To Progression, CI: Confidence interval, IRC: Independent Response Committee
Cut-off date: 07FEB2020 HR<1 favors IKd arm
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] Two-sided significance level is 0.05.
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables and the treatment-by-subgroup interaction as covariates.
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16.2.6.3 Secondary efficacy endpoints - Time to progression
16.2.6.3.1 ITT population
16.2.6.3.1.14 Subgroup analyses by previous autologous stem-cell
16.2.6.3.1.14.1 Time to progression based on disease assessment by the IRC by treatment group according to previous autologous stem-cell - ITT population

	Yes		No		
	Kd (N=69)	**IKd (N=116)**	**Kd (N=54)**	**IKd (N=63)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	29 (42.0)	28 (24.1)	19 (35.2)	12 (19.0)	0.8917
Number (%) of patients censored	40 (58.0)	88 (75.9)	35 (64.8)	51 (81.0)	
Kaplan-Meier estimates of TTP in months					
25% quantile (95% CI)	10.18 (7.326 to 15.376)	17.08 (12.550 to NC)	12.19 (6.078 to 18.201)	NC (10.283 to NC)	
Median (95% CI)	19.15 (15.376 to NC)	NC (NC to NC)	NC (16.099 to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.0060		0.0336	
Hazard ratio (95% CI) vs Kd	-	0.49 (0.29 to 0.82)		0.46 (0.23 to 0.96)	
P-value	-	0.0071		0.0380	
TTP probability (95% CI)[b]					
6 Months	0.893 (0.788 to 0.947)	0.926 (0.858 to 0.963)	0.899 (0.774 to 0.957)	0.982 (0.882 to 0.998)	

TTP: Time To Progression, CI: Confidence interval, IRC: Independent Response Committee
Cut-off date: 07FEB2020 HR<1 favors IKd arm
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] Two-sided significance level is 0.05.
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables and the treatment-by-subgroup interaction as covariates.
PGM=DEVOPS/SAR650984/EFC15246/CIR_RWE/REPORT/PGM/eff_km_subgp_sr_de_i_t.sas OUT=REPORT/OUTPUT/eff_km_ttp_auto_de_i_t_x.rtf (19FEB2021 15:19)

16.2.6.3 Secondary efficacy endpoints - Time to progression
16.2.6.3.1 ITT population
16.2.6.3.1.15 Subgroup analyses by baseline eGFR (MDRD)
16.2.6.3.1.15.1 Time to progression based on disease assessment by the IRC by treatment group according to baseline eGFR (MDRD) - ITT population

	>=60 mL/min/1.73m2		<60 mL/min/1.73m2		
	Kd (N=93)	**IKd (N=122)**	**Kd (N=18)**	**IKd (N=43)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	35 (37.6)	24 (19.7)	7 (38.9)	10 (23.3)	0.6261
Number (%) of patients censored	58 (62.4)	98 (80.3)	11 (61.1)	33 (76.7)	
Kaplan-Meier estimates of TTP in months					
25% quantile (95% CI)	13.24 (9.298 to 15.770)	NC (11.433 to NC)	11.14 (2.825 to 16.099)	18.76 (11.893 to NC)	
Median (95% CI)	NC (16.986 to NC)	NC (NC to NC)	16.10 (6.834 to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (16.099 to NC)	NC (NC to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.0083		0.0359	
Hazard ratio (95% CI) vs Kd	-	0.50 (0.30 to 0.85)		0.37 (0.14 to 0.97)	
P-value	-	0.0096		0.0439	
TTP probability (95% CI)[b]					
6 Months	0.911 (0.829 to 0.954)	0.947 (0.885 to 0.976)	0.862 (0.550 to 0.964)	0.951 (0.817 to 0.987)	

TTP: Time To Progression, CI: Confidence interval, IRC: Independent Response Committee
Cut-off date: 07FEB2020 HR<1 favors IKd arm
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] Two-sided significance level is 0.05.
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables and the treatment-by-subgroup interaction as covariates.
PGM=DEVOPS/SAR650984/EFC15246/CIR_RWE/REPORT/PGM/eff_km_subgp_sr_de_i_t.sas OUT=REPORT/OUTPUT/eff_km_ttp_crcl_de_i_t_x.rtf (19FEB2021 15:19)

16.2.6.3 Secondary efficacy endpoints - Time to progression
16.2.6.3.1 ITT population
16.2.6.3.1.16 Subgroup analyses by previous treatment with PI
16.2.6.3.1.16.1 Time to progression based on disease assessment by the IRC by treatment group according to previous treatment with PI - ITT population

	Yes		No		
	Kd (N=47)	**IKd (N=81)**	**Kd (N=76)**	**IKd (N=98)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	17 (36.2)	18 (22.2)	31 (40.8)	22 (22.4)	0.8712
Number (%) of patients censored	30 (63.8)	63 (77.8)	45 (59.2)	76 (77.6)	
Kaplan-Meier estimates of TTP in months					
25% quantile (95% CI)	8.57 (4.830 to 15.770)	16.43 (10.283 to NC)	13.96 (9.363 to 16.164)	18.76 (12.550 to NC)	
Median (95% CI)	NC (11.138 to NC)	NC (NC to NC)	19.45 (16.164 to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.0531		0.0050	
Hazard ratio (95% CI) vs Kd	-	0.53 (0.27 to 1.02)		0.47 (0.27 to 0.80)	
P-value	-	0.0573		0.0061	
TTP probability (95% CI)[b]					
6 Months	0.865 (0.723 to 0.937)	0.959 (0.877 to 0.987)	0.915 (0.820 to 0.961)	0.935 (0.862 to 0.970)	

TTP: Time To Progression, CI: Confidence interval, IRC: Independent Response Committee
Cut-off date: 07FEB2020 HR<1 favors IKd arm
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] Two-sided significance level is 0.05.
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables and the treatment-by-subgroup interaction as covariates.
PGM=DEVOPS/SAR650984/EFC15246/CIR_RWE/REPORT/PGM/eff_km_subgp_sr_de_i_t.sas OUT=REPORT/OUTPUT/eff_km_ttp_pi_de_i_t_x.rtf (19FEB2021 15:19)

16.2.6.3 Secondary efficacy endpoints - Time to progression
16.2.6.3.1 ITT population
16.2.6.3.1.17 Subgroup analyses by previous treatment with IMiD
16.2.6.3.1.17.1 Time to progression based on disease assessment by the IRC by treatment group according to previous treatment with IMiD - ITT population

	Yes		No		
	Kd (N=62)	**IKd (N=81)**	**Kd (N=61)**	**IKd (N=98)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	25 (40.3)	20 (24.7)	23 (37.7)	20 (20.4)	0.7642
Number (%) of patients censored	37 (59.7)	61 (75.3)	38 (62.3)	78 (79.6)	
Kaplan-Meier estimates of TTP in months					
25% quantile (95% CI)	13.24 (8.674 to 16.099)	16.99 (9.232 to NC)	9.43 (4.830 to 18.201)	18.76 (13.372 to NC)	
Median (95% CI)	19.15 (15.704 to NC)	NC (NC to NC)	NC (18.201 to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.0269		0.0092	
Hazard ratio (95% CI) vs Kd	-	0.52 (0.29 to 0.94)		0.46 (0.25 to 0.84)	
P-value	-	0.0296		0.0111	
TTP probability (95% CI)[b]					
6 Months	0.947 (0.844 to 0.982)	0.922 (0.835 to 0.964)	0.847 (0.726 to 0.917)	0.965 (0.896 to 0.989)	

TTP: Time To Progression, CI: Confidence interval, IRC: Independent Response Committee
Cut-off date: 07FEB2020 HR<1 favors IKd arm
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] Two-sided significance level is 0.05.
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables and the treatment-by-subgroup interaction as covariates.
PGM=DEVOPS/SAR650984/EFC15246/CIR_RWE/REPORT/PGM/eff_km_subgp_sr_de_i_t.sas OUT=REPORT/OUTPUT/eff_km_ttp_imid_de_i_t_x.rtf (19FEB2021 15:19)

16.2.6.3 Secondary efficacy endpoints - Time to progression
16.2.6.3.1 ITT population
16.2.6.3.1.18 Subgroup analyses by previous treatment with PI and IMiD
16.2.6.3.1.18.1 Time to progression based on disease assessment by the IRC by treatment group according to previous treatment with PI and IMiD - ITT population

	Yes		No		
	Kd (N=17)	**IKd (N=23)**	**Kd (N=106)**	**IKd (N=156)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	5 (29.4)	6 (26.1)	43 (40.6)	34 (21.8)	0.4636
Number (%) of patients censored	12 (70.6)	17 (73.9)	63 (59.4)	122 (78.2)	
Kaplan-Meier estimates of TTP in months					
25% quantile (95% CI)	11.14 (8.411 to NC)	20.34 (0.131 to NC)	11.99 (8.312 to 15.376)	18.46 (13.372 to NC)	
Median (95% CI)	NC (9.922 to NC)	NC (20.337 to NC)	19.45 (16.164 to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.6852		0.0005	
Hazard ratio (95% CI) vs Kd	-	0.78 (0.24 to 2.57)		0.46 (0.29 to 0.72)	
P-value	-	0.6860		0.0007	
TTP probability (95% CI)[b]					
6 Months	1.000 (1.000 to 1.000)	0.909 (0.681 to 0.976)	0.880 (0.798 to 0.930)	0.951 (0.901 to 0.977)	

TTP: Time To Progression, CI: Confidence interval, IRC: Independent Response Committee
Cut-off date: 07FEB2020 HR<1 favors IKd arm
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] Two-sided significance level is 0.05.
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables and the treatment-by-subgroup interaction as covariates.
PGM=DEVOPS/SAR650984/EFC15246/CIR_RWE/REPORT/PGM/eff_km_subgp_sr_de_i_t.sas OUT=REPORT/OUTPUT/eff_km_ttp_piimid_de_i_t_x.rtf (19FEB2021 15:19)

16.2.6.5 Secondary efficacy endpoints - Time to first response
16.2.6.5.1 ITT population
16.2.6.5.1.3 Subgroup analyses by age
16.2.6.5.1.3.1 Time to first response based on disease assessment by the IRC by treatment group according to age - ITT population

	<65 years		>=65 years		
	Kd (N=66)	**IKd (N=88)**	**Kd (N=57)**	**IKd (N=91)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	54 (81.8)	75 (85.2)	48 (84.2)	80 (87.9)	0.6037
Number (%) of patients censored	12 (18.2)	13 (14.8)	9 (15.8)	11 (12.1)	
Kaplan-Meier estimates of TT1R in months					
25% quantile (95% CI)	1.02 (0.986 to 1.051)	0.99 (0.986 to 1.018)	0.99 (0.953 to 1.018)	0.99 (0.986 to 1.018)	
Median (95% CI)	1.12 (1.051 to 1.873)	1.05 (1.018 to 1.117)	1.08 (1.018 to 1.873)	1.08 (1.051 to 1.150)	
75% quantile (95% CI)	1.97 (1.873 to 3.713)	1.91 (1.150 to 2.004)	2.00 (1.314 to 3.055)	1.97 (1.314 to 2.530)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.3770		0.8200	
Hazard ratio (95% CI) vs Kd	-	1.17 (0.82 to 1.66)		1.04 (0.73 to 1.49)	
P-value	-	0.3775		0.8209	
TT1R probability (95% CI)[b]					
6 Months	0.074 (0.024 to 0.162)	0.089 (0.038 to 0.167)	0.078 (0.023 to 0.179)	0.071 (0.025 to 0.148)	

TT1R: Time to first response, CI: Confidence interval, IRC: Independent Response Committee
Cut-off date: 07FEB2020 HR<1 favors IKd arm
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] Two-sided significance level is 0.05.
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables and the treatment-by-subgroup interaction as covariates.
PGM=DEVOPS/SAR650984/EFC15246/CIR_RWE/REPORT/PGM/eff_km_subgp_sr_de_i_t.sas OUT=REPORT/OUTPUT/eff_km_tt1r_age_de_i_t_x.rtf (19FEB2021 15:19)

16.2.6.5 Secondary efficacy endpoints - Time to first response
16.2.6.5.1 ITT population
16.2.6.5.1.4 Subgroup analyses by gender
16.2.6.5.1.4.1 Time to first response based on disease assessment by the IRC by treatment group according to gender - ITT population

	Male		Female		
	Kd (N=68)	**IKd (N=101)**	**Kd (N=55)**	**IKd (N=78)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	55 (80.9)	85 (84.2)	47 (85.5)	70 (89.7)	0.2645
Number (%) of patients censored	13 (19.1)	16 (15.8)	8 (14.5)	8 (10.3)	
Kaplan-Meier estimates of TT1R in months					
25% quantile (95% CI)	1.02 (0.986 to 1.051)	0.99 (0.986 to 1.018)	1.00 (0.986 to 1.018)	0.99 (0.986 to 1.018)	
Median (95% CI)	1.12 (1.084 to 1.216)	1.08 (1.051 to 1.150)	1.05 (1.018 to 1.906)	1.05 (1.018 to 1.117)	
75% quantile (95% CI)	1.94 (1.281 to 2.037)	1.97 (1.577 to 2.136)	2.79 (1.906 to 4.764)	1.46 (1.150 to 2.037)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.8586		0.1972	
Hazard ratio (95% CI) vs Kd	-	0.97 (0.69 to 1.36)		1.28 (0.88 to 1.86)	
P-value	-	0.8581		0.1982	
TT1R probability (95% CI)[b]					
6 Months	0.059 (0.016 to 0.144)	0.099 (0.045 to 0.178)	0.101 (0.037 to 0.202)	0.064 (0.022 to 0.139)	

TT1R: Time to first response, CI: Confidence interval, IRC: Independent Response Committee
Cut-off date: 07FEB2020 HR<1 favors IKd arm
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] Two-sided significance level is 0.05.
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables and the treatment-by-subgroup interaction as covariates.
PGM=DEVOPS/SAR650984/EFC15246/CIR_RWE/REPORT/PGM/eff_km_subgp_sr_de_i_t.sas OUT=REPORT/OUTPUT/eff_km_tt1r_sex_de_i_t_x.rtf (19FEB2021 15:19)

16.2.6.5 Secondary efficacy endpoints - Time to first response
16.2.6.5.1 ITT population
16.2.6.5.1.5 Subgroup analyses by ethnic origin
16.2.6.5.1.5.1 Time to first response based on disease assessment by the IRC by treatment group according to ethnic origin - ITT population

	White		Other		
	Kd (N=83)	**IKd (N=131)**	**Kd (N=28)**	**IKd (N=34)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	70 (84.3)	113 (86.3)	24 (85.7)	29 (85.3)	0.1333
Number (%) of patients censored	13 (15.7)	18 (13.7)	4 (14.3)	5 (14.7)	
Kaplan-Meier estimates of TT1R in months					
25% quantile (95% CI)	0.99 (0.986 to 1.018)	0.99 (0.986 to 1.018)	1.12 (0.986 to 1.150)	0.99 (0.953 to 1.018)	
Median (95% CI)	1.05 (1.018 to 1.117)	1.08 (1.051 to 1.150)	1.18 (1.117 to 1.971)	1.03 (0.986 to 1.117)	
75% quantile (95% CI)	1.94 (1.873 to 3.055)	1.94 (1.314 to 2.070)	2.00 (1.873 to 8.246)	1.51 (1.051 to 2.957)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.8956		0.0831	
Hazard ratio (95% CI) vs Kd	-	1.02 (0.76 to 1.38)		1.61 (0.93 to 2.79)	
P-value	-	0.8958		0.0859	
TT1R probability (95% CI)[b]					
6 Months	0.068 (0.023 to 0.145)	0.087 (0.043 to 0.151)	0.121 (0.031 to 0.278)	0.078 (0.015 to 0.212)	

TT1R: Time to first response, CI: Confidence interval, IRC: Independent Response Committee
Cut-off date: 07FEB2020 HR<1 favors IKd arm
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] Two-sided significance level is 0.05.
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables and the treatment-by-subgroup interaction as covariates.
PGM=DEVOPS/SAR650984/EFC15246/CIR_RWE/REPORT/PGM/eff_km_subgp_sr_de_i_t.sas OUT=REPORT/OUTPUT/eff_km_tt1r_race_de_i_t_x.rtf (19FEB2021 15:19)

16.2.6.5 Secondary efficacy endpoints - Time to first response
16.2.6.5.1 ITT population
16.2.6.5.1.6 Subgroup analyses by geographical region
16.2.6.5.1.6.1 Time to first response based on disease assessment by the IRC by treatment group according to geographical region - ITT population

	Europe		America		Asia		Other countries		
	Kd (N=60)	**IKd (N=85)**	**Kd (N=20)**	**IKd (N=24)**	**Kd (N=21)**	**IKd (N=25)**	**Kd (N=22)**	**IKd (N=45)**	**p-value of treatment-by-subgroup interaction[c]**
Number (%) of events	46 (76.7)	73 (85.9)	19 (95.0)	21 (87.5)	17 (81.0)	22 (88.0)	20 (90.9)	39 (86.7)	0.3137
Number (%) of patients censored	14 (23.3)	12 (14.1)	1 (5.0)	3 (12.5)	4 (19.0)	3 (12.0)	2 (9.1)	6 (13.3)	
Kaplan-Meier estimates of event in months									
25% quantile (95% CI)	0.99 (0.953 to 0.986)	0.99 (0.986 to 1.018)	1.00 (0.920 to 1.051)	1.05 (0.953 to 1.084)	1.10 (0.986 to 1.150)	0.99 (0.920 to 0.986)	1.05 (0.953 to 1.084)	1.02 (0.986 to 1.018)	
Median (95% CI)	1.05 (0.986 to 1.873)	1.05 (1.018 to 1.150)	1.07 (0.986 to 1.281)	1.08 (1.051 to 1.840)	1.17 (1.084 to 2.037)	1.02 (0.986 to 1.117)	1.12 (1.051 to 1.906)	1.08 (1.018 to 1.938)	
75% quantile (95% CI)	1.94 (1.873 to 3.055)	1.87 (1.183 to 2.070)	1.61 (1.084 to 5.585)	1.91 (1.084 to 2.530)	2.83 (1.183 to NC)	1.13 (1.051 to 2.957)	2.00 (1.117 to 4.764)	2.89 (1.938 to 3.680)	
Comparison vs. Kd									
Log-Rank test p-value[a] vs Kd	-	0.8102		0.9488		0.0507		0.8700	

TT1R: Time to first response, CI: Confidence interval, IRC: Independent Response Committee
Cut-off date: 07FEB2020 HR<1 favors IKd arm
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] Two-sided significance level is 0.05.
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables and the treatment-by-subgroup interaction as covariates.
PGM=DEVOPS/SAR650984/EFC15246/CIR_RWE/REPORT/PGM/eff_km_subgp_sr_de_i_t.sas OUT=REPORT/OUTPUT/eff_km_tt1r_greg_de_i_t_x.rtf (19FEB2021 15:19)

16.2.6.5 Secondary efficacy endpoints - Time to first response
16.2.6.5.1 ITT population
16.2.6.5.1.6 Subgroup analyses by geographical region
16.2.6.5.1.6.1 Time to first response based on disease assessment by the IRC by treatment group according to geographical region - ITT population

	Europe		America		Asia		Other countries		
	Kd (N=60)	**IKd (N=85)**	**Kd (N=20)**	**IKd (N=24)**	**Kd (N=21)**	**IKd (N=25)**	**Kd (N=22)**	**IKd (N=45)**	**p-value of treatment-by-subgroup interaction[c]**
Hazard ratio (95% CI) vs Kd	-	1.05 (0.72 to 1.52)		0.98 (0.52 to 1.84)		1.88 (0.99 to 3.57)		0.96 (0.56 to 1.64)	
P-value	-	0.8111		0.9488		0.0543		0.8690	
TT1R probability (95% CI)[b]									
6 Months	0.070 (0.018 to 0.169)	0.096 (0.040 to 0.182)	0.050 (0.003 to 0.205)	0.045 (0.003 to 0.189)	0.169 (0.043 to 0.366)	0.083 (0.014 to 0.233)	0.048 (0.003 to 0.197)	0.088 (0.024 to 0.206)	
12 Months	0.070 (0.018 to 0.169)	0.096 (0.040 to 0.182)	0.050 (0.003 to 0.205)	0.045 (0.003 to 0.189)	0.084 (0.007 to 0.291)	0.083 (0.014 to 0.233)	0.048 (0.003 to 0.197)	0.088 (0.024 to 0.206)	
18 Months	0.070 (0.018 to 0.169)	0.096 (0.040 to 0.182)	0.050 (0.003 to 0.205)	0.045 (0.003 to 0.189)	0.084 (0.007 to 0.291)	0.083 (0.014 to 0.233)	0.048 (0.003 to 0.197)	0.088 (0.024 to 0.206)	

TT1R: Time to first response, CI: Confidence interval, IRC: Independent Response Committee
Cut-off date: 07FEB2020 HR<1 favors IKd arm
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] Two-sided significance level is 0.05.
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables and the treatment-by-subgroup interaction as covariates.
PGM=DEVOPS/SAR650984/EFC15246/CIR_RWE/REPORT/PGM/eff_km_subgp_sr_de_i_t.sas OUT=REPORT/OUTPUT/eff_km_tt1r_greg_de_i_t_x.rtf (19FEB2021 15:19)

16.2.6.5 Secondary efficacy endpoints - Time to first response
16.2.6.5.1 ITT population
16.2.6.5.1.7 Subgroup analyses by regulatory region
16.2.6.5.1.7.1 Time to first response based on disease assessment by the IRC by treatment group according to regulatory region - ITT population

	Western countries		Other countries		
	Kd (N=55)	**IKd (N=97)**	**Kd (N=68)**	**IKd (N=82)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	46 (83.6)	85 (87.6)	56 (82.4)	70 (85.4)	0.0500
Number (%) of patients censored	9 (16.4)	12 (12.4)	12 (17.6)	12 (14.6)	
Kaplan-Meier estimates of TT1R in months					
25% quantile (95% CI)	0.99 (0.986 to 1.018)	1.02 (0.986 to 1.018)	1.02 (0.986 to 1.051)	0.99 (NC to NC)	
Median (95% CI)	1.05 (1.018 to 1.314)	1.12 (1.051 to 1.150)	1.12 (1.084 to 1.873)	1.05 (1.018 to 1.084)	
75% quantile (95% CI)	1.92 (1.117 to 2.793)	1.97 (1.314 to 2.136)	2.04 (1.906 to 4.107)	1.91 (1.117 to 2.004)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.4145		0.0946	
Hazard ratio (95% CI) vs Kd	-	0.86 (0.60 to 1.23)		1.35 (0.95 to 1.92)	
P-value	-	0.4150		0.0958	
TT1R probability (95% CI)[b]					
6 Months	0.023 (0.002 to 0.103)	0.083 (0.034 to 0.159)	0.117 (0.050 to 0.215)	0.080 (0.031 to 0.160)	

TT1R: Time to first response, CI: Confidence interval, IRC: Independent Response Committee
Cut-off date: 07FEB2020 HR<1 favors IKd arm
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] Two-sided significance level is 0.05.
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables and the treatment-by-subgroup interaction as covariates.
PGM=DEVOPS/SAR650984/EFC15246/CIR_RWE/REPORT/PGM/eff_km_subgp_sr_de_i_t.sas OUT=REPORT/OUTPUT/eff_km_tt1r_rreg_de_i_t_x.rtf (19FEB2021 15:19)

16.2.6.5 Secondary efficacy endpoints - Time to first response
16.2.6.5.1 ITT population
16.2.6.5.1.8 Subgroup analyses by baseline ECOG PS
16.2.6.5.1.8.1 Time to first response based on disease assessment by the IRC by treatment group according to baseline ECOG PS - ITT population

	0 or 1		>1		
	Kd (N=118)	**IKd (N=168)**	**Kd (N=5)**	**IKd (N=11)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	97 (82.2)	147 (87.5)	5 (100.0)	8 (72.7)	0.5009
Number (%) of patients censored	21 (17.8)	21 (12.5)	0 (0.0)	3 (27.3)	
Kaplan-Meier estimates of TT1R in months					
25% quantile (95% CI)	1.02 (0.986 to 1.018)	0.99 (0.986 to 1.018)	1.02 (0.986 to 1.938)	0.99 (0.986 to 1.906)	
Median (95% CI)	1.12 (1.051 to 1.183)	1.07 (1.051 to 1.117)	1.18 (0.986 to 2.037)	1.91 (0.986 to 2.530)	
75% quantile (95% CI)	1.97 (1.906 to 2.825)	1.94 (1.248 to 2.037)	1.94 (0.986 to 2.037)	2.10 (1.018 to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.3577		0.4473	
Hazard ratio (95% CI) vs Kd	-	1.13 (0.87 to 1.46)		0.63 (0.19 to 2.08)	
P-value	-	0.3580		0.4511	
TT1R probability (95% CI)[b]					
6 Months	0.080 (0.036 to 0.145)	0.080 (0.042 to 0.134)	0.200 (0.008 to 0.582)	0.111 (0.006 to 0.388)	

TT1R: Time to first response, CI: Confidence interval, IRC: Independent Response Committee
Cut-off date: 07FEB2020 HR<1 favors IKd arm
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] Two-sided significance level is 0.05.
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables and the treatment-by-subgroup interaction as covariates.
PGM=DEVOPS/SAR650984/EFC15246/CIR_RWE/REPORT/PGM/eff_km_subgp_sr_de_i_t.sas OUT=REPORT/OUTPUT/eff_km_tt1r_ecog_de_i_t_x.rtf (19FEB2021 15:19)

16.2.6.5 Secondary efficacy endpoints - Time to first response
16.2.6.5.1 ITT population
16.2.6.5.1.9 Subgroup analyses by ISS staging at SE
16.2.6.5.1.9.1 Time to first response based on disease assessment by the IRC by treatment group according to ISS staging at SE - ITT population

	I		II		III		
	Kd (N=71)	**IKd (N=89)**	**Kd (N=31)**	**IKd (N=63)**	**Kd (N=20)**	**IKd (N=26)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	61 (85.9)	81 (91.0)	26 (83.9)	57 (90.5)	15 (75.0)	16 (61.5)	0.4497
Number (%) of patients censored	10 (14.1)	8 (9.0)	5 (16.1)	6 (9.5)	5 (25.0)	10 (38.5)	
Kaplan-Meier estimates of TT1R in months							
25% quantile (95% CI)	0.99 (0.986 to 1.018)	0.99 (0.986 to 1.018)	0.99 (0.986 to 1.051)	0.99 (0.986 to 1.018)	1.05 (0.953 to 1.150)	1.05 (0.953 to 1.314)	
Median (95% CI)	1.08 (1.018 to 1.117)	1.08 (1.018 to 1.150)	1.23 (1.018 to 1.906)	1.05 (1.018 to 1.084)	1.18 (1.051 to 1.971)	1.92 (1.051 to 2.924)	
75% quantile (95% CI)	1.91 (1.117 to 2.793)	1.51 (1.150 to 2.004)	2.04 (1.873 to 3.055)	1.94 (1.084 to 2.136)	1.97 (1.183 to NC)	2.96 (1.938 to NC)	
Comparison vs. Kd							
Log-Rank test p-value[a] vs Kd	-	0.7905		0.3064		0.5201	
Hazard ratio (95% CI) vs Kd	-	1.05 (0.75 to 1.46)		1.27 (0.80 to 2.03)		0.79 (0.39 to 1.61)	
P-value	-	0.7911		0.3076		0.5210	
TT1R probability (95% CI)[b]							

TT1R: Time to first response, CI: Confidence interval, IRC: Independent Response Committee
Cut-off date: 07FEB2020 HR<1 favors IKd arm
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] Two-sided significance level is 0.05.
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables and the treatment-by-subgroup interaction as covariates.
PGM=DEVOPS/SAR650984/EFC15246/CIR_RWE/REPORT/PGM/eff_km_subgp_sr_de_i_t.sas OUT=REPORT/OUTPUT/eff_km_tt1r_seiss_de_i_t_x.rtf (19FEB2021 15:19)

16.2.6.5 Secondary efficacy endpoints - Time to first response
16.2.6.5.1 ITT population
16.2.6.5.1.10 Subgroup analyses by R-ISS stage at SE
16.2.6.5.1.10.1 Time to first response based on disease assessment by the IRC by treatment group according to R-ISS stage at SE - ITT population

	I or II		III		Not classified		
	Kd (N=103)	**IKd (N=155)**	**Kd (N=8)**	**IKd (N=16)**	**Kd (N=12)**	**IKd (N=8)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	86 (83.5)	141 (91.0)	5 (62.5)	9 (56.3)	11 (91.7)	5 (62.5)	0.5409
Number (%) of patients censored	17 (16.5)	14 (9.0)	3 (37.5)	7 (43.8)	1 (8.3)	3 (37.5)	
Kaplan-Meier estimates of TT1R in months							
25% quantile (95% CI)	1.02 (0.986 to 1.018)	0.99 (0.986 to 1.018)	1.12 (1.018 to 3.055)	1.91 (0.953 to 2.103)	0.99 (0.953 to 0.986)	1.02 (0.986 to 1.150)	
Median (95% CI)	1.12 (1.051 to 1.183)	1.05 (1.051 to 1.084)	3.06 (1.018 to NC)	2.10 (1.084 to NC)	1.03 (0.953 to 1.906)	1.15 (0.986 to NC)	
75% quantile (95% CI)	1.94 (1.873 to 2.793)	1.84 (1.183 to 1.971)	NC (1.971 to NC)	2.96 (1.971 to NC)	1.89 (0.986 to NC)	2.00 (1.018 to NC)	
Comparison vs. Kd							
Log-Rank test p-value[a] vs Kd	-	0.2686		0.5686		0.3710	
Hazard ratio (95% CI) vs Kd	-	1.16 (0.89 to 1.52)		1.38 (0.45 to 4.23)		0.62 (0.21 to 1.80)	
P-value	-	0.2691		0.5701		0.3754	
TT1R probability (95% CI)[b]							

TT1R: Time to first response, CI: Confidence interval, IRC: Independent Response Committee
Cut-off date: 07FEB2020 HR<1 favors IKd arm
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] Two-sided significance level is 0.05.
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables and the treatment-by-subgroup interaction as covariates.
PGM=DEVOPS/SAR650984/EFC15246/CIR_RWE/REPORT/PGM/eff_km_subgp_sr_de_i_t.sas OUT=REPORT/OUTPUT/eff_km_tt1r_seriss_de_i_t_x.rtf (19FEB2021 15:19)

16.2.6.5 Secondary efficacy endpoints - Time to first response
16.2.6.5.1 ITT population
16.2.6.5.1.11 Subgroup analyses by nb of prior lines
16.2.6.5.1.11.1 Time to first response based on disease assessment by the IRC by treatment group according to nb of prior lines - ITT population

	1		>1		
	Kd (N=55)	**IKd (N=79)**	**Kd (N=68)**	**IKd (N=100)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	47 (85.5)	69 (87.3)	55 (80.9)	86 (86.0)	0.6615
Number (%) of patients censored	8 (14.5)	10 (12.7)	13 (19.1)	14 (14.0)	
Kaplan-Meier estimates of TT1R in months					
25% quantile (95% CI)	0.99 (0.953 to 1.051)	0.99 (0.986 to 1.018)	1.02 (0.986 to 1.018)	0.99 (0.986 to 1.018)	
Median (95% CI)	1.12 (1.051 to 1.183)	1.05 (1.018 to 1.150)	1.12 (1.018 to 1.873)	1.08 (1.051 to 1.150)	
75% quantile (95% CI)	1.97 (1.150 to 2.858)	1.91 (1.216 to 2.891)	1.94 (1.873 to 3.055)	1.94 (1.183 to 2.103)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.8128		0.3657	
Hazard ratio (95% CI) vs Kd	-	1.05 (0.72 to 1.52)		1.17 (0.83 to 1.64)	
P-value	-	0.8135		0.3662	
TT1R probability (95% CI)[b]					
6 Months	0.066 (0.017 to 0.162)	0.086 (0.034 to 0.169)	0.083 (0.029 to 0.176)	0.078 (0.033 to 0.150)	

TT1R: Time to first response, CI: Confidence interval, IRC: Independent Response Committee
Cut-off date: 07FEB2020 HR<1 favors IKd arm
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] Two-sided significance level is 0.05.
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables and the treatment-by-subgroup interaction as covariates.
PGM=DEVOPS/SAR650984/EFC15246/CIR_RWE/REPORT/PGM/eff_km_subgp_sr_de_i_t.sas OUT=REPORT/OUTPUT/eff_km_tt1r_plne_de_i_t_x.rtf (19FEB2021 15:19)

16.2.6.5 Secondary efficacy endpoints - Time to first response
16.2.6.5.1 ITT population
16.2.6.5.1.12 Subgroup analyses by cytogenetic abnormality
16.2.6.5.1.12.1 Time to first response based on disease assessment by the IRC by treatment group according to cytogenetic abnormality - ITT population

	At least one		None		
	Kd (N=31)	**IKd (N=42)**	**Kd (N=77)**	**IKd (N=114)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	24 (77.4)	33 (78.6)	66 (85.7)	104 (91.2)	0.1997
Number (%) of patients censored	7 (22.6)	9 (21.4)	11 (14.3)	10 (8.8)	
Kaplan-Meier estimates of TT1R in months					
25% quantile (95% CI)	1.02 (0.953 to 1.117)	0.99 (0.953 to 1.018)	1.02 (0.986 to 1.051)	0.99 (0.986 to 1.018)	
Median (95% CI)	1.13 (1.018 to 1.906)	1.10 (1.018 to 2.037)	1.12 (1.051 to 1.216)	1.05 (1.018 to 1.117)	
75% quantile (95% CI)	1.97 (1.314 to NC)	3.42 (1.971 to NC)	1.97 (1.873 to 2.858)	1.58 (1.150 to 1.938)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.7827		0.0674	
Hazard ratio (95% CI) vs Kd	-	0.93 (0.55 to 1.57)		1.34 (0.98 to 1.84)	
P-value	-	0.7828		0.0683	
TT1R probability (95% CI)[b]					
6 Months	0.117 (0.030 to 0.269)	0.190 (0.082 to 0.333)	0.073 (0.027 to 0.150)	0.033 (0.008 to 0.094)	

TT1R: Time to first response, CI: Confidence interval, IRC: Independent Response Committee
Cut-off date: 07FEB2020 HR<1 favors IKd arm
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] Two-sided significance level is 0.05.
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables and the treatment-by-subgroup interaction as covariates.
PGM=DEVOPS/SAR650984/EFC15246/CIR_RWE/REPORT/PGM/eff_km_subgp_sr_de_i_t.sas OUT=REPORT/OUTPUT/eff_km_tt1r_cyto_de_i_t_x.rtf (19FEB2021 15:19)

16.2.6.5 Secondary efficacy endpoints - Time to first response
16.2.6.5.1 ITT population
16.2.6.5.1.13 Subgroup analyses by MM type at SE
16.2.6.5.1.13.1 Time to first response based on disease assessment by the IRC by treatment group according to MM type at SE - ITT population

	IgG		Non-IgG		
	Kd (N=85)	**IKd (N=126)**	**Kd (N=38)**	**IKd (N=53)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	72 (84.7)	109 (86.5)	30 (78.9)	46 (86.8)	0.5031
Number (%) of patients censored	13 (15.3)	17 (13.5)	8 (21.1)	7 (13.2)	
Kaplan-Meier estimates of TT1R in months					
25% quantile (95% CI)	1.02 (0.986 to 1.051)	1.02 (0.986 to 1.018)	0.99 (0.953 to 0.986)	0.99 (0.953 to 0.986)	
Median (95% CI)	1.13 (1.084 to 1.906)	1.08 (1.051 to 1.150)	1.05 (0.986 to 1.084)	1.03 (0.986 to 1.117)	
75% quantile (95% CI)	2.00 (1.906 to 2.858)	1.97 (1.478 to 2.136)	1.18 (1.051 to 3.055)	1.22 (1.117 to 2.037)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.3147		0.9040	
Hazard ratio (95% CI) vs Kd	-	1.17 (0.86 to 1.57)		0.97 (0.61 to 1.54)	
P-value	-	0.3152		0.9037	
TT1R probability (95% CI)[b]					
6 Months	0.083 (0.034 to 0.159)	0.079 (0.037 to 0.142)	0.071 (0.013 to 0.199)	0.092 (0.029 to 0.199)	

TT1R: Time to first response, CI: Confidence interval, IRC: Independent Response Committee
Cut-off date: 07FEB2020 HR<1 favors IKd arm
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] Two-sided significance level is 0.05.
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables and the treatment-by-subgroup interaction as covariates.
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16.2.6.5 Secondary efficacy endpoints - Time to first response
16.2.6.5.1 ITT population
16.2.6.5.1.14 Subgroup analyses by previous autologous stem-cell
16.2.6.5.1.14.1 Time to first response based on disease assessment by the IRC by treatment group according to previous autologous stem-cell - ITT population

	Yes		No		
	Kd (N=69)	**IKd (N=116)**	**Kd (N=54)**	**IKd (N=63)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	59 (85.5)	102 (87.9)	43 (79.6)	53 (84.1)	0.5839
Number (%) of patients censored	10 (14.5)	14 (12.1)	11 (20.4)	10 (15.9)	
Kaplan-Meier estimates of TT1R in months					
25% quantile (95% CI)	0.99 (0.986 to 1.051)	0.99 (0.986 to 1.018)	1.02 (0.986 to 1.051)	1.02 (0.986 to 1.051)	
Median (95% CI)	1.12 (1.051 to 1.281)	1.05 (1.018 to 1.117)	1.12 (1.018 to 1.873)	1.12 (1.051 to 1.938)	
75% quantile (95% CI)	1.94 (1.873 to 2.793)	1.45 (1.150 to 1.971)	2.04 (1.314 to 3.811)	2.04 (1.938 to 3.417)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.3587		0.9576	
Hazard ratio (95% CI) vs Kd	-	1.16 (0.84 to 1.60)		1.01 (0.67 to 1.51)	
P-value	-	0.3591		0.9576	
TT1R probability (95% CI)[b]					
6 Months	0.035 (0.007 to 0.107)	0.072 (0.031 to 0.135)	0.134 (0.055 to 0.248)	0.098 (0.034 to 0.201)	

TT1R: Time to first response, CI: Confidence interval, IRC: Independent Response Committee
Cut-off date: 07FEB2020 HR<1 favors IKd arm
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] Two-sided significance level is 0.05.
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables and the treatment-by-subgroup interaction as covariates.
PGM=DEVOPS/SAR650984/EFC15246/CIR_RWE/REPORT/PGM/eff_km_subgp_sr_de_i_t.sas OUT=REPORT/OUTPUT/eff_km_tt1r_auto_de_i_t_x.rtf (19FEB2021 15:19)

16.2.6.5 Secondary efficacy endpoints - Time to first response
16.2.6.5.1 ITT population
16.2.6.5.1.15 Subgroup analyses by baseline eGFR (MDRD)
16.2.6.5.1.15.1 Time to first response based on disease assessment by the IRC by treatment group according to baseline eGFR (MDRD) - ITT population

	>=60 mL/min/1.73m2		<60 mL/min/1.73m2		
	Kd (N=93)	**IKd (N=122)**	**Kd (N=18)**	**IKd (N=43)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	83 (89.2)	102 (83.6)	11 (61.1)	40 (93.0)	0.2514
Number (%) of patients censored	10 (10.8)	20 (16.4)	7 (38.9)	3 (7.0)	
Kaplan-Meier estimates of TT1R in months					
25% quantile (95% CI)	1.02 (0.986 to 1.018)	0.99 (0.986 to 1.018)	0.99 (0.920 to 1.084)	1.02 (0.986 to 1.051)	
Median (95% CI)	1.12 (1.051 to 1.183)	1.05 (1.018 to 1.117)	1.15 (0.986 to 3.055)	1.08 (1.051 to 1.314)	
75% quantile (95% CI)	1.94 (1.873 to 2.793)	1.94 (1.183 to 2.136)	3.06 (1.150 to NC)	1.94 (1.248 to 2.004)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.6789		0.1727	
Hazard ratio (95% CI) vs Kd	-	1.06 (0.80 to 1.42)		1.60 (0.81 to 3.15)	
P-value	-	0.6797		0.1762	
TT1R probability (95% CI)[b]					
6 Months	0.062 (0.023 to 0.128)	0.105 (0.055 to 0.174)	0.233 (0.059 to 0.473)	0.034 (0.003 to 0.141)	

TT1R: Time to first response, CI: Confidence interval, IRC: Independent Response Committee
Cut-off date: 07FEB2020 HR<1 favors IKd arm
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] Two-sided significance level is 0.05.
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables and the treatment-by-subgroup interaction as covariates.
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16.2.6.5 Secondary efficacy endpoints - Time to first response
16.2.6.5.1 ITT population
16.2.6.5.1.16 Subgroup analyses by previous treatment with PI
16.2.6.5.1.16.1 Time to first response based on disease assessment by the IRC by treatment group according to previous treatment with PI - ITT population

	Yes		No		
	Kd (N=47)	**IKd (N=81)**	**Kd (N=76)**	**IKd (N=98)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	37 (78.7)	69 (85.2)	65 (85.5)	86 (87.8)	0.9525
Number (%) of patients censored	10 (21.3)	12 (14.8)	11 (14.5)	12 (12.2)	
Kaplan-Meier estimates of TT1R in months					
25% quantile (95% CI)	1.02 (0.986 to 1.051)	0.99 (0.986 to 1.018)	0.99 (0.986 to 1.018)	0.99 (0.986 to 1.018)	
Median (95% CI)	1.12 (1.051 to 1.873)	1.05 (1.018 to 1.150)	1.12 (1.051 to 1.281)	1.08 (1.051 to 1.117)	
75% quantile (95% CI)	2.04 (1.314 to 3.713)	2.00 (1.216 to 2.957)	1.94 (1.873 to 2.825)	1.84 (1.183 to 1.971)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.6144		0.4948	
Hazard ratio (95% CI) vs Kd	-	1.11 (0.74 to 1.65)		1.12 (0.81 to 1.55)	
P-value	-	0.6146		0.4950	
TT1R probability (95% CI)[b]					
6 Months	0.087 (0.023 to 0.205)	0.084 (0.033 to 0.167)	0.068 (0.023 to 0.147)	0.084 (0.037 to 0.156)	

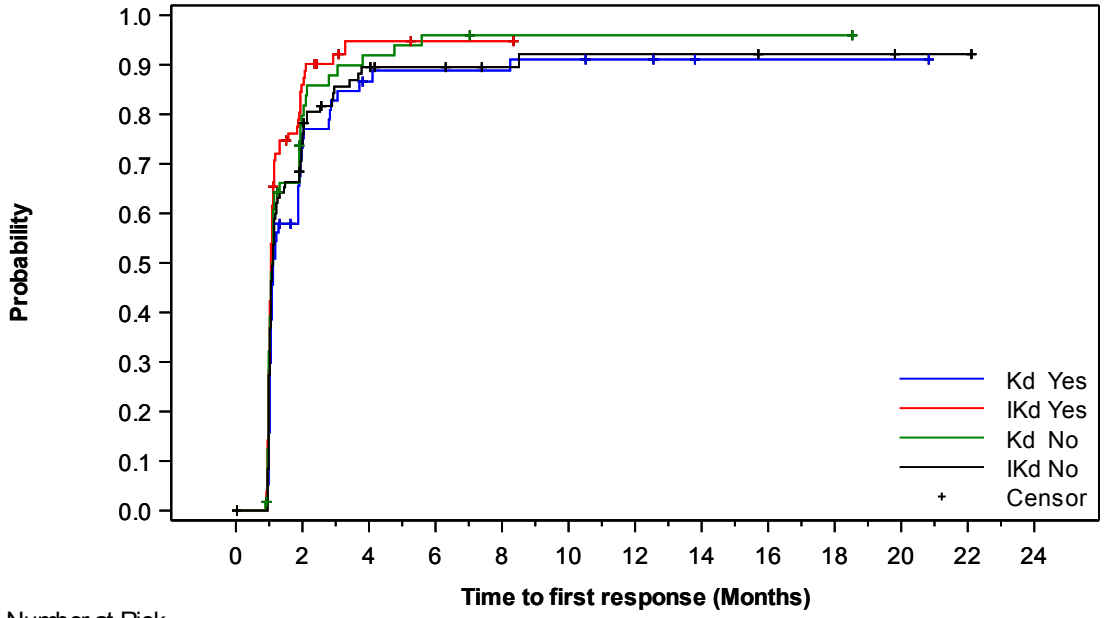
TT1R: Time to first response, CI: Confidence interval, IRC: Independent Response Committee
Cut-off date: 07FEB2020 HR<1 favors IKd arm
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] Two-sided significance level is 0.05.
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables and the treatment-by-subgroup interaction as covariates.
PGM=DEVOPS/SAR650984/EFC15246/CIR_RWE/REPORT/PGM/eff_km_subgp_sr_de_i_t.sas OUT=REPORT/OUTPUT/eff_km_tt1r_pi_de_i_t_x.rtf (19FEB2021 15:19)

16.2.6.5 Secondary efficacy endpoints - Time to first response
16.2.6.5.1 ITT population
16.2.6.5.1.17 Subgroup analyses by previous treatment with IMiD
16.2.6.5.1.17.1 Time to first response based on disease assessment by the IRC by treatment group according to previous treatment with IMiD - ITT population

	Yes		No		
	Kd (N=62)	**IKd (N=81)**	**Kd (N=61)**	**IKd (N=98)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	50 (80.6)	71 (87.7)	52 (85.2)	84 (85.7)	0.0296
Number (%) of patients censored	12 (19.4)	10 (12.3)	9 (14.8)	14 (14.3)	
Kaplan-Meier estimates of TT1R in months					
25% quantile (95% CI)	1.02 (0.986 to 1.051)	0.99 (0.986 to 1.018)	0.99 (0.986 to 1.018)	0.99 (0.986 to 1.018)	
Median (95% CI)	1.12 (1.051 to 1.873)	1.05 (1.018 to 1.084)	1.12 (1.018 to 1.150)	1.12 (1.051 to 1.183)	
75% quantile (95% CI)	2.00 (1.873 to 3.713)	1.58 (1.117 to 1.938)	1.94 (1.150 to 2.136)	2.00 (1.478 to 2.924)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.0391		0.4106	
Hazard ratio (95% CI) vs Kd	-	1.47 (1.02 to 2.12)		0.86 (0.61 to 1.22)	
P-value	-	0.0403		0.4110	
Hazard ratio inverted (95% CI) vs IKd		-		1.16 (0.82 to 1.64)	
TT1R probability (95% CI)[b]					

TT1R: Time to first response, CI: Confidence interval, IRC: Independent Response Committee
Cut-off date: 07FEB2020 HR<1 favors IKd arm
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] Two-sided significance level is 0.05.
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables and the treatment-by-subgroup interaction as covariates.
PGM=DEVOPS/SAR650984/EFC15246/CIR_RWE/REPORT/PGM/eff_km_subgp_sr_de_i_t.sas OUT=REPORT/OUTPUT/eff_km_tt1r_imid_de_i_t_x.rtf (19FEB2021 15:19)

16.2.6.5 Secondary efficacy endpoints - Time to first response
16.2.6.5.1 ITT population
16.2.6.5.1.17 Subgroup analyses by previous treatment with IMiD
16.2.6.5.1.17.2 Time to first response based on disease assessment by the IRC by treatment group according to previous treatment with IMiD - Kaplan-Meier curve - ITT population



Number at Risk

Kd Yes	62	9	5	4	3	1	1	0	0
IKd Yes	81	4	1	0	0	0	0	0	0
Kd No	61	6	2	1	1	1	1	0	0
IKd No	98	11	6	3	3	3	2	1	0

16.2.6.5 Secondary efficacy endpoints - Time to first response
16.2.6.5.1 ITT population
16.2.6.5.1.18 Subgroup analyses by previous treatment with PI and IMiD
16.2.6.5.1.18.1 Time to first response based on disease assessment by the IRC by treatment group according to previous treatment with PI and IMiD - ITT population

	Yes		No		
	Kd (N=17)	**IKd (N=23)**	**Kd (N=106)**	**IKd (N=156)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	13 (76.5)	19 (82.6)	89 (84.0)	136 (87.2)	0.2796
Number (%) of patients censored	4 (23.5)	4 (17.4)	17 (16.0)	20 (12.8)	
Kaplan-Meier estimates of TT1R in months					
25% quantile (95% CI)	1.02 (0.986 to 1.183)	1.02 (0.920 to 1.018)	0.99 (0.986 to 1.018)	0.99 (0.986 to 1.018)	
Median (95% CI)	1.53 (1.018 to 3.055)	1.05 (1.018 to 1.873)	1.12 (1.051 to 1.150)	1.08 (1.051 to 1.117)	
75% quantile (95% CI)	3.06 (1.183 to NC)	1.94 (1.051 to NC)	1.94 (1.873 to 2.136)	1.94 (1.314 to 2.037)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.2631		0.7734	
Hazard ratio (95% CI) vs Kd	-	1.50 (0.73 to 3.07)		1.04 (0.80 to 1.36)	
P-value	-	0.2661		0.7743	
TT1R probability (95% CI)[b]					
6 Months	0.143 (0.024 to 0.363)	0.080 (0.007 to 0.276)	0.064 (0.025 to 0.129)	0.082 (0.043 to 0.138)	

TT1R: Time to first response, CI: Confidence interval, IRC: Independent Response Committee
Cut-off date: 07FEB2020 HR<1 favors IKd arm
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] Two-sided significance level is 0.05.
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables and the treatment-by-subgroup interaction as covariates.
PGM=DEVOPS/SAR650984/EFC15246/CIR_RWE/REPORT/PGM/eff_km_subgp_sr_de_i_t.sas OUT=REPORT/OUTPUT/eff_km_tt1r_piimid_de_i_t_x.rtf (19FEB2021 15:19)

16.2.6.7 Secondary efficacy endpoints - MRD
16.2.6.7.1 ITT population
16.2.6.7.1.2 Subgroup analyses by age
16.2.6.7.1.2.1 Summary of MRD negativity rate as per IRC - 2-sided p-value according to age - ITT population

	<65 years		>=65 years		
	Kd (N=66)	**IKd (N=88)**	**Kd (N=57)**	**IKd (N=91)**	**Treat.-by-subgroup[b]**
MRD negativity rate					
MRD positive rate or missing	58 (87.9)	59 (67.0)	49 (86.0)	67 (73.6)	
95% CI[a]	(0.7751 to 0.9462)	(0.5621 to 0.7670)	(0.7421 to 0.9374)	(0.6335 to 0.8231)	
MRD negativity rate	8 (12.1)	29 (33.0)	8 (14.0)	24 (26.4)	
95% CI[a]	(0.0538 to 0.2249)	(0.2330 to 0.4379)	(0.0626 to 0.2579)	(0.1769 to 0.3665)	
Risk ratio 95% CI vs Kd[b]	-	2.72 (1.327 to 5.572)	-	1.88 (0.904 to 3.905)	
P-value [b]	-	0.0065	-	0.0907	
P-value heterogeneity[b]					0.4786
Odds ratio 95% CI vs Kd[b]	-	3.56 (1.499 to 8.472)	-	2.19 (0.906 to 5.313)	
P-value [b]	-	0.0042	-	0.0815	
P-value heterogeneity[b]					0.4413
Percent difference 95% CI vs Kd(%)[b]	-	20.83 (8.194 to 33.472)	-	12.34 (-0.492 to 25.169)	
P-value [b]	-	0.0013	-	0.0594	
P-value heterogeneity[b]					0.3540

CI: Confidence interval, IRC: Independent Response Committee
[a] Estimated using Clopper-Pearson method.
[b] Estimation, CI and P-value are calculated from PROC GLIMMIX procedure and a model with treatment, subgroup variables and the treatment-by-subgroup interaction as covariates.
PGM=DEVOPS/SAR650984/EFC15246/CIR_RWE/REPORT/PGM/eff_mrd_subgrp_sr_de_i_t.sas OUT=REPORT/OUTPUT/eff_mrd_2sid_age_de_i_t_x.rtf (19FEB2021 15:23)

16.2.6.7 Secondary efficacy endpoints - MRD
16.2.6.7.1 ITT population
16.2.6.7.1.3 Subgroup analyses by gender
16.2.6.7.1.3.1 Summary of MRD negativity rate as per IRC - 2-sided p-value according to gender - ITT population

	Male		Female		
	Kd (N=68)	**IKd (N=101)**	**Kd (N=55)**	**IKd (N=78)**	**Treat.-by-subgroup[b]**
MRD negativity rate					
MRD positive rate or missing	61 (89.7)	69 (68.3)	46 (83.6)	57 (73.1)	
95% CI[a]	(0.7993 to 0.9576)	(0.5831 to 0.7722)	(0.7120 to 0.9223)	(0.6184 to 0.8250)	
MRD negativity rate	7 (10.3)	32 (31.7)	9 (16.4)	21 (26.9)	
95% CI[a]	(0.0424 to 0.2007)	(0.2278 to 0.4169)	(0.0777 to 0.2880)	(0.1750 to 0.3816)	
Risk ratio 95% CI vs Kd[b]	-	3.08 (1.438 to 6.587)	-	1.65 (0.814 to 3.324)	
P-value [b]	-	0.0039	-	0.1646	
P-value heterogeneity[b]					0.2352
Odds ratio 95% CI vs Kd[b]	-	4.04 (1.658 to 9.851)	-	1.88 (0.784 to 4.520)	
P-value [b]	-	0.0022	-	0.1560	
P-value heterogeneity[b]					0.2299
Percent difference 95% CI vs Kd(%)[b]	-	21.39 (9.745 to 33.033)	-	10.56 (-3.371 to 24.490)	
P-value [b]	-	0.0004	-	0.1368	
P-value heterogeneity[b]					0.2414

CI: Confidence interval, IRC: Independent Response Committee
[a] Estimated using Clopper-Pearson method.
[b] Estimation, CI and P-value are calculated from PROC GLIMMIX procedure and a model with treatment, subgroup variables and the treatment-by-subgroup interaction as covariates.
PGM=DEVOPS/SAR650984/EFC15246/CIR_RWE/REPORT/PGM/eff_mrd_subgrp_sr_de_i_t.sas OUT=REPORT/OUTPUT/eff_mrd_2sid_sex_de_i_t_x.rtf (19FEB2021 15:23)

16.2.6.7 Secondary efficacy endpoints - MRD
16.2.6.7.1 ITT population
16.2.6.7.1.4 Subgroup analyses by ethnic origin
16.2.6.7.1.4.1 Summary of MRD negativity rate as per IRC - 2-sided p-value according to ethnic origin - ITT population

	White		Other		
	Kd (N=83)	**IKd (N=131)**	**Kd (N=28)**	**IKd (N=34)**	**Treat.-by-subgroup[b]**
MRD negativity rate					
MRD positive rate or missing	71 (85.5)	96 (73.3)	25 (89.3)	20 (58.8)	
95% CI[a]	(0.7611 to 0.9230)	(0.6485 to 0.8063)	(0.7177 to 0.9773)	(0.4070 to 0.7535)	
MRD negativity rate	12 (14.5)	35 (26.7)	3 (10.7)	14 (41.2)	
95% CI[a]	(0.0770 to 0.2389)	(0.1937 to 0.3515)	(0.0227 to 0.2823)	(0.2465 to 0.5930)	
Risk ratio 95% CI vs Kd[b]	-	1.85 (1.016 to 3.360)	-	3.84 (1.220 to 12.105)	
P-value [b]	-	0.0441	-	0.0216	
P-value heterogeneity[b]					0.2662
Odds ratio 95% CI vs Kd[b]	-	2.16 (1.043 to 4.463)	-	5.83 (1.461 to 23.298)	
P-value [b]	-	0.0383	-	0.0128	
P-value heterogeneity[b]					0.2116
Percent difference 95% CI vs Kd(%)[b]	-	12.26 (1.504 to 23.015)	-	30.46 (10.250 to 50.674)	
P-value [b]	-	0.0256	-	0.0033	
P-value heterogeneity[b]					0.1187

CI: Confidence interval, IRC: Independent Response Committee
[a] Estimated using Clopper-Pearson method.
[b] Estimation, CI and P-value are calculated from PROC GLIMMIX procedure and a model with treatment, subgroup variables and the treatment-by-subgroup interaction as covariates.
PGM=DEVOPS/SAR650984/EFC15246/CIR_RWE/REPORT/PGM/eff_mrd_subgrp_sr_de_i_t.sas OUT=REPORT/OUTPUT/eff_mrd_2sid_race_de_i_t_x.rtf (19FEB2021 15:23)

16.2.6.7 Secondary efficacy endpoints - MRD
16.2.6.7.1 ITT population
16.2.6.7.1.5 Subgroup analyses by geographical region
16.2.6.7.1.5.1 Summary of MRD negativity rate as per IRC - 2-sided p-value according to geographical region - ITT population

	Europe		America		Asia		Other countries		
	Kd (N=60)	**IKd (N=85)**	**Kd (N=20)**	**IKd (N=24)**	**Kd (N=21)**	**IKd (N=25)**	**Kd (N=22)**	**IKd (N=45)**	**Treat.-by-subgroup[b]**
MRD negativity rate									
MRD positive rate or missing	50 (83.3)	61 (71.8)	18 (90.0)	15 (62.5)	19 (90.5)	14 (56.0)	20 (90.9)	36 (80.0)	
95% CI[a]	(0.7148 to 0.9171)	(0.6096 to 0.8100)	(0.6830 to 0.9877)	(0.4059 to 0.8120)	(0.6962 to 0.9883)	(0.3493 to 0.7560)	(0.7084 to 0.9888)	(0.6540 to 0.9042)	
MRD negativity rate	10 (16.7)	24 (28.2)	2 (10.0)	9 (37.5)	2 (9.5)	11 (44.0)	2 (9.1)	9 (20.0)	
95% CI[a]	(0.0829 to 0.2852)	(0.1900 to 0.3904)	(0.0123 to 0.3170)	(0.1880 to 0.5941)	(0.0117 to 0.3038)	(0.2440 to 0.6507)	(0.0112 to 0.2916)	(0.0958 to 0.3460)	
Risk ratio 95% CI vs Kd[b]	-	1.69 (0.874 to 3.285)	-	3.75 (0.908 to 15.490)	-	4.62 (1.144 to 18.664)	-	2.20 (0.516 to 9.387)	
P-value [b]	-	0.1183	-	0.0677	-	0.0318	-	0.2857	
P-value heterogeneity[b]									0.5247
Odds ratio 95% CI vs Kd[b]	-	1.97 (0.857 to 4.514)	-	5.40 (1.001 to 29.129)	-	7.46 (1.413 to 39.419)	-	2.50 (0.488 to 12.804)	
P-value [b]	-	0.1099	-	0.0499	-	0.0181	-	0.2705	
P-value heterogeneity[b]									0.4501

CI: Confidence interval, IRC: Independent Response Committee
[a] Estimated using Clopper-Pearson method.
[b] Estimation, CI and P-value are calculated from PROC GLIMMIX procedure and a model with treatment, subgroup variables and the treatment-by-subgroup interaction as covariates.
PGM=DEVOPS/SAR650984/EFC15246/CIR_RWE/REPORT/PGM/eff_mrd_subgrp_sr_de_i_t.sas OUT=REPORT/OUTPUT/eff_mrd_2sid_greg_de_i_t_x.rtf (19FEB2021 15:23)

16.2.6.7 Secondary efficacy endpoints - MRD
16.2.6.7.1 ITT population
16.2.6.7.1.5 Subgroup analyses by geographical region
16.2.6.7.1.5.1 Summary of MRD negativity rate as per IRC - 2-sided p-value according to geographical region - ITT population

	Europe		America		Asia		Other countries		
	Kd (N=60)	**IKd (N=85)**	**Kd (N=20)**	**IKd (N=24)**	**Kd (N=21)**	**IKd (N=25)**	**Kd (N=22)**	**IKd (N=45)**	**Treat.-by-subgroup[b]**
Percent difference 95% CI vs Kd(%)[b]	-	11.57 (-1.922 to 25.059)	-	27.50 (3.994 to 51.006)	-	34.48 (11.224 to 57.729)	-	10.91 (-5.920 to 27.738)	
P-value [b]	-	0.0925	-	0.0220	-	0.0038	-	0.2030	
P-value heterogeneity[b]									0.2535

CI: Confidence interval, IRC: Independent Response Committee
[a] Estimated using Clopper-Pearson method.
[b] Estimation, CI and P-value are calculated from PROC GLIMMIX procedure and a model with treatment, subgroup variables and the treatment-by-subgroup interaction as covariates.
PGM=DEVOPS/SAR650984/EFC15246/CIR_RWE/REPORT/PGM/eff_mrd_subgrp_sr_de_i_t.sas OUT=REPORT/OUTPUT/eff_mrd_2sid_greg_de_i_t_x.rtf (19FEB2021 15:23)

16.2.6.7 Secondary efficacy endpoints - MRD
16.2.6.7.1 ITT population
16.2.6.7.1.6 Subgroup analyses by regulatory region
16.2.6.7.1.6.1 Summary of MRD negativity rate as per IRC - 2-sided p-value according to regulatory region - ITT population

	Western countries		Other countries		
	Kd (N=55)	**IKd (N=97)**	**Kd (N=68)**	**IKd (N=82)**	**Treat.-by-subgroup[b]**
MRD negativity rate					
MRD positive rate or missing	45 (81.8)	66 (68.0)	62 (91.2)	60 (73.2)	
95% CI[a]	(0.6910 to 0.9092)	(0.5780 to 0.7715)	(0.8178 to 0.9669)	(0.6224 to 0.8236)	
MRD negativity rate	10 (18.2)	31 (32.0)	6 (8.8)	22 (26.8)	
95% CI[a]	(0.0908 to 0.3090)	(0.2285 to 0.4220)	(0.0331 to 0.1822)	(0.1764 to 0.3776)	
Risk ratio 95% CI vs Kd[b]	-	1.76 (0.932 to 3.313)	-	3.04 (1.304 to 7.092)	
P-value [b]	-	0.0810	-	0.0102	
P-value heterogeneity[b]					0.3088
Odds ratio 95% CI vs Kd[b]	-	2.11 (0.940 to 4.754)	-	3.79 (1.431 to 10.034)	
P-value [b]	-	0.0702	-	0.0075	
P-value heterogeneity[b]					0.3654
Percent difference 95% CI vs Kd(%)[b]	-	13.78 (-0.064 to 27.618)	-	18.01 (6.236 to 29.776)	
P-value [b]	-	0.0511	-	0.0028	
P-value heterogeneity[b]					0.6473

CI: Confidence interval, IRC: Independent Response Committee
[a] Estimated using Clopper-Pearson method.
[b] Estimation, CI and P-value are calculated from PROC GLIMMIX procedure and a model with treatment, subgroup variables and the treatment-by-subgroup interaction as covariates.
PGM=DEVOPS/SAR650984/EFC15246/CIR_RWE/REPORT/PGM/eff_mrd_subgrp_sr_de_i_t.sas OUT=REPORT/OUTPUT/eff_mrd_2sid_rreg_de_i_t_x.rtf (19FEB2021 15:23)

16.2.6.7 Secondary efficacy endpoints - MRD
16.2.6.7.1 ITT population
16.2.6.7.1.7 Subgroup analyses by baseline ECOG PS
16.2.6.7.1.7.1 Summary of MRD negativity rate as per IRC - 2-sided p-value according to baseline ECOG PS - ITT population

	0 or 1		>1		
	Kd (N=118)	**IKd (N=168)**	**Kd (N=5)**	**IKd (N=11)**	**Treat.-by-subgroup[b]**
MRD negativity rate					
MRD positive rate or missing	102 (86.4)	116 (69.0)	5 (100.0)	10 (90.9)	
95% CI[a]	(0.7892 to 0.9205)	(0.6147 to 0.7594)	(0.4782 to 1.0000)	(0.5872 to 0.9977)	
MRD negativity rate	16 (13.6)	52 (31.0)	5 (100.0)	1 (9.1)	
95% CI[a]	(0.0795 to 0.2108)	(0.2406 to 0.3853)	(0.4782 to 1.0000)	(0.0023 to 0.4128)	
Risk ratio 95% CI vs Kd[b]	-	2.28 (1.370 to 3.804)	-	50858.34 (0.000 to 3.91E290)	
P-value [b]	-	0.0016	-	0.9742	
P-value heterogeneity[b]					0.9761
Odds ratio 95% CI vs Kd[b]	-	2.86 (1.533 to 5.327)	-	77923.39 (0.000 to .)	
P-value [b]	-	0.0010	-	0.9773	
P-value heterogeneity[b]					0.9794
Peto Odds ratio 95% CI vs Kd[b]	-	0.38 (0.220 to 0.670)	-	0.23 (0.000 to 16.020)	
P-value [b]	-	0.0007	-	0.5002	
P-value heterogeneity[b]					0.8189

CI: Confidence interval, IRC: Independent Response Committee
[a] Estimated using Clopper-Pearson method.
[b] Estimation, CI and P-value are calculated from PROC GLIMMIX procedure and a model with treatment, subgroup variables and the treatment-by-subgroup interaction as covariates.
PGM=DEVOPS/SAR650984/EFC15246/CIR_RWE/REPORT/PGM/eff_mrd_subgrp_sr_de_i_t.sas OUT=REPORT/OUTPUT/eff_mrd_2sid_ecog_de_i_t_x.rtf (19FEB2021 15:23)

16.2.6.7 Secondary efficacy endpoints - MRD
16.2.6.7.1 ITT population
16.2.6.7.1.7 Subgroup analyses by baseline ECOG PS
16.2.6.7.1.7.1 Summary of MRD negativity rate as per IRC - 2-sided p-value according to baseline ECOG PS - ITT population

	0 or 1		>1		
	Kd (N=118)	**IKd (N=168)**	**Kd (N=5)**	**IKd (N=11)**	**Treat.-by-subgroup[b]**
Percent difference 95% CI vs Kd(%)[b]	-	17.39 (8.026 to 26.760)	-	9.09 (-0.276 to 18.458)	
P-value [b]	-	0.0003	-	0.0571	
P-value heterogeneity[b]					<.0001

CI: Confidence interval, IRC: Independent Response Committee
[a] Estimated using Clopper-Pearson method.
[b] Estimation, CI and P-value are calculated from PROC GLIMMIX procedure and a model with treatment, subgroup variables and the treatment-by-subgroup interaction as covariates.
PGM=DEVOPS/SAR650984/EFC15246/CIR_RWE/REPORT/PGM/eff_mrd_subgrp_sr_de_i_t.sas OUT=REPORT/OUTPUT/eff_mrd_2sid_ecog_de_i_t_x.rtf (19FEB2021 15:23)

16.2.6.7 Secondary efficacy endpoints - MRD
16.2.6.7.1 ITT population
16.2.6.7.1.8 Subgroup analyses by ISS staging at SE
16.2.6.7.1.8.1 Summary of MRD negativity rate as per IRC - 2-sided p-value according to ISS staging at SE - ITT population

	I		II		III		
	Kd (N=71)	**IKd (N=89)**	**Kd (N=31)**	**IKd (N=63)**	**Kd (N=20)**	**IKd (N=26)**	**Treat.-by-subgroup[b]**
MRD negativity rate							
MRD positive rate or missing	61 (85.9)	57 (64.0)	27 (87.1)	45 (71.4)	18 (90.0)	23 (88.5)	
95% CI[a]	(0.7562 to 0.9303)	(0.5318 to 0.7395)	(0.7017 to 0.9637)	(0.5865 to 0.8211)	(0.6830 to 0.9877)	(0.6985 to 0.9755)	
MRD negativity rate	10 (14.1)	32 (36.0)	4 (12.9)	18 (28.6)	2 (10.0)	3 (11.5)	
95% CI[a]	(0.0697 to 0.2438)	(0.2605 to 0.4682)	(0.0363 to 0.2983)	(0.1789 to 0.4135)	(0.0123 to 0.3170)	(0.0245 to 0.3015)	
Risk ratio 95% CI vs Kd[b]	-	2.55 (1.345 to 4.844)	-	2.21 (0.816 to 6.010)	-	1.15 (0.211 to 6.307)	
P-value [b]	-	0.0043	-	0.1182	-	0.8684	
P-value heterogeneity[b]							0.6888
Odds ratio 95% CI vs Kd[b]	-	3.42 (1.539 to 7.621)	-	2.70 (0.822 to 8.864)	-	1.17 (0.176 to 7.851)	
P-value [b]	-	0.0027	-	0.1012	-	0.8682	
P-value heterogeneity[b]							0.5903
Percent difference 95% CI vs Kd(%)[b]	-	21.87 (8.978 to 34.764)	-	15.67 (-0.638 to 31.974)	-	1.54 (-16.527 to 19.604)	

CI: Confidence interval, IRC: Independent Response Committee
[a] Estimated using Clopper-Pearson method.
[b] Estimation, CI and P-value are calculated from PROC GLIMMIX procedure and a model with treatment, subgroup variables and the treatment-by-subgroup interaction as covariates.
PGM=DEVOPS/SAR650984/EFC15246/CIR_RWE/REPORT/PGM/eff_mrd_subgrp_sr_de_i_t.sas OUT=REPORT/OUTPUT/eff_mrd_2sid_seiss_de_i_t_x.rtf (19FEB2021 15:23)

16.2.6.7 Secondary efficacy endpoints - MRD
16.2.6.7.1 ITT population
16.2.6.7.1.8 Subgroup analyses by ISS staging at SE
16.2.6.7.1.8.1 Summary of MRD negativity rate as per IRC - 2-sided p-value according to ISS staging at SE - ITT population

	I		II		III		
	Kd (N=71)	**IKd (N=89)**	**Kd (N=31)**	**IKd (N=63)**	**Kd (N=20)**	**IKd (N=26)**	**Treat.-by-subgroup[b]**
P-value [b]	-	0.0010	-	0.0596	-	0.8670	
P-value heterogeneity[b]							0.1982

CI: Confidence interval, IRC: Independent Response Committee
[a] Estimated using Clopper-Pearson method.
[b] Estimation, CI and P-value are calculated from PROC GLIMMIX procedure and a model with treatment, subgroup variables and the treatment-by-subgroup interaction as covariates.
PGM=DEVOPS/SAR650984/EFC15246/CIR_RWE/REPORT/PGM/eff_mrd_subgrp_sr_de_i_t.sas OUT=REPORT/OUTPUT/eff_mrd_2sid_seiss_de_i_t_x.rtf (19FEB2021 15:23)

16.2.6.7 Secondary efficacy endpoints - MRD
16.2.6.7.1 ITT population
16.2.6.7.1.9 Subgroup analyses by R-ISS stage at SE
16.2.6.7.1.9.1 Summary of MRD negativity rate as per IRC - 2-sided p-value according to R-ISS stage at SE - ITT population

	I or II		III		Not classified		
	Kd (N=103)	IKd (N=155)	Kd (N=8)	IKd (N=16)	Kd (N=12)	IKd (N=8)	Treat.-by-subgroup[b]
MRD negativity rate							
MRD positive rate or missing	89 (86.4)	102 (65.8)	7 (87.5)	16 (100.0)	11 (91.7)	8 (100.0)	
95% CI[a]	(0.7825 to 0.9237)	(0.5777 to 0.7323)	(0.4735 to 0.9968)	(0.7941 to 1.0000)	(0.6152 to 0.9979)	(0.6306 to 1.0000)	
MRD negativity rate	14 (13.6)	53 (34.2)	1 (12.5)	16 (100.0)	1 (8.3)	0	
95% CI[a]	(0.0763 to 0.2175)	(0.2677 to 0.4223)	(0.0032 to 0.5265)	(0.7941 to 1.0000)	(0.0021 to 0.3848)	-	
Risk ratio 95% CI vs Kd[b]	-	2.52 (1.472 to 4.299)	-	0.00 (0.000 to .)	-	0.00 (0.000 to .)	
P-value [b]	-	0.0008	-	0.9794	-	0.9859	
P-value heterogeneity[b]							0.9994
Odds ratio 95% CI vs Kd[b]	-	3.30 (1.713 to 6.370)	-	0.00 (0.000 to .)	-	0.00 (0.000 to .)	
P-value [b]	-	0.0004	-	0.9819	-	0.9876	
P-value heterogeneity[b]							0.9996
Peto Odds ratio 95% CI vs Kd[b]	-	0.34 (0.200 to 0.610)	-	20.09 (0.310 to 1283.970)	-	5.29 (0.100 to 289.290)	

CI: Confidence interval, IRC: Independent Response Committee
[a] Estimated using Clopper-Pearson method.
[b] Estimation, CI and P-value are calculated from PROC GLIMMIX procedure and a model with treatment, subgroup variables and the treatment-by-subgroup interaction as covariates.
PGM=DEVOPS/SAR650984/EFC15246/CIR_RWE/REPORT/PGM/eff_mrd_subgrp_sr_de_i_t.sas OUT=REPORT/OUTPUT/eff_mrd_2sid_seriss_de_i_t_x.rtf (19FEB2021 15:23)

16.2.6.7 Secondary efficacy endpoints - MRD
16.2.6.7.1 ITT population
16.2.6.7.1.9 Subgroup analyses by R-ISS stage at SE
16.2.6.7.1.9.1 Summary of MRD negativity rate as per IRC - 2-sided p-value according to R-ISS stage at SE - ITT population

	I or II		III		Not classified		
	Kd (N=103)	**IKd (N=155)**	**Kd (N=8)**	**IKd (N=16)**	**Kd (N=12)**	**IKd (N=8)**	**Treat.-by-subgroup[b]**
P-value [b]	-	0.0002	-	0.1573	-	0.4142	
P-value heterogeneity[b]							0.0716
Percent difference 95% CI vs Kd(%)[b]	-	20.60 (10.582 to 30.621)	-	-12.50 (-22.519 to -2.481)	-	-8.33 (-18.353 to 1.686)	
P-value [b]	-	<.0001	-	0.0147	-	0.1027	
P-value heterogeneity[b]							<.0001

CI: Confidence interval, IRC: Independent Response Committee
[a] Estimated using Clopper-Pearson method.
[b] Estimation, CI and P-value are calculated from PROC GLIMMIX procedure and a model with treatment, subgroup variables and the treatment-by-subgroup interaction as covariates.
PGM=DEVOPS/SAR650984/EFC15246/CIR_RWE/REPORT/PGM/eff_mrd_subgrp_sr_de_i_t.sas OUT=REPORT/OUTPUT/eff_mrd_2sid_seriss_de_i_t_x.rtf (19FEB2021 15:23)

16.2.6.7 Secondary efficacy endpoints - MRD
16.2.6.7.1 ITT population
16.2.6.7.1.10 Subgroup analyses by nb of prior lines
16.2.6.7.1.10.1 Summary of MRD negativity rate as per IRC - 2-sided p-value according to nb of prior lines - ITT population

	1		>1		
	Kd (N=55)	**IKd (N=79)**	**Kd (N=68)**	**IKd (N=100)**	**Treat.-by-subgroup[b]**
MRD negativity rate					
MRD positive rate or missing	45 (81.8)	51 (64.6)	62 (91.2)	75 (75.0)	
95% CI[a]	(0.6910 to 0.9092)	(0.5299 to 0.7500)	(0.8178 to 0.9669)	(0.6534 to 0.8312)	
MRD negativity rate	10 (18.2)	28 (35.4)	6 (8.8)	25 (25.0)	
95% CI[a]	(0.0908 to 0.3090)	(0.2500 to 0.4701)	(0.0331 to 0.1822)	(0.1688 to 0.3466)	
Risk ratio 95% CI vs Kd[b]	-	1.95 (1.031 to 3.687)	-	2.83 (1.224 to 6.560)	
P-value [b]	-	0.0402	-	0.0152	
P-value heterogeneity[b]					0.4856
Odds ratio 95% CI vs Kd[b]	-	2.47 (1.078 to 5.661)	-	3.44 (1.324 to 8.963)	
P-value [b]	-	0.0326	-	0.0114	
P-value heterogeneity[b]					0.6058
Percent difference 95% CI vs Kd(%)[b]	-	17.26 (2.533 to 31.989)	-	16.18 (5.294 to 27.059)	
P-value [b]	-	0.0218	-	0.0037	
P-value heterogeneity[b]					0.9073

CI: Confidence interval, IRC: Independent Response Committee
[a] Estimated using Clopper-Pearson method.
[b] Estimation, CI and P-value are calculated from PROC GLIMMIX procedure and a model with treatment, subgroup variables and the treatment-by-subgroup interaction as covariates.
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16.2.6.7 Secondary efficacy endpoints - MRD
16.2.6.7.1 ITT population
16.2.6.7.1.11 Subgroup analyses by cytogenetic abnormality
16.2.6.7.1.11.1 Summary of MRD negativity rate as per IRC - 2-sided p-value according to cytogenetic abnormality - ITT population

	At least one		None		
	Kd (N=31)	**IKd (N=42)**	**Kd (N=77)**	**IKd (N=114)**	**Treat.-by-subgroup[b]**
MRD negativity rate					
MRD positive rate or missing	24 (77.4)	33 (78.6)	68 (88.3)	73 (64.0)	
95% CI[a]	(0.5890 to 0.9041)	(0.6319 to 0.8970)	(0.7897 to 0.9451)	(0.5451 to 0.7281)	
MRD negativity rate	7 (22.6)	9 (21.4)	9 (11.7)	41 (36.0)	
95% CI[a]	(0.0959 to 0.4110)	(0.1030 to 0.3681)	(0.0549 to 0.2103)	(0.2719 to 0.4549)	
Risk ratio 95% CI vs Kd[b]	-	0.95 (0.395 to 2.279)	-	3.08 (1.584 to 5.978)	
P-value [b]	-	0.9064	-	0.0010	
P-value heterogeneity[b]					0.0361
Odds ratio 95% CI vs Kd[b]	-	0.94 (0.304 to 2.878)	-	4.24 (1.912 to 9.418)	
P-value [b]	-	0.9065	-	0.0004	
P-value heterogeneity[b]					0.0316
Percent difference 95% CI vs Kd(%)[b]	-	-1.15 (-20.494 to 18.190)	-	24.28 (12.861 to 35.692)	
P-value [b]	-	0.9067	-	<.0001	
P-value heterogeneity[b]					0.0266

CI: Confidence interval, IRC: Independent Response Committee
[a] Estimated using Clopper-Pearson method.
[b] Estimation, CI and P-value are calculated from PROC GLIMMIX procedure and a model with treatment, subgroup variables and the treatment-by-subgroup interaction as covariates.
PGM=DEVOPS/SAR650984/EFC15246/CIR_RWE/REPORT/PGM/eff_mrd_subgrp_sr_de_i_t.sas OUT=REPORT/OUTPUT/eff_mrd_2sid_cyto_de_i_t_x.rtf (19FEB2021 15:23)

16.2.6.7 Secondary efficacy endpoints - MRD
16.2.6.7.1 ITT population
16.2.6.7.1.12 Subgroup analyses by MM type at SE
16.2.6.7.1.12.1 Summary of MRD negativity rate as per IRC - 2-sided p-value according to MM type at SE - ITT population

	IgG		Non-IgG		
	Kd (N=85)	**IKd (N=126)**	**Kd (N=38)**	**IKd (N=53)**	**Treat.-by-subgroup[b]**
MRD negativity rate					
MRD positive rate or missing	76 (89.4)	91 (72.2)	31 (81.6)	35 (66.0)	
95% CI[a]	(0.8085 to 0.9504)	(0.6354 to 0.7983)	(0.6567 to 0.9226)	(0.5173 to 0.7848)	
MRD negativity rate	9 (10.6)	35 (27.8)	7 (18.4)	18 (34.0)	
95% CI[a]	(0.0496 to 0.1915)	(0.2017 to 0.3646)	(0.0774 to 0.3433)	(0.2152 to 0.4827)	
Risk ratio 95% CI vs Kd[b]	-	2.62 (1.327 to 5.187)	-	1.84 (0.853 to 3.983)	
P-value [b]	-	0.0057	-	0.1192	
P-value heterogeneity[b]					0.5003
Odds ratio 95% CI vs Kd[b]	-	3.25 (1.464 to 7.203)	-	2.28 (0.836 to 6.203)	
P-value [b]	-	0.0039	-	0.1070	
P-value heterogeneity[b]					0.5857
Percent difference 95% CI vs Kd(%)[b]	-	17.19 (6.952 to 27.427)	-	15.54 (-2.265 to 33.347)	
P-value [b]	-	0.0011	-	0.0869	
P-value heterogeneity[b]					0.8746

CI: Confidence interval, IRC: Independent Response Committee
[a] Estimated using Clopper-Pearson method.
[b] Estimation, CI and P-value are calculated from PROC GLIMMIX procedure and a model with treatment, subgroup variables and the treatment-by-subgroup interaction as covariates.
PGM=DEVOPS/SAR650984/EFC15246/CIR_RWE/REPORT/PGM/eff_mrd_subgrp_sr_de_i_t.sas OUT=REPORT/OUTPUT/eff_mrd_2sid_semm_de_i_t_x.rtf (19FEB2021 15:23)

16.2.6.7 Secondary efficacy endpoints - MRD
16.2.6.7.1 ITT population
16.2.6.7.1.13 Subgroup analyses by previous autologous stem-cell
16.2.6.7.1.13.1 Summary of MRD negativity rate as per IRC - 2-sided p-value according to previous autologous stem-cell - ITT population

	Yes		No		
	Kd (N=69)	**IKd (N=116)**	**Kd (N=54)**	**IKd (N=63)**	**Treat.-by-subgroup[b]**
MRD negativity rate					
MRD positive rate or missing	60 (87.0)	79 (68.1)	47 (87.0)	47 (74.6)	
95% CI[a]	(0.7668 to 0.9386)	(0.5881 to 0.7645)	(0.7510 to 0.9463)	(0.6206 to 0.8473)	
MRD negativity rate	9 (13.0)	37 (31.9)	7 (13.0)	16 (25.4)	
95% CI[a]	(0.0614 to 0.2332)	(0.2355 to 0.4119)	(0.0537 to 0.2490)	(0.1527 to 0.3794)	
Risk ratio 95% CI vs Kd[b]	-	2.45 (1.255 to 4.767)	-	1.96 (0.868 to 4.420)	
P-value [b]	-	0.0088	-	0.1049	
P-value heterogeneity[b]					0.6788
Odds ratio 95% CI vs Kd[b]	-	3.12 (1.396 to 6.986)	-	2.29 (0.858 to 6.089)	
P-value [b]	-	0.0057	-	0.0979	
P-value heterogeneity[b]					0.6288
Percent difference 95% CI vs Kd(%)[b]	-	18.85 (7.183 to 30.523)	-	12.43 (-1.616 to 26.483)	
P-value [b]	-	0.0016	-	0.0826	
P-value heterogeneity[b]					0.4897

CI: Confidence interval, IRC: Independent Response Committee
[a] Estimated using Clopper-Pearson method.
[b] Estimation, CI and P-value are calculated from PROC GLIMMIX procedure and a model with treatment, subgroup variables and the treatment-by-subgroup interaction as covariates.
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16.2.6.7 Secondary efficacy endpoints - MRD
16.2.6.7.1 ITT population
16.2.6.7.1.14 Subgroup analyses by baseline eGFR (MDRD)
16.2.6.7.1.14.1 Summary of MRD negativity rate as per IRC - 2-sided p-value according to baseline eGFR (MDRD) - ITT population

	>=60 mL/min/1.73m2		<60 mL/min/1.73m2		
	Kd (N=93)	**IKd (N=122)**	**Kd (N=18)**	**IKd (N=43)**	**Treat.-by-subgroup[b]**
MRD negativity rate					
MRD positive rate or missing	80 (86.0)	86 (70.5)	16 (88.9)	30 (69.8)	
95% CI[a]	(0.7728 to 0.9234)	(0.6156 to 0.7840)	(0.6529 to 0.9862)	(0.5387 to 0.8282)	
MRD negativity rate	13 (14.0)	36 (29.5)	2 (11.1)	13 (30.2)	
95% CI[a]	(0.0766 to 0.2272)	(0.2160 to 0.3844)	(0.0138 to 0.3471)	(0.1718 to 0.4613)	
Risk ratio 95% CI vs Kd[b]	-	2.11 (1.186 to 3.757)	-	2.72 (0.678 to 10.918)	
P-value [b]	-	0.0113	-	0.1573	
P-value heterogeneity[b]					0.7400
Odds ratio 95% CI vs Kd[b]	-	2.58 (1.271 to 5.222)	-	3.47 (0.690 to 17.426)	
P-value [b]	-	0.0089	-	0.1308	
P-value heterogeneity[b]					0.7404
Percent difference 95% CI vs Kd(%)[b]	-	15.53 (4.750 to 26.309)	-	19.12 (-0.948 to 39.191)	
P-value [b]	-	0.0049	-	0.0618	
P-value heterogeneity[b]					0.7565

CI: Confidence interval, IRC: Independent Response Committee
[a] Estimated using Clopper-Pearson method.
[b] Estimation, CI and P-value are calculated from PROC GLIMMIX procedure and a model with treatment, subgroup variables and the treatment-by-subgroup interaction as covariates.
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16.2.6.7 Secondary efficacy endpoints - MRD
16.2.6.7.1 ITT population
16.2.6.7.1.15 Subgroup analyses by previous treatment with PI
16.2.6.7.1.15.1 Summary of MRD negativity rate as per IRC - 2-sided p-value according to previous treatment with PI - ITT population

	Yes		No		
	Kd (N=47)	**IKd (N=81)**	**Kd (N=76)**	**IKd (N=98)**	**Treat.-by-subgroup[b]**
MRD negativity rate					
MRD positive rate or missing	41 (87.2)	58 (71.6)	66 (86.8)	68 (69.4)	
95% CI[a]	(0.7426 to 0.9517)	(0.6050 to 0.8107)	(0.7713 to 0.9351)	(0.5926 to 0.7830)	
MRD negativity rate	6 (12.8)	23 (28.4)	10 (13.2)	30 (30.6)	
95% CI[a]	(0.0483 to 0.2574)	(0.1893 to 0.3950)	(0.0649 to 0.2287)	(0.2170 to 0.4074)	
Risk ratio 95% CI vs Kd[b]	-	2.22 (0.973 to 5.085)	-	2.33 (1.211 to 4.468)	
P-value [b]	-	0.0580	-	0.0114	
P-value heterogeneity[b]					0.9331
Odds ratio 95% CI vs Kd[b]	-	2.71 (1.009 to 7.274)	-	2.91 (1.315 to 6.448)	
P-value [b]	-	0.0479	-	0.0086	
P-value heterogeneity[b]					0.9112
Percent difference 95% CI vs Kd(%)[b]	-	15.63 (1.882 to 29.376)	-	17.45 (5.531 to 29.378)	
P-value [b]	-	0.0260	-	0.0043	
P-value heterogeneity[b]					0.8437

CI: Confidence interval, IRC: Independent Response Committee
[a] Estimated using Clopper-Pearson method.
[b] Estimation, CI and P-value are calculated from PROC GLIMMIX procedure and a model with treatment, subgroup variables and the treatment-by-subgroup interaction as covariates.
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16.2.6.7 Secondary efficacy endpoints - MRD
16.2.6.7.1 ITT population
16.2.6.7.1.16 Subgroup analyses by previous treatment with IMiD
16.2.6.7.1.16.1 Summary of MRD negativity rate as per IRC - 2-sided p-value according to previous treatment with IMiD - ITT population

	Yes		No		
	Kd (N=62)	**IKd (N=81)**	**Kd (N=61)**	**IKd (N=98)**	**Treat.-by-subgroup[b]**
MRD negativity rate					
MRD positive rate or missing	52 (83.9)	52 (64.2)	55 (90.2)	74 (75.5)	
95% CI[a]	(0.7233 to 0.9198)	(0.5277 to 0.7455)	(0.7981 to 0.9630)	(0.6579 to 0.8364)	
MRD negativity rate	10 (16.1)	29 (35.8)	6 (9.8)	24 (24.5)	
95% CI[a]	(0.0802 to 0.2767)	(0.2545 to 0.4723)	(0.0370 to 0.2019)	(0.1636 to 0.3421)	
Risk ratio 95% CI vs Kd[b]	-	2.22 (1.170 to 4.213)	-	2.49 (1.076 to 5.761)	
P-value [b]	-	0.0149	-	0.0332	
P-value heterogeneity[b]					0.8307
Odds ratio 95% CI vs Kd[b]	-	2.90 (1.279 to 6.574)	-	2.97 (1.134 to 7.797)	
P-value [b]	-	0.0110	-	0.0269	
P-value heterogeneity[b]					0.9692
Percent difference 95% CI vs Kd(%)[b]	-	19.67 (5.731 to 33.616)	-	14.65 (3.279 to 26.029)	
P-value [b]	-	0.0058	-	0.0117	
P-value heterogeneity[b]					0.5834

CI: Confidence interval, IRC: Independent Response Committee
[a] Estimated using Clopper-Pearson method.
[b] Estimation, CI and P-value are calculated from PROC GLIMMIX procedure and a model with treatment, subgroup variables and the treatment-by-subgroup interaction as covariates.
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16.2.6.7 Secondary efficacy endpoints - MRD
16.2.6.7.1 ITT population
16.2.6.7.1.17 Subgroup analyses by previous treatment with PI and IMiD
16.2.6.7.1.17.1 Summary of MRD negativity rate as per IRC - 2-sided p-value according to previous treatment with PI and IMiD - ITT population

	Yes		No		
	Kd (N=17)	**IKd (N=23)**	**Kd (N=106)**	**IKd (N=156)**	**Treat.-by-subgroup[b]**
MRD negativity rate					
MRD positive rate or missing	13 (76.5)	13 (56.5)	94 (88.7)	113 (72.4)	
95% CI[a]	(0.5010 to 0.9319)	(0.3449 to 0.7681)	(0.8106 to 0.9401)	(0.6472 to 0.7928)	
MRD negativity rate	4 (23.5)	10 (43.5)	12 (11.3)	43 (27.6)	
95% CI[a]	(0.0681 to 0.4990)	(0.2319 to 0.6551)	(0.0599 to 0.1894)	(0.2072 to 0.3528)	
Risk ratio 95% CI vs Kd[b]	-	1.85 (0.694 to 4.921)	-	2.43 (1.346 to 4.405)	
P-value [b]	-	0.2183	-	0.0034	
P-value heterogeneity[b]					0.6357
Odds ratio 95% CI vs Kd[b]	-	2.50 (0.618 to 10.107)	-	2.98 (1.482 to 5.995)	
P-value [b]	-	0.1977	-	0.0023	
P-value heterogeneity[b]					0.8247
Percent difference 95% CI vs Kd(%)[b]	-	19.95 (-8.751 to 48.649)	-	16.24 (6.956 to 25.530)	
P-value [b]	-	0.1724	-	0.0007	
P-value heterogeneity[b]					0.8091

CI: Confidence interval, IRC: Independent Response Committee
[a] Estimated using Clopper-Pearson method.
[b] Estimation, CI and P-value are calculated from PROC GLIMMIX procedure and a model with treatment, subgroup variables and the treatment-by-subgroup interaction as covariates.
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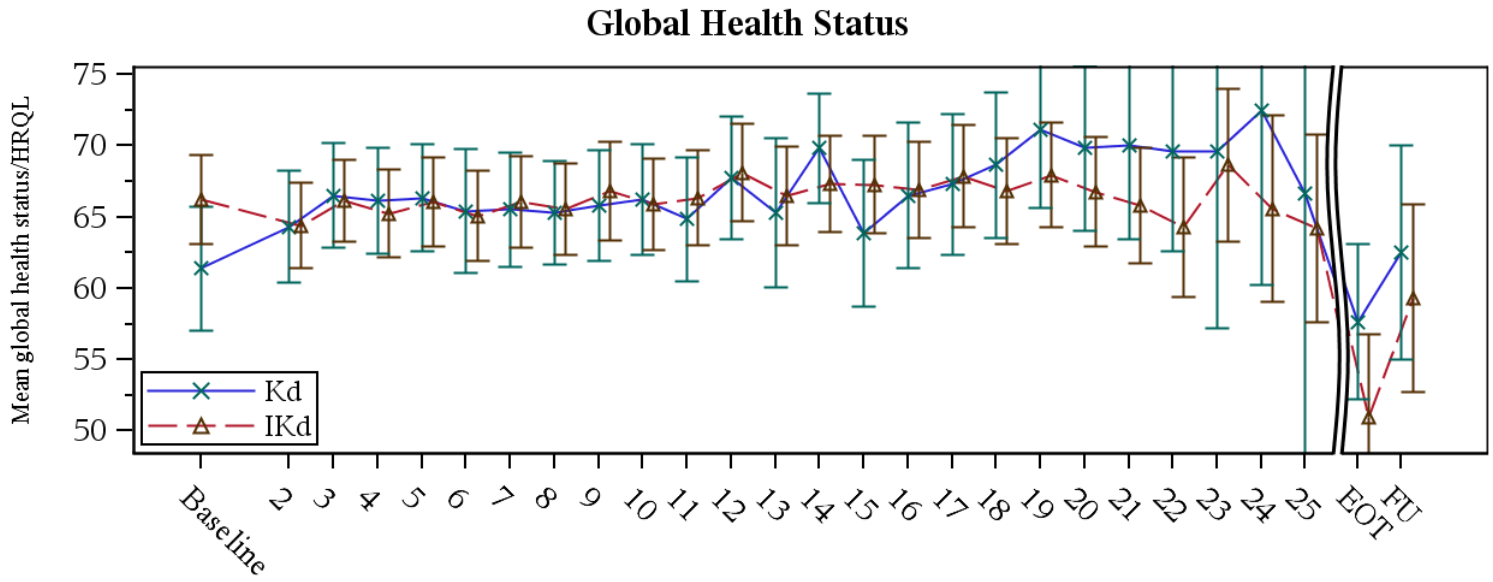
16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Global health status
16.2.6.1.2.1 Efficacy response data
16.2.6.1.2.1.1 QLQ-C30 - Mean and 95% CI for global health status score over time (LOCF) - ITT population



#patients																									
Kd	112	114	112	110	104	100	95	91	88	84	78	72	67	66	62	57	52	50	45	37	30	23	17	10	6	62	34
IKd	166	169	168	164	161	155	150	145	138	133	130	127	121	118	112	109	105	102	97	91	78	56	38	23	17	59	34

A higher score represents a better level of quality of life. Cycles with less than 20 patients overall are not presented.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
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16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Global health status
16.2.6.1.2.1 Efficacy response data
16.2.6.1.2.1.15 QLQ-C30 - Time to first improvement by 15 pt in Global health status (LOCF) - ITT population

First improvement 15 points Global health status	**Kd (N=123)**	**IKd (N=179)**
Number (%) of events	61 (49.6)	92 (51.4)
Number (%) of patients censored	62 (50.4)	87 (48.6)
Kaplan-Meier estimates of Global health status in months		
25% quantile (95% CI)	1.87 (1.051 to 2.004)	1.91 (1.150 to 2.103)
Median (95% CI)	16.16 (4.205 to NC)	15.11 (4.797 to NC)
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)
Comparison vs. Kd		
Stratified[a] Log-Rank test p-value[b] vs Kd	-	0.8581
Stratified[a] Hazard ratio (95% CI) vs Kd	-	1.03 (0.74 to 1.43)
P-value	-	0.8585
Improvement probability (95% CI)[c]		
3 Months	0.392 (0.304 to 0.478)	0.367 (0.296 to 0.438)
6 Months	0.452 (0.361 to 0.539)	0.450 (0.375 to 0.522)

A lower score represents a better level of quality of life. Clinical meaningful improvement change from baseline less than or equal to -15 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] Stratified on number of prior lines of therapy (1 vs. >1) and Revised International Staging System (R-ISS) stage (I or II vs. III vs. not classified) according to IRT
[b] One-sided significance level is 0.025
[c] Estimated using the Kaplan-Meier method
NA/NC = Not Applicable / Not Calculable
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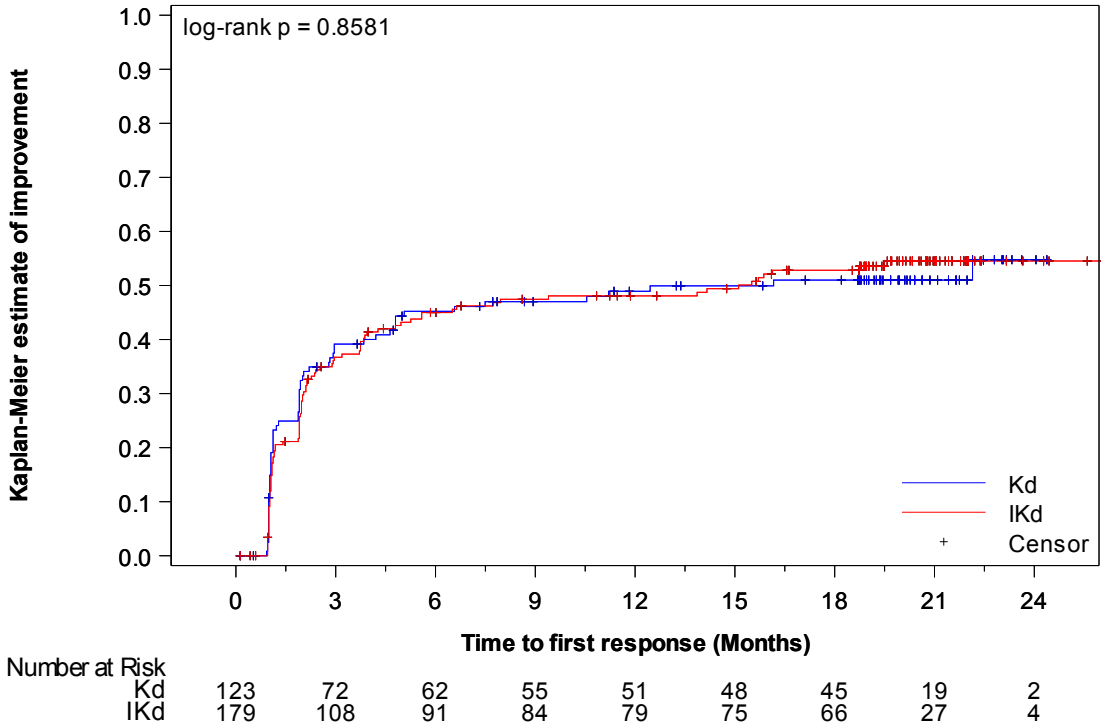
16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Global health status
16.2.6.1.2.1 Efficacy response data
16.2.6.1.2.1.16 QLQ-C30 - Time to first improvement by 15 pt in Global health status - Kaplan-Meier curve (LOCF) - ITT population



A lower score represents a better level of quality of life. Clinical meaningful improvement change from baseline less than or equal to -15 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
PGM=DEVOPS/SAR650984/EFC15246/CIR_RWE/REPORT/PGM/eff_qlq_km_i_f.sas OUT=REPORT/OUTPUT/eff_km_c30_glb_imp15l_de_i_f_x.rtf (07APR2021 14:23)

16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Global health status
16.2.6.1.2.1 Efficacy response data
16.2.6.1.2.1.17 QLQ-C30 - Time to first deterioration by 15 pt in Global health status (LOCF) - ITT population

First deterioration 15 points Global health status	**Kd (N=123)**	**IKd (N=179)**
Number (%) of events	71 (57.7)	115 (64.2)
Number (%) of patients censored	52 (42.3)	64 (35.8)
Kaplan-Meier estimates of Global health status in months		
25% quantile (95% CI)	2.00 (1.216 to 2.825)	1.87 (1.117 to 1.971)
Median (95% CI)	5.82 (3.844 to 13.536)	5.91 (3.778 to 10.875)
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)
Comparison vs. Kd		
Stratified[a] Log-Rank test p-value[b] vs Kd	-	0.2552
Stratified[a] Hazard ratio (95% CI) vs Kd	-	1.19 (0.88 to 1.61)
P-value	-	0.2558
Deterioration probability (95% CI)[c]		
3 Months	0.641 (0.548 to 0.720)	0.628 (0.551 to 0.695)
6 Months	0.495 (0.402 to 0.581)	0.499 (0.423 to 0.571)

A lower score represents a better level of quality of life. Clinical meaningful deterioration change from baseline greater than or equal to 15 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] Stratified on number of prior lines of therapy (1 vs. >1) and Revised International Staging System (R-ISS) stage (I or II vs. III vs. not classified) according to IRT
[b] One-sided significance level is 0.025
[c] Estimated using the Kaplan-Meier method
NA/NC = Not Applicable / Not Calculable
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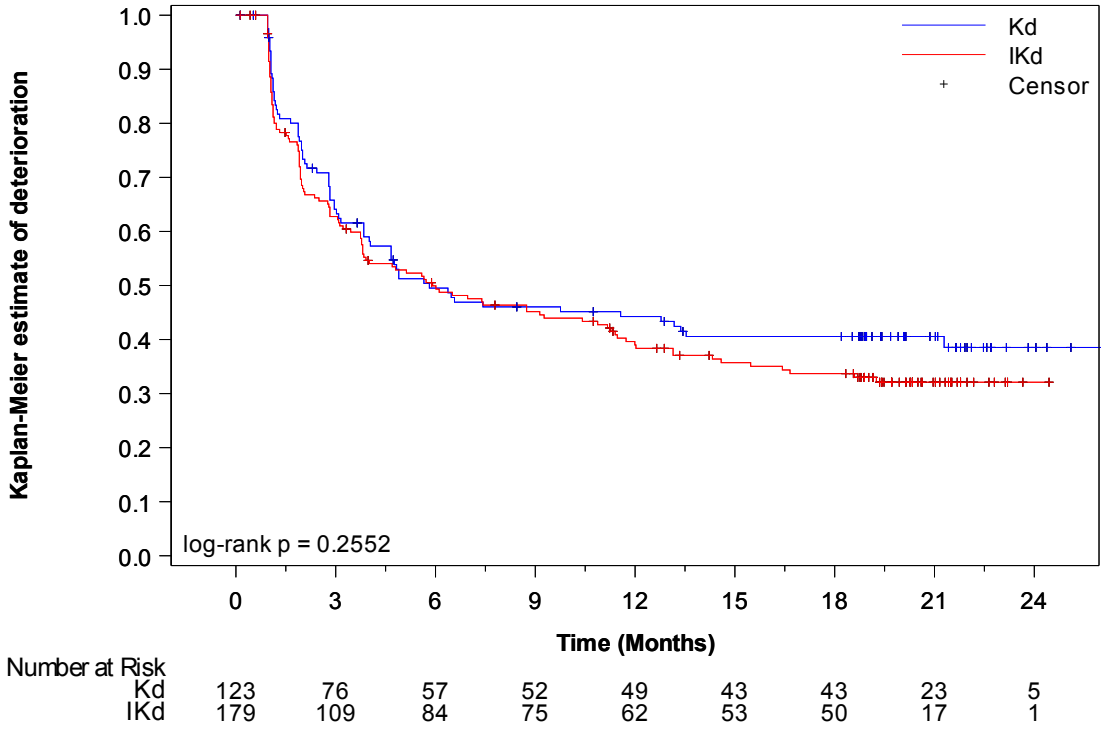
16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Global health status
16.2.6.1.2.1 Efficacy response data
16.2.6.1.2.1.18 QLQ-C30 - Time to first deterioration by 15 pt in Global health status - Kaplan-Meier curve (LOCF) - ITT population



A lower score represents a better level of quality of life. Clinical meaningful deterioration change from baseline greater than or equal to 15 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
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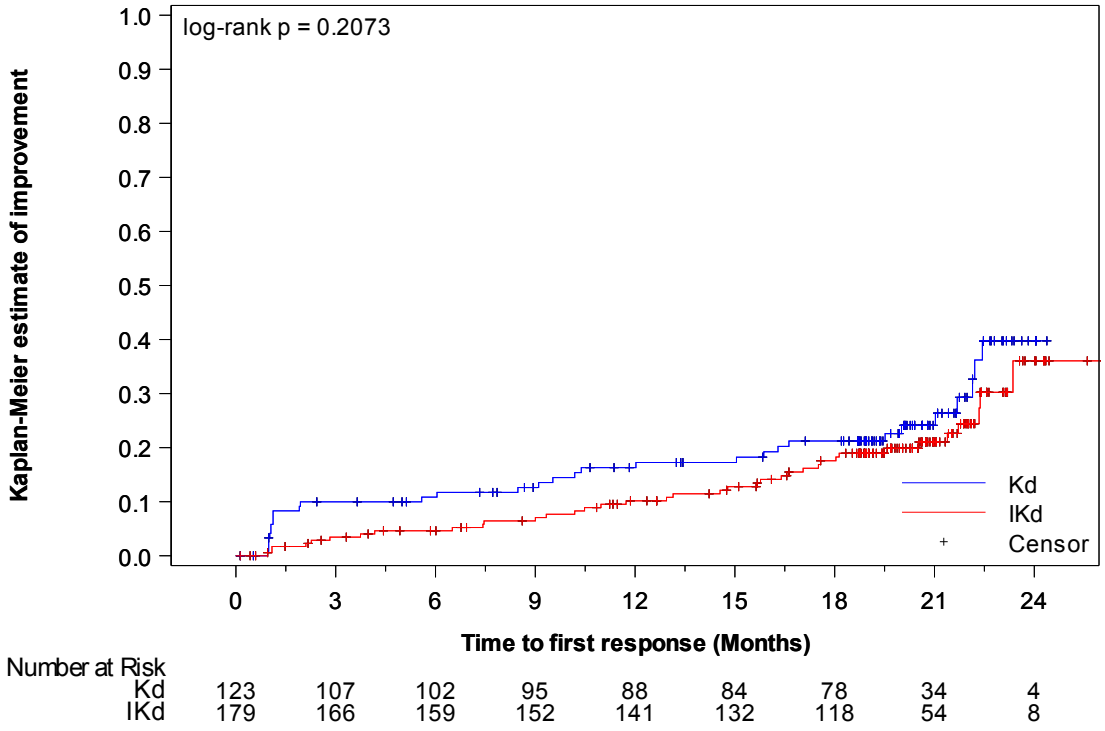
16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Global health status
16.2.6.1.2.1 Efficacy response data
16.2.6.1.2.1.19 QLQ-C30 - Time until permanent improvement by 15 pt in Global health status (LOCF) - ITT population

First permanent improvement 15 points Global health status	**Kd (N=123)**	**IKd (N=179)**
Number (%) of events	31 (25.2)	37 (20.7)
Number (%) of patients censored	92 (74.8)	142 (79.3)
Kaplan-Meier estimates of Global health status in months		
25% quantile (95% CI)	21.03 (12.025 to 22.439)	22.34 (18.037 to NC)
Median (95% CI)	NC (22.209 to NC)	NC (23.359 to NC)
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)
Comparison vs. Kd		
Stratified[a] Log-Rank test p-value[b] vs Kd	-	0.2073
Stratified[a] Hazard ratio (95% CI) vs Kd	-	0.74 (0.46 to 1.19)
P-value	-	0.2090
Improvement probability (95% CI)[c]		
3 Months	0.100 (0.054 to 0.161)	0.034 (0.014 to 0.069)
6 Months	0.108 (0.061 to 0.172)	0.046 (0.022 to 0.085)

A lower score represents a better level of quality of life. Clinical meaningful improvement change from baseline less than or equal to -15 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] Stratified on number of prior lines of therapy (1 vs. >1) and Revised International Staging System (R-ISS) stage (I or II vs. III vs. not classified) according to IRT
[b] One-sided significance level is 0.025
[c] Estimated using the Kaplan-Meier method
NA/NC = Not Applicable / Not Calculable
PGM=DEVOPS/SAR650984/EFC15246/CIR_RWE/REPORT/PGM/eff_km_invhr_sr_i_t.sas OUT=REPORT/OUTPUT/eff_km_c30_glb_imp15pl_de_i_t_x.rtf (07APR2021 14:22)

16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Global health status
16.2.6.1.2.1 Efficacy response data
16.2.6.1.2.1.20 QLQ-C30 - Time until permanent improvement by 15 pt in Global health status - Kaplan-Meier curve (LOCF) - ITT population



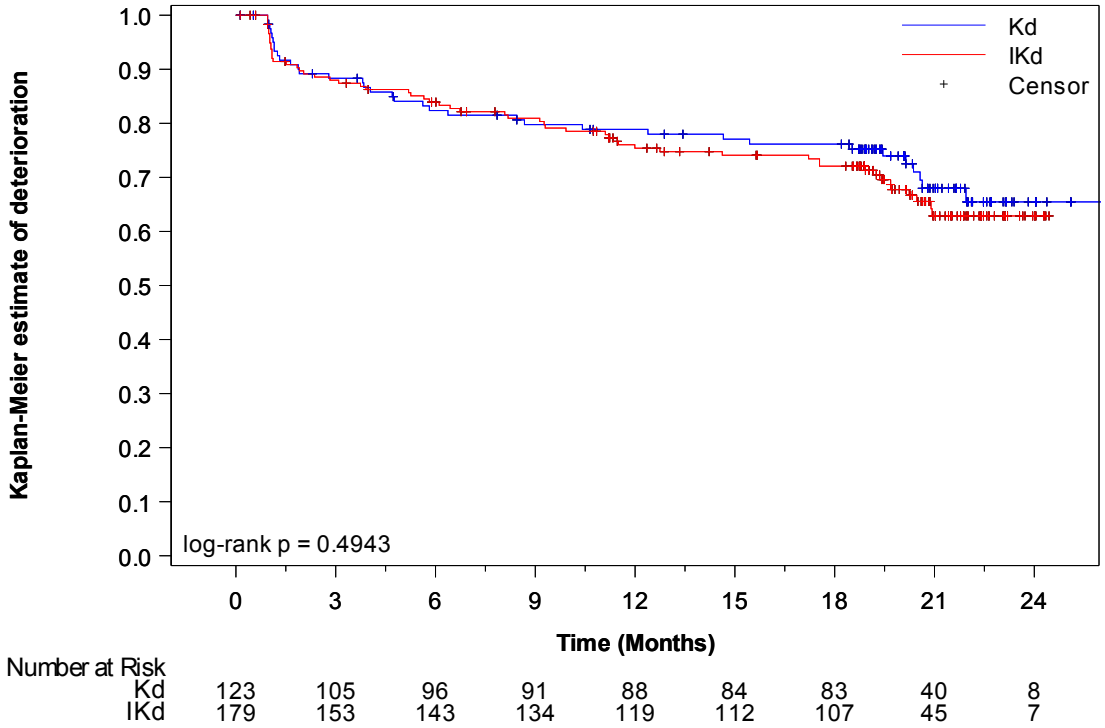
A lower score represents a better level of quality of life. Clinical meaningful improvement change from baseline less than or equal to -15 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
PGM=DEVOPS/SAR650984/EFC15246/CIR_RWE/REPORT/PGM/eff_qlq_km_i_f.sas OUT=REPORT/OUTPUT/eff_km_c30_glb_imp15pl_de_i_f_x.rtf (07APR2021 14:23)

16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Global health status
16.2.6.1.2.1 Efficacy response data
16.2.6.1.2.1.21 QLQ-C30 - Time until permanent deterioration by 15 pt in Global health status (LOCF) - ITT population

First permanent deterioration 15 points Global health status	**Kd (N=123)**	**IKd (N=179)**
Number (%) of events	35 (28.5)	56 (31.3)
Number (%) of patients censored	88 (71.5)	123 (68.7)
Kaplan-Meier estimates of Global health status in months		
25% quantile (95% CI)	19.45 (5.815 to 21.947)	12.75 (8.082 to 19.713)
Median (95% CI)	NC (NC to NC)	NC (NC to NC)
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)
Comparison vs. Kd		
Stratified[a] Log-Rank test p-value[b] vs Kd	-	0.4943
Stratified[a] Hazard ratio (95% CI) vs Kd	-	1.16 (0.76 to 1.78)
P-value	-	0.4947
Deterioration probability (95% CI)[c]		
3 Months	0.883 (0.811 to 0.929)	0.880 (0.822 to 0.920)
6 Months	0.824 (0.742 to 0.881)	0.839 (0.776 to 0.886)

A lower score represents a better level of quality of life. Clinical meaningful deterioration change from baseline greater than or equal to 15 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] Stratified on number of prior lines of therapy (1 vs. >1) and Revised International Staging System (R-ISS) stage (I or II vs. III vs. not classified) according to IRT
[b] One-sided significance level is 0.025
[c] Estimated using the Kaplan-Meier method
NA/NC = Not Applicable / Not Calculable
PGM=DEVOPS/SAR650984/EFC15246/CIR_RWE/REPORT/PGM/eff_km_invhr_sr_i_t.sas OUT=REPORT/OUTPUT/eff_km_c30_glb_det15pl_de_i_t_x.rtf (07APR2021 14:22)

16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Global health status
16.2.6.1.2.1 Efficacy response data
16.2.6.1.2.1.22 QLQ-C30 - Time until permanent deterioration by 15 pt in Global health status - Kaplan-Meier curve (LOCF) - ITT population



A lower score represents a better level of quality of life. Clinical meaningful deterioration change from baseline greater than or equal to 15 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
PGM=DEVOPS/SAR650984/EFC15246/CIR_RWE/REPORT/PGM/eff_qlq_km_i_f.sas OUT=REPORT/OUTPUT/eff_km_c30_glb_det15pl_de_i_f_x.rtf (07APR2021 14:23)

16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Global health status
16.2.6.1.2.2 Efficacy response data - Subgroup analyses by age
16.2.6.1.2.2.3 QLQ-C30 - Time to first improvement by 10 pt in global health status according to age (LOCF) - ITT population

	<65 years		>=65 years		
	Kd (N=66)	**IKd (N=88)**	**Kd (N=57)**	**IKd (N=91)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	35 (53.0)	45 (51.1)	26 (45.6)	47 (51.6)	0.5746
Number (%) of patients censored	31 (47.0)	43 (48.9)	31 (54.4)	44 (48.4)	
Kaplan-Meier estimates of Global health status in months					
25% quantile (95% CI)	1.12 (1.018 to 1.906)	1.18 (1.018 to 2.004)	1.94 (1.051 to 4.205)	2.00 (1.150 to 3.187)	
Median (95% CI)	11.20 (1.938 to NC)	14.16 (2.366 to NC)	NC (4.205 to NC)	15.51 (4.271 to NC)	
75% quantile (95% CI)	NC (22.144 to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.7790		0.6437	
Hazard ratio (95% CI) vs Kd	-	0.94 (0.60 to 1.46)		1.12 (0.69 to 1.81)	
P-value	-	0.7780		0.6439	
Improvement probability (95% CI)[b]					

A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
PGM=DEVOPS/SAR650984/EFC15246/CIR_RWE/REPORT/PGM/eff_km_subgp_sr_sig_de_i_t.sas OUT=REPORT/OUTPUT/eff_km_c30_glb_impl_age_de_i_t_x.rtf (07APR2021 14:20)

16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Global health status
16.2.6.1.2.2 Efficacy response data - Subgroup analyses by age
16.2.6.1.2.2.4 QLQ-C30 - Time to first deterioration by 10 pt in global health status according to age (LOCF) - ITT population

	<65 years		>=65 years		
	Kd (N=66)	**IKd (N=88)**	**Kd (N=57)**	**IKd (N=91)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	33 (50.0)	56 (63.6)	38 (66.7)	59 (64.8)	0.1751
Number (%) of patients censored	33 (50.0)	32 (36.4)	19 (33.3)	32 (35.2)	
Kaplan-Meier estimates of Global health status in months					
25% quantile (95% CI)	2.79 (1.643 to 3.844)	1.91 (1.084 to 2.825)	1.31 (1.051 to 2.431)	1.86 (1.084 to 2.004)	
Median (95% CI)	13.17 (3.844 to NC)	5.72 (3.778 to 11.729)	4.67 (2.431 to 7.425)	6.01 (3.055 to 11.466)	
75% quantile (95% CI)	NC (NC to NC)	NC (14.587 to NC)	NC (7.425 to NC)	NC (16.427 to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.1122		0.7946	
Hazard ratio (95% CI) vs Kd	-	1.41 (0.92 to 2.18)		0.95 (0.63 to 1.42)	
P-value	-	0.1140		0.7934	
Deterioration probability (95% CI)[b]					

A higher score represents a better level of quality of life. Clinical meaningful deterioration change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
PGM=DEVOPS/SAR650984/EFC15246/CIR_RWE/REPORT/PGM/eff_km_subgp_sr_sig_de_i_t.sas OUT=REPORT/OUTPUT/eff_km_c30_glb_detl_age_de_i_t_x.rtf (07APR2021 14:20)

16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Global health status
16.2.6.1.2.2 Efficacy response data - Subgroup analyses by age
16.2.6.1.2.2.5 QLQ-C30 - Time until permanent improvement by 10 pt in global health status according to age (LOCF) - ITT population

	<65 years		>=65 years		
	Kd (N=66)	**IKd (N=88)**	**Kd (N=57)**	**IKd (N=91)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	20 (30.3)	17 (19.3)	11 (19.3)	20 (22.0)	0.1993
Number (%) of patients censored	46 (69.7)	71 (80.7)	46 (80.7)	71 (78.0)	
Kaplan-Meier estimates of Global health status in months					
25% quantile (95% CI)	12.02 (5.585 to 22.439)	22.34 (14.554 to NC)	21.68 (16.624 to NC)	21.72 (17.511 to NC)	
Median (95% CI)	NC (22.144 to NC)	NC (NC to NC)	NC (22.209 to NC)	NC (23.359 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.1066		0.7984	
Hazard ratio (95% CI) vs Kd	-	0.59 (0.31 to 1.13)		1.10 (0.53 to 2.30)	
P-value	-	0.1107		0.7985	
Improvement probability (95% CI)[b]					

A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
PGM=DEVOPS/SAR650984/EFC15246/CIR_RWE/REPORT/PGM/eff_km_subgp_sr_sig_de_i_t.sas OUT=REPORT/OUTPUT/eff_km_c30_glb_imppl_age_de_i_t_x.rtf (07APR2021 14:21)

16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Global health status
16.2.6.1.2.2 Efficacy response data - Subgroup analyses by age
16.2.6.1.2.2.6 QLQ-C30 - Time until permanent deterioration by 10 pt in global health status according to age (LOCF) - ITT population

	<65 years		>=65 years		
	Kd (N=66)	**IKd (N=88)**	**Kd (N=57)**	**IKd (N=91)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	17 (25.8)	27 (30.7)	18 (31.6)	29 (31.9)	0.6384
Number (%) of patients censored	49 (74.2)	61 (69.3)	39 (68.4)	62 (68.1)	
Kaplan-Meier estimates of Global health status in months					
25% quantile (95% CI)	20.37 (5.618 to NC)	12.75 (6.111 to 20.928)	15.44 (3.811 to NC)	14.62 (5.257 to 20.468)	
Median (95% CI)	NC (21.947 to NC)	NC (NC to NC)	NC (20.567 to NC)	NC (20.895 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.4585		0.9217	
Hazard ratio (95% CI) vs Kd	-	1.26 (0.69 to 2.31)		1.03 (0.57 to 1.85)	
P-value	-	0.4595		0.9220	
Deterioration probability (95% CI)[b]					

A higher score represents a better level of quality of life. Clinical meaningful deterioration change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
PGM=DEVOPS/SAR650984/EFC15246/CIR_RWE/REPORT/PGM/eff_km_subgp_sr_sig_de_i_t.sas OUT=REPORT/OUTPUT/eff_km_c30_glb_detpl_age_de_i_t_x.rtf (07APR2021 14:21)

16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Global health status
16.2.6.1.2.3 Efficacy response data - Subgroup analyses by gender
16.2.6.1.2.3.3 QLQ-C30 - Time to first improvement by 10 pt in global health status according to gender (LOCF) - ITT population

	Male		Female		
	Kd (N=68)	**IKd (N=101)**	**Kd (N=55)**	**IKd (N=78)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	27 (39.7)	51 (50.5)	34 (61.8)	41 (52.6)	0.0724
Number (%) of patients censored	41 (60.3)	50 (49.5)	21 (38.2)	37 (47.4)	
Kaplan-Meier estimates of Global health status in months					
25% quantile (95% CI)	2.00 (1.117 to 6.571)	1.91 (1.084 to 2.530)	1.05 (1.018 to 1.906)	1.97 (1.051 to 2.366)	
Median (95% CI)	NC (12.452 to NC)	15.87 (4.961 to NC)	3.40 (1.906 to 11.203)	7.72 (3.187 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (11.203 to NC)	NC (NC to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.1934		0.2033	
Hazard ratio (95% CI) vs Kd	-	1.36 (0.85 to 2.18)		0.75 (0.47 to 1.17)	
P-value	-	0.1951		0.2050	
Improvement probability (95% CI)[b]					

A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
PGM=DEVOPS/SAR650984/EFC15246/CIR_RWE/REPORT/PGM/eff_km_subgp_sr_sig_de_i_t.sas OUT=REPORT/OUTPUT/eff_km_c30_glb_impl_sex_de_i_t_x.rtf (07APR2021 14:21)

16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Global health status
16.2.6.1.2.3 Efficacy response data - Subgroup analyses by gender
16.2.6.1.2.3.4 QLQ-C30 - Time to first deterioration by 10 pt in global health status according to gender (LOCF) - ITT population

	Male		Female		
	Kd (N=68)	**IKd (N=101)**	**Kd (N=55)**	**IKd (N=78)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	44 (64.7)	67 (66.3)	27 (49.1)	48 (61.5)	0.4257
Number (%) of patients censored	24 (35.3)	34 (33.7)	28 (50.9)	30 (38.5)	
Kaplan-Meier estimates of Global health status in months					
25% quantile (95% CI)	2.00 (1.150 to 2.825)	1.51 (1.051 to 2.366)	1.91 (1.051 to 4.764)	1.94 (1.117 to 2.497)	
Median (95% CI)	4.04 (2.957 to 6.374)	5.13 (3.055 to 9.265)	21.29 (4.764 to NC)	9.13 (3.778 to 14.324)	
75% quantile (95% CI)	NC (7.425 to NC)	NC (14.587 to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.7989		0.2171	
Hazard ratio (95% CI) vs Kd	-	1.05 (0.72 to 1.54)		1.34 (0.84 to 2.16)	
P-value	-	0.7998		0.2188	
Deterioration probability (95% CI)[b]					

A higher score represents a better level of quality of life. Clinical meaningful deterioration change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
PGM=DEVOPS/SAR650984/EFC15246/CIR_RWE/REPORT/PGM/eff_km_subgp_sr_sig_de_i_t.sas OUT=REPORT/OUTPUT/eff_km_c30_glb_detl_sex_de_i_t_x.rtf (07APR2021 14:20)

16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Global health status
16.2.6.1.2.3 Efficacy response data - Subgroup analyses by gender
16.2.6.1.2.3.5 QLQ-C30 - Time until permanent improvement by 10 pt in global health status according to gender (LOCF) - ITT population

	Male		Female		
	Kd (N=68)	**IKd (N=101)**	**Kd (N=55)**	**IKd (N=78)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	11 (16.2)	20 (19.8)	20 (36.4)	17 (21.8)	0.0709
Number (%) of patients censored	57 (83.8)	81 (80.2)	35 (63.6)	61 (78.2)	
Kaplan-Meier estimates of Global health status in months					
25% quantile (95% CI)	22.14 (20.008 to NC)	21.72 (16.394 to NC)	15.05 (1.906 to 21.027)	22.37 (17.051 to NC)	
Median (95% CI)	NC (22.144 to NC)	NC (NC to NC)	22.44 (21.027 to NC)	NC (23.359 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.5839		0.0278	
Hazard ratio (95% CI) vs Kd	-	1.23 (0.59 to 2.56)		0.49 (0.25 to 0.94)	
P-value	-	0.5846		0.0313	
Improvement probability (95% CI)[b]					

A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
PGM=DEVOPS/SAR650984/EFC15246/CIR_RWE/REPORT/PGM/eff_km_subgp_sr_sig_de_i_t.sas OUT=REPORT/OUTPUT/eff_km_c30_glb_imppl_sex_de_i_t_x.rtf (07APR2021 14:21)

16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Global health status
16.2.6.1.2.3 Efficacy response data - Subgroup analyses by gender
16.2.6.1.2.3.6 QLQ-C30 - Time until permanent deterioration by 10 pt in global health status according to gender (LOCF) - ITT population

	Male		Female		
	Kd (N=68)	**IKd (N=101)**	**Kd (N=55)**	**IKd (N=78)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	23 (33.8)	30 (29.7)	12 (21.8)	26 (33.3)	0.2033
Number (%) of patients censored	45 (66.2)	71 (70.3)	43 (78.2)	52 (66.7)	
Kaplan-Meier estimates of Global health status in months					
25% quantile (95% CI)	10.41 (3.844 to 20.370)	12.75 (3.910 to 20.895)	21.95 (4.698 to NC)	11.99 (6.439 to 20.468)	
Median (95% CI)	NC (20.370 to NC)	NC (NC to NC)	NC (NC to NC)	NC (20.928 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.7189		0.1640	
Hazard ratio (95% CI) vs Kd	-	0.91 (0.53 to 1.56)		1.62 (0.82 to 3.21)	
P-value	-	0.7190		0.1681	
Deterioration probability (95% CI)[b]					

A higher score represents a better level of quality of life. Clinical meaningful deterioration change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
PGM=DEVOPS/SAR650984/EFC15246/CIR_RWE/REPORT/PGM/eff_km_subgp_sr_sig_de_i_t.sas OUT=REPORT/OUTPUT/eff_km_c30_glb_detpl_sex_de_i_t_x.rtf (07APR2021 14:21)

16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Global health status
16.2.6.1.2.4 Efficacy response data - Subgroup analyses by ethnic origin
16.2.6.1.2.4.3 QLQ-C30 - Time to first improvement by 10 pt in global health status according to ethnic origin (LOCF) - ITT population

	White		Other		
	Kd (N=83)	**IKd (N=131)**	**Kd (N=28)**	**IKd (N=34)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	43 (51.8)	69 (52.7)	16 (57.1)	17 (50.0)	0.8155
Number (%) of patients censored	40 (48.2)	62 (47.3)	12 (42.9)	17 (50.0)	
Kaplan-Meier estimates of Global health status in months					
25% quantile (95% CI)	1.87 (1.018 to 1.938)	1.97 (1.117 to 2.136)	1.12 (1.018 to 2.924)	1.15 (0.953 to 3.745)	
Median (95% CI)	7.49 (2.825 to NC)	15.11 (3.877 to NC)	10.55 (1.117 to NC)	13.86 (1.906 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (12.452 to NC)	NC (NC to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.9014		0.7085	
Hazard ratio (95% CI) vs Kd	-	0.98 (0.67 to 1.43)		0.88 (0.44 to 1.74)	
P-value	-	0.9011		0.7087	
Improvement probability (95% CI)[b]					

A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
PGM=DEVOPS/SAR650984/EFC15246/CIR_RWE/REPORT/PGM/eff_km_subgp_sr_sig_de_i_t.sas OUT=REPORT/OUTPUT/eff_km_c30_glb_impl_race_de_i_t_x.rtf (07APR2021 14:21)

16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Global health status
16.2.6.1.2.4 Efficacy response data - Subgroup analyses by ethnic origin
16.2.6.1.2.4.4 QLQ-C30 - Time to first deterioration by 10 pt in global health status according to ethnic origin (LOCF) - ITT population

	White		Other		
	Kd (N=83)	**IKd (N=131)**	**Kd (N=28)**	**IKd (N=34)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	51 (61.4)	85 (64.9)	15 (53.6)	24 (70.6)	0.1989
Number (%) of patients censored	32 (38.6)	46 (35.1)	13 (46.4)	10 (29.4)	
Kaplan-Meier estimates of Global health status in months					
25% quantile (95% CI)	1.87 (1.117 to 2.793)	1.91 (1.117 to 2.760)	2.79 (1.051 to 3.023)	1.13 (0.986 to 1.906)	
Median (95% CI)	4.90 (3.844 to 12.780)	6.51 (3.811 to 11.170)	5.65 (2.825 to NC)	2.94 (1.840 to 11.269)	
75% quantile (95% CI)	NC (21.290 to NC)	NC (18.595 to NC)	NC (13.175 to NC)	14.59 (3.811 to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.7082		0.1066	
Hazard ratio (95% CI) vs Kd	-	1.07 (0.75 to 1.51)		1.69 (0.89 to 3.23)	
P-value	-	0.7083		0.1107	
Deterioration probability (95% CI)[b]					

A higher score represents a better level of quality of life. Clinical meaningful deterioration change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
PGM=DEVOPS/SAR650984/EFC15246/CIR_RWE/REPORT/PGM/eff_km_subgp_sr_sig_de_i_t.sas OUT=REPORT/OUTPUT/eff_km_c30_glb_detl_race_de_i_t_x.rtf (07APR2021 14:20)

16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Global health status
16.2.6.1.2.4 Efficacy response data - Subgroup analyses by ethnic origin
16.2.6.1.2.4.5 QLQ-C30 - Time until permanent improvement by 10 pt in global health status according to ethnic origin (LOCF) - ITT population

	White		Other		
	Kd (N=83)	**IKd (N=131)**	**Kd (N=28)**	**IKd (N=34)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	21 (25.3)	29 (22.1)	8 (28.6)	7 (20.6)	0.7237
Number (%) of patients censored	62 (74.7)	102 (77.9)	20 (71.4)	27 (79.4)	
Kaplan-Meier estimates of Global health status in months					
25% quantile (95% CI)	21.68 (12.025 to 22.439)	21.72 (17.511 to NC)	19.52 (1.051 to NC)	22.34 (6.505 to NC)	
Median (95% CI)	NC (22.144 to NC)	NC (23.359 to NC)	NC (20.008 to NC)	NC (22.341 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.5009		0.5122	
Hazard ratio (95% CI) vs Kd	-	0.82 (0.47 to 1.45)		0.71 (0.26 to 1.97)	
P-value	-	0.5016		0.5142	
Improvement probability (95% CI)[b]					

A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Global health status
16.2.6.1.2.4 Efficacy response data - Subgroup analyses by ethnic origin
16.2.6.1.2.4.6 QLQ-C30 - Time until permanent deterioration by 10 pt in global health status according to ethnic origin (LOCF) - ITT population

	White		Other		
	Kd (N=83)	**IKd (N=131)**	**Kd (N=28)**	**IKd (N=34)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	26 (31.3)	40 (30.5)	6 (21.4)	11 (32.4)	0.2934
Number (%) of patients censored	57 (68.7)	91 (69.5)	22 (78.6)	23 (67.6)	
Kaplan-Meier estimates of Global health status in months					
25% quantile (95% CI)	18.53 (4.698 to 21.947)	12.75 (8.181 to 20.468)	NC (1.117 to NC)	4.55 (1.018 to NC)	
Median (95% CI)	NC (21.947 to NC)	NC (NC to NC)	NC (NC to NC)	NC (17.544 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.9734		0.2759	
Hazard ratio (95% CI) vs Kd	-	0.99 (0.61 to 1.62)		1.73 (0.64 to 4.68)	
P-value	-	0.9733		0.2819	
Deterioration probability (95% CI)[b]					

A higher score represents a better level of quality of life. Clinical meaningful deterioration change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
PGM=DEVOPS/SAR650984/EFC15246/CIR_RWE/REPORT/PGM/eff_km_subgp_sr_sig_de_i_t.sas OUT=REPORT/OUTPUT/eff_km_c30_glb_detpl_race_de_i_t_x.rtf (07APR2021 14:21)

16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Global health status
16.2.6.1.2.5 Efficacy response data - Subgroup analyses by geographical region
16.2.6.1.2.5.3 QLQ-C30 - Time to first improvement by 10 pt in global health status according to geographical region (LOCF) - ITT population

	Europe		America		Asia		Other countries		
	Kd (N=60)	**IKd (N=85)**	**Kd (N=20)**	**IKd (N=24)**	**Kd (N=21)**	**IKd (N=25)**	**Kd (N=22)**	**IKd (N=45)**	**p-value of treatment-by-subgroup interaction[c]**
Number (%) of events	27 (45.0)	41 (48.2)	12 (60.0)	12 (50.0)	13 (61.9)	14 (56.0)	9 (40.9)	25 (55.6)	0.4248
Number (%) of patients censored	33 (55.0)	44 (51.8)	8 (40.0)	12 (50.0)	8 (38.1)	11 (44.0)	13 (59.1)	20 (44.4)	
Kaplan-Meier estimates of event in months									
25% quantile (95% CI)	1.91 (1.018 to 2.004)	1.91 (1.150 to 3.187)	1.02 (0.920 to 1.906)	2.00 (0.953 to 7.721)	1.12 (0.986 to 2.037)	1.12 (0.953 to 3.745)	4.80 (1.018 to 22.144)	1.91 (1.018 to 2.136)	
Median (95% CI)	NC (2.793 to NC)	16.13 (3.943 to NC)	4.85 (0.986 to NC)	7.95 (2.366 to NC)	2.92 (1.117 to NC)	9.72 (1.150 to NC)	22.14 (4.797 to NC)	6.64 (2.004 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (7.491 to NC)	NC (18.760 to NC)	NC (2.957 to NC)	NC (13.864 to NC)	NC (22.144 to NC)	NC (NC to NC)	

A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Global health status
16.2.6.1.2.5 Efficacy response data - Subgroup analyses by geographical region
16.2.6.1.2.5.3 QLQ-C30 - Time to first improvement by 10 pt in global health status according to geographical region (LOCF) - ITT population

	Europe		America		Asia		Other countries		
	Kd (N=60)	**IKd (N=85)**	**Kd (N=20)**	**IKd (N=24)**	**Kd (N=21)**	**IKd (N=25)**	**Kd (N=22)**	**IKd (N=45)**	**p-value of treatment-by-subgroup interaction[c]**
Comparison vs. Kd									
Log-Rank test p-value[a] vs Kd	-	0.9571		0.4514		0.5517		0.1618	
Hazard ratio (95% CI) vs Kd	-	1.01 (0.62 to 1.65)		0.74 (0.33 to 1.64)		0.79 (0.37 to 1.70)		1.71 (0.80 to 3.67)	
P-value	-	0.9571		0.4532		0.5525		0.1671	
Improvement probability (95% CI)[b]									
3 Months	0.378 (0.255 to 0.500)	0.338 (0.239 to 0.440)	0.500 (0.271 to 0.692)	0.402 (0.204 to 0.594)	0.560 (0.318 to 0.746)	0.375 (0.190 to 0.560)	0.182 (0.057 to 0.363)	0.400 (0.258 to 0.538)	

A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Global health status
16.2.6.1.2.5 Efficacy response data - Subgroup analyses by geographical region
16.2.6.1.2.5.4 QLQ-C30 - Time to first deterioration by 10 pt in global health status according to geographical region (LOCF) - ITT population

	Europe		America		Asia		Other countries		
	Kd (N=60)	**IKd (N=85)**	**Kd (N=20)**	**IKd (N=24)**	**Kd (N=21)**	**IKd (N=25)**	**Kd (N=22)**	**IKd (N=45)**	**p-value of treatment-by-subgroup interaction[c]**
Number (%) of events	29 (48.3)	52 (61.2)	13 (65.0)	14 (58.3)	9 (42.9)	18 (72.0)	20 (90.9)	31 (68.9)	0.0428
Number (%) of patients censored	31 (51.7)	33 (38.8)	7 (35.0)	10 (41.7)	12 (57.1)	7 (28.0)	2 (9.1)	14 (31.1)	
Kaplan-Meier estimates of event in months									
25% quantile (95% CI)	2.83 (1.643 to 4.895)	1.94 (1.084 to 3.745)	1.51 (0.953 to 2.825)	1.91 (1.084 to 3.450)	2.48 (1.051 to 13.175)	1.12 (0.986 to 1.906)	1.18 (0.986 to 2.793)	1.31 (1.018 to 2.004)	
Median (95% CI)	13.37 (4.895 to NC)	10.87 (5.717 to 15.474)	3.06 (1.051 to NC)	3.81 (1.906 to NC)	NC (2.004 to NC)	2.43 (1.117 to 11.269)	3.32 (1.183 to 4.830)	4.80 (1.971 to 14.587)	
75% quantile (95% CI)	NC (NC to NC)	NC (19.253 to NC)	NC (3.088 to NC)	NC (3.811 to NC)	NC (NC to NC)	13.14 (3.121 to NC)	5.65 (3.844 to 21.290)	NC (7.392 to NC)	

A higher score represents a better level of quality of life. Clinical meaningful deterioration change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Global health status
16.2.6.1.2.5 Efficacy response data - Subgroup analyses by geographical region
16.2.6.1.2.5.4 QLQ-C30 - Time to first deterioration by 10 pt in global health status according to geographical region (LOCF) - ITT population

	Europe		America		Asia		Other countries		
	Kd (N=60)	**IKd (N=85)**	**Kd (N=20)**	**IKd (N=24)**	**Kd (N=21)**	**IKd (N=25)**	**Kd (N=22)**	**IKd (N=45)**	**p-value of treatment-by-subgroup interaction[c]**
Comparison vs. Kd									
Log-Rank test p-value[a] vs Kd	-	0.2405		0.6815		0.0406		0.1078	
Hazard ratio (95% CI) vs Kd	-	1.31 (0.83 to 2.07)		0.85 (0.40 to 1.82)		2.27 (1.01 to 5.06)		0.63 (0.36 to 1.11)	
P-value	-	0.2419		0.6818		0.0462		0.1107	
Hazard ratio inverted (95% CI) vs IKd		-		1.17 (0.55 to 2.50)		0.44 (0.20 to 0.99)		1.59 (0.90 to 2.80)	
Deterioration probability (95% CI)[b]									
3 Months	0.724 (0.589 to 0.821)	0.699 (0.588 to 0.785)	0.550 (0.313 to 0.735)	0.595 (0.365 to 0.765)	0.650 (0.403 to 0.815)	0.458 (0.256 to 0.640)	0.500 (0.282 to 0.684)	0.600 (0.443 to 0.726)	

A higher score represents a better level of quality of life. Clinical meaningful deterioration change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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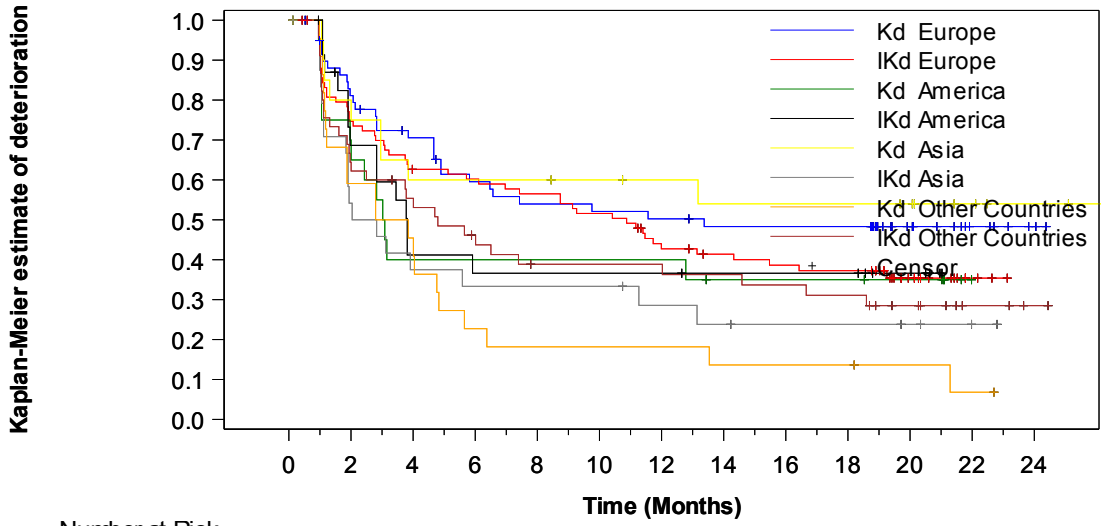
16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Global health status
16.2.6.1.2.5 Efficacy response data - Subgroup analyses by geographical region
16.2.6.1.2.5.5 QLQ-C30 - Time to first deterioration by 10 pt in global health status according to geographical region- Kaplan-Meier curve (LOCF) - ITT population



Number at Risk									
Kd Europe	60	41	32	29	27	25	25	10	2
IKd Europe	85	58	49	44	33	29	27	8	0
Kd America	20	11	8	8	8	6	6	5	0
IKd America	24	13	8	8	8	7	7	1	0
Kd Asia	21	13	12	11	10	9	9	6	3
IKd Asia	25	11	8	8	6	4	4	2	0
Kd Other Countries	22	11	5	4	4	3	3	2	0
IKd Other Countries	45	27	19	15	15	13	12	6	1

A higher score represents a better level of quality of life. Clinical meaningful deterioration change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
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16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Global health status
16.2.6.1.2.5 Efficacy response data - Subgroup analyses by geographical region
16.2.6.1.2.5.6 QLQ-C30 - Time until permanent improvement by 10 pt in global health status according to geographical region (LOCF) - ITT population

	Europe		America		Asia		Other countries		
	Kd (N=60)	**IKd (N=85)**	**Kd (N=20)**	**IKd (N=24)**	**Kd (N=21)**	**IKd (N=25)**	**Kd (N=22)**	**IKd (N=45)**	**p-value of treatment-by-subgroup interaction[c]**
Number (%) of events	10 (16.7)	16 (18.8)	6 (30.0)	3 (12.5)	8 (38.1)	6 (24.0)	7 (31.8)	12 (26.7)	0.4542
Number (%) of patients censored	50 (83.3)	69 (81.2)	14 (70.0)	21 (87.5)	13 (61.9)	19 (76.0)	15 (68.2)	33 (73.3)	
Kaplan-Meier estimates of event in months									
25% quantile (95% CI)	22.44 (10.185 to NC)	22.37 (17.577 to NC)	12.02 (0.986 to NC)	NC (0.953 to NC)	1.12 (1.018 to 20.008)	22.34 (1.084 to NC)	21.03 (8.476 to 22.209)	19.58 (11.729 to NC)	
Median (95% CI)	NC (NC to NC)	NC (23.359 to NC)	NC (12.025 to NC)	NC (NC to NC)	NC (1.117 to NC)	NC (22.341 to NC)	22.21 (21.027 to NC)	NC (21.717 to NC)	

A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Global health status
16.2.6.1.2.5 Efficacy response data - Subgroup analyses by geographical region
16.2.6.1.2.5.6 QLQ-C30 - Time until permanent improvement by 10 pt in global health status according to geographical region (LOCF) - ITT population

	Europe		America		Asia		Other countries		
	Kd (N=60)	**IKd (N=85)**	**Kd (N=20)**	**IKd (N=24)**	**Kd (N=21)**	**IKd (N=25)**	**Kd (N=22)**	**IKd (N=45)**	**p-value of treatment-by-subgroup interaction[c]**
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (22.144 to NC)	NC (NC to NC)	
Comparison vs. Kd									
Log-Rank test p-value[a] vs Kd	-	0.7864		0.2086		0.2228		0.8938	
Hazard ratio (95% CI) vs Kd	-	1.12 (0.50 to 2.47)		0.42 (0.11 to 1.69)		0.52 (0.18 to 1.51)		0.94 (0.37 to 2.39)	
P-value	-	0.7865		0.2227		0.2309		0.8938	
Improvement probability (95% CI)[b]									

A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Global health status
16.2.6.1.2.5 Efficacy response data - Subgroup analyses by geographical region
16.2.6.1.2.5.7 QLQ-C30 - Time until permanent deterioration by 10 pt in global health status according to geographical region (LOCF) - ITT population

	Europe		America		Asia		Other countries		
	Kd (N=60)	**IKd (N=85)**	**Kd (N=20)**	**IKd (N=24)**	**Kd (N=21)**	**IKd (N=25)**	**Kd (N=22)**	**IKd (N=45)**	**p-value of treatment-by-subgroup interaction[c]**
Number (%) of events	16 (26.7)	29 (34.1)	6 (30.0)	5 (20.8)	5 (23.8)	9 (36.0)	8 (36.4)	13 (28.9)	0.6863
Number (%) of patients censored	44 (73.3)	56 (65.9)	14 (70.0)	19 (79.2)	16 (76.2)	16 (64.0)	14 (63.6)	32 (71.1)	
Kaplan-Meier estimates of event in months									
25% quantile (95% CI)	20.37 (3.811 to NC)	17.22 (8.082 to 19.713)	18.53 (4.698 to NC)	20.90 (1.084 to NC)	20.63 (1.051 to NC)	2.97 (0.986 to NC)	6.37 (1.018 to NC)	9.30 (5.257 to NC)	
Median (95% CI)	NC (21.947 to NC)	NC (20.928 to NC)	NC (18.530 to NC)	NC (20.895 to NC)	NC (20.632 to NC)	NC (3.910 to NC)	NC (6.374 to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	

A higher score represents a better level of quality of life. Clinical meaningful deterioration change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
PGM=DEVOPS/SAR650984/EFC15246/CIR_RWE/REPORT/PGM/eff_km_subgp_sr_sig_de_i_t.sas OUT=REPORT/OUTPUT/eff_km_c30_glb_detpl_greg_de_i_t_x.rtf (07APR2021 14:21)

16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Global health status
16.2.6.1.2.5 Efficacy response data - Subgroup analyses by geographical region
16.2.6.1.2.5.7 QLQ-C30 - Time until permanent deterioration by 10 pt in global health status according to geographical region (LOCF) - ITT population

	Europe		America		Asia		Other countries		
	Kd (N=60)	**IKd (N=85)**	**Kd (N=20)**	**IKd (N=24)**	**Kd (N=21)**	**IKd (N=25)**	**Kd (N=22)**	**IKd (N=45)**	**p-value of treatment-by-subgroup interaction[c]**
Comparison vs. Kd									
Log-Rank test p-value[a] vs Kd	-	0.4208		0.8040		0.3992		0.6011	
Hazard ratio (95% CI) vs Kd	-	1.28 (0.70 to 2.37)		0.86 (0.26 to 2.83)		1.59 (0.53 to 4.76)		0.79 (0.33 to 1.91)	
P-value	-	0.4220		0.8042		0.4034		0.6019	
Deterioration probability (95% CI)[b]									
3 Months	0.880 (0.764 to 0.941)	0.892 (0.802 to 0.942)	1.000 (1.000 to 1.000)	0.911 (0.688 to 0.977)	0.800 (0.551 to 0.920)	0.750 (0.526 to 0.879)	0.864 (0.634 to 0.954)	0.911 (0.780 to 0.966)	

A higher score represents a better level of quality of life. Clinical meaningful deterioration change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
PGM=DEVOPS/SAR650984/EFC15246/CIR_RWE/REPORT/PGM/eff_km_subgp_sr_sig_de_i_t.sas OUT=REPORT/OUTPUT/eff_km_c30_glb_detpl_greg_de_i_t_x.rtf (07APR2021 14:21)

16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Global health status
16.2.6.1.2.6 Efficacy response data - Subgroup analyses by regulatory region
16.2.6.1.2.6.3 QLQ-C30 - Time to first improvement by 10 pt in global health status according to regulatory region (LOCF) - ITT population

	Western countries		Other countries		
	Kd (N=55)	**IKd (N=97)**	**Kd (N=68)**	**IKd (N=82)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	25 (45.5)	44 (45.4)	36 (52.9)	48 (58.5)	0.6523
Number (%) of patients censored	30 (54.5)	53 (54.6)	32 (47.1)	34 (41.5)	
Kaplan-Meier estimates of Global health status in months					
25% quantile (95% CI)	1.94 (1.018 to 4.797)	1.97 (1.413 to 3.745)	1.12 (1.018 to 1.906)	1.17 (0.986 to 2.004)	
Median (95% CI)	22.14 (4.797 to NC)	NC (6.505 to NC)	5.06 (1.938 to NC)	5.59 (2.366 to 15.704)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.9186		0.6147	
Hazard ratio (95% CI) vs Kd	-	0.97 (0.60 to 1.59)		1.12 (0.73 to 1.72)	
P-value	-	0.9183		0.6149	
Improvement probability (95% CI)[b]					

A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
PGM=DEVOPS/SAR650984/EFC15246/CIR_RWE/REPORT/PGM/eff_km_subgp_sr_sig_de_i_t.sas OUT=REPORT/OUTPUT/eff_km_c30_glb_impl_rreg_de_i_t_x.rtf (07APR2021 14:21)

16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Global health status
16.2.6.1.2.6 Efficacy response data - Subgroup analyses by regulatory region
16.2.6.1.2.6.4 QLQ-C30 - Time to first deterioration by 10 pt in global health status according to regulatory region (LOCF) - ITT population

	Western countries		Other countries		
	Kd (N=55)	**IKd (N=97)**	**Kd (N=68)**	**IKd (N=82)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	29 (52.7)	62 (63.9)	42 (61.8)	53 (64.6)	0.4769
Number (%) of patients censored	26 (47.3)	35 (36.1)	26 (38.2)	29 (35.4)	
Kaplan-Meier estimates of Global health status in months					
25% quantile (95% CI)	2.83 (1.216 to 4.764)	1.87 (1.117 to 2.366)	1.64 (1.051 to 2.004)	1.84 (1.051 to 2.497)	
Median (95% CI)	11.56 (4.665 to NC)	8.74 (3.745 to 12.025)	4.01 (2.431 to 13.175)	4.80 (3.055 to 11.269)	
75% quantile (95% CI)	NC (21.290 to NC)	NC (18.595 to NC)	NC (NC to NC)	NC (13.142 to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.1925		0.7678	
Hazard ratio (95% CI) vs Kd	-	1.34 (0.86 to 2.08)		1.06 (0.71 to 1.59)	
P-value	-	0.1941		0.7685	
Deterioration probability (95% CI)[b]					

A higher score represents a better level of quality of life. Clinical meaningful deterioration change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Global health status
16.2.6.1.2.6 Efficacy response data - Subgroup analyses by regulatory region
16.2.6.1.2.6.5 QLQ-C30 - Time until permanent improvement by 10 pt in global health status according to regulatory region (LOCF) - ITT population

	Western countries		Other countries		
	Kd (N=55)	**IKd (N=97)**	**Kd (N=68)**	**IKd (N=82)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	14 (25.5)	16 (16.5)	17 (25.0)	21 (25.6)	0.4712
Number (%) of patients censored	41 (74.5)	81 (83.5)	51 (75.0)	61 (74.4)	
Kaplan-Meier estimates of Global health status in months					
25% quantile (95% CI)	21.68 (9.528 to 22.439)	NC (18.136 to NC)	19.52 (9.101 to NC)	20.53 (11.729 to 23.359)	
Median (95% CI)	NC (22.144 to NC)	NC (NC to NC)	NC (NC to NC)	NC (22.374 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.2758		0.8460	
Hazard ratio (95% CI) vs Kd	-	0.67 (0.33 to 1.38)		0.94 (0.49 to 1.78)	
P-value	-	0.2789		0.8454	
Improvement probability (95% CI)[b]					

A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Global health status
16.2.6.1.2.6 Efficacy response data - Subgroup analyses by regulatory region
16.2.6.1.2.6.6 QLQ-C30 - Time until permanent deterioration by 10 pt in global health status according to regulatory region (LOCF) - ITT population

	Western countries		Other countries		
	Kd (N=55)	**IKd (N=97)**	**Kd (N=68)**	**IKd (N=82)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	11 (20.0)	33 (34.0)	24 (35.3)	23 (28.0)	0.0554
Number (%) of patients censored	44 (80.0)	64 (66.0)	44 (64.7)	59 (72.0)	
Kaplan-Meier estimates of Global health status in months					
25% quantile (95% CI)	NC (8.444 to NC)	12.75 (6.735 to 19.713)	8.67 (1.643 to 20.632)	17.22 (3.745 to NC)	
Median (95% CI)	NC (NC to NC)	NC (20.895 to NC)	NC (20.632 to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.0605		0.4099	
Hazard ratio (95% CI) vs Kd	-	1.90 (0.96 to 3.77)		0.79 (0.44 to 1.39)	
P-value	-	0.0650		0.4110	
Deterioration probability (95% CI)[b]					

A higher score represents a better level of quality of life. Clinical meaningful deterioration change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Global health status
16.2.6.1.2.7 Efficacy response data - Subgroup analyses by baseline ECOG PS
16.2.6.1.2.7.3 QLQ-C30 - Time to first improvement by 10 pt in global health status according to baseline ECOG PS (LOCF) - ITT population

	0 or 1		>1		
	Kd (N=118)	**IKd (N=168)**	**Kd (N=5)**	**IKd (N=11)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	58 (49.2)	88 (52.4)	3 (60.0)	4 (36.4)	0.3613
Number (%) of patients censored	60 (50.8)	80 (47.6)	2 (40.0)	7 (63.6)	
Kaplan-Meier estimates of Global health status in months					
25% quantile (95% CI)	1.87 (1.051 to 2.037)	1.91 (1.117 to 2.103)	1.05 (0.986 to NC)	2.53 (1.906 to NC)	
Median (95% CI)	16.16 (4.632 to NC)	15.11 (4.271 to NC)	1.91 (0.986 to NC)	NC (1.906 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (0.986 to NC)	NC (4.961 to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.7834		0.3147	
Hazard ratio (95% CI) vs Kd	-	1.05 (0.75 to 1.46)		0.47 (0.10 to 2.12)	
P-value	-	0.7843		0.3257	
Improvement probability (95% CI)[b]					

A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Global health status
16.2.6.1.2.7 Efficacy response data - Subgroup analyses by baseline ECOG PS
16.2.6.1.2.7.4 QLQ-C30 - Time to first deterioration by 10 pt in global health status according to baseline ECOG PS (LOCF) - ITT population

	0 or 1		>1		
	Kd (N=118)	**IKd (N=168)**	**Kd (N=5)**	**IKd (N=11)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	69 (58.5)	108 (64.3)	2 (40.0)	7 (63.6)	0.3902
Number (%) of patients censored	49 (41.5)	60 (35.7)	3 (60.0)	4 (36.4)	
Kaplan-Meier estimates of Global health status in months					
25% quantile (95% CI)	1.97 (1.183 to 2.825)	1.84 (1.117 to 1.971)	2.79 (2.070 to NC)	3.12 (1.906 to 4.698)	
Median (95% CI)	5.65 (3.844 to 13.372)	6.11 (3.778 to 11.400)	NC (2.070 to NC)	4.70 (1.906 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (2.070 to NC)	10.41 (3.450 to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.3922		0.3227	
Hazard ratio (95% CI) vs Kd	-	1.14 (0.84 to 1.54)		2.18 (0.45 to 10.56)	
P-value	-	0.3926		0.3344	
Deterioration probability (95% CI)[b]					

A higher score represents a better level of quality of life. Clinical meaningful deterioration change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Global health status
16.2.6.1.2.7 Efficacy response data - Subgroup analyses by baseline ECOG PS
16.2.6.1.2.7.5 QLQ-C30 - Time until permanent improvement by 10 pt in global health status according to baseline ECOG PS (LOCF) - ITT population

	0 or 1		>1		
	Kd (N=118)	**IKd (N=168)**	**Kd (N=5)**	**IKd (N=11)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	30 (25.4)	36 (21.4)	1 (20.0)	1 (9.1)	0.6449
Number (%) of patients censored	88 (74.6)	132 (78.6)	4 (80.0)	10 (90.9)	
Kaplan-Meier estimates of Global health status in months					
25% quantile (95% CI)	21.03 (12.025 to 22.209)	21.72 (17.577 to NC)	NC (0.986 to NC)	NC (7.458 to NC)	
Median (95% CI)	NC (22.209 to NC)	NC (23.359 to NC)	NC (0.986 to NC)	NC (7.458 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (0.986 to NC)	NC (NC to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.3422		0.5430	
Hazard ratio (95% CI) vs Kd	-	0.79 (0.49 to 1.28)		0.43 (0.03 to 7.04)	
P-value	-	0.3433		0.5543	
Improvement probability (95% CI)[b]					

A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Global health status
16.2.6.1.2.7 Efficacy response data - Subgroup analyses by baseline ECOG PS
16.2.6.1.2.7.6 QLQ-C30 - Time until permanent deterioration by 10 pt in global health status according to baseline ECOG PS (LOCF) - ITT population

	0 or 1		>1		
	Kd (N=118)	**IKd (N=168)**	**Kd (N=5)**	**IKd (N=11)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	33 (28.0)	53 (31.5)	2 (40.0)	3 (27.3)	0.5890
Number (%) of patients censored	85 (72.0)	115 (68.5)	3 (60.0)	8 (72.7)	
Kaplan-Meier estimates of Global health status in months					
25% quantile (95% CI)	19.45 (5.815 to NC)	12.75 (6.735 to 19.713)	14.65 (2.793 to NC)	17.22 (5.191 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	14.65 (2.793 to NC)	NC (5.191 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (2.793 to NC)	NC (NC to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.4777		0.5374	
Hazard ratio (95% CI) vs Kd	-	1.17 (0.76 to 1.81)		0.57 (0.09 to 3.52)	
P-value	-	0.4782		0.5422	
Deterioration probability (95% CI)[b]					

A higher score represents a better level of quality of life. Clinical meaningful deterioration change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Global health status
16.2.6.1.2.8 Efficacy response data - Subgroup analyses by ISS staging at SE
16.2.6.1.2.8.3 QLQ-C30 - Time to first improvement by 10 pt in global health status according to ISS staging at SE (LOCF) - ITT population

	I		II		III		
	Kd (N=71)	**IKd (N=89)**	**Kd (N=31)**	**IKd (N=63)**	**Kd (N=20)**	**IKd (N=26)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	38 (53.5)	39 (43.8)	16 (51.6)	37 (58.7)	7 (35.0)	15 (57.7)	0.0624
Number (%) of patients censored	33 (46.5)	50 (56.2)	15 (48.4)	26 (41.3)	13 (65.0)	11 (42.3)	
Kaplan-Meier estimates of Global health status in months							
25% quantile (95% CI)	1.12 (1.018 to 1.938)	2.14 (1.117 to 4.961)	1.91 (1.018 to 4.797)	1.94 (1.051 to 2.398)	1.91 (0.953 to NC)	1.08 (0.953 to 2.004)	
Median (95% CI)	5.06 (2.793 to NC)	NC (13.864 to NC)	16.16 (2.004 to NC)	7.95 (2.530 to NC)	NC (1.906 to NC)	2.10 (1.084 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (22.144 to NC)	NC (NC to NC)	NC (NC to NC)	NC (2.136 to NC)	
Comparison vs. Kd							
Log-Rank test p-value[a] vs Kd	-	0.1569		0.5347		0.0855	
Hazard ratio (95% CI) vs Kd	-	0.72 (0.46 to 1.13)		1.21 (0.67 to 2.18)		2.17 (0.88 to 5.35)	
P-value	-	0.1587		0.5353		0.0932	

A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Global health status
16.2.6.1.2.8 Efficacy response data - Subgroup analyses by ISS staging at SE
16.2.6.1.2.8.4 QLQ-C30 - Time to first deterioration by 10 pt in global health status according to ISS staging at SE (LOCF) - ITT population

	I		II		III		
	Kd (N=71)	**IKd (N=89)**	**Kd (N=31)**	**IKd (N=63)**	**Kd (N=20)**	**IKd (N=26)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	41 (57.7)	58 (65.2)	18 (58.1)	43 (68.3)	11 (55.0)	13 (50.0)	0.5326
Number (%) of patients censored	30 (42.3)	31 (34.8)	13 (41.9)	20 (31.7)	9 (45.0)	13 (50.0)	
Kaplan-Meier estimates of Global health status in months							
25% quantile (95% CI)	2.43 (1.117 to 3.844)	1.61 (1.117 to 1.938)	2.79 (1.248 to 4.665)	1.94 (1.051 to 3.055)	1.12 (0.953 to 2.004)	1.91 (0.986 to 4.698)	
Median (95% CI)	7.43 (4.041 to NC)	5.72 (2.825 to 12.025)	6.37 (2.957 to NC)	5.91 (3.220 to 11.170)	2.79 (1.117 to NC)	11.47 (2.004 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (16.657 to NC)	NC (13.175 to NC)	NC (11.170 to NC)	NC (2.793 to NC)	NC (11.466 to NC)	
Comparison vs. Kd							
Log-Rank test p-value[a] vs Kd	-	0.2851		0.3821		0.5964	
Hazard ratio (95% CI) vs Kd	-	1.24 (0.83 to 1.86)		1.28 (0.74 to 2.22)		0.80 (0.36 to 1.80)	
P-value	-	0.2860		0.3833		0.5972	

A higher score represents a better level of quality of life. Clinical meaningful deterioration change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
PGM=DEVOPS/SAR650984/EFC15246/CIR_RWE/REPORT/PGM/eff_km_subgp_sr_sig_de_i_t.sas OUT=REPORT/OUTPUT/eff_km_c30_glb_detl_seiss_de_i_t_x.rtf (07APR2021 14:20)

16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Global health status
16.2.6.1.2.8 Efficacy response data - Subgroup analyses by ISS staging at SE
16.2.6.1.2.8.5 QLQ-C30 - Time until permanent improvement by 10 pt in global health status according to ISS staging at SE (LOCF) - ITT population

	I		II		III		
	Kd (N=71)	**IKd (N=89)**	**Kd (N=31)**	**IKd (N=63)**	**Kd (N=20)**	**IKd (N=26)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	23 (32.4)	19 (21.3)	5 (16.1)	12 (19.0)	3 (15.0)	6 (23.1)	0.3126
Number (%) of patients censored	48 (67.6)	70 (78.7)	26 (83.9)	51 (81.0)	17 (85.0)	20 (76.9)	
Kaplan-Meier estimates of Global health status in months							
25% quantile (95% CI)	16.30 (8.476 to 22.209)	21.39 (16.394 to NC)	22.14 (15.047 to NC)	22.37 (18.136 to NC)	NC (0.953 to NC)	10.18 (0.953 to NC)	
Median (95% CI)	NC (21.684 to NC)	NC (NC to NC)	NC (21.027 to NC)	NC (22.374 to NC)	NC (NC to NC)	NC (10.185 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (23.359 to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Kd							
Log-Rank test p-value[a] vs Kd	-	0.1165		0.9300		0.5124	
Hazard ratio (95% CI) vs Kd	-	0.62 (0.34 to 1.13)		1.05 (0.37 to 2.98)		1.58 (0.40 to 6.33)	
P-value	-	0.1200		0.9307		0.5161	

A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Global health status
16.2.6.1.2.8 Efficacy response data - Subgroup analyses by ISS staging at SE
16.2.6.1.2.8.6 QLQ-C30 - Time until permanent deterioration by 10 pt in global health status according to ISS staging at SE (LOCF) - ITT population

	I		II		III		
	Kd (N=71)	**IKd (N=89)**	**Kd (N=31)**	**IKd (N=63)**	**Kd (N=20)**	**IKd (N=26)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	17 (23.9)	28 (31.5)	9 (29.0)	20 (31.7)	8 (40.0)	7 (26.9)	0.3528
Number (%) of patients censored	54 (76.1)	61 (68.5)	22 (71.0)	43 (68.3)	12 (60.0)	19 (73.1)	
Kaplan-Meier estimates of Global health status in months							
25% quantile (95% CI)	20.63 (8.444 to NC)	17.54 (5.191 to 20.895)	14.65 (1.906 to NC)	11.47 (2.825 to NC)	3.81 (0.953 to 8.674)	14.62 (0.986 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (20.370 to NC)	NC (NC to NC)	NC (3.811 to NC)	NC (14.620 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Kd							
Log-Rank test p-value[a] vs Kd	-	0.2239		0.7342		0.3073	
Hazard ratio (95% CI) vs Kd	-	1.45 (0.79 to 2.65)		1.15 (0.52 to 2.52)		0.59 (0.21 to 1.64)	
P-value	-	0.2266		0.7344		0.3127	

A higher score represents a better level of quality of life. Clinical meaningful deterioration change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Global health status
16.2.6.1.2.9 Efficacy response data - Subgroup analyses by R-ISS stage at SE
16.2.6.1.2.9.3 QLQ-C30 - Time to first improvement by 10 pt in global health status according to R-ISS stage at SE (LOCF) - ITT population

	I or II		III		Not classified		
	Kd (N=103)	**IKd (N=155)**	**Kd (N=8)**	**IKd (N=16)**	**Kd (N=12)**	**IKd (N=8)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	49 (47.6)	79 (51.0)	5 (62.5)	9 (56.3)	7 (58.3)	4 (50.0)	0.9357
Number (%) of patients censored	54 (52.4)	76 (49.0)	3 (37.5)	7 (43.8)	5 (41.7)	4 (50.0)	
Kaplan-Meier estimates of Global health status in months							
25% quantile (95% CI)	1.87 (1.051 to 2.201)	1.94 (1.150 to 2.398)	1.05 (0.953 to 1.906)	1.08 (0.953 to 2.103)	1.89 (0.953 to 4.632)	2.14 (1.084 to 3.943)	
Median (95% CI)	22.14 (4.797 to NC)	15.87 (5.585 to NC)	1.91 (0.953 to NC)	2.10 (1.084 to NC)	4.85 (0.986 to NC)	3.84 (1.084 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (1.117 to NC)	NC (2.103 to NC)	NC (4.632 to NC)	NC (2.136 to NC)	
Comparison vs. Kd							
Log-Rank test p-value[a] vs Kd	-	0.8666		0.8352		0.8169	
Hazard ratio (95% CI) vs Kd	-	1.03 (0.72 to 1.47)		0.89 (0.30 to 2.66)		1.16 (0.34 to 3.98)	
P-value	-	0.8671		0.8353		0.8170	

A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Global health status
16.2.6.1.2.9 Efficacy response data - Subgroup analyses by R-ISS stage at SE
16.2.6.1.2.9.4 QLQ-C30 - Time to first deterioration by 10 pt in global health status according to R-ISS stage at SE (LOCF) - ITT population

	I or II		III		Not classified		
	Kd (N=103)	**IKd (N=155)**	**Kd (N=8)**	**IKd (N=16)**	**Kd (N=12)**	**IKd (N=8)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	61 (59.2)	106 (68.4)	4 (50.0)	6 (37.5)	6 (50.0)	3 (37.5)	0.6649
Number (%) of patients censored	42 (40.8)	49 (31.6)	4 (50.0)	10 (62.5)	6 (50.0)	5 (62.5)	
Kaplan-Meier estimates of Global health status in months							
25% quantile (95% CI)	2.00 (1.216 to 2.825)	1.61 (1.117 to 1.938)	1.12 (1.051 to 2.793)	2.37 (1.051 to NC)	2.86 (1.051 to 7.425)	5.13 (1.018 to NC)	
Median (95% CI)	5.65 (3.844 to 13.372)	5.65 (3.450 to 9.133)	2.79 (1.051 to NC)	NC (2.004 to NC)	NC (1.150 to NC)	11.73 (1.018 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (16.657 to NC)	NC (2.004 to NC)	NC (10.415 to NC)	NC (7.425 to NC)	NC (5.125 to NC)	
Comparison vs. Kd							
Log-Rank test p-value[a] vs Kd	-	0.2483		0.5111		0.9280	
Hazard ratio (95% CI) vs Kd	-	1.20 (0.88 to 1.65)		0.66 (0.18 to 2.33)		0.94 (0.23 to 3.76)	
P-value	-	0.2489		0.5141		0.9280	

A higher score represents a better level of quality of life. Clinical meaningful deterioration change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Global health status
16.2.6.1.2.9 Efficacy response data - Subgroup analyses by R-ISS stage at SE
16.2.6.1.2.9.5 QLQ-C30 - Time until permanent improvement by 10 pt in global health status according to R-ISS stage at SE (LOCF) - ITT population

	I or II		III		Not classified		
	Kd (N=103)	**IKd (N=155)**	**Kd (N=8)**	**IKd (N=16)**	**Kd (N=12)**	**IKd (N=8)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	25 (24.3)	31 (20.0)	2 (25.0)	5 (31.3)	4 (33.3)	1 (12.5)	0.7900
Number (%) of patients censored	78 (75.7)	124 (80.0)	6 (75.0)	11 (68.8)	8 (66.7)	7 (87.5)	
Kaplan-Meier estimates of Global health status in months							
25% quantile (95% CI)	21.68 (10.382 to 22.439)	22.34 (19.581 to NC)	1.12 (0.953 to NC)	7.46 (0.953 to NC)	18.32 (10.185 to NC)	NC (7.425 to NC)	
Median (95% CI)	NC (22.209 to NC)	NC (23.359 to NC)	NC (0.953 to NC)	NC (2.103 to NC)	NC (12.025 to NC)	NC (7.425 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (20.008 to NC)	NC (7.425 to NC)	
Comparison vs. Kd							
Log-Rank test p-value[a] vs Kd	-	0.2424		0.8629		0.6421	
Hazard ratio (95% CI) vs Kd	-	0.73 (0.43 to 1.24)		1.16 (0.22 to 5.99)		0.60 (0.07 to 5.38)	
P-value	-	0.2443		0.8630		0.6457	

A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
PGM=DEVOPS/SAR650984/EFC15246/CIR_RWE/REPORT/PGM/eff_km_subgp_sr_sig_de_i_t.sas OUT=REPORT/OUTPUT/eff_km_c30_glb_imppl_seriss_de_i_t_x.rtf (07APR2021 14:21)

16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Global health status
16.2.6.1.2.9 Efficacy response data - Subgroup analyses by R-ISS stage at SE
16.2.6.1.2.9.6 QLQ-C30 - Time until permanent deterioration by 10 pt in global health status according to R-ISS stage at SE (LOCF) - ITT population

	I or II		III		Not classified		
	Kd (N=103)	**IKd (N=155)**	**Kd (N=8)**	**IKd (N=16)**	**Kd (N=12)**	**IKd (N=8)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	30 (29.1)	51 (32.9)	3 (37.5)	4 (25.0)	2 (16.7)	1 (12.5)	0.7595
Number (%) of patients censored	73 (70.9)	104 (67.1)	5 (62.5)	12 (75.0)	10 (83.3)	7 (87.5)	
Kaplan-Meier estimates of Global health status in months							
25% quantile (95% CI)	18.53 (5.815 to 21.947)	11.99 (6.111 to 19.680)	2.79 (1.117 to NC)	14.62 (2.366 to NC)	NC (1.150 to NC)	20.93 (20.928 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (1.117 to NC)	NC (8.181 to NC)	NC (20.632 to NC)	NC (20.928 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (3.811 to NC)	NC (NC to NC)	NC (NC to NC)	NC (20.928 to NC)	
Comparison vs. Kd							
Log-Rank test p-value[a] vs Kd	-	0.5650		0.5300		0.9165	
Hazard ratio (95% CI) vs Kd	-	1.14 (0.73 to 1.79)		0.62 (0.14 to 2.79)		1.14 (0.10 to 12.66)	
P-value	-	0.5653		0.5338		0.9166	

A higher score represents a better level of quality of life. Clinical meaningful deterioration change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Global health status
16.2.6.1.2.10 Efficacy response data - Subgroup analyses by nb of prior lines
16.2.6.1.2.10.3 QLQ-C30 - Time to first improvement by 10 pt in global health status according to nb of prior lines (LOCF) - ITT population

	1		>1		
	Kd (N=55)	**IKd (N=79)**	**Kd (N=68)**	**IKd (N=100)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	24 (43.6)	37 (46.8)	37 (54.4)	55 (55.0)	0.6540
Number (%) of patients censored	31 (56.4)	42 (53.2)	31 (45.6)	45 (45.0)	
Kaplan-Meier estimates of Global health status in months					
25% quantile (95% CI)	2.79 (1.051 to 5.060)	2.10 (1.117 to 4.271)	1.12 (0.986 to 1.906)	1.91 (1.051 to 2.004)	
Median (95% CI)	22.14 (5.060 to NC)	NC (5.585 to NC)	4.80 (1.906 to NC)	4.96 (2.530 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.6912		0.7936	
Hazard ratio (95% CI) vs Kd	-	1.11 (0.66 to 1.86)		0.95 (0.62 to 1.43)	
P-value	-	0.6913		0.7924	
Improvement probability (95% CI)[b]					

A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Global health status
16.2.6.1.2.10 Efficacy response data - Subgroup analyses by nb of prior lines
16.2.6.1.2.10.4 QLQ-C30 - Time to first deterioration by 10 pt in global health status according to nb of prior lines (LOCF) - ITT population

	1		>1		
	Kd (N=55)	**IKd (N=79)**	**Kd (N=68)**	**IKd (N=100)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	33 (60.0)	50 (63.3)	38 (55.9)	65 (65.0)	0.9377
Number (%) of patients censored	22 (40.0)	29 (36.7)	30 (44.1)	35 (35.0)	
Kaplan-Meier estimates of Global health status in months					
25% quantile (95% CI)	1.87 (1.117 to 3.844)	1.22 (1.051 to 1.906)	2.07 (1.216 to 2.957)	1.94 (1.150 to 3.121)	
Median (95% CI)	5.73 (3.844 to NC)	3.81 (1.971 to 11.466)	6.37 (3.023 to NC)	7.39 (3.844 to 11.729)	
75% quantile (95% CI)	NC (21.290 to NC)	NC (16.427 to NC)	NC (NC to NC)	NC (15.474 to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.4632		0.4673	
Hazard ratio (95% CI) vs Kd	-	1.18 (0.76 to 1.83)		1.16 (0.78 to 1.73)	
P-value	-	0.4637		0.4677	
Deterioration probability (95% CI)[b]					

A higher score represents a better level of quality of life. Clinical meaningful deterioration change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Global health status
16.2.6.1.2.10 Efficacy response data - Subgroup analyses by nb of prior lines
16.2.6.1.2.10.5 QLQ-C30 - Time until permanent improvement by 10 pt in global health status according to nb of prior lines (LOCF) - ITT population

	1		>1		
	Kd (N=55)	**IKd (N=79)**	**Kd (N=68)**	**IKd (N=100)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	13 (23.6)	16 (20.3)	18 (26.5)	21 (21.0)	0.7482
Number (%) of patients censored	42 (76.4)	63 (79.7)	50 (73.5)	79 (79.0)	
Kaplan-Meier estimates of Global health status in months					
25% quantile (95% CI)	22.14 (9.101 to NC)	22.37 (18.037 to NC)	16.62 (9.528 to 22.439)	21.72 (14.784 to NC)	
Median (95% CI)	NC (22.144 to NC)	NC (22.374 to NC)	NC (21.684 to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.6733		0.3040	
Hazard ratio (95% CI) vs Kd	-	0.85 (0.41 to 1.78)		0.72 (0.38 to 1.35)	
P-value	-	0.6737		0.3062	
Improvement probability (95% CI)[b]					

A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
PGM=DEVOPS/SAR650984/EFC15246/CIR_RWE/REPORT/PGM/eff_km_subgp_sr_sig_de_i_t.sas OUT=REPORT/OUTPUT/eff_km_c30_glb_imppl_plne_de_i_t_x.rtf (07APR2021 14:21)

16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Global health status
16.2.6.1.2.10 Efficacy response data - Subgroup analyses by nb of prior lines
16.2.6.1.2.10.6 QLQ-C30 - Time until permanent deterioration by 10 pt in global health status according to nb of prior lines (LOCF) - ITT population

	1		>1		
	Kd (N=55)	**IKd (N=79)**	**Kd (N=68)**	**IKd (N=100)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	17 (30.9)	25 (31.6)	18 (26.5)	31 (31.0)	0.6515
Number (%) of patients censored	38 (69.1)	54 (68.4)	50 (73.5)	69 (69.0)	
Kaplan-Meier estimates of Global health status in months					
25% quantile (95% CI)	10.41 (1.314 to NC)	17.54 (5.651 to 20.895)	20.14 (6.374 to NC)	11.50 (6.111 to 19.713)	
Median (95% CI)	NC (NC to NC)	NC (20.895 to NC)	NC (21.947 to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.9110		0.4394	
Hazard ratio (95% CI) vs Kd	-	1.04 (0.56 to 1.92)		1.26 (0.70 to 2.25)	
P-value	-	0.9112		0.4404	
Deterioration probability (95% CI)[b]					

A higher score represents a better level of quality of life. Clinical meaningful deterioration change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
PGM=DEVOPS/SAR650984/EFC15246/CIR_RWE/REPORT/PGM/eff_km_subgp_sr_sig_de_i_t.sas OUT=REPORT/OUTPUT/eff_km_c30_glb_detpl_plne_de_i_t_x.rtf (07APR2021 14:21)

16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Global health status
16.2.6.1.2.11 Efficacy response data - Subgroup analyses by cytogenetic abnormality
16.2.6.1.2.11.3 QLQ-C30 - Time to first improvement by 10 pt in global health status according to cytogenetic abnormality (LOCF) - ITT population

	At least one		None		
	Kd (N=31)	**IKd (N=42)**	**Kd (N=77)**	**IKd (N=114)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	17 (54.8)	24 (57.1)	35 (45.5)	57 (50.0)	0.9085
Number (%) of patients censored	14 (45.2)	18 (42.9)	42 (54.5)	57 (50.0)	
Kaplan-Meier estimates of Global health status in months					
25% quantile (95% CI)	1.12 (0.986 to 2.793)	1.41 (0.986 to 2.004)	1.87 (1.051 to 2.004)	1.97 (1.117 to 2.398)	
Median (95% CI)	4.50 (1.906 to NC)	4.96 (1.906 to NC)	22.14 (2.957 to NC)	16.13 (4.797 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.9866		0.7509	
Hazard ratio (95% CI) vs Kd	-	1.01 (0.54 to 1.87)		1.07 (0.70 to 1.63)	
P-value	-	0.9866		0.7510	
Improvement probability (95% CI)[b]					

A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
PGM=DEVOPS/SAR650984/EFC15246/CIR_RWE/REPORT/PGM/eff_km_subgp_sr_sig_de_i_t.sas OUT=REPORT/OUTPUT/eff_km_c30_glb_impl_cyto_de_i_t_x.rtf (07APR2021 14:20)

16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Global health status
16.2.6.1.2.11 Efficacy response data - Subgroup analyses by cytogenetic abnormality
16.2.6.1.2.11.4 QLQ-C30 - Time to first deterioration by 10 pt in global health status according to cytogenetic abnormality (LOCF) - ITT population

	At least one		None		
	Kd (N=31)	**IKd (N=42)**	**Kd (N=77)**	**IKd (N=114)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	21 (67.7)	27 (64.3)	43 (55.8)	75 (65.8)	0.2733
Number (%) of patients censored	10 (32.3)	15 (35.7)	34 (44.2)	39 (34.2)	
Kaplan-Meier estimates of Global health status in months					
25% quantile (95% CI)	1.87 (1.018 to 2.793)	1.12 (0.986 to 1.971)	2.14 (1.183 to 3.154)	1.87 (1.117 to 2.070)	
Median (95% CI)	2.96 (2.004 to 9.758)	5.65 (1.938 to 18.595)	6.57 (4.008 to NC)	5.72 (3.450 to 11.466)	
75% quantile (95% CI)	NC (5.815 to NC)	NC (12.025 to NC)	NC (NC to NC)	NC (16.427 to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.6987		0.1731	
Hazard ratio (95% CI) vs Kd	-	0.89 (0.50 to 1.58)		1.30 (0.89 to 1.89)	
P-value	-	0.6989		0.1743	
Deterioration probability (95% CI)[b]					

A higher score represents a better level of quality of life. Clinical meaningful deterioration change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Global health status
16.2.6.1.2.11 Efficacy response data - Subgroup analyses by cytogenetic abnormality
16.2.6.1.2.11.5 QLQ-C30 - Time until permanent improvement by 10 pt in global health status according to cytogenetic abnormality (LOCF) - ITT population

	At least one		None		
	Kd (N=31)	**IKd (N=42)**	**Kd (N=77)**	**IKd (N=114)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	8 (25.8)	12 (28.6)	19 (24.7)	20 (17.5)	0.2569
Number (%) of patients censored	23 (74.2)	30 (71.4)	58 (75.3)	94 (82.5)	
Kaplan-Meier estimates of Global health status in months					
25% quantile (95% CI)	21.68 (1.051 to NC)	14.78 (10.185 to NC)	19.52 (9.528 to NC)	22.34 (20.534 to NC)	
Median (95% CI)	NC (21.684 to NC)	23.36 (23.359 to NC)	NC (22.144 to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (23.359 to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.8904		0.1085	
Hazard ratio (95% CI) vs Kd	-	1.06 (0.43 to 2.62)		0.60 (0.32 to 1.13)	
P-value	-	0.8911		0.1123	
Improvement probability (95% CI)[b]					

A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Global health status
16.2.6.1.2.11 Efficacy response data - Subgroup analyses by cytogenetic abnormality
16.2.6.1.2.11.6 QLQ-C30 - Time until permanent deterioration by 10 pt in global health status according to cytogenetic abnormality (LOCF) - ITT population

	At least one		None		
	Kd (N=31)	**IKd (N=42)**	**Kd (N=77)**	**IKd (N=114)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	12 (38.7)	15 (35.7)	21 (27.3)	36 (31.6)	0.5898
Number (%) of patients censored	19 (61.3)	27 (64.3)	56 (72.7)	78 (68.4)	
Kaplan-Meier estimates of Global health status in months					
25% quantile (95% CI)	6.37 (1.873 to 21.947)	5.19 (1.840 to NC)	19.45 (4.698 to NC)	17.22 (9.133 to 20.468)	
Median (95% CI)	NC (14.653 to NC)	NC (14.620 to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.8755		0.5130	
Hazard ratio (95% CI) vs Kd	-	0.94 (0.44 to 2.01)		1.20 (0.70 to 2.05)	
P-value	-	0.8750		0.5136	
Deterioration probability (95% CI)[b]					

A higher score represents a better level of quality of life. Clinical meaningful deterioration change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Global health status
16.2.6.1.2.12 Efficacy response data - Subgroup analyses by MM type at SE
16.2.6.1.2.12.3 QLQ-C30 - Time to first improvement by 10 pt in global health status according to MM type at SE (LOCF) - ITT population

	IgG		Non-IgG		
	Kd (N=85)	**IKd (N=126)**	**Kd (N=38)**	**IKd (N=53)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	42 (49.4)	59 (46.8)	19 (50.0)	33 (62.3)	0.3748
Number (%) of patients censored	43 (50.6)	67 (53.2)	19 (50.0)	20 (37.7)	
Kaplan-Meier estimates of Global health status in months					
25% quantile (95% CI)	1.87 (1.051 to 2.825)	1.97 (1.150 to 2.924)	1.49 (0.986 to 1.938)	1.18 (0.986 to 2.004)	
Median (95% CI)	22.14 (4.205 to NC)	NC (6.505 to NC)	10.48 (1.906 to NC)	3.75 (1.971 to 19.581)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (16.131 to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.6858		0.4608	
Hazard ratio (95% CI) vs Kd	-	0.92 (0.62 to 1.37)		1.24 (0.70 to 2.18)	
P-value	-	0.6859		0.4616	
Improvement probability (95% CI)[b]					

A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Global health status
16.2.6.1.2.12 Efficacy response data - Subgroup analyses by MM type at SE
16.2.6.1.2.12.4 QLQ-C30 - Time to first deterioration by 10 pt in global health status according to MM type at SE (LOCF) - ITT population

	IgG		Non-IgG		
	Kd (N=85)	**IKd (N=126)**	**Kd (N=38)**	**IKd (N=53)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	52 (61.2)	82 (65.1)	19 (50.0)	33 (62.3)	0.6264
Number (%) of patients censored	33 (38.8)	44 (34.9)	19 (50.0)	20 (37.7)	
Kaplan-Meier estimates of Global health status in months					
25% quantile (95% CI)	2.00 (1.150 to 2.825)	1.91 (1.150 to 2.497)	1.95 (1.051 to 4.665)	1.08 (0.986 to 2.037)	
Median (95% CI)	4.83 (3.088 to 13.536)	5.65 (3.450 to 9.265)	12.78 (2.793 to NC)	10.41 (1.938 to 15.474)	
75% quantile (95% CI)	NC (NC to NC)	NC (16.657 to NC)	NC (NC to NC)	NC (13.142 to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.5246		0.3355	
Hazard ratio (95% CI) vs Kd	-	1.12 (0.79 to 1.59)		1.32 (0.75 to 2.32)	
P-value	-	0.5248		0.3370	
Deterioration probability (95% CI)[b]					

A higher score represents a better level of quality of life. Clinical meaningful deterioration change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
PGM=DEVOPS/SAR650984/EFC15246/CIR_RWE/REPORT/PGM/eff_km_subgp_sr_sig_de_i_t.sas OUT=REPORT/OUTPUT/eff_km_c30_glb_detl_semm_de_i_t_x.rtf (07APR2021 14:20)

16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Global health status
16.2.6.1.2.12 Efficacy response data - Subgroup analyses by MM type at SE
16.2.6.1.2.12.5 QLQ-C30 - Time until permanent improvement by 10 pt in global health status according to MM type at SE (LOCF) - ITT population

	IgG		Non-IgG		
	Kd (N=85)	**IKd (N=126)**	**Kd (N=38)**	**IKd (N=53)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	25 (29.4)	23 (18.3)	6 (15.8)	14 (26.4)	0.0793
Number (%) of patients censored	60 (70.6)	103 (81.7)	32 (84.2)	39 (73.6)	
Kaplan-Meier estimates of Global health status in months					
25% quantile (95% CI)	19.52 (10.185 to 22.209)	22.37 (20.534 to NC)	21.68 (1.906 to NC)	19.58 (10.185 to NC)	
Median (95% CI)	NC (22.144 to NC)	NC (23.359 to NC)	NC (21.684 to NC)	NC (22.341 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.0592		0.3773	
Hazard ratio (95% CI) vs Kd	-	0.58 (0.33 to 1.03)		1.53 (0.59 to 3.99)	
P-value	-	0.0623		0.3810	
Improvement probability (95% CI)[b]					

A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
PGM=DEVOPS/SAR650984/EFC15246/CIR_RWE/REPORT/PGM/eff_km_subgp_sr_sig_de_i_t.sas OUT=REPORT/OUTPUT/eff_km_c30_glb_imppl_semm_de_i_t_x.rtf (07APR2021 14:21)

16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Global health status
16.2.6.1.2.12 Efficacy response data - Subgroup analyses by MM type at SE
16.2.6.1.2.12.6 QLQ-C30 - Time until permanent deterioration by 10 pt in global health status according to MM type at SE (LOCF) - ITT population

	IgG		Non-IgG		
	Kd (N=85)	**IKd (N=126)**	**Kd (N=38)**	**IKd (N=53)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	24 (28.2)	41 (32.5)	11 (28.9)	15 (28.3)	0.5026
Number (%) of patients censored	61 (71.8)	85 (67.5)	27 (71.1)	38 (71.7)	
Kaplan-Meier estimates of Global health status in months					
25% quantile (95% CI)	20.14 (5.815 to NC)	11.50 (6.111 to 19.713)	6.37 (1.906 to NC)	12.75 (2.037 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (20.567 to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.3704		0.8100	
Hazard ratio (95% CI) vs Kd	-	1.26 (0.76 to 2.08)		0.91 (0.42 to 1.98)	
P-value	-	0.3714		0.8101	
Deterioration probability (95% CI)[b]					

A higher score represents a better level of quality of life. Clinical meaningful deterioration change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
PGM=DEVOPS/SAR650984/EFC15246/CIR_RWE/REPORT/PGM/eff_km_subgp_sr_sig_de_i_t.sas OUT=REPORT/OUTPUT/eff_km_c30_glb_detpl_semm_de_i_t_x.rtf (07APR2021 14:21)

16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Global health status
16.2.6.1.2.13 Efficacy response data - Subgroup analyses by previous autologous stem-cell
16.2.6.1.2.13.3 QLQ-C30 - Time to first improvement by 10 pt in global health status according to previous autologous stem-cell (LOCF) - ITT population

	Yes		No		
	Kd (N=69)	**IKd (N=116)**	**Kd (N=54)**	**IKd (N=63)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	32 (46.4)	59 (50.9)	29 (53.7)	33 (52.4)	0.4929
Number (%) of patients censored	37 (53.6)	57 (49.1)	25 (46.3)	30 (47.6)	
Kaplan-Meier estimates of Global health status in months					
25% quantile (95% CI)	1.58 (1.018 to 3.844)	1.91 (1.084 to 2.136)	1.87 (1.018 to 2.201)	1.97 (1.084 to 3.745)	
Median (95% CI)	22.14 (5.060 to NC)	15.51 (3.745 to NC)	4.80 (2.004 to NC)	15.11 (3.745 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.5714		0.6610	
Hazard ratio (95% CI) vs Kd	-	1.13 (0.74 to 1.74)		0.89 (0.54 to 1.47)	
P-value	-	0.5717		0.6612	
Improvement probability (95% CI)[b]					

A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Global health status
16.2.6.1.2.13 Efficacy response data - Subgroup analyses by previous autologous stem-cell
16.2.6.1.2.13.4 QLQ-C30 - Time to first deterioration by 10 pt in global health status according to previous autologous stem-cell (LOCF) - ITT population

	Yes		No		
	Kd (N=69)	**IKd (N=116)**	**Kd (N=54)**	**IKd (N=63)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	36 (52.2)	74 (63.8)	35 (64.8)	41 (65.1)	0.3384
Number (%) of patients censored	33 (47.8)	42 (36.2)	19 (35.2)	22 (34.9)	
Kaplan-Meier estimates of Global health status in months					
25% quantile (95% CI)	2.38 (1.051 to 3.154)	1.31 (1.051 to 1.938)	2.00 (1.150 to 2.793)	1.99 (1.216 to 3.088)	
Median (95% CI)	9.76 (3.844 to NC)	5.72 (3.220 to 11.729)	4.90 (2.793 to 13.175)	6.97 (3.088 to 11.400)	
75% quantile (95% CI)	NC (NC to NC)	NC (19.253 to NC)	NC (13.175 to NC)	NC (11.400 to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.1716		0.9866	
Hazard ratio (95% CI) vs Kd	-	1.32 (0.89 to 1.97)		1.00 (0.63 to 1.56)	
P-value	-	0.1730		0.9866	
Deterioration probability (95% CI)[b]					

A higher score represents a better level of quality of life. Clinical meaningful deterioration change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Global health status
16.2.6.1.2.13 Efficacy response data - Subgroup analyses by previous autologous stem-cell
16.2.6.1.2.13.5 QLQ-C30 - Time until permanent improvement by 10 pt in global health status according to previous autologous stem-cell (LOCF) - ITT population

	Yes		No		
	Kd (N=69)	**IKd (N=116)**	**Kd (N=54)**	**IKd (N=63)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	18 (26.1)	23 (19.8)	13 (24.1)	14 (22.2)	0.7899
Number (%) of patients censored	51 (73.9)	93 (80.2)	41 (75.9)	49 (77.8)	
Kaplan-Meier estimates of Global health status in months					
25% quantile (95% CI)	21.03 (9.528 to 22.439)	22.34 (18.037 to NC)	19.52 (9.101 to NC)	21.72 (15.770 to NC)	
Median (95% CI)	NC (22.144 to NC)	NC (NC to NC)	NC (22.209 to NC)	NC (22.374 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (23.359 to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.3275		0.6309	
Hazard ratio (95% CI) vs Kd	-	0.74 (0.40 to 1.36)		0.83 (0.39 to 1.77)	
P-value	-	0.3293		0.6314	
Improvement probability (95% CI)[b]					

A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Global health status
16.2.6.1.2.13 Efficacy response data - Subgroup analyses by previous autologous stem-cell
16.2.6.1.2.13.6 QLQ-C30 - Time until permanent deterioration by 10 pt in global health status according to previous autologous stem-cell (LOCF) - ITT population

	Yes		No		
	Kd (N=69)	**IKd (N=116)**	**Kd (N=54)**	**IKd (N=63)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	18 (26.1)	33 (28.4)	17 (31.5)	23 (36.5)	0.8057
Number (%) of patients censored	51 (73.9)	83 (71.6)	37 (68.5)	40 (63.5)	
Kaplan-Meier estimates of Global health status in months					
25% quantile (95% CI)	20.37 (4.041 to NC)	19.25 (8.082 to 20.928)	14.65 (3.811 to NC)	11.10 (3.088 to 18.924)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (20.567 to NC)	NC (18.924 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.6759		0.4724	
Hazard ratio (95% CI) vs Kd	-	1.13 (0.64 to 2.01)		1.26 (0.67 to 2.36)	
P-value	-	0.6761		0.4734	
Deterioration probability (95% CI)[b]					

A higher score represents a better level of quality of life. Clinical meaningful deterioration change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Global health status
16.2.6.1.2.14 Efficacy response data - Subgroup analyses by baseline eGFR (MDRD)
16.2.6.1.2.14.3 QLQ-C30 - Time to first improvement by 10 pt in global health status according to baseline eGFR (MDRD) (LOCF) - ITT population

	>=60 mL/min/1.73m2		<60 mL/min/1.73m2		
	Kd (N=93)	**IKd (N=122)**	**Kd (N=18)**	**IKd (N=43)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	53 (57.0)	62 (50.8)	6 (33.3)	24 (55.8)	0.2877
Number (%) of patients censored	40 (43.0)	60 (49.2)	12 (66.7)	19 (44.2)	
Kaplan-Meier estimates of Global health status in months					
25% quantile (95% CI)	1.12 (1.051 to 1.906)	1.91 (1.051 to 2.136)	2.04 (0.920 to NC)	1.97 (1.084 to 2.530)	
Median (95% CI)	5.82 (2.825 to NC)	15.51 (4.961 to NC)	NC (1.906 to NC)	7.95 (2.366 to NC)	
75% quantile (95% CI)	NC (22.144 to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.5029		0.4017	
Hazard ratio (95% CI) vs Kd	-	0.88 (0.61 to 1.27)		1.46 (0.60 to 3.58)	
P-value	-	0.5031		0.4049	
Improvement probability (95% CI)[b]					

A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Global health status
16.2.6.1.2.14 Efficacy response data - Subgroup analyses by baseline eGFR (MDRD)
16.2.6.1.2.14.4 QLQ-C30 - Time to first deterioration by 10 pt in global health status according to baseline eGFR (MDRD) (LOCF) - ITT population

	>=60 mL/min/1.73m2		<60 mL/min/1.73m2		
	Kd (N=93)	**IKd (N=122)**	**Kd (N=18)**	**IKd (N=43)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	53 (57.0)	81 (66.4)	13 (72.2)	28 (65.1)	0.0265
Number (%) of patients censored	40 (43.0)	41 (33.6)	5 (27.8)	15 (34.9)	
Kaplan-Meier estimates of Global health status in months					
25% quantile (95% CI)	2.28 (1.216 to 2.957)	1.87 (1.117 to 2.004)	1.05 (0.953 to 1.906)	1.61 (1.018 to 2.825)	
Median (95% CI)	6.95 (4.008 to NC)	5.59 (3.220 to 10.415)	2.96 (1.051 to 4.665)	6.97 (2.037 to 16.427)	
75% quantile (95% CI)	NC (NC to NC)	NC (14.587 to NC)	4.83 (1.906 to NC)	NC (11.466 to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.0922		0.1096	
Hazard ratio (95% CI) vs Kd	-	1.35 (0.95 to 1.90)		0.59 (0.30 to 1.14)	
P-value	-	0.0934		0.1138	
Deterioration probability (95% CI)[b]					

A higher score represents a better level of quality of life. Clinical meaningful deterioration change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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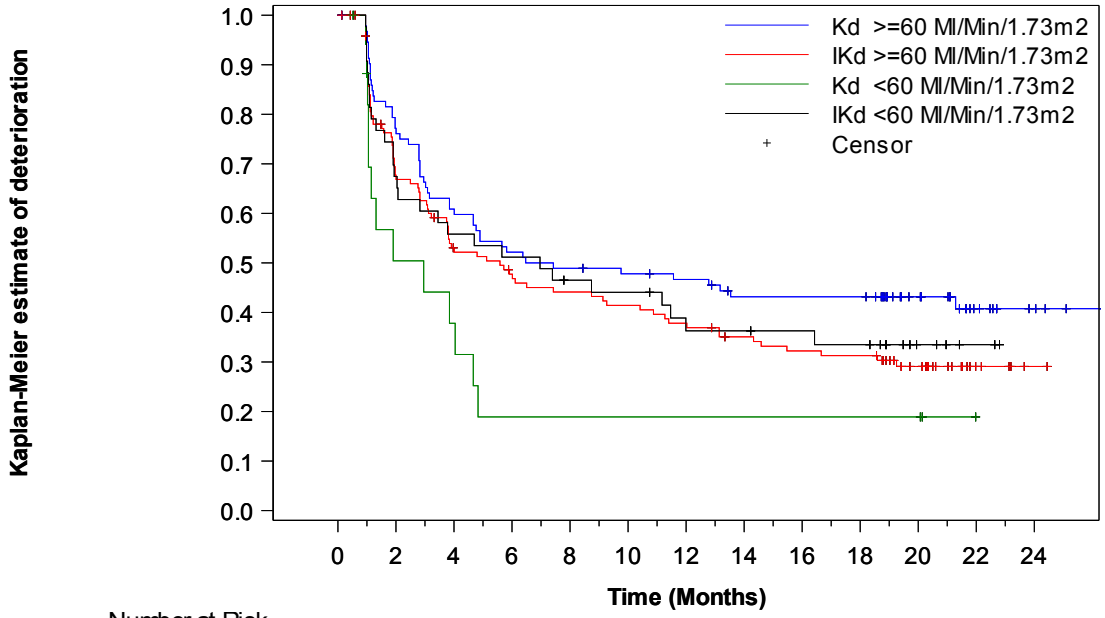
16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Global health status
16.2.6.1.2.14 Efficacy response data - Subgroup analyses by baseline eGFR (MDRD)
16.2.6.1.2.14.5 QLQ-C30 - Time to first deterioration by 10 pt in global health status according to baseline eGFR (MDRD)- Kaplan-Meier curve (LOCF) - ITT population



Number at Risk

Kd >=60 Ml/Min/1.73m2	93	61	48	44	41	36	36	21	5
lKd >=60 Ml/Min/1.73m2	122	73	53	48	42	35	33	12	1
Kd <60 Ml/Min/1.73m2	18	7	3	3	3	3	3	1	0
lKd <60 Ml/Min/1.73m2	43	26	22	18	14	13	12	3	0

A higher score represents a better level of quality of life. Clinical meaningful deterioration change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
PGM=DEVOPS/SAR650984/EFC15246/CIR_RWE/REPORT/PGM/eff_qlq_km_subgp_de_i_f.sas OUT=REPORT/OUTPUT/eff_km_c30_glb_detl_crcl_de_i_f_x.rtf (07APR2021 14:48)

16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Global health status
16.2.6.1.2.14 Efficacy response data - Subgroup analyses by baseline eGFR (MDRD)
16.2.6.1.2.14.6 QLQ-C30 - Time until permanent improvement by 10 pt in global health status according to baseline eGFR (MDRD) (LOCF) - ITT population

	>=60 mL/min/1.73m2		<60 mL/min/1.73m2		
	Kd (N=93)	**IKd (N=122)**	**Kd (N=18)**	**IKd (N=43)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	27 (29.0)	27 (22.1)	2 (11.1)	9 (20.9)	0.3953
Number (%) of patients censored	66 (71.0)	95 (77.9)	16 (88.9)	34 (79.1)	
Kaplan-Meier estimates of Global health status in months					
25% quantile (95% CI)	19.52 (9.101 to 22.209)	21.39 (16.624 to NC)	21.03 (15.869 to NC)	23.36 (12.945 to NC)	
Median (95% CI)	NC (22.144 to NC)	NC (22.374 to NC)	NC (21.027 to NC)	NC (23.359 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (21.027 to NC)	NC (23.359 to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.2808		0.6272	
Hazard ratio (95% CI) vs Kd	-	0.75 (0.44 to 1.27)		1.46 (0.31 to 6.76)	
P-value	-	0.2825		0.6296	
Improvement probability (95% CI)[b]					

A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Global health status
16.2.6.1.2.14 Efficacy response data - Subgroup analyses by baseline eGFR (MDRD)
16.2.6.1.2.14.7 QLQ-C30 - Time until permanent deterioration by 10 pt in global health status according to baseline eGFR (MDRD) (LOCF) - ITT population

	>=60 mL/min/1.73m2		<60 mL/min/1.73m2		
	Kd (N=93)	**IKd (N=122)**	**Kd (N=18)**	**IKd (N=43)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	23 (24.7)	35 (28.7)	9 (50.0)	16 (37.2)	0.0977
Number (%) of patients censored	70 (75.3)	87 (71.3)	9 (50.0)	27 (62.8)	
Kaplan-Meier estimates of Global health status in months					
25% quantile (95% CI)	20.37 (10.415 to NC)	12.75 (8.082 to 20.895)	3.81 (0.953 to 8.674)	8.18 (1.051 to 20.468)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	20.63 (1.906 to NC)	NC (18.924 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (8.674 to NC)	NC (NC to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.3464		0.1958	
Hazard ratio (95% CI) vs Kd	-	1.29 (0.76 to 2.18)		0.59 (0.26 to 1.33)	
P-value	-	0.3476		0.2011	
Deterioration probability (95% CI)[b]					

A higher score represents a better level of quality of life. Clinical meaningful deterioration change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Global health status
16.2.6.1.2.15 Efficacy response data - Subgroup analyses by previous treatment with PI
16.2.6.1.2.15.3 QLQ-C30 - Time to first improvement by 10 pt in global health status according to previous treatment with PI (LOCF) - ITT population

	Yes		No		
	Kd (N=47)	**IKd (N=81)**	**Kd (N=76)**	**IKd (N=98)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	24 (51.1)	36 (44.4)	37 (48.7)	56 (57.1)	0.2746
Number (%) of patients censored	23 (48.9)	45 (55.6)	39 (51.3)	42 (42.9)	
Kaplan-Meier estimates of Global health status in months					
25% quantile (95% CI)	1.87 (1.018 to 2.957)	2.04 (1.150 to 3.745)	1.28 (1.051 to 2.201)	1.87 (1.051 to 2.004)	
Median (95% CI)	16.16 (2.037 to NC)	NC (6.505 to NC)	12.45 (2.957 to NC)	5.59 (2.891 to 19.581)	
75% quantile (95% CI)	NC (22.144 to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.4783		0.4298	
Hazard ratio (95% CI) vs Kd	-	0.83 (0.49 to 1.39)		1.18 (0.78 to 1.79)	
P-value	-	0.4789		0.4304	
Improvement probability (95% CI)[b]					

A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Global health status
16.2.6.1.2.15 Efficacy response data - Subgroup analyses by previous treatment with PI
16.2.6.1.2.15.4 QLQ-C30 - Time to first deterioration by 10 pt in global health status according to previous treatment with PI (LOCF) - ITT population

	Yes		No		
	Kd (N=47)	**IKd (N=81)**	**Kd (N=76)**	**IKd (N=98)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	30 (63.8)	52 (64.2)	41 (53.9)	63 (64.3)	0.8320
Number (%) of patients censored	17 (36.2)	29 (35.8)	35 (46.1)	35 (35.7)	
Kaplan-Meier estimates of Global health status in months					
25% quantile (95% CI)	1.97 (1.216 to 2.957)	1.22 (1.051 to 2.004)	2.00 (1.117 to 3.154)	1.94 (1.150 to 3.088)	
Median (95% CI)	4.75 (2.431 to 13.536)	4.01 (2.497 to 11.170)	6.47 (3.844 to NC)	6.97 (3.811 to 13.142)	
75% quantile (95% CI)	NC (13.175 to NC)	NC (11.992 to NC)	NC (NC to NC)	NC (16.657 to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.6151		0.3649	
Hazard ratio (95% CI) vs Kd	-	1.12 (0.72 to 1.76)		1.20 (0.81 to 1.78)	
P-value	-	0.6153		0.3655	
Deterioration probability (95% CI)[b]					

A higher score represents a better level of quality of life. Clinical meaningful deterioration change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Global health status
16.2.6.1.2.15 Efficacy response data - Subgroup analyses by previous treatment with PI
16.2.6.1.2.15.5 QLQ-C30 - Time until permanent improvement by 10 pt in global health status according to previous treatment with PI (LOCF) - ITT population

	Yes		No		
	Kd (N=47)	**IKd (N=81)**	**Kd (N=76)**	**IKd (N=98)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	10 (21.3)	15 (18.5)	21 (27.6)	22 (22.4)	0.6999
Number (%) of patients censored	37 (78.7)	66 (81.5)	55 (72.4)	76 (77.6)	
Kaplan-Meier estimates of Global health status in months					
25% quantile (95% CI)	22.14 (9.528 to NC)	22.37 (17.511 to NC)	20.01 (9.101 to 22.209)	21.72 (15.671 to NC)	
Median (95% CI)	NC (22.144 to NC)	NC (22.374 to NC)	NC (21.684 to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (23.359 to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.7850		0.2959	
Hazard ratio (95% CI) vs Kd	-	0.89 (0.40 to 2.00)		0.73 (0.40 to 1.32)	
P-value	-	0.7851		0.2979	
Improvement probability (95% CI)[b]					

A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Global health status
16.2.6.1.2.15 Efficacy response data - Subgroup analyses by previous treatment with PI
16.2.6.1.2.15.6 QLQ-C30 - Time until permanent deterioration by 10 pt in global health status according to previous treatment with PI (LOCF) - ITT population

	Yes		No		
	Kd (N=47)	**IKd (N=81)**	**Kd (N=76)**	**IKd (N=98)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	14 (29.8)	31 (38.3)	21 (27.6)	25 (25.5)	0.1730
Number (%) of patients censored	33 (70.2)	50 (61.7)	55 (72.4)	73 (74.5)	
Kaplan-Meier estimates of Global health status in months					
25% quantile (95% CI)	18.53 (4.698 to NC)	6.44 (1.906 to 14.620)	20.14 (3.811 to NC)	20.24 (11.499 to NC)	
Median (95% CI)	NC (20.567 to NC)	NC (17.544 to NC)	NC (21.947 to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.1730		0.6309	
Hazard ratio (95% CI) vs Kd	-	1.55 (0.82 to 2.91)		0.87 (0.49 to 1.55)	
P-value	-	0.1764		0.6312	
Deterioration probability (95% CI)[b]					

A higher score represents a better level of quality of life. Clinical meaningful deterioration change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Global health status
16.2.6.1.2.16 Efficacy response data - Subgroup analyses by previous treatment with IMiD
16.2.6.1.2.16.3 QLQ-C30 - Time to first improvement by 10 pt in global health status according to previous treatment with IMiD (LOCF) - ITT population

	Yes		No		
	Kd (N=62)	**IKd (N=81)**	**Kd (N=61)**	**IKd (N=98)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	33 (53.2)	42 (51.9)	28 (45.9)	50 (51.0)	0.4398
Number (%) of patients censored	29 (46.8)	39 (48.1)	33 (54.1)	48 (49.0)	
Kaplan-Meier estimates of Global health status in months					
25% quantile (95% CI)	1.22 (1.018 to 1.938)	1.91 (1.084 to 2.891)	1.91 (1.051 to 2.924)	1.91 (1.084 to 2.136)	
Median (95% CI)	10.55 (1.938 to NC)	15.87 (3.877 to NC)	NC (2.924 to NC)	9.40 (3.713 to NC)	
75% quantile (95% CI)	NC (22.144 to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.6455		0.5656	
Hazard ratio (95% CI) vs Kd	-	0.90 (0.57 to 1.42)		1.15 (0.72 to 1.82)	
P-value	-	0.6457		0.5659	
Improvement probability (95% CI)[b]					

A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Global health status
16.2.6.1.2.16 Efficacy response data - Subgroup analyses by previous treatment with IMiD
16.2.6.1.2.16.4 QLQ-C30 - Time to first deterioration by 10 pt in global health status according to previous treatment with IMiD (LOCF) - ITT population

	Yes		No		
	Kd (N=62)	**IKd (N=81)**	**Kd (N=61)**	**IKd (N=98)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	32 (51.6)	51 (63.0)	39 (63.9)	64 (65.3)	0.5557
Number (%) of patients censored	30 (48.4)	30 (37.0)	22 (36.1)	34 (34.7)	
Kaplan-Meier estimates of Global health status in months					
25% quantile (95% CI)	2.07 (1.084 to 3.844)	1.87 (1.084 to 2.825)	1.97 (1.183 to 2.825)	1.91 (1.084 to 2.037)	
Median (95% CI)	6.57 (3.844 to NC)	7.39 (3.745 to 14.324)	4.83 (2.825 to 12.780)	5.59 (3.055 to 11.269)	
75% quantile (95% CI)	NC (NC to NC)	NC (15.474 to NC)	NC (13.372 to NC)	NC (16.427 to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.2702		0.7421	
Hazard ratio (95% CI) vs Kd	-	1.28 (0.82 to 2.00)		1.07 (0.72 to 1.59)	
P-value	-	0.2715		0.7422	
Deterioration probability (95% CI)[b]					

A higher score represents a better level of quality of life. Clinical meaningful deterioration change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Global health status
16.2.6.1.2.16 Efficacy response data - Subgroup analyses by previous treatment with IMiD
16.2.6.1.2.16.5 QLQ-C30 - Time until permanent improvement by 10 pt in global health status according to previous treatment with IMiD (LOCF) - ITT population

	Yes		No		
	Kd (N=62)	**IKd (N=81)**	**Kd (N=61)**	**IKd (N=98)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	22 (35.5)	21 (25.9)	9 (14.8)	16 (16.3)	0.2423
Number (%) of patients censored	40 (64.5)	60 (74.1)	52 (85.2)	82 (83.7)	
Kaplan-Meier estimates of Global health status in months					
25% quantile (95% CI)	15.05 (6.045 to 21.027)	21.39 (15.671 to 22.374)	NC (16.624 to NC)	NC (17.051 to NC)	
Median (95% CI)	22.21 (21.027 to NC)	23.36 (22.341 to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (22.439 to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.1129		0.8030	
Hazard ratio (95% CI) vs Kd	-	0.62 (0.34 to 1.13)		1.11 (0.49 to 2.51)	
P-value	-	0.1163		0.8031	
Improvement probability (95% CI)[b]					

A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Global health status
16.2.6.1.2.16 Efficacy response data - Subgroup analyses by previous treatment with IMiD
16.2.6.1.2.16.6 QLQ-C30 - Time until permanent deterioration by 10 pt in global health status according to previous treatment with IMiD (LOCF) - ITT population

	Yes		No		
	Kd (N=62)	**IKd (N=81)**	**Kd (N=61)**	**IKd (N=98)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	14 (22.6)	26 (32.1)	21 (34.4)	30 (30.6)	0.2417
Number (%) of patients censored	48 (77.4)	55 (67.9)	40 (65.6)	68 (69.4)	
Kaplan-Meier estimates of Global health status in months					
25% quantile (95% CI)	20.63 (3.811 to NC)	11.50 (3.088 to 20.928)	12.39 (4.698 to 20.567)	14.62 (8.082 to 20.468)	
Median (95% CI)	NC (NC to NC)	NC (20.928 to NC)	NC (20.370 to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.2215		0.7269	
Hazard ratio (95% CI) vs Kd	-	1.50 (0.78 to 2.87)		0.91 (0.52 to 1.58)	
P-value	-	0.2246		0.7270	
Deterioration probability (95% CI)[b]					

A higher score represents a better level of quality of life. Clinical meaningful deterioration change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Global health status
16.2.6.1.2.17 Efficacy response data - Subgroup analyses by previous treatment with PI and IMiD
16.2.6.1.2.17.3 QLQ-C30 - Time to first improvement by 10 pt in global health status according to previous treatment with PI and IMiD (LOCF) - ITT population

	Yes		No		
	Kd (N=17)	**IKd (N=23)**	**Kd (N=106)**	**IKd (N=156)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	10 (58.8)	7 (30.4)	51 (48.1)	85 (54.5)	0.0247
Number (%) of patients censored	7 (41.2)	16 (69.6)	55 (51.9)	71 (45.5)	
Kaplan-Meier estimates of Global health status in months					
25% quantile (95% CI)	1.03 (0.953 to 4.797)	15.70 (0.986 to NC)	1.91 (1.051 to 2.201)	1.91 (1.084 to 2.004)	
Median (95% CI)	4.80 (1.018 to NC)	NC (15.704 to NC)	NC (4.205 to NC)	7.72 (3.745 to NC)	
75% quantile (95% CI)	NC (4.797 to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.0544		0.3926	
Hazard ratio (95% CI) vs Kd	-	0.40 (0.15 to 1.05)		1.16 (0.82 to 1.65)	
P-value	-	0.0630		0.3931	
Improvement probability (95% CI)[b]					

A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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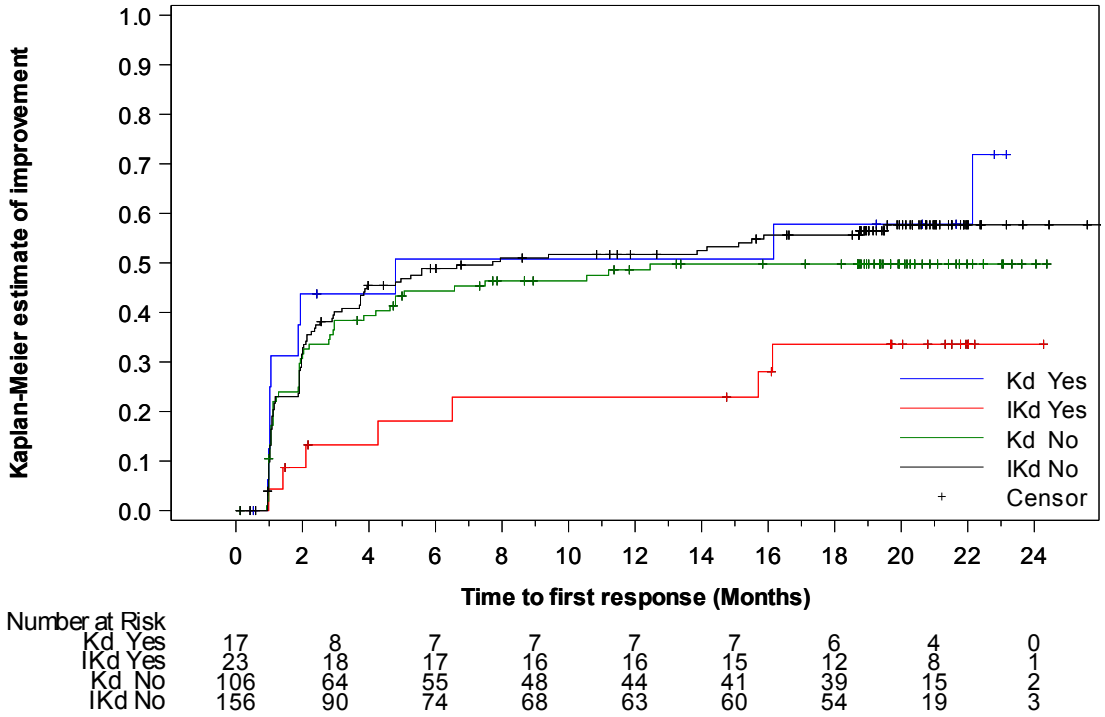
16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Global health status
16.2.6.1.2.17 Efficacy response data - Subgroup analyses by previous treatment with PI and IMiD
16.2.6.1.2.17.4 QLQ-C30 - Time to first improvement by 10 pt in global health status according to previous treatment with PI and IMiD- Kaplan-Meier curve (LOCF) - ITT population



A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
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16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Global health status
16.2.6.1.2.17 Efficacy response data - Subgroup analyses by previous treatment with PI and IMiD
16.2.6.1.2.17.5 QLQ-C30 - Time to first deterioration by 10 pt in global health status according to previous treatment with PI and IMiD (LOCF) - ITT population

	Yes		No		
	Kd (N=17)	**IKd (N=23)**	**Kd (N=106)**	**IKd (N=156)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	7 (41.2)	15 (65.2)	64 (60.4)	100 (64.1)	0.1413
Number (%) of patients censored	10 (58.8)	8 (34.8)	42 (39.6)	56 (35.9)	
Kaplan-Meier estimates of Global health status in months					
25% quantile (95% CI)	3.73 (1.051 to NC)	1.51 (0.986 to 2.497)	1.97 (1.150 to 2.825)	1.91 (1.117 to 2.037)	
Median (95% CI)	NC (2.793 to NC)	3.78 (1.873 to NC)	4.90 (3.154 to 12.780)	6.51 (3.811 to 11.400)	
75% quantile (95% CI)	NC (NC to NC)	NC (3.778 to NC)	NC (NC to NC)	NC (19.253 to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.0951		0.6611	
Hazard ratio (95% CI) vs Kd	-	2.12 (0.86 to 5.23)		1.07 (0.78 to 1.47)	
P-value	-	0.1028		0.6611	
Deterioration probability (95% CI)[b]					

A higher score represents a better level of quality of life. Clinical meaningful deterioration change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Global health status
16.2.6.1.2.17 Efficacy response data - Subgroup analyses by previous treatment with PI and IMiD
16.2.6.1.2.17.6 QLQ-C30 - Time until permanent improvement by 10 pt in global health status according to previous treatment with PI and IMiD (LOCF) - ITT population

	Yes		No		
	Kd (N=17)	**IKd (N=23)**	**Kd (N=106)**	**IKd (N=156)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	6 (35.3)	4 (17.4)	25 (23.6)	33 (21.2)	0.2764
Number (%) of patients censored	11 (64.7)	19 (82.6)	81 (76.4)	123 (78.8)	
Kaplan-Meier estimates of Global health status in months					
25% quantile (95% CI)	9.53 (0.953 to NC)	22.37 (18.136 to 23.359)	21.03 (15.869 to NC)	21.72 (16.624 to NC)	
Median (95% CI)	NC (9.528 to NC)	23.36 (22.374 to NC)	NC (22.439 to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (22.144 to NC)	NC (22.374 to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.1930		0.5760	
Hazard ratio (95% CI) vs Kd	-	0.44 (0.12 to 1.57)		0.86 (0.51 to 1.45)	
P-value	-	0.2051		0.5764	
Improvement probability (95% CI)[b]					

A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Global health status
16.2.6.1.2.17 Efficacy response data - Subgroup analyses by previous treatment with PI and IMiD
16.2.6.1.2.17.7 QLQ-C30 - Time until permanent deterioration by 10 pt in global health status according to previous treatment with PI and IMiD (LOCF) - ITT population

	Yes		No		
	Kd (N=17)	**IKd (N=23)**	**Kd (N=106)**	**IKd (N=156)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	2 (11.8)	11 (47.8)	33 (31.1)	45 (28.8)	0.0275
Number (%) of patients censored	15 (88.2)	12 (52.2)	73 (68.9)	111 (71.2)	
Kaplan-Meier estimates of Global health status in months					
25% quantile (95% CI)	NC (1.314 to NC)	2.37 (0.986 to 17.216)	15.44 (4.698 to 20.632)	18.92 (9.265 to 20.895)	
Median (95% CI)	NC (NC to NC)	17.54 (5.257 to NC)	NC (21.947 to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.0179		0.7484	
Hazard ratio (95% CI) vs Kd	-	5.15 (1.14 to 23.30)		0.93 (0.59 to 1.46)	
P-value	-	0.0335		0.7484	
Hazard ratio inverted (95% CI) vs IKd		-		1.08 (0.69 to 1.69)	

A higher score represents a better level of quality of life. Clinical meaningful deterioration change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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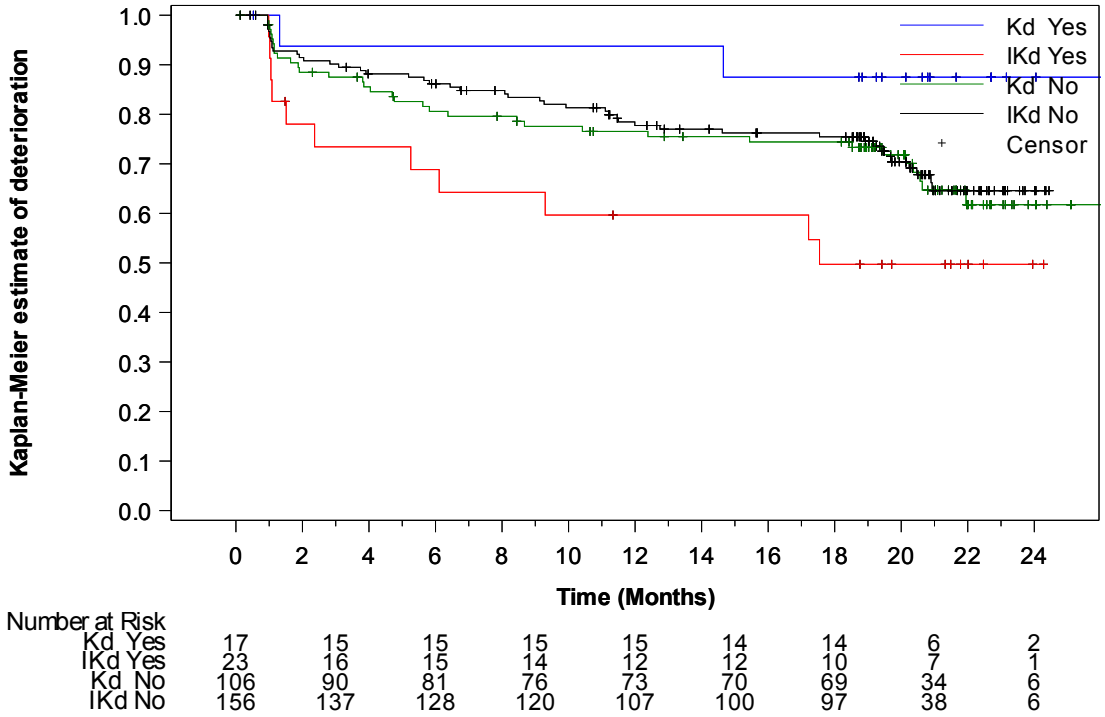
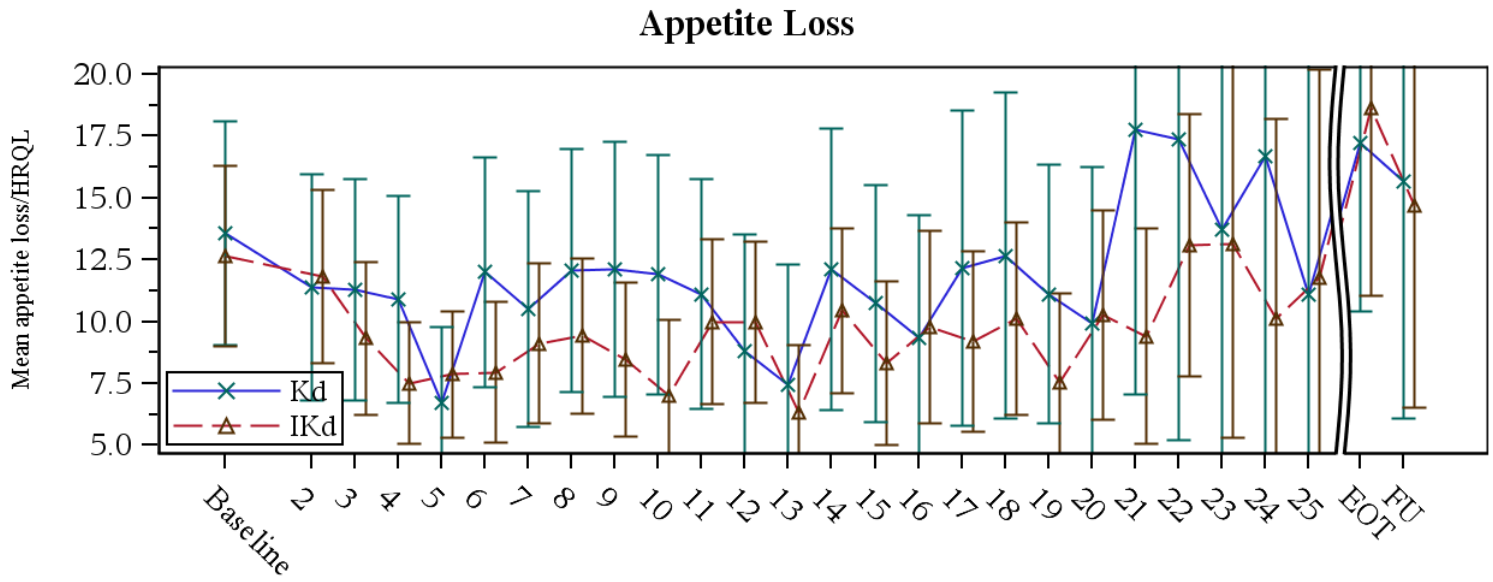
16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Global health status
16.2.6.1.2.17 Efficacy response data - Subgroup analyses by previous treatment with PI and IMiD
16.2.6.1.2.17.8 QLQ-C30 - Time until permanent deterioration by 10 pt in global health status according to previous treatment with PI and IMiD- Kaplan-Meier curve (LOCF) - ITT population



A higher score represents a better level of quality of life. Clinical meaningful deterioration change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
PGM=DEVOPS/SAR650984/EFC15246/CIR_RWE/REPORT/PGM/eff_qlq_km_subgp_de_i_f.sas OUT=REPORT/OUTPUT/eff_km_c30_glb_detpl_piimid_de_i_f_x.rtf (07APR2021 15:06)

16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Appetite loss
16.2.6.1.2.1 Efficacy response data
16.2.6.1.2.1.1 QLQ-C30 - Mean and 95% CI for appetite loss score over time (LOCF) - ITT population



#patients

Kd	113	114	112	110	104	100	95	91	88	84	78	72	67	66	62	57	52	50	45	37	30	23	17	10	6	62	34
IKd	166	169	168	164	161	155	150	145	138	133	130	127	121	118	112	109	105	102	97	91	78	56	38	23	17	59	34

A lower score represents a better level of quality of life. Cycles with less than 20 patients overall are not presented.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
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16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Appetite loss
16.2.6.1.2.1 Efficacy response data
16.2.6.1.2.1.15 QLQ-C30 - Time to first improvement by 15 pt in Appetite loss (LOCF) - ITT population

First improvement 15 points Appetite loss (%)	**Kd (N=123)**	**IKd (N=179)**
Number (%) of events	26 (21.1)	40 (22.3)
Number (%) of patients censored	97 (78.9)	139 (77.7)
Kaplan-Meier estimates of Appetite loss in months		
25% quantile (95% CI)	NC (1.971 to NC)	NC (2.103 to NC)
Median (95% CI)	NC (NC to NC)	NC (NC to NC)
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)
Comparison vs. Kd		
Stratified[a] Log-Rank test p-value[b] vs Kd	-	0.8366
Stratified[a] Hazard ratio (95% CI) vs Kd	-	1.05 (0.64 to 1.73)
P-value	-	0.8374
Improvement probability (95% CI)[c]		
3 Months	0.183 (0.120 to 0.257)	0.206 (0.150 to 0.269)
6 Months	0.217 (0.148 to 0.294)	0.218 (0.160 to 0.281)

A lower score represents a better level of quality of life. Clinical meaningful improvement change from baseline less than or equal to -15 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] Stratified on number of prior lines of therapy (1 vs. >1) and Revised International Staging System (R-ISS) stage (I or II vs. III vs. not classified) according to IRT
[b] One-sided significance level is 0.025
[c] Estimated using the Kaplan-Meier method
NA/NC = Not Applicable / Not Calculable
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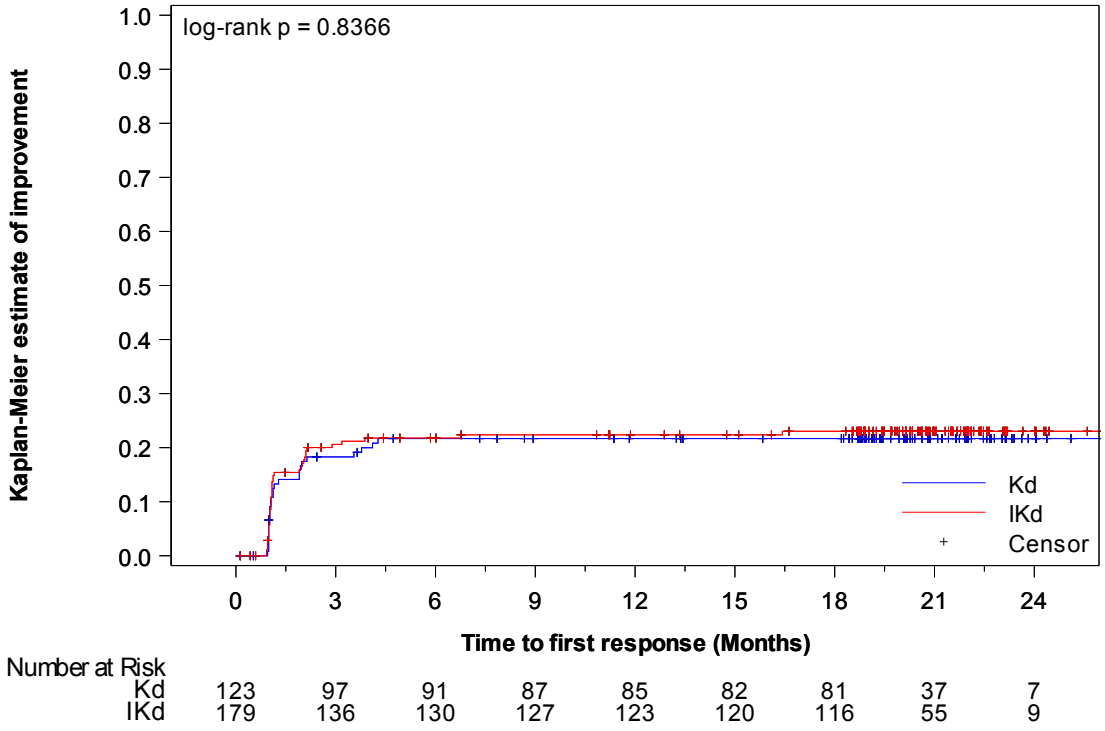
16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Appetite loss
16.2.6.1.2.1 Efficacy response data
16.2.6.1.2.1.16 QLQ-C30 - Time to first improvement by 15 pt in Appetite loss - Kaplan-Meier curve (LOCF) - ITT population



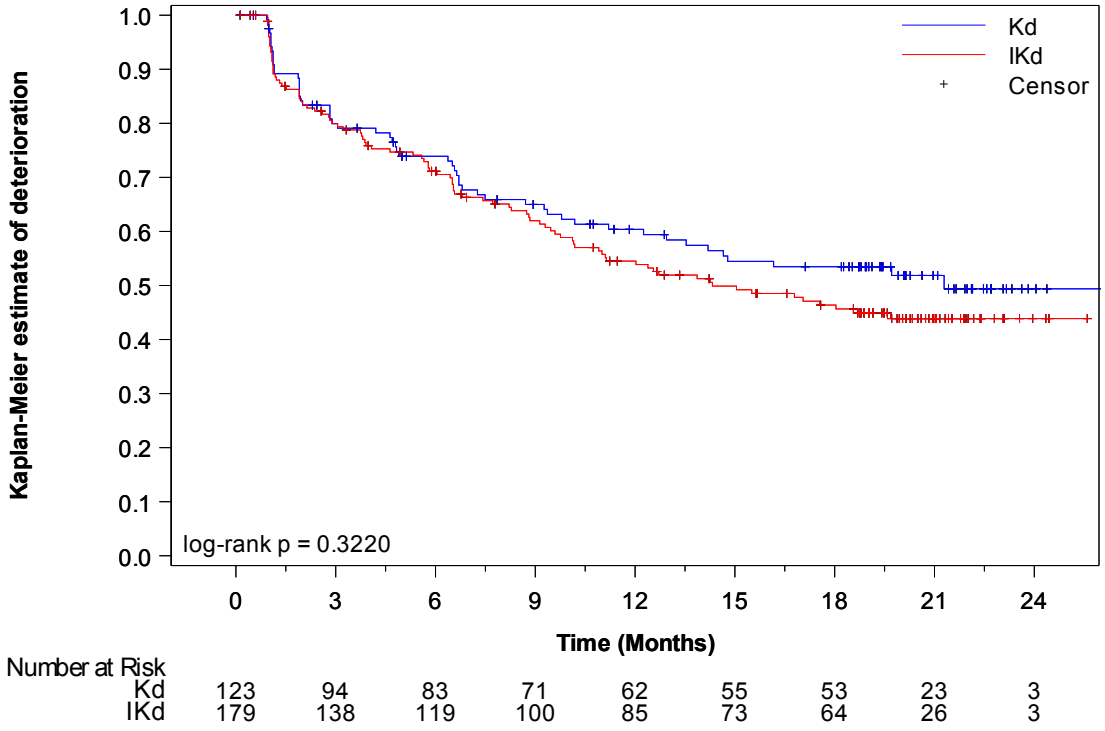
A lower score represents a better level of quality of life. Clinical meaningful improvement change from baseline less than or equal to -15 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
PGM=DEVOPS/SAR650984/EFC15246/CIR_RWE/REPORT/PGM/eff_qlq_km_i_f.sas OUT=REPORT/OUTPUT/eff_km_c30_apt_imp15l_de_i_f_x.rtf (07APR2021 14:24)

16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Appetite loss
16.2.6.1.2.1 Efficacy response data
16.2.6.1.2.1.17 QLQ-C30 - Time to first deterioration by 15 pt in Appetite loss (LOCF) - ITT population

First deterioration 15 points Appetite loss (%)	**Kd (N=123)**	**IKd (N=179)**
Number (%) of events	55 (44.7)	92 (51.4)
Number (%) of patients censored	68 (55.3)	87 (48.6)
Kaplan-Meier estimates of Appetite loss in months		
25% quantile (95% CI)	4.83 (2.825 to 7.261)	4.63 (2.793 to 6.538)
Median (95% CI)	21.29 (12.255 to NC)	14.32 (10.152 to NC)
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)
Comparison vs. Kd		
Stratified[a] Log-Rank test p-value[b] vs Kd	-	0.3220
Stratified[a] Hazard ratio (95% CI) vs Kd	-	1.18 (0.85 to 1.66)
P-value	-	0.3225
Deterioration probability (95% CI)[c]		
3 Months	0.799 (0.716 to 0.861)	0.799 (0.732 to 0.852)
6 Months	0.739 (0.650 to 0.809)	0.711 (0.638 to 0.773)

A lower score represents a better level of quality of life. Clinical meaningful deterioration change from baseline greater than or equal to 15 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] Stratified on number of prior lines of therapy (1 vs. >1) and Revised International Staging System (R-ISS) stage (I or II vs. III vs. not classified) according to IRT
[b] One-sided significance level is 0.025
[c] Estimated using the Kaplan-Meier method
NA/NC = Not Applicable / Not Calculable
PGM=DEVOPS/SAR650984/EFC15246/CIR_RWE/REPORT/PGM/eff_km_invhr_sr_i_t.sas OUT=REPORT/OUTPUT/eff_km_c30_apt_det15l_de_i_t_x.rtf (07APR2021 14:23)

16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Appetite loss
16.2.6.1.2.1 Efficacy response data
16.2.6.1.2.1.18 QLQ-C30 - Time to first deterioration by 15 pt in Appetite loss - Kaplan-Meier curve (LOCF) - ITT population



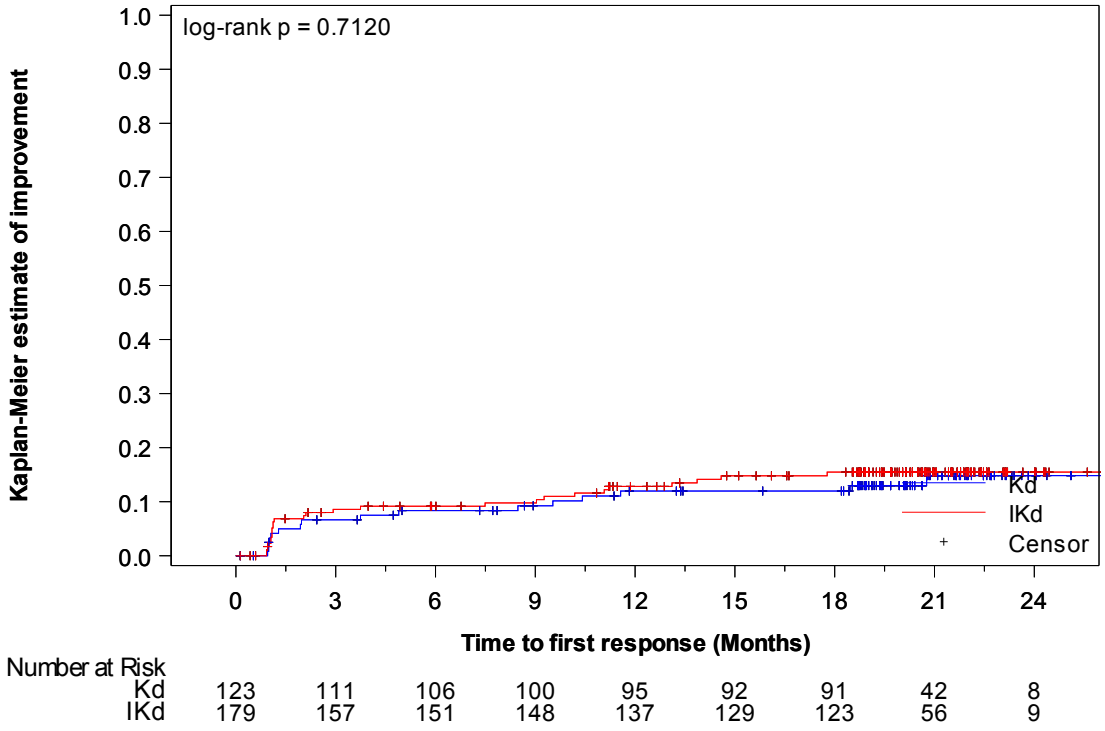
A lower score represents a better level of quality of life. Clinical meaningful deterioration change from baseline greater than or equal to 15 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
PGM=DEVOPS/SAR650984/EFC15246/CIR_RWE/REPORT/PGM/eff_qlq_km_i_f.sas OUT=REPORT/OUTPUT/eff_km_c30_apt_det15l_de_i_f_x.rtf (07APR2021 14:24)

16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Appetite loss
16.2.6.1.2.1 Efficacy response data
16.2.6.1.2.1.19 QLQ-C30 - Time until permanent improvement by 15 pt in Appetite loss (LOCF) - ITT population

First permanent improvement 15 points Appetite loss (%)	**Kd (N=123)**	**IKd (N=179)**
Number (%) of events	16 (13.0)	26 (14.5)
Number (%) of patients censored	107 (87.0)	153 (85.5)
Kaplan-Meier estimates of Appetite loss in months		
25% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)
Median (95% CI)	NC (NC to NC)	NC (NC to NC)
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)
Comparison vs. Kd		
Stratified[a] Log-Rank test p-value[b] vs Kd	-	0.7120
Stratified[a] Hazard ratio (95% CI) vs Kd	-	1.12 (0.60 to 2.10)
P-value	-	0.7122
Improvement probability (95% CI)[c]		
3 Months	0.066 (0.031 to 0.120)	0.086 (0.050 to 0.133)
6 Months	0.084 (0.043 to 0.142)	0.092 (0.055 to 0.140)

A lower score represents a better level of quality of life. Clinical meaningful improvement change from baseline less than or equal to -15 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] Stratified on number of prior lines of therapy (1 vs. >1) and Revised International Staging System (R-ISS) stage (I or II vs. III vs. not classified) according to IRT
[b] One-sided significance level is 0.025
[c] Estimated using the Kaplan-Meier method
NA/NC = Not Applicable / Not Calculable
PGM=DEVOPS/SAR650984/EFC15246/CIR_RWE/REPORT/PGM/eff_km_invhr_sr_i_t.sas OUT=REPORT/OUTPUT/eff_km_c30_apt_imp15pl_de_i_t_x.rtf (07APR2021 14:23)

16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Appetite loss
16.2.6.1.2.1 Efficacy response data
16.2.6.1.2.1.20 QLQ-C30 - Time until permanent improvement by 15 pt in Appetite loss - Kaplan-Meier curve (LOCF) - ITT population



A lower score represents a better level of quality of life. Clinical meaningful improvement change from baseline less than or equal to -15 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
PGM=DEVOPS/SAR650984/EFC15246/CIR_RWE/REPORT/PGM/eff_qlq_km_i_f.sas OUT=REPORT/OUTPUT/eff_km_c30_apt_imp15pl_de_i_f_x.rtf (07APR2021 14:24)

16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Appetite loss
16.2.6.1.2.1 Efficacy response data
16.2.6.1.2.1.21 QLQ-C30 - Time until permanent deterioration by 15 pt in Appetite loss (LOCF) - ITT population

First permanent deterioration 15 points Appetite loss (%)	**Kd (N=123)**	**IKd (N=179)**
Number (%) of events	22 (17.9)	36 (20.1)
Number (%) of patients censored	101 (82.1)	143 (79.9)
Kaplan-Meier estimates of Appetite loss in months		
25% quantile (95% CI)	NC (19.220 to NC)	21.39 (19.713 to NC)
Median (95% CI)	NC (NC to NC)	NC (NC to NC)
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)
Comparison vs. Kd		
Stratified[a] Log-Rank test p-value[b] vs Kd	-	0.7269
Stratified[a] Hazard ratio (95% CI) vs Kd	-	1.10 (0.65 to 1.87)
P-value	-	0.7270
Deterioration probability (95% CI)[c]		
3 Months	0.983 (0.934 to 0.996)	0.971 (0.932 to 0.988)
6 Months	0.957 (0.900 to 0.982)	0.930 (0.881 to 0.960)

A lower score represents a better level of quality of life. Clinical meaningful deterioration change from baseline greater than or equal to 15 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] Stratified on number of prior lines of therapy (1 vs. >1) and Revised International Staging System (R-ISS) stage (I or II vs. III vs. not classified) according to IRT
[b] One-sided significance level is 0.025
[c] Estimated using the Kaplan-Meier method
NA/NC = Not Applicable / Not Calculable
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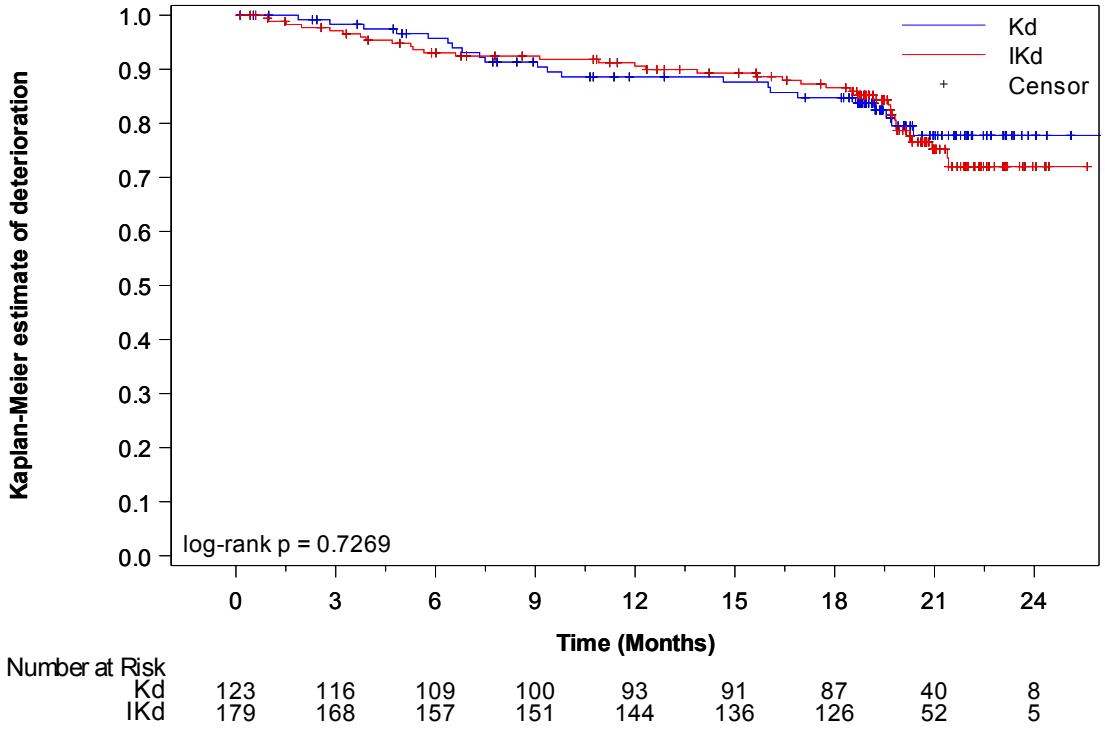
16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Appetite loss
16.2.6.1.2.1 Efficacy response data
16.2.6.1.2.1.22 QLQ-C30 - Time until permanent deterioration by 15 pt in Appetite loss - Kaplan-Meier curve (LOCF) - ITT population



A lower score represents a better level of quality of life. Clinical meaningful deterioration change from baseline greater than or equal to 15 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
PGM=DEVOPS/SAR650984/EFC15246/CIR_RWE/REPORT/PGM/eff_qlq_km_i_f.sas OUT=REPORT/OUTPUT/eff_km_c30_apt_det15pl_de_i_f_x.rtf (07APR2021 14:24)

16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Appetite loss
16.2.6.1.2.2 Efficacy response data - Subgroup analyses by age
16.2.6.1.2.2.3 QLQ-C30 - Time to first improvement by 10 pt in appetite loss according to age (LOCF) - ITT population

	<65 years		>=65 years		
	Kd (N=66)	**IKd (N=88)**	**Kd (N=57)**	**IKd (N=91)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	13 (19.7)	21 (23.9)	13 (22.8)	19 (20.9)	0.5582
Number (%) of patients censored	53 (80.3)	67 (76.1)	44 (77.2)	72 (79.1)	
Kaplan-Meier estimates of Appetite loss in months					
25% quantile (95% CI)	NC (1.281 to NC)	NC (1.084 to NC)	NC (1.906 to NC)	NC (2.037 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.5565		0.8160	
Hazard ratio (95% CI) vs Kd	-	1.23 (0.62 to 2.46)		0.92 (0.45 to 1.86)	
P-value	-	0.5572		0.8161	
Improvement probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful improvement change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Appetite loss
16.2.6.1.2.2 Efficacy response data - Subgroup analyses by age
16.2.6.1.2.2.4 QLQ-C30 - Time to first deterioration by 10 pt in appetite loss according to age (LOCF) - ITT population

	<65 years		>=65 years		
	Kd (N=66)	**IKd (N=88)**	**Kd (N=57)**	**IKd (N=91)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	26 (39.4)	41 (46.6)	29 (50.9)	51 (56.0)	0.6892
Number (%) of patients censored	40 (60.6)	47 (53.4)	28 (49.1)	40 (44.0)	
Kaplan-Meier estimates of Appetite loss in months					
25% quantile (95% CI)	6.70 (1.906 to 12.255)	3.81 (1.511 to 6.801)	4.80 (1.906 to 6.702)	5.59 (2.595 to 7.721)	
Median (95% CI)	NC (14.193 to NC)	19.68 (10.152 to NC)	14.65 (6.702 to NC)	12.02 (8.805 to 17.544)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (21.290 to NC)	NC (NC to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.3743		0.6755	
Hazard ratio (95% CI) vs Kd	-	1.25 (0.76 to 2.04)		1.10 (0.70 to 1.74)	
P-value	-	0.3753		0.6756	
Deterioration probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful deterioration change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
PGM=DEVOPS/SAR650984/EFC15246/CIR_RWE/REPORT/PGM/eff_km_subgp_sr_sig_de_i_t.sas OUT=REPORT/OUTPUT/eff_km_c30_apt_detl_age_de_i_t_x.rtf (07APR2021 14:34)

16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Appetite loss
16.2.6.1.2.2 Efficacy response data - Subgroup analyses by age
16.2.6.1.2.2.5 QLQ-C30 - Time until permanent improvement by 10 pt in appetite loss according to age (LOCF) - ITT population

	<65 years		>=65 years		
	Kd (N=66)	**IKd (N=88)**	**Kd (N=57)**	**IKd (N=91)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	8 (12.1)	13 (14.8)	8 (14.0)	13 (14.3)	0.7837
Number (%) of patients censored	58 (87.9)	75 (85.2)	49 (86.0)	78 (85.7)	
Kaplan-Meier estimates of Appetite loss in months					
25% quantile (95% CI)	NC (20.764 to NC)	NC (14.587 to NC)	NC (11.565 to NC)	NC (NC to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.6443		0.9384	
Hazard ratio (95% CI) vs Kd	-	1.23 (0.51 to 2.97)		1.04 (0.43 to 2.50)	
P-value	-	0.6449		0.9386	
Improvement probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful improvement change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Appetite loss
16.2.6.1.2.2 Efficacy response data - Subgroup analyses by age
16.2.6.1.2.2.6 QLQ-C30 - Time until permanent deterioration by 10 pt in appetite loss according to age (LOCF) - ITT population

	<65 years		>=65 years		
	Kd (N=66)	**IKd (N=88)**	**Kd (N=57)**	**IKd (N=91)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	12 (18.2)	16 (18.2)	10 (17.5)	20 (22.0)	0.7139
Number (%) of patients censored	54 (81.8)	72 (81.8)	47 (82.5)	71 (78.0)	
Kaplan-Meier estimates of Appetite loss in months					
25% quantile (95% CI)	NC (18.628 to NC)	21.39 (19.680 to NC)	NC (14.653 to NC)	20.30 (16.986 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.9909		0.6258	
Hazard ratio (95% CI) vs Kd	-	1.00 (0.47 to 2.11)		1.21 (0.57 to 2.58)	
P-value	-	0.9909		0.6263	
Deterioration probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful deterioration change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Appetite loss
16.2.6.1.2.3 Efficacy response data - Subgroup analyses by gender
16.2.6.1.2.3.3 QLQ-C30 - Time to first improvement by 10 pt in appetite loss according to gender (LOCF) - ITT population

	Male		Female		
	Kd (N=68)	**IKd (N=101)**	**Kd (N=55)**	**IKd (N=78)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	11 (16.2)	26 (25.7)	15 (27.3)	14 (17.9)	0.0431
Number (%) of patients censored	57 (83.8)	75 (74.3)	40 (72.7)	64 (82.1)	
Kaplan-Meier estimates of Appetite loss in months					
25% quantile (95% CI)	NC (3.548 to NC)	3.19 (1.084 to NC)	3.78 (1.018 to NC)	NC (2.891 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.1259		0.1764	
Hazard ratio (95% CI) vs Kd	-	1.72 (0.85 to 3.49)		0.61 (0.29 to 1.26)	
P-value	-	0.1308		0.1809	
Improvement probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful improvement change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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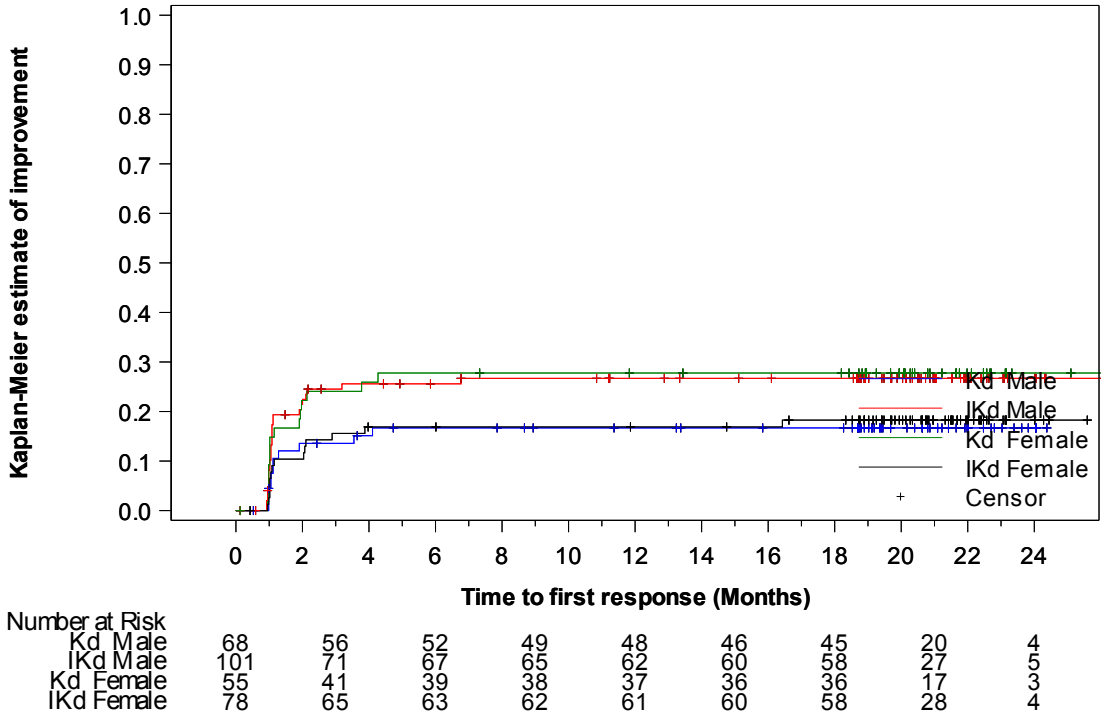
16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Appetite loss
16.2.6.1.2.3 Efficacy response data - Subgroup analyses by gender
16.2.6.1.2.3.4 QLQ-C30 - Time to first improvement by 10 pt in appetite loss according to gender - Kaplan-Meier curve (LOCF) - ITT population



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The last observation carried forward (LOCF) procedure was applied to impute missing data.
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16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Appetite loss
16.2.6.1.2.3 Efficacy response data - Subgroup analyses by gender
16.2.6.1.2.3.5 QLQ-C30 - Time to first deterioration by 10 pt in appetite loss according to gender (LOCF) - ITT population

	Male		Female		
	Kd (N=68)	**IKd (N=101)**	**Kd (N=55)**	**IKd (N=78)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	30 (44.1)	45 (44.6)	25 (45.5)	47 (60.3)	0.3012
Number (%) of patients censored	38 (55.9)	56 (55.4)	30 (54.5)	31 (39.7)	
Kaplan-Meier estimates of Appetite loss in months					
25% quantile (95% CI)	6.64 (3.055 to 10.185)	6.51 (2.891 to 10.119)	2.83 (1.117 to 6.702)	3.22 (1.906 to 5.782)	
Median (95% CI)	19.71 (11.203 to NC)	19.68 (12.386 to NC)	NC (6.702 to NC)	9.46 (6.538 to 15.047)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.9765		0.1654	
Hazard ratio (95% CI) vs Kd	-	1.01 (0.63 to 1.60)		1.41 (0.87 to 2.29)	
P-value	-	0.9765		0.1675	
Deterioration probability (95% CI)[b]					

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The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Appetite loss
16.2.6.1.2.3 Efficacy response data - Subgroup analyses by gender
16.2.6.1.2.3.6 QLQ-C30 - Time until permanent improvement by 10 pt in appetite loss according to gender (LOCF) - ITT population

	Male		Female		
	Kd (N=68)	**IKd (N=101)**	**Kd (N=55)**	**IKd (N=78)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	4 (5.9)	19 (18.8)	12 (21.8)	7 (9.0)	0.0025
Number (%) of patients censored	64 (94.1)	82 (81.2)	43 (78.2)	71 (91.0)	
Kaplan-Meier estimates of Appetite loss in months					
25% quantile (95% CI)	NC (NC to NC)	NC (11.203 to NC)	NC (4.895 to NC)	NC (NC to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.0176		0.0364	
Hazard ratio (95% CI) vs Kd	-	3.41 (1.16 to 10.03)		0.38 (0.15 to 0.97)	
P-value	-	0.0257		0.0440	
Hazard ratio inverted (95% CI) vs IKd		-		2.61 (1.03 to 6.62)	

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The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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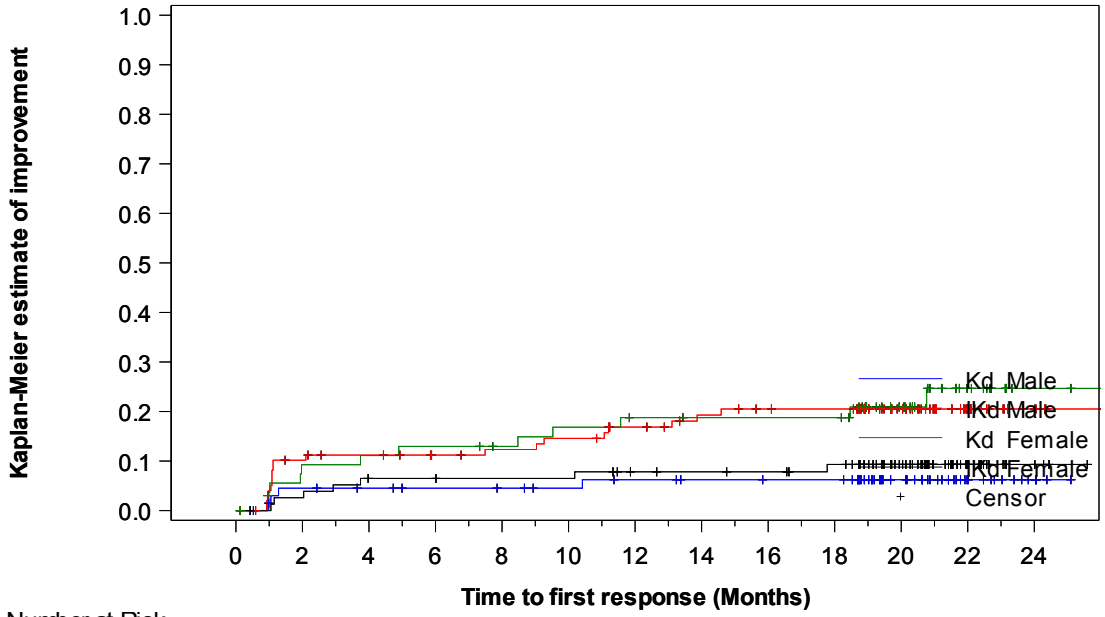
16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Appetite loss
16.2.6.1.2.3 Efficacy response data - Subgroup analyses by gender
16.2.6.1.2.3.7 QLQ-C30 - Time until permanent improvement by 10 pt in appetite loss according to gender - Kaplan-Meier curve (LOCF) - ITT population



Number at Risk

Kd Male	68	62	59	56	54	52	51	24	5
IKd Male	101	84	80	78	71	65	62	28	5
Kd Female	55	49	47	44	41	40	40	18	3
IKd Female	78	73	71	70	66	64	61	28	4

A lower score represents a better level of quality of life. Clinical meaningful improvement change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
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16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Appetite loss
16.2.6.1.2.3 Efficacy response data - Subgroup analyses by gender
16.2.6.1.2.3.8 QLQ-C30 - Time until permanent deterioration by 10 pt in appetite loss according to gender (LOCF) - ITT population

	Male		Female		
	Kd (N=68)	**IKd (N=101)**	**Kd (N=55)**	**IKd (N=78)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	12 (17.6)	13 (12.9)	10 (18.2)	23 (29.5)	0.1624
Number (%) of patients censored	56 (82.4)	88 (87.1)	45 (81.8)	55 (70.5)	
Kaplan-Meier estimates of Appetite loss in months					
25% quantile (95% CI)	NC (16.887 to NC)	NC (19.844 to NC)	NC (9.068 to NC)	19.81 (13.864 to 21.421)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (21.421 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.4080		0.2350	
Hazard ratio (95% CI) vs Kd	-	0.72 (0.33 to 1.58)		1.56 (0.74 to 3.28)	
P-value	-	0.4101		0.2390	
Deterioration probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful deterioration change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Appetite loss
16.2.6.1.2.4 Efficacy response data - Subgroup analyses by ethnic origin
16.2.6.1.2.4.3 QLQ-C30 - Time to first improvement by 10 pt in appetite loss according to ethnic origin (LOCF) - ITT population

	White		Other		
	Kd (N=83)	**IKd (N=131)**	**Kd (N=28)**	**IKd (N=34)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	16 (19.3)	27 (20.6)	8 (28.6)	10 (29.4)	0.8844
Number (%) of patients censored	67 (80.7)	104 (79.4)	20 (71.4)	24 (70.6)	
Kaplan-Meier estimates of Appetite loss in months					
25% quantile (95% CI)	NC (1.906 to NC)	NC (2.103 to NC)	4.11 (1.117 to NC)	2.07 (0.986 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (4.271 to NC)	NC (6.768 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.8354		0.7772	
Hazard ratio (95% CI) vs Kd	-	1.07 (0.58 to 1.98)		1.14 (0.45 to 2.90)	
P-value	-	0.8355		0.7774	
Improvement probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful improvement change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Appetite loss
16.2.6.1.2.4 Efficacy response data - Subgroup analyses by ethnic origin
16.2.6.1.2.4.4 QLQ-C30 - Time to first deterioration by 10 pt in appetite loss according to ethnic origin (LOCF) - ITT population

	White		Other		
	Kd (N=83)	**IKd (N=131)**	**Kd (N=28)**	**IKd (N=34)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	36 (43.4)	63 (48.1)	15 (53.6)	24 (70.6)	0.5974
Number (%) of patients censored	47 (56.6)	68 (51.9)	13 (46.4)	10 (29.4)	
Kaplan-Meier estimates of Appetite loss in months					
25% quantile (95% CI)	4.70 (1.906 to 7.491)	4.63 (2.136 to 6.505)	6.64 (1.117 to 11.203)	3.84 (1.117 to 8.214)	
Median (95% CI)	NC (9.791 to NC)	14.32 (9.758 to NC)	14.19 (6.702 to NC)	11.10 (3.910 to 17.544)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (16.164 to NC)	19.68 (15.507 to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.4778		0.2169	
Hazard ratio (95% CI) vs Kd	-	1.16 (0.77 to 1.75)		1.50 (0.78 to 2.86)	
P-value	-	0.4782		0.2200	
Deterioration probability (95% CI)[b]					

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The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Appetite loss
16.2.6.1.2.4 Efficacy response data - Subgroup analyses by ethnic origin
16.2.6.1.2.4.5 QLQ-C30 - Time until permanent improvement by 10 pt in appetite loss according to ethnic origin (LOCF) - ITT population

	White		Other		
	Kd (N=83)	**IKd (N=131)**	**Kd (N=28)**	**IKd (N=34)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	10 (12.0)	20 (15.3)	4 (14.3)	5 (14.7)	0.8001
Number (%) of patients censored	73 (88.0)	111 (84.7)	24 (85.7)	29 (85.3)	
Kaplan-Meier estimates of Appetite loss in months					
25% quantile (95% CI)	NC (20.764 to NC)	NC (NC to NC)	NC (1.281 to NC)	NC (1.084 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.4812		0.9203	
Hazard ratio (95% CI) vs Kd	-	1.31 (0.61 to 2.80)		1.07 (0.29 to 3.98)	
P-value	-	0.4826		0.9206	
Improvement probability (95% CI)[b]					

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CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Appetite loss
16.2.6.1.2.4 Efficacy response data - Subgroup analyses by ethnic origin
16.2.6.1.2.4.6 QLQ-C30 - Time until permanent deterioration by 10 pt in appetite loss according to ethnic origin (LOCF) - ITT population

	White		Other		
	Kd (N=83)	**IKd (N=131)**	**Kd (N=28)**	**IKd (N=34)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	18 (21.7)	25 (19.1)	2 (7.1)	8 (23.5)	0.0797
Number (%) of patients censored	65 (78.3)	106 (80.9)	26 (92.9)	26 (76.5)	
Kaplan-Meier estimates of Appetite loss in months					
25% quantile (95% CI)	20.37 (16.000 to NC)	21.39 (19.713 to NC)	NC (19.713 to NC)	20.30 (3.910 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.5975		0.0784	
Hazard ratio (95% CI) vs Kd	-	0.85 (0.46 to 1.56)		3.66 (0.78 to 17.27)	
P-value	-	0.5979		0.1005	
Deterioration probability (95% CI)[b]					

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The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Appetite loss
16.2.6.1.2.5 Efficacy response data - Subgroup analyses by geographical region
16.2.6.1.2.5.3 QLQ-C30 - Time to first improvement by 10 pt in appetite loss according to geographical region (LOCF) - ITT population

	Europe		America		Asia		Other countries		
	Kd (N=60)	**IKd (N=85)**	**Kd (N=20)**	**IKd (N=24)**	**Kd (N=21)**	**IKd (N=25)**	**Kd (N=22)**	**IKd (N=45)**	**p-value of treatment-by-subgroup interaction[c]**
Number (%) of events	12 (20.0)	16 (18.8)	4 (20.0)	4 (16.7)	7 (33.3)	8 (32.0)	3 (13.6)	12 (26.7)	0.6784
Number (%) of patients censored	48 (80.0)	69 (81.2)	16 (80.0)	20 (83.3)	14 (66.7)	17 (68.0)	19 (86.4)	33 (73.3)	
Kaplan-Meier estimates of event in months									
25% quantile (95% CI)	NC (1.018 to NC)	NC (2.103 to NC)	NC (0.986 to NC)	NC (0.953 to NC)	3.55 (1.018 to NC)	1.99 (0.920 to NC)	NC (1.018 to NC)	3.88 (1.051 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (3.548 to NC)	NC (2.070 to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Kd									

A lower score represents a better level of quality of life. Clinical meaningful improvement change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Appetite loss
16.2.6.1.2.5 Efficacy response data - Subgroup analyses by geographical region
16.2.6.1.2.5.3 QLQ-C30 - Time to first improvement by 10 pt in appetite loss according to geographical region (LOCF) - ITT population

	Europe		America		Asia		Other countries		
	Kd (N=60)	**IKd (N=85)**	**Kd (N=20)**	**IKd (N=24)**	**Kd (N=21)**	**IKd (N=25)**	**Kd (N=22)**	**IKd (N=45)**	**p-value of treatment-by-subgroup interaction[c]**
Log-Rank test p-value[a] vs Kd	-	0.7727		0.9181		0.9920		0.2205	
Hazard ratio (95% CI) vs Kd	-	0.90 (0.42 to 1.89)		0.93 (0.23 to 3.72)		1.01 (0.36 to 2.77)		2.16 (0.61 to 7.67)	
P-value	-	0.7728		0.9181		0.9920		0.2319	
Improvement probability (95% CI)[b]									
3 Months	0.205 (0.113 to 0.316)	0.169 (0.098 to 0.256)	0.200 (0.062 to 0.393)	0.172 (0.054 to 0.347)	0.200 (0.062 to 0.393)	0.292 (0.130 to 0.476)	0.091 (0.016 to 0.251)	0.244 (0.132 to 0.376)	
6 Months	0.205 (0.113 to 0.316)	0.181 (0.107 to 0.271)	0.200 (0.062 to 0.393)	0.172 (0.054 to 0.347)	0.360 (0.161 to 0.565)	0.292 (0.130 to 0.476)	0.136 (0.034 to 0.309)	0.267 (0.149 to 0.400)	

A lower score represents a better level of quality of life. Clinical meaningful improvement change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Appetite loss
16.2.6.1.2.5 Efficacy response data - Subgroup analyses by geographical region
16.2.6.1.2.5.4 QLQ-C30 - Time to first deterioration by 10 pt in appetite loss according to geographical region (LOCF) - ITT population

	Europe		America		Asia		Other countries		
	Kd (N=60)	**IKd (N=85)**	**Kd (N=20)**	**IKd (N=24)**	**Kd (N=21)**	**IKd (N=25)**	**Kd (N=22)**	**IKd (N=45)**	**p-value of treatment-by-subgroup interaction[c]**
Number (%) of events	20 (33.3)	40 (47.1)	11 (55.0)	14 (58.3)	10 (47.6)	18 (72.0)	14 (63.6)	20 (44.4)	0.1814
Number (%) of patients censored	40 (66.7)	45 (52.9)	9 (45.0)	10 (41.7)	11 (52.4)	7 (28.0)	8 (36.4)	25 (55.6)	
Kaplan-Meier estimates of event in months									
25% quantile (95% CI)	7.26 (2.891 to 14.784)	5.78 (1.906 to 9.133)	3.37 (0.920 to 6.801)	3.81 (1.051 to 6.801)	6.70 (1.051 to 14.193)	2.40 (0.986 to 8.279)	2.00 (0.986 to 6.374)	5.65 (1.380 to 10.185)	
Median (95% CI)	NC (14.784 to NC)	17.54 (10.152 to NC)	9.36 (1.938 to NC)	7.72 (3.811 to NC)	19.71 (6.702 to NC)	11.10 (2.825 to 18.037)	10.09 (2.004 to NC)	NC (8.838 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (9.791 to NC)	NC (8.214 to NC)	NC (19.713 to NC)	19.68 (13.864 to NC)	NC (13.536 to NC)	NC (NC to NC)	

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The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Appetite loss
16.2.6.1.2.5 Efficacy response data - Subgroup analyses by geographical region
16.2.6.1.2.5.4 QLQ-C30 - Time to first deterioration by 10 pt in appetite loss according to geographical region (LOCF) - ITT population

	Europe		America		Asia		Other countries		
	Kd (N=60)	**IKd (N=85)**	**Kd (N=20)**	**IKd (N=24)**	**Kd (N=21)**	**IKd (N=25)**	**Kd (N=22)**	**IKd (N=45)**	**p-value of treatment-by-subgroup interaction[c]**
Comparison vs. Kd									
Log-Rank test p-value[a] vs Kd	-	0.1346		0.7434		0.1478		0.1938	
Hazard ratio (95% CI) vs Kd	-	1.50 (0.88 to 2.57)		1.14 (0.52 to 2.52)		1.76 (0.81 to 3.84)		0.64 (0.32 to 1.26)	
P-value	-	0.1373		0.7436		0.1531		0.1974	
Deterioration probability (95% CI)[b]									
3 Months	0.861 (0.741 to 0.928)	0.807 (0.704 to 0.877)	0.750 (0.500 to 0.887)	0.824 (0.596 to 0.930)	0.800 (0.551 to 0.920)	0.708 (0.484 to 0.849)	0.682 (0.446 to 0.834)	0.822 (0.676 to 0.907)	

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The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Appetite loss
16.2.6.1.2.5 Efficacy response data - Subgroup analyses by geographical region
16.2.6.1.2.5.5 QLQ-C30 - Time until permanent improvement by 10 pt in appetite loss according to geographical region (LOCF) - ITT population

	Europe		America		Asia		Other countries		
	Kd (N=60)	**IKd (N=85)**	**Kd (N=20)**	**IKd (N=24)**	**Kd (N=21)**	**IKd (N=25)**	**Kd (N=22)**	**IKd (N=45)**	**p-value of treatment-by-subgroup interaction[c]**
Number (%) of events	7 (11.7)	11 (12.9)	4 (20.0)	3 (12.5)	3 (14.3)	4 (16.0)	2 (9.1)	8 (17.8)	0.7987
Number (%) of patients censored	53 (88.3)	74 (87.1)	16 (80.0)	21 (87.5)	18 (85.7)	21 (84.0)	20 (90.9)	37 (82.2)	
Kaplan-Meier estimates of event in months									
25% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	20.76 (1.281 to NC)	NC (0.953 to NC)	NC (1.018 to NC)	NC (0.920 to NC)	NC (4.895 to NC)	NC (11.072 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (20.764 to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	

A lower score represents a better level of quality of life. Clinical meaningful improvement change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Appetite loss
16.2.6.1.2.5 Efficacy response data - Subgroup analyses by geographical region
16.2.6.1.2.5.5 QLQ-C30 - Time until permanent improvement by 10 pt in appetite loss according to geographical region (LOCF) - ITT population

	Europe		America		Asia		Other countries		
	Kd (N=60)	**IKd (N=85)**	**Kd (N=20)**	**IKd (N=24)**	**Kd (N=21)**	**IKd (N=25)**	**Kd (N=22)**	**IKd (N=45)**	**p-value of treatment-by-subgroup interaction[c]**
Comparison vs. Kd									
Log-Rank test p-value[a] vs Kd	-	0.8558		0.6278		0.8958		0.3400	
Hazard ratio (95% CI) vs Kd	-	1.09 (0.42 to 2.82)		0.69 (0.15 to 3.09)		1.11 (0.25 to 4.94)		2.09 (0.44 to 9.85)	
P-value	-	0.8558		0.6297		0.8958		0.3508	
Improvement probability (95% CI)[b]									
3 Months	0.068 (0.022 to 0.151)	0.061 (0.022 to 0.126)	0.100 (0.017 to 0.272)	0.129 (0.032 to 0.294)	0.100 (0.017 to 0.272)	0.125 (0.031 to 0.287)		0.089 (0.028 to 0.193)	

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The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Appetite loss
16.2.6.1.2.5 Efficacy response data - Subgroup analyses by geographical region
16.2.6.1.2.5.6 QLQ-C30 - Time until permanent deterioration by 10 pt in appetite loss according to geographical region (LOCF) - ITT population

	Europe		America		Asia		Other countries		
	Kd (N=60)	**IKd (N=85)**	**Kd (N=20)**	**IKd (N=24)**	**Kd (N=21)**	**IKd (N=25)**	**Kd (N=22)**	**IKd (N=45)**	**p-value of treatment-by-subgroup interaction[c]**
Number (%) of events	10 (16.7)	19 (22.4)	5 (25.0)	2 (8.3)	2 (9.5)	7 (28.0)	5 (22.7)	8 (17.8)	0.2597
Number (%) of patients censored	50 (83.3)	66 (77.6)	15 (75.0)	22 (91.7)	19 (90.5)	18 (72.0)	17 (77.3)	37 (82.2)	
Kaplan-Meier estimates of event in months									
25% quantile (95% CI)	NC (16.066 to NC)	20.93 (18.464 to NC)	18.63 (6.801 to NC)	NC (12.320 to NC)	NC (4.830 to NC)	13.86 (0.986 to NC)	19.22 (3.844 to NC)	21.42 (18.694 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (18.628 to NC)	NC (19.844 to NC)	NC (NC to NC)	NC (19.680 to NC)	NC (19.220 to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	

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The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Appetite loss
16.2.6.1.2.5 Efficacy response data - Subgroup analyses by geographical region
16.2.6.1.2.5.6 QLQ-C30 - Time until permanent deterioration by 10 pt in appetite loss according to geographical region (LOCF) - ITT population

	Europe		America		Asia		Other countries		
	Kd (N=60)	**IKd (N=85)**	**Kd (N=20)**	**IKd (N=24)**	**Kd (N=21)**	**IKd (N=25)**	**Kd (N=22)**	**IKd (N=45)**	**p-value of treatment-by-subgroup interaction[c]**
Comparison vs. Kd									
Log-Rank test p-value[a] vs Kd	-	0.5943		0.1856		0.1294		0.6961	
Hazard ratio (95% CI) vs Kd	-	1.23 (0.57 to 2.65)		0.35 (0.07 to 1.79)		3.16 (0.66 to 15.24)		0.80 (0.26 to 2.45)	
P-value	-	0.5949		0.2062		0.1510		0.6967	
Deterioration probability (95% CI)[b]									
3 Months	0.965 (0.868 to 0.991)	0.964 (0.892 to 0.988)	1.000 (1.000 to 1.000)	1.000 (1.000 to 1.000)	1.000 (1.000 to 1.000)	0.917 (0.706 to 0.978)	1.000 (1.000 to 1.000)	1.000 (1.000 to 1.000)	

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The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Appetite loss
16.2.6.1.2.6 Efficacy response data - Subgroup analyses by regulatory region
16.2.6.1.2.6.3 QLQ-C30 - Time to first improvement by 10 pt in appetite loss according to regulatory region (LOCF) - ITT population

	Western countries		Other countries		
	Kd (N=55)	**IKd (N=97)**	**Kd (N=68)**	**IKd (N=82)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	11 (20.0)	22 (22.7)	15 (22.1)	18 (22.0)	0.9493
Number (%) of patients censored	44 (80.0)	75 (77.3)	53 (77.9)	64 (78.0)	
Kaplan-Meier estimates of Appetite loss in months					
25% quantile (95% CI)	NC (1.018 to NC)	NC (2.004 to NC)	NC (1.938 to NC)	NC (1.084 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.8047		0.8885	
Hazard ratio (95% CI) vs Kd	-	1.10 (0.53 to 2.26)		1.05 (0.53 to 2.08)	
P-value	-	0.8048		0.8887	
Improvement probability (95% CI)[b]					

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The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Appetite loss
16.2.6.1.2.6 Efficacy response data - Subgroup analyses by regulatory region
16.2.6.1.2.6.4 QLQ-C30 - Time to first deterioration by 10 pt in appetite loss according to regulatory region (LOCF) - ITT population

	Western countries		Other countries		
	Kd (N=55)	**IKd (N=97)**	**Kd (N=68)**	**IKd (N=82)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	24 (43.6)	42 (43.3)	31 (45.6)	50 (61.0)	0.1697
Number (%) of patients censored	31 (56.4)	55 (56.7)	37 (54.4)	32 (39.0)	
Kaplan-Meier estimates of Appetite loss in months					
25% quantile (95% CI)	6.37 (1.906 to 9.265)	6.51 (3.220 to 10.908)	4.83 (1.150 to 9.363)	2.83 (1.511 to 5.782)	
Median (95% CI)	21.29 (6.702 to NC)	NC (12.550 to NC)	19.71 (9.791 to NC)	9.76 (6.571 to 17.051)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (18.694 to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.8697		0.0636	
Hazard ratio (95% CI) vs Kd	-	0.96 (0.58 to 1.58)		1.52 (0.97 to 2.39)	
P-value	-	0.8689		0.0656	
Deterioration probability (95% CI)[b]					

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CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Appetite loss
16.2.6.1.2.6 Efficacy response data - Subgroup analyses by regulatory region
16.2.6.1.2.6.5 QLQ-C30 - Time until permanent improvement by 10 pt in appetite loss according to regulatory region (LOCF) - ITT population

	Western countries		Other countries		
	Kd (N=55)	**IKd (N=97)**	**Kd (N=68)**	**IKd (N=82)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	7 (12.7)	14 (14.4)	9 (13.2)	12 (14.6)	0.9836
Number (%) of patients censored	48 (87.3)	83 (85.6)	59 (86.8)	70 (85.4)	
Kaplan-Meier estimates of Appetite loss in months					
25% quantile (95% CI)	NC (10.415 to NC)	NC (NC to NC)	NC (20.764 to NC)	NC (17.774 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.8166		0.7758	
Hazard ratio (95% CI) vs Kd	-	1.11 (0.45 to 2.76)		1.13 (0.48 to 2.69)	
P-value	-	0.8167		0.7760	
Improvement probability (95% CI)[b]					

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CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Appetite loss
16.2.6.1.2.6 Efficacy response data - Subgroup analyses by regulatory region
16.2.6.1.2.6.6 QLQ-C30 - Time until permanent deterioration by 10 pt in appetite loss according to regulatory region (LOCF) - ITT population

	Western countries		Other countries		
	Kd (N=55)	**IKd (N=97)**	**Kd (N=68)**	**IKd (N=82)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	9 (16.4)	16 (16.5)	13 (19.1)	20 (24.4)	0.6833
Number (%) of patients censored	46 (83.6)	81 (83.5)	55 (80.9)	62 (75.6)	
Kaplan-Meier estimates of Appetite loss in months					
25% quantile (95% CI)	NC (16.066 to NC)	21.39 (19.844 to NC)	NC (16.000 to NC)	19.81 (13.864 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.9631		0.5062	
Hazard ratio (95% CI) vs Kd	-	1.02 (0.45 to 2.31)		1.27 (0.63 to 2.55)	
P-value	-	0.9632		0.5072	
Deterioration probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful deterioration change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
PGM=DEVOPS/SAR650984/EFC15246/CIR_RWE/REPORT/PGM/eff_km_subgp_sr_sig_de_i_t.sas OUT=REPORT/OUTPUT/eff_km_c30_apt_detpl_rreg_de_i_t_x.rtf (07APR2021 14:34)

16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Appetite loss
16.2.6.1.2.7 Efficacy response data - Subgroup analyses by baseline ECOG PS
16.2.6.1.2.7.3 QLQ-C30 - Time to first improvement by 10 pt in appetite loss according to baseline ECOG PS (LOCF) - ITT population

	0 or 1		>1		
	Kd (N=118)	**IKd (N=168)**	**Kd (N=5)**	**IKd (N=11)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	24 (20.3)	37 (22.0)	2 (40.0)	3 (27.3)	0.6791
Number (%) of patients censored	94 (79.7)	131 (78.0)	3 (60.0)	8 (72.7)	
Kaplan-Meier estimates of Appetite loss in months					
25% quantile (95% CI)	NC (2.136 to NC)	NC (2.103 to NC)	1.05 (0.986 to NC)	2.10 (0.986 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (0.986 to NC)	NC (0.986 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (0.986 to NC)	NC (NC to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.7481		0.7852	
Hazard ratio (95% CI) vs Kd	-	1.09 (0.65 to 1.82)		0.78 (0.13 to 4.68)	
P-value	-	0.7482		0.7858	
Improvement probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful improvement change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Appetite loss
16.2.6.1.2.7 Efficacy response data - Subgroup analyses by baseline ECOG PS
16.2.6.1.2.7.4 QLQ-C30 - Time to first deterioration by 10 pt in appetite loss according to baseline ECOG PS (LOCF) - ITT population

	0 or 1		>1		
	Kd (N=118)	**IKd (N=168)**	**Kd (N=5)**	**IKd (N=11)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	53 (44.9)	87 (51.8)	2 (40.0)	5 (45.5)	0.7942
Number (%) of patients censored	65 (55.1)	81 (48.2)	3 (60.0)	6 (54.5)	
Kaplan-Meier estimates of Appetite loss in months					
25% quantile (95% CI)	4.80 (2.004 to 7.261)	5.32 (2.793 to 6.538)	10.73 (6.801 to NC)	3.06 (1.906 to 10.908)	
Median (95% CI)	21.29 (11.203 to NC)	15.05 (10.152 to NC)	14.65 (6.801 to NC)	10.91 (1.906 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (6.801 to NC)	NC (10.119 to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.3382		0.6381	
Hazard ratio (95% CI) vs Kd	-	1.18 (0.84 to 1.66)		1.48 (0.29 to 7.64)	
P-value	-	0.3388		0.6404	
Deterioration probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful deterioration change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Appetite loss
16.2.6.1.2.7 Efficacy response data - Subgroup analyses by baseline ECOG PS
16.2.6.1.2.7.5 QLQ-C30 - Time until permanent improvement by 10 pt in appetite loss according to baseline ECOG PS (LOCF) - ITT population

	0 or 1		>1		
	Kd (N=118)	**IKd (N=168)**	**Kd (N=5)**	**IKd (N=11)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	14 (11.9)	25 (14.9)	2 (40.0)	1 (9.1)	0.1504
Number (%) of patients censored	104 (88.1)	143 (85.1)	3 (60.0)	10 (90.9)	
Kaplan-Meier estimates of Appetite loss in months					
25% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	1.05 (0.986 to NC)	NC (0.986 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (0.986 to NC)	NC (0.986 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (0.986 to NC)	NC (NC to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.4752		0.2486	
Hazard ratio (95% CI) vs Kd	-	1.27 (0.66 to 2.44)		0.27 (0.02 to 2.96)	
P-value	-	0.4763		0.2826	
Improvement probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful improvement change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Appetite loss
16.2.6.1.2.7 Efficacy response data - Subgroup analyses by baseline ECOG PS
16.2.6.1.2.7.6 QLQ-C30 - Time until permanent deterioration by 10 pt in appetite loss according to baseline ECOG PS (LOCF) - ITT population

	0 or 1		>1		
	Kd (N=118)	**IKd (N=168)**	**Kd (N=5)**	**IKd (N=11)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	20 (16.9)	34 (20.2)	2 (40.0)	2 (18.2)	0.2237
Number (%) of patients censored	98 (83.1)	134 (79.8)	3 (60.0)	9 (81.8)	
Kaplan-Meier estimates of Appetite loss in months					
25% quantile (95% CI)	NC (19.548 to NC)	20.93 (19.713 to NC)	10.73 (6.801 to NC)	NC (1.971 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	14.65 (6.801 to NC)	NC (1.971 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (6.801 to NC)	NC (NC to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.5589		0.3692	
Hazard ratio (95% CI) vs Kd	-	1.18 (0.68 to 2.05)		0.42 (0.06 to 3.00)	
P-value	-	0.5594		0.3839	
Deterioration probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful deterioration change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Appetite loss
16.2.6.1.2.8 Efficacy response data - Subgroup analyses by ISS staging at SE
16.2.6.1.2.8.3 QLQ-C30 - Time to first improvement by 10 pt in appetite loss according to ISS staging at SE (LOCF) - ITT population

	I		II		III		
	Kd (N=71)	**IKd (N=89)**	**Kd (N=31)**	**IKd (N=63)**	**Kd (N=20)**	**IKd (N=26)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	12 (16.9)	17 (19.1)	8 (25.8)	12 (19.0)	6 (30.0)	11 (42.3)	0.4976
Number (%) of patients censored	59 (83.1)	72 (80.9)	23 (74.2)	51 (81.0)	14 (70.0)	15 (57.7)	
Kaplan-Meier estimates of Appetite loss in months							
25% quantile (95% CI)	NC (4.107 to NC)	NC (2.136 to NC)	3.55 (1.018 to NC)	NC (1.971 to NC)	1.05 (0.953 to NC)	1.05 (0.953 to 2.103)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (1.051 to NC)	NC (1.084 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Kd							
Log-Rank test p-value[a] vs Kd	-	0.7002		0.4499		0.4285	
Hazard ratio (95% CI) vs Kd	-	1.16 (0.55 to 2.42)		0.71 (0.29 to 1.74)		1.49 (0.55 to 4.03)	
P-value	-	0.7004		0.4521		0.4315	

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The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Appetite loss
16.2.6.1.2.8 Efficacy response data - Subgroup analyses by ISS staging at SE
16.2.6.1.2.8.4 QLQ-C30 - Time to first deterioration by 10 pt in appetite loss according to ISS staging at SE (LOCF) - ITT population

	I		II		III		
	Kd (N=71)	**IKd (N=89)**	**Kd (N=31)**	**IKd (N=63)**	**Kd (N=20)**	**IKd (N=26)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	36 (50.7)	46 (51.7)	13 (41.9)	38 (60.3)	5 (25.0)	7 (26.9)	0.4267
Number (%) of patients censored	35 (49.3)	43 (48.3)	18 (58.1)	25 (39.7)	15 (75.0)	19 (73.1)	
Kaplan-Meier estimates of Appetite loss in months							
25% quantile (95% CI)	4.21 (1.873 to 6.637)	5.78 (1.906 to 8.214)	6.37 (1.906 to 12.255)	2.89 (1.117 to 5.815)	14.19 (1.150 to NC)	12.55 (1.906 to NC)	
Median (95% CI)	19.71 (6.702 to NC)	16.79 (10.152 to NC)	NC (6.801 to NC)	9.76 (5.815 to 18.037)	NC (11.203 to NC)	NC (10.908 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (19.680 to NC)	
Comparison vs. Kd							
Log-Rank test p-value[a] vs Kd	-	0.9720		0.1199		0.7000	
Hazard ratio (95% CI) vs Kd	-	0.99 (0.64 to 1.54)		1.64 (0.87 to 3.08)		1.25 (0.40 to 3.96)	

A lower score represents a better level of quality of life. Clinical meaningful deterioration change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Appetite loss
16.2.6.1.2.8 Efficacy response data - Subgroup analyses by ISS staging at SE
16.2.6.1.2.8.5 QLQ-C30 - Time until permanent improvement by 10 pt in appetite loss according to ISS staging at SE (LOCF) - ITT population

	I		II		III		
	Kd (N=71)	**IKd (N=89)**	**Kd (N=31)**	**IKd (N=63)**	**Kd (N=20)**	**IKd (N=26)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	6 (8.5)	10 (11.2)	5 (16.1)	8 (12.7)	5 (25.0)	8 (30.8)	0.6831
Number (%) of patients censored	65 (91.5)	79 (88.8)	26 (83.9)	55 (87.3)	15 (75.0)	18 (69.2)	
Kaplan-Meier estimates of Appetite loss in months							
25% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (4.895 to NC)	NC (NC to NC)	11.56 (0.953 to NC)	3.75 (0.953 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (11.565 to NC)	NC (3.745 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Kd							
Log-Rank test p-value[a] vs Kd	-	0.5420		0.6146		0.6429	
Hazard ratio (95% CI) vs Kd	-	1.37 (0.50 to 3.77)		0.75 (0.25 to 2.30)		1.30 (0.43 to 3.98)	
P-value	-	0.5437		0.6157		0.6439	

A lower score represents a better level of quality of life. Clinical meaningful improvement change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Appetite loss
16.2.6.1.2.8 Efficacy response data - Subgroup analyses by ISS staging at SE
16.2.6.1.2.8.6 QLQ-C30 - Time until permanent deterioration by 10 pt in appetite loss according to ISS staging at SE (LOCF) - ITT population

	I		II		III		
	Kd (N=71)	**IKd (N=89)**	**Kd (N=31)**	**IKd (N=63)**	**Kd (N=20)**	**IKd (N=26)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	11 (15.5)	22 (24.7)	8 (25.8)	10 (15.9)	2 (10.0)	3 (11.5)	0.1859
Number (%) of patients censored	60 (84.5)	67 (75.3)	23 (74.2)	53 (84.1)	18 (90.0)	23 (88.5)	
Kaplan-Meier estimates of Appetite loss in months							
25% quantile (95% CI)	NC (19.220 to NC)	20.27 (18.464 to NC)	20.37 (6.801 to NC)	NC (18.694 to NC)	NC (4.830 to NC)	NC (10.908 to NC)	
Median (95% CI)	NC (NC to NC)	NC (21.421 to NC)	NC (20.370 to NC)	NC (NC to NC)	NC (NC to NC)	NC (19.680 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Kd							
Log-Rank test p-value[a] vs Kd	-	0.1789		0.2285		0.8704	
Hazard ratio (95% CI) vs Kd	-	1.64 (0.79 to 3.37)		0.57 (0.22 to 1.44)		1.16 (0.19 to 6.98)	
P-value	-	0.1833		0.2346		0.8705	

A lower score represents a better level of quality of life. Clinical meaningful deterioration change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Appetite loss
16.2.6.1.2.9 Efficacy response data - Subgroup analyses by R-ISS stage at SE
16.2.6.1.2.9.3 QLQ-C30 - Time to first improvement by 10 pt in appetite loss according to R-ISS stage at SE (LOCF) - ITT population

	I or II		III		Not classified		
	Kd (N=103)	**IKd (N=155)**	**Kd (N=8)**	**IKd (N=16)**	**Kd (N=12)**	**IKd (N=8)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	20 (19.4)	29 (18.7)	3 (37.5)	8 (50.0)	3 (25.0)	3 (37.5)	0.4610
Number (%) of patients censored	83 (80.6)	126 (81.3)	5 (62.5)	8 (50.0)	9 (75.0)	5 (62.5)	
Kaplan-Meier estimates of Appetite loss in months							
25% quantile (95% CI)	NC (2.136 to NC)	NC (6.768 to NC)	1.05 (0.986 to NC)	1.08 (0.953 to 2.103)	NC (0.953 to NC)	1.02 (1.018 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (0.986 to NC)	2.10 (1.018 to NC)	NC (1.906 to NC)	NC (1.018 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (1.051 to NC)	NC (2.103 to NC)	NC (NC to NC)	NC (1.018 to NC)	
Comparison vs. Kd							
Log-Rank test p-value[a] vs Kd	-	0.8418		0.6285		0.2739	
Hazard ratio (95% CI) vs Kd	-	0.94 (0.53 to 1.67)		1.39 (0.37 to 5.25)		2.40 (0.48 to 12.14)	
P-value	-	0.8409		0.6300		0.2884	

A lower score represents a better level of quality of life. Clinical meaningful improvement change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
PGM=DEVOPS/SAR650984/EFC15246/CIR_RWE/REPORT/PGM/eff_km_subgp_sr_sig_de_i_t.sas OUT=REPORT/OUTPUT/eff_km_c30_apt_impl_seriss_de_i_t_x.rtf (07APR2021 14:34)

16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Appetite loss
16.2.6.1.2.9 Efficacy response data - Subgroup analyses by R-ISS stage at SE
16.2.6.1.2.9.4 QLQ-C30 - Time to first deterioration by 10 pt in appetite loss according to R-ISS stage at SE (LOCF) - ITT population

	I or II		III		Not classified		
	Kd (N=103)	**IKd (N=155)**	**Kd (N=8)**	**IKd (N=16)**	**Kd (N=12)**	**IKd (N=8)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	47 (45.6)	87 (56.1)	2 (25.0)	3 (18.8)	6 (50.0)	2 (25.0)	0.6839
Number (%) of patients censored	56 (54.4)	68 (43.9)	6 (75.0)	13 (81.3)	6 (50.0)	6 (75.0)	
Kaplan-Meier estimates of Appetite loss in months							
25% quantile (95% CI)	4.83 (2.004 to 6.801)	3.88 (2.004 to 6.045)	14.19 (11.203 to NC)	12.55 (1.906 to NC)	2.89 (0.986 to 19.713)	8.74 (3.055 to NC)	
Median (95% CI)	21.29 (9.363 to NC)	12.71 (9.298 to 19.680)	NC (11.203 to NC)	NC (10.908 to NC)	19.71 (0.986 to NC)	NC (3.055 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (11.203 to NC)	NC (NC to NC)	NC (19.713 to NC)	NC (8.739 to NC)	
Comparison vs. Kd							
Log-Rank test p-value[a] vs Kd	-	0.2098		0.7857		0.6823	
Hazard ratio (95% CI) vs Kd	-	1.25 (0.88 to 1.79)		0.78 (0.13 to 4.68)		0.71 (0.14 to 3.60)	

A lower score represents a better level of quality of life. Clinical meaningful deterioration change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Appetite loss
16.2.6.1.2.9 Efficacy response data - Subgroup analyses by R-ISS stage at SE
16.2.6.1.2.9.5 QLQ-C30 - Time until permanent improvement by 10 pt in appetite loss according to R-ISS stage at SE (LOCF) - ITT population

	I or II		III		Not classified		
	Kd (N=103)	**IKd (N=155)**	**Kd (N=8)**	**IKd (N=16)**	**Kd (N=12)**	**IKd (N=8)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	11 (10.7)	17 (11.0)	2 (25.0)	6 (37.5)	3 (25.0)	3 (37.5)	0.5832
Number (%) of patients censored	92 (89.3)	138 (89.0)	6 (75.0)	10 (62.5)	9 (75.0)	5 (62.5)	
Kaplan-Meier estimates of Appetite loss in months							
25% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	11.56 (1.051 to NC)	1.08 (0.953 to NC)	NC (0.953 to NC)	10.18 (3.745 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (1.051 to NC)	NC (1.084 to NC)	NC (3.745 to NC)	NC (3.745 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (11.565 to NC)	NC (11.203 to NC)	NC (NC to NC)	NC (10.185 to NC)	
Comparison vs. Kd							
Log-Rank test p-value[a] vs Kd	-	0.9941		0.4236		0.3441	
Hazard ratio (95% CI) vs Kd	-	1.00 (0.47 to 2.13)		1.91 (0.38 to 9.52)		2.14 (0.43 to 10.70)	
P-value	-	0.9941		0.4314		0.3553	

A lower score represents a better level of quality of life. Clinical meaningful improvement change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Appetite loss
16.2.6.1.2.9 Efficacy response data - Subgroup analyses by R-ISS stage at SE
16.2.6.1.2.9.6 QLQ-C30 - Time until permanent deterioration by 10 pt in appetite loss according to R-ISS stage at SE (LOCF) - ITT population

	I or II		III		Not classified		
	Kd (N=103)	**IKd (N=155)**	**Kd (N=8)**	**IKd (N=16)**	**Kd (N=12)**	**IKd (N=8)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	20 (19.4)	34 (21.9)	0 (0.0)	1 (6.3)	2 (16.7)	1 (12.5)	0.9973
Number (%) of patients censored	83 (80.6)	121 (78.1)	8 (100.0)	15 (93.8)	10 (83.3)	7 (87.5)	
Kaplan-Meier estimates of Appetite loss in months							
25% quantile (95% CI)	NC (16.887 to NC)	21.39 (19.614 to NC)	NC (NC to NC)	NC (10.908 to NC)	NC (9.068 to NC)	20.93 (20.928 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (19.713 to NC)	NC (20.928 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (20.928 to NC)	
Comparison vs. Kd							
Log-Rank test p-value[a] vs Kd	-	0.8499		0.5002		0.9277	
Hazard ratio (95% CI) vs Kd	-	1.05 (0.61 to 1.83)				1.12 (0.10 to 12.35)	
P-value	-	0.8509		0.9986		0.9278	

A lower score represents a better level of quality of life. Clinical meaningful deterioration change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Appetite loss
16.2.6.1.2.10 Efficacy response data - Subgroup analyses by nb of prior lines
16.2.6.1.2.10.3 QLQ-C30 - Time to first improvement by 10 pt in appetite loss according to nb of prior lines (LOCF) - ITT population

	1		>1		
	Kd (N=55)	**IKd (N=79)**	**Kd (N=68)**	**IKd (N=100)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	3 (5.5)	21 (26.6)	23 (33.8)	19 (19.0)	0.0006
Number (%) of patients censored	52 (94.5)	58 (73.4)	45 (66.2)	81 (81.0)	
Kaplan-Meier estimates of Appetite loss in months					
25% quantile (95% CI)	NC (NC to NC)	6.77 (1.084 to NC)	1.91 (1.018 to NC)	NC (2.004 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.0019		0.0346	
Hazard ratio (95% CI) vs Kd	-	5.48 (1.63 to 18.37)		0.52 (0.29 to 0.96)	
P-value	-	0.0059		0.0378	
Hazard ratio inverted (95% CI) vs IKd		-		1.90 (1.04 to 3.50)	

A lower score represents a better level of quality of life. Clinical meaningful improvement change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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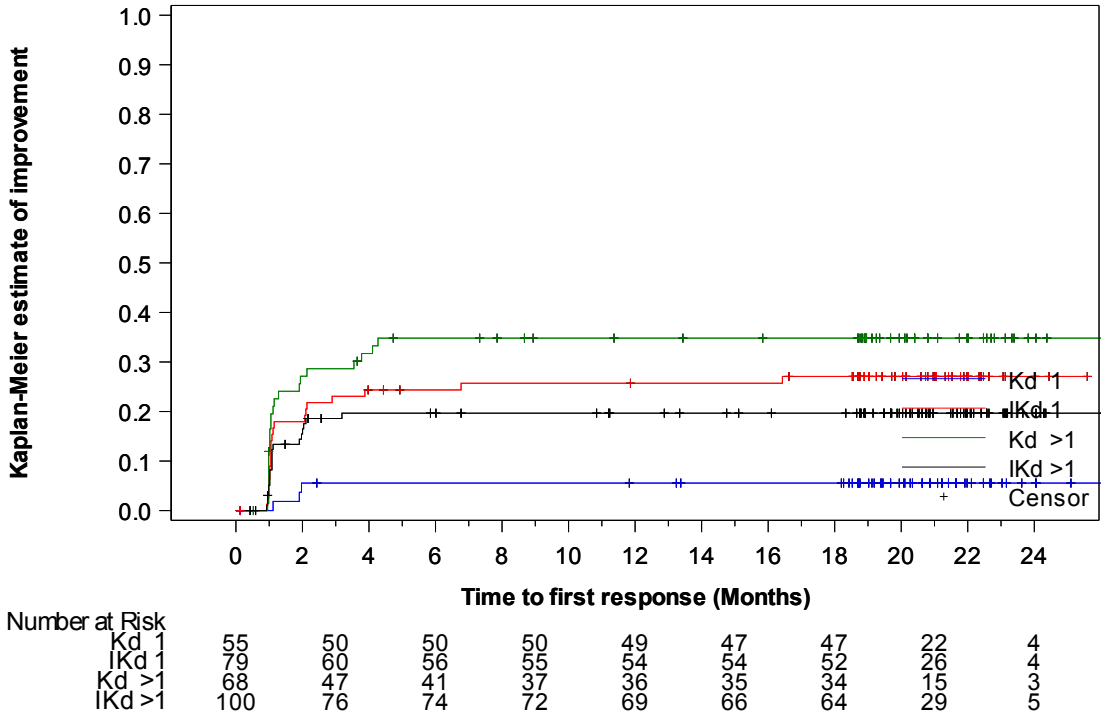
16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Appetite loss
16.2.6.1.2.10 Efficacy response data - Subgroup analyses by nb of prior lines
16.2.6.1.2.10.4 QLQ-C30 - Time to first improvement by 10 pt in appetite loss according to nb of prior lines - Kaplan-Meier curve (LOCF) - ITT population



A lower score represents a better level of quality of life. Clinical meaningful improvement change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
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16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Appetite loss
16.2.6.1.2.10 Efficacy response data - Subgroup analyses by nb of prior lines
16.2.6.1.2.10.5 QLQ-C30 - Time to first deterioration by 10 pt in appetite loss according to nb of prior lines (LOCF) - ITT population

	1		>1		
	Kd (N=55)	**IKd (N=79)**	**Kd (N=68)**	**IKd (N=100)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	24 (43.6)	35 (44.3)	31 (45.6)	57 (57.0)	0.4655
Number (%) of patients censored	31 (56.4)	44 (55.7)	37 (54.4)	43 (43.0)	
Kaplan-Meier estimates of Appetite loss in months					
25% quantile (95% CI)	4.83 (1.873 to 12.945)	6.51 (3.055 to 10.152)	4.90 (1.938 to 8.706)	3.78 (1.380 to 6.439)	
Median (95% CI)	NC (12.255 to NC)	NC (12.550 to NC)	16.16 (9.265 to NC)	10.91 (8.739 to 17.051)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.9247		0.2113	
Hazard ratio (95% CI) vs Kd	-	1.03 (0.61 to 1.72)		1.32 (0.85 to 2.05)	
P-value	-	0.9249		0.2128	
Deterioration probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful deterioration change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Appetite loss
16.2.6.1.2.10 Efficacy response data - Subgroup analyses by nb of prior lines
16.2.6.1.2.10.6 QLQ-C30 - Time until permanent improvement by 10 pt in appetite loss according to nb of prior lines (LOCF) - ITT population

	1		>1		
	Kd (N=55)	**IKd (N=79)**	**Kd (N=68)**	**IKd (N=100)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	2 (3.6)	13 (16.5)	14 (20.6)	13 (13.0)	0.0133
Number (%) of patients censored	53 (96.4)	66 (83.5)	54 (79.4)	87 (87.0)	
Kaplan-Meier estimates of Appetite loss in months					
25% quantile (95% CI)	NC (NC to NC)	NC (11.072 to NC)	NC (8.476 to NC)	NC (NC to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.0206		0.1799	
Hazard ratio (95% CI) vs Kd	-	4.89 (1.10 to 21.68)		0.60 (0.28 to 1.28)	
P-value	-	0.0367		0.1846	
Hazard ratio inverted (95% CI) vs IKd		-		1.67 (0.78 to 3.55)	

A lower score represents a better level of quality of life. Clinical meaningful improvement change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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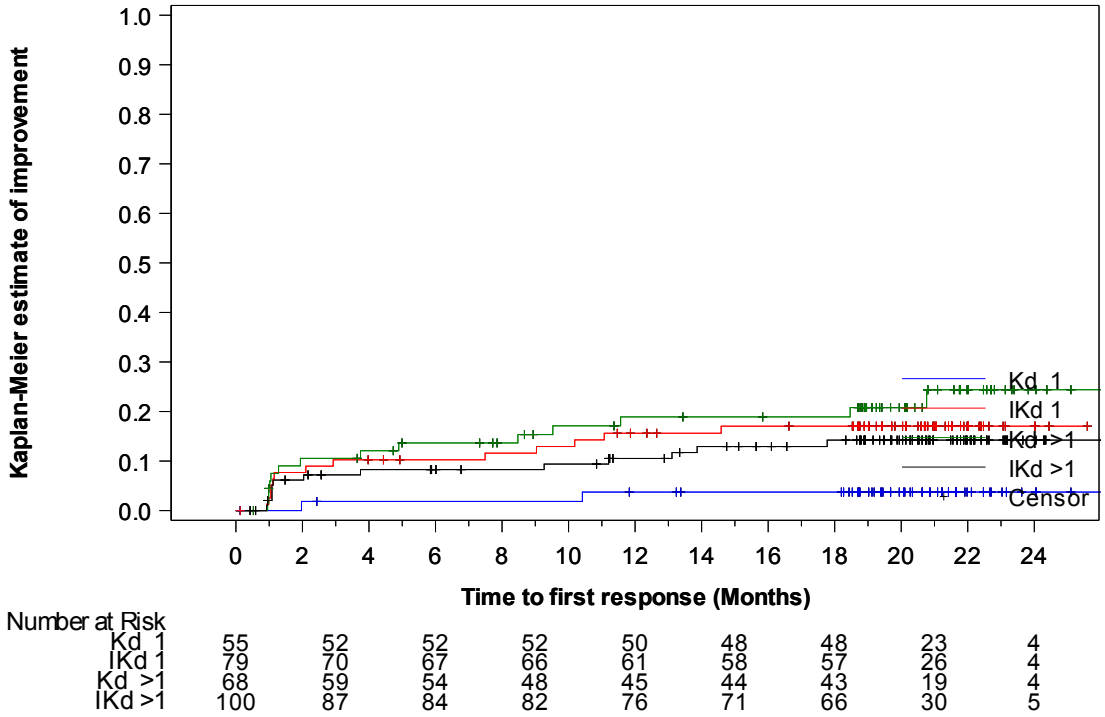
16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Appetite loss
16.2.6.1.2.10 Efficacy response data - Subgroup analyses by nb of prior lines
16.2.6.1.2.10.7 QLQ-C30 - Time until permanent improvement by 10 pt in appetite loss according to nb of prior lines - Kaplan-Meier curve (LOCF) - ITT population



A lower score represents a better level of quality of life. Clinical meaningful improvement change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
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16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Appetite loss
16.2.6.1.2.10 Efficacy response data - Subgroup analyses by nb of prior lines
16.2.6.1.2.10.8 QLQ-C30 - Time until permanent deterioration by 10 pt in appetite loss according to nb of prior lines (LOCF) - ITT population

	1		>1		
	Kd (N=55)	**IKd (N=79)**	**Kd (N=68)**	**IKd (N=100)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	8 (14.5)	14 (17.7)	14 (20.6)	22 (22.0)	0.7366
Number (%) of patients censored	47 (85.5)	65 (82.3)	54 (79.4)	78 (78.0)	
Kaplan-Meier estimates of Appetite loss in months					
25% quantile (95% CI)	NC (19.548 to NC)	NC (19.811 to NC)	20.37 (9.791 to NC)	20.27 (19.253 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.6301		0.9581	
Hazard ratio (95% CI) vs Kd	-	1.24 (0.52 to 2.95)		1.02 (0.52 to 1.99)	
P-value	-	0.6307		0.9581	
Deterioration probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful deterioration change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Appetite loss
16.2.6.1.2.11 Efficacy response data - Subgroup analyses by cytogenetic abnormality
16.2.6.1.2.11.3 QLQ-C30 - Time to first improvement by 10 pt in appetite loss according to cytogenetic abnormality (LOCF) - ITT population

	At least one		None		
	Kd (N=31)	**IKd (N=42)**	**Kd (N=77)**	**IKd (N=114)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	8 (25.8)	13 (31.0)	14 (18.2)	20 (17.5)	0.6932
Number (%) of patients censored	23 (74.2)	29 (69.0)	63 (81.8)	94 (82.5)	
Kaplan-Meier estimates of Appetite loss in months					
25% quantile (95% CI)	3.55 (1.051 to NC)	2.07 (1.051 to NC)	NC (2.136 to NC)	NC (3.877 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.6929		0.9088	
Hazard ratio (95% CI) vs Kd	-	1.19 (0.49 to 2.88)		0.96 (0.49 to 1.90)	
P-value	-	0.6933		0.9085	
Improvement probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful improvement change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Appetite loss
16.2.6.1.2.11 Efficacy response data - Subgroup analyses by cytogenetic abnormality
16.2.6.1.2.11.4 QLQ-C30 - Time to first deterioration by 10 pt in appetite loss according to cytogenetic abnormality (LOCF) - ITT population

	At least one		None		
	Kd (N=31)	**IKd (N=42)**	**Kd (N=77)**	**IKd (N=114)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	13 (41.9)	21 (50.0)	38 (49.4)	62 (54.4)	0.8686
Number (%) of patients censored	18 (58.1)	21 (50.0)	39 (50.6)	52 (45.6)	
Kaplan-Meier estimates of Appetite loss in months					
25% quantile (95% CI)	4.83 (1.873 to 11.203)	3.91 (1.906 to 8.279)	4.63 (1.906 to 6.801)	4.63 (1.906 to 6.801)	
Median (95% CI)	NC (6.374 to NC)	13.86 (5.782 to NC)	14.78 (7.491 to NC)	14.26 (9.593 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.6534		0.6108	
Hazard ratio (95% CI) vs Kd	-	1.17 (0.59 to 2.34)		1.11 (0.74 to 1.66)	
P-value	-	0.6538		0.6110	
Deterioration probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful deterioration change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Appetite loss
16.2.6.1.2.11 Efficacy response data - Subgroup analyses by cytogenetic abnormality
16.2.6.1.2.11.5 QLQ-C30 - Time until permanent improvement by 10 pt in appetite loss according to cytogenetic abnormality (LOCF) - ITT population

	At least one		None		
	Kd (N=31)	**IKd (N=42)**	**Kd (N=77)**	**IKd (N=114)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	4 (12.9)	10 (23.8)	8 (10.4)	11 (9.6)	0.3340
Number (%) of patients censored	27 (87.1)	32 (76.2)	69 (89.6)	103 (90.4)	
Kaplan-Meier estimates of Appetite loss in months					
25% quantile (95% CI)	NC (1.971 to NC)	NC (1.117 to NC)	NC (20.764 to NC)	NC (NC to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.2805		0.8576	
Hazard ratio (95% CI) vs Kd	-	1.87 (0.59 to 5.98)		0.92 (0.37 to 2.29)	
P-value	-	0.2887		0.8576	
Improvement probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful improvement change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Appetite loss
16.2.6.1.2.11 Efficacy response data - Subgroup analyses by cytogenetic abnormality
16.2.6.1.2.11.6 QLQ-C30 - Time until permanent deterioration by 10 pt in appetite loss according to cytogenetic abnormality (LOCF) - ITT population

	At least one		None		
	Kd (N=31)	**IKd (N=42)**	**Kd (N=77)**	**IKd (N=114)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	7 (22.6)	8 (19.0)	14 (18.2)	25 (21.9)	0.4738
Number (%) of patients censored	24 (77.4)	34 (81.0)	63 (81.8)	89 (78.1)	
Kaplan-Meier estimates of Appetite loss in months					
25% quantile (95% CI)	16.89 (6.374 to NC)	NC (5.322 to NC)	NC (18.628 to NC)	20.30 (19.614 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.6197		0.6334	
Hazard ratio (95% CI) vs Kd	-	0.77 (0.28 to 2.14)		1.17 (0.61 to 2.26)	
P-value	-	0.6207		0.6337	
Deterioration probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful deterioration change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Appetite loss
16.2.6.1.2.12 Efficacy response data - Subgroup analyses by MM type at SE
16.2.6.1.2.12.3 QLQ-C30 - Time to first improvement by 10 pt in appetite loss according to MM type at SE (LOCF) - ITT population

	IgG		Non-IgG		
	Kd (N=85)	**IKd (N=126)**	**Kd (N=38)**	**IKd (N=53)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	18 (21.2)	26 (20.6)	8 (21.1)	14 (26.4)	0.6862
Number (%) of patients censored	67 (78.8)	100 (79.4)	30 (78.9)	39 (73.6)	
Kaplan-Meier estimates of Appetite loss in months					
25% quantile (95% CI)	NC (1.906 to NC)	NC (2.103 to NC)	NC (1.051 to NC)	6.77 (1.018 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.9928		0.6441	
Hazard ratio (95% CI) vs Kd	-	1.00 (0.55 to 1.82)		1.23 (0.51 to 2.92)	
P-value	-	0.9928		0.6447	
Improvement probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful improvement change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Appetite loss
16.2.6.1.2.12 Efficacy response data - Subgroup analyses by MM type at SE
16.2.6.1.2.12.4 QLQ-C30 - Time to first deterioration by 10 pt in appetite loss according to MM type at SE (LOCF) - ITT population

	IgG		Non-IgG		
	Kd (N=85)	**IKd (N=126)**	**Kd (N=38)**	**IKd (N=53)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	42 (49.4)	66 (52.4)	13 (34.2)	26 (49.1)	0.2228
Number (%) of patients censored	43 (50.6)	60 (47.6)	25 (65.8)	27 (50.9)	
Kaplan-Meier estimates of Appetite loss in months					
25% quantile (95% CI)	2.89 (1.873 to 6.637)	5.65 (2.793 to 7.425)	9.26 (4.205 to NC)	3.88 (1.216 to 6.538)	
Median (95% CI)	19.71 (7.491 to NC)	15.05 (10.119 to NC)	NC (11.203 to NC)	12.55 (6.538 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.8241		0.1313	
Hazard ratio (95% CI) vs Kd	-	1.04 (0.71 to 1.54)		1.66 (0.85 to 3.24)	
P-value	-	0.8249		0.1355	
Deterioration probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful deterioration change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Appetite loss
16.2.6.1.2.12 Efficacy response data - Subgroup analyses by MM type at SE
16.2.6.1.2.12.5 QLQ-C30 - Time until permanent improvement by 10 pt in appetite loss according to MM type at SE (LOCF) - ITT population

	IgG		Non-IgG		
	Kd (N=85)	**IKd (N=126)**	**Kd (N=38)**	**IKd (N=53)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	12 (14.1)	18 (14.3)	4 (10.5)	8 (15.1)	0.7340
Number (%) of patients censored	73 (85.9)	108 (85.7)	34 (89.5)	45 (84.9)	
Kaplan-Meier estimates of Appetite loss in months					
25% quantile (95% CI)	NC (20.764 to NC)	NC (NC to NC)	NC (4.895 to NC)	NC (13.864 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.8800		0.6198	
Hazard ratio (95% CI) vs Kd	-	1.06 (0.51 to 2.20)		1.35 (0.41 to 4.50)	
P-value	-	0.8806		0.6212	
Improvement probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful improvement change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Appetite loss
16.2.6.1.2.12 Efficacy response data - Subgroup analyses by MM type at SE
16.2.6.1.2.12.6 QLQ-C30 - Time until permanent deterioration by 10 pt in appetite loss according to MM type at SE (LOCF) - ITT population

	IgG		Non-IgG		
	Kd (N=85)	**IKd (N=126)**	**Kd (N=38)**	**IKd (N=53)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	15 (17.6)	26 (20.6)	7 (18.4)	10 (18.9)	0.6850
Number (%) of patients censored	70 (82.4)	100 (79.4)	31 (81.6)	43 (81.1)	
Kaplan-Meier estimates of Appetite loss in months					
25% quantile (95% CI)	NC (18.628 to NC)	21.39 (19.680 to NC)	NC (6.374 to NC)	20.93 (16.427 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.6073		0.8774	
Hazard ratio (95% CI) vs Kd	-	1.18 (0.63 to 2.23)		0.93 (0.35 to 2.44)	
P-value	-	0.6077		0.8774	
Deterioration probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful deterioration change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Appetite loss
16.2.6.1.2.13 Efficacy response data - Subgroup analyses by previous autologous stem-cell
16.2.6.1.2.13.3 QLQ-C30 - Time to first improvement by 10 pt in appetite loss according to previous autologous stem-cell (LOCF) - ITT population

	Yes		No		
	Kd (N=69)	**IKd (N=116)**	**Kd (N=54)**	**IKd (N=63)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	13 (18.8)	26 (22.4)	13 (24.1)	14 (22.2)	0.6001
Number (%) of patients censored	56 (81.2)	90 (77.6)	41 (75.9)	49 (77.8)	
Kaplan-Meier estimates of Appetite loss in months					
25% quantile (95% CI)	NC (1.281 to NC)	NC (1.971 to NC)	4.11 (1.051 to NC)	NC (1.150 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.5653		0.8426	
Hazard ratio (95% CI) vs Kd	-	1.22 (0.62 to 2.37)		0.93 (0.44 to 1.97)	
P-value	-	0.5660		0.8423	
Improvement probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful improvement change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Appetite loss
16.2.6.1.2.13 Efficacy response data - Subgroup analyses by previous autologous stem-cell
16.2.6.1.2.13.4 QLQ-C30 - Time to first deterioration by 10 pt in appetite loss according to previous autologous stem-cell (LOCF) - ITT population

	Yes		No		
	Kd (N=69)	**IKd (N=116)**	**Kd (N=54)**	**IKd (N=63)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	28 (40.6)	60 (51.7)	27 (50.0)	32 (50.8)	0.4133
Number (%) of patients censored	41 (59.4)	56 (48.3)	27 (50.0)	31 (49.2)	
Kaplan-Meier estimates of Appetite loss in months					
25% quantile (95% CI)	6.64 (1.938 to 10.185)	5.32 (2.366 to 6.801)	4.70 (1.117 to 6.801)	3.81 (1.216 to 7.721)	
Median (95% CI)	NC (14.193 to NC)	17.05 (10.152 to NC)	13.54 (6.571 to NC)	12.55 (8.279 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (21.290 to NC)	NC (NC to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.1710		0.9043	
Hazard ratio (95% CI) vs Kd	-	1.37 (0.87 to 2.14)		1.03 (0.62 to 1.72)	
P-value	-	0.1728		0.9044	
Deterioration probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful deterioration change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Appetite loss
16.2.6.1.2.13 Efficacy response data - Subgroup analyses by previous autologous stem-cell
16.2.6.1.2.13.5 QLQ-C30 - Time until permanent improvement by 10 pt in appetite loss according to previous autologous stem-cell (LOCF) - ITT population

	Yes		No		
	Kd (N=69)	**IKd (N=116)**	**Kd (N=54)**	**IKd (N=63)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	8 (11.6)	17 (14.7)	8 (14.8)	9 (14.3)	0.6624
Number (%) of patients censored	61 (88.4)	99 (85.3)	46 (85.2)	54 (85.7)	
Kaplan-Meier estimates of Appetite loss in months					
25% quantile (95% CI)	NC (20.764 to NC)	NC (NC to NC)	NC (10.415 to NC)	NC (11.203 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.5482		0.9569	
Hazard ratio (95% CI) vs Kd	-	1.29 (0.56 to 3.00)		0.97 (0.38 to 2.52)	
P-value	-	0.5493		0.9569	
Improvement probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful improvement change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Appetite loss
16.2.6.1.2.13 Efficacy response data - Subgroup analyses by previous autologous stem-cell
16.2.6.1.2.13.6 QLQ-C30 - Time until permanent deterioration by 10 pt in appetite loss according to previous autologous stem-cell (LOCF) - ITT population

	Yes		No		
	Kd (N=69)	**IKd (N=116)**	**Kd (N=54)**	**IKd (N=63)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	10 (14.5)	21 (18.1)	12 (22.2)	15 (23.8)	0.6414
Number (%) of patients censored	59 (85.5)	95 (81.9)	42 (77.8)	48 (76.2)	
Kaplan-Meier estimates of Appetite loss in months					
25% quantile (95% CI)	NC (19.548 to NC)	21.42 (19.811 to NC)	19.22 (9.068 to NC)	19.84 (15.671 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.4941		0.9936	
Hazard ratio (95% CI) vs Kd	-	1.30 (0.61 to 2.76)		1.00 (0.47 to 2.13)	
P-value	-	0.4954		0.9936	
Deterioration probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful deterioration change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Appetite loss
16.2.6.1.2.14 Efficacy response data - Subgroup analyses by baseline eGFR (MDRD)
16.2.6.1.2.14.3 QLQ-C30 - Time to first improvement by 10 pt in appetite loss according to baseline eGFR (MDRD) (LOCF) - ITT population

	>=60 mL/min/1.73m2		<60 mL/min/1.73m2		
	Kd (N=93)	**IKd (N=122)**	**Kd (N=18)**	**IKd (N=43)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	19 (20.4)	25 (20.5)	5 (27.8)	12 (27.9)	0.8080
Number (%) of patients censored	74 (79.6)	97 (79.5)	13 (72.2)	31 (72.1)	
Kaplan-Meier estimates of Appetite loss in months					
25% quantile (95% CI)	NC (1.971 to NC)	NC (2.004 to NC)	3.55 (0.986 to NC)	2.89 (1.051 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (1.938 to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.8704		0.8312	
Hazard ratio (95% CI) vs Kd	-	1.05 (0.58 to 1.91)		0.89 (0.31 to 2.54)	
P-value	-	0.8708		0.8313	
Improvement probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful improvement change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Appetite loss
16.2.6.1.2.14 Efficacy response data - Subgroup analyses by baseline eGFR (MDRD)
16.2.6.1.2.14.4 QLQ-C30 - Time to first deterioration by 10 pt in appetite loss according to baseline eGFR (MDRD) (LOCF) - ITT population

	>=60 mL/min/1.73m2		<60 mL/min/1.73m2		
	Kd (N=93)	**IKd (N=122)**	**Kd (N=18)**	**IKd (N=43)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	43 (46.2)	65 (53.3)	8 (44.4)	22 (51.2)	0.4921
Number (%) of patients censored	50 (53.8)	57 (46.7)	10 (55.6)	21 (48.8)	
Kaplan-Meier estimates of Appetite loss in months					
25% quantile (95% CI)	4.85 (1.906 to 7.261)	3.75 (1.906 to 6.505)	2.83 (0.920 to 9.363)	4.63 (2.366 to 6.571)	
Median (95% CI)	NC (11.203 to NC)	14.26 (9.298 to NC)	19.71 (2.825 to NC)	12.02 (6.538 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (19.713 to NC)	NC (NC to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.1924		0.8927	
Hazard ratio (95% CI) vs Kd	-	1.29 (0.88 to 1.90)		0.95 (0.42 to 2.13)	
P-value	-	0.1936		0.8927	
Deterioration probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful deterioration change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
PGM=DEVOPS/SAR650984/EFC15246/CIR_RWE/REPORT/PGM/eff_km_subgp_sr_sig_de_i_t.sas OUT=REPORT/OUTPUT/eff_km_c30_apt_detl_crcl_de_i_t_x.rtf (07APR2021 14:34)

16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Appetite loss
16.2.6.1.2.14 Efficacy response data - Subgroup analyses by baseline eGFR (MDRD)
16.2.6.1.2.14.5 QLQ-C30 - Time until permanent improvement by 10 pt in appetite loss according to baseline eGFR (MDRD) (LOCF) - ITT population

	>=60 mL/min/1.73m2		<60 mL/min/1.73m2		
	Kd (N=93)	**IKd (N=122)**	**Kd (N=18)**	**IKd (N=43)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	11 (11.8)	16 (13.1)	3 (16.7)	9 (20.9)	0.9172
Number (%) of patients censored	82 (88.2)	106 (86.9)	15 (83.3)	34 (79.1)	
Kaplan-Meier estimates of Appetite loss in months					
25% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (1.938 to NC)	NC (1.084 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (11.565 to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.6723		0.9016	
Hazard ratio (95% CI) vs Kd	-	1.18 (0.55 to 2.54)		1.09 (0.29 to 4.02)	
P-value	-	0.6727		0.9016	
Improvement probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful improvement change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Appetite loss
16.2.6.1.2.14 Efficacy response data - Subgroup analyses by baseline eGFR (MDRD)
16.2.6.1.2.14.6 QLQ-C30 - Time until permanent deterioration by 10 pt in appetite loss according to baseline eGFR (MDRD) (LOCF) - ITT population

	>=60 mL/min/1.73m2		<60 mL/min/1.73m2		
	Kd (N=93)	**IKd (N=122)**	**Kd (N=18)**	**IKd (N=43)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	14 (15.1)	27 (22.1)	6 (33.3)	6 (14.0)	0.0086
Number (%) of patients censored	79 (84.9)	95 (77.9)	12 (66.7)	37 (86.0)	
Kaplan-Meier estimates of Appetite loss in months					
25% quantile (95% CI)	NC (19.548 to NC)	20.30 (19.253 to NC)	9.36 (2.825 to NC)	NC (19.713 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (9.068 to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (19.713 to NC)	NC (NC to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.1415		0.0212	
Hazard ratio (95% CI) vs Kd	-	1.62 (0.85 to 3.08)		0.29 (0.09 to 0.89)	
P-value	-	0.1454		0.0305	
Deterioration probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful deterioration change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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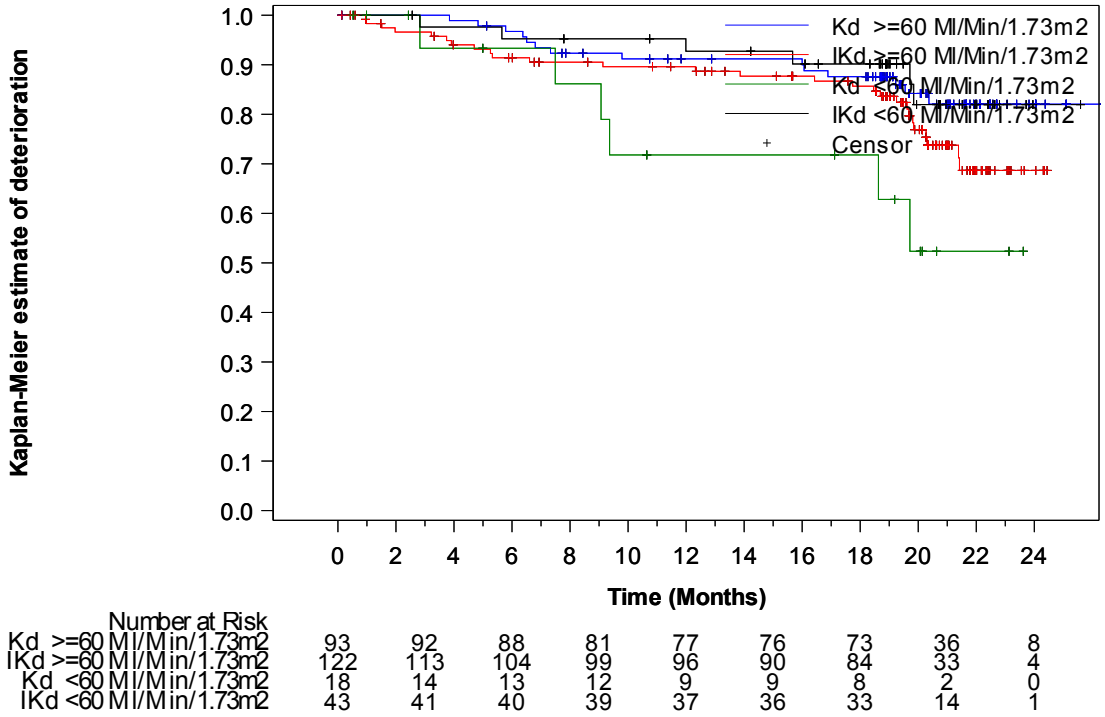
16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Appetite loss
16.2.6.1.2.14 Efficacy response data - Subgroup analyses by baseline eGFR (MDRD)
16.2.6.1.2.14.7 QLQ-C30 - Time until permanent deterioration by 10 pt in appetite loss according to baseline eGFR (MDRD) - Kaplan-Meier curve (LOCF) - ITT population



Number at Risk

Kd >=60 Ml/Min/1.73m2	93	92	88	81	77	76	73	36	8
IKd >=60 Ml/Min/1.73m2	122	113	104	99	96	90	84	33	4
Kd <60 Ml/Min/1.73m2	18	14	13	12	9	9	8	2	0
IKd <60 Ml/Min/1.73m2	43	41	40	39	37	36	33	14	1

A lower score represents a better level of quality of life. Clinical meaningful deterioration change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
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16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Appetite loss
16.2.6.1.2.15 Efficacy response data - Subgroup analyses by previous treatment with PI
16.2.6.1.2.15.3 QLQ-C30 - Time to first improvement by 10 pt in appetite loss according to previous treatment with PI (LOCF) - ITT population

	Yes		No		
	Kd (N=47)	**IKd (N=81)**	**Kd (N=76)**	**IKd (N=98)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	10 (21.3)	21 (25.9)	16 (21.1)	19 (19.4)	0.4636
Number (%) of patients censored	37 (78.7)	60 (74.1)	60 (78.9)	79 (80.6)	
Kaplan-Meier estimates of Appetite loss in months					
25% quantile (95% CI)	NC (2.136 to NC)	3.88 (1.906 to NC)	NC (1.051 to NC)	NC (1.117 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.4634		0.7892	
Hazard ratio (95% CI) vs Kd	-	1.32 (0.62 to 2.81)		0.91 (0.47 to 1.78)	
P-value	-	0.4649		0.7893	
Improvement probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful improvement change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Appetite loss
16.2.6.1.2.15 Efficacy response data - Subgroup analyses by previous treatment with PI
16.2.6.1.2.15.4 QLQ-C30 - Time to first deterioration by 10 pt in appetite loss according to previous treatment with PI (LOCF) - ITT population

	Yes		No		
	Kd (N=47)	**IKd (N=81)**	**Kd (N=76)**	**IKd (N=98)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	22 (46.8)	41 (50.6)	33 (43.4)	51 (52.0)	0.9520
Number (%) of patients censored	25 (53.2)	40 (49.4)	43 (56.6)	47 (48.0)	
Kaplan-Meier estimates of Appetite loss in months					
25% quantile (95% CI)	4.83 (1.906 to 9.791)	5.59 (1.906 to 8.214)	4.90 (1.906 to 9.265)	3.78 (2.004 to 6.571)	
Median (95% CI)	14.78 (7.491 to NC)	12.71 (9.133 to NC)	21.29 (9.363 to NC)	15.51 (9.593 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.5298		0.4068	
Hazard ratio (95% CI) vs Kd	-	1.18 (0.70 to 1.98)		1.20 (0.78 to 1.86)	
P-value	-	0.5303		0.4074	
Deterioration probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful deterioration change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Appetite loss
16.2.6.1.2.15 Efficacy response data - Subgroup analyses by previous treatment with PI
16.2.6.1.2.15.5 QLQ-C30 - Time until permanent improvement by 10 pt in appetite loss according to previous treatment with PI (LOCF) - ITT population

	Yes		No		
	Kd (N=47)	**IKd (N=81)**	**Kd (N=76)**	**IKd (N=98)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	6 (12.8)	12 (14.8)	10 (13.2)	14 (14.3)	0.8676
Number (%) of patients censored	41 (87.2)	69 (85.2)	66 (86.8)	84 (85.7)	
Kaplan-Meier estimates of Appetite loss in months					
25% quantile (95% CI)	NC (9.528 to NC)	NC (17.774 to NC)	NC (20.764 to NC)	NC (NC to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.7012		0.8522	
Hazard ratio (95% CI) vs Kd	-	1.21 (0.45 to 3.23)		1.08 (0.48 to 2.43)	
P-value	-	0.7017		0.8530	
Improvement probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful improvement change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Appetite loss
16.2.6.1.2.15 Efficacy response data - Subgroup analyses by previous treatment with PI
16.2.6.1.2.15.6 QLQ-C30 - Time until permanent deterioration by 10 pt in appetite loss according to previous treatment with PI (LOCF) - ITT population

	Yes		No		
	Kd (N=47)	**IKd (N=81)**	**Kd (N=76)**	**IKd (N=98)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	9 (19.1)	18 (22.2)	13 (17.1)	18 (18.4)	0.8126
Number (%) of patients censored	38 (80.9)	63 (77.8)	63 (82.9)	80 (81.6)	
Kaplan-Meier estimates of Appetite loss in months					
25% quantile (95% CI)	NC (9.791 to NC)	20.30 (15.671 to NC)	NC (19.220 to NC)	21.39 (19.713 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.6790		0.9309	
Hazard ratio (95% CI) vs Kd	-	1.18 (0.53 to 2.64)		1.03 (0.51 to 2.11)	
P-value	-	0.6793		0.9310	
Deterioration probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful deterioration change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Appetite loss
16.2.6.1.2.16 Efficacy response data - Subgroup analyses by previous treatment with IMiD
16.2.6.1.2.16.3 QLQ-C30 - Time to first improvement by 10 pt in appetite loss according to previous treatment with IMiD (LOCF) - ITT population

	Yes		No		
	Kd (N=62)	**IKd (N=81)**	**Kd (N=61)**	**IKd (N=98)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	12 (19.4)	14 (17.3)	14 (23.0)	26 (26.5)	0.5086
Number (%) of patients censored	50 (80.6)	67 (82.7)	47 (77.0)	72 (73.5)	
Kaplan-Meier estimates of Appetite loss in months					
25% quantile (95% CI)	NC (1.051 to NC)	NC (2.103 to NC)	NC (1.938 to NC)	3.88 (1.150 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.7315		0.5539	
Hazard ratio (95% CI) vs Kd	-	0.87 (0.40 to 1.89)		1.22 (0.64 to 2.33)	
P-value	-	0.7317		0.5545	
Improvement probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful improvement change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Appetite loss
16.2.6.1.2.16 Efficacy response data - Subgroup analyses by previous treatment with IMiD
16.2.6.1.2.16.4 QLQ-C30 - Time to first deterioration by 10 pt in appetite loss according to previous treatment with IMiD (LOCF) - ITT population

	Yes		No		
	Kd (N=62)	**IKd (N=81)**	**Kd (N=61)**	**IKd (N=98)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	25 (40.3)	43 (53.1)	30 (49.2)	49 (50.0)	0.4798
Number (%) of patients censored	37 (59.7)	38 (46.9)	31 (50.8)	49 (50.0)	
Kaplan-Meier estimates of Appetite loss in months					
25% quantile (95% CI)	6.64 (1.906 to 14.653)	3.78 (1.511 to 8.739)	4.21 (1.906 to 6.801)	5.32 (2.793 to 6.538)	
Median (95% CI)	NC (14.653 to NC)	15.51 (10.908 to NC)	14.19 (6.801 to NC)	13.86 (8.805 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.2152		0.8182	
Hazard ratio (95% CI) vs Kd	-	1.36 (0.83 to 2.23)		1.05 (0.67 to 1.66)	
P-value	-	0.2170		0.8193	
Deterioration probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful deterioration change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
PGM=DEVOPS/SAR650984/EFC15246/CIR_RWE/REPORT/PGM/eff_km_subgp_sr_sig_de_i_t.sas OUT=REPORT/OUTPUT/eff_km_c30_apt_detl_imid_de_i_t_x.rtf (07APR2021 14:34)

16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Appetite loss
16.2.6.1.2.16 Efficacy response data - Subgroup analyses by previous treatment with IMiD
16.2.6.1.2.16.5 QLQ-C30 - Time until permanent improvement by 10 pt in appetite loss according to previous treatment with IMiD (LOCF) - ITT population

	Yes		No		
	Kd (N=62)	**IKd (N=81)**	**Kd (N=61)**	**IKd (N=98)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	7 (11.3)	10 (12.3)	9 (14.8)	16 (16.3)	0.9263
Number (%) of patients censored	55 (88.7)	71 (87.7)	52 (85.2)	82 (83.7)	
Kaplan-Meier estimates of Appetite loss in months					
25% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (18.464 to NC)	NC (14.587 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.8839		0.7341	
Hazard ratio (95% CI) vs Kd	-	1.07 (0.41 to 2.82)		1.15 (0.51 to 2.61)	
P-value	-	0.8845		0.7343	
Improvement probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful improvement change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Appetite loss
16.2.6.1.2.16 Efficacy response data - Subgroup analyses by previous treatment with IMiD
16.2.6.1.2.16.6 QLQ-C30 - Time until permanent deterioration by 10 pt in appetite loss according to previous treatment with IMiD (LOCF) - ITT population

	Yes		No		
	Kd (N=62)	**IKd (N=81)**	**Kd (N=61)**	**IKd (N=98)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	9 (14.5)	18 (22.2)	13 (21.3)	18 (18.4)	0.3054
Number (%) of patients censored	53 (85.5)	63 (77.8)	48 (78.7)	80 (81.6)	
Kaplan-Meier estimates of Appetite loss in months					
25% quantile (95% CI)	NC (18.628 to NC)	20.30 (19.680 to NC)	20.37 (9.791 to NC)	NC (17.741 to NC)	
Median (95% CI)	NC (NC to NC)	NC (21.421 to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.3132		0.7013	
Hazard ratio (95% CI) vs Kd	-	1.51 (0.68 to 3.35)		0.87 (0.43 to 1.78)	
P-value	-	0.3166		0.7015	
Deterioration probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful deterioration change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Appetite loss
16.2.6.1.2.17 Efficacy response data - Subgroup analyses by previous treatment with PI and IMiD
16.2.6.1.2.17.3 QLQ-C30 - Time to first improvement by 10 pt in appetite loss according to previous treatment with PI and IMiD (LOCF) - ITT population

	Yes		No		
	Kd (N=17)	**IKd (N=23)**	**Kd (N=106)**	**IKd (N=156)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	2 (11.8)	3 (13.0)	24 (22.6)	37 (23.7)	0.9945
Number (%) of patients censored	15 (88.2)	20 (87.0)	82 (77.4)	119 (76.3)	
Kaplan-Meier estimates of Appetite loss in months					
25% quantile (95% CI)	NC (1.018 to NC)	NC (1.051 to NC)	NC (1.906 to NC)	NC (2.004 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.9366		0.7990	
Hazard ratio (95% CI) vs Kd	-	1.08 (0.18 to 6.44)		1.07 (0.64 to 1.79)	
P-value	-	0.9366		0.8002	
Improvement probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful improvement change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Appetite loss
16.2.6.1.2.17 Efficacy response data - Subgroup analyses by previous treatment with PI and IMiD
16.2.6.1.2.17.4 QLQ-C30 - Time to first deterioration by 10 pt in appetite loss according to previous treatment with PI and IMiD (LOCF) - ITT population

	Yes		No		
	Kd (N=17)	**IKd (N=23)**	**Kd (N=106)**	**IKd (N=156)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	7 (41.2)	12 (52.2)	48 (45.3)	80 (51.3)	0.7850
Number (%) of patients censored	10 (58.8)	11 (47.8)	58 (54.7)	76 (48.7)	
Kaplan-Meier estimates of Appetite loss in months					
25% quantile (95% CI)	7.49 (1.906 to 14.784)	7.43 (0.986 to 11.138)	4.70 (1.938 to 6.801)	3.91 (2.366 to 6.505)	
Median (95% CI)	NC (7.491 to NC)	12.71 (7.425 to NC)	21.29 (10.185 to NC)	15.05 (9.593 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (17.544 to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.4761		0.3949	
Hazard ratio (95% CI) vs Kd	-	1.40 (0.55 to 3.56)		1.17 (0.82 to 1.67)	
P-value	-	0.4782		0.3954	
Deterioration probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful deterioration change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Appetite loss
16.2.6.1.2.17 Efficacy response data - Subgroup analyses by previous treatment with PI and IMiD
16.2.6.1.2.17.5 QLQ-C30 - Time until permanent improvement by 10 pt in appetite loss according to previous treatment with PI and IMiD (LOCF) - ITT population

	Yes		No		
	Kd (N=17)	**IKd (N=23)**	**Kd (N=106)**	**IKd (N=156)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	1 (5.9)	1 (4.3)	15 (14.2)	25 (16.0)	0.7671
Number (%) of patients censored	16 (94.1)	22 (95.7)	91 (85.8)	131 (84.0)	
Kaplan-Meier estimates of Appetite loss in months					
25% quantile (95% CI)	NC (9.528 to NC)	NC (1.051 to NC)	NC (20.764 to NC)	NC (NC to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.8317		0.6768	
Hazard ratio (95% CI) vs Kd	-	0.74 (0.05 to 11.86)		1.15 (0.60 to 2.17)	
P-value	-	0.8323		0.6771	
Improvement probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful improvement change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Appetite loss
16.2.6.1.2.17 Efficacy response data - Subgroup analyses by previous treatment with PI and IMiD
16.2.6.1.2.17.6 QLQ-C30 - Time until permanent deterioration by 10 pt in appetite loss according to previous treatment with PI and IMiD (LOCF) - ITT population

	Yes		No		
	Kd (N=17)	**IKd (N=23)**	**Kd (N=106)**	**IKd (N=156)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	2 (11.8)	7 (30.4)	20 (18.9)	29 (18.6)	0.2587
Number (%) of patients censored	15 (88.2)	16 (69.6)	86 (81.1)	127 (81.4)	
Kaplan-Meier estimates of Appetite loss in months					
25% quantile (95% CI)	NC (7.491 to NC)	20.27 (1.511 to NC)	NC (18.628 to NC)	21.39 (19.713 to NC)	
Median (95% CI)	NC (NC to NC)	NC (20.271 to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.2367		0.9056	
Hazard ratio (95% CI) vs Kd	-	2.50 (0.52 to 12.05)		0.97 (0.55 to 1.71)	
P-value	-	0.2531		0.9053	
Deterioration probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful deterioration change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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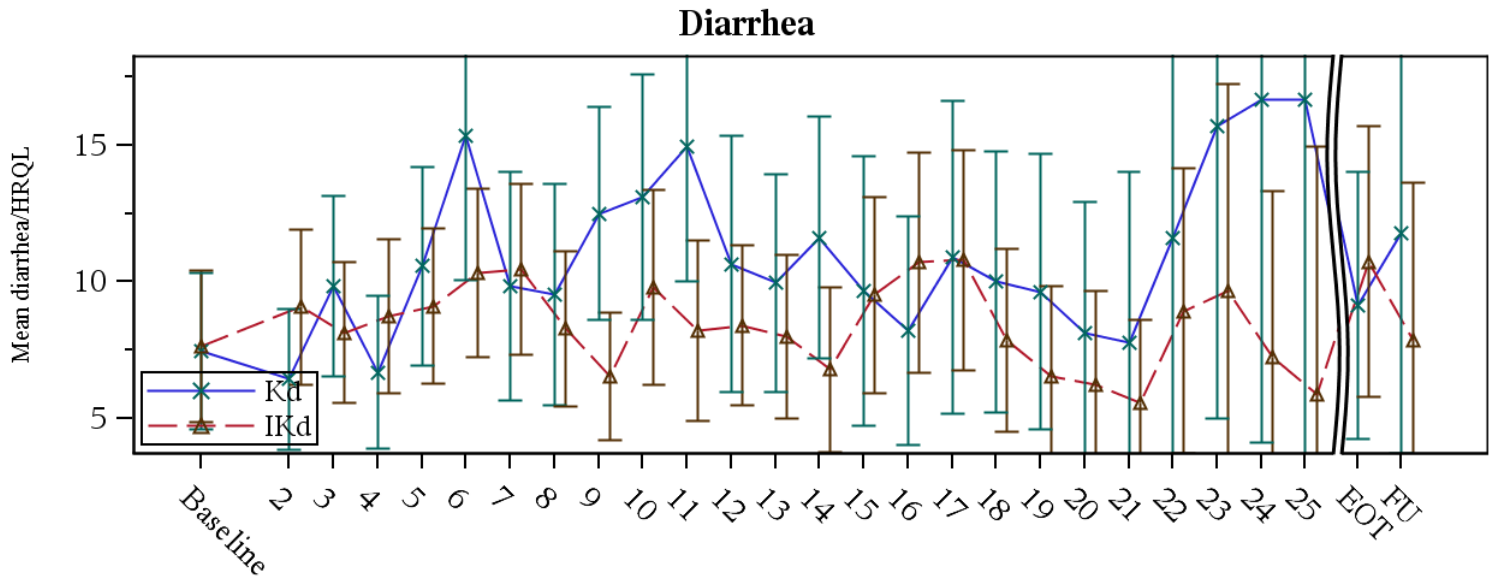
16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Diarrhea
16.2.6.1.2.1 Efficacy response data
16.2.6.1.2.1.1 QLQ-C30 - Mean and 95% CI for diarrhea score over time (LOCF) - ITT population



#patients																									
Kd	112	114	112	110	104	100	95	91	88	84	78	72	67	66	62	57	52	50	45	37	30	23	17	10	6	62	34
IKd	166	169	168	164	161	155	150	145	138	133	130	127	121	118	112	109	105	102	97	91	78	56	38	23	17	59	34

A lower score represents a better level of quality of life. Cycles with less than 20 patients overall are not presented.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
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16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Diarrhea
16.2.6.1.2.1 Efficacy response data
16.2.6.1.2.1.15 QLQ-C30 - Time to first improvement by 15 pt in Diarrhea (LOCF) - ITT population

First improvement 15 points Diarrhea (%)	**Kd (N=123)**	**IKd (N=179)**
Number (%) of events	21 (17.1)	28 (15.6)
Number (%) of patients censored	102 (82.9)	151 (84.4)
Kaplan-Meier estimates of Diarrhea in months		
25% quantile (95% CI)	NC (12.255 to NC)	NC (NC to NC)
Median (95% CI)	NC (NC to NC)	NC (NC to NC)
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)
Comparison vs. Kd		
Stratified[a] Log-Rank test p-value[b] vs Kd	-	0.6402
Stratified[a] Hazard ratio (95% CI) vs Kd	-	0.87 (0.50 to 1.54)
P-value	-	0.6404
Improvement probability (95% CI)[c]		
3 Months	0.133 (0.080 to 0.201)	0.126 (0.082 to 0.180)
6 Months	0.142 (0.087 to 0.210)	0.150 (0.102 to 0.207)

A lower score represents a better level of quality of life. Clinical meaningful improvement change from baseline less than or equal to -15 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] Stratified on number of prior lines of therapy (1 vs. >1) and Revised International Staging System (R-ISS) stage (I or II vs. III vs. not classified) according to IRT
[b] One-sided significance level is 0.025
[c] Estimated using the Kaplan-Meier method
NA/NC = Not Applicable / Not Calculable
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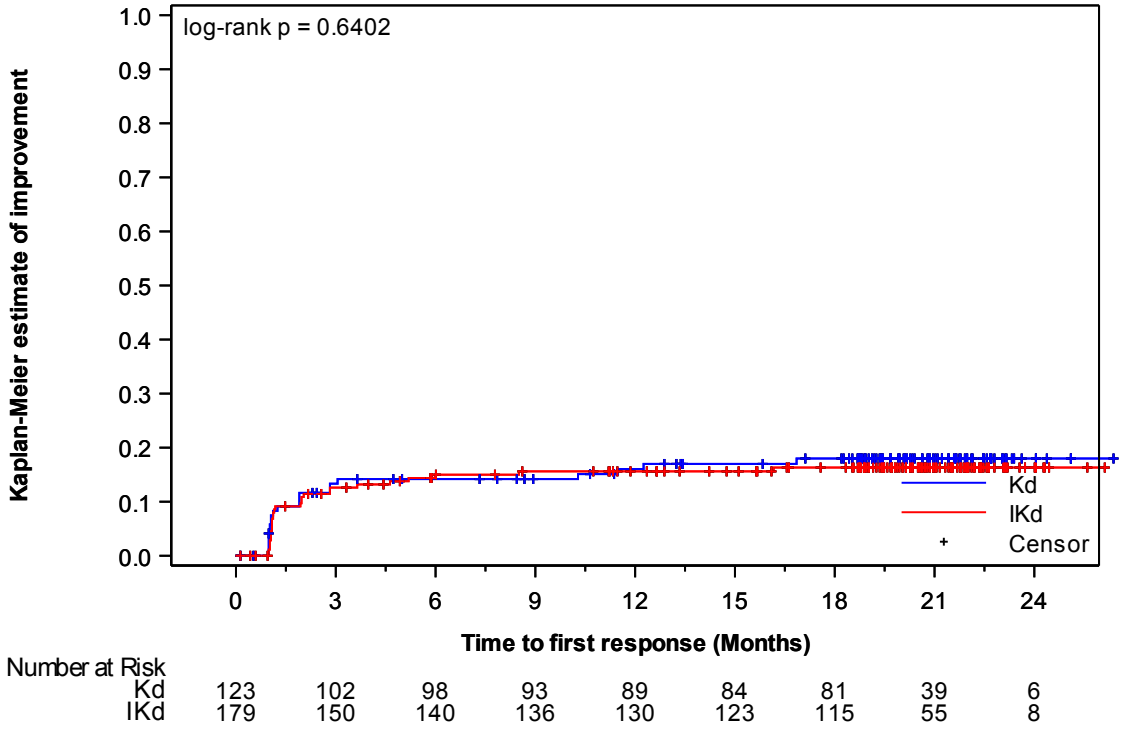
16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Diarrhea
16.2.6.1.2.1 Efficacy response data
16.2.6.1.2.1.16 QLQ-C30 - Time to first improvement by 15 pt in Diarrhea - Kaplan-Meier curve (LOCF) - ITT population



A lower score represents a better level of quality of life. Clinical meaningful improvement change from baseline less than or equal to -15 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.

16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Diarrhea
16.2.6.1.2.1 Efficacy response data
16.2.6.1.2.1.17 QLQ-C30 - Time to first deterioration by 15 pt in Diarrhea (LOCF) - ITT population

First deterioration 15 points Diarrhea (%)	**Kd (N=123)**	**IKd (N=179)**
Number (%) of events	54 (43.9)	99 (55.3)
Number (%) of patients censored	69 (56.1)	80 (44.7)
Kaplan-Meier estimates of Diarrhea in months		
25% quantile (95% CI)	3.78 (2.103 to 4.895)	2.99 (2.136 to 4.140)
Median (95% CI)	NC (9.495 to NC)	11.07 (6.538 to 17.281)
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)
Comparison vs. Kd		
Stratified[a] Log-Rank test p-value[b] vs Kd	-	0.0903
Stratified[a] Hazard ratio (95% CI) vs Kd	-	1.33 (0.95 to 1.86)
P-value	-	0.0914
Deterioration probability (95% CI)[c]		
3 Months	0.783 (0.698 to 0.847)	0.741 (0.669 to 0.800)
6 Months	0.671 (0.578 to 0.748)	0.593 (0.516 to 0.663)

A lower score represents a better level of quality of life. Clinical meaningful deterioration change from baseline greater than or equal to 15 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] Stratified on number of prior lines of therapy (1 vs. >1) and Revised International Staging System (R-ISS) stage (I or II vs. III vs. not classified) according to IRT
[b] One-sided significance level is 0.025
[c] Estimated using the Kaplan-Meier method
NA/NC = Not Applicable / Not Calculable
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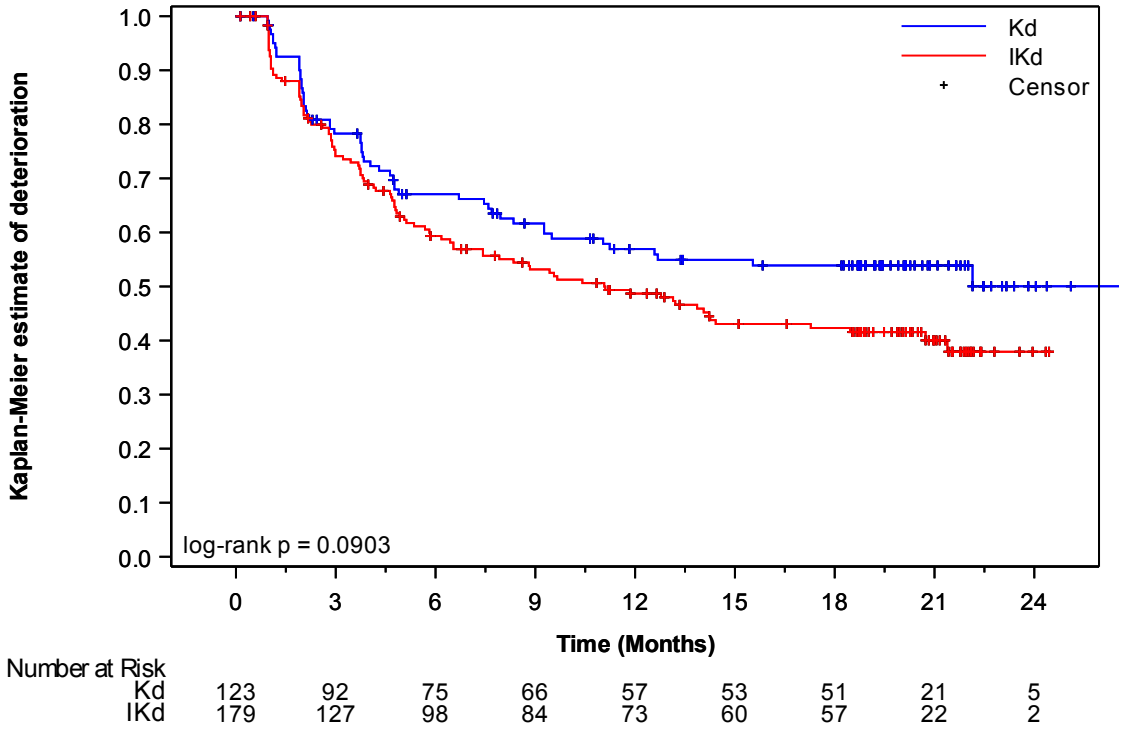
16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Diarrhea
16.2.6.1.2.1 Efficacy response data
16.2.6.1.2.1.18 QLQ-C30 - Time to first deterioration by 15 pt in Diarrhea - Kaplan-Meier curve (LOCF) - ITT population



A lower score represents a better level of quality of life. Clinical meaningful deterioration change from baseline greater than or equal to 15 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
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16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Diarrhea
16.2.6.1.2.1 Efficacy response data
16.2.6.1.2.1.19 QLQ-C30 - Time until permanent improvement by 15 pt in Diarrhea (LOCF) - ITT population

First permanent improvement 15 points Diarrhea (%)	**Kd (N=123)**	**IKd (N=179)**
Number (%) of events	16 (13.0)	18 (10.1)
Number (%) of patients censored	107 (87.0)	161 (89.9)
Kaplan-Meier estimates of Diarrhea in months		
25% quantile (95% CI)	NC (21.684 to NC)	NC (NC to NC)
Median (95% CI)	NC (NC to NC)	NC (NC to NC)
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)
Comparison vs. Kd		
Stratified[a] Log-Rank test p-value[b] vs Kd	-	0.4138
Stratified[a] Hazard ratio (95% CI) vs Kd	-	0.76 (0.38 to 1.48)
P-value	-	0.4153
Improvement probability (95% CI)[c]		
3 Months	0.050 (0.021 to 0.100)	0.046 (0.022 to 0.084)
6 Months	0.059 (0.026 to 0.111)	0.052 (0.025 to 0.092)

A lower score represents a better level of quality of life. Clinical meaningful improvement change from baseline less than or equal to -15 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] Stratified on number of prior lines of therapy (1 vs. >1) and Revised International Staging System (R-ISS) stage (I or II vs. III vs. not classified) according to IRT
[b] One-sided significance level is 0.025
[c] Estimated using the Kaplan-Meier method
NA/NC = Not Applicable / Not Calculable
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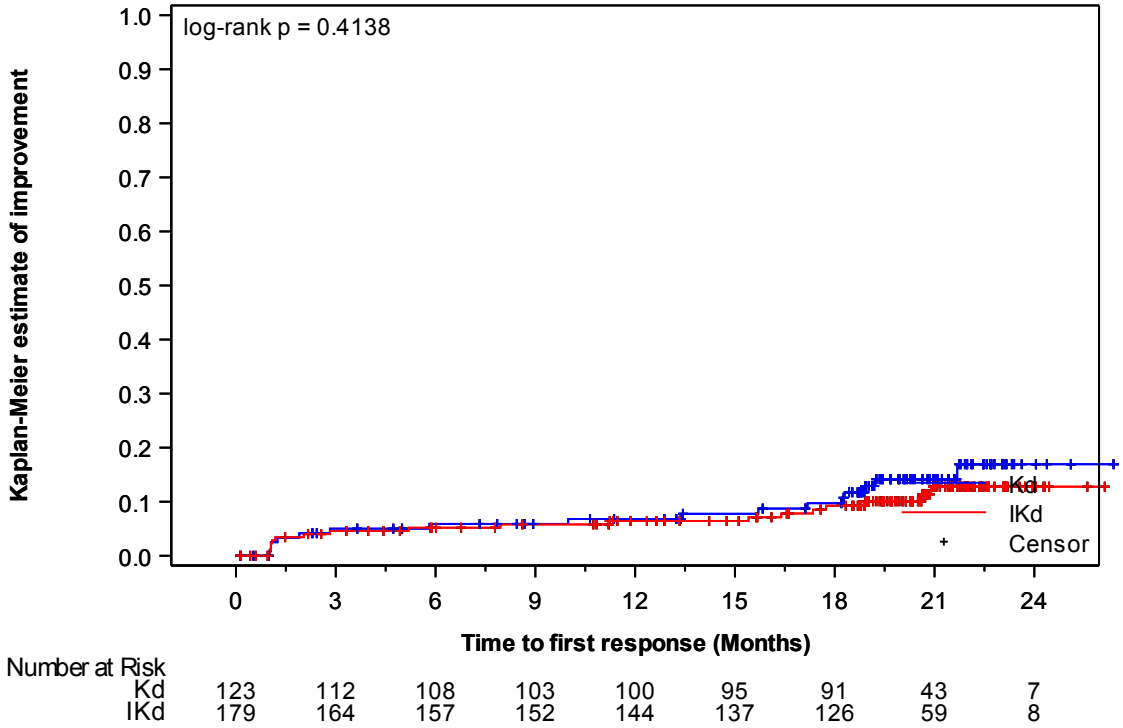
16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Diarrhea
16.2.6.1.2.1 Efficacy response data
16.2.6.1.2.1.20 QLQ-C30 - Time until permanent improvement by 15 pt in Diarrhea - Kaplan-Meier curve (LOCF) - ITT population



A lower score represents a better level of quality of life. Clinical meaningful improvement change from baseline less than or equal to -15 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
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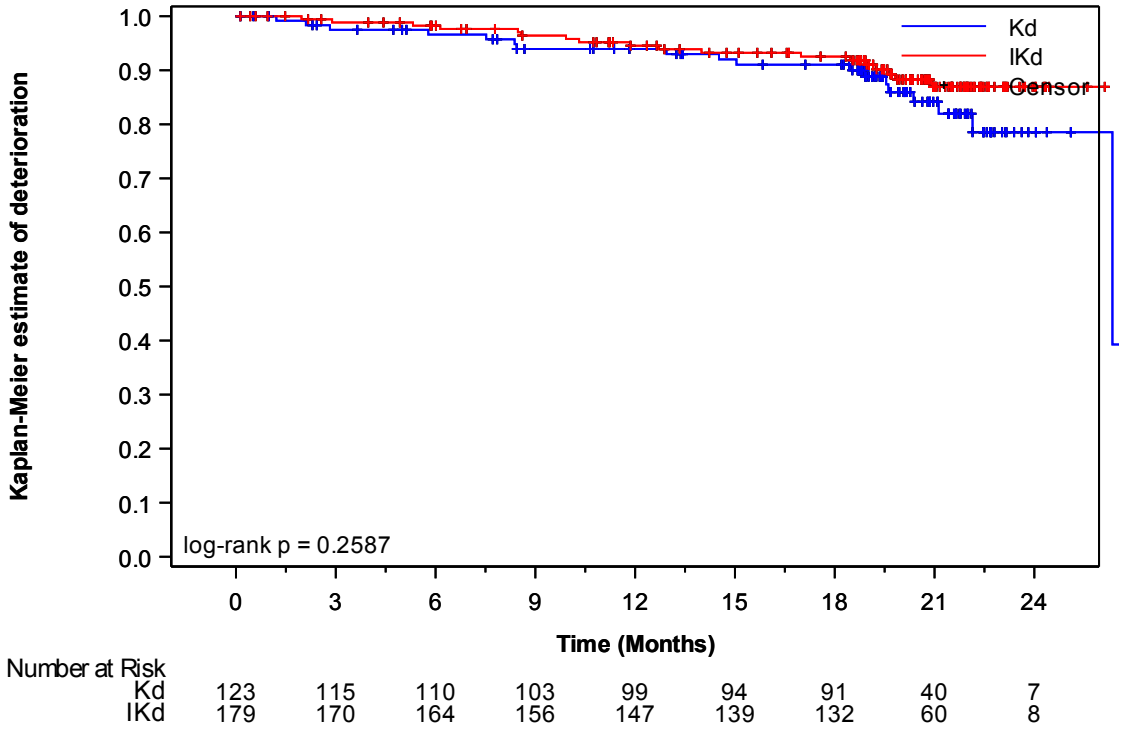
16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Diarrhea
16.2.6.1.2.1 Efficacy response data
16.2.6.1.2.1.21 QLQ-C30 - Time until permanent deterioration by 15 pt in Diarrhea (LOCF) - ITT population

First permanent deterioration 15 points Diarrhea (%)	**Kd (N=123)**	**IKd (N=179)**
Number (%) of events	18 (14.6)	18 (10.1)
Number (%) of patients censored	105 (85.4)	161 (89.9)
Kaplan-Meier estimates of Diarrhea in months		
25% quantile (95% CI)	26.35 (20.370 to NC)	NC (NC to NC)
Median (95% CI)	26.35 (26.349 to NC)	NC (NC to NC)
75% quantile (95% CI)	NC (26.349 to NC)	NC (NC to NC)
Comparison vs. Kd		
Stratified[a] Log-Rank test p-value[b] vs Kd	-	0.2587
Stratified[a] Hazard ratio (95% CI) vs Kd	-	0.68 (0.35 to 1.33)
P-value	-	0.2615
Deterioration probability (95% CI)[c]		
3 Months	0.975 (0.924 to 0.992)	0.988 (0.955 to 0.997)
6 Months	0.966 (0.912 to 0.987)	0.983 (0.947 to 0.994)

A lower score represents a better level of quality of life. Clinical meaningful deterioration change from baseline greater than or equal to 15 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] Stratified on number of prior lines of therapy (1 vs. >1) and Revised International Staging System (R-ISS) stage (I or II vs. III vs. not classified) according to IRT
[b] One-sided significance level is 0.025
[c] Estimated using the Kaplan-Meier method
NA/NC = Not Applicable / Not Calculable
PGM=DEVOPS/SAR650984/EFC15246/CIR_RWE/REPORT/PGM/eff_km_invhr_sr_i_t.sas OUT=REPORT/OUTPUT/eff_km_c30_dia_det15pl_de_i_t_x.rtf (07APR2021 14:23)

16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Diarrhea
16.2.6.1.2.1 Efficacy response data
16.2.6.1.2.1.22 QLQ-C30 - Time until permanent deterioration by 15 pt in Diarrhea - Kaplan-Meier curve (LOCF) - ITT population



A lower score represents a better level of quality of life. Clinical meaningful deterioration change from baseline greater than or equal to 15 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
PGM=DEVOPS/SAR650984/EFC15246/CIR_RWE/REPORT/PGM/eff_qlq_km_i_f.sas OUT=REPORT/OUTPUT/eff_km_c30_dia_det15pl_de_i_f_x.rtf (07APR2021 14:24)

16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Diarrhea
16.2.6.1.2.2 Efficacy response data - Subgroup analyses by age
16.2.6.1.2.2.3 QLQ-C30 - Time to first improvement by 10 pt in diarrhea according to age (LOCF) - ITT population

	<65 years		>=65 years		
	Kd (N=66)	**IKd (N=88)**	**Kd (N=57)**	**IKd (N=91)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	13 (19.7)	14 (15.9)	8 (14.0)	14 (15.4)	0.6113
Number (%) of patients censored	53 (80.3)	74 (84.1)	49 (86.0)	77 (84.6)	
Kaplan-Meier estimates of Diarrhea in months					
25% quantile (95% CI)	NC (3.055 to NC)	NC (5.979 to NC)	NC (11.466 to NC)	NC (16.164 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.5623		0.8513	
Hazard ratio (95% CI) vs Kd	-	0.80 (0.38 to 1.70)		1.09 (0.46 to 2.59)	
P-value	-	0.5631		0.8513	
Improvement probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful improvement change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
PGM=DEVOPS/SAR650984/EFC15246/CIR_RWE/REPORT/PGM/eff_km_subgp_sr_sig_de_i_t.sas OUT=REPORT/OUTPUT/eff_km_c30_dia_impl_age_de_i_t_x.rtf (07APR2021 14:37)

16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Diarrhea
16.2.6.1.2.2 Efficacy response data - Subgroup analyses by age
16.2.6.1.2.2.4 QLQ-C30 - Time to first deterioration by 10 pt in diarrhea according to age (LOCF) - ITT population

	<65 years		>=65 years		
	Kd (N=66)	**IKd (N=88)**	**Kd (N=57)**	**IKd (N=91)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	31 (47.0)	45 (51.1)	23 (40.4)	54 (59.3)	0.2222
Number (%) of patients censored	35 (53.0)	43 (48.9)	34 (59.6)	37 (40.7)	
Kaplan-Meier estimates of Diarrhea in months					
25% quantile (95% CI)	3.84 (2.004 to 4.895)	3.71 (1.938 to 5.815)	3.78 (2.037 to 11.236)	2.89 (1.971 to 3.811)	
Median (95% CI)	22.14 (6.702 to NC)	13.21 (9.429 to NC)	NC (11.236 to NC)	7.92 (4.698 to 18.464)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (21.388 to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.6541		0.0356	
Hazard ratio (95% CI) vs Kd	-	1.11 (0.70 to 1.76)		1.68 (1.03 to 2.74)	
P-value	-	0.6543		0.0377	
Hazard ratio inverted (95% CI) vs IKd		-		0.60 (0.37 to 0.97)	

A lower score represents a better level of quality of life. Clinical meaningful deterioration change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
PGM=DEVOPS/SAR650984/EFC15246/CIR_RWE/REPORT/PGM/eff_km_subgp_sr_sig_de_i_t.sas OUT=REPORT/OUTPUT/eff_km_c30_dia_detl_age_de_i_t_x.rtf (07APR2021 14:36)

16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Diarrhea
16.2.6.1.2.2 Efficacy response data - Subgroup analyses by age
16.2.6.1.2.2.5 QLQ-C30 - Time until permanent improvement by 10 pt in diarrhea according to age (LOCF) - ITT population

	<65 years		>=65 years		
	Kd (N=66)	**IKd (N=88)**	**Kd (N=57)**	**IKd (N=91)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	9 (13.6)	10 (11.4)	7 (12.3)	8 (8.8)	0.8549
Number (%) of patients censored	57 (86.4)	78 (88.6)	50 (87.7)	83 (91.2)	
Kaplan-Meier estimates of Diarrhea in months					
25% quantile (95% CI)	NC (18.300 to NC)	NC (NC to NC)	NC (19.220 to NC)	NC (NC to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.7072		0.5548	
Hazard ratio (95% CI) vs Kd	-	0.84 (0.34 to 2.07)		0.74 (0.27 to 2.03)	
P-value	-	0.7075		0.5563	
Improvement probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful improvement change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
PGM=DEVOPS/SAR650984/EFC15246/CIR_RWE/REPORT/PGM/eff_km_subgp_sr_sig_de_i_t.sas OUT=REPORT/OUTPUT/eff_km_c30_dia_imppl_age_de_i_t_x.rtf (07APR2021 14:37)

16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Diarrhea
16.2.6.1.2.2 Efficacy response data - Subgroup analyses by age
16.2.6.1.2.2.6 QLQ-C30 - Time until permanent deterioration by 10 pt in diarrhea according to age (LOCF) - ITT population

	<65 years		>=65 years		
	Kd (N=66)	**IKd (N=88)**	**Kd (N=57)**	**IKd (N=91)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	10 (15.2)	9 (10.2)	8 (14.0)	9 (9.9)	0.9571
Number (%) of patients censored	56 (84.8)	79 (89.8)	49 (86.0)	82 (90.1)	
Kaplan-Meier estimates of Diarrhea in months					
25% quantile (95% CI)	26.35 (19.614 to 26.349)	NC (20.928 to NC)	NC (18.464 to NC)	NC (NC to NC)	
Median (95% CI)	26.35 (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	26.35 (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.4933		0.4248	
Hazard ratio (95% CI) vs Kd	-	0.72 (0.29 to 1.83)		0.68 (0.26 to 1.76)	
P-value	-	0.4951		0.4276	
Deterioration probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful deterioration change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
PGM=DEVOPS/SAR650984/EFC15246/CIR_RWE/REPORT/PGM/eff_km_subgp_sr_sig_de_i_t.sas OUT=REPORT/OUTPUT/eff_km_c30_dia_detpl_age_de_i_t_x.rtf (07APR2021 14:37)

16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Diarrhea
16.2.6.1.2.3 Efficacy response data - Subgroup analyses by gender
16.2.6.1.2.3.3 QLQ-C30 - Time to first improvement by 10 pt in diarrhea according to gender (LOCF) - ITT population

	Male		Female		
	Kd (N=68)	**IKd (N=101)**	**Kd (N=55)**	**IKd (N=78)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	11 (16.2)	16 (15.8)	10 (18.2)	12 (15.4)	0.7466
Number (%) of patients censored	57 (83.8)	85 (84.2)	45 (81.8)	66 (84.6)	
Kaplan-Meier estimates of Diarrhea in months					
25% quantile (95% CI)	NC (10.283 to NC)	NC (16.164 to NC)	NC (1.906 to NC)	NC (5.979 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.9699		0.6482	
Hazard ratio (95% CI) vs Kd	-	0.99 (0.46 to 2.12)		0.82 (0.36 to 1.90)	
P-value	-	0.9699		0.6487	
Improvement probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful improvement change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
PGM=DEVOPS/SAR650984/EFC15246/CIR_RWE/REPORT/PGM/eff_km_subgp_sr_sig_de_i_t.sas OUT=REPORT/OUTPUT/eff_km_c30_dia_impl_sex_de_i_t_x.rtf (07APR2021 14:37)

16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Diarrhea
16.2.6.1.2.3 Efficacy response data - Subgroup analyses by gender
16.2.6.1.2.3.4 QLQ-C30 - Time to first deterioration by 10 pt in diarrhea according to gender (LOCF) - ITT population

	Male		Female		
	Kd (N=68)	**IKd (N=101)**	**Kd (N=55)**	**IKd (N=78)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	24 (35.3)	51 (50.5)	30 (54.5)	48 (61.5)	0.2982
Number (%) of patients censored	44 (64.7)	50 (49.5)	25 (45.5)	30 (38.5)	
Kaplan-Meier estimates of Diarrhea in months					
25% quantile (95% CI)	4.73 (2.037 to 12.682)	2.96 (2.037 to 4.698)	3.78 (1.938 to 4.895)	3.22 (1.906 to 4.764)	
Median (95% CI)	NC (12.682 to NC)	11.10 (5.684 to NC)	9.26 (4.895 to NC)	10.41 (5.355 to 18.464)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (22.144 to NC)	NC (20.731 to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.0541		0.5266	
Hazard ratio (95% CI) vs Kd	-	1.60 (0.99 to 2.61)		1.16 (0.73 to 1.83)	
P-value	-	0.0564		0.5270	
Deterioration probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful deterioration change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
PGM=DEVOPS/SAR650984/EFC15246/CIR_RWE/REPORT/PGM/eff_km_subgp_sr_sig_de_i_t.sas OUT=REPORT/OUTPUT/eff_km_c30_dia_detl_sex_de_i_t_x.rtf (07APR2021 14:37)

16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Diarrhea
16.2.6.1.2.3 Efficacy response data - Subgroup analyses by gender
16.2.6.1.2.3.5 QLQ-C30 - Time until permanent improvement by 10 pt in diarrhea according to gender (LOCF) - ITT population

	Male		Female		
	Kd (N=68)	**IKd (N=101)**	**Kd (N=55)**	**IKd (N=78)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	8 (11.8)	9 (8.9)	8 (14.5)	9 (11.5)	0.9657
Number (%) of patients censored	60 (88.2)	92 (91.1)	47 (85.5)	69 (88.5)	
Kaplan-Meier estimates of Diarrhea in months					
25% quantile (95% CI)	NC (19.220 to NC)	NC (NC to NC)	NC (15.704 to NC)	NC (20.632 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.6102		0.5816	
Hazard ratio (95% CI) vs Kd	-	0.78 (0.30 to 2.02)		0.77 (0.30 to 1.98)	
P-value	-	0.6111		0.5827	
Improvement probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful improvement change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
PGM=DEVOPS/SAR650984/EFC15246/CIR_RWE/REPORT/PGM/eff_km_subgp_sr_sig_de_i_t.sas OUT=REPORT/OUTPUT/eff_km_c30_dia_imppl_sex_de_i_t_x.rtf (07APR2021 14:37)

16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Diarrhea
16.2.6.1.2.3 Efficacy response data - Subgroup analyses by gender
16.2.6.1.2.3.6 QLQ-C30 - Time until permanent deterioration by 10 pt in diarrhea according to gender (LOCF) - ITT population

	Male		Female		
	Kd (N=68)	**IKd (N=101)**	**Kd (N=55)**	**IKd (N=78)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	5 (7.4)	9 (8.9)	13 (23.6)	9 (11.5)	0.1630
Number (%) of patients censored	63 (92.6)	92 (91.1)	42 (76.4)	69 (88.5)	
Kaplan-Meier estimates of Diarrhea in months					
25% quantile (95% CI)	NC (21.125 to NC)	NC (NC to NC)	22.14 (12.945 to NC)	NC (20.928 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	26.35 (26.349 to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (26.349 to NC)	NC (NC to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.6675		0.0822	
Hazard ratio (95% CI) vs Kd	-	1.27 (0.43 to 3.79)		0.47 (0.20 to 1.12)	
P-value	-	0.6682		0.0895	
Deterioration probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful deterioration change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
PGM=DEVOPS/SAR650984/EFC15246/CIR_RWE/REPORT/PGM/eff_km_subgp_sr_sig_de_i_t.sas OUT=REPORT/OUTPUT/eff_km_c30_dia_detpl_sex_de_i_t_x.rtf (07APR2021 14:37)

16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Diarrhea
16.2.6.1.2.4 Efficacy response data - Subgroup analyses by ethnic origin
16.2.6.1.2.4.3 QLQ-C30 - Time to first improvement by 10 pt in diarrhea according to ethnic origin (LOCF) - ITT population

	White		Other		
	Kd (N=83)	**IKd (N=131)**	**Kd (N=28)**	**IKd (N=34)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	13 (15.7)	22 (16.8)	7 (25.0)	5 (14.7)	0.3930
Number (%) of patients censored	70 (84.3)	109 (83.2)	21 (75.0)	29 (85.3)	
Kaplan-Meier estimates of Diarrhea in months					
25% quantile (95% CI)	NC (16.854 to NC)	NC (16.164 to NC)	11.47 (1.117 to NC)	NC (1.150 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.8534		0.3694	
Hazard ratio (95% CI) vs Kd	-	1.07 (0.54 to 2.12)		0.59 (0.19 to 1.87)	
P-value	-	0.8535		0.3747	
Improvement probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful improvement change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
PGM=DEVOPS/SAR650984/EFC15246/CIR_RWE/REPORT/PGM/eff_km_subgp_sr_sig_de_i_t.sas OUT=REPORT/OUTPUT/eff_km_c30_dia_impl_race_de_i_t_x.rtf (07APR2021 14:37)

16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Diarrhea
16.2.6.1.2.4 Efficacy response data - Subgroup analyses by ethnic origin
16.2.6.1.2.4.4 QLQ-C30 - Time to first deterioration by 10 pt in diarrhea according to ethnic origin (LOCF) - ITT population

	White		Other		
	Kd (N=83)	**IKd (N=131)**	**Kd (N=28)**	**IKd (N=34)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	36 (43.4)	72 (55.0)	11 (39.3)	20 (58.8)	0.7765
Number (%) of patients censored	47 (56.6)	59 (45.0)	17 (60.7)	14 (41.2)	
Kaplan-Meier estimates of Diarrhea in months					
25% quantile (95% CI)	3.75 (1.971 to 7.688)	2.89 (1.971 to 3.975)	4.04 (1.906 to 11.236)	5.45 (1.018 to 7.918)	
Median (95% CI)	NC (9.265 to NC)	11.10 (5.125 to 21.388)	NC (4.304 to NC)	11.07 (6.538 to 14.226)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (13.207 to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.1090		0.2383	
Hazard ratio (95% CI) vs Kd	-	1.39 (0.93 to 2.07)		1.55 (0.74 to 3.25)	
P-value	-	0.1106		0.2421	
Deterioration probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful deterioration change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
PGM=DEVOPS/SAR650984/EFC15246/CIR_RWE/REPORT/PGM/eff_km_subgp_sr_sig_de_i_t.sas OUT=REPORT/OUTPUT/eff_km_c30_dia_detl_race_de_i_t_x.rtf (07APR2021 14:36)

16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Diarrhea
16.2.6.1.2.4 Efficacy response data - Subgroup analyses by ethnic origin
16.2.6.1.2.4.5 QLQ-C30 - Time until permanent improvement by 10 pt in diarrhea according to ethnic origin (LOCF) - ITT population

	White		Other		
	Kd (N=83)	**IKd (N=131)**	**Kd (N=28)**	**IKd (N=34)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	10 (12.0)	14 (10.7)	5 (17.9)	4 (11.8)	0.7141
Number (%) of patients censored	73 (88.0)	117 (89.3)	23 (82.1)	30 (88.2)	
Kaplan-Meier estimates of Diarrhea in months					
25% quantile (95% CI)	NC (21.684 to NC)	NC (NC to NC)	NC (2.825 to NC)	NC (17.347 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.8004		0.5595	
Hazard ratio (95% CI) vs Kd	-	0.90 (0.40 to 2.03)		0.68 (0.18 to 2.52)	
P-value	-	0.8005		0.5620	
Improvement probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful improvement change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
PGM=DEVOPS/SAR650984/EFC15246/CIR_RWE/REPORT/PGM/eff_km_subgp_sr_sig_de_i_t.sas OUT=REPORT/OUTPUT/eff_km_c30_dia_imppl_race_de_i_t_x.rtf (07APR2021 14:37)

16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Diarrhea
16.2.6.1.2.4 Efficacy response data - Subgroup analyses by ethnic origin
16.2.6.1.2.4.6 QLQ-C30 - Time until permanent deterioration by 10 pt in diarrhea according to ethnic origin (LOCF) - ITT population

	White		Other		
	Kd (N=83)	**IKd (N=131)**	**Kd (N=28)**	**IKd (N=34)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	13 (15.7)	14 (10.7)	2 (7.1)	0 (0.0)	0.9895
Number (%) of patients censored	70 (84.3)	117 (89.3)	26 (92.9)	34 (100.0)	
Kaplan-Meier estimates of Diarrhea in months					
25% quantile (95% CI)	NC (19.548 to NC)	NC (NC to NC)	26.35 (14.522 to NC)	NC (NC to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	26.35 (26.349 to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (26.349 to NC)	NC (NC to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.2679		0.2752	
Hazard ratio (95% CI) vs Kd	-	0.65 (0.31 to 1.39)			
P-value	-	0.2715		0.9975	
Deterioration probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful deterioration change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Diarrhea
16.2.6.1.2.5 Efficacy response data - Subgroup analyses by geographical region
16.2.6.1.2.5.3 QLQ-C30 - Time to first improvement by 10 pt in diarrhea according to geographical region (LOCF) - ITT population

	Europe		America		Asia		Other countries		
	Kd (N=60)	**IKd (N=85)**	**Kd (N=20)**	**IKd (N=24)**	**Kd (N=21)**	**IKd (N=25)**	**Kd (N=22)**	**IKd (N=45)**	**p-value of treatment-by-subgroup interaction[c]**
Number (%) of events	10 (16.7)	10 (11.8)	2 (10.0)	6 (25.0)	7 (33.3)	4 (16.0)	2 (9.1)	8 (17.8)	0.2005
Number (%) of patients censored	50 (83.3)	75 (88.2)	18 (90.0)	18 (75.0)	14 (66.7)	21 (84.0)	20 (90.9)	37 (82.2)	
Kaplan-Meier estimates of event in months									
25% quantile (95% CI)	NC (2.825 to NC)	NC (NC to NC)	NC (0.986 to NC)	5.19 (0.986 to NC)	3.06 (1.051 to NC)	NC (1.051 to NC)	NC (0.986 to NC)	NC (1.938 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (5.191 to NC)	NC (3.055 to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Kd									

A lower score represents a better level of quality of life. Clinical meaningful improvement change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
PGM=DEVOPS/SAR650984/EFC15246/CIR_RWE/REPORT/PGM/eff_km_subgp_sr_sig_de_i_t.sas OUT=REPORT/OUTPUT/eff_km_c30_dia_impl_greg_de_i_t_x.rtf (07APR2021 14:37)

16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Diarrhea
16.2.6.1.2.5 Efficacy response data - Subgroup analyses by geographical region
16.2.6.1.2.5.3 QLQ-C30 - Time to first improvement by 10 pt in diarrhea according to geographical region (LOCF) - ITT population

	Europe		America		Asia		Other countries		
	Kd (N=60)	**IKd (N=85)**	**Kd (N=20)**	**IKd (N=24)**	**Kd (N=21)**	**IKd (N=25)**	**Kd (N=22)**	**IKd (N=45)**	**p-value of treatment-by-subgroup interaction[c]**
Log-Rank test p-value[a] vs Kd	-	0.3693		0.1883		0.1963		0.3790	
Hazard ratio (95% CI) vs Kd	-	0.67 (0.28 to 1.61)		2.80 (0.56 to 13.88)		0.45 (0.13 to 1.55)		1.98 (0.42 to 9.32)	
P-value	-	0.3725		0.2079		0.2080		0.3882	
Improvement probability (95% CI)[b]									
3 Months	0.137 (0.064 to 0.238)	0.085 (0.037 to 0.157)	0.100 (0.017 to 0.272)	0.176 (0.055 to 0.354)	0.203 (0.063 to 0.399)	0.167 (0.052 to 0.337)	0.091 (0.016 to 0.251)	0.156 (0.068 to 0.275)	
6 Months	0.137 (0.064 to 0.238)	0.110 (0.054 to 0.189)	0.100 (0.017 to 0.272)	0.268 (0.109 to 0.457)	0.256 (0.093 to 0.458)	0.167 (0.052 to 0.337)	0.091 (0.016 to 0.251)	0.156 (0.068 to 0.275)	

A lower score represents a better level of quality of life. Clinical meaningful improvement change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Diarrhea
16.2.6.1.2.5 Efficacy response data - Subgroup analyses by geographical region
16.2.6.1.2.5.4 QLQ-C30 - Time to first deterioration by 10 pt in diarrhea according to geographical region (LOCF) - ITT population

	Europe		America		Asia		Other countries		
	Kd (N=60)	**IKd (N=85)**	**Kd (N=20)**	**IKd (N=24)**	**Kd (N=21)**	**IKd (N=25)**	**Kd (N=22)**	**IKd (N=45)**	**p-value of treatment-by-subgroup interaction[c]**
Number (%) of events	24 (40.0)	40 (47.1)	13 (65.0)	12 (50.0)	8 (38.1)	15 (60.0)	9 (40.9)	32 (71.1)	0.2182
Number (%) of patients censored	36 (60.0)	45 (52.9)	7 (35.0)	12 (50.0)	13 (61.9)	10 (40.0)	13 (59.1)	13 (28.9)	
Kaplan-Meier estimates of event in months									
25% quantile (95% CI)	4.63 (2.103 to 12.583)	3.68 (2.267 to 4.830)	4.06 (0.953 to 7.458)	5.06 (1.906 to 11.105)	4.04 (1.971 to NC)	6.54 (0.986 to 8.805)	1.91 (0.986 to NC)	1.12 (0.986 to 2.234)	
Median (95% CI)	NC (11.039 to NC)	20.73 (9.659 to NC)	7.77 (3.811 to NC)	11.86 (5.060 to NC)	NC (4.041 to NC)	11.07 (7.425 to NC)	NC (1.906 to NC)	4.70 (2.037 to 6.177)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (7.951 to NC)	NC (14.423 to NC)	NC (NC to NC)	NC (13.142 to NC)	NC (NC to NC)	NC (5.684 to NC)	

A lower score represents a better level of quality of life. Clinical meaningful deterioration change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Diarrhea
16.2.6.1.2.5 Efficacy response data - Subgroup analyses by geographical region
16.2.6.1.2.5.4 QLQ-C30 - Time to first deterioration by 10 pt in diarrhea according to geographical region (LOCF) - ITT population

	Europe		America		Asia		Other countries		
	Kd (N=60)	**IKd (N=85)**	**Kd (N=20)**	**IKd (N=24)**	**Kd (N=21)**	**IKd (N=25)**	**Kd (N=22)**	**IKd (N=45)**	**p-value of treatment-by-subgroup interaction[c]**
Comparison vs. Kd									
Log-Rank test p-value[a] vs Kd	-	0.3986		0.4080		0.3286		0.0538	
Hazard ratio (95% CI) vs Kd	-	1.24 (0.75 to 2.06)		0.72 (0.33 to 1.58)		1.53 (0.65 to 3.62)		2.04 (0.97 to 4.29)	
P-value	-	0.3995		0.4101		0.3322		0.0590	
Deterioration probability (95% CI)[b]									
3 Months	0.827 (0.702 to 0.903)	0.769 (0.662 to 0.846)	0.800 (0.551 to 0.920)	0.864 (0.634 to 0.954)	0.797 (0.545 to 0.919)	0.917 (0.706 to 0.978)	0.636 (0.403 to 0.799)	0.533 (0.379 to 0.666)	
6 Months	0.719 (0.582 to 0.817)	0.643 (0.528 to 0.737)	0.600 (0.357 to 0.776)	0.636 (0.403 to 0.799)	0.691 (0.436 to 0.848)	0.792 (0.570 to 0.908)	0.591 (0.361 to 0.762)	0.378 (0.239 to 0.516)	

A lower score represents a better level of quality of life. Clinical meaningful deterioration change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Diarrhea
16.2.6.1.2.5 Efficacy response data - Subgroup analyses by geographical region
16.2.6.1.2.5.5 QLQ-C30 - Time until permanent improvement by 10 pt in diarrhea according to geographical region (LOCF) - ITT population

	Europe		America		Asia		Other countries		
	Kd (N=60)	**IKd (N=85)**	**Kd (N=20)**	**IKd (N=24)**	**Kd (N=21)**	**IKd (N=25)**	**Kd (N=22)**	**IKd (N=45)**	**p-value of treatment-by-subgroup interaction[c]**
Number (%) of events	9 (15.0)	6 (7.1)	0 (0.0)	3 (12.5)	5 (23.8)	3 (12.0)	2 (9.1)	6 (13.3)	0.5845
Number (%) of patients censored	51 (85.0)	79 (92.9)	20 (100.0)	21 (87.5)	16 (76.2)	22 (88.0)	20 (90.9)	39 (86.7)	
Kaplan-Meier estimates of event in months									
25% quantile (95% CI)	NC (18.300 to NC)	NC (NC to NC)	NC (NC to NC)	NC (1.084 to NC)	18.23 (1.051 to NC)	NC (1.051 to NC)	NC (15.704 to NC)	NC (16.394 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (20.895 to NC)	NC (18.234 to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	

A lower score represents a better level of quality of life. Clinical meaningful improvement change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Diarrhea
16.2.6.1.2.5 Efficacy response data - Subgroup analyses by geographical region
16.2.6.1.2.5.5 QLQ-C30 - Time until permanent improvement by 10 pt in diarrhea according to geographical region (LOCF) - ITT population

	Europe		America		Asia		Other countries		
	Kd (N=60)	**IKd (N=85)**	**Kd (N=20)**	**IKd (N=24)**	**Kd (N=21)**	**IKd (N=25)**	**Kd (N=22)**	**IKd (N=45)**	**p-value of treatment-by-subgroup interaction[c]**
Comparison vs. Kd									
Log-Rank test p-value[a] vs Kd	-	0.1192		0.0820		0.3010		0.5541	
Hazard ratio (95% CI) vs Kd	-	0.45 (0.16 to 1.26)				0.48 (0.11 to 2.00)		1.61 (0.33 to 8.00)	
P-value	-	0.1292		0.9972		0.3120		0.5581	
Improvement probability (95% CI)[b]									
3 Months	0.069 (0.022 to 0.153)	0.048 (0.016 to 0.109)		0.043 (0.003 to 0.182)	0.103 (0.017 to 0.279)	0.042 (0.003 to 0.176)		0.044 (0.008 to 0.133)	

A lower score represents a better level of quality of life. Clinical meaningful improvement change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Diarrhea
16.2.6.1.2.5 Efficacy response data - Subgroup analyses by geographical region
16.2.6.1.2.5.6 QLQ-C30 - Time until permanent deterioration by 10 pt in diarrhea according to geographical region (LOCF) - ITT population

	Europe		America		Asia		Other countries		
	Kd (N=60)	**IKd (N=85)**	**Kd (N=20)**	**IKd (N=24)**	**Kd (N=21)**	**IKd (N=25)**	**Kd (N=22)**	**IKd (N=45)**	**p-value of treatment-by-subgroup interaction[c]**
Number (%) of events	7 (11.7)	10 (11.8)	5 (25.0)	3 (12.5)	1 (4.8)	0 (0.0)	5 (22.7)	5 (11.1)	0.8064
Number (%) of patients censored	53 (88.3)	75 (88.2)	15 (75.0)	21 (87.5)	20 (95.2)	25 (100.0)	17 (77.3)	40 (88.9)	
Kaplan-Meier estimates of event in months									
25% quantile (95% CI)	NC (20.370 to NC)	NC (20.928 to NC)	19.55 (8.444 to NC)	NC (5.322 to NC)	26.35 (26.349 to NC)	NC (NC to NC)	21.13 (1.216 to NC)	NC (19.614 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (18.924 to NC)	NC (NC to NC)	NC (26.349 to NC)	NC (NC to NC)	NC (21.125 to NC)	NC (NC to NC)	

A lower score represents a better level of quality of life. Clinical meaningful deterioration change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Diarrhea
16.2.6.1.2.5 Efficacy response data - Subgroup analyses by geographical region
16.2.6.1.2.5.6 QLQ-C30 - Time until permanent deterioration by 10 pt in diarrhea according to geographical region (LOCF) - ITT population

	Europe		America		Asia		Other countries		
	Kd (N=60)	**IKd (N=85)**	**Kd (N=20)**	**IKd (N=24)**	**Kd (N=21)**	**IKd (N=25)**	**Kd (N=22)**	**IKd (N=45)**	**p-value of treatment-by-subgroup interaction[c]**
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (26.349 to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Kd									
Log-Rank test p-value[a] vs Kd	-	0.9499		0.5035				0.2147	
Hazard ratio (95% CI) vs Kd	-	0.97 (0.37 to 2.55)		0.62 (0.15 to 2.58)				0.46 (0.13 to 1.61)	
P-value	-	0.9497		0.5077				0.2260	
Deterioration probability (95% CI)[b]									

A lower score represents a better level of quality of life. Clinical meaningful deterioration change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
PGM=DEVOPS/SAR650984/EFC15246/CIR_RWE/REPORT/PGM/eff_km_subgp_sr_sig_de_i_t.sas OUT=REPORT/OUTPUT/eff_km_c30_dia_detpl_greg_de_i_t_x.rtf (07APR2021 14:37)

16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Diarrhea
16.2.6.1.2.6 Efficacy response data - Subgroup analyses by regulatory region
16.2.6.1.2.6.3 QLQ-C30 - Time to first improvement by 10 pt in diarrhea according to regulatory region (LOCF) - ITT population

	Western countries		Other countries		
	Kd (N=55)	**IKd (N=97)**	**Kd (N=68)**	**IKd (N=82)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	8 (14.5)	17 (17.5)	13 (19.1)	11 (13.4)	0.3566
Number (%) of patients censored	47 (85.5)	80 (82.5)	55 (80.9)	71 (86.6)	
Kaplan-Meier estimates of Diarrhea in months					
25% quantile (95% CI)	NC (12.255 to NC)	NC (8.509 to NC)	NC (2.825 to NC)	NC (NC to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.6651		0.3683	
Hazard ratio (95% CI) vs Kd	-	1.20 (0.52 to 2.79)		0.69 (0.31 to 1.55)	
P-value	-	0.6656		0.3710	
Improvement probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful improvement change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
PGM=DEVOPS/SAR650984/EFC15246/CIR_RWE/REPORT/PGM/eff_km_subgp_sr_sig_de_i_t.sas OUT=REPORT/OUTPUT/eff_km_c30_dia_impl_rreg_de_i_t_x.rtf (07APR2021 14:37)

16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Diarrhea
16.2.6.1.2.6 Efficacy response data - Subgroup analyses by regulatory region
16.2.6.1.2.6.4 QLQ-C30 - Time to first deterioration by 10 pt in diarrhea according to regulatory region (LOCF) - ITT population

	Western countries		Other countries		
	Kd (N=55)	**IKd (N=97)**	**Kd (N=68)**	**IKd (N=82)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	22 (40.0)	48 (49.5)	32 (47.1)	51 (62.2)	0.5825
Number (%) of patients censored	33 (60.0)	49 (50.5)	36 (52.9)	31 (37.8)	
Kaplan-Meier estimates of Diarrhea in months					
25% quantile (95% CI)	2.83 (1.906 to 9.265)	2.89 (2.037 to 4.140)	4.04 (2.201 to 7.589)	3.71 (1.906 to 4.830)	
Median (95% CI)	NC (9.265 to NC)	17.28 (5.684 to NC)	15.54 (7.688 to NC)	8.84 (5.355 to 13.207)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (14.226 to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.3957		0.0563	
Hazard ratio (95% CI) vs Kd	-	1.24 (0.75 to 2.06)		1.53 (0.99 to 2.39)	
P-value	-	0.3967		0.0582	
Deterioration probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful deterioration change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Diarrhea
16.2.6.1.2.6 Efficacy response data - Subgroup analyses by regulatory region
16.2.6.1.2.6.5 QLQ-C30 - Time until permanent improvement by 10 pt in diarrhea according to regulatory region (LOCF) - ITT population

	Western countries		Other countries		
	Kd (N=55)	**IKd (N=97)**	**Kd (N=68)**	**IKd (N=82)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	7 (12.7)	10 (10.3)	9 (13.2)	8 (9.8)	0.8586
Number (%) of patients censored	48 (87.3)	87 (89.7)	59 (86.8)	74 (90.2)	
Kaplan-Meier estimates of Diarrhea in months					
25% quantile (95% CI)	NC (18.924 to NC)	NC (20.895 to NC)	NC (18.234 to NC)	NC (NC to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.7143		0.5356	
Hazard ratio (95% CI) vs Kd	-	0.84 (0.32 to 2.20)		0.74 (0.29 to 1.92)	
P-value	-	0.7147		0.5371	
Improvement probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful improvement change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Diarrhea
16.2.6.1.2.6 Efficacy response data - Subgroup analyses by regulatory region
16.2.6.1.2.6.6 QLQ-C30 - Time until permanent deterioration by 10 pt in diarrhea according to regulatory region (LOCF) - ITT population

	Western countries		Other countries		
	Kd (N=55)	**IKd (N=97)**	**Kd (N=68)**	**IKd (N=82)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	10 (18.2)	14 (14.4)	8 (11.8)	4 (4.9)	0.4366
Number (%) of patients censored	45 (81.8)	83 (85.6)	60 (88.2)	78 (95.1)	
Kaplan-Meier estimates of Diarrhea in months					
25% quantile (95% CI)	22.14 (15.047 to NC)	NC (19.253 to NC)	26.35 (19.548 to NC)	NC (NC to NC)	
Median (95% CI)	NC (22.144 to NC)	NC (NC to NC)	26.35 (26.349 to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (26.349 to NC)	NC (NC to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.5928		0.1831	
Hazard ratio (95% CI) vs Kd	-	0.80 (0.36 to 1.81)		0.44 (0.13 to 1.52)	
P-value	-	0.5935		0.1952	
Deterioration probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful deterioration change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Diarrhea
16.2.6.1.2.7 Efficacy response data - Subgroup analyses by baseline ECOG PS
16.2.6.1.2.7.3 QLQ-C30 - Time to first improvement by 10 pt in diarrhea according to baseline ECOG PS (LOCF) - ITT population

	0 or 1		>1		
	Kd (N=118)	**IKd (N=168)**	**Kd (N=5)**	**IKd (N=11)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	20 (16.9)	27 (16.1)	1 (20.0)	1 (9.1)	0.6578
Number (%) of patients censored	98 (83.1)	141 (83.9)	4 (80.0)	10 (90.9)	
Kaplan-Meier estimates of Diarrhea in months					
25% quantile (95% CI)	NC (12.255 to NC)	NC (NC to NC)	NC (1.051 to NC)	NC (1.971 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (1.051 to NC)	NC (1.971 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (1.051 to NC)	NC (NC to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.8145		0.6144	
Hazard ratio (95% CI) vs Kd	-	0.93 (0.52 to 1.66)		0.50 (0.03 to 7.98)	
P-value	-	0.8135		0.6215	
Improvement probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful improvement change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Diarrhea
16.2.6.1.2.7 Efficacy response data - Subgroup analyses by baseline ECOG PS
16.2.6.1.2.7.4 QLQ-C30 - Time to first deterioration by 10 pt in diarrhea according to baseline ECOG PS (LOCF) - ITT population

	0 or 1		>1		
	Kd (N=118)	**IKd (N=168)**	**Kd (N=5)**	**IKd (N=11)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	52 (44.1)	95 (56.5)	2 (40.0)	4 (36.4)	0.7190
Number (%) of patients censored	66 (55.9)	73 (43.5)	3 (60.0)	7 (63.6)	
Kaplan-Meier estimates of Diarrhea in months					
25% quantile (95% CI)	3.78 (2.103 to 4.895)	2.96 (2.037 to 3.975)	12.58 (1.938 to NC)	5.13 (1.216 to NC)	
Median (95% CI)	NC (9.265 to NC)	11.07 (6.439 to 14.423)	NC (1.938 to NC)	NC (1.216 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (1.938 to NC)	NC (10.415 to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.0557		0.9002	
Hazard ratio (95% CI) vs Kd	-	1.39 (0.99 to 1.95)		1.11 (0.20 to 6.09)	
P-value	-	0.0568		0.9003	
Deterioration probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful deterioration change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Diarrhea
16.2.6.1.2.7 Efficacy response data - Subgroup analyses by baseline ECOG PS
16.2.6.1.2.7.5 QLQ-C30 - Time until permanent improvement by 10 pt in diarrhea according to baseline ECOG PS (LOCF) - ITT population

	0 or 1		>1		
	Kd (N=118)	**IKd (N=168)**	**Kd (N=5)**	**IKd (N=11)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	15 (12.7)	17 (10.1)	1 (20.0)	1 (9.1)	0.6732
Number (%) of patients censored	103 (87.3)	151 (89.9)	4 (80.0)	10 (90.9)	
Kaplan-Meier estimates of Diarrhea in months					
25% quantile (95% CI)	NC (21.684 to NC)	NC (NC to NC)	NC (1.051 to NC)	NC (5.191 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (1.051 to NC)	NC (5.191 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (1.051 to NC)	NC (NC to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.5294		0.6144	
Hazard ratio (95% CI) vs Kd	-	0.80 (0.40 to 1.60)		0.50 (0.03 to 7.98)	
P-value	-	0.5302		0.6215	
Improvement probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful improvement change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Diarrhea
16.2.6.1.2.7 Efficacy response data - Subgroup analyses by baseline ECOG PS
16.2.6.1.2.7.6 QLQ-C30 - Time until permanent deterioration by 10 pt in diarrhea according to baseline ECOG PS (LOCF) - ITT population

	0 or 1		>1		
	Kd (N=118)	**IKd (N=168)**	**Kd (N=5)**	**IKd (N=11)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	17 (14.4)	18 (10.7)	1 (20.0)	0 (0.0)	0.9886
Number (%) of patients censored	101 (85.6)	150 (89.3)	4 (80.0)	11 (100.0)	
Kaplan-Meier estimates of Diarrhea in months					
25% quantile (95% CI)	26.35 (20.370 to NC)	NC (NC to NC)	NC (8.378 to NC)	NC (NC to NC)	
Median (95% CI)	26.35 (26.349 to NC)	NC (NC to NC)	NC (8.378 to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (26.349 to NC)	NC (NC to NC)	NC (8.378 to NC)	NC (NC to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.4402		0.1336	
Hazard ratio (95% CI) vs Kd	-	0.77 (0.39 to 1.51)			
P-value	-	0.4415		0.9986	
Deterioration probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful deterioration change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Diarrhea
16.2.6.1.2.8 Efficacy response data - Subgroup analyses by ISS staging at SE
16.2.6.1.2.8.3 QLQ-C30 - Time to first improvement by 10 pt in diarrhea according to ISS staging at SE (LOCF) - ITT population

	I		II		III		
	Kd (N=71)	**IKd (N=89)**	**Kd (N=31)**	**IKd (N=63)**	**Kd (N=20)**	**IKd (N=26)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	11 (15.5)	13 (14.6)	7 (22.6)	12 (19.0)	3 (15.0)	2 (7.7)	0.8601
Number (%) of patients censored	60 (84.5)	76 (85.4)	24 (77.4)	51 (81.0)	17 (85.0)	24 (92.3)	
Kaplan-Meier estimates of Diarrhea in months							
25% quantile (95% CI)	NC (11.466 to NC)	NC (NC to NC)	NC (1.906 to NC)	NC (1.117 to NC)	NC (0.986 to NC)	NC (1.018 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Kd							
Log-Rank test p-value[a] vs Kd	-	0.8120		0.7554		0.4610	
Hazard ratio (95% CI) vs Kd	-	0.91 (0.41 to 2.03)		0.86 (0.34 to 2.19)		0.52 (0.09 to 3.09)	
P-value	-	0.8121		0.7557		0.4690	

A lower score represents a better level of quality of life. Clinical meaningful improvement change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Diarrhea
16.2.6.1.2.8 Efficacy response data - Subgroup analyses by ISS staging at SE
16.2.6.1.2.8.4 QLQ-C30 - Time to first deterioration by 10 pt in diarrhea according to ISS staging at SE (LOCF) - ITT population

	I		II		III		
	Kd (N=71)	**IKd (N=89)**	**Kd (N=31)**	**IKd (N=63)**	**Kd (N=20)**	**IKd (N=26)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	32 (45.1)	50 (56.2)	14 (45.2)	41 (65.1)	7 (35.0)	7 (26.9)	0.5087
Number (%) of patients censored	39 (54.9)	39 (43.8)	17 (54.8)	22 (34.9)	13 (65.0)	19 (73.1)	
Kaplan-Meier estimates of Diarrhea in months							
25% quantile (95% CI)	3.81 (2.037 to 7.951)	3.84 (2.037 to 4.928)	2.83 (1.216 to 4.895)	2.04 (1.051 to 2.891)	4.76 (1.938 to NC)	10.41 (1.216 to NC)	
Median (95% CI)	22.14 (9.265 to NC)	12.78 (6.538 to NC)	NC (3.745 to NC)	5.68 (3.220 to 13.142)	NC (4.764 to NC)	NC (10.415 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (14.226 to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Kd							
Log-Rank test p-value[a] vs Kd	-	0.1956		0.1381		0.6580	
Hazard ratio (95% CI) vs Kd	-	1.34 (0.86 to 2.09)		1.58 (0.86 to 2.89)		0.79 (0.28 to 2.25)	
P-value	-	0.1972		0.1418		0.6588	

A lower score represents a better level of quality of life. Clinical meaningful deterioration change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Diarrhea
16.2.6.1.2.8 Efficacy response data - Subgroup analyses by ISS staging at SE
16.2.6.1.2.8.5 QLQ-C30 - Time until permanent improvement by 10 pt in diarrhea according to ISS staging at SE (LOCF) - ITT population

	I		II		III		
	Kd (N=71)	**IKd (N=89)**	**Kd (N=31)**	**IKd (N=63)**	**Kd (N=20)**	**IKd (N=26)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	8 (11.3)	9 (10.1)	6 (19.4)	7 (11.1)	2 (10.0)	2 (7.7)	0.6811
Number (%) of patients censored	63 (88.7)	80 (89.9)	25 (80.6)	56 (88.9)	18 (90.0)	24 (92.3)	
Kaplan-Meier estimates of Diarrhea in months							
25% quantile (95% CI)	NC (21.684 to NC)	NC (20.895 to NC)	NC (5.815 to NC)	NC (NC to NC)	NC (1.051 to NC)	NC (1.051 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Kd							
Log-Rank test p-value[a] vs Kd	-	0.9346		0.2294		0.8545	
Hazard ratio (95% CI) vs Kd	-	0.96 (0.37 to 2.49)		0.52 (0.17 to 1.54)		0.83 (0.12 to 5.92)	
P-value	-	0.9345		0.2376		0.8547	

A lower score represents a better level of quality of life. Clinical meaningful improvement change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
PGM=DEVOPS/SAR650984/EFC15246/CIR_RWE/REPORT/PGM/eff_km_subgp_sr_sig_de_i_t.sas OUT=REPORT/OUTPUT/eff_km_c30_dia_imppl_seiss_de_i_t_x.rtf (07APR2021 14:37)

16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Diarrhea
16.2.6.1.2.8 Efficacy response data - Subgroup analyses by ISS staging at SE
16.2.6.1.2.8.6 QLQ-C30 - Time until permanent deterioration by 10 pt in diarrhea according to ISS staging at SE (LOCF) - ITT population

	I		II		III		
	Kd (N=71)	**IKd (N=89)**	**Kd (N=31)**	**IKd (N=63)**	**Kd (N=20)**	**IKd (N=26)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	11 (15.5)	9 (10.1)	5 (16.1)	8 (12.7)	2 (10.0)	0 (0.0)	0.9803
Number (%) of patients censored	60 (84.5)	80 (89.9)	26 (83.9)	55 (87.3)	18 (90.0)	26 (100.0)	
Kaplan-Meier estimates of Diarrhea in months							
25% quantile (95% CI)	NC (19.548 to NC)	NC (NC to NC)	26.35 (15.047 to 26.349)	NC (19.614 to NC)	NC (8.378 to NC)	NC (NC to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	26.35 (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	26.35 (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Kd							
Log-Rank test p-value[a] vs Kd	-	0.3389		0.8394		0.1150	
Hazard ratio (95% CI) vs Kd	-	0.65 (0.27 to 1.58)		0.88 (0.27 to 2.94)			
P-value	-	0.3425		0.8395		0.9977	

A lower score represents a better level of quality of life. Clinical meaningful deterioration change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
PGM=DEVOPS/SAR650984/EFC15246/CIR_RWE/REPORT/PGM/eff_km_subgp_sr_sig_de_i_t.sas OUT=REPORT/OUTPUT/eff_km_c30_dia_detpl_seiss_de_i_t_x.rtf (07APR2021 14:37)

16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Diarrhea
16.2.6.1.2.9 Efficacy response data - Subgroup analyses by R-ISS stage at SE
16.2.6.1.2.9.3 QLQ-C30 - Time to first improvement by 10 pt in diarrhea according to R-ISS stage at SE (LOCF) - ITT population

	I or II		III		Not classified		
	Kd (N=103)	**IKd (N=155)**	**Kd (N=8)**	**IKd (N=16)**	**Kd (N=12)**	**IKd (N=8)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	15 (14.6)	26 (16.8)	3 (37.5)	0 (0.0)	3 (25.0)	2 (25.0)	0.9830
Number (%) of patients censored	88 (85.4)	129 (83.2)	5 (62.5)	16 (100.0)	9 (75.0)	6 (75.0)	
Kaplan-Meier estimates of Diarrhea in months							
25% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	1.05 (0.986 to NC)	NC (NC to NC)	NC (0.986 to NC)	5.98 (1.018 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (0.986 to NC)	NC (NC to NC)	NC (1.117 to NC)	NC (1.018 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (10.283 to NC)	NC (NC to NC)	NC (NC to NC)	NC (5.979 to NC)	
Comparison vs. Kd							
Log-Rank test p-value[a] vs Kd	-	0.6890		0.0095		0.7688	
Hazard ratio (95% CI) vs Kd	-	1.14 (0.60 to 2.15)				1.31 (0.22 to 7.83)	
P-value	-	0.6892		0.9975		0.7694	

A lower score represents a better level of quality of life. Clinical meaningful improvement change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
PGM=DEVOPS/SAR650984/EFC15246/CIR_RWE/REPORT/PGM/eff_km_subgp_sr_sig_de_i_t.sas OUT=REPORT/OUTPUT/eff_km_c30_dia_impl_seriss_de_i_t_x.rtf (07APR2021 14:37)

16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Diarrhea
16.2.6.1.2.9 Efficacy response data - Subgroup analyses by R-ISS stage at SE
16.2.6.1.2.9.4 QLQ-C30 - Time to first deterioration by 10 pt in diarrhea according to R-ISS stage at SE (LOCF) - ITT population

	I or II		III		Not classified		
	Kd (N=103)	**IKd (N=155)**	**Kd (N=8)**	**IKd (N=16)**	**Kd (N=12)**	**IKd (N=8)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	45 (43.7)	92 (59.4)	3 (37.5)	4 (25.0)	6 (50.0)	3 (37.5)	0.4899
Number (%) of patients censored	58 (56.3)	63 (40.6)	5 (62.5)	12 (75.0)	6 (50.0)	5 (62.5)	
Kaplan-Meier estimates of Diarrhea in months							
25% quantile (95% CI)	3.78 (2.004 to 7.458)	2.86 (1.971 to 3.745)	4.04 (2.957 to NC)	10.41 (1.216 to NC)	4.68 (2.136 to 9.495)	5.13 (2.990 to NC)	
Median (95% CI)	NC (11.039 to NC)	9.66 (5.815 to 14.259)	NC (2.957 to NC)	NC (5.060 to NC)	NC (3.745 to NC)	7.43 (2.990 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (4.764 to NC)	NC (NC to NC)	NC (9.495 to NC)	NC (5.125 to NC)	
Comparison vs. Kd							
Log-Rank test p-value[a] vs Kd	-	0.0378		0.4289		0.8663	
Hazard ratio (95% CI) vs Kd	-	1.46 (1.02 to 2.08)		0.55 (0.12 to 2.48)		1.13 (0.28 to 4.56)	
P-value	-	0.0390		0.4354		0.8664	

A lower score represents a better level of quality of life. Clinical meaningful deterioration change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Diarrhea
16.2.6.1.2.9 Efficacy response data - Subgroup analyses by R-ISS stage at SE
16.2.6.1.2.9.5 QLQ-C30 - Time until permanent improvement by 10 pt in diarrhea according to R-ISS stage at SE (LOCF) - ITT population

	I or II		III		Not classified		
	Kd (N=103)	**IKd (N=155)**	**Kd (N=8)**	**IKd (N=16)**	**Kd (N=12)**	**IKd (N=8)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	12 (11.7)	17 (11.0)	2 (25.0)	0 (0.0)	2 (16.7)	1 (12.5)	0.9781
Number (%) of patients censored	91 (88.3)	138 (89.0)	6 (75.0)	16 (100.0)	10 (83.3)	7 (87.5)	
Kaplan-Meier estimates of Diarrhea in months							
25% quantile (95% CI)	NC (21.684 to NC)	NC (NC to NC)	13.40 (1.051 to NC)	NC (NC to NC)	NC (15.704 to NC)	NC (2.825 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (1.051 to NC)	NC (NC to NC)	NC (17.183 to NC)	NC (2.825 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (13.405 to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Kd							
Log-Rank test p-value[a] vs Kd	-	0.7985		0.0514		0.8471	
Hazard ratio (95% CI) vs Kd	-	0.91 (0.43 to 1.90)				1.27 (0.11 to 14.09)	
P-value	-	0.7986		0.9978		0.8474	

A lower score represents a better level of quality of life. Clinical meaningful improvement change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Diarrhea
16.2.6.1.2.9 Efficacy response data - Subgroup analyses by R-ISS stage at SE
16.2.6.1.2.9.6 QLQ-C30 - Time until permanent deterioration by 10 pt in diarrhea according to R-ISS stage at SE (LOCF) - ITT population

	I or II		III		Not classified		
	Kd (N=103)	**IKd (N=155)**	**Kd (N=8)**	**IKd (N=16)**	**Kd (N=12)**	**IKd (N=8)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	16 (15.5)	17 (11.0)	0 (0.0)	0 (0.0)	2 (16.7)	1 (12.5)	0.9091
Number (%) of patients censored	87 (84.5)	138 (89.0)	8 (100.0)	16 (100.0)	10 (83.3)	7 (87.5)	
Kaplan-Meier estimates of Diarrhea in months							
25% quantile (95% CI)	26.35 (20.370 to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (12.945 to NC)	20.93 (20.928 to NC)	
Median (95% CI)	26.35 (26.349 to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (18.464 to NC)	NC (20.928 to NC)	
75% quantile (95% CI)	NC (26.349 to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (20.928 to NC)	
Comparison vs. Kd							
Log-Rank test p-value[a] vs Kd	-	0.2993				0.8471	
Hazard ratio (95% CI) vs Kd	-	0.69 (0.35 to 1.39)				1.27 (0.11 to 14.09)	
P-value	-	0.3020				0.8474	

A lower score represents a better level of quality of life. Clinical meaningful deterioration change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Diarrhea
16.2.6.1.2.10 Efficacy response data - Subgroup analyses by nb of prior lines
16.2.6.1.2.10.3 QLQ-C30 - Time to first improvement by 10 pt in diarrhea according to nb of prior lines (LOCF) - ITT population

	1		>1		
	Kd (N=55)	**IKd (N=79)**	**Kd (N=68)**	**IKd (N=100)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	5 (9.1)	10 (12.7)	16 (23.5)	18 (18.0)	0.3151
Number (%) of patients censored	50 (90.9)	69 (87.3)	52 (76.5)	82 (82.0)	
Kaplan-Meier estimates of Diarrhea in months					
25% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	16.85 (1.906 to NC)	NC (2.825 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.5229		0.3793	
Hazard ratio (95% CI) vs Kd	-	1.42 (0.48 to 4.14)		0.74 (0.38 to 1.45)	
P-value	-	0.5250		0.3811	
Improvement probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful improvement change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Diarrhea
16.2.6.1.2.10 Efficacy response data - Subgroup analyses by nb of prior lines
16.2.6.1.2.10.4 QLQ-C30 - Time to first deterioration by 10 pt in diarrhea according to nb of prior lines (LOCF) - ITT population

	1		>1		
	Kd (N=55)	**IKd (N=79)**	**Kd (N=68)**	**IKd (N=100)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	23 (41.8)	46 (58.2)	31 (45.6)	53 (53.0)	0.5800
Number (%) of patients censored	32 (58.2)	33 (41.8)	37 (54.4)	47 (47.0)	
Kaplan-Meier estimates of Diarrhea in months					
25% quantile (95% CI)	3.84 (1.971 to 11.039)	3.68 (1.971 to 4.830)	3.78 (2.037 to 7.458)	2.86 (1.938 to 4.632)	
Median (95% CI)	NC (11.039 to NC)	13.21 (5.848 to 21.388)	22.14 (7.589 to NC)	9.56 (5.060 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (21.388 to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.1027		0.3182	
Hazard ratio (95% CI) vs Kd	-	1.51 (0.92 to 2.50)		1.25 (0.80 to 1.95)	
P-value	-	0.1052		0.3192	
Deterioration probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful deterioration change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Diarrhea
16.2.6.1.2.10 Efficacy response data - Subgroup analyses by nb of prior lines
16.2.6.1.2.10.5 QLQ-C30 - Time until permanent improvement by 10 pt in diarrhea according to nb of prior lines (LOCF) - ITT population

	1		>1		
	Kd (N=55)	**IKd (N=79)**	**Kd (N=68)**	**IKd (N=100)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	4 (7.3)	6 (7.6)	12 (17.6)	12 (12.0)	0.5387
Number (%) of patients censored	51 (92.7)	73 (92.4)	56 (82.4)	88 (88.0)	
Kaplan-Meier estimates of Diarrhea in months					
25% quantile (95% CI)	NC (NC to NC)	NC (20.895 to NC)	NC (15.704 to NC)	NC (NC to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.8853		0.3235	
Hazard ratio (95% CI) vs Kd	-	1.10 (0.31 to 3.89)		0.67 (0.30 to 1.49)	
P-value	-	0.8853		0.3267	
Improvement probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful improvement change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Diarrhea
16.2.6.1.2.10 Efficacy response data - Subgroup analyses by nb of prior lines
16.2.6.1.2.10.6 QLQ-C30 - Time until permanent deterioration by 10 pt in diarrhea according to nb of prior lines (LOCF) - ITT population

	1		>1		
	Kd (N=55)	**IKd (N=79)**	**Kd (N=68)**	**IKd (N=100)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	7 (12.7)	11 (13.9)	11 (16.2)	7 (7.0)	0.1187
Number (%) of patients censored	48 (87.3)	68 (86.1)	57 (83.8)	93 (93.0)	
Kaplan-Meier estimates of Diarrhea in months					
25% quantile (95% CI)	26.35 (21.125 to 26.349)	NC (19.811 to NC)	22.14 (18.924 to NC)	NC (NC to NC)	
Median (95% CI)	26.35 (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	26.35 (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.5896		0.0442	
Hazard ratio (95% CI) vs Kd	-	1.31 (0.49 to 3.55)		0.39 (0.15 to 1.01)	
P-value	-	0.5908		0.0524	
Deterioration probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful deterioration change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Diarrhea
16.2.6.1.2.11 Efficacy response data - Subgroup analyses by cytogenetic abnormality
16.2.6.1.2.11.3 QLQ-C30 - Time to first improvement by 10 pt in diarrhea according to cytogenetic abnormality (LOCF) - ITT population

	At least one		None		
	Kd (N=31)	**IKd (N=42)**	**Kd (N=77)**	**IKd (N=114)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	7 (22.6)	10 (23.8)	9 (11.7)	15 (13.2)	0.9404
Number (%) of patients censored	24 (77.4)	32 (76.2)	68 (88.3)	99 (86.8)	
Kaplan-Meier estimates of Diarrhea in months					
25% quantile (95% CI)	NC (1.906 to NC)	NC (1.117 to NC)	NC (NC to NC)	NC (NC to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.8913		0.7995	
Hazard ratio (95% CI) vs Kd	-	1.07 (0.41 to 2.81)		1.11 (0.49 to 2.54)	
P-value	-	0.8919		0.7996	
Improvement probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful improvement change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
PGM=DEVOPS/SAR650984/EFC15246/CIR_RWE/REPORT/PGM/eff_km_subgp_sr_sig_de_i_t.sas OUT=REPORT/OUTPUT/eff_km_c30_dia_impl_cyto_de_i_t_x.rtf (07APR2021 14:37)

16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Diarrhea
16.2.6.1.2.11 Efficacy response data - Subgroup analyses by cytogenetic abnormality
16.2.6.1.2.11.4 QLQ-C30 - Time to first deterioration by 10 pt in diarrhea according to cytogenetic abnormality (LOCF) - ITT population

	At least one		None		
	Kd (N=31)	**IKd (N=42)**	**Kd (N=77)**	**IKd (N=114)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	14 (45.2)	20 (47.6)	35 (45.5)	69 (60.5)	0.3356
Number (%) of patients censored	17 (54.8)	22 (52.4)	42 (54.5)	45 (39.5)	
Kaplan-Meier estimates of Diarrhea in months					
25% quantile (95% CI)	3.81 (1.906 to 7.688)	4.67 (0.986 to 9.429)	3.75 (2.004 to 4.895)	2.89 (1.938 to 3.844)	
Median (95% CI)	NC (4.764 to NC)	20.73 (5.848 to NC)	22.14 (7.589 to NC)	8.84 (5.060 to 13.864)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (21.388 to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.9899		0.0546	
Hazard ratio (95% CI) vs Kd	-	1.00 (0.51 to 1.99)		1.49 (0.99 to 2.24)	
P-value	-	0.9899		0.0562	
Deterioration probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful deterioration change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Diarrhea
16.2.6.1.2.11 Efficacy response data - Subgroup analyses by cytogenetic abnormality
16.2.6.1.2.11.5 QLQ-C30 - Time until permanent improvement by 10 pt in diarrhea according to cytogenetic abnormality (LOCF) - ITT population

	At least one		None		
	Kd (N=31)	**IKd (N=42)**	**Kd (N=77)**	**IKd (N=114)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	6 (19.4)	7 (16.7)	6 (7.8)	10 (8.8)	0.7166
Number (%) of patients censored	25 (80.6)	35 (83.3)	71 (92.2)	104 (91.2)	
Kaplan-Meier estimates of Diarrhea in months					
25% quantile (95% CI)	21.68 (9.988 to NC)	NC (15.409 to NC)	NC (NC to NC)	NC (NC to NC)	
Median (95% CI)	NC (21.684 to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.7914		0.8122	
Hazard ratio (95% CI) vs Kd	-	0.86 (0.29 to 2.57)		1.13 (0.41 to 3.11)	
P-value	-	0.7916		0.8123	
Improvement probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful improvement change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Diarrhea
16.2.6.1.2.11 Efficacy response data - Subgroup analyses by cytogenetic abnormality
16.2.6.1.2.11.6 QLQ-C30 - Time until permanent deterioration by 10 pt in diarrhea according to cytogenetic abnormality (LOCF) - ITT population

	At least one		None		
	Kd (N=31)	**IKd (N=42)**	**Kd (N=77)**	**IKd (N=114)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	2 (6.5)	0 (0.0)	13 (16.9)	16 (14.0)	0.9867
Number (%) of patients censored	29 (93.5)	42 (100.0)	64 (83.1)	98 (86.0)	
Kaplan-Meier estimates of Diarrhea in months					
25% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	22.14 (19.548 to NC)	NC (19.811 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	26.35 (26.349 to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (26.349 to NC)	NC (NC to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.0896		0.7323	
Hazard ratio (95% CI) vs Kd	-			0.88 (0.42 to 1.86)	
P-value	-	0.9965		0.7325	
Deterioration probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful deterioration change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Diarrhea
16.2.6.1.2.12 Efficacy response data - Subgroup analyses by MM type at SE
16.2.6.1.2.12.3 QLQ-C30 - Time to first improvement by 10 pt in diarrhea according to MM type at SE (LOCF) - ITT population

	IgG		Non-IgG		
	Kd (N=85)	**IKd (N=126)**	**Kd (N=38)**	**IKd (N=53)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	15 (17.6)	20 (15.9)	6 (15.8)	8 (15.1)	0.9912
Number (%) of patients censored	70 (82.4)	106 (84.1)	32 (84.2)	45 (84.9)	
Kaplan-Meier estimates of Diarrhea in months					
25% quantile (95% CI)	NC (11.466 to NC)	NC (NC to NC)	NC (2.825 to NC)	NC (2.825 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.7747		0.8637	
Hazard ratio (95% CI) vs Kd	-	0.91 (0.46 to 1.77)		0.91 (0.32 to 2.63)	
P-value	-	0.7748		0.8637	
Improvement probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful improvement change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Diarrhea
16.2.6.1.2.12 Efficacy response data - Subgroup analyses by MM type at SE
16.2.6.1.2.12.4 QLQ-C30 - Time to first deterioration by 10 pt in diarrhea according to MM type at SE (LOCF) - ITT population

	IgG		Non-IgG		
	Kd (N=85)	**IKd (N=126)**	**Kd (N=38)**	**IKd (N=53)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	44 (51.8)	69 (54.8)	10 (26.3)	30 (56.6)	0.0236
Number (%) of patients censored	41 (48.2)	57 (45.2)	28 (73.7)	23 (43.4)	
Kaplan-Meier estimates of Diarrhea in months					
25% quantile (95% CI)	2.96 (1.971 to 4.304)	3.22 (2.234 to 4.698)	12.68 (2.825 to NC)	2.86 (1.018 to 4.764)	
Median (95% CI)	9.49 (4.895 to NC)	11.07 (6.177 to 21.388)	NC (NC to NC)	12.78 (4.632 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (18.464 to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.7202		0.0041	
Hazard ratio (95% CI) vs Kd	-	1.07 (0.73 to 1.57)		2.75 (1.34 to 5.64)	
P-value	-	0.7202		0.0059	
Hazard ratio inverted (95% CI) vs IKd		-		0.36 (0.18 to 0.75)	

A lower score represents a better level of quality of life. Clinical meaningful deterioration change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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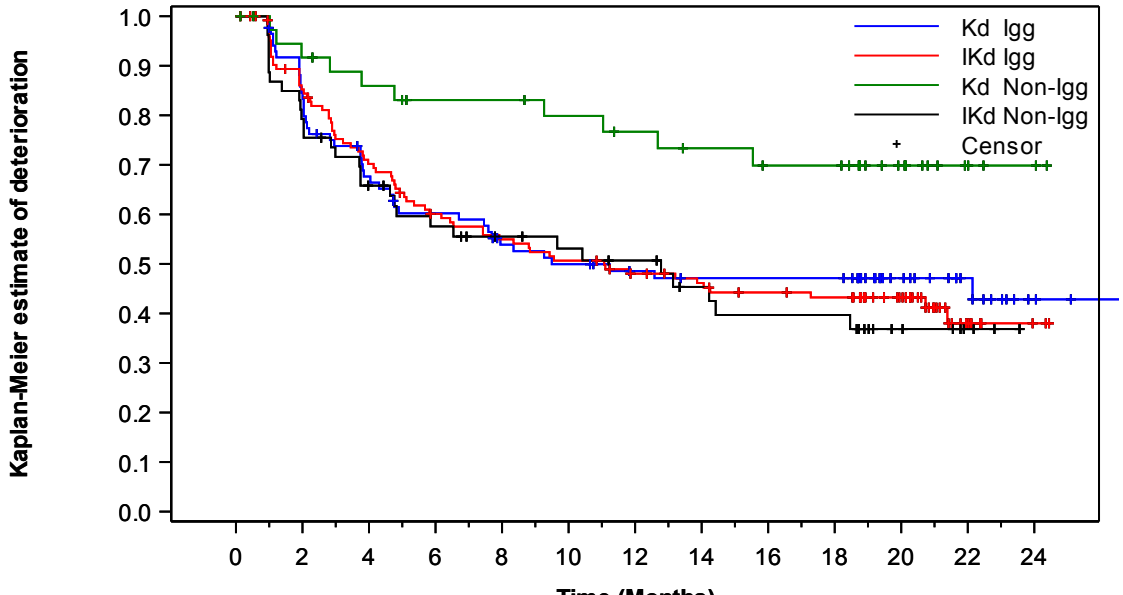
16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Diarrhea
16.2.6.1.2.12 Efficacy response data - Subgroup analyses by MM type at SE
16.2.6.1.2.12.5 QLQ-C30 - Time to first deterioration by 10 pt in diarrhea according to MM type at SE - Kaplan-Meier curve (LOCF) - ITT population



Number at Risk

Kd Igg	85	61	48	40	34	32	32	15	3
IKd Igg	126	90	70	61	53	46	43	16	2
Kd Non-Igg	38	31	27	26	23	21	19	6	2
IKd Non-Igg	53	37	28	23	20	14	14	6	0

A lower score represents a better level of quality of life. Clinical meaningful deterioration change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
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16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Diarrhea
16.2.6.1.2.12 Efficacy response data - Subgroup analyses by MM type at SE
16.2.6.1.2.12.6 QLQ-C30 - Time until permanent improvement by 10 pt in diarrhea according to MM type at SE (LOCF) - ITT population

	IgG		Non-IgG		
	Kd (N=85)	**IKd (N=126)**	**Kd (N=38)**	**IKd (N=53)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	11 (12.9)	13 (10.3)	5 (13.2)	5 (9.4)	0.7935
Number (%) of patients censored	74 (87.1)	113 (89.7)	33 (86.8)	48 (90.6)	
Kaplan-Meier estimates of Diarrhea in months					
25% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	21.68 (18.234 to NC)	NC (NC to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (21.684 to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.6404		0.5095	
Hazard ratio (95% CI) vs Kd	-	0.83 (0.37 to 1.84)		0.66 (0.19 to 2.29)	
P-value	-	0.6409		0.5125	
Improvement probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful improvement change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Diarrhea
16.2.6.1.2.12 Efficacy response data - Subgroup analyses by MM type at SE
16.2.6.1.2.12.7 QLQ-C30 - Time until permanent deterioration by 10 pt in diarrhea according to MM type at SE (LOCF) - ITT population

	IgG		Non-IgG		
	Kd (N=85)	**IKd (N=126)**	**Kd (N=38)**	**IKd (N=53)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	14 (16.5)	12 (9.5)	4 (10.5)	6 (11.3)	0.4849
Number (%) of patients censored	71 (83.5)	114 (90.5)	34 (89.5)	47 (88.7)	
Kaplan-Meier estimates of Diarrhea in months					
25% quantile (95% CI)	NC (19.614 to NC)	NC (NC to NC)	26.35 (NC to NC)	NC (19.614 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	26.35 (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	26.35 (NC to NC)	NC (NC to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.1744		0.7641	
Hazard ratio (95% CI) vs Kd	-	0.59 (0.27 to 1.28)		1.24 (0.31 to 4.95)	
P-value	-	0.1794		0.7646	
Deterioration probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful deterioration change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Diarrhea
16.2.6.1.2.13 Efficacy response data - Subgroup analyses by previous autologous stem-cell
16.2.6.1.2.13.3 QLQ-C30 - Time to first improvement by 10 pt in diarrhea according to previous autologous stem-cell (LOCF) - ITT population

	Yes		No		
	Kd (N=69)	**IKd (N=116)**	**Kd (N=54)**	**IKd (N=63)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	10 (14.5)	18 (15.5)	11 (20.4)	10 (15.9)	0.6152
Number (%) of patients censored	59 (85.5)	98 (84.5)	43 (79.6)	53 (84.1)	
Kaplan-Meier estimates of Diarrhea in months					
25% quantile (95% CI)	NC (16.854 to NC)	NC (NC to NC)	NC (2.825 to NC)	NC (2.825 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.8901		0.5793	
Hazard ratio (95% CI) vs Kd	-	1.06 (0.49 to 2.29)		0.79 (0.33 to 1.85)	
P-value	-	0.8909		0.5802	
Improvement probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful improvement change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Diarrhea
16.2.6.1.2.13 Efficacy response data - Subgroup analyses by previous autologous stem-cell
16.2.6.1.2.13.4 QLQ-C30 - Time to first deterioration by 10 pt in diarrhea according to previous autologous stem-cell (LOCF) - ITT population

	Yes		No		
	Kd (N=69)	**IKd (N=116)**	**Kd (N=54)**	**IKd (N=63)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	30 (43.5)	68 (58.6)	24 (44.4)	31 (49.2)	0.3503
Number (%) of patients censored	39 (56.5)	48 (41.4)	30 (55.6)	32 (50.8)	
Kaplan-Meier estimates of Diarrhea in months					
25% quantile (95% CI)	3.84 (2.004 to 7.688)	2.86 (1.906 to 3.745)	3.75 (1.971 to 7.589)	4.67 (2.136 to 6.439)	
Median (95% CI)	NC (8.345 to NC)	9.66 (5.060 to 14.423)	NC (7.589 to NC)	14.23 (6.439 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (21.388 to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.0476		0.6929	
Hazard ratio (95% CI) vs Kd	-	1.54 (1.00 to 2.37)		1.11 (0.65 to 1.90)	
P-value	-	0.0494		0.6930	
Hazard ratio inverted (95% CI) vs IKd		-		0.90 (0.53 to 1.53)	

A lower score represents a better level of quality of life. Clinical meaningful deterioration change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Diarrhea
16.2.6.1.2.13 Efficacy response data - Subgroup analyses by previous autologous stem-cell
16.2.6.1.2.13.5 QLQ-C30 - Time until permanent improvement by 10 pt in diarrhea according to previous autologous stem-cell (LOCF) - ITT population

	Yes		No		
	Kd (N=69)	**IKd (N=116)**	**Kd (N=54)**	**IKd (N=63)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	7 (10.1)	12 (10.3)	9 (16.7)	6 (9.5)	0.4191
Number (%) of patients censored	62 (89.9)	104 (89.7)	45 (83.3)	57 (90.5)	
Kaplan-Meier estimates of Diarrhea in months					
25% quantile (95% CI)	NC (21.684 to NC)	NC (NC to NC)	NC (18.234 to NC)	NC (20.632 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.9650		0.2845	
Hazard ratio (95% CI) vs Kd	-	1.02 (0.40 to 2.59)		0.57 (0.20 to 1.61)	
P-value	-	0.9651		0.2907	
Improvement probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful improvement change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
PGM=DEVOPS/SAR650984/EFC15246/CIR_RWE/REPORT/PGM/eff_km_subgp_sr_sig_de_i_t.sas OUT=REPORT/OUTPUT/eff_km_c30_dia_imppl_auto_de_i_t_x.rtf (07APR2021 14:37)

16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Diarrhea
16.2.6.1.2.13 Efficacy response data - Subgroup analyses by previous autologous stem-cell
16.2.6.1.2.13.6 QLQ-C30 - Time until permanent deterioration by 10 pt in diarrhea according to previous autologous stem-cell (LOCF) - ITT population

	Yes		No		
	Kd (N=69)	**IKd (N=116)**	**Kd (N=54)**	**IKd (N=63)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	9 (13.0)	13 (11.2)	9 (16.7)	5 (7.9)	0.3648
Number (%) of patients censored	60 (87.0)	103 (88.8)	45 (83.3)	58 (92.1)	
Kaplan-Meier estimates of Diarrhea in months					
25% quantile (95% CI)	NC (20.370 to NC)	NC (NC to NC)	26.35 (18.464 to 26.349)	NC (NC to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	26.35 (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	26.35 (NC to NC)	NC (NC to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.7287		0.2140	
Hazard ratio (95% CI) vs Kd	-	0.86 (0.37 to 2.01)		0.50 (0.16 to 1.53)	
P-value	-	0.7289		0.2232	
Deterioration probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful deterioration change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
PGM=DEVOPS/SAR650984/EFC15246/CIR_RWE/REPORT/PGM/eff_km_subgp_sr_sig_de_i_t.sas OUT=REPORT/OUTPUT/eff_km_c30_dia_detpl_auto_de_i_t_x.rtf (07APR2021 14:37)

16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Diarrhea
16.2.6.1.2.14 Efficacy response data - Subgroup analyses by baseline eGFR (MDRD)
16.2.6.1.2.14.3 QLQ-C30 - Time to first improvement by 10 pt in diarrhea according to baseline eGFR (MDRD) (LOCF) - ITT population

	>=60 mL/min/1.73m2		<60 mL/min/1.73m2		
	Kd (N=93)	**IKd (N=122)**	**Kd (N=18)**	**IKd (N=43)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	18 (19.4)	23 (18.9)	2 (11.1)	4 (9.3)	0.6973
Number (%) of patients censored	75 (80.6)	99 (81.1)	16 (88.9)	39 (90.7)	
Kaplan-Meier estimates of Diarrhea in months					
25% quantile (95% CI)	NC (10.283 to NC)	NC (4.632 to NC)	NC (0.986 to NC)	NC (NC to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.9623		0.7476	
Hazard ratio (95% CI) vs Kd	-	1.01 (0.55 to 1.88)		0.76 (0.14 to 4.14)	
P-value	-	0.9623		0.7483	
Improvement probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful improvement change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Diarrhea
16.2.6.1.2.14 Efficacy response data - Subgroup analyses by baseline eGFR (MDRD)
16.2.6.1.2.14.4 QLQ-C30 - Time to first deterioration by 10 pt in diarrhea according to baseline eGFR (MDRD) (LOCF) - ITT population

	>=60 mL/min/1.73m2		<60 mL/min/1.73m2		
	Kd (N=93)	**IKd (N=122)**	**Kd (N=18)**	**IKd (N=43)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	40 (43.0)	66 (54.1)	7 (38.9)	26 (60.5)	0.9828
Number (%) of patients censored	53 (57.0)	56 (45.9)	11 (61.1)	17 (39.5)	
Kaplan-Meier estimates of Diarrhea in months					
25% quantile (95% CI)	3.76 (1.971 to 6.702)	3.22 (1.938 to 4.764)	3.75 (1.906 to 12.682)	3.45 (1.906 to 5.355)	
Median (95% CI)	NC (9.265 to NC)	12.78 (6.177 to 20.731)	NC (3.745 to NC)	11.10 (4.632 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (12.682 to NC)	NC (21.388 to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.0829		0.4151	
Hazard ratio (95% CI) vs Kd	-	1.41 (0.95 to 2.09)		1.41 (0.61 to 3.26)	
P-value	-	0.0844		0.4177	
Deterioration probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful deterioration change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Diarrhea
16.2.6.1.2.14 Efficacy response data - Subgroup analyses by baseline eGFR (MDRD)
16.2.6.1.2.14.5 QLQ-C30 - Time until permanent improvement by 10 pt in diarrhea according to baseline eGFR (MDRD) (LOCF) - ITT population

	>=60 mL/min/1.73m2		<60 mL/min/1.73m2		
	Kd (N=93)	**IKd (N=122)**	**Kd (N=18)**	**IKd (N=43)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	13 (14.0)	17 (13.9)	2 (11.1)	1 (2.3)	0.1278
Number (%) of patients censored	80 (86.0)	105 (86.1)	16 (88.9)	42 (97.7)	
Kaplan-Meier estimates of Diarrhea in months					
25% quantile (95% CI)	NC (21.684 to NC)	NC (20.632 to NC)	NC (9.988 to NC)	NC (NC to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (13.405 to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.7988		0.0897	
Hazard ratio (95% CI) vs Kd	-	1.10 (0.53 to 2.26)		0.16 (0.01 to 1.79)	
P-value	-	0.7998		0.1375	
Improvement probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful improvement change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Diarrhea
16.2.6.1.2.14 Efficacy response data - Subgroup analyses by baseline eGFR (MDRD)
16.2.6.1.2.14.6 QLQ-C30 - Time until permanent deterioration by 10 pt in diarrhea according to baseline eGFR (MDRD) (LOCF) - ITT population

	>=60 mL/min/1.73m2		<60 mL/min/1.73m2		
	Kd (N=93)	**IKd (N=122)**	**Kd (N=18)**	**IKd (N=43)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	13 (14.0)	10 (8.2)	2 (11.1)	4 (9.3)	0.9869
Number (%) of patients censored	80 (86.0)	112 (91.8)	16 (88.9)	39 (90.7)	
Kaplan-Meier estimates of Diarrhea in months					
25% quantile (95% CI)	26.35 (20.370 to NC)	NC (NC to NC)	NC (2.825 to NC)	NC (18.957 to NC)	
Median (95% CI)	26.35 (26.349 to NC)	NC (NC to NC)	NC (19.548 to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (26.349 to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.3174		0.6676	
Hazard ratio (95% CI) vs Kd	-	0.65 (0.28 to 1.51)		0.69 (0.13 to 3.77)	
P-value	-	0.3211		0.6692	
Deterioration probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful deterioration change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Diarrhea
16.2.6.1.2.15 Efficacy response data - Subgroup analyses by previous treatment with PI
16.2.6.1.2.15.3 QLQ-C30 - Time to first improvement by 10 pt in diarrhea according to previous treatment with PI (LOCF) - ITT population

	Yes		No		
	Kd (N=47)	**IKd (N=81)**	**Kd (N=76)**	**IKd (N=98)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	8 (17.0)	7 (8.6)	13 (17.1)	21 (21.4)	0.1367
Number (%) of patients censored	39 (83.0)	74 (91.4)	63 (82.9)	77 (78.6)	
Kaplan-Meier estimates of Diarrhea in months					
25% quantile (95% CI)	NC (1.906 to NC)	NC (NC to NC)	NC (11.466 to NC)	NC (3.647 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.1663		0.5141	
Hazard ratio (95% CI) vs Kd	-	0.50 (0.18 to 1.37)		1.26 (0.63 to 2.51)	
P-value	-	0.1751		0.5150	
Improvement probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful improvement change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Diarrhea
16.2.6.1.2.15 Efficacy response data - Subgroup analyses by previous treatment with PI
16.2.6.1.2.15.4 QLQ-C30 - Time to first deterioration by 10 pt in diarrhea according to previous treatment with PI (LOCF) - ITT population

	Yes		No		
	Kd (N=47)	**IKd (N=81)**	**Kd (N=76)**	**IKd (N=98)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	20 (42.6)	45 (55.6)	34 (44.7)	54 (55.1)	0.8181
Number (%) of patients censored	27 (57.4)	36 (44.4)	42 (55.3)	44 (44.9)	
Kaplan-Meier estimates of Diarrhea in months					
25% quantile (95% CI)	3.75 (2.004 to 7.458)	2.86 (1.906 to 4.764)	4.30 (1.938 to 7.688)	3.45 (2.037 to 4.698)	
Median (95% CI)	NC (4.632 to NC)	11.07 (6.177 to 20.731)	22.14 (9.265 to NC)	11.10 (5.125 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.1800		0.1989	
Hazard ratio (95% CI) vs Kd	-	1.43 (0.84 to 2.42)		1.32 (0.86 to 2.03)	
P-value	-	0.1824		0.2004	
Deterioration probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful deterioration change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Diarrhea
16.2.6.1.2.15 Efficacy response data - Subgroup analyses by previous treatment with PI
16.2.6.1.2.15.5 QLQ-C30 - Time until permanent improvement by 10 pt in diarrhea according to previous treatment with PI (LOCF) - ITT population

	Yes		No		
	Kd (N=47)	**IKd (N=81)**	**Kd (N=76)**	**IKd (N=98)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	8 (17.0)	5 (6.2)	8 (10.5)	13 (13.3)	0.0736
Number (%) of patients censored	39 (83.0)	76 (93.8)	68 (89.5)	85 (86.7)	
Kaplan-Meier estimates of Diarrhea in months					
25% quantile (95% CI)	NC (9.988 to NC)	NC (NC to NC)	NC (21.684 to NC)	NC (20.895 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.0553		0.5733	
Hazard ratio (95% CI) vs Kd	-	0.35 (0.12 to 1.08)		1.29 (0.53 to 3.11)	
P-value	-	0.0669		0.5744	
Improvement probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful improvement change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Diarrhea
16.2.6.1.2.15 Efficacy response data - Subgroup analyses by previous treatment with PI
16.2.6.1.2.15.6 QLQ-C30 - Time until permanent deterioration by 10 pt in diarrhea according to previous treatment with PI (LOCF) - ITT population

	Yes		No		
	Kd (N=47)	**IKd (N=81)**	**Kd (N=76)**	**IKd (N=98)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	6 (12.8)	8 (9.9)	12 (15.8)	10 (10.2)	0.6268
Number (%) of patients censored	41 (87.2)	73 (90.1)	64 (84.2)	88 (89.8)	
Kaplan-Meier estimates of Diarrhea in months					
25% quantile (95% CI)	26.35 (19.614 to 26.349)	NC (19.614 to NC)	NC (19.548 to NC)	NC (NC to NC)	
Median (95% CI)	26.35 (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	26.35 (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.9317		0.2171	
Hazard ratio (95% CI) vs Kd	-	0.95 (0.31 to 2.91)		0.59 (0.26 to 1.37)	
P-value	-	0.9313		0.2223	
Deterioration probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful deterioration change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Diarrhea
16.2.6.1.2.16 Efficacy response data - Subgroup analyses by previous treatment with IMiD
16.2.6.1.2.16.3 QLQ-C30 - Time to first improvement by 10 pt in diarrhea according to previous treatment with IMiD (LOCF) - ITT population

	Yes		No		
	Kd (N=62)	**IKd (N=81)**	**Kd (N=61)**	**IKd (N=98)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	10 (16.1)	15 (18.5)	11 (18.0)	13 (13.3)	0.4891
Number (%) of patients censored	52 (83.9)	66 (81.5)	50 (82.0)	85 (86.7)	
Kaplan-Meier estimates of Diarrhea in months					
25% quantile (95% CI)	NC (3.055 to NC)	NC (5.191 to NC)	NC (10.283 to NC)	NC (NC to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.8051		0.4691	
Hazard ratio (95% CI) vs Kd	-	1.11 (0.50 to 2.46)		0.74 (0.33 to 1.66)	
P-value	-	0.8052		0.4707	
Improvement probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful improvement change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
PGM=DEVOPS/SAR650984/EFC15246/CIR_RWE/REPORT/PGM/eff_km_subgp_sr_sig_de_i_t.sas OUT=REPORT/OUTPUT/eff_km_c30_dia_impl_imid_de_i_t_x.rtf (07APR2021 14:37)

16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Diarrhea
16.2.6.1.2.16 Efficacy response data - Subgroup analyses by previous treatment with IMiD
16.2.6.1.2.16.4 QLQ-C30 - Time to first deterioration by 10 pt in diarrhea according to previous treatment with IMiD (LOCF) - ITT population

	Yes		No		
	Kd (N=62)	**IKd (N=81)**	**Kd (N=61)**	**IKd (N=98)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	27 (43.5)	45 (55.6)	27 (44.3)	54 (55.1)	0.8775
Number (%) of patients censored	35 (56.5)	36 (44.4)	34 (55.7)	44 (44.9)	
Kaplan-Meier estimates of Diarrhea in months					
25% quantile (95% CI)	3.75 (1.938 to 4.764)	2.86 (1.938 to 4.205)	3.84 (2.037 to 9.265)	3.45 (1.971 to 4.797)	
Median (95% CI)	NC (4.764 to NC)	9.66 (4.928 to NC)	22.14 (9.265 to NC)	12.78 (5.848 to 21.388)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (22.144 to NC)	NC (21.388 to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.2785		0.1379	
Hazard ratio (95% CI) vs Kd	-	1.30 (0.81 to 2.10)		1.42 (0.89 to 2.25)	
P-value	-	0.2799		0.1399	
Deterioration probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful deterioration change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Diarrhea
16.2.6.1.2.16 Efficacy response data - Subgroup analyses by previous treatment with IMiD
16.2.6.1.2.16.5 QLQ-C30 - Time until permanent improvement by 10 pt in diarrhea according to previous treatment with IMiD (LOCF) - ITT population

	Yes		No		
	Kd (N=62)	**IKd (N=81)**	**Kd (N=61)**	**IKd (N=98)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	8 (12.9)	8 (9.9)	8 (13.1)	10 (10.2)	0.9348
Number (%) of patients censored	54 (87.1)	73 (90.1)	53 (86.9)	88 (89.8)	
Kaplan-Meier estimates of Diarrhea in months					
25% quantile (95% CI)	NC (18.924 to NC)	NC (20.895 to NC)	NC (21.684 to NC)	NC (NC to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.5741		0.6310	
Hazard ratio (95% CI) vs Kd	-	0.76 (0.28 to 2.01)		0.80 (0.31 to 2.02)	
P-value	-	0.5754		0.6317	
Improvement probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful improvement change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
PGM=DEVOPS/SAR650984/EFC15246/CIR_RWE/REPORT/PGM/eff_km_subgp_sr_sig_de_i_t.sas OUT=REPORT/OUTPUT/eff_km_c30_dia_imppl_imid_de_i_t_x.rtf (07APR2021 14:37)

16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Diarrhea
16.2.6.1.2.16 Efficacy response data - Subgroup analyses by previous treatment with IMiD
16.2.6.1.2.16.6 QLQ-C30 - Time until permanent deterioration by 10 pt in diarrhea according to previous treatment with IMiD (LOCF) - ITT population

	Yes		No		
	Kd (N=62)	**IKd (N=81)**	**Kd (N=61)**	**IKd (N=98)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	9 (14.5)	8 (9.9)	9 (14.8)	10 (10.2)	0.8987
Number (%) of patients censored	53 (85.5)	73 (90.1)	52 (85.2)	88 (89.8)	
Kaplan-Meier estimates of Diarrhea in months					
25% quantile (95% CI)	26.35 (19.548 to NC)	NC (20.928 to NC)	22.14 (20.370 to NC)	NC (NC to NC)	
Median (95% CI)	26.35 (26.349 to NC)	NC (NC to NC)	NC (22.144 to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (26.349 to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.5277		0.3938	
Hazard ratio (95% CI) vs Kd	-	0.73 (0.27 to 1.95)		0.68 (0.27 to 1.67)	
P-value	-	0.5294		0.3968	
Deterioration probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful deterioration change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
PGM=DEVOPS/SAR650984/EFC15246/CIR_RWE/REPORT/PGM/eff_km_subgp_sr_sig_de_i_t.sas OUT=REPORT/OUTPUT/eff_km_c30_dia_detpl_imid_de_i_t_x.rtf (07APR2021 14:37)

16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Diarrhea
16.2.6.1.2.17 Efficacy response data - Subgroup analyses by previous treatment with PI and IMiD
16.2.6.1.2.17.3 QLQ-C30 - Time to first improvement by 10 pt in diarrhea according to previous treatment with PI and IMiD (LOCF) - ITT population

	Yes		No		
	Kd (N=17)	**IKd (N=23)**	**Kd (N=106)**	**IKd (N=156)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	3 (17.6)	1 (4.3)	18 (17.0)	27 (17.3)	0.2046
Number (%) of patients censored	14 (82.4)	22 (95.7)	88 (83.0)	129 (82.7)	
Kaplan-Meier estimates of Diarrhea in months					
25% quantile (95% CI)	NC (1.018 to NC)	NC (1.051 to NC)	NC (12.255 to NC)	NC (16.164 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.1582		0.9416	
Hazard ratio (95% CI) vs Kd	-	0.23 (0.02 to 2.17)		1.02 (0.56 to 1.86)	
P-value	-	0.1975		0.9417	
Improvement probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful improvement change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Diarrhea
16.2.6.1.2.17 Efficacy response data - Subgroup analyses by previous treatment with PI and IMiD
16.2.6.1.2.17.4 QLQ-C30 - Time to first deterioration by 10 pt in diarrhea according to previous treatment with PI and IMiD (LOCF) - ITT population

	Yes		No		
	Kd (N=17)	**IKd (N=23)**	**Kd (N=106)**	**IKd (N=156)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	8 (47.1)	13 (56.5)	46 (43.4)	86 (55.1)	0.9018
Number (%) of patients censored	9 (52.9)	10 (43.5)	60 (56.6)	70 (44.9)	
Kaplan-Meier estimates of Diarrhea in months					
25% quantile (95% CI)	3.75 (0.986 to 12.583)	2.60 (0.986 to 4.928)	3.84 (2.103 to 7.589)	2.99 (2.136 to 4.665)	
Median (95% CI)	12.58 (3.745 to NC)	6.18 (2.595 to NC)	22.14 (9.495 to NC)	11.86 (6.538 to 20.731)	
75% quantile (95% CI)	NC (12.583 to NC)	NC (9.659 to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.5970		0.0742	
Hazard ratio (95% CI) vs Kd	-	1.27 (0.52 to 3.06)		1.38 (0.97 to 1.98)	
P-value	-	0.5978		0.0755	
Deterioration probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful deterioration change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Diarrhea
16.2.6.1.2.17 Efficacy response data - Subgroup analyses by previous treatment with PI and IMiD
16.2.6.1.2.17.5 QLQ-C30 - Time until permanent improvement by 10 pt in diarrhea according to previous treatment with PI and IMiD (LOCF) - ITT population

	Yes		No		
	Kd (N=17)	**IKd (N=23)**	**Kd (N=106)**	**IKd (N=156)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	3 (17.6)	0 (0.0)	13 (12.3)	18 (11.5)	0.9890
Number (%) of patients censored	14 (82.4)	23 (100.0)	93 (87.7)	138 (88.5)	
Kaplan-Meier estimates of Diarrhea in months					
25% quantile (95% CI)	NC (1.018 to NC)	NC (NC to NC)	NC (21.684 to NC)	NC (NC to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.0411		0.9181	
Hazard ratio (95% CI) vs Kd	-			0.96 (0.47 to 1.97)	
P-value	-	0.9972		0.9178	
Improvement probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful improvement change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Diarrhea
16.2.6.1.2.17 Efficacy response data - Subgroup analyses by previous treatment with PI and IMiD
16.2.6.1.2.17.6 QLQ-C30 - Time until permanent deterioration by 10 pt in diarrhea according to previous treatment with PI and IMiD (LOCF) - ITT population

	Yes		No		
	Kd (N=17)	**IKd (N=23)**	**Kd (N=106)**	**IKd (N=156)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	2 (11.8)	2 (8.7)	16 (15.1)	16 (10.3)	0.7308
Number (%) of patients censored	15 (88.2)	21 (91.3)	90 (84.9)	140 (89.7)	
Kaplan-Meier estimates of Diarrhea in months					
25% quantile (95% CI)	26.35 (19.614 to 26.349)	NC (18.957 to NC)	NC (20.370 to NC)	NC (NC to NC)	
Median (95% CI)	26.35 (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	26.35 (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.7028		0.2167	
Hazard ratio (95% CI) vs Kd	-	1.59 (0.14 to 17.53)		0.65 (0.32 to 1.30)	
P-value	-	0.7053		0.2203	
Deterioration probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful deterioration change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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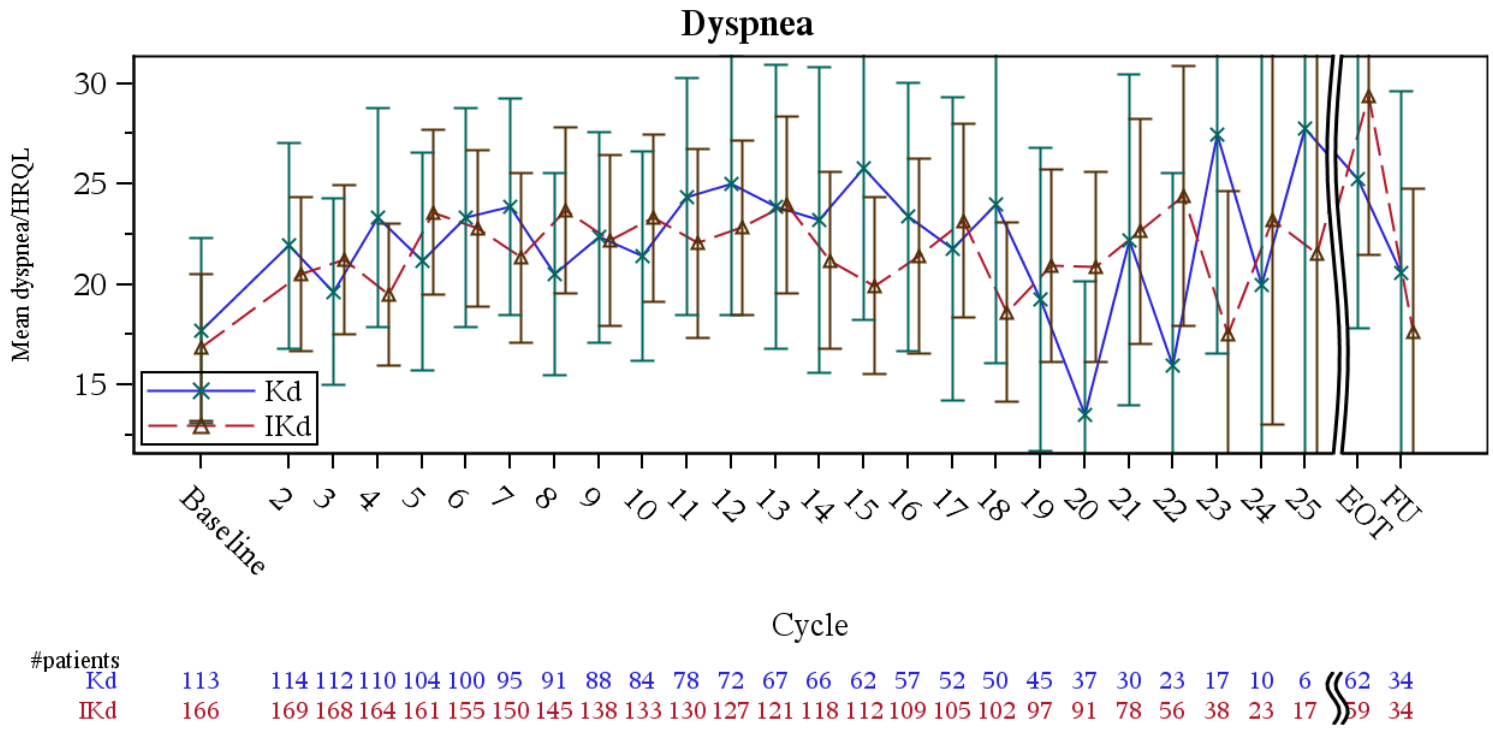
16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Dyspnea
16.2.6.1.2.1 Efficacy response data
16.2.6.1.2.1.1 QLQ-C30 - Mean and 95% CI for dyspnea score over time (LOCF) - ITT population



A lower score represents a better level of quality of life. Cycles with less than 20 patients overall are not presented.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
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16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Dyspnea
16.2.6.1.2.1 Efficacy response data
16.2.6.1.2.1.15 QLQ-C30 - Time to first improvement by 15 pt in Dyspnea (LOCF) - ITT population

First improvement 15 points Dyspnea (%)	**Kd (N=123)**	**IKd (N=179)**
Number (%) of events	33 (26.8)	53 (29.6)
Number (%) of patients censored	90 (73.2)	126 (70.4)
Kaplan-Meier estimates of Dyspnea in months		
25% quantile (95% CI)	5.65 (2.070 to NC)	6.47 (2.793 to NC)
Median (95% CI)	NC (NC to NC)	NC (NC to NC)
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)
Comparison vs. Kd		
Stratified[a] Log-Rank test p-value[b] vs Kd	-	0.6149
Stratified[a] Hazard ratio (95% CI) vs Kd	-	1.12 (0.72 to 1.73)
P-value	-	0.6150
Improvement probability (95% CI)[c]		
3 Months	0.191 (0.127 to 0.266)	0.213 (0.155 to 0.276)
6 Months	0.252 (0.178 to 0.332)	0.248 (0.186 to 0.314)

A lower score represents a better level of quality of life. Clinical meaningful improvement change from baseline less than or equal to -15 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] Stratified on number of prior lines of therapy (1 vs. >1) and Revised International Staging System (R-ISS) stage (I or II vs. III vs. not classified) according to IRT
[b] One-sided significance level is 0.025
[c] Estimated using the Kaplan-Meier method
NA/NC = Not Applicable / Not Calculable
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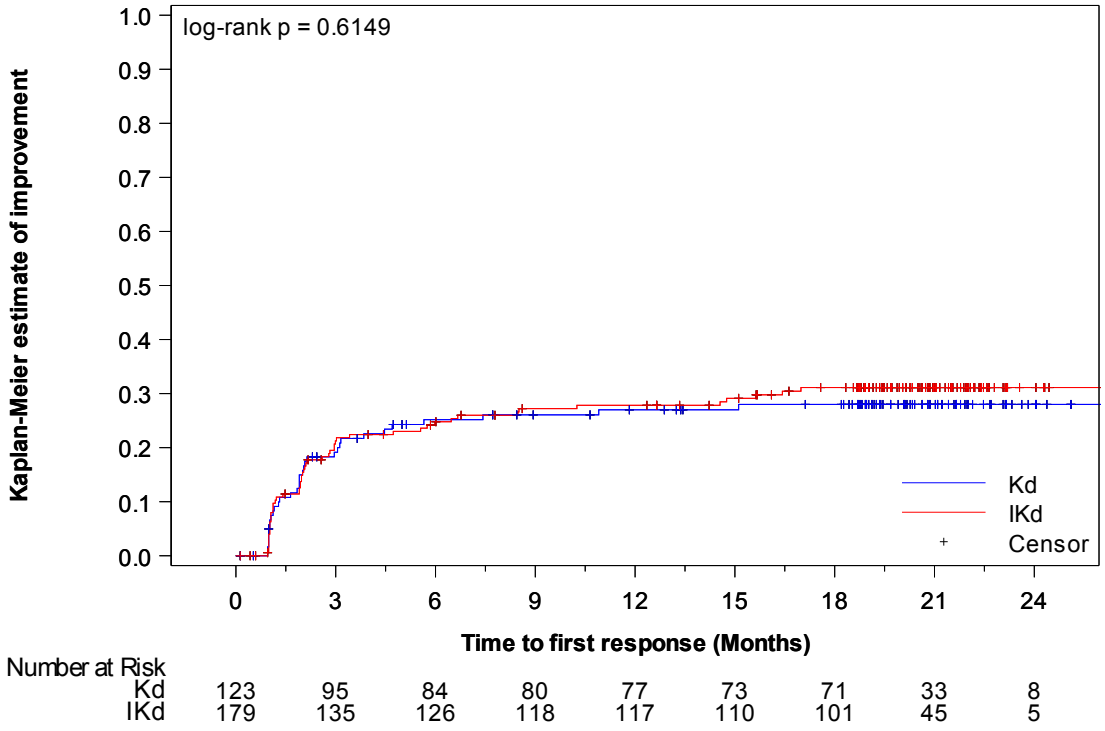
16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Dyspnea
16.2.6.1.2.1 Efficacy response data
16.2.6.1.2.1.16 QLQ-C30 - Time to first improvement by 15 pt in Dyspnea - Kaplan-Meier curve (LOCF) - ITT population



A lower score represents a better level of quality of life. Clinical meaningful improvement change from baseline less than or equal to -15 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.

16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Dyspnea
16.2.6.1.2.1 Efficacy response data
16.2.6.1.2.1.17 QLQ-C30 - Time to first deterioration by 15 pt in Dyspnea (LOCF) - ITT population

First deterioration 15 points Dyspnea (%)	**Kd (N=123)**	**IKd (N=179)**
Number (%) of events	71 (57.7)	116 (64.8)
Number (%) of patients censored	52 (42.3)	63 (35.2)
Kaplan-Meier estimates of Dyspnea in months		
25% quantile (95% CI)	1.91 (1.150 to 2.070)	1.91 (1.248 to 2.004)
Median (95% CI)	5.82 (3.943 to 12.912)	5.22 (3.713 to 8.345)
75% quantile (95% CI)	NC (NC to NC)	NC (19.811 to NC)
Comparison vs. Kd		
Stratified[a] Log-Rank test p-value[b] vs Kd	-	0.3384
Stratified[a] Hazard ratio (95% CI) vs Kd	-	1.16 (0.86 to 1.56)
P-value	-	0.3389
Deterioration probability (95% CI)[c]		
3 Months	0.625 (0.532 to 0.705)	0.592 (0.516 to 0.661)
6 Months	0.495 (0.402 to 0.581)	0.474 (0.398 to 0.546)

A lower score represents a better level of quality of life. Clinical meaningful deterioration change from baseline greater than or equal to 15 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] Stratified on number of prior lines of therapy (1 vs. >1) and Revised International Staging System (R-ISS) stage (I or II vs. III vs. not classified) according to IRT
[b] One-sided significance level is 0.025
[c] Estimated using the Kaplan-Meier method
NA/NC = Not Applicable / Not Calculable
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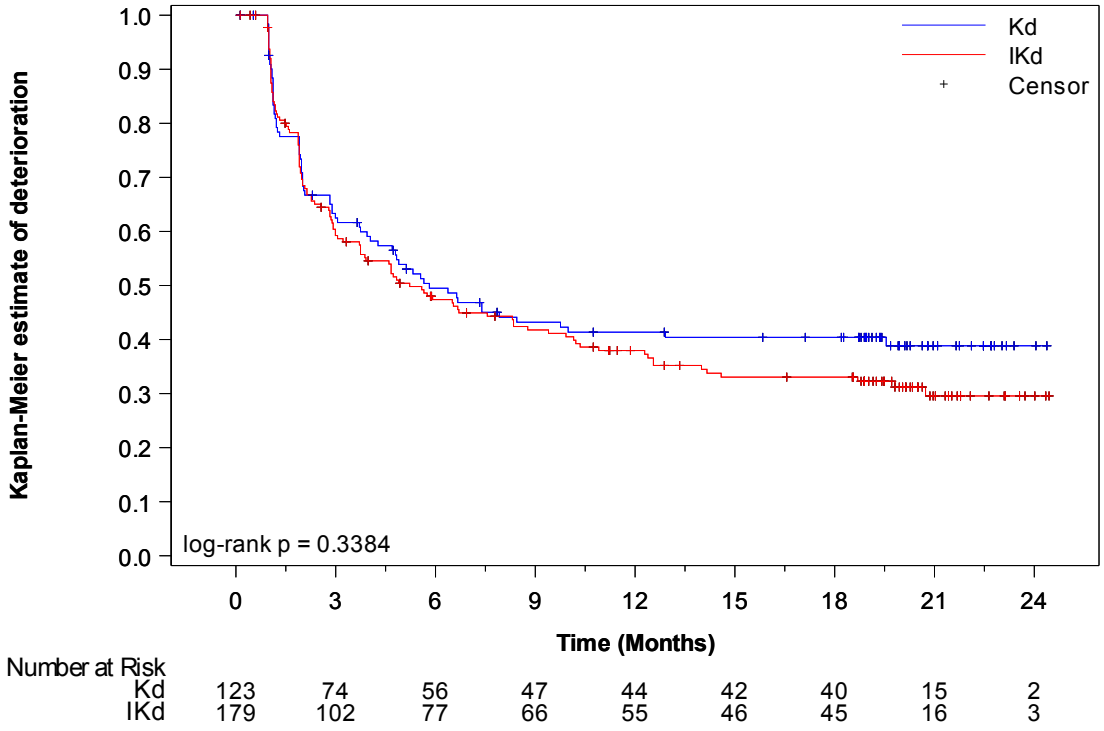
16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Dyspnea
16.2.6.1.2.1 Efficacy response data
16.2.6.1.2.1.18 QLQ-C30 - Time to first deterioration by 15 pt in Dyspnea - Kaplan-Meier curve (LOCF) - ITT population



A lower score represents a better level of quality of life. Clinical meaningful deterioration change from baseline greater than or equal to 15 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
PGM=DEVOPS/SAR650984/EFC15246/CIR_RWE/REPORT/PGM/eff_qlq_km_i_f.sas OUT=REPORT/OUTPUT/eff_km_c30_dys_det15l_de_i_f_x.rtf (07APR2021 14:24)

16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Dyspnea
16.2.6.1.2.1 Efficacy response data
16.2.6.1.2.1.19 QLQ-C30 - Time until permanent improvement by 15 pt in Dyspnea (LOCF) - ITT population

First permanent improvement 15 points Dyspnea (%)	**Kd (N=123)**	**IKd (N=179)**
Number (%) of events	20 (16.3)	18 (10.1)
Number (%) of patients censored	103 (83.7)	161 (89.9)
Kaplan-Meier estimates of Dyspnea in months		
25% quantile (95% CI)	NC (19.187 to NC)	NC (NC to NC)
Median (95% CI)	NC (NC to NC)	NC (NC to NC)
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)
Comparison vs. Kd		
Stratified[a] Log-Rank test p-value[b] vs Kd	-	0.1087
Stratified[a] Hazard ratio (95% CI) vs Kd	-	0.60 (0.31 to 1.13)
P-value	-	0.1126
Improvement probability (95% CI)[c]		
3 Months	0.050 (0.020 to 0.099)	0.023 (0.008 to 0.054)
6 Months	0.067 (0.031 to 0.121)	0.035 (0.014 to 0.070)

A lower score represents a better level of quality of life. Clinical meaningful improvement change from baseline less than or equal to -15 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] Stratified on number of prior lines of therapy (1 vs. >1) and Revised International Staging System (R-ISS) stage (I or II vs. III vs. not classified) according to IRT
[b] One-sided significance level is 0.025
[c] Estimated using the Kaplan-Meier method
NA/NC = Not Applicable / Not Calculable
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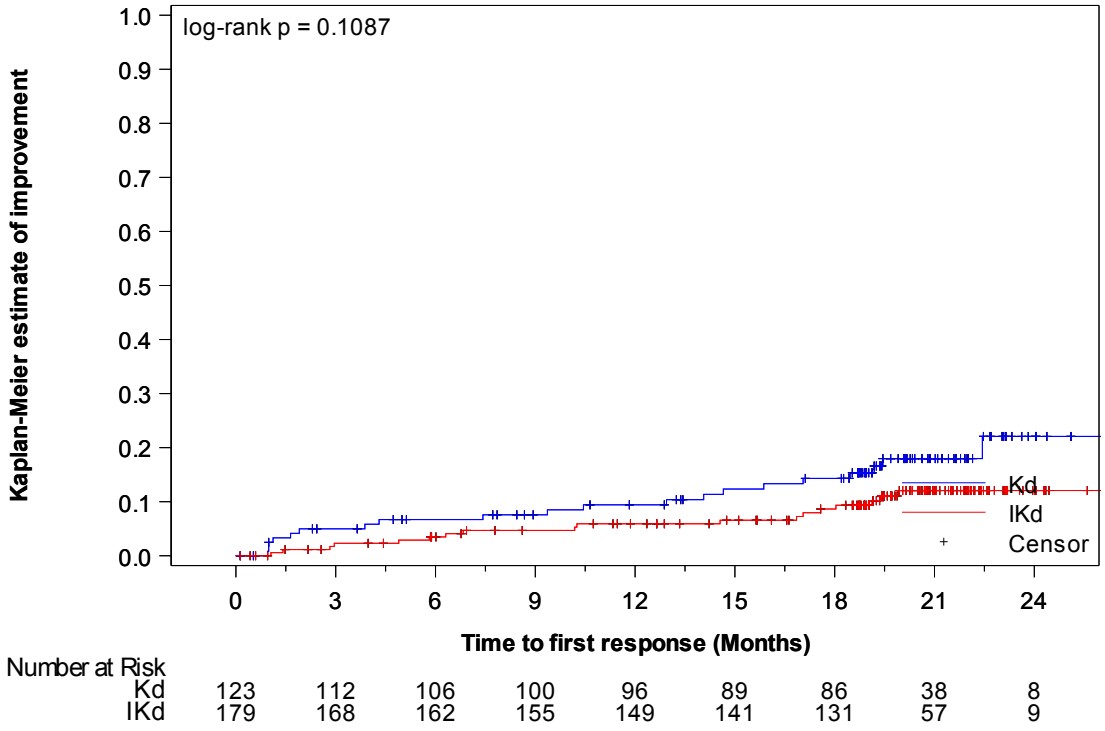
16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Dyspnea
16.2.6.1.2.1 Efficacy response data
16.2.6.1.2.1.20 QLQ-C30 - Time until permanent improvement by 15 pt in Dyspnea - Kaplan-Meier curve (LOCF) - ITT population



A lower score represents a better level of quality of life. Clinical meaningful improvement change from baseline less than or equal to -15 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
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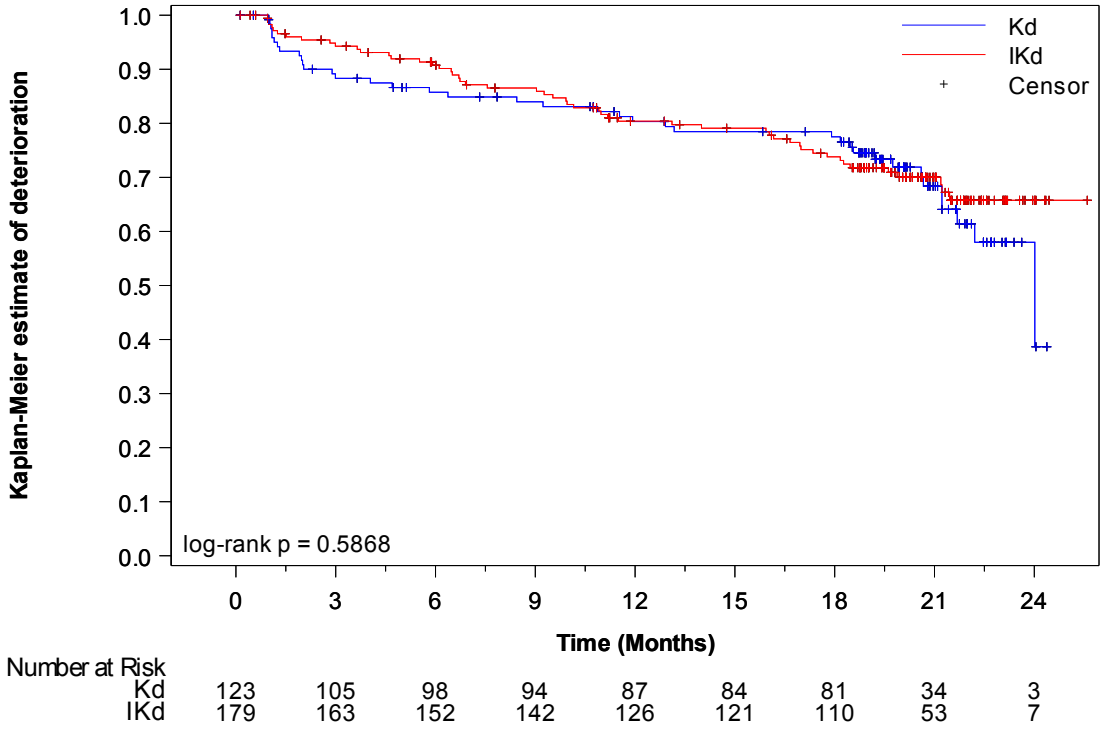
16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Dyspnea
16.2.6.1.2.1 Efficacy response data
16.2.6.1.2.1.21 QLQ-C30 - Time until permanent deterioration by 15 pt in Dyspnea (LOCF) - ITT population

First permanent deterioration 15 points Dyspnea (%)	**Kd (N=123)**	**IKd (N=179)**
Number (%) of events	38 (30.9)	51 (28.5)
Number (%) of patients censored	85 (69.1)	128 (71.5)
Kaplan-Meier estimates of Dyspnea in months		
25% quantile (95% CI)	18.56 (10.875 to 21.224)	17.35 (10.973 to 21.224)
Median (95% CI)	24.02 (21.684 to NC)	NC (NC to NC)
75% quantile (95% CI)	NC (24.016 to NC)	NC (NC to NC)
Comparison vs. Kd		
Stratified[a] Log-Rank test p-value[b] vs Kd	-	0.5868
Stratified[a] Hazard ratio (95% CI) vs Kd	-	0.89 (0.58 to 1.36)
P-value	-	0.5870
Deterioration probability (95% CI)[c]		
3 Months	0.883 (0.811 to 0.929)	0.943 (0.896 to 0.969)
6 Months	0.858 (0.781 to 0.909)	0.907 (0.853 to 0.942)

A lower score represents a better level of quality of life. Clinical meaningful deterioration change from baseline greater than or equal to 15 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] Stratified on number of prior lines of therapy (1 vs. >1) and Revised International Staging System (R-ISS) stage (I or II vs. III vs. not classified) according to IRT
[b] One-sided significance level is 0.025
[c] Estimated using the Kaplan-Meier method
NA/NC = Not Applicable / Not Calculable
PGM=DEVOPS/SAR650984/EFC15246/CIR_RWE/REPORT/PGM/eff_km_invhr_sr_i_t.sas OUT=REPORT/OUTPUT/eff_km_c30_dys_det15pl_de_i_t_x.rtf (07APR2021 14:23)

16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Dyspnea
16.2.6.1.2.1 Efficacy response data
16.2.6.1.2.1.22 QLQ-C30 - Time until permanent deterioration by 15 pt in Dyspnea - Kaplan-Meier curve (LOCF) - ITT population



A lower score represents a better level of quality of life. Clinical meaningful deterioration change from baseline greater than or equal to 15 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
PGM=DEVOPS/SAR650984/EFC15246/CIR_RWE/REPORT/PGM/eff_qlq_km_i_f.sas OUT=REPORT/OUTPUT/eff_km_c30_dys_det15pl_de_i_f_x.rtf (07APR2021 14:24)

16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Dyspnea
16.2.6.1.2.2 Efficacy response data - Subgroup analyses by age
16.2.6.1.2.2.3 QLQ-C30 - Time to first improvement by 10 pt in dyspnea according to age (LOCF) - ITT population

	<65 years		>=65 years		
	Kd (N=66)	**IKd (N=88)**	**Kd (N=57)**	**IKd (N=91)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	17 (25.8)	22 (25.0)	16 (28.1)	31 (34.1)	0.5408
Number (%) of patients censored	49 (74.2)	66 (75.0)	41 (71.9)	60 (65.9)	
Kaplan-Meier estimates of Dyspnea in months					
25% quantile (95% CI)	15.11 (1.906 to NC)	15.64 (2.957 to NC)	5.65 (2.004 to NC)	2.96 (1.906 to 16.427)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.8395		0.4943	
Hazard ratio (95% CI) vs Kd	-	0.94 (0.50 to 1.76)		1.23 (0.67 to 2.26)	
P-value	-	0.8388		0.4951	
Improvement probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful improvement change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
PGM=DEVOPS/SAR650984/EFC15246/CIR_RWE/REPORT/PGM/eff_km_subgp_sr_sig_de_i_t.sas OUT=REPORT/OUTPUT/eff_km_c30_dys_impl_age_de_i_t_x.rtf (07APR2021 14:31)

16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Dyspnea
16.2.6.1.2.2 Efficacy response data - Subgroup analyses by age
16.2.6.1.2.2.4 QLQ-C30 - Time to first deterioration by 10 pt in dyspnea according to age (LOCF) - ITT population

	<65 years		>=65 years		
	Kd (N=66)	**IKd (N=88)**	**Kd (N=57)**	**IKd (N=91)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	37 (56.1)	53 (60.2)	34 (59.6)	63 (69.2)	0.4149
Number (%) of patients censored	29 (43.9)	35 (39.8)	23 (40.4)	28 (30.8)	
Kaplan-Meier estimates of Dyspnea in months					
25% quantile (95% CI)	1.91 (1.117 to 2.004)	1.87 (1.084 to 2.793)	2.00 (1.117 to 3.943)	1.91 (1.183 to 2.136)	
Median (95% CI)	5.55 (2.037 to NC)	6.51 (2.990 to 18.694)	6.37 (3.943 to NC)	4.67 (2.924 to 8.345)	
75% quantile (95% CI)	NC (NC to NC)	NC (20.731 to NC)	NC (NC to NC)	19.81 (10.349 to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.8795		0.1847	
Hazard ratio (95% CI) vs Kd	-	1.03 (0.68 to 1.57)		1.33 (0.87 to 2.01)	
P-value	-	0.8799		0.1862	
Deterioration probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful deterioration change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Dyspnea
16.2.6.1.2.2 Efficacy response data - Subgroup analyses by age
16.2.6.1.2.2.5 QLQ-C30 - Time until permanent improvement by 10 pt in dyspnea according to age (LOCF) - ITT population

	<65 years		>=65 years		
	Kd (N=66)	**IKd (N=88)**	**Kd (N=57)**	**IKd (N=91)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	11 (16.7)	8 (9.1)	9 (15.8)	10 (11.0)	0.7037
Number (%) of patients censored	55 (83.3)	80 (90.9)	48 (84.2)	81 (89.0)	
Kaplan-Meier estimates of Dyspnea in months					
25% quantile (95% CI)	22.44 (15.869 to NC)	NC (NC to NC)	NC (17.051 to NC)	NC (NC to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.1514		0.3522	
Hazard ratio (95% CI) vs Kd	-	0.52 (0.21 to 1.29)		0.65 (0.27 to 1.61)	
P-value	-	0.1588		0.3557	
Improvement probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful improvement change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
PGM=DEVOPS/SAR650984/EFC15246/CIR_RWE/REPORT/PGM/eff_km_subgp_sr_sig_de_i_t.sas OUT=REPORT/OUTPUT/eff_km_c30_dys_imppl_age_de_i_t_x.rtf (07APR2021 14:32)

16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Dyspnea
16.2.6.1.2.2 Efficacy response data - Subgroup analyses by age
16.2.6.1.2.2.6 QLQ-C30 - Time until permanent deterioration by 10 pt in dyspnea according to age (LOCF) - ITT population

	<65 years		>=65 years		
	Kd (N=66)	**IKd (N=88)**	**Kd (N=57)**	**IKd (N=91)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	21 (31.8)	29 (33.0)	17 (29.8)	22 (24.2)	0.6352
Number (%) of patients censored	45 (68.2)	59 (67.0)	40 (70.2)	69 (75.8)	
Kaplan-Meier estimates of Dyspnea in months					
25% quantile (95% CI)	13.17 (2.891 to 21.224)	11.50 (6.735 to 19.614)	19.22 (8.444 to 22.209)	19.88 (13.996 to NC)	
Median (95% CI)	24.02 (21.224 to NC)	NC (NC to NC)	NC (21.684 to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (24.016 to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.9807		0.5453	
Hazard ratio (95% CI) vs Kd	-	0.99 (0.57 to 1.74)		0.82 (0.44 to 1.55)	
P-value	-	0.9807		0.5460	
Deterioration probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful deterioration change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Dyspnea
16.2.6.1.2.3 Efficacy response data - Subgroup analyses by gender
16.2.6.1.2.3.3 QLQ-C30 - Time to first improvement by 10 pt in dyspnea according to gender (LOCF) - ITT population

	Male		Female		
	Kd (N=68)	**IKd (N=101)**	**Kd (N=55)**	**IKd (N=78)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	16 (23.5)	25 (24.8)	17 (30.9)	28 (35.9)	0.8576
Number (%) of patients censored	52 (76.5)	76 (75.2)	38 (69.1)	50 (64.1)	
Kaplan-Meier estimates of Dyspnea in months					
25% quantile (95% CI)	15.11 (2.957 to NC)	14.75 (2.957 to NC)	3.06 (1.117 to NC)	2.99 (1.906 to 16.427)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.8694		0.6608	
Hazard ratio (95% CI) vs Kd	-	1.05 (0.56 to 1.97)		1.14 (0.63 to 2.09)	
P-value	-	0.8701		0.6611	
Improvement probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful improvement change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Dyspnea
16.2.6.1.2.3 Efficacy response data - Subgroup analyses by gender
16.2.6.1.2.3.4 QLQ-C30 - Time to first deterioration by 10 pt in dyspnea according to gender (LOCF) - ITT population

	Male		Female		
	Kd (N=68)	**IKd (N=101)**	**Kd (N=55)**	**IKd (N=78)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	39 (57.4)	67 (66.3)	32 (58.2)	49 (62.8)	0.7907
Number (%) of patients censored	29 (42.6)	34 (33.7)	23 (41.8)	29 (37.2)	
Kaplan-Meier estimates of Dyspnea in months					
25% quantile (95% CI)	1.91 (1.117 to 2.825)	1.91 (1.216 to 2.793)	1.94 (1.084 to 3.055)	1.91 (1.051 to 2.136)	
Median (95% CI)	6.37 (2.891 to 19.548)	4.67 (2.990 to 8.345)	5.68 (3.055 to NC)	6.54 (2.563 to 14.160)	
75% quantile (95% CI)	NC (19.548 to NC)	NC (10.152 to NC)	NC (NC to NC)	NC (19.811 to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.3530		0.6404	
Hazard ratio (95% CI) vs Kd	-	1.21 (0.81 to 1.79)		1.11 (0.71 to 1.74)	
P-value	-	0.3537		0.6405	
Deterioration probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful deterioration change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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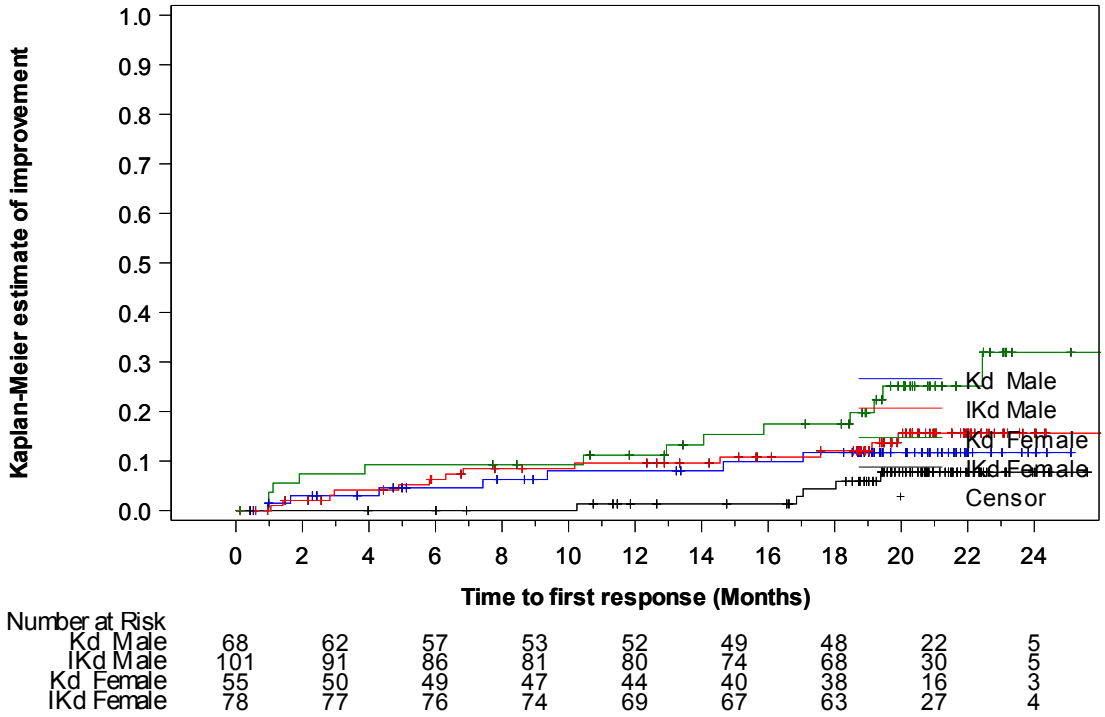
16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Dyspnea
16.2.6.1.2.3 Efficacy response data - Subgroup analyses by gender
16.2.6.1.2.3.5 QLQ-C30 - Time until permanent improvement by 10 pt in dyspnea according to gender (LOCF) - ITT population

	Male		Female		
	Kd (N=68)	**IKd (N=101)**	**Kd (N=55)**	**IKd (N=78)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	7 (10.3)	13 (12.9)	13 (23.6)	5 (6.4)	0.0210
Number (%) of patients censored	61 (89.7)	88 (87.1)	42 (76.4)	73 (93.6)	
Kaplan-Meier estimates of Dyspnea in months					
25% quantile (95% CI)	NC (NC to NC)	NC (19.910 to NC)	19.45 (12.945 to NC)	NC (NC to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (22.439 to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.6380		0.0039	
Hazard ratio (95% CI) vs Kd	-	1.25 (0.50 to 3.12)		0.25 (0.09 to 0.69)	
P-value	-	0.6387		0.0078	
Improvement probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful improvement change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
PGM=DEVOPS/SAR650984/EFC15246/CIR_RWE/REPORT/PGM/eff_km_subgp_sr_sig_de_i_t.sas OUT=REPORT/OUTPUT/eff_km_c30_dys_imppl_sex_de_i_t_x.rtf (07APR2021 14:32)

16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Dyspnea
16.2.6.1.2.3 Efficacy response data - Subgroup analyses by gender
16.2.6.1.2.3.6 QLQ-C30 - Time until permanent improvement by 10 pt in dyspnea according to gender - Kaplan-Meier curve (LOCF) - ITT population



Number at Risk

Kd Male	68	62	57	53	52	49	48	22	5
IKd Male	101	91	86	81	80	74	68	30	5
Kd Female	55	50	49	47	44	40	38	16	3
IKd Female	78	77	76	74	69	67	63	27	4

A lower score represents a better level of quality of life. Clinical meaningful improvement change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
PGM=DEVOPS/SAR650984/EFC15246/CIR_RWE/REPORT/PGM/eff_qlq_km_subgp_de_i_f.sas OUT=REPORT/OUTPUT/eff_km_c30_dys_imppl_sex_de_i_f_x.rtf (07APR2021 14:23)

16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Dyspnea
16.2.6.1.2.3 Efficacy response data - Subgroup analyses by gender
16.2.6.1.2.3.7 QLQ-C30 - Time until permanent deterioration by 10 pt in dyspnea according to gender (LOCF) - ITT population

	Male		Female		
	Kd (N=68)	**IKd (N=101)**	**Kd (N=55)**	**IKd (N=78)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	23 (33.8)	31 (30.7)	15 (27.3)	20 (25.6)	0.9934
Number (%) of patients censored	45 (66.2)	70 (69.3)	40 (72.7)	58 (74.4)	
Kaplan-Meier estimates of Dyspnea in months					
25% quantile (95% CI)	18.17 (5.815 to 21.224)	15.93 (7.556 to 21.224)	20.60 (4.698 to NC)	19.61 (13.996 to NC)	
Median (95% CI)	24.02 (21.224 to NC)	NC (NC to NC)	NC (21.224 to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (24.016 to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.6848		0.7734	
Hazard ratio (95% CI) vs Kd	-	0.89 (0.52 to 1.53)		0.91 (0.46 to 1.77)	
P-value	-	0.6849		0.7735	
Deterioration probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful deterioration change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
PGM=DEVOPS/SAR650984/EFC15246/CIR_RWE/REPORT/PGM/eff_km_subgp_sr_sig_de_i_t.sas OUT=REPORT/OUTPUT/eff_km_c30_dys_detpl_sex_de_i_t_x.rtf (07APR2021 14:32)

16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Dyspnea
16.2.6.1.2.4 Efficacy response data - Subgroup analyses by ethnic origin
16.2.6.1.2.4.3 QLQ-C30 - Time to first improvement by 10 pt in dyspnea according to ethnic origin (LOCF) - ITT population

	White		Other		
	Kd (N=83)	**IKd (N=131)**	**Kd (N=28)**	**IKd (N=34)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	24 (28.9)	39 (29.8)	7 (25.0)	9 (26.5)	0.9473
Number (%) of patients censored	59 (71.1)	92 (70.2)	21 (75.0)	25 (73.5)	
Kaplan-Meier estimates of Dyspnea in months					
25% quantile (95% CI)	3.84 (1.906 to NC)	6.47 (2.070 to NC)	15.11 (1.117 to NC)	6.67 (1.117 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.9308		0.8900	
Hazard ratio (95% CI) vs Kd	-	1.02 (0.62 to 1.70)		1.07 (0.40 to 2.88)	
P-value	-	0.9309		0.8905	
Improvement probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful improvement change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
PGM=DEVOPS/SAR650984/EFC15246/CIR_RWE/REPORT/PGM/eff_km_subgp_sr_sig_de_i_t.sas OUT=REPORT/OUTPUT/eff_km_c30_dys_impl_race_de_i_t_x.rtf (07APR2021 14:32)

16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Dyspnea
16.2.6.1.2.4 Efficacy response data - Subgroup analyses by ethnic origin
16.2.6.1.2.4.4 QLQ-C30 - Time to first deterioration by 10 pt in dyspnea according to ethnic origin (LOCF) - ITT population

	White		Other		
	Kd (N=83)	**IKd (N=131)**	**Kd (N=28)**	**IKd (N=34)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	50 (60.2)	90 (68.7)	18 (64.3)	20 (58.8)	0.2697
Number (%) of patients censored	33 (39.8)	41 (31.3)	10 (35.7)	14 (41.2)	
Kaplan-Meier estimates of Dyspnea in months					
25% quantile (95% CI)	1.94 (1.117 to 2.891)	1.87 (1.183 to 1.971)	1.15 (1.051 to 1.971)	1.91 (1.018 to 2.990)	
Median (95% CI)	5.32 (3.745 to 12.912)	4.67 (2.858 to 6.538)	2.07 (1.150 to NC)	6.11 (2.136 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (10.152 to NC)	NC (5.651 to NC)	NC (12.287 to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.2022		0.5753	
Hazard ratio (95% CI) vs Kd	-	1.25 (0.89 to 1.77)		0.83 (0.44 to 1.58)	
P-value	-	0.2032		0.5758	
Deterioration probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful deterioration change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Dyspnea
16.2.6.1.2.4 Efficacy response data - Subgroup analyses by ethnic origin
16.2.6.1.2.4.5 QLQ-C30 - Time until permanent improvement by 10 pt in dyspnea according to ethnic origin (LOCF) - ITT population

	White		Other		
	Kd (N=83)	**IKd (N=131)**	**Kd (N=28)**	**IKd (N=34)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	13 (15.7)	13 (9.9)	5 (17.9)	2 (5.9)	0.4365
Number (%) of patients censored	70 (84.3)	118 (90.1)	23 (82.1)	32 (94.1)	
Kaplan-Meier estimates of Dyspnea in months					
25% quantile (95% CI)	NC (19.187 to NC)	NC (NC to NC)	NC (1.906 to NC)	NC (18.037 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.2249		0.1366	
Hazard ratio (95% CI) vs Kd	-	0.62 (0.29 to 1.35)		0.31 (0.06 to 1.59)	
P-value	-	0.2292		0.1598	
Improvement probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful improvement change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Dyspnea
16.2.6.1.2.4 Efficacy response data - Subgroup analyses by ethnic origin
16.2.6.1.2.4.6 QLQ-C30 - Time until permanent deterioration by 10 pt in dyspnea according to ethnic origin (LOCF) - ITT population

	White		Other		
	Kd (N=83)	**IKd (N=131)**	**Kd (N=28)**	**IKd (N=34)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	23 (27.7)	38 (29.0)	13 (46.4)	9 (26.5)	0.2297
Number (%) of patients censored	60 (72.3)	93 (71.0)	15 (53.6)	25 (73.5)	
Kaplan-Meier estimates of Dyspnea in months					
25% quantile (95% CI)	19.75 (6.374 to 22.209)	16.95 (9.922 to 21.224)	11.93 (1.150 to 20.600)	17.35 (4.600 to NC)	
Median (95% CI)	NC (21.684 to NC)	NC (NC to NC)	24.02 (17.906 to 24.016)	NC (18.267 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	24.02 (NC to NC)	NC (NC to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.9296		0.1669	
Hazard ratio (95% CI) vs Kd	-	1.02 (0.61 to 1.72)		0.55 (0.24 to 1.30)	
P-value	-	0.9298		0.1731	
Deterioration probability (95% CI)[b]					

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The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Dyspnea
16.2.6.1.2.5 Efficacy response data - Subgroup analyses by geographical region
16.2.6.1.2.5.3 QLQ-C30 - Time to first improvement by 10 pt in dyspnea according to geographical region (LOCF) - ITT population

	Europe		America		Asia		Other countries		
	Kd (N=60)	**IKd (N=85)**	**Kd (N=20)**	**IKd (N=24)**	**Kd (N=21)**	**IKd (N=25)**	**Kd (N=22)**	**IKd (N=45)**	**p-value of treatment-by-subgroup interaction[c]**
Number (%) of events	16 (26.7)	25 (29.4)	5 (25.0)	3 (12.5)	4 (19.0)	9 (36.0)	8 (36.4)	16 (35.6)	0.5215
Number (%) of patients censored	44 (73.3)	60 (70.6)	15 (75.0)	21 (87.5)	17 (81.0)	16 (64.0)	14 (63.6)	29 (64.4)	
Kaplan-Meier estimates of event in months									
25% quantile (95% CI)	4.70 (1.906 to NC)	5.98 (2.070 to NC)	NC (1.281 to NC)	NC (0.986 to NC)	NC (1.117 to NC)	3.88 (0.986 to NC)	2.00 (0.953 to NC)	2.96 (1.117 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (5.651 to NC)	NC (NC to NC)	NC (NC to NC)	NC (4.731 to NC)	NC (2.004 to NC)	NC (14.752 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Kd									

A lower score represents a better level of quality of life. Clinical meaningful improvement change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Dyspnea
16.2.6.1.2.5 Efficacy response data - Subgroup analyses by geographical region
16.2.6.1.2.5.3 QLQ-C30 - Time to first improvement by 10 pt in dyspnea according to geographical region (LOCF) - ITT population

	Europe		America		Asia		Other countries		
	Kd (N=60)	**IKd (N=85)**	**Kd (N=20)**	**IKd (N=24)**	**Kd (N=21)**	**IKd (N=25)**	**Kd (N=22)**	**IKd (N=45)**	**p-value of treatment-by-subgroup interaction[c]**
Log-Rank test p-value[a] vs Kd	-	0.8239		0.3423		0.2284		0.8917	
Hazard ratio (95% CI) vs Kd	-	1.07 (0.57 to 2.01)		0.51 (0.12 to 2.12)		2.03 (0.63 to 6.60)		0.94 (0.40 to 2.20)	
P-value	-	0.8239		0.3516		0.2383		0.8917	
Improvement probability (95% CI)[b]									
3 Months	0.189 (0.101 to 0.298)	0.218 (0.136 to 0.312)	0.150 (0.037 to 0.335)	0.089 (0.015 to 0.247)	0.100 (0.017 to 0.272)	0.208 (0.076 to 0.385)	0.318 (0.142 to 0.511)	0.267 (0.149 to 0.400)	
6 Months	0.260 (0.155 to 0.377)	0.256 (0.168 to 0.354)	0.250 (0.091 to 0.449)	0.089 (0.015 to 0.247)	0.153 (0.038 to 0.340)	0.292 (0.130 to 0.476)	0.318 (0.142 to 0.511)	0.289 (0.166 to 0.424)	

A lower score represents a better level of quality of life. Clinical meaningful improvement change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Dyspnea
16.2.6.1.2.5 Efficacy response data - Subgroup analyses by geographical region
16.2.6.1.2.5.4 QLQ-C30 - Time to first deterioration by 10 pt in dyspnea according to geographical region (LOCF) - ITT population

	Europe		America		Asia		Other countries		
	Kd (N=60)	**IKd (N=85)**	**Kd (N=20)**	**IKd (N=24)**	**Kd (N=21)**	**IKd (N=25)**	**Kd (N=22)**	**IKd (N=45)**	**p-value of treatment-by-subgroup interaction[c]**
Number (%) of events	27 (45.0)	55 (64.7)	13 (65.0)	15 (62.5)	15 (71.4)	15 (60.0)	16 (72.7)	31 (68.9)	0.1498
Number (%) of patients censored	33 (55.0)	30 (35.3)	7 (35.0)	9 (37.5)	6 (28.6)	10 (40.0)	6 (27.3)	14 (31.1)	
Kaplan-Meier estimates of event in months									
25% quantile (95% CI)	2.99 (1.906 to 5.322)	1.91 (1.183 to 2.793)	1.17 (0.953 to 1.971)	1.61 (1.051 to 2.924)	1.15 (1.051 to 1.971)	2.86 (0.986 to 4.600)	1.18 (0.986 to 4.041)	1.25 (1.051 to 1.971)	
Median (95% CI)	19.55 (5.322 to NC)	6.67 (3.055 to 10.908)	4.48 (1.117 to NC)	4.67 (1.906 to NC)	2.02 (1.150 to 9.988)	7.56 (2.891 to NC)	4.98 (1.183 to 7.918)	3.75 (1.938 to 9.396)	
75% quantile (95% CI)	NC (NC to NC)	NC (14.160 to NC)	NC (4.698 to NC)	NC (4.665 to NC)	NC (2.037 to NC)	NC (12.287 to NC)	NC (5.125 to NC)	20.73 (8.345 to NC)	

A lower score represents a better level of quality of life. Clinical meaningful deterioration change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Dyspnea
16.2.6.1.2.5 Efficacy response data - Subgroup analyses by geographical region
16.2.6.1.2.5.4 QLQ-C30 - Time to first deterioration by 10 pt in dyspnea according to geographical region (LOCF) - ITT population

	Europe		America		Asia		Other countries		
	Kd (N=60)	**IKd (N=85)**	**Kd (N=20)**	**IKd (N=24)**	**Kd (N=21)**	**IKd (N=25)**	**Kd (N=22)**	**IKd (N=45)**	**p-value of treatment-by-subgroup interaction[c]**
Comparison vs. Kd									
Log-Rank test p-value[a] vs Kd	-	0.0360		0.9652		0.1712		0.9662	
Hazard ratio (95% CI) vs Kd	-	1.63 (1.03 to 2.58)		0.98 (0.47 to 2.07)		0.61 (0.30 to 1.25)		1.01 (0.55 to 1.85)	
P-value	-	0.0379		0.9651		0.1754		0.9662	
Hazard ratio inverted (95% CI) vs IKd		-		1.02 (0.48 to 2.14)		1.65 (0.80 to 3.39)		0.99 (0.54 to 1.81)	
Deterioration probability (95% CI)[b]									
3 Months	0.741 (0.608 to 0.835)	0.626 (0.512 to 0.720)	0.550 (0.313 to 0.735)	0.551 (0.326 to 0.728)	0.350 (0.157 to 0.552)	0.667 (0.443 to 0.817)	0.636 (0.403 to 0.799)	0.511 (0.358 to 0.645)	

A lower score represents a better level of quality of life. Clinical meaningful deterioration change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Dyspnea
16.2.6.1.2.5 Efficacy response data - Subgroup analyses by geographical region
16.2.6.1.2.5.5 QLQ-C30 - Time until permanent improvement by 10 pt in dyspnea according to geographical region (LOCF) - ITT population

	Europe		America		Asia		Other countries		
	Kd (N=60)	**IKd (N=85)**	**Kd (N=20)**	**IKd (N=24)**	**Kd (N=21)**	**IKd (N=25)**	**Kd (N=22)**	**IKd (N=45)**	**p-value of treatment-by-subgroup interaction[c]**
Number (%) of events	10 (16.7)	8 (9.4)	4 (20.0)	3 (12.5)	2 (9.5)	2 (8.0)	4 (18.2)	5 (11.1)	0.9754
Number (%) of patients censored	50 (83.3)	77 (90.6)	16 (80.0)	21 (87.5)	19 (90.5)	23 (92.0)	18 (81.8)	40 (88.9)	
Kaplan-Meier estimates of event in months									
25% quantile (95% CI)	22.44 (14.653 to NC)	NC (NC to NC)	19.45 (4.304 to NC)	NC (6.834 to NC)	NC (1.117 to NC)	NC (2.825 to NC)	NC (12.945 to NC)	NC (17.577 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (19.450 to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	

A lower score represents a better level of quality of life. Clinical meaningful improvement change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Dyspnea
16.2.6.1.2.5 Efficacy response data - Subgroup analyses by geographical region
16.2.6.1.2.5.5 QLQ-C30 - Time until permanent improvement by 10 pt in dyspnea according to geographical region (LOCF) - ITT population

	Europe		America		Asia		Other countries		
	Kd (N=60)	**IKd (N=85)**	**Kd (N=20)**	**IKd (N=24)**	**Kd (N=21)**	**IKd (N=25)**	**Kd (N=22)**	**IKd (N=45)**	**p-value of treatment-by-subgroup interaction[c]**
Comparison vs. Kd									
Log-Rank test p-value[a] vs Kd	-	0.1649		0.6463		0.7965		0.5087	
Hazard ratio (95% CI) vs Kd	-	0.52 (0.21 to 1.33)		0.71 (0.16 to 3.15)		0.77 (0.11 to 5.49)		0.64 (0.17 to 2.40)	
P-value	-	0.1722		0.6479		0.7971		0.5121	
Improvement probability (95% CI)[b]									
3 Months	0.068 (0.022 to 0.151)	0.024 (0.005 to 0.077)			0.100 (0.017 to 0.272)	0.042 (0.003 to 0.176)		0.022 (0.002 to 0.101)	

A lower score represents a better level of quality of life. Clinical meaningful improvement change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
PGM=DEVOPS/SAR650984/EFC15246/CIR_RWE/REPORT/PGM/eff_km_subgp_sr_sig_de_i_t.sas OUT=REPORT/OUTPUT/eff_km_c30_dys_imppl_greg_de_i_t_x.rtf (07APR2021 14:32)

16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Dyspnea
16.2.6.1.2.5 Efficacy response data - Subgroup analyses by geographical region
16.2.6.1.2.5.6 QLQ-C30 - Time until permanent deterioration by 10 pt in dyspnea according to geographical region (LOCF) - ITT population

	Europe		America		Asia		Other countries		
	Kd (N=60)	**IKd (N=85)**	**Kd (N=20)**	**IKd (N=24)**	**Kd (N=21)**	**IKd (N=25)**	**Kd (N=22)**	**IKd (N=45)**	**p-value of treatment-by-subgroup interaction[c]**
Number (%) of events	12 (20.0)	27 (31.8)	6 (30.0)	7 (29.2)	11 (52.4)	7 (28.0)	9 (40.9)	10 (22.2)	0.1221
Number (%) of patients censored	48 (80.0)	58 (68.2)	14 (70.0)	17 (70.8)	10 (47.6)	18 (72.0)	13 (59.1)	35 (77.8)	
Kaplan-Meier estimates of event in months									
25% quantile (95% CI)	21.22 (13.175 to NC)	16.99 (9.265 to 21.224)	14.85 (0.986 to NC)	11.17 (1.117 to NC)	7.41 (1.051 to 20.600)	16.16 (0.986 to NC)	9.23 (1.018 to 22.209)	19.61 (6.505 to NC)	
Median (95% CI)	NC (21.684 to NC)	NC (21.454 to NC)	NC (11.532 to NC)	NC (11.170 to NC)	20.60 (2.891 to 24.016)	NC (16.164 to NC)	22.21 (9.232 to NC)	NC (NC to NC)	

A lower score represents a better level of quality of life. Clinical meaningful deterioration change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Dyspnea
16.2.6.1.2.5 Efficacy response data - Subgroup analyses by geographical region
16.2.6.1.2.5.6 QLQ-C30 - Time until permanent deterioration by 10 pt in dyspnea according to geographical region (LOCF) - ITT population

	Europe		America		Asia		Other countries		
	Kd (N=60)	**IKd (N=85)**	**Kd (N=20)**	**IKd (N=24)**	**Kd (N=21)**	**IKd (N=25)**	**Kd (N=22)**	**IKd (N=45)**	**p-value of treatment-by-subgroup interaction[c]**
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	24.02 (20.600 to 24.016)	NC (NC to NC)	NC (22.209 to NC)	NC (NC to NC)	
Comparison vs. Kd									
Log-Rank test p-value[a] vs Kd	-	0.2031		0.9038		0.1201		0.1425	
Hazard ratio (95% CI) vs Kd	-	1.55 (0.78 to 3.06)		1.07 (0.36 to 3.18)		0.48 (0.19 to 1.24)		0.52 (0.21 to 1.27)	
P-value	-	0.2068		0.9040		0.1284		0.1497	
Deterioration probability (95% CI)[b]									

A lower score represents a better level of quality of life. Clinical meaningful deterioration change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Dyspnea
16.2.6.1.2.6 Efficacy response data - Subgroup analyses by regulatory region
16.2.6.1.2.6.3 QLQ-C30 - Time to first improvement by 10 pt in dyspnea according to regulatory region (LOCF) - ITT population

	Western countries		Other countries		
	Kd (N=55)	**IKd (N=97)**	**Kd (N=68)**	**IKd (N=82)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	15 (27.3)	27 (27.8)	18 (26.5)	26 (31.7)	0.4458
Number (%) of patients censored	40 (72.7)	70 (72.2)	50 (73.5)	56 (68.3)	
Kaplan-Meier estimates of Dyspnea in months					
25% quantile (95% CI)	3.84 (1.051 to NC)	10.25 (2.825 to NC)	10.91 (2.004 to NC)	3.02 (1.906 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.8093		0.3934	
Hazard ratio (95% CI) vs Kd	-	0.93 (0.49 to 1.74)		1.30 (0.71 to 2.37)	
P-value	-	0.8094		0.3947	
Improvement probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful improvement change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Dyspnea
16.2.6.1.2.6 Efficacy response data - Subgroup analyses by regulatory region
16.2.6.1.2.6.4 QLQ-C30 - Time to first deterioration by 10 pt in dyspnea according to regulatory region (LOCF) - ITT population

	Western countries		Other countries		
	Kd (N=55)	**IKd (N=97)**	**Kd (N=68)**	**IKd (N=82)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	25 (45.5)	65 (67.0)	46 (67.6)	51 (62.2)	0.0513
Number (%) of patients censored	30 (54.5)	32 (33.0)	22 (32.4)	31 (37.8)	
Kaplan-Meier estimates of Dyspnea in months					
25% quantile (95% CI)	2.00 (1.084 to 4.041)	1.87 (1.117 to 2.004)	1.31 (1.117 to 2.037)	1.91 (1.216 to 2.924)	
Median (95% CI)	NC (3.943 to NC)	4.73 (2.793 to 8.345)	5.13 (2.070 to 8.444)	6.54 (3.713 to 12.550)	
75% quantile (95% CI)	NC (NC to NC)	NC (10.349 to NC)	NC (9.758 to NC)	NC (14.587 to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.0406		0.5625	
Hazard ratio (95% CI) vs Kd	-	1.61 (1.02 to 2.56)		0.89 (0.60 to 1.32)	
P-value	-	0.0426		0.5627	
Hazard ratio inverted (95% CI) vs IKd		-		1.12 (0.76 to 1.68)	

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The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Dyspnea
16.2.6.1.2.6 Efficacy response data - Subgroup analyses by regulatory region
16.2.6.1.2.6.5 QLQ-C30 - Time until permanent improvement by 10 pt in dyspnea according to regulatory region (LOCF) - ITT population

	Western countries		Other countries		
	Kd (N=55)	**IKd (N=97)**	**Kd (N=68)**	**IKd (N=82)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	9 (16.4)	12 (12.4)	11 (16.2)	6 (7.3)	0.4378
Number (%) of patients censored	46 (83.6)	85 (87.6)	57 (83.8)	76 (92.7)	
Kaplan-Meier estimates of Dyspnea in months					
25% quantile (95% CI)	22.44 (14.653 to NC)	NC (NC to NC)	NC (18.464 to NC)	NC (NC to NC)	
Median (95% CI)	NC (22.439 to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.4823		0.0847	
Hazard ratio (95% CI) vs Kd	-	0.73 (0.31 to 1.75)		0.43 (0.16 to 1.16)	
P-value	-	0.4840		0.0943	
Improvement probability (95% CI)[b]					

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The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Dyspnea
16.2.6.1.2.6 Efficacy response data - Subgroup analyses by regulatory region
16.2.6.1.2.6.6 QLQ-C30 - Time until permanent deterioration by 10 pt in dyspnea according to regulatory region (LOCF) - ITT population

	Western countries		Other countries		
	Kd (N=55)	**IKd (N=97)**	**Kd (N=68)**	**IKd (N=82)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	16 (29.1)	29 (29.9)	22 (32.4)	22 (26.8)	0.5514
Number (%) of patients censored	39 (70.9)	68 (70.1)	46 (67.6)	60 (73.2)	
Kaplan-Meier estimates of Dyspnea in months					
25% quantile (95% CI)	19.75 (5.815 to 22.209)	16.99 (9.528 to 21.454)	18.46 (4.698 to 20.665)	17.35 (9.955 to NC)	
Median (95% CI)	NC (21.224 to NC)	NC (21.454 to NC)	24.02 (20.665 to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (24.016 to NC)	NC (NC to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.9033		0.4857	
Hazard ratio (95% CI) vs Kd	-	1.04 (0.56 to 1.91)		0.81 (0.45 to 1.46)	
P-value	-	0.9038		0.4865	
Deterioration probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful deterioration change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Dyspnea
16.2.6.1.2.7 Efficacy response data - Subgroup analyses by baseline ECOG PS
16.2.6.1.2.7.3 QLQ-C30 - Time to first improvement by 10 pt in dyspnea according to baseline ECOG PS (LOCF) - ITT population

	0 or 1		>1		
	Kd (N=118)	**IKd (N=168)**	**Kd (N=5)**	**IKd (N=11)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	32 (27.1)	50 (29.8)	1 (20.0)	3 (27.3)	0.7384
Number (%) of patients censored	86 (72.9)	118 (70.2)	4 (80.0)	8 (72.7)	
Kaplan-Meier estimates of Dyspnea in months					
25% quantile (95% CI)	5.65 (2.037 to NC)	6.47 (2.793 to NC)	NC (2.070 to NC)	14.55 (1.216 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (2.070 to NC)	NC (1.216 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (2.070 to NC)	NC (NC to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.7329		0.7541	
Hazard ratio (95% CI) vs Kd	-	1.08 (0.69 to 1.68)		1.45 (0.14 to 14.69)	
P-value	-	0.7329		0.7554	
Improvement probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful improvement change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Dyspnea
16.2.6.1.2.7 Efficacy response data - Subgroup analyses by baseline ECOG PS
16.2.6.1.2.7.4 QLQ-C30 - Time to first deterioration by 10 pt in dyspnea according to baseline ECOG PS (LOCF) - ITT population

	0 or 1		>1		
	Kd (N=118)	**IKd (N=168)**	**Kd (N=5)**	**IKd (N=11)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	70 (59.3)	110 (65.5)	1 (20.0)	6 (54.5)	0.2371
Number (%) of patients censored	48 (40.7)	58 (34.5)	4 (80.0)	5 (45.5)	
Kaplan-Meier estimates of Dyspnea in months					
25% quantile (95% CI)	1.91 (1.117 to 2.004)	1.91 (1.183 to 2.004)	NC (4.698 to NC)	3.06 (1.610 to 6.505)	
Median (95% CI)	5.65 (3.713 to 9.758)	5.22 (3.220 to 8.345)	NC (4.698 to NC)	6.51 (1.610 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (18.694 to NC)	NC (4.698 to NC)	NC (4.665 to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.4473		0.1400	
Hazard ratio (95% CI) vs Kd	-	1.12 (0.83 to 1.52)		4.33 (0.52 to 36.11)	
P-value	-	0.4475		0.1759	
Deterioration probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful deterioration change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Dyspnea
16.2.6.1.2.7 Efficacy response data - Subgroup analyses by baseline ECOG PS
16.2.6.1.2.7.5 QLQ-C30 - Time until permanent improvement by 10 pt in dyspnea according to baseline ECOG PS (LOCF) - ITT population

	0 or 1		>1		
	Kd (N=118)	**IKd (N=168)**	**Kd (N=5)**	**IKd (N=11)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	19 (16.1)	17 (10.1)	1 (20.0)	1 (9.1)	0.7358
Number (%) of patients censored	99 (83.9)	151 (89.9)	4 (80.0)	10 (90.9)	
Kaplan-Meier estimates of Dyspnea in months					
25% quantile (95% CI)	NC (19.450 to NC)	NC (NC to NC)	14.65 (14.653 to NC)	NC (14.554 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (14.653 to NC)	NC (14.554 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (14.653 to NC)	NC (NC to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.1262		0.3166	
Hazard ratio (95% CI) vs Kd	-	0.60 (0.31 to 1.16)		0.27 (0.02 to 4.28)	
P-value	-	0.1302		0.3511	
Improvement probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful improvement change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Dyspnea
16.2.6.1.2.7 Efficacy response data - Subgroup analyses by baseline ECOG PS
16.2.6.1.2.7.6 QLQ-C30 - Time until permanent deterioration by 10 pt in dyspnea according to baseline ECOG PS (LOCF) - ITT population

	0 or 1		>1		
	Kd (N=118)	**IKd (N=168)**	**Kd (N=5)**	**IKd (N=11)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	37 (31.4)	50 (29.8)	1 (20.0)	1 (9.1)	0.5293
Number (%) of patients censored	81 (68.6)	118 (70.2)	4 (80.0)	10 (90.9)	
Kaplan-Meier estimates of Dyspnea in months					
25% quantile (95% CI)	18.56 (10.875 to 21.224)	16.99 (10.973 to 21.191)	NC (4.698 to NC)	NC (10.908 to NC)	
Median (95% CI)	24.02 (21.684 to NC)	NC (NC to NC)	NC (4.698 to NC)	NC (10.908 to NC)	
75% quantile (95% CI)	NC (24.016 to NC)	NC (NC to NC)	NC (4.698 to NC)	NC (NC to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.7405		0.5430	
Hazard ratio (95% CI) vs Kd	-	0.93 (0.61 to 1.42)		0.43 (0.03 to 7.04)	
P-value	-	0.7390		0.5543	
Deterioration probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful deterioration change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
PGM=DEVOPS/SAR650984/EFC15246/CIR_RWE/REPORT/PGM/eff_km_subgp_sr_sig_de_i_t.sas OUT=REPORT/OUTPUT/eff_km_c30_dys_detpl_ecog_de_i_t_x.rtf (07APR2021 14:32)

16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Dyspnea
16.2.6.1.2.8 Efficacy response data - Subgroup analyses by ISS staging at SE
16.2.6.1.2.8.3 QLQ-C30 - Time to first improvement by 10 pt in dyspnea according to ISS staging at SE (LOCF) - ITT population

	I		II		III		
	Kd (N=71)	**IKd (N=89)**	**Kd (N=31)**	**IKd (N=63)**	**Kd (N=20)**	**IKd (N=26)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	18 (25.4)	21 (23.6)	9 (29.0)	22 (34.9)	5 (25.0)	9 (34.6)	0.7201
Number (%) of patients censored	53 (74.6)	68 (76.4)	22 (71.0)	41 (65.1)	15 (75.0)	17 (65.4)	
Kaplan-Meier estimates of Dyspnea in months							
25% quantile (95% CI)	15.11 (2.957 to NC)	NC (2.990 to NC)	2.07 (1.051 to NC)	2.96 (1.938 to 16.986)	3.12 (0.953 to NC)	1.94 (0.986 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (3.121 to NC)	NC (2.103 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Kd							
Log-Rank test p-value[a] vs Kd	-	0.7907		0.7098		0.4626	
Hazard ratio (95% CI) vs Kd	-	0.92 (0.49 to 1.72)		1.16 (0.53 to 2.52)		1.50 (0.50 to 4.49)	
P-value	-	0.7898		0.7100		0.4657	

A lower score represents a better level of quality of life. Clinical meaningful improvement change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Dyspnea
16.2.6.1.2.8 Efficacy response data - Subgroup analyses by ISS staging at SE
16.2.6.1.2.8.4 QLQ-C30 - Time to first deterioration by 10 pt in dyspnea according to ISS staging at SE (LOCF) - ITT population

	I		II		III		
	Kd (N=71)	**IKd (N=89)**	**Kd (N=31)**	**IKd (N=63)**	**Kd (N=20)**	**IKd (N=26)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	47 (66.2)	57 (64.0)	17 (54.8)	48 (76.2)	7 (35.0)	11 (42.3)	0.1570
Number (%) of patients censored	24 (33.8)	32 (36.0)	14 (45.2)	15 (23.8)	13 (65.0)	15 (57.7)	
Kaplan-Meier estimates of Dyspnea in months							
25% quantile (95% CI)	1.12 (1.084 to 1.971)	1.91 (1.183 to 2.563)	1.97 (1.150 to 3.943)	1.48 (1.051 to 1.906)	5.32 (1.150 to NC)	6.51 (1.051 to 10.908)	
Median (95% CI)	4.80 (2.004 to 7.392)	4.90 (3.055 to 10.218)	6.37 (2.990 to NC)	2.92 (1.938 to 6.538)	NC (5.322 to NC)	12.55 (6.505 to NC)	
75% quantile (95% CI)	NC (9.758 to NC)	NC (20.731 to NC)	NC (NC to NC)	14.16 (6.702 to NC)	NC (NC to NC)	NC (12.550 to NC)	
Comparison vs. Kd							
Log-Rank test p-value[a] vs Kd	-	0.5817		0.0588		0.5709	
Hazard ratio (95% CI) vs Kd	-	0.90 (0.61 to 1.32)		1.70 (0.97 to 2.95)		1.31 (0.51 to 3.40)	

A lower score represents a better level of quality of life. Clinical meaningful deterioration change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Dyspnea
16.2.6.1.2.8 Efficacy response data - Subgroup analyses by ISS staging at SE
16.2.6.1.2.8.5 QLQ-C30 - Time until permanent improvement by 10 pt in dyspnea according to ISS staging at SE (LOCF) - ITT population

	I		II		III		
	Kd (N=71)	**IKd (N=89)**	**Kd (N=31)**	**IKd (N=63)**	**Kd (N=20)**	**IKd (N=26)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	10 (14.1)	7 (7.9)	5 (16.1)	7 (11.1)	4 (20.0)	4 (15.4)	0.9462
Number (%) of patients censored	61 (85.9)	82 (92.1)	26 (83.9)	56 (88.9)	16 (80.0)	22 (84.6)	
Kaplan-Meier estimates of Dyspnea in months							
25% quantile (95% CI)	NC (19.450 to NC)	NC (NC to NC)	NC (4.304 to NC)	NC (NC to NC)	17.05 (0.953 to NC)	19.91 (1.413 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (17.051 to NC)	NC (19.910 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Kd							
Log-Rank test p-value[a] vs Kd	-	0.2531		0.3786		0.6579	
Hazard ratio (95% CI) vs Kd	-	0.57 (0.22 to 1.51)		0.60 (0.19 to 1.89)		0.73 (0.18 to 2.93)	
P-value	-	0.2592		0.3835		0.6592	

A lower score represents a better level of quality of life. Clinical meaningful improvement change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Dyspnea
16.2.6.1.2.8 Efficacy response data - Subgroup analyses by ISS staging at SE
16.2.6.1.2.8.6 QLQ-C30 - Time until permanent deterioration by 10 pt in dyspnea according to ISS staging at SE (LOCF) - ITT population

	I		II		III		
	Kd (N=71)	**IKd (N=89)**	**Kd (N=31)**	**IKd (N=63)**	**Kd (N=20)**	**IKd (N=26)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	22 (31.0)	30 (33.7)	12 (38.7)	16 (25.4)	4 (20.0)	5 (19.2)	0.2857
Number (%) of patients censored	49 (69.0)	59 (66.3)	19 (61.3)	47 (74.6)	16 (80.0)	21 (80.8)	
Kaplan-Meier estimates of Dyspnea in months							
25% quantile (95% CI)	19.75 (9.232 to 21.684)	13.11 (6.505 to 21.191)	10.87 (2.004 to 24.016)	19.88 (13.996 to NC)	18.56 (1.150 to NC)	16.03 (7.556 to NC)	
Median (95% CI)	NC (21.224 to NC)	NC (21.454 to NC)	24.02 (12.912 to 24.016)	NC (NC to NC)	NC (18.563 to NC)	NC (16.033 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	24.02 (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Kd							
Log-Rank test p-value[a] vs Kd	-	0.6056		0.1260		0.9763	
Hazard ratio (95% CI) vs Kd	-	1.16 (0.67 to 2.00)		0.56 (0.26 to 1.19)		0.98 (0.26 to 3.66)	

A lower score represents a better level of quality of life. Clinical meaningful deterioration change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Dyspnea
16.2.6.1.2.9 Efficacy response data - Subgroup analyses by R-ISS stage at SE
16.2.6.1.2.9.3 QLQ-C30 - Time to first improvement by 10 pt in dyspnea according to R-ISS stage at SE (LOCF) - ITT population

	I or II		III		Not classified		
	Kd (N=103)	**IKd (N=155)**	**Kd (N=8)**	**IKd (N=16)**	**Kd (N=12)**	**IKd (N=8)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	26 (25.2)	45 (29.0)	3 (37.5)	5 (31.3)	4 (33.3)	3 (37.5)	0.7332
Number (%) of patients censored	77 (74.8)	110 (71.0)	5 (62.5)	11 (68.8)	8 (66.7)	5 (62.5)	
Kaplan-Meier estimates of Dyspnea in months							
25% quantile (95% CI)	7.43 (2.136 to NC)	8.48 (2.825 to NC)	1.12 (0.953 to NC)	2.10 (1.216 to NC)	8.51 (0.986 to NC)	1.91 (1.018 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (0.953 to NC)	NC (1.938 to NC)	NC (1.150 to NC)	NC (1.018 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (3.055 to NC)	NC (NC to NC)	NC (NC to NC)	NC (1.906 to NC)	
Comparison vs. Kd							
Log-Rank test p-value[a] vs Kd	-	0.6277		0.6765		0.5273	
Hazard ratio (95% CI) vs Kd	-	1.13 (0.70 to 1.83)		0.74 (0.18 to 3.10)		1.62 (0.36 to 7.25)	
P-value	-	0.6279		0.6776		0.5311	

A lower score represents a better level of quality of life. Clinical meaningful improvement change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Dyspnea
16.2.6.1.2.9 Efficacy response data - Subgroup analyses by R-ISS stage at SE
16.2.6.1.2.9.4 QLQ-C30 - Time to first deterioration by 10 pt in dyspnea according to R-ISS stage at SE (LOCF) - ITT population

	I or II		III		Not classified		
	Kd (N=103)	**IKd (N=155)**	**Kd (N=8)**	**IKd (N=16)**	**Kd (N=12)**	**IKd (N=8)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	59 (57.3)	108 (69.7)	4 (50.0)	6 (37.5)	8 (66.7)	2 (25.0)	0.2176
Number (%) of patients censored	44 (42.7)	47 (30.3)	4 (50.0)	10 (62.5)	4 (33.3)	6 (75.0)	
Kaplan-Meier estimates of Dyspnea in months							
25% quantile (95% CI)	1.91 (1.117 to 2.004)	1.87 (1.117 to 1.938)	2.04 (2.004 to 5.815)	7.56 (2.004 to 12.550)	2.45 (0.953 to 4.895)	5.22 (3.055 to NC)	
Median (95% CI)	6.37 (3.943 to 19.548)	4.60 (2.858 to 6.669)	5.82 (2.004 to NC)	12.55 (6.505 to NC)	5.22 (0.986 to NC)	NC (3.055 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (13.996 to NC)	NC (2.891 to NC)	NC (12.550 to NC)	NC (4.895 to NC)	NC (5.224 to NC)	
Comparison vs. Kd							
Log-Rank test p-value[a] vs Kd	-	0.1307		0.3196		0.2236	
Hazard ratio (95% CI) vs Kd	-	1.28 (0.93 to 1.75)		0.53 (0.15 to 1.90)		0.39 (0.08 to 1.86)	

A lower score represents a better level of quality of life. Clinical meaningful deterioration change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Dyspnea
16.2.6.1.2.9 Efficacy response data - Subgroup analyses by R-ISS stage at SE
16.2.6.1.2.9.5 QLQ-C30 - Time until permanent improvement by 10 pt in dyspnea according to R-ISS stage at SE (LOCF) - ITT population

	I or II		III		Not classified		
	Kd (N=103)	**IKd (N=155)**	**Kd (N=8)**	**IKd (N=16)**	**Kd (N=12)**	**IKd (N=8)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	16 (15.5)	15 (9.7)	2 (25.0)	3 (18.8)	2 (16.7)	0 (0.0)	0.9934
Number (%) of patients censored	87 (84.5)	140 (90.3)	6 (75.0)	13 (81.3)	10 (83.3)	8 (100.0)	
Kaplan-Meier estimates of Dyspnea in months							
25% quantile (95% CI)	NC (19.450 to NC)	NC (NC to NC)	1.12 (0.953 to NC)	14.55 (1.413 to NC)	NC (12.945 to NC)	NC (NC to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (0.953 to NC)	NC (14.554 to NC)	NC (18.464 to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Kd							
Log-Rank test p-value[a] vs Kd	-	0.1154		0.5675		0.4038	
Hazard ratio (95% CI) vs Kd	-	0.57 (0.28 to 1.16)		0.59 (0.10 to 3.61)			
P-value	-	0.1202		0.5715		0.9971	

A lower score represents a better level of quality of life. Clinical meaningful improvement change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Dyspnea
16.2.6.1.2.9 Efficacy response data - Subgroup analyses by R-ISS stage at SE
16.2.6.1.2.9.6 QLQ-C30 - Time until permanent deterioration by 10 pt in dyspnea according to R-ISS stage at SE (LOCF) - ITT population

	I or II		III		Not classified		
	Kd (N=103)	**IKd (N=155)**	**Kd (N=8)**	**IKd (N=16)**	**Kd (N=12)**	**IKd (N=8)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	35 (34.0)	48 (31.0)	2 (25.0)	2 (12.5)	1 (8.3)	1 (12.5)	0.6403
Number (%) of patients censored	68 (66.0)	107 (69.0)	6 (75.0)	14 (87.5)	11 (91.7)	7 (87.5)	
Kaplan-Meier estimates of Dyspnea in months							
25% quantile (95% CI)	17.91 (6.374 to 21.224)	16.99 (10.152 to 21.191)	18.56 (2.037 to NC)	NC (7.556 to NC)	NC (18.464 to NC)	NC (11.499 to NC)	
Median (95% CI)	24.02 (21.224 to NC)	NC (NC to NC)	NC (2.037 to NC)	NC (10.908 to NC)	NC (NC to NC)	NC (11.499 to NC)	
75% quantile (95% CI)	NC (24.016 to NC)	NC (NC to NC)	NC (18.563 to NC)	NC (NC to NC)	NC (NC to NC)	NC (11.499 to NC)	
Comparison vs. Kd							
Log-Rank test p-value[a] vs Kd	-	0.4370		0.4409		0.3508	
Hazard ratio (95% CI) vs Kd	-	0.84 (0.54 to 1.30)		0.47 (0.06 to 3.38)		3.46 (0.22 to 55.78)	
P-value	-	0.4376		0.4513		0.3809	

A lower score represents a better level of quality of life. Clinical meaningful deterioration change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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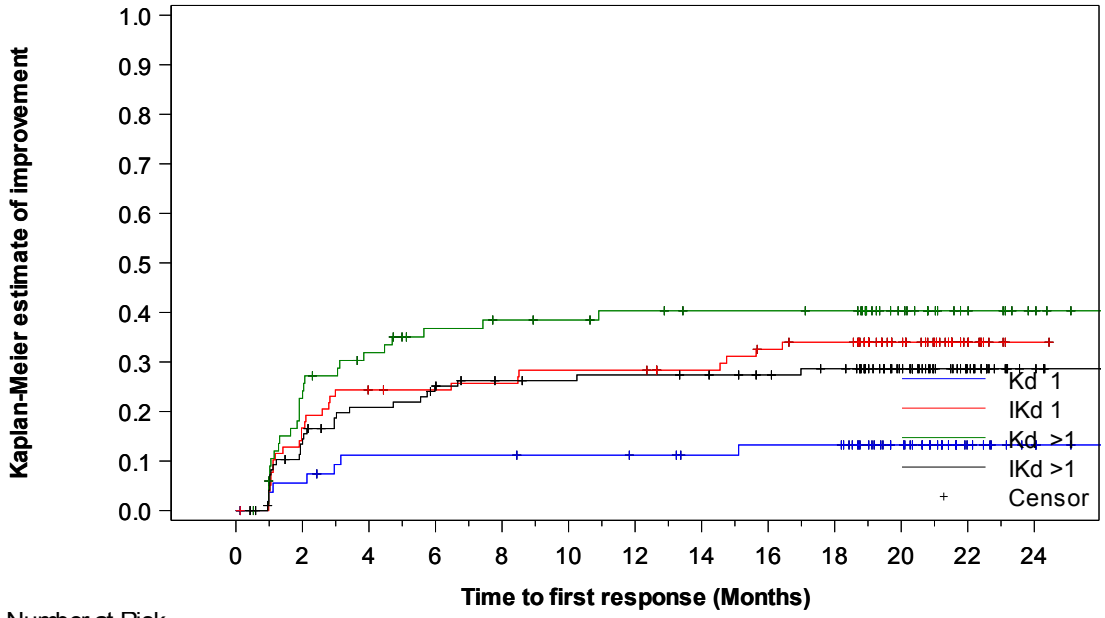
16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Dyspnea
16.2.6.1.2.10 Efficacy response data - Subgroup analyses by nb of prior lines
16.2.6.1.2.10.3 QLQ-C30 - Time to first improvement by 10 pt in dyspnea according to nb of prior lines (LOCF) - ITT population

	1		>1		
	Kd (N=55)	**IKd (N=79)**	**Kd (N=68)**	**IKd (N=100)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	7 (12.7)	26 (32.9)	26 (38.2)	27 (27.0)	0.0031
Number (%) of patients censored	48 (87.3)	53 (67.1)	42 (61.8)	73 (73.0)	
Kaplan-Meier estimates of Dyspnea in months					
25% quantile (95% CI)	NC (15.113 to NC)	6.47 (1.971 to NC)	2.04 (1.314 to 5.651)	5.98 (2.136 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (7.425 to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.0099		0.1034	
Hazard ratio (95% CI) vs Kd	-	2.86 (1.24 to 6.59)		0.64 (0.37 to 1.10)	
P-value	-	0.0137		0.1062	
Hazard ratio inverted (95% CI) vs IKd		-		1.56 (0.91 to 2.67)	

A lower score represents a better level of quality of life. Clinical meaningful improvement change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
PGM=DEVOPS/SAR650984/EFC15246/CIR_RWE/REPORT/PGM/eff_km_subgp_sr_sig_de_i_t.sas OUT=REPORT/OUTPUT/eff_km_c30_dys_impl_plne_de_i_t_x.rtf (07APR2021 14:32)

16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Dyspnea
16.2.6.1.2.10 Efficacy response data - Subgroup analyses by nb of prior lines
16.2.6.1.2.10.4 QLQ-C30 - Time to first improvement by 10 pt in dyspnea according to nb of prior lines - Kaplan-Meier curve (LOCF) - ITT population



Number at Risk

Kd 1	55	48	47	46	45	43	42	20	4
IKd 1	79	59	57	54	54	49	45	20	1
Kd >1	68	47	37	34	32	30	29	13	4
IKd >1	100	76	69	64	63	61	56	25	4

A lower score represents a better level of quality of life. Clinical meaningful improvement change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
PGM=DEVOPS/SAR650984/EFC15246/CIR_RWE/REPORT/PGM/eff_qlq_km_subgp_de_i_f.sas OUT=REPORT/OUTPUT/eff_km_c30_dys_impl_plne_de_i_f_x.rtf (07APR2021 15:11)

16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Dyspnea
16.2.6.1.2.10 Efficacy response data - Subgroup analyses by nb of prior lines
16.2.6.1.2.10.5 QLQ-C30 - Time to first deterioration by 10 pt in dyspnea according to nb of prior lines (LOCF) - ITT population

	1		>1		
	Kd (N=55)	**IKd (N=79)**	**Kd (N=68)**	**IKd (N=100)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	37 (67.3)	52 (65.8)	34 (50.0)	64 (64.0)	0.2539
Number (%) of patients censored	18 (32.7)	27 (34.2)	34 (50.0)	36 (36.0)	
Kaplan-Meier estimates of Dyspnea in months					
25% quantile (95% CI)	1.91 (1.084 to 2.004)	1.58 (1.051 to 2.070)	1.94 (1.117 to 3.713)	1.94 (1.314 to 2.366)	
Median (95% CI)	4.53 (2.004 to 6.637)	4.83 (2.858 to 9.922)	9.76 (4.698 to NC)	5.91 (2.924 to 10.218)	
75% quantile (95% CI)	NC (6.637 to NC)	NC (12.550 to NC)	NC (NC to NC)	NC (13.996 to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.9011		0.1301	
Hazard ratio (95% CI) vs Kd	-	0.97 (0.64 to 1.48)		1.38 (0.91 to 2.09)	
P-value	-	0.9008		0.1317	
Deterioration probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful deterioration change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
PGM=DEVOPS/SAR650984/EFC15246/CIR_RWE/REPORT/PGM/eff_km_subgp_sr_sig_de_i_t.sas OUT=REPORT/OUTPUT/eff_km_c30_dys_detl_plne_de_i_t_x.rtf (07APR2021 14:31)

16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Dyspnea
16.2.6.1.2.10 Efficacy response data - Subgroup analyses by nb of prior lines
16.2.6.1.2.10.6 QLQ-C30 - Time until permanent improvement by 10 pt in dyspnea according to nb of prior lines (LOCF) - ITT population

	1		>1		
	Kd (N=55)	**IKd (N=79)**	**Kd (N=68)**	**IKd (N=100)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	3 (5.5)	9 (11.4)	17 (25.0)	9 (9.0)	0.0160
Number (%) of patients censored	52 (94.5)	70 (88.6)	51 (75.0)	91 (91.0)	
Kaplan-Meier estimates of Dyspnea in months					
25% quantile (95% CI)	NC (NC to NC)	NC (19.910 to NC)	19.19 (12.945 to NC)	NC (NC to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (22.439 to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.2511		0.0036	
Hazard ratio (95% CI) vs Kd	-	2.11 (0.57 to 7.81)		0.32 (0.14 to 0.72)	
P-value	-	0.2621		0.0058	
Improvement probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful improvement change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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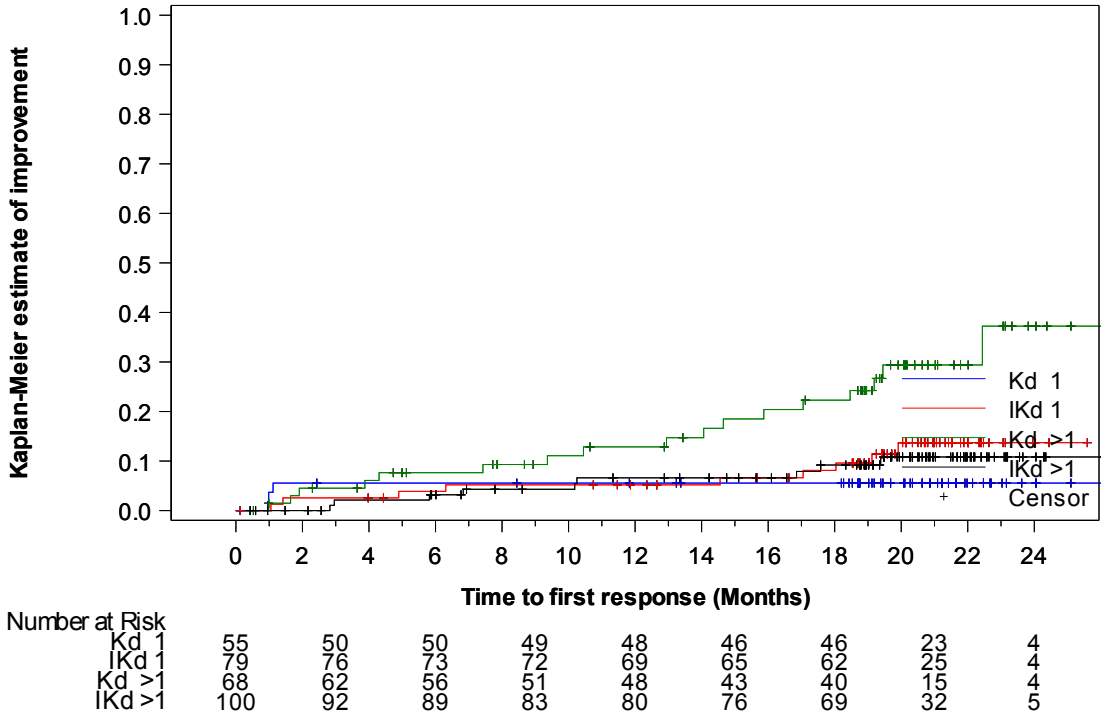
16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Dyspnea
16.2.6.1.2.10 Efficacy response data - Subgroup analyses by nb of prior lines
16.2.6.1.2.10.7 QLQ-C30 - Time until permanent improvement by 10 pt in dyspnea according to nb of prior lines - Kaplan-Meier curve (LOCF) - ITT population



A lower score represents a better level of quality of life. Clinical meaningful improvement change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
PGM=DEVOPS/SAR650984/EFC15246/CIR_RWE/REPORT/PGM/eff_qlq_km_subgp_de_i_f.sas OUT=REPORT/OUTPUT/eff_km_c30_dys_imppl_plne_de_i_f_x.rtf (07APR2021 15:11)

16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Dyspnea
16.2.6.1.2.10 Efficacy response data - Subgroup analyses by nb of prior lines
16.2.6.1.2.10.8 QLQ-C30 - Time until permanent deterioration by 10 pt in dyspnea according to nb of prior lines (LOCF) - ITT population

	1		>1		
	Kd (N=55)	**IKd (N=79)**	**Kd (N=68)**	**IKd (N=100)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	20 (36.4)	23 (29.1)	18 (26.5)	28 (28.0)	0.4571
Number (%) of patients censored	35 (63.6)	56 (70.9)	50 (73.5)	72 (72.0)	
Kaplan-Meier estimates of Dyspnea in months					
25% quantile (95% CI)	11.53 (1.971 to 22.209)	18.17 (9.922 to NC)	20.67 (11.926 to 21.684)	16.95 (9.265 to NC)	
Median (95% CI)	24.02 (20.600 to 24.016)	NC (NC to NC)	NC (21.224 to NC)	NC (NC to NC)	
75% quantile (95% CI)	24.02 (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.3504		0.8708	
Hazard ratio (95% CI) vs Kd	-	0.75 (0.41 to 1.37)		1.05 (0.58 to 1.90)	
P-value	-	0.3520		0.8715	
Deterioration probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful deterioration change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Dyspnea
16.2.6.1.2.11 Efficacy response data - Subgroup analyses by cytogenetic abnormality
16.2.6.1.2.11.3 QLQ-C30 - Time to first improvement by 10 pt in dyspnea according to cytogenetic abnormality (LOCF) - ITT population

	At least one		None		
	Kd (N=31)	**IKd (N=42)**	**Kd (N=77)**	**IKd (N=114)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	13 (41.9)	10 (23.8)	16 (20.8)	35 (30.7)	0.0215
Number (%) of patients censored	18 (58.1)	32 (76.2)	61 (79.2)	79 (69.3)	
Kaplan-Meier estimates of Dyspnea in months					
25% quantile (95% CI)	2.07 (0.986 to 5.651)	NC (2.037 to NC)	NC (2.957 to NC)	5.55 (1.971 to NC)	
Median (95% CI)	NC (4.468 to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.0630		0.1529	
Hazard ratio (95% CI) vs Kd	-	0.47 (0.20 to 1.06)		1.53 (0.85 to 2.77)	
P-value	-	0.0696		0.1561	
Improvement probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful improvement change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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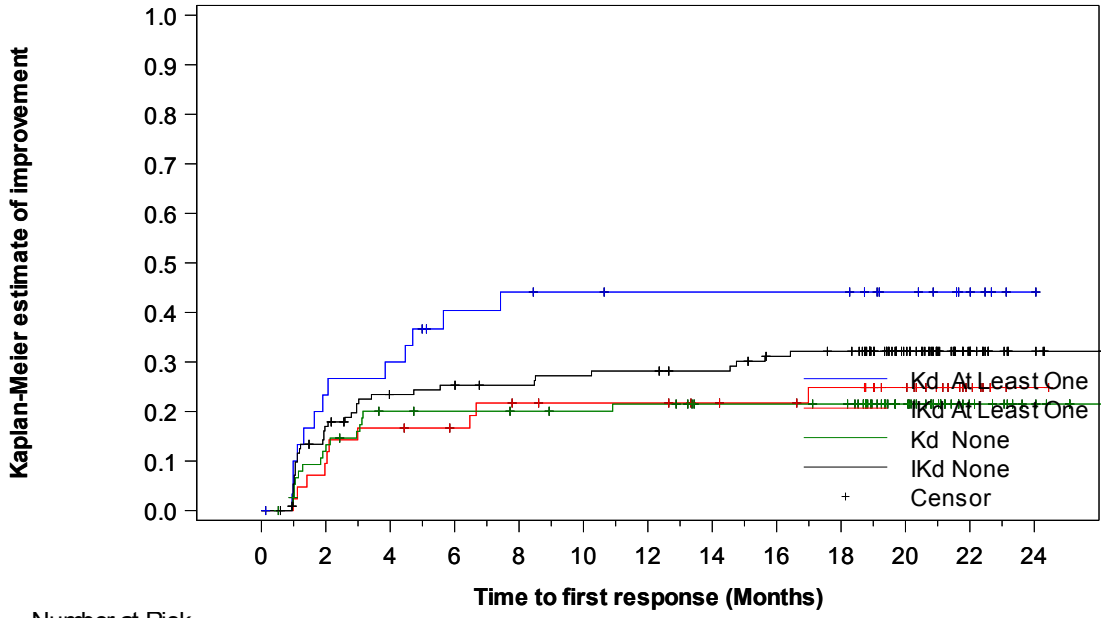
16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Dyspnea
16.2.6.1.2.11 Efficacy response data - Subgroup analyses by cytogenetic abnormality
16.2.6.1.2.11.4 QLQ-C30 - Time to first improvement by 10 pt in dyspnea according to cytogenetic abnormality - Kaplan-Meier curve (LOCF) - ITT population



Number at Risk									
Kd At Least One	31	22	16	14	13	13	13	7	1
IKd At Least One	42	35	33	29	29	26	24	12	1
Kd None	77	62	57	55	54	50	49	22	6
IKd None	114	85	80	76	75	71	66	26	4

A lower score represents a better level of quality of life. Clinical meaningful improvement change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
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16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Dyspnea
16.2.6.1.2.11 Efficacy response data - Subgroup analyses by cytogenetic abnormality
16.2.6.1.2.11.5 QLQ-C30 - Time to first deterioration by 10 pt in dyspnea according to cytogenetic abnormality (LOCF) - ITT population

	At least one		None		
	Kd (N=31)	**IKd (N=42)**	**Kd (N=77)**	**IKd (N=114)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	19 (61.3)	27 (64.3)	42 (54.5)	76 (66.7)	0.2548
Number (%) of patients censored	12 (38.7)	15 (35.7)	35 (45.5)	38 (33.3)	
Kaplan-Meier estimates of Dyspnea in months					
25% quantile (95% CI)	1.91 (1.018 to 2.891)	2.99 (1.051 to 4.895)	1.91 (1.117 to 2.037)	1.51 (1.084 to 1.906)	
Median (95% CI)	5.75 (2.825 to NC)	10.15 (4.665 to 19.811)	6.67 (3.943 to NC)	3.91 (2.267 to 6.702)	
75% quantile (95% CI)	NC (9.758 to NC)	NC (14.160 to NC)	NC (NC to NC)	NC (12.287 to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.7622		0.1136	
Hazard ratio (95% CI) vs Kd	-	0.91 (0.51 to 1.64)		1.35 (0.93 to 1.98)	
P-value	-	0.7623		0.1150	
Deterioration probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful deterioration change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Dyspnea
16.2.6.1.2.11 Efficacy response data - Subgroup analyses by cytogenetic abnormality
16.2.6.1.2.11.6 QLQ-C30 - Time until permanent improvement by 10 pt in dyspnea according to cytogenetic abnormality (LOCF) - ITT population

	At least one		None		
	Kd (N=31)	**IKd (N=42)**	**Kd (N=77)**	**IKd (N=114)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	10 (32.3)	2 (4.8)	8 (10.4)	13 (11.4)	0.0148
Number (%) of patients censored	21 (67.7)	40 (95.2)	69 (89.6)	101 (88.6)	
Kaplan-Meier estimates of Dyspnea in months					
25% quantile (95% CI)	19.19 (1.117 to 22.439)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Median (95% CI)	NC (19.187 to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (22.439 to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.0018		0.8971	
Hazard ratio (95% CI) vs Kd	-	0.13 (0.03 to 0.59)		1.06 (0.44 to 2.56)	
P-value	-	0.0083		0.8978	
Improvement probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful improvement change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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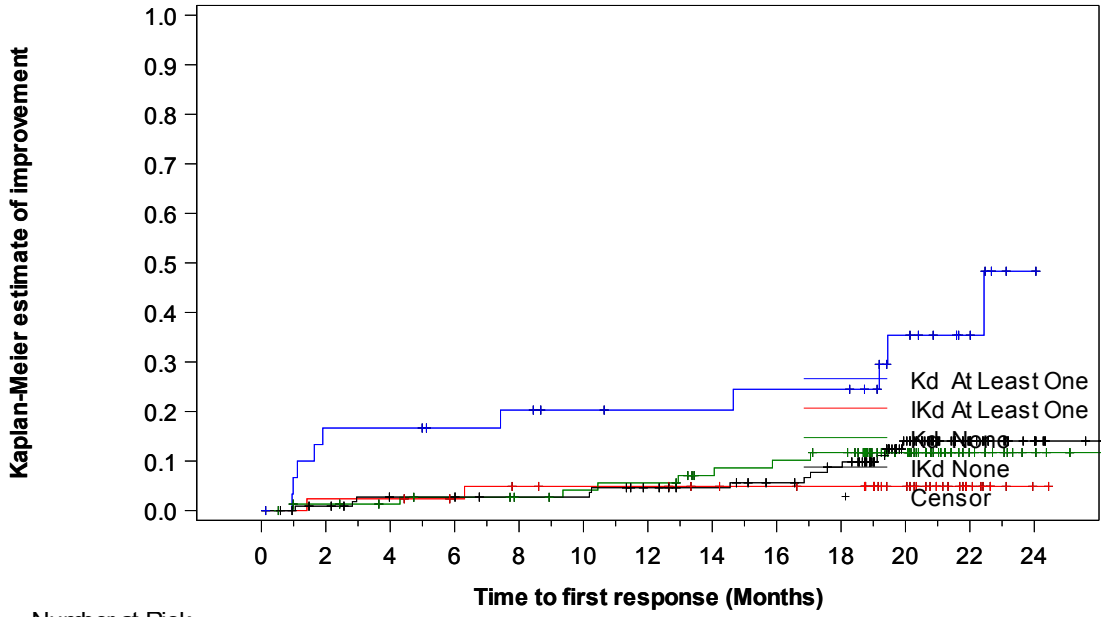
16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Dyspnea
16.2.6.1.2.11 Efficacy response data - Subgroup analyses by cytogenetic abnormality
16.2.6.1.2.11.7 QLQ-C30 - Time until permanent improvement by 10 pt in dyspnea according to cytogenetic abnormality - Kaplan-Meier curve (LOCF) - ITT population



Number at Risk									
Kd At Least One	31	25	23	20	19	18	18	8	1
IKd At Least One	42	41	39	36	36	33	32	15	1
Kd None	77	73	70	67	65	59	56	24	6
IKd None	114	106	105	103	98	93	86	33	8

A lower score represents a better level of quality of life. Clinical meaningful improvement change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
PGM=DEVOPS/SAR650984/EFC15246/CIR_RWE/REPORT/PGM/eff_qlq_km_subgp_de_i_f.sas OUT=REPORT/OUTPUT/eff_km_c30_dys_imppl_cyto_de_i_f_x.rtf (07APR2021 14:57)

16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Dyspnea
16.2.6.1.2.11 Efficacy response data - Subgroup analyses by cytogenetic abnormality
16.2.6.1.2.11.8 QLQ-C30 - Time until permanent deterioration by 10 pt in dyspnea according to cytogenetic abnormality (LOCF) - ITT population

	At least one		None		
	Kd (N=31)	**IKd (N=42)**	**Kd (N=77)**	**IKd (N=114)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	9 (29.0)	14 (33.3)	25 (32.5)	33 (28.9)	0.5507
Number (%) of patients censored	22 (71.0)	28 (66.7)	52 (67.5)	81 (71.1)	
Kaplan-Meier estimates of Dyspnea in months					
25% quantile (95% CI)	18.56 (6.374 to NC)	14.00 (4.665 to NC)	19.22 (5.815 to 21.224)	17.35 (10.152 to NC)	
Median (95% CI)	NC (19.745 to NC)	NC (21.224 to NC)	24.02 (21.224 to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (24.016 to NC)	NC (NC to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.7684		0.5491	
Hazard ratio (95% CI) vs Kd	-	1.13 (0.49 to 2.62)		0.85 (0.51 to 1.44)	
P-value	-	0.7686		0.5495	
Deterioration probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful deterioration change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Dyspnea
16.2.6.1.2.12 Efficacy response data - Subgroup analyses by MM type at SE
16.2.6.1.2.12.3 QLQ-C30 - Time to first improvement by 10 pt in dyspnea according to MM type at SE (LOCF) - ITT population

	IgG		Non-IgG		
	Kd (N=85)	**IKd (N=126)**	**Kd (N=38)**	**IKd (N=53)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	23 (27.1)	40 (31.7)	10 (26.3)	13 (24.5)	0.4679
Number (%) of patients censored	62 (72.9)	86 (68.3)	28 (73.7)	40 (75.5)	
Kaplan-Meier estimates of Dyspnea in months					
25% quantile (95% CI)	7.43 (1.906 to NC)	5.75 (2.004 to 16.427)	3.15 (1.314 to NC)	16.99 (2.037 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.4670		0.6893	
Hazard ratio (95% CI) vs Kd	-	1.21 (0.72 to 2.02)		0.85 (0.37 to 1.93)	
P-value	-	0.4677		0.6896	
Improvement probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful improvement change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
PGM=DEVOPS/SAR650984/EFC15246/CIR_RWE/REPORT/PGM/eff_km_subgp_sr_sig_de_i_t.sas OUT=REPORT/OUTPUT/eff_km_c30_dys_impl_semm_de_i_t_x.rtf (07APR2021 14:32)

16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Dyspnea
16.2.6.1.2.12 Efficacy response data - Subgroup analyses by MM type at SE
16.2.6.1.2.12.4 QLQ-C30 - Time to first deterioration by 10 pt in dyspnea according to MM type at SE (LOCF) - ITT population

	IgG		Non-IgG		
	Kd (N=85)	**IKd (N=126)**	**Kd (N=38)**	**IKd (N=53)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	50 (58.8)	84 (66.7)	21 (55.3)	32 (60.4)	0.4754
Number (%) of patients censored	35 (41.2)	42 (33.3)	17 (44.7)	21 (39.6)	
Kaplan-Meier estimates of Dyspnea in months					
25% quantile (95% CI)	1.31 (1.117 to 2.037)	1.87 (1.117 to 1.938)	1.99 (1.018 to 3.713)	2.83 (1.084 to 4.895)	
Median (95% CI)	5.65 (2.990 to 12.912)	3.75 (2.793 to 6.702)	6.37 (2.891 to NC)	8.34 (4.665 to 20.731)	
75% quantile (95% CI)	NC (NC to NC)	NC (12.287 to NC)	NC (19.548 to NC)	NC (13.996 to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.2309		0.9298	
Hazard ratio (95% CI) vs Kd	-	1.24 (0.87 to 1.76)		0.98 (0.56 to 1.69)	
P-value	-	0.2318		0.9296	
Deterioration probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful deterioration change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
PGM=DEVOPS/SAR650984/EFC15246/CIR_RWE/REPORT/PGM/eff_km_subgp_sr_sig_de_i_t.sas OUT=REPORT/OUTPUT/eff_km_c30_dys_detl_semm_de_i_t_x.rtf (07APR2021 14:31)

16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Dyspnea
16.2.6.1.2.12 Efficacy response data - Subgroup analyses by MM type at SE
16.2.6.1.2.12.5 QLQ-C30 - Time until permanent improvement by 10 pt in dyspnea according to MM type at SE (LOCF) - ITT population

	IgG		Non-IgG		
	Kd (N=85)	**IKd (N=126)**	**Kd (N=38)**	**IKd (N=53)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	15 (17.6)	15 (11.9)	5 (13.2)	3 (5.7)	0.5058
Number (%) of patients censored	70 (82.4)	111 (88.1)	33 (86.8)	50 (94.3)	
Kaplan-Meier estimates of Dyspnea in months					
25% quantile (95% CI)	22.44 (18.464 to NC)	NC (NC to NC)	NC (3.877 to NC)	NC (NC to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.2560		0.1747	
Hazard ratio (95% CI) vs Kd	-	0.66 (0.32 to 1.36)		0.38 (0.09 to 1.61)	
P-value	-	0.2594		0.1912	
Improvement probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful improvement change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Dyspnea
16.2.6.1.2.12 Efficacy response data - Subgroup analyses by MM type at SE
16.2.6.1.2.12.6 QLQ-C30 - Time until permanent deterioration by 10 pt in dyspnea according to MM type at SE (LOCF) - ITT population

	IgG		Non-IgG		
	Kd (N=85)	**IKd (N=126)**	**Kd (N=38)**	**IKd (N=53)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	27 (31.8)	34 (27.0)	11 (28.9)	17 (32.1)	0.6479
Number (%) of patients censored	58 (68.2)	92 (73.0)	27 (71.1)	36 (67.9)	
Kaplan-Meier estimates of Dyspnea in months					
25% quantile (95% CI)	18.46 (2.990 to 21.224)	17.35 (11.170 to NC)	20.60 (6.374 to 24.016)	15.93 (5.520 to NC)	
Median (95% CI)	NC (21.224 to NC)	NC (NC to NC)	24.02 (20.600 to NC)	NC (21.224 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (24.016 to NC)	NC (NC to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.5411		0.8770	
Hazard ratio (95% CI) vs Kd	-	0.85 (0.52 to 1.42)		1.06 (0.49 to 2.28)	
P-value	-	0.5415		0.8777	
Deterioration probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful deterioration change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Dyspnea
16.2.6.1.2.13 Efficacy response data - Subgroup analyses by previous autologous stem-cell
16.2.6.1.2.13.3 QLQ-C30 - Time to first improvement by 10 pt in dyspnea according to previous autologous stem-cell (LOCF) - ITT population

	Yes		No		
	Kd (N=69)	**IKd (N=116)**	**Kd (N=54)**	**IKd (N=63)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	18 (26.1)	32 (27.6)	15 (27.8)	21 (33.3)	0.7039
Number (%) of patients censored	51 (73.9)	84 (72.4)	39 (72.2)	42 (66.7)	
Kaplan-Meier estimates of Dyspnea in months					
25% quantile (95% CI)	5.65 (1.906 to NC)	8.51 (2.957 to NC)	4.47 (1.840 to NC)	2.60 (1.906 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.8997		0.5377	
Hazard ratio (95% CI) vs Kd	-	1.04 (0.58 to 1.85)		1.23 (0.63 to 2.39)	
P-value	-	0.9002		0.5384	
Improvement probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful improvement change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Dyspnea
16.2.6.1.2.13 Efficacy response data - Subgroup analyses by previous autologous stem-cell
16.2.6.1.2.13.4 QLQ-C30 - Time to first deterioration by 10 pt in dyspnea according to previous autologous stem-cell (LOCF) - ITT population

	Yes		No		
	Kd (N=69)	**IKd (N=116)**	**Kd (N=54)**	**IKd (N=63)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	40 (58.0)	75 (64.7)	31 (57.4)	41 (65.1)	0.7683
Number (%) of patients censored	29 (42.0)	41 (35.3)	23 (42.6)	22 (34.9)	
Kaplan-Meier estimates of Dyspnea in months					
25% quantile (95% CI)	1.20 (1.051 to 2.037)	1.87 (1.117 to 1.971)	2.00 (1.216 to 3.713)	1.97 (1.248 to 2.924)	
Median (95% CI)	5.65 (2.825 to NC)	4.90 (2.990 to 10.152)	6.37 (3.713 to NC)	5.65 (2.924 to 10.349)	
75% quantile (95% CI)	NC (NC to NC)	NC (18.694 to NC)	NC (NC to NC)	NC (10.349 to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.5625		0.3848	
Hazard ratio (95% CI) vs Kd	-	1.12 (0.76 to 1.64)		1.23 (0.77 to 1.96)	
P-value	-	0.5628		0.3856	
Deterioration probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful deterioration change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Dyspnea
16.2.6.1.2.13 Efficacy response data - Subgroup analyses by previous autologous stem-cell
16.2.6.1.2.13.5 QLQ-C30 - Time until permanent improvement by 10 pt in dyspnea according to previous autologous stem-cell (LOCF) - ITT population

	Yes		No		
	Kd (N=69)	**IKd (N=116)**	**Kd (N=54)**	**IKd (N=63)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	11 (15.9)	12 (10.3)	9 (16.7)	6 (9.5)	0.8048
Number (%) of patients censored	58 (84.1)	104 (89.7)	45 (83.3)	57 (90.5)	
Kaplan-Meier estimates of Dyspnea in months					
25% quantile (95% CI)	NC (19.187 to NC)	NC (NC to NC)	NC (14.062 to NC)	NC (NC to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.2756		0.2344	
Hazard ratio (95% CI) vs Kd	-	0.64 (0.28 to 1.44)		0.54 (0.19 to 1.52)	
P-value	-	0.2797		0.2418	
Improvement probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful improvement change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Dyspnea
16.2.6.1.2.13 Efficacy response data - Subgroup analyses by previous autologous stem-cell
16.2.6.1.2.13.6 QLQ-C30 - Time until permanent deterioration by 10 pt in dyspnea according to previous autologous stem-cell (LOCF) - ITT population

	Yes		No		
	Kd (N=69)	**IKd (N=116)**	**Kd (N=54)**	**IKd (N=63)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	18 (26.1)	34 (29.3)	20 (37.0)	17 (27.0)	0.3029
Number (%) of patients censored	51 (73.9)	82 (70.7)	34 (63.0)	46 (73.0)	
Kaplan-Meier estimates of Dyspnea in months					
25% quantile (95% CI)	21.22 (2.990 to NC)	16.03 (9.035 to NC)	18.46 (6.374 to 20.600)	19.61 (11.499 to NC)	
Median (95% CI)	NC (21.684 to NC)	NC (NC to NC)	22.21 (19.745 to 24.016)	NC (21.224 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	24.02 (NC to NC)	NC (NC to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.7466		0.2537	
Hazard ratio (95% CI) vs Kd	-	1.10 (0.62 to 1.95)		0.69 (0.36 to 1.31)	
P-value	-	0.7467		0.2564	
Deterioration probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful deterioration change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Dyspnea
16.2.6.1.2.14 Efficacy response data - Subgroup analyses by baseline eGFR (MDRD)
16.2.6.1.2.14.3 QLQ-C30 - Time to first improvement by 10 pt in dyspnea according to baseline eGFR (MDRD) (LOCF) - ITT population

	>=60 mL/min/1.73m2		<60 mL/min/1.73m2		
	Kd (N=93)	**IKd (N=122)**	**Kd (N=18)**	**IKd (N=43)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	24 (25.8)	32 (26.2)	7 (38.9)	16 (37.2)	0.5684
Number (%) of patients censored	69 (74.2)	90 (73.8)	11 (61.1)	27 (62.8)	
Kaplan-Meier estimates of Dyspnea in months					
25% quantile (95% CI)	7.43 (2.004 to NC)	8.51 (2.793 to NC)	3.06 (0.986 to 15.113)	5.55 (1.938 to 16.986)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (3.055 to NC)	NC (16.427 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (15.113 to NC)	NC (NC to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.8543		0.5178	
Hazard ratio (95% CI) vs Kd	-	1.05 (0.62 to 1.78)		0.75 (0.31 to 1.82)	
P-value	-	0.8547		0.5192	
Improvement probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful improvement change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Dyspnea
16.2.6.1.2.14 Efficacy response data - Subgroup analyses by baseline eGFR (MDRD)
16.2.6.1.2.14.4 QLQ-C30 - Time to first deterioration by 10 pt in dyspnea according to baseline eGFR (MDRD) (LOCF) - ITT population

	>=60 mL/min/1.73m2		<60 mL/min/1.73m2		
	Kd (N=93)	**IKd (N=122)**	**Kd (N=18)**	**IKd (N=43)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	58 (62.4)	80 (65.6)	10 (55.6)	30 (69.8)	0.6701
Number (%) of patients censored	35 (37.6)	42 (34.4)	8 (44.4)	13 (30.2)	
Kaplan-Meier estimates of Dyspnea in months					
25% quantile (95% CI)	1.23 (1.117 to 1.971)	1.87 (1.117 to 1.971)	4.44 (1.150 to 5.815)	1.91 (1.084 to 2.924)	
Median (95% CI)	4.48 (2.070 to 7.918)	4.67 (2.825 to 6.538)	6.24 (4.041 to NC)	4.83 (2.793 to 12.386)	
75% quantile (95% CI)	NC (NC to NC)	NC (13.996 to NC)	NC (5.815 to NC)	NC (10.152 to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.5440		0.4641	
Hazard ratio (95% CI) vs Kd	-	1.11 (0.79 to 1.56)		1.31 (0.64 to 2.68)	
P-value	-	0.5442		0.4655	
Deterioration probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful deterioration change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Dyspnea
16.2.6.1.2.14 Efficacy response data - Subgroup analyses by baseline eGFR (MDRD)
16.2.6.1.2.14.5 QLQ-C30 - Time until permanent improvement by 10 pt in dyspnea according to baseline eGFR (MDRD) (LOCF) - ITT population

	>=60 mL/min/1.73m2		<60 mL/min/1.73m2		
	Kd (N=93)	**IKd (N=122)**	**Kd (N=18)**	**IKd (N=43)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	14 (15.1)	9 (7.4)	4 (22.2)	6 (14.0)	0.9353
Number (%) of patients censored	79 (84.9)	113 (92.6)	14 (77.8)	37 (86.0)	
Kaplan-Meier estimates of Dyspnea in months					
25% quantile (95% CI)	NC (19.450 to NC)	NC (NC to NC)	15.87 (0.986 to NC)	NC (19.384 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (12.945 to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.0993		0.2049	
Hazard ratio (95% CI) vs Kd	-	0.50 (0.22 to 1.16)		0.45 (0.13 to 1.60)	
P-value	-	0.1061		0.2168	
Improvement probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful improvement change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
PGM=DEVOPS/SAR650984/EFC15246/CIR_RWE/REPORT/PGM/eff_km_subgp_sr_sig_de_i_t.sas OUT=REPORT/OUTPUT/eff_km_c30_dys_imppl_crcl_de_i_t_x.rtf (07APR2021 14:32)

16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Dyspnea
16.2.6.1.2.14 Efficacy response data - Subgroup analyses by baseline eGFR (MDRD)
16.2.6.1.2.14.6 QLQ-C30 - Time until permanent deterioration by 10 pt in dyspnea according to baseline eGFR (MDRD) (LOCF) - ITT population

	>=60 mL/min/1.73m2		<60 mL/min/1.73m2		
	Kd (N=93)	**IKd (N=122)**	**Kd (N=18)**	**IKd (N=43)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	34 (36.6)	36 (29.5)	2 (11.1)	11 (25.6)	0.3165
Number (%) of patients censored	59 (63.4)	86 (70.5)	16 (88.9)	32 (74.4)	
Kaplan-Meier estimates of Dyspnea in months					
25% quantile (95% CI)	17.91 (5.815 to 20.600)	15.93 (9.035 to 21.191)	NC (1.314 to NC)	19.88 (10.973 to NC)	
Median (95% CI)	24.02 (21.224 to NC)	NC (NC to NC)	NC (NC to NC)	NC (21.224 to NC)	
75% quantile (95% CI)	NC (24.016 to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.4329		0.4149	
Hazard ratio (95% CI) vs Kd	-	0.83 (0.52 to 1.33)		1.85 (0.41 to 8.38)	
P-value	-	0.4336		0.4222	
Deterioration probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful deterioration change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
PGM=DEVOPS/SAR650984/EFC15246/CIR_RWE/REPORT/PGM/eff_km_subgp_sr_sig_de_i_t.sas OUT=REPORT/OUTPUT/eff_km_c30_dys_detpl_crcl_de_i_t_x.rtf (07APR2021 14:32)

16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Dyspnea
16.2.6.1.2.15 Efficacy response data - Subgroup analyses by previous treatment with PI
16.2.6.1.2.15.3 QLQ-C30 - Time to first improvement by 10 pt in dyspnea according to previous treatment with PI (LOCF) - ITT population

	Yes		No		
	Kd (N=47)	**IKd (N=81)**	**Kd (N=76)**	**IKd (N=98)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	11 (23.4)	22 (27.2)	22 (28.9)	31 (31.6)	0.8800
Number (%) of patients censored	36 (76.6)	59 (72.8)	54 (71.1)	67 (68.4)	
Kaplan-Meier estimates of Dyspnea in months					
25% quantile (95% CI)	NC (1.906 to NC)	14.55 (2.037 to NC)	4.70 (1.906 to NC)	5.55 (2.004 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.6794		0.7786	
Hazard ratio (95% CI) vs Kd	-	1.16 (0.56 to 2.40)		1.08 (0.63 to 1.87)	
P-value	-	0.6797		0.7798	
Improvement probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful improvement change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
PGM=DEVOPS/SAR650984/EFC15246/CIR_RWE/REPORT/PGM/eff_km_subgp_sr_sig_de_i_t.sas OUT=REPORT/OUTPUT/eff_km_c30_dys_impl_pi_de_i_t_x.rtf (07APR2021 14:32)

16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Dyspnea
16.2.6.1.2.15 Efficacy response data - Subgroup analyses by previous treatment with PI
16.2.6.1.2.15.4 QLQ-C30 - Time to first deterioration by 10 pt in dyspnea according to previous treatment with PI (LOCF) - ITT population

	Yes		No		
	Kd (N=47)	**IKd (N=81)**	**Kd (N=76)**	**IKd (N=98)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	27 (57.4)	55 (67.9)	44 (57.9)	61 (62.2)	0.5032
Number (%) of patients censored	20 (42.6)	26 (32.1)	32 (42.1)	37 (37.8)	
Kaplan-Meier estimates of Dyspnea in months					
25% quantile (95% CI)	1.94 (1.117 to 2.990)	1.87 (1.051 to 2.136)	1.91 (1.084 to 2.891)	1.91 (1.183 to 2.267)	
Median (95% CI)	5.96 (2.004 to NC)	5.22 (2.924 to 10.908)	5.82 (3.943 to 19.548)	4.90 (2.891 to 10.152)	
75% quantile (95% CI)	NC (NC to NC)	20.73 (12.550 to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.2292		0.7534	
Hazard ratio (95% CI) vs Kd	-	1.33 (0.84 to 2.10)		1.06 (0.72 to 1.57)	
P-value	-	0.2308		0.7545	
Deterioration probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful deterioration change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
PGM=DEVOPS/SAR650984/EFC15246/CIR_RWE/REPORT/PGM/eff_km_subgp_sr_sig_de_i_t.sas OUT=REPORT/OUTPUT/eff_km_c30_dys_detl_pi_de_i_t_x.rtf (07APR2021 14:31)

16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Dyspnea
16.2.6.1.2.15 Efficacy response data - Subgroup analyses by previous treatment with PI
16.2.6.1.2.15.5 QLQ-C30 - Time until permanent improvement by 10 pt in dyspnea according to previous treatment with PI (LOCF) - ITT population

	Yes		No		
	Kd (N=47)	**IKd (N=81)**	**Kd (N=76)**	**IKd (N=98)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	8 (17.0)	4 (4.9)	12 (15.8)	14 (14.3)	0.1450
Number (%) of patients censored	39 (83.0)	77 (95.1)	64 (84.2)	84 (85.7)	
Kaplan-Meier estimates of Dyspnea in months					
25% quantile (95% CI)	NC (14.653 to NC)	NC (NC to NC)	22.44 (17.051 to NC)	NC (19.910 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (22.439 to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.0267		0.6401	
Hazard ratio (95% CI) vs Kd	-	0.28 (0.08 to 0.93)		0.83 (0.38 to 1.80)	
P-value	-	0.0381		0.6406	
Improvement probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful improvement change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
PGM=DEVOPS/SAR650984/EFC15246/CIR_RWE/REPORT/PGM/eff_km_subgp_sr_sig_de_i_t.sas OUT=REPORT/OUTPUT/eff_km_c30_dys_imppl_pi_de_i_t_x.rtf (07APR2021 14:32)

16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Dyspnea
16.2.6.1.2.15 Efficacy response data - Subgroup analyses by previous treatment with PI
16.2.6.1.2.15.6 QLQ-C30 - Time until permanent deterioration by 10 pt in dyspnea according to previous treatment with PI (LOCF) - ITT population

	Yes		No		
	Kd (N=47)	**IKd (N=81)**	**Kd (N=76)**	**IKd (N=98)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	16 (34.0)	26 (32.1)	22 (28.9)	25 (25.5)	0.5936
Number (%) of patients censored	31 (66.0)	55 (67.9)	54 (71.1)	73 (74.5)	
Kaplan-Meier estimates of Dyspnea in months					
25% quantile (95% CI)	18.46 (2.990 to 20.665)	14.00 (7.556 to 21.191)	19.22 (5.815 to 22.209)	17.77 (9.955 to NC)	
Median (95% CI)	24.02 (20.600 to NC)	NC (21.191 to NC)	NC (21.684 to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (24.016 to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.9727		0.4847	
Hazard ratio (95% CI) vs Kd	-	1.01 (0.54 to 1.89)		0.82 (0.46 to 1.45)	
P-value	-	0.9727		0.4855	
Deterioration probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful deterioration change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Dyspnea
16.2.6.1.2.16 Efficacy response data - Subgroup analyses by previous treatment with IMiD
16.2.6.1.2.16.3 QLQ-C30 - Time to first improvement by 10 pt in dyspnea according to previous treatment with IMiD (LOCF) - ITT population

	Yes		No		
	Kd (N=62)	**IKd (N=81)**	**Kd (N=61)**	**IKd (N=98)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	20 (32.3)	25 (30.9)	13 (21.3)	28 (28.6)	0.2710
Number (%) of patients censored	42 (67.7)	56 (69.1)	48 (78.7)	70 (71.4)	
Kaplan-Meier estimates of Dyspnea in months					
25% quantile (95% CI)	3.12 (1.281 to NC)	5.75 (2.595 to NC)	NC (3.055 to NC)	6.67 (1.971 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.6641		0.2765	
Hazard ratio (95% CI) vs Kd	-	0.88 (0.49 to 1.58)		1.44 (0.74 to 2.78)	
P-value	-	0.6643		0.2792	
Improvement probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful improvement change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Dyspnea
16.2.6.1.2.16 Efficacy response data - Subgroup analyses by previous treatment with IMiD
16.2.6.1.2.16.4 QLQ-C30 - Time to first deterioration by 10 pt in dyspnea according to previous treatment with IMiD (LOCF) - ITT population

	Yes		No		
	Kd (N=62)	**IKd (N=81)**	**Kd (N=61)**	**IKd (N=98)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	31 (50.0)	54 (66.7)	40 (65.6)	62 (63.3)	0.1512
Number (%) of patients censored	31 (50.0)	27 (33.3)	21 (34.4)	36 (36.7)	
Kaplan-Meier estimates of Dyspnea in months					
25% quantile (95% CI)	1.97 (1.117 to 4.041)	1.87 (1.150 to 1.938)	1.58 (1.117 to 2.037)	1.97 (1.084 to 2.563)	
Median (95% CI)	8.44 (4.041 to NC)	4.90 (2.793 to 10.152)	4.80 (2.037 to 7.392)	5.59 (2.990 to 10.218)	
75% quantile (95% CI)	NC (NC to NC)	NC (12.287 to NC)	NC (9.758 to NC)	NC (13.996 to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.0960		0.7862	
Hazard ratio (95% CI) vs Kd	-	1.45 (0.93 to 2.26)		0.95 (0.64 to 1.41)	
P-value	-	0.0979		0.7849	
Deterioration probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful deterioration change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Dyspnea
16.2.6.1.2.16 Efficacy response data - Subgroup analyses by previous treatment with IMiD
16.2.6.1.2.16.5 QLQ-C30 - Time until permanent improvement by 10 pt in dyspnea according to previous treatment with IMiD (LOCF) - ITT population

	Yes		No		
	Kd (N=62)	**IKd (N=81)**	**Kd (N=61)**	**IKd (N=98)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	14 (22.6)	10 (12.3)	6 (9.8)	8 (8.2)	0.4241
Number (%) of patients censored	48 (77.4)	71 (87.7)	55 (90.2)	90 (91.8)	
Kaplan-Meier estimates of Dyspnea in months					
25% quantile (95% CI)	22.44 (10.448 to NC)	NC (NC to NC)	NC (19.450 to NC)	NC (NC to NC)	
Median (95% CI)	NC (22.439 to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.0802		0.7207	
Hazard ratio (95% CI) vs Kd	-	0.49 (0.22 to 1.11)		0.82 (0.29 to 2.38)	
P-value	-	0.0867		0.7211	
Improvement probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful improvement change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Dyspnea
16.2.6.1.2.16 Efficacy response data - Subgroup analyses by previous treatment with IMiD
16.2.6.1.2.16.6 QLQ-C30 - Time until permanent deterioration by 10 pt in dyspnea according to previous treatment with IMiD (LOCF) - ITT population

	Yes		No		
	Kd (N=62)	**IKd (N=81)**	**Kd (N=61)**	**IKd (N=98)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	16 (25.8)	19 (23.5)	22 (36.1)	32 (32.7)	0.9410
Number (%) of patients censored	46 (74.2)	62 (76.5)	39 (63.9)	66 (67.3)	
Kaplan-Meier estimates of Dyspnea in months					
25% quantile (95% CI)	21.22 (8.444 to 24.016)	21.22 (10.908 to NC)	13.17 (2.990 to 20.665)	14.00 (9.528 to 18.464)	
Median (95% CI)	24.02 (22.209 to 24.016)	NC (NC to NC)	21.68 (20.665 to NC)	NC (21.191 to NC)	
75% quantile (95% CI)	24.02 (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.6455		0.7079	
Hazard ratio (95% CI) vs Kd	-	0.86 (0.44 to 1.67)		0.90 (0.52 to 1.55)	
P-value	-	0.6458		0.7080	
Deterioration probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful deterioration change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Dyspnea
16.2.6.1.2.17 Efficacy response data - Subgroup analyses by previous treatment with PI and IMiD
16.2.6.1.2.17.3 QLQ-C30 - Time to first improvement by 10 pt in dyspnea according to previous treatment with PI and IMiD (LOCF) - ITT population

	Yes		No		
	Kd (N=17)	**IKd (N=23)**	**Kd (N=106)**	**IKd (N=156)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	5 (29.4)	6 (26.1)	28 (26.4)	47 (30.1)	0.5815
Number (%) of patients censored	12 (70.6)	17 (73.9)	78 (73.6)	109 (69.9)	
Kaplan-Meier estimates of Dyspnea in months					
25% quantile (95% CI)	3.27 (0.953 to NC)	3.42 (1.216 to NC)	7.43 (2.136 to NC)	6.47 (2.793 to NC)	
Median (95% CI)	NC (2.070 to NC)	NC (3.417 to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.7535		0.5594	
Hazard ratio (95% CI) vs Kd	-	0.83 (0.25 to 2.71)		1.15 (0.72 to 1.84)	
P-value	-	0.7539		0.5597	
Improvement probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful improvement change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
PGM=DEVOPS/SAR650984/EFC15246/CIR_RWE/REPORT/PGM/eff_km_subgp_sr_sig_de_i_t.sas OUT=REPORT/OUTPUT/eff_km_c30_dys_impl_piimid_de_i_t_x.rtf (07APR2021 14:32)

16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Dyspnea
16.2.6.1.2.17 Efficacy response data - Subgroup analyses by previous treatment with PI and IMiD
16.2.6.1.2.17.4 QLQ-C30 - Time to first deterioration by 10 pt in dyspnea according to previous treatment with PI and IMiD (LOCF) - ITT population

	Yes		No		
	Kd (N=17)	**IKd (N=23)**	**Kd (N=106)**	**IKd (N=156)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	8 (47.1)	16 (69.6)	63 (59.4)	100 (64.1)	0.3276
Number (%) of patients censored	9 (52.9)	7 (30.4)	43 (40.6)	56 (35.9)	
Kaplan-Meier estimates of Dyspnea in months					
25% quantile (95% CI)	1.95 (0.986 to 9.988)	1.51 (0.986 to 2.825)	1.91 (1.117 to 2.825)	1.91 (1.216 to 2.136)	
Median (95% CI)	NC (1.938 to NC)	6.54 (1.873 to 18.694)	5.65 (3.745 to 9.758)	5.22 (3.745 to 8.772)	
75% quantile (95% CI)	NC (9.988 to NC)	NC (6.538 to NC)	NC (NC to NC)	NC (19.811 to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.1962		0.5576	
Hazard ratio (95% CI) vs Kd	-	1.74 (0.74 to 4.08)		1.10 (0.80 to 1.51)	
P-value	-	0.2019		0.5577	
Deterioration probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful deterioration change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
PGM=DEVOPS/SAR650984/EFC15246/CIR_RWE/REPORT/PGM/eff_km_subgp_sr_sig_de_i_t.sas OUT=REPORT/OUTPUT/eff_km_c30_dys_detl_piimid_de_i_t_x.rtf (07APR2021 14:31)

16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Dyspnea
16.2.6.1.2.17 Efficacy response data - Subgroup analyses by previous treatment with PI and IMiD
16.2.6.1.2.17.5 QLQ-C30 - Time until permanent improvement by 10 pt in dyspnea according to previous treatment with PI and IMiD (LOCF) - ITT population

	Yes		No		
	Kd (N=17)	**IKd (N=23)**	**Kd (N=106)**	**IKd (N=156)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	4 (23.5)	1 (4.3)	16 (15.1)	17 (10.9)	0.2211
Number (%) of patients censored	13 (76.5)	22 (95.7)	90 (84.9)	139 (89.1)	
Kaplan-Meier estimates of Dyspnea in months					
25% quantile (95% CI)	14.65 (0.953 to NC)	NC (1.413 to NC)	NC (19.450 to NC)	NC (NC to NC)	
Median (95% CI)	NC (14.653 to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.0675		0.2966	
Hazard ratio (95% CI) vs Kd	-	0.17 (0.02 to 1.49)		0.70 (0.35 to 1.38)	
P-value	-	0.1086		0.2992	

A lower score represents a better level of quality of life. Clinical meaningful improvement change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Dyspnea
16.2.6.1.2.17 Efficacy response data - Subgroup analyses by previous treatment with PI and IMiD
16.2.6.1.2.17.6 QLQ-C30 - Time until permanent deterioration by 10 pt in dyspnea according to previous treatment with PI and IMiD (LOCF) - ITT population

	Yes		No		
	Kd (N=17)	**IKd (N=23)**	**Kd (N=106)**	**IKd (N=156)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	4 (23.5)	6 (26.1)	34 (32.1)	45 (28.8)	0.6054
Number (%) of patients censored	13 (76.5)	17 (73.9)	72 (67.9)	111 (71.2)	
Kaplan-Meier estimates of Dyspnea in months					
25% quantile (95% CI)	24.02 (1.314 to 24.016)	21.45 (1.248 to NC)	18.17 (8.444 to 21.224)	16.95 (10.973 to 21.224)	
Median (95% CI)	24.02 (20.600 to 24.016)	NC (21.454 to NC)	NC (21.224 to NC)	NC (NC to NC)	
75% quantile (95% CI)	24.02 (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.5609		0.5294	
Hazard ratio (95% CI) vs Kd	-	1.50 (0.38 to 6.02)		0.87 (0.56 to 1.35)	
P-value	-	0.5637		0.5297	
Deterioration probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful deterioration change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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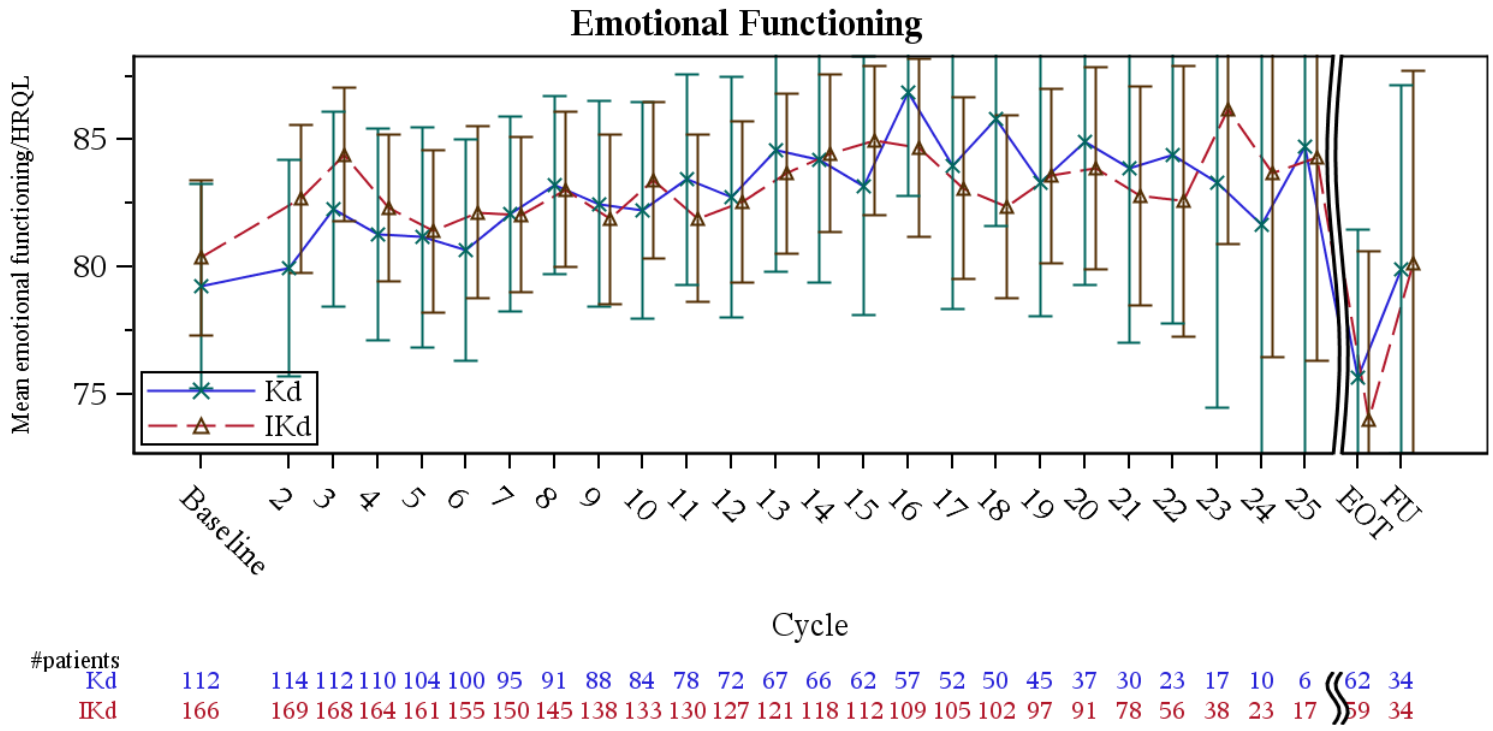
16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Emotional functioning
16.2.6.1.2.1 Efficacy response data
16.2.6.1.2.1.1 QLQ-C30 - Mean and 95% CI for emotional functioning score over time (LOCF) - ITT population



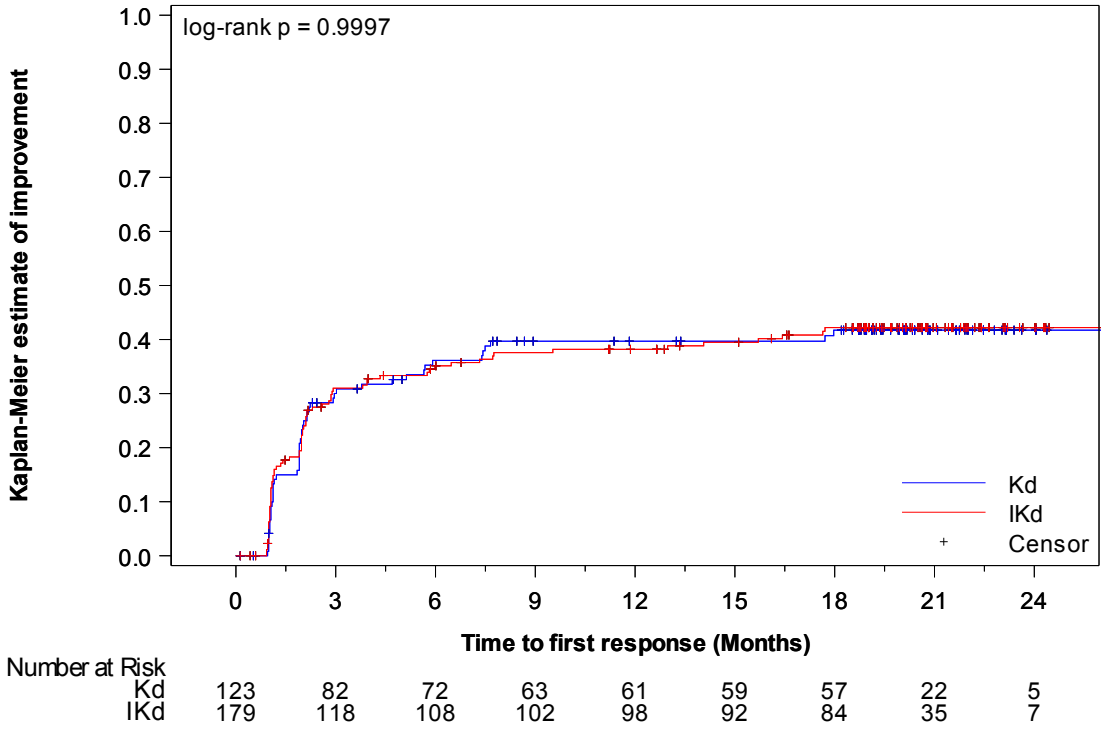
A higher score represents a better level of quality of life. Cycles with less than 20 patients overall are not presented.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
PGM=DEVOPS/SAR650984/EFC15246/CIR_RWE/REPORT/PGM/eff_qlq_line_i_f.sas OUT=REPORT/OUTPUT/eff_qlq_line_c30_emo_de_i_f_x.rtf (12FEB2021 15:16)

16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Emotional functioning
16.2.6.1.2.1 Efficacy response data
16.2.6.1.2.1.15 QLQ-C30 - Time to first improvement by 15 pt in Emotional functioning (LOCF) - ITT population

First improvement 15 points Emotional functioning (%)	**Kd (N=123)**	**IKd (N=179)**
Number (%) of events	49 (39.8)	72 (40.2)
Number (%) of patients censored	74 (60.2)	107 (59.8)
Kaplan-Meier estimates of Emotional functioning in months		
25% quantile (95% CI)	2.14 (1.906 to 5.125)	2.10 (1.906 to 3.811)
Median (95% CI)	NC (17.708 to NC)	NC (17.708 to NC)
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)
Comparison vs. Kd		
Stratified[a] Log-Rank test p-value[b] vs Kd	-	0.9997
Stratified[a] Hazard ratio (95% CI) vs Kd	-	1.00 (0.69 to 1.44)
P-value	-	1.0000
Improvement probability (95% CI)[c]		
3 Months	0.300 (0.221 to 0.383)	0.310 (0.243 to 0.379)
6 Months	0.361 (0.276 to 0.447)	0.351 (0.281 to 0.422)

A lower score represents a better level of quality of life. Clinical meaningful improvement change from baseline less than or equal to -15 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] Stratified on number of prior lines of therapy (1 vs. >1) and Revised International Staging System (R-ISS) stage (I or II vs. III vs. not classified) according to IRT
[b] One-sided significance level is 0.025
[c] Estimated using the Kaplan-Meier method
NA/NC = Not Applicable / Not Calculable
PGM=DEVOPS/SAR650984/EFC15246/CIR_RWE/REPORT/PGM/eff_km_invhr_sr_i_t.sas OUT=REPORT/OUTPUT/eff_km_c30_emo_imp15l_de_i_t_x.rtf (07APR2021 14:22)

16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Emotional functioning
16.2.6.1.2.1 Efficacy response data
16.2.6.1.2.1.16 QLQ-C30 - Time to first improvement by 15 pt in Emotional functioning - Kaplan-Meier curve (LOCF) - ITT population



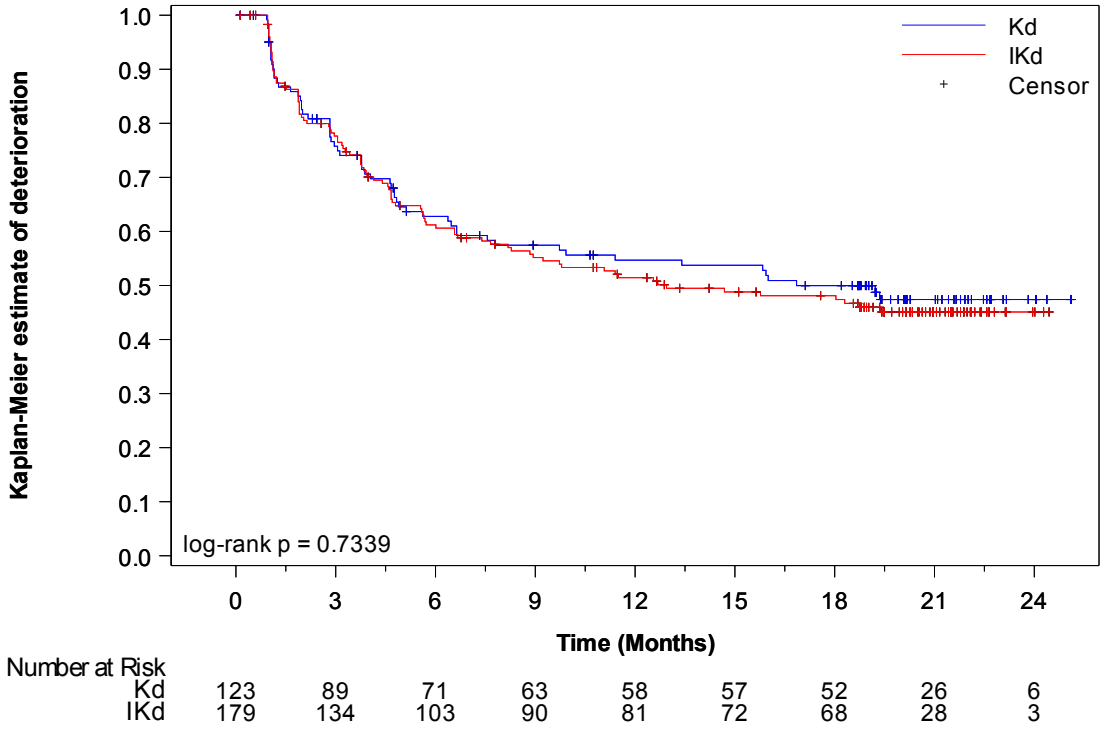
A lower score represents a better level of quality of life. Clinical meaningful improvement change from baseline less than or equal to -15 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
PGM=DEVOPS/SAR650984/EFC15246/CIR_RWE/REPORT/PGM/eff_qlq_km_i_f.sas OUT=REPORT/OUTPUT/eff_km_c30_emo_imp15l_de_i_f_x.rtf (07APR2021 14:23)

16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Emotional functioning
16.2.6.1.2.1 Efficacy response data
16.2.6.1.2.1.17 QLQ-C30 - Time to first deterioration by 15 pt in Emotional functioning (LOCF) - ITT population

First deterioration 15 points Emotional functioning (%)	**Kd (N=123)**	**IKd (N=179)**
Number (%) of events	60 (48.8)	92 (51.4)
Number (%) of patients censored	63 (51.2)	87 (48.6)
Kaplan-Meier estimates of Emotional functioning in months		
25% quantile (95% CI)	3.06 (1.971 to 4.764)	3.29 (1.971 to 4.567)
Median (95% CI)	16.85 (6.637 to NC)	12.94 (7.655 to NC)
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)
Comparison vs. Kd		
Stratified[a] Log-Rank test p-value[b] vs Kd	-	0.7339
Stratified[a] Hazard ratio (95% CI) vs Kd	-	1.06 (0.76 to 1.47)
P-value	-	0.7353
Deterioration probability (95% CI)[c]		
3 Months	0.758 (0.670 to 0.825)	0.776 (0.707 to 0.831)
6 Months	0.628 (0.534 to 0.708)	0.612 (0.535 to 0.680)

A lower score represents a better level of quality of life. Clinical meaningful deterioration change from baseline greater than or equal to 15 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] Stratified on number of prior lines of therapy (1 vs. >1) and Revised International Staging System (R-ISS) stage (I or II vs. III vs. not classified) according to IRT
[b] One-sided significance level is 0.025
[c] Estimated using the Kaplan-Meier method
NA/NC = Not Applicable / Not Calculable
PGM=DEVOPS/SAR650984/EFC15246/CIR_RWE/REPORT/PGM/eff_km_invhr_sr_i_t.sas OUT=REPORT/OUTPUT/eff_km_c30_emo_det15l_de_i_t_x.rtf (07APR2021 14:22)

16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Emotional functioning
16.2.6.1.2.1 Efficacy response data
16.2.6.1.2.1.18 QLQ-C30 - Time to first deterioration by 15 pt in Emotional functioning - Kaplan-Meier curve (LOCF) - ITT population



A lower score represents a better level of quality of life. Clinical meaningful deterioration change from baseline greater than or equal to 15 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
PGM=DEVOPS/SAR650984/EFC15246/CIR_RWE/REPORT/PGM/eff_qlq_km_i_f.sas OUT=REPORT/OUTPUT/eff_km_c30_emo_det15l_de_i_f_x.rtf (07APR2021 14:23)

16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Emotional functioning
16.2.6.1.2.1 Efficacy response data
16.2.6.1.2.1.19 QLQ-C30 - Time until permanent improvement by 15 pt in Emotional functioning (LOCF) - ITT population

First permanent improvement 15 points Emotional functioning (%)	Kd (N=123)	IKd (N=179)
Number (%) of events	21 (17.1)	34 (19.0)
Number (%) of patients censored	102 (82.9)	145 (81.0)
Kaplan-Meier estimates of Emotional functioning in months		
25% quantile (95% CI)	22.21 (19.450 to NC)	22.11 (19.351 to NC)
Median (95% CI)	NC (NC to NC)	NC (NC to NC)
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)
Comparison vs. Kd		
Stratified[a] Log-Rank test p-value[b] vs Kd	-	0.6602
Stratified[a] Hazard ratio (95% CI) vs Kd	-	1.13 (0.65 to 1.96)
P-value	-	0.6604
Improvement probability (95% CI)[c]		
3 Months	0.050 (0.021 to 0.100)	0.063 (0.033 to 0.106)
6 Months	0.059 (0.026 to 0.111)	0.081 (0.046 to 0.127)

A lower score represents a better level of quality of life. Clinical meaningful improvement change from baseline less than or equal to -15 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] Stratified on number of prior lines of therapy (1 vs. >1) and Revised International Staging System (R-ISS) stage (I or II vs. III vs. not classified) according to IRT
[b] One-sided significance level is 0.025
[c] Estimated using the Kaplan-Meier method
NA/NC = Not Applicable / Not Calculable
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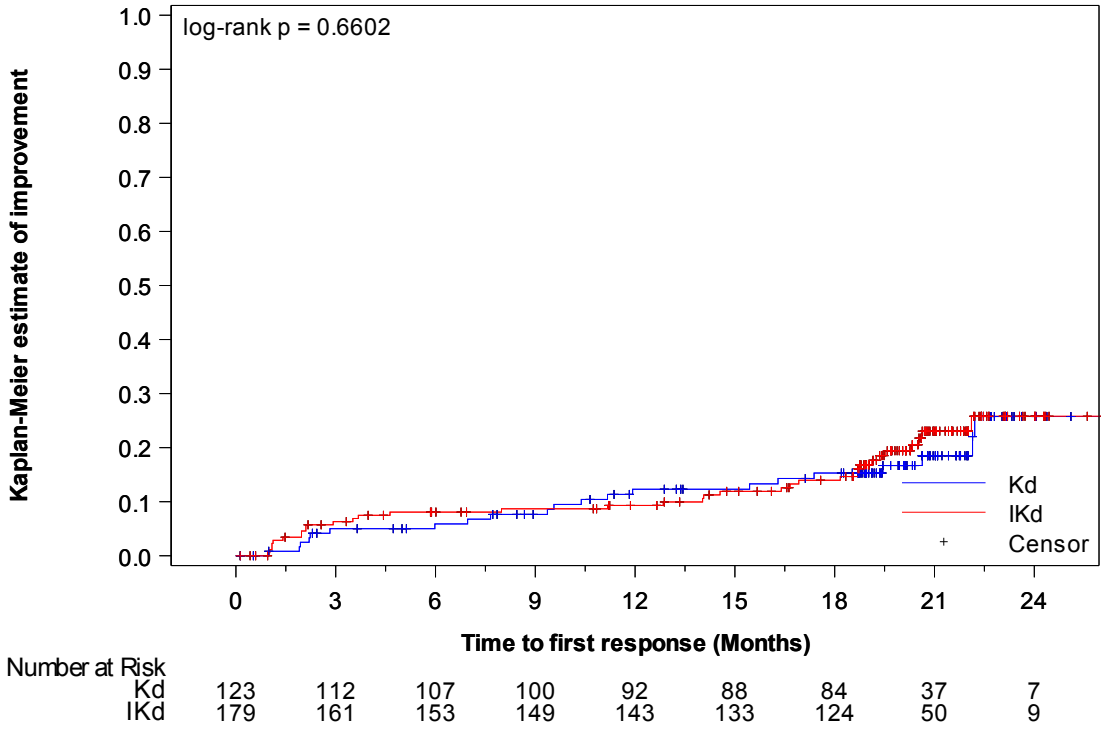
16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Emotional functioning
16.2.6.1.2.1 Efficacy response data
16.2.6.1.2.1.20 QLQ-C30 - Time until permanent improvement by 15 pt in Emotional functioning - Kaplan-Meier curve (LOCF) - ITT population



A lower score represents a better level of quality of life. Clinical meaningful improvement change from baseline less than or equal to -15 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
PGM=DEVOPS/SAR650984/EFC15246/CIR_RWE/REPORT/PGM/eff_qlq_km_i_f.sas OUT=REPORT/OUTPUT/eff_km_c30_emo_imp15pl_de_i_f_x.rtf (07APR2021 14:23)

16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Emotional functioning
16.2.6.1.2.1 Efficacy response data
16.2.6.1.2.1.21 QLQ-C30 - Time until permanent deterioration by 15 pt in Emotional functioning (LOCF) - ITT population

First permanent deterioration 15 points Emotional functioning (%)	**Kd (N=123)**	**IKd (N=179)**
Number (%) of events	20 (16.3)	34 (19.0)
Number (%) of patients censored	103 (83.7)	145 (81.0)
Kaplan-Meier estimates of Emotional functioning in months		
25% quantile (95% CI)	NC (20.370 to NC)	NC (19.121 to NC)
Median (95% CI)	NC (NC to NC)	NC (NC to NC)
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)
Comparison vs. Kd		
Stratified[a] Log-Rank test p-value[b] vs Kd	-	0.6473
Stratified[a] Hazard ratio (95% CI) vs Kd	-	1.14 (0.65 to 1.98)
P-value	-	0.6475
Deterioration probability (95% CI)[c]		
3 Months	0.933 (0.871 to 0.966)	0.954 (0.910 to 0.977)
6 Months	0.898 (0.828 to 0.941)	0.937 (0.889 to 0.964)

A lower score represents a better level of quality of life. Clinical meaningful deterioration change from baseline greater than or equal to 15 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] Stratified on number of prior lines of therapy (1 vs. >1) and Revised International Staging System (R-ISS) stage (I or II vs. III vs. not classified) according to IRT
[b] One-sided significance level is 0.025
[c] Estimated using the Kaplan-Meier method
NA/NC = Not Applicable / Not Calculable
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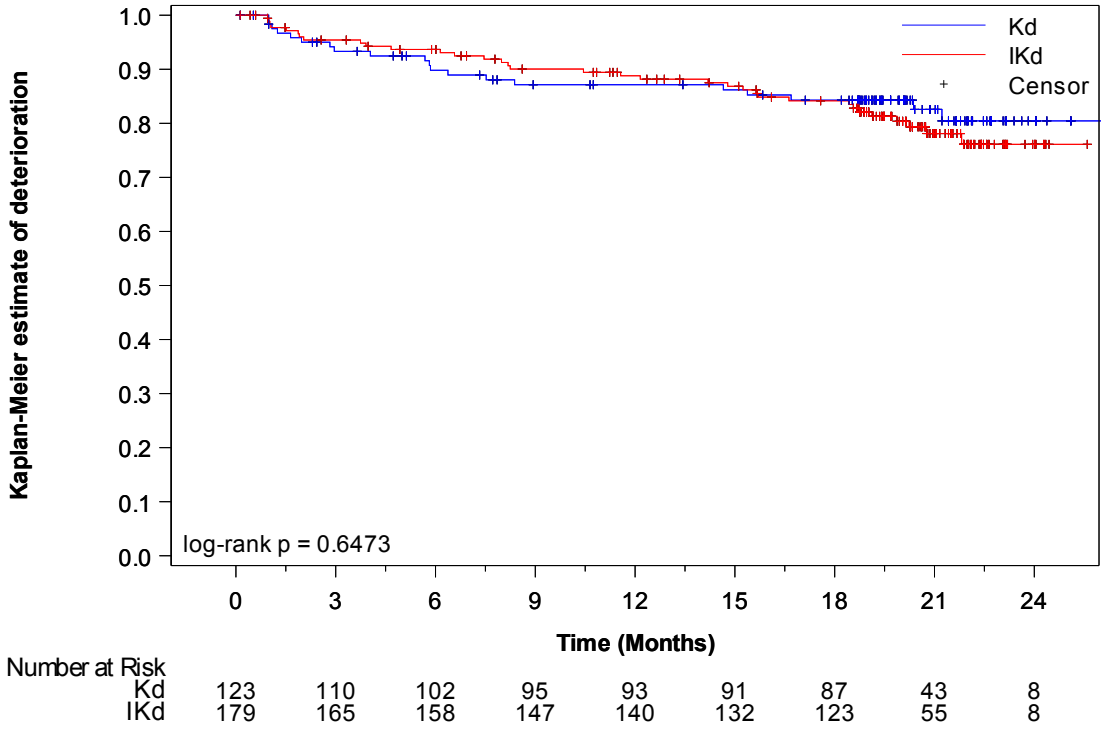
16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Emotional functioning
16.2.6.1.2.1 Efficacy response data
16.2.6.1.2.1.22 QLQ-C30 - Time until permanent deterioration by 15 pt in Emotional functioning - Kaplan-Meier curve (LOCF) - ITT population



A lower score represents a better level of quality of life. Clinical meaningful deterioration change from baseline greater than or equal to 15 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
PGM=DEVOPS/SAR650984/EFC15246/CIR_RWE/REPORT/PGM/eff_qlq_km_i_f.sas OUT=REPORT/OUTPUT/eff_km_c30_emo_det15pl_de_i_f_x.rtf (07APR2021 14:23)

16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Emotional functioning
16.2.6.1.2.2 Efficacy response data - Subgroup analyses by age
16.2.6.1.2.2.3 QLQ-C30 - Time to first improvement by 10 pt in emotional functioning according to age (LOCF) - ITT population

	<65 years		>=65 years		
	Kd (N=66)	**IKd (N=88)**	**Kd (N=57)**	**IKd (N=91)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	31 (47.0)	29 (33.0)	18 (31.6)	43 (47.3)	0.0130
Number (%) of patients censored	35 (53.0)	59 (67.0)	39 (68.4)	48 (52.7)	
Kaplan-Meier estimates of Emotional functioning in months					
25% quantile (95% CI)	1.94 (1.216 to 5.125)	3.81 (1.971 to 17.643)	2.96 (1.150 to NC)	1.94 (1.117 to 2.300)	
Median (95% CI)	NC (5.651 to NC)	NC (NC to NC)	NC (NC to NC)	NC (4.337 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.0836		0.0723	
Hazard ratio (95% CI) vs Kd	-	0.64 (0.39 to 1.07)		1.65 (0.95 to 2.86)	
P-value	-	0.0861		0.0754	

A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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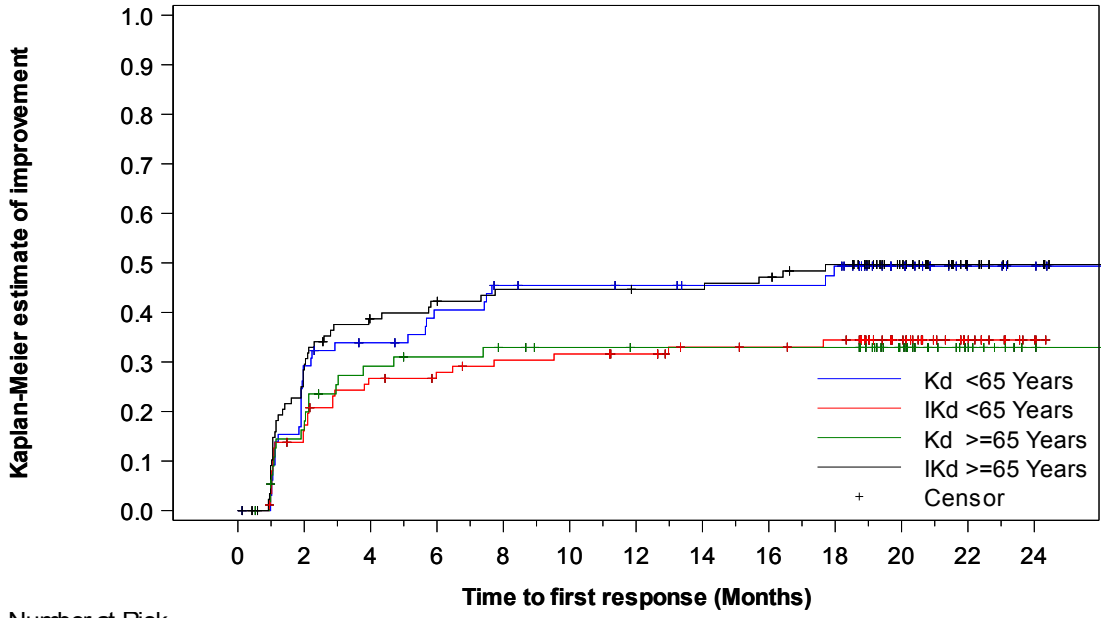
16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Emotional functioning
16.2.6.1.2.2 Efficacy response data - Subgroup analyses by age
16.2.6.1.2.2.4 QLQ-C30 - Time to first improvement by 10 pt in emotional functioning according to age - Kaplan-Meier curve (LOCF) - ITT population



Number at Risk									
Kd <65 Years	66	42	36	31	30	28	26	8	3
IKd <65 Years	88	64	59	56	53	48	45	18	3
Kd >=65 Years	57	40	36	32	31	31	31	14	2
IKd >=65 Years	91	54	49	46	45	44	39	17	4

A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
PGM=DEVOPS/SAR650984/EFC15246/CIR_RWE/REPORT/PGM/eff_qlq_km_subgp_de_i_f.sas OUT=REPORT/OUTPUT/eff_km_c30_emo_impl_age_de_i_f_x.rtf (07APR2021 14:25)

16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Emotional functioning
16.2.6.1.2.2 Efficacy response data - Subgroup analyses by age
16.2.6.1.2.2.5 QLQ-C30 - Time to first deterioration by 10 pt in emotional functioning according to age (LOCF) - ITT population

	<65 years		>=65 years		
	Kd (N=66)	**IKd (N=88)**	**Kd (N=57)**	**IKd (N=91)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	32 (48.5)	42 (47.7)	28 (49.1)	50 (54.9)	0.5014
Number (%) of patients censored	34 (51.5)	46 (52.3)	29 (50.9)	41 (45.1)	
Kaplan-Meier estimates of Emotional functioning in months					
25% quantile (95% CI)	2.83 (1.150 to 4.764)	2.86 (1.873 to 4.665)	4.04 (1.971 to 6.374)	3.42 (1.906 to 5.552)	
Median (95% CI)	19.35 (4.764 to NC)	18.76 (8.181 to NC)	15.84 (6.374 to NC)	8.94 (5.717 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.8702		0.4387	
Hazard ratio (95% CI) vs Kd	-	0.96 (0.61 to 1.52)		1.20 (0.76 to 1.91)	
P-value	-	0.8698		0.4393	

A higher score represents a better level of quality of life. Clinical meaningful deterioration change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
PGM=DEVOPS/SAR650984/EFC15246/CIR_RWE/REPORT/PGM/eff_km_subgp_sr_sig_de_i_t.sas OUT=REPORT/OUTPUT/eff_km_c30_emo_detl_age_de_i_t_x.rtf (07APR2021 14:24)

16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Emotional functioning
16.2.6.1.2.2 Efficacy response data - Subgroup analyses by age
16.2.6.1.2.2.6 QLQ-C30 - Time until permanent improvement by 10 pt in emotional functioning according to age (LOCF) - ITT population

	<65 years		>=65 years		
	Kd (N=66)	**IKd (N=88)**	**Kd (N=57)**	**IKd (N=91)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	15 (22.7)	15 (17.0)	6 (10.5)	19 (20.9)	0.0703
Number (%) of patients censored	51 (77.3)	73 (83.0)	51 (89.5)	72 (79.1)	
Kaplan-Meier estimates of Emotional functioning in months					
25% quantile (95% CI)	22.14 (9.561 to NC)	NC (18.694 to NC)	NC (22.209 to NC)	22.11 (16.920 to NC)	
Median (95% CI)	NC (22.144 to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.3827		0.0977	
Hazard ratio (95% CI) vs Kd	-	0.73 (0.36 to 1.49)		2.14 (0.85 to 5.35)	
P-value	-	0.3847		0.1057	

A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
PGM=DEVOPS/SAR650984/EFC15246/CIR_RWE/REPORT/PGM/eff_km_subgp_sr_sig_de_i_t.sas OUT=REPORT/OUTPUT/eff_km_c30_emo_imppl_age_de_i_t_x.rtf (07APR2021 14:24)

16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Emotional functioning
16.2.6.1.2.2 Efficacy response data - Subgroup analyses by age
16.2.6.1.2.2.7 QLQ-C30 - Time until permanent deterioration by 10 pt in emotional functioning according to age (LOCF) - ITT population

	<65 years		>=65 years		
	Kd (N=66)	**IKd (N=88)**	**Kd (N=57)**	**IKd (N=91)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	10 (15.2)	20 (22.7)	10 (17.5)	14 (15.4)	0.2732
Number (%) of patients censored	56 (84.8)	68 (77.3)	47 (82.5)	77 (84.6)	
Kaplan-Meier estimates of Emotional functioning in months					
25% quantile (95% CI)	NC (20.370 to NC)	20.76 (12.156 to NC)	NC (6.374 to NC)	NC (19.877 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.2523		0.6600	
Hazard ratio (95% CI) vs Kd	-	1.55 (0.73 to 3.32)		0.83 (0.37 to 1.88)	
P-value	-	0.2562		0.6605	

A higher score represents a better level of quality of life. Clinical meaningful deterioration change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
PGM=DEVOPS/SAR650984/EFC15246/CIR_RWE/REPORT/PGM/eff_km_subgp_sr_sig_de_i_t.sas OUT=REPORT/OUTPUT/eff_km_c30_emo_detpl_age_de_i_t_x.rtf (07APR2021 14:24)

16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Emotional functioning
16.2.6.1.2.3 Efficacy response data - Subgroup analyses by gender
16.2.6.1.2.3.3 QLQ-C30 - Time to first improvement by 10 pt in emotional functioning according to gender (LOCF) - ITT population

	Male		Female		
	Kd (N=68)	**IKd (N=101)**	**Kd (N=55)**	**IKd (N=78)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	20 (29.4)	32 (31.7)	29 (52.7)	40 (51.3)	0.7286
Number (%) of patients censored	48 (70.6)	69 (68.3)	26 (47.3)	38 (48.7)	
Kaplan-Meier estimates of Emotional functioning in months					
25% quantile (95% CI)	5.91 (1.906 to NC)	2.89 (1.971 to NC)	1.94 (1.018 to 2.136)	1.91 (1.051 to 2.595)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	7.41 (2.136 to NC)	17.64 (3.943 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.7463		0.8717	
Hazard ratio (95% CI) vs Kd	-	1.10 (0.63 to 1.92)		0.96 (0.60 to 1.55)	
P-value	-	0.7464		0.8713	

A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Emotional functioning
16.2.6.1.2.3 Efficacy response data - Subgroup analyses by gender
16.2.6.1.2.3.4 QLQ-C30 - Time to first deterioration by 10 pt in emotional functioning according to gender (LOCF) - ITT population

	Male		Female		
	Kd (N=68)	**IKd (N=101)**	**Kd (N=55)**	**IKd (N=78)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	32 (47.1)	51 (50.5)	28 (50.9)	41 (52.6)	0.7783
Number (%) of patients censored	36 (52.9)	50 (49.5)	27 (49.1)	37 (47.4)	
Kaplan-Meier estimates of Emotional functioning in months					
25% quantile (95% CI)	3.12 (2.004 to 6.374)	3.06 (1.906 to 4.600)	3.06 (1.051 to 4.764)	3.42 (1.478 to 5.552)	
Median (95% CI)	19.22 (6.637 to NC)	15.77 (7.392 to NC)	15.84 (4.764 to NC)	12.68 (5.684 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.6220		0.9452	
Hazard ratio (95% CI) vs Kd	-	1.12 (0.72 to 1.74)		1.02 (0.63 to 1.64)	
P-value	-	0.6222		0.9453	

A higher score represents a better level of quality of life. Clinical meaningful deterioration change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Emotional functioning
16.2.6.1.2.3 Efficacy response data - Subgroup analyses by gender
16.2.6.1.2.3.5 QLQ-C30 - Time until permanent improvement by 10 pt in emotional functioning according to gender (LOCF) - ITT population

	Male		Female		
	Kd (N=68)	**IKd (N=101)**	**Kd (N=55)**	**IKd (N=78)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	9 (13.2)	17 (16.8)	12 (21.8)	17 (21.8)	0.5980
Number (%) of patients censored	59 (86.8)	84 (83.2)	43 (78.2)	61 (78.2)	
Kaplan-Meier estimates of Emotional functioning in months					
25% quantile (95% CI)	NC (16.296 to NC)	NC (19.351 to NC)	22.21 (9.561 to NC)	22.11 (18.694 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (22.209 to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.5247		0.9730	
Hazard ratio (95% CI) vs Kd	-	1.30 (0.58 to 2.91)		0.99 (0.47 to 2.07)	
P-value	-	0.5259		0.9730	

A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Emotional functioning
16.2.6.1.2.3 Efficacy response data - Subgroup analyses by gender
16.2.6.1.2.3.6 QLQ-C30 - Time until permanent deterioration by 10 pt in emotional functioning according to gender (LOCF) - ITT population

	Male		Female		
	Kd (N=68)	**IKd (N=101)**	**Kd (N=55)**	**IKd (N=78)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	11 (16.2)	19 (18.8)	9 (16.4)	15 (19.2)	0.9467
Number (%) of patients censored	57 (83.8)	82 (81.2)	46 (83.6)	63 (80.8)	
Kaplan-Meier estimates of Emotional functioning in months					
25% quantile (95% CI)	NC (14.653 to NC)	NC (15.704 to NC)	NC (8.378 to NC)	NC (16.624 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.6563		0.7462	
Hazard ratio (95% CI) vs Kd	-	1.18 (0.56 to 2.49)		1.15 (0.50 to 2.62)	
P-value	-	0.6567		0.7464	

A higher score represents a better level of quality of life. Clinical meaningful deterioration change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Emotional functioning
16.2.6.1.2.4 Efficacy response data - Subgroup analyses by ethnic origin
16.2.6.1.2.4.3 QLQ-C30 - Time to first improvement by 10 pt in emotional functioning according to ethnic origin (LOCF) - ITT population

	White		Other		
	Kd (N=83)	**IKd (N=131)**	**Kd (N=28)**	**IKd (N=34)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	39 (47.0)	56 (42.7)	9 (32.1)	11 (32.4)	0.8236
Number (%) of patients censored	44 (53.0)	75 (57.3)	19 (67.9)	23 (67.6)	
Kaplan-Meier estimates of Emotional functioning in months					
25% quantile (95% CI)	1.97 (1.906 to 2.924)	2.10 (1.150 to 3.811)	1.22 (1.117 to NC)	2.10 (1.051 to NC)	
Median (95% CI)	NC (5.125 to NC)	NC (12.977 to NC)	NC (3.023 to NC)	NC (7.721 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.5956		0.9642	
Hazard ratio (95% CI) vs Kd	-	0.90 (0.59 to 1.35)		1.02 (0.42 to 2.46)	
P-value	-	0.5958		0.9642	

A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
PGM=DEVOPS/SAR650984/EFC15246/CIR_RWE/REPORT/PGM/eff_km_subgp_sr_sig_de_i_t.sas OUT=REPORT/OUTPUT/eff_km_c30_emo_impl_race_de_i_t_x.rtf (07APR2021 14:24)

16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Emotional functioning
16.2.6.1.2.4 Efficacy response data - Subgroup analyses by ethnic origin
16.2.6.1.2.4.4 QLQ-C30 - Time to first deterioration by 10 pt in emotional functioning according to ethnic origin (LOCF) - ITT population

	White		Other		
	Kd (N=83)	**IKd (N=131)**	**Kd (N=28)**	**IKd (N=34)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	42 (50.6)	65 (49.6)	14 (50.0)	20 (58.8)	0.4548
Number (%) of patients censored	41 (49.4)	66 (50.4)	14 (50.0)	14 (41.2)	
Kaplan-Meier estimates of Emotional functioning in months					
25% quantile (95% CI)	3.06 (1.971 to 4.632)	3.75 (1.971 to 4.797)	2.83 (1.084 to 7.556)	2.86 (1.018 to 3.943)	
Median (95% CI)	19.22 (4.895 to NC)	18.30 (7.392 to NC)	15.84 (4.764 to NC)	8.84 (2.957 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (11.072 to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.9105		0.4411	
Hazard ratio (95% CI) vs Kd	-	0.98 (0.66 to 1.44)		1.31 (0.66 to 2.59)	
P-value	-	0.9102		0.4425	

A higher score represents a better level of quality of life. Clinical meaningful deterioration change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Emotional functioning
16.2.6.1.2.4 Efficacy response data - Subgroup analyses by ethnic origin
16.2.6.1.2.4.5 QLQ-C30 - Time until permanent improvement by 10 pt in emotional functioning according to ethnic origin (LOCF) - ITT population

	White		Other		
	Kd (N=83)	**IKd (N=131)**	**Kd (N=28)**	**IKd (N=34)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	16 (19.3)	25 (19.1)	5 (17.9)	6 (17.6)	0.8826
Number (%) of patients censored	67 (80.7)	106 (80.9)	23 (82.1)	28 (82.4)	
Kaplan-Meier estimates of Emotional functioning in months					
25% quantile (95% CI)	22.14 (17.380 to NC)	22.11 (19.121 to NC)	NC (5.979 to NC)	NC (1.971 to NC)	
Median (95% CI)	NC (22.209 to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.9229		0.9601	
Hazard ratio (95% CI) vs Kd	-	0.97 (0.52 to 1.82)		1.03 (0.31 to 3.38)	
P-value	-	0.9226		0.9601	

A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Emotional functioning
16.2.6.1.2.4 Efficacy response data - Subgroup analyses by ethnic origin
16.2.6.1.2.4.6 QLQ-C30 - Time until permanent deterioration by 10 pt in emotional functioning according to ethnic origin (LOCF) - ITT population

	White		Other		
	Kd (N=83)	**IKd (N=131)**	**Kd (N=28)**	**IKd (N=34)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	13 (15.7)	24 (18.3)	4 (14.3)	9 (26.5)	0.4803
Number (%) of patients censored	70 (84.3)	107 (81.7)	24 (85.7)	25 (73.5)	
Kaplan-Meier estimates of Emotional functioning in months					
25% quantile (95% CI)	NC (16.690 to NC)	NC (19.121 to NC)	NC (1.971 to NC)	15.70 (3.910 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (20.238 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.6428		0.2805	
Hazard ratio (95% CI) vs Kd	-	1.17 (0.60 to 2.30)		1.89 (0.58 to 6.15)	
P-value	-	0.6432		0.2887	

A higher score represents a better level of quality of life. Clinical meaningful deterioration change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Emotional functioning
16.2.6.1.2.5 Efficacy response data - Subgroup analyses by geographical region
16.2.6.1.2.5.3 QLQ-C30 - Time to first improvement by 10 pt in emotional functioning according to geographical region (LOCF) - ITT population

	Europe		America		Asia		Other countries		
	Kd (N=60)	**IKd (N=85)**	**Kd (N=20)**	**IKd (N=24)**	**Kd (N=21)**	**IKd (N=25)**	**Kd (N=22)**	**IKd (N=45)**	**p-value of treatment-by-subgroup interaction[c]**
Number (%) of events	18 (30.0)	35 (41.2)	15 (75.0)	11 (45.8)	7 (33.3)	8 (32.0)	9 (40.9)	18 (40.0)	0.3649
Number (%) of patients censored	42 (70.0)	50 (58.8)	5 (25.0)	13 (54.2)	14 (66.7)	17 (68.0)	13 (59.1)	27 (60.0)	
Kaplan-Meier estimates of event in months									
25% quantile (95% CI)	5.13 (1.906 to NC)	2.79 (1.971 to 5.815)	1.91 (1.018 to 3.023)	2.04 (0.986 to 7.754)	1.13 (1.018 to NC)	4.86 (0.920 to NC)	2.14 (0.986 to NC)	1.12 (1.018 to 3.811)	
Median (95% CI)	NC (NC to NC)	NC (12.977 to NC)	5.31 (1.906 to 17.708)	14.06 (2.037 to NC)	NC (1.117 to NC)	NC (7.721 to NC)	NC (2.136 to NC)	NC (2.004 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	17.71 (5.914 to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	

A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
PGM=DEVOPS/SAR650984/EFC15246/CIR_RWE/REPORT/PGM/eff_km_subgp_sr_sig_de_i_t.sas OUT=REPORT/OUTPUT/eff_km_c30_emo_impl_greg_de_i_t_x.rtf (07APR2021 14:24)

16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Emotional functioning
16.2.6.1.2.5 Efficacy response data - Subgroup analyses by geographical region
16.2.6.1.2.5.3 QLQ-C30 - Time to first improvement by 10 pt in emotional functioning according to geographical region (LOCF) - ITT population

	Europe		America		Asia		Other countries		
	Kd (N=60)	**IKd (N=85)**	**Kd (N=20)**	**IKd (N=24)**	**Kd (N=21)**	**IKd (N=25)**	**Kd (N=22)**	**IKd (N=45)**	**p-value of treatment-by-subgroup interaction[c]**
Comparison vs. Kd									
Log-Rank test p-value[a] vs Kd	-	0.2285		0.1625		0.8226		0.8651	
Hazard ratio (95% CI) vs Kd	-	1.42 (0.80 to 2.50)		0.58 (0.26 to 1.26)		0.89 (0.32 to 2.46)		1.07 (0.48 to 2.39)	
P-value	-	0.2308		0.1677		0.8227		0.8651	
Improvement probability (95% CI)[b]									
3 Months	0.241 (0.141 to 0.356)	0.291 (0.198 to 0.391)	0.400 (0.193 to 0.600)	0.359 (0.172 to 0.552)	0.350 (0.157 to 0.552)	0.250 (0.102 to 0.431)	0.318 (0.142 to 0.511)	0.356 (0.220 to 0.493)	

A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
PGM=DEVOPS/SAR650984/EFC15246/CIR_RWE/REPORT/PGM/eff_km_subgp_sr_sig_de_i_t.sas OUT=REPORT/OUTPUT/eff_km_c30_emo_impl_greg_de_i_t_x.rtf (07APR2021 14:24)

16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Emotional functioning
16.2.6.1.2.5 Efficacy response data - Subgroup analyses by geographical region
16.2.6.1.2.5.4 QLQ-C30 - Time to first deterioration by 10 pt in emotional functioning according to geographical region (LOCF) - ITT population

	Europe		America		Asia		Other countries		
	Kd (N=60)	**IKd (N=85)**	**Kd (N=20)**	**IKd (N=24)**	**Kd (N=21)**	**IKd (N=25)**	**Kd (N=22)**	**IKd (N=45)**	**p-value of treatment-by-subgroup interaction[c]**
Number (%) of events	27 (45.0)	45 (52.9)	12 (60.0)	11 (45.8)	9 (42.9)	14 (56.0)	12 (54.5)	22 (48.9)	0.7491
Number (%) of patients censored	33 (55.0)	40 (47.1)	8 (40.0)	13 (54.2)	12 (57.1)	11 (44.0)	10 (45.5)	23 (51.1)	
Kaplan-Meier estimates of event in months									
25% quantile (95% CI)	3.78 (1.248 to 5.618)	3.29 (1.873 to 5.552)	1.91 (0.920 to 2.858)	1.15 (0.953 to 4.567)	4.76 (1.051 to 16.000)	3.35 (1.018 to 4.665)	4.83 (1.150 to 9.725)	3.78 (1.906 to 6.571)	
Median (95% CI)	NC (5.618 to NC)	12.94 (5.717 to NC)	3.45 (1.873 to NC)	18.30 (2.037 to NC)	NC (4.764 to NC)	10.15 (3.745 to NC)	18.04 (4.830 to NC)	9.79 (6.012 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (3.778 to NC)	NC (NC to NC)	NC (NC to NC)	NC (18.037 to NC)	NC (19.220 to NC)	NC (NC to NC)	

A higher score represents a better level of quality of life. Clinical meaningful deterioration change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
PGM=DEVOPS/SAR650984/EFC15246/CIR_RWE/REPORT/PGM/eff_km_subgp_sr_sig_de_i_t.sas OUT=REPORT/OUTPUT/eff_km_c30_emo_detl_greg_de_i_t_x.rtf (07APR2021 14:24)

16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Emotional functioning
16.2.6.1.2.5 Efficacy response data - Subgroup analyses by geographical region
16.2.6.1.2.5.4 QLQ-C30 - Time to first deterioration by 10 pt in emotional functioning according to geographical region (LOCF) - ITT population

	Europe		America		Asia		Other countries		
	Kd (N=60)	**IKd (N=85)**	**Kd (N=20)**	**IKd (N=24)**	**Kd (N=21)**	**IKd (N=25)**	**Kd (N=22)**	**IKd (N=45)**	**p-value of treatment-by-subgroup interaction[c]**
Comparison vs. Kd									
Log-Rank test p-value[a] vs Kd	-	0.5523		0.5519		0.4454		0.9836	
Hazard ratio (95% CI) vs Kd	-	1.16 (0.72 to 1.86)		0.78 (0.34 to 1.77)		1.38 (0.60 to 3.20)		0.99 (0.49 to 2.01)	
P-value	-	0.5527		0.5529		0.4474		0.9836	
Deterioration probability (95% CI)[b]									
3 Months	0.759 (0.627 to 0.849)	0.807 (0.705 to 0.877)	0.550 (0.313 to 0.735)	0.648 (0.417 to 0.806)	0.800 (0.551 to 0.920)	0.750 (0.526 to 0.879)	0.909 (0.683 to 0.976)	0.800 (0.651 to 0.891)	

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The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Emotional functioning
16.2.6.1.2.5 Efficacy response data - Subgroup analyses by geographical region
16.2.6.1.2.5.5 QLQ-C30 - Time until permanent improvement by 10 pt in emotional functioning according to geographical region (LOCF) - ITT population

	Europe		America		Asia		Other countries		
	Kd (N=60)	**IKd (N=85)**	**Kd (N=20)**	**IKd (N=24)**	**Kd (N=21)**	**IKd (N=25)**	**Kd (N=22)**	**IKd (N=45)**	**p-value of treatment-by-subgroup interaction[c]**
Number (%) of events	6 (10.0)	15 (17.6)	6 (30.0)	6 (25.0)	4 (19.0)	4 (16.0)	5 (22.7)	9 (20.0)	0.7303
Number (%) of patients censored	54 (90.0)	70 (82.4)	14 (70.0)	18 (75.0)	17 (81.0)	21 (84.0)	17 (77.3)	36 (80.0)	
Kaplan-Meier estimates of event in months									
25% quantile (95% CI)	NC (20.632 to NC)	22.11 (18.760 to NC)	17.38 (2.201 to NC)	18.69 (11.170 to NC)	NC (2.825 to NC)	NC (1.018 to NC)	22.14 (6.965 to NC)	20.63 (18.168 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (17.380 to NC)	NC (18.694 to NC)	NC (11.926 to NC)	NC (NC to NC)	NC (22.144 to NC)	NC (NC to NC)	

A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Emotional functioning
16.2.6.1.2.5 Efficacy response data - Subgroup analyses by geographical region
16.2.6.1.2.5.5 QLQ-C30 - Time until permanent improvement by 10 pt in emotional functioning according to geographical region (LOCF) - ITT population

	Europe		America		Asia		Other countries		
	Kd (N=60)	**IKd (N=85)**	**Kd (N=20)**	**IKd (N=24)**	**Kd (N=21)**	**IKd (N=25)**	**Kd (N=22)**	**IKd (N=45)**	**p-value of treatment-by-subgroup interaction[c]**
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (22.209 to NC)	NC (NC to NC)	
Comparison vs. Kd									
Log-Rank test p-value[a] vs Kd	-	0.2394		0.9390		0.8361		0.9601	
Hazard ratio (95% CI) vs Kd	-	1.75 (0.68 to 4.52)		0.96 (0.31 to 2.98)		0.86 (0.22 to 3.46)		0.97 (0.33 to 2.91)	
P-value	-	0.2457		0.9390		0.8362		0.9600	
Improvement probability (95% CI)[b]									

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The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Emotional functioning
16.2.6.1.2.5 Efficacy response data - Subgroup analyses by geographical region
16.2.6.1.2.5.6 QLQ-C30 - Time until permanent deterioration by 10 pt in emotional functioning according to geographical region (LOCF) - ITT population

	Europe		America		Asia		Other countries		
	Kd (N=60)	**IKd (N=85)**	**Kd (N=20)**	**IKd (N=24)**	**Kd (N=21)**	**IKd (N=25)**	**Kd (N=22)**	**IKd (N=45)**	**p-value of treatment-by-subgroup interaction[c]**
Number (%) of events	12 (20.0)	16 (18.8)	1 (5.0)	3 (12.5)	3 (14.3)	6 (24.0)	4 (18.2)	9 (20.0)	0.7057
Number (%) of patients censored	48 (80.0)	69 (81.2)	19 (95.0)	21 (87.5)	18 (85.7)	19 (76.0)	18 (81.8)	36 (80.0)	
Kaplan-Meier estimates of event in months									
25% quantile (95% CI)	21.22 (8.378 to NC)	21.82 (18.760 to NC)	NC (15.376 to NC)	NC (0.986 to NC)	NC (1.084 to NC)	15.70 (1.018 to NC)	NC (4.041 to NC)	NC (10.448 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	

A higher score represents a better level of quality of life. Clinical meaningful deterioration change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Emotional functioning
16.2.6.1.2.5 Efficacy response data - Subgroup analyses by geographical region
16.2.6.1.2.5.6 QLQ-C30 - Time until permanent deterioration by 10 pt in emotional functioning according to geographical region (LOCF) - ITT population

	Europe		America		Asia		Other countries		
	Kd (N=60)	**IKd (N=85)**	**Kd (N=20)**	**IKd (N=24)**	**Kd (N=21)**	**IKd (N=25)**	**Kd (N=22)**	**IKd (N=45)**	**p-value of treatment-by-subgroup interaction[c]**
Comparison vs. Kd									
Log-Rank test p-value[a] vs Kd	-	0.7498		0.3310		0.5060		0.8703	
Hazard ratio (95% CI) vs Kd	-	0.89 (0.42 to 1.87)		2.92 (0.30 to 28.13)		1.59 (0.40 to 6.38)		1.10 (0.34 to 3.58)	
P-value	-	0.7499		0.3538		0.5099		0.8704	
Deterioration probability (95% CI)[b]									
3 Months	0.914 (0.806 to 0.963)	0.964 (0.892 to 0.988)	1.000 (1.000 to 1.000)	0.867 (0.643 to 0.955)	0.847 (0.597 to 0.948)	0.917 (0.706 to 0.978)	1.000 (1.000 to 1.000)	1.000 (1.000 to 1.000)	
6 Months	0.876 (0.757 to 0.939)	0.952 (0.876 to 0.982)	1.000 (1.000 to 1.000)	0.867 (0.643 to 0.955)	0.847 (0.597 to 0.948)	0.875 (0.661 to 0.958)	0.909 (0.683 to 0.976)	0.977 (0.849 to 0.997)	

A higher score represents a better level of quality of life. Clinical meaningful deterioration change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Emotional functioning
16.2.6.1.2.6 Efficacy response data - Subgroup analyses by regulatory region
16.2.6.1.2.6.3 QLQ-C30 - Time to first improvement by 10 pt in emotional functioning according to regulatory region (LOCF) - ITT population

	Western countries		Other countries		
	Kd (N=55)	**IKd (N=97)**	**Kd (N=68)**	**IKd (N=82)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	19 (34.5)	38 (39.2)	30 (44.1)	34 (41.5)	0.4922
Number (%) of patients censored	36 (65.5)	59 (60.8)	38 (55.9)	48 (58.5)	
Kaplan-Meier estimates of Emotional functioning in months					
25% quantile (95% CI)	2.96 (1.906 to 17.971)	2.10 (1.150 to 5.749)	1.91 (1.117 to 4.698)	2.10 (1.610 to 5.815)	
Median (95% CI)	NC (17.971 to NC)	NC (17.643 to NC)	NC (5.651 to NC)	NC (7.721 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.5454		0.7393	
Hazard ratio (95% CI) vs Kd	-	1.18 (0.68 to 2.06)		0.92 (0.56 to 1.50)	
P-value	-	0.5459		0.7384	

A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Emotional functioning
16.2.6.1.2.6 Efficacy response data - Subgroup analyses by regulatory region
16.2.6.1.2.6.4 QLQ-C30 - Time to first deterioration by 10 pt in emotional functioning according to regulatory region (LOCF) - ITT population

	Western countries		Other countries		
	Kd (N=55)	**IKd (N=97)**	**Kd (N=68)**	**IKd (N=82)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	24 (43.6)	43 (44.3)	36 (52.9)	49 (59.8)	0.5884
Number (%) of patients censored	31 (56.4)	54 (55.7)	32 (47.1)	33 (40.2)	
Kaplan-Meier estimates of Emotional functioning in months					
25% quantile (95% CI)	4.76 (2.004 to 6.472)	3.78 (2.037 to 5.717)	2.83 (1.248 to 3.778)	2.79 (1.478 to 3.943)	
Median (95% CI)	NC (6.472 to NC)	NC (9.725 to NC)	16.00 (4.632 to NC)	8.18 (4.698 to 18.037)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.9976		0.4164	
Hazard ratio (95% CI) vs Kd	-	1.00 (0.61 to 1.65)		1.20 (0.78 to 1.84)	
P-value	-	0.9976		0.4170	

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The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Emotional functioning
16.2.6.1.2.6 Efficacy response data - Subgroup analyses by regulatory region
16.2.6.1.2.6.5 QLQ-C30 - Time until permanent improvement by 10 pt in emotional functioning according to regulatory region (LOCF) - ITT population

	Western countries		Other countries		
	Kd (N=55)	**IKd (N=97)**	**Kd (N=68)**	**IKd (N=82)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	7 (12.7)	21 (21.6)	14 (20.6)	13 (15.9)	0.1275
Number (%) of patients censored	48 (87.3)	76 (78.4)	54 (79.4)	69 (84.1)	
Kaplan-Meier estimates of Emotional functioning in months					
25% quantile (95% CI)	22.21 (20.632 to NC)	20.63 (16.920 to NC)	NC (10.382 to NC)	NC (18.760 to NC)	
Median (95% CI)	NC (22.209 to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.1399		0.4504	
Hazard ratio (95% CI) vs Kd	-	1.89 (0.80 to 4.45)		0.75 (0.35 to 1.59)	
P-value	-	0.1465		0.4520	

A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Emotional functioning
16.2.6.1.2.6 Efficacy response data - Subgroup analyses by regulatory region
16.2.6.1.2.6.6 QLQ-C30 - Time until permanent deterioration by 10 pt in emotional functioning according to regulatory region (LOCF) - ITT population

	Western countries		Other countries		
	Kd (N=55)	**IKd (N=97)**	**Kd (N=68)**	**IKd (N=82)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	11 (20.0)	16 (16.5)	9 (13.2)	18 (22.0)	0.2162
Number (%) of patients censored	44 (80.0)	81 (83.5)	59 (86.8)	64 (78.0)	
Kaplan-Meier estimates of Emotional functioning in months					
25% quantile (95% CI)	21.22 (8.378 to NC)	NC (19.877 to NC)	NC (NC to NC)	21.82 (11.565 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.6336		0.2060	
Hazard ratio (95% CI) vs Kd	-	0.83 (0.38 to 1.79)		1.67 (0.75 to 3.71)	
P-value	-	0.6341		0.2110	

A higher score represents a better level of quality of life. Clinical meaningful deterioration change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
PGM=DEVOPS/SAR650984/EFC15246/CIR_RWE/REPORT/PGM/eff_km_subgp_sr_sig_de_i_t.sas OUT=REPORT/OUTPUT/eff_km_c30_emo_detpl_rreg_de_i_t_x.rtf (07APR2021 14:24)

16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Emotional functioning
16.2.6.1.2.7 Efficacy response data - Subgroup analyses by baseline ECOG PS
16.2.6.1.2.7.3 QLQ-C30 - Time to first improvement by 10 pt in emotional functioning according to baseline ECOG PS (LOCF) - ITT population

	0 or 1		>1		
	Kd (N=118)	**IKd (N=168)**	**Kd (N=5)**	**IKd (N=11)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	46 (39.0)	68 (40.5)	3 (60.0)	4 (36.4)	0.5979
Number (%) of patients censored	72 (61.0)	100 (59.5)	2 (40.0)	7 (63.6)	
Kaplan-Meier estimates of Emotional functioning in months					
25% quantile (95% CI)	2.14 (1.906 to 5.125)	2.14 (1.413 to 3.943)	1.91 (1.051 to NC)	1.97 (1.610 to NC)	
Median (95% CI)	NC (17.971 to NC)	NC (17.708 to NC)	7.39 (1.051 to NC)	NC (1.610 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (1.051 to NC)	NC (2.103 to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.8598		0.5964	
Hazard ratio (95% CI) vs Kd	-	1.03 (0.71 to 1.50)		0.67 (0.15 to 2.99)	
P-value	-	0.8603		0.5988	

A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
PGM=DEVOPS/SAR650984/EFC15246/CIR_RWE/REPORT/PGM/eff_km_subgp_sr_sig_de_i_t.sas OUT=REPORT/OUTPUT/eff_km_c30_emo_impl_ecog_de_i_t_x.rtf (07APR2021 14:24)

16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Emotional functioning
16.2.6.1.2.7 Efficacy response data - Subgroup analyses by baseline ECOG PS
16.2.6.1.2.7.4 QLQ-C30 - Time to first deterioration by 10 pt in emotional functioning according to baseline ECOG PS (LOCF) - ITT population

	0 or 1		>1		
	Kd (N=118)	**IKd (N=168)**	**Kd (N=5)**	**IKd (N=11)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	57 (48.3)	87 (51.8)	3 (60.0)	5 (45.5)	0.6857
Number (%) of patients censored	61 (51.7)	81 (48.2)	2 (40.0)	6 (54.5)	
Kaplan-Meier estimates of Emotional functioning in months					
25% quantile (95% CI)	2.96 (1.971 to 4.764)	3.29 (1.971 to 4.402)	3.78 (3.778 to 6.637)	4.80 (0.986 to 19.384)	
Median (95% CI)	19.22 (7.556 to NC)	12.68 (7.392 to NC)	6.64 (3.778 to NC)	19.38 (0.986 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (3.778 to NC)	NC (8.181 to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.6535		0.6771	
Hazard ratio (95% CI) vs Kd	-	1.08 (0.77 to 1.51)		0.73 (0.17 to 3.18)	
P-value	-	0.6535		0.6782	

A higher score represents a better level of quality of life. Clinical meaningful deterioration change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
PGM=DEVOPS/SAR650984/EFC15246/CIR_RWE/REPORT/PGM/eff_km_subgp_sr_sig_de_i_t.sas OUT=REPORT/OUTPUT/eff_km_c30_emo_detl_ecog_de_i_t_x.rtf (07APR2021 14:24)

16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Emotional functioning
16.2.6.1.2.7 Efficacy response data - Subgroup analyses by baseline ECOG PS
16.2.6.1.2.7.5 QLQ-C30 - Time until permanent improvement by 10 pt in emotional functioning according to baseline ECOG PS (LOCF) - ITT population

	0 or 1		>1		
	Kd (N=118)	**IKd (N=168)**	**Kd (N=5)**	**IKd (N=11)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	21 (17.8)	30 (17.9)	0 (0.0)	4 (36.4)	0.9853
Number (%) of patients censored	97 (82.2)	138 (82.1)	5 (100.0)	7 (63.6)	
Kaplan-Meier estimates of Emotional functioning in months					
25% quantile (95% CI)	22.21 (19.450 to NC)	NC (19.515 to NC)	NC (NC to NC)	12.85 (1.971 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (1.971 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (14.554 to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.9935		0.1497	
Hazard ratio (95% CI) vs Kd	-	1.00 (0.57 to 1.74)			
P-value	-	0.9935		0.9971	

A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Emotional functioning
16.2.6.1.2.7 Efficacy response data - Subgroup analyses by baseline ECOG PS
16.2.6.1.2.7.6 QLQ-C30 - Time until permanent deterioration by 10 pt in emotional functioning according to baseline ECOG PS (LOCF) - ITT population

	0 or 1		>1		
	Kd (N=118)	**IKd (N=168)**	**Kd (N=5)**	**IKd (N=11)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	18 (15.3)	31 (18.5)	2 (40.0)	3 (27.3)	0.4586
Number (%) of patients censored	100 (84.7)	137 (81.5)	3 (60.0)	8 (72.7)	
Kaplan-Meier estimates of Emotional functioning in months					
25% quantile (95% CI)	NC (20.370 to NC)	NC (19.121 to NC)	11.52 (8.378 to NC)	21.82 (7.458 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	14.65 (8.378 to NC)	NC (7.458 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (8.378 to NC)	NC (21.815 to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.5433		0.4200	
Hazard ratio (95% CI) vs Kd	-	1.20 (0.67 to 2.14)		0.45 (0.06 to 3.25)	
P-value	-	0.5438		0.4317	

A higher score represents a better level of quality of life. Clinical meaningful deterioration change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Emotional functioning
16.2.6.1.2.8 Efficacy response data - Subgroup analyses by ISS staging at SE
16.2.6.1.2.8.3 QLQ-C30 - Time to first improvement by 10 pt in emotional functioning according to ISS staging at SE (LOCF) - ITT population

	I		II		III		
	Kd (N=71)	**IKd (N=89)**	**Kd (N=31)**	**IKd (N=63)**	**Kd (N=20)**	**IKd (N=26)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	31 (43.7)	31 (34.8)	11 (35.5)	28 (44.4)	7 (35.0)	12 (46.2)	0.3638
Number (%) of patients censored	40 (56.3)	58 (65.2)	20 (64.5)	35 (55.6)	13 (65.0)	14 (53.8)	
Kaplan-Meier estimates of Emotional functioning in months							
25% quantile (95% CI)	2.14 (1.906 to 5.125)	2.92 (1.150 to 17.643)	1.97 (1.150 to NC)	1.97 (1.051 to 7.754)	1.12 (0.986 to NC)	2.00 (1.018 to 2.103)	
Median (95% CI)	NC (5.684 to NC)	NC (NC to NC)	NC (3.778 to NC)	NC (7.754 to NC)	NC (1.117 to NC)	7.72 (2.004 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (7.721 to NC)	
Comparison vs. Kd							
Log-Rank test p-value[a] vs Kd	-	0.3213		0.5141		0.4906	
Hazard ratio (95% CI) vs Kd	-	0.78 (0.47 to 1.28)		1.26 (0.63 to 2.53)		1.39 (0.54 to 3.53)	
P-value	-	0.3226		0.5151		0.4925	

A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Emotional functioning
16.2.6.1.2.8 Efficacy response data - Subgroup analyses by ISS staging at SE
16.2.6.1.2.8.4 QLQ-C30 - Time to first deterioration by 10 pt in emotional functioning according to ISS staging at SE (LOCF) - ITT population

	I		II		III		
	Kd (N=71)	**IKd (N=89)**	**Kd (N=31)**	**IKd (N=63)**	**Kd (N=20)**	**IKd (N=26)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	36 (50.7)	47 (52.8)	14 (45.2)	38 (60.3)	9 (45.0)	6 (23.1)	0.2049
Number (%) of patients censored	35 (49.3)	42 (47.2)	17 (54.8)	25 (39.7)	11 (55.0)	20 (76.9)	
Kaplan-Meier estimates of Emotional functioning in months							
25% quantile (95% CI)	2.86 (1.643 to 4.764)	3.84 (1.906 to 5.552)	3.78 (1.248 to 9.725)	2.86 (1.084 to 3.745)	4.76 (1.150 to 9.922)	12.55 (0.953 to NC)	
Median (95% CI)	16.85 (4.895 to NC)	12.94 (6.669 to NC)	NC (6.374 to NC)	6.57 (3.778 to 18.760)	19.35 (4.764 to NC)	NC (12.550 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (19.351 to NC)	NC (NC to NC)	
Comparison vs. Kd							
Log-Rank test p-value[a] vs Kd	-	0.9889		0.2068		0.1898	
Hazard ratio (95% CI) vs Kd	-	1.00 (0.65 to 1.55)		1.48 (0.80 to 2.73)		0.51 (0.18 to 1.43)	
P-value	-	0.9889		0.2098		0.1981	

A higher score represents a better level of quality of life. Clinical meaningful deterioration change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
PGM=DEVOPS/SAR650984/EFC15246/CIR_RWE/REPORT/PGM/eff_km_subgp_sr_sig_de_i_t.sas OUT=REPORT/OUTPUT/eff_km_c30_emo_detl_seiss_de_i_t_x.rtf (07APR2021 14:24)

16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Emotional functioning
16.2.6.1.2.8 Efficacy response data - Subgroup analyses by ISS staging at SE
16.2.6.1.2.8.5 QLQ-C30 - Time until permanent improvement by 10 pt in emotional functioning according to ISS staging at SE (LOCF) - ITT population

	I		II		III		
	Kd (N=71)	**IKd (N=89)**	**Kd (N=31)**	**IKd (N=63)**	**Kd (N=20)**	**IKd (N=26)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	14 (19.7)	13 (14.6)	5 (16.1)	14 (22.2)	2 (10.0)	7 (26.9)	0.2566
Number (%) of patients censored	57 (80.3)	76 (85.4)	26 (83.9)	49 (77.8)	18 (90.0)	19 (73.1)	
Kaplan-Meier estimates of Emotional functioning in months							
25% quantile (95% CI)	22.21 (16.296 to NC)	NC (20.534 to NC)	NC (6.965 to NC)	20.63 (18.694 to NC)	NC (9.363 to NC)	14.55 (1.084 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (22.144 to NC)	NC (NC to NC)	NC (NC to NC)	NC (14.554 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Kd							
Log-Rank test p-value[a] vs Kd	-	0.4992		0.6804		0.1530	
Hazard ratio (95% CI) vs Kd	-	0.77 (0.36 to 1.64)		1.24 (0.45 to 3.45)		2.98 (0.62 to 14.35)	
P-value	-	0.5004		0.6810		0.1736	

A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Emotional functioning
16.2.6.1.2.8 Efficacy response data - Subgroup analyses by ISS staging at SE
16.2.6.1.2.8.6 QLQ-C30 - Time until permanent deterioration by 10 pt in emotional functioning according to ISS staging at SE (LOCF) - ITT population

	I		II		III		
	Kd (N=71)	**IKd (N=89)**	**Kd (N=31)**	**IKd (N=63)**	**Kd (N=20)**	**IKd (N=26)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	10 (14.1)	16 (18.0)	7 (22.6)	16 (25.4)	2 (10.0)	2 (7.7)	0.9133
Number (%) of patients censored	61 (85.9)	73 (82.0)	24 (77.4)	47 (74.6)	18 (90.0)	24 (92.3)	
Kaplan-Meier estimates of Emotional functioning in months							
25% quantile (95% CI)	NC (21.224 to NC)	NC (16.624 to NC)	20.37 (5.684 to NC)	20.76 (10.448 to NC)	NC (2.957 to NC)	NC (7.458 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (20.370 to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Kd							
Log-Rank test p-value[a] vs Kd	-	0.5310		0.9161		0.8438	
Hazard ratio (95% CI) vs Kd	-	1.29 (0.58 to 2.84)		1.05 (0.43 to 2.55)		0.82 (0.12 to 5.84)	
P-value	-	0.5321		0.9169		0.8441	

A higher score represents a better level of quality of life. Clinical meaningful deterioration change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Emotional functioning
16.2.6.1.2.9 Efficacy response data - Subgroup analyses by R-ISS stage at SE
16.2.6.1.2.9.3 QLQ-C30 - Time to first improvement by 10 pt in emotional functioning according to R-ISS stage at SE (LOCF) - ITT population

	I or II		III		Not classified		
	Kd (N=103)	**IKd (N=155)**	**Kd (N=8)**	**IKd (N=16)**	**Kd (N=12)**	**IKd (N=8)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	41 (39.8)	60 (38.7)	3 (37.5)	8 (50.0)	5 (41.7)	4 (50.0)	0.6509
Number (%) of patients censored	62 (60.2)	95 (61.3)	5 (62.5)	8 (50.0)	7 (58.3)	4 (50.0)	
Kaplan-Meier estimates of Emotional functioning in months							
25% quantile (95% CI)	2.20 (1.906 to 5.651)	2.60 (1.347 to 5.815)	1.05 (0.986 to NC)	2.00 (1.084 to 2.103)	1.51 (0.953 to NC)	1.91 (1.018 to 5.979)	
Median (95% CI)	NC (17.708 to NC)	NC (NC to NC)	NC (0.986 to NC)	2.10 (1.906 to NC)	NC (0.986 to NC)	4.45 (1.018 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (1.117 to NC)	NC (2.103 to NC)	NC (NC to NC)	NC (1.906 to NC)	
Comparison vs. Kd							
Log-Rank test p-value[a] vs Kd	-	0.8213		0.8541		0.4530	
Hazard ratio (95% CI) vs Kd	-	0.96 (0.64 to 1.42)		1.13 (0.30 to 4.29)		1.65 (0.44 to 6.22)	
P-value	-	0.8205		0.8542		0.4575	

A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Emotional functioning
16.2.6.1.2.9 Efficacy response data - Subgroup analyses by R-ISS stage at SE
16.2.6.1.2.9.4 QLQ-C30 - Time to first deterioration by 10 pt in emotional functioning according to R-ISS stage at SE (LOCF) - ITT population

	I or II		III		Not classified		
	Kd (N=103)	**IKd (N=155)**	**Kd (N=8)**	**IKd (N=16)**	**Kd (N=12)**	**IKd (N=8)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	53 (51.5)	85 (54.8)	3 (37.5)	5 (31.3)	4 (33.3)	2 (25.0)	0.9792
Number (%) of patients censored	50 (48.5)	70 (45.2)	5 (62.5)	11 (68.8)	8 (66.7)	6 (75.0)	
Kaplan-Meier estimates of Emotional functioning in months							
25% quantile (95% CI)	2.96 (1.938 to 4.632)	3.19 (1.906 to 3.943)	4.76 (1.971 to NC)	8.18 (0.953 to NC)	5.68 (1.084 to NC)	16.03 (12.682 to NC)	
Median (95% CI)	15.93 (6.374 to NC)	11.07 (6.012 to NC)	NC (1.971 to NC)	NC (1.216 to NC)	NC (1.150 to NC)	19.38 (12.682 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (7.556 to NC)	NC (NC to NC)	NC (NC to NC)	NC (12.682 to NC)	
Comparison vs. Kd							
Log-Rank test p-value[a] vs Kd	-	0.8208		0.8698		0.9449	
Hazard ratio (95% CI) vs Kd	-	1.04 (0.74 to 1.47)		0.89 (0.21 to 3.74)		0.94 (0.17 to 5.17)	
P-value	-	0.8216		0.8699		0.9449	

A higher score represents a better level of quality of life. Clinical meaningful deterioration change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Emotional functioning
16.2.6.1.2.9 Efficacy response data - Subgroup analyses by R-ISS stage at SE
16.2.6.1.2.9.5 QLQ-C30 - Time until permanent improvement by 10 pt in emotional functioning according to R-ISS stage at SE (LOCF) - ITT population

	I or II		III		Not classified		
	Kd (N=103)	**IKd (N=155)**	**Kd (N=8)**	**IKd (N=16)**	**Kd (N=12)**	**IKd (N=8)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	18 (17.5)	27 (17.4)	1 (12.5)	6 (37.5)	2 (16.7)	1 (12.5)	0.4518
Number (%) of patients censored	85 (82.5)	128 (82.6)	7 (87.5)	10 (62.5)	10 (83.3)	7 (87.5)	
Kaplan-Meier estimates of Emotional functioning in months							
25% quantile (95% CI)	22.21 (19.450 to NC)	NC (20.304 to NC)	NC (9.561 to NC)	2.10 (1.084 to 19.351)	NC (5.979 to NC)	NC (2.924 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (9.561 to NC)	19.35 (2.103 to NC)	NC (7.655 to NC)	NC (2.924 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (9.561 to NC)	NC (19.351 to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Kd							
Log-Rank test p-value[a] vs Kd	-	0.8642		0.2073		0.8935	
Hazard ratio (95% CI) vs Kd	-	0.95 (0.52 to 1.72)		3.58 (0.43 to 29.80)		1.18 (0.11 to 13.05)	

A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
PGM=DEVOPS/SAR650984/EFC15246/CIR_RWE/REPORT/PGM/eff_km_subgp_sr_sig_de_i_t.sas OUT=REPORT/OUTPUT/eff_km_c30_emo_imppl_seriss_de_i_t_x.rtf (07APR2021 14:25)

16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Emotional functioning
16.2.6.1.2.9 Efficacy response data - Subgroup analyses by R-ISS stage at SE
16.2.6.1.2.9.6 QLQ-C30 - Time until permanent deterioration by 10 pt in emotional functioning according to R-ISS stage at SE (LOCF) - ITT population

	I or II		III		Not classified		
	Kd (N=103)	**IKd (N=155)**	**Kd (N=8)**	**IKd (N=16)**	**Kd (N=12)**	**IKd (N=8)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	18 (17.5)	32 (20.6)	0 (0.0)	2 (12.5)	2 (16.7)	0 (0.0)	0.9998
Number (%) of patients censored	85 (82.5)	123 (79.4)	8 (100.0)	14 (87.5)	10 (83.3)	8 (100.0)	
Kaplan-Meier estimates of Emotional functioning in months							
25% quantile (95% CI)	NC (16.690 to NC)	NC (18.760 to NC)	NC (NC to NC)	NC (7.458 to NC)	NC (1.084 to NC)	NC (NC to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (8.181 to NC)	NC (5.848 to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Kd							
Log-Rank test p-value[a] vs Kd	-	0.6925		0.3385		0.3066	
Hazard ratio (95% CI) vs Kd	-	1.12 (0.63 to 2.00)					
P-value	-	0.6927		0.9980		0.9979	

A higher score represents a better level of quality of life. Clinical meaningful deterioration change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
PGM=DEVOPS/SAR650984/EFC15246/CIR_RWE/REPORT/PGM/eff_km_subgp_sr_sig_de_i_t.sas OUT=REPORT/OUTPUT/eff_km_c30_emo_detpl_seriss_de_i_t_x.rtf (07APR2021 14:24)

16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Emotional functioning
16.2.6.1.2.10 Efficacy response data - Subgroup analyses by nb of prior lines
16.2.6.1.2.10.3 QLQ-C30 - Time to first improvement by 10 pt in emotional functioning according to nb of prior lines (LOCF) - ITT population

	1		>1		
	Kd (N=55)	**IKd (N=79)**	**Kd (N=68)**	**IKd (N=100)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	17 (30.9)	36 (45.6)	32 (47.1)	36 (36.0)	0.0394
Number (%) of patients censored	38 (69.1)	43 (54.4)	36 (52.9)	64 (64.0)	
Kaplan-Meier estimates of Emotional functioning in months					
25% quantile (95% CI)	2.23 (1.906 to NC)	2.14 (1.216 to 3.943)	1.91 (1.051 to 4.698)	2.10 (1.084 to 7.721)	
Median (95% CI)	NC (NC to NC)	NC (6.472 to NC)	17.97 (5.125 to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.1190		0.1847	
Hazard ratio (95% CI) vs Kd	-	1.58 (0.89 to 2.81)		0.73 (0.45 to 1.17)	
P-value	-	0.1222		0.1865	

A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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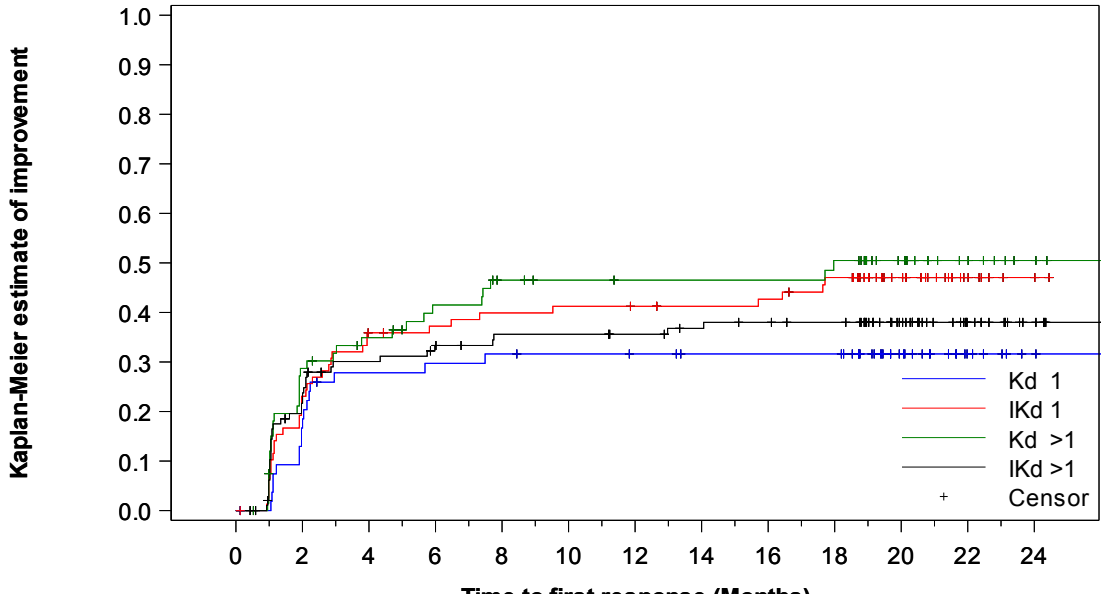
16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Emotional functioning
16.2.6.1.2.10 Efficacy response data - Subgroup analyses by nb of prior lines
16.2.6.1.2.10.4 QLQ-C30 - Time to first improvement by 10 pt in emotional functioning according to nb of prior lines - Kaplan-Meier curve (LOCF) - ITT population



Number at Risk

Kd 1	55	38	37	35	34	32	32	12	2
IKd 1	79	53	47	45	43	41	36	14	2
Kd >1	68	44	35	28	27	27	25	10	3
IKd >1	100	65	61	57	55	51	48	21	5

A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
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16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Emotional functioning
16.2.6.1.2.10 Efficacy response data - Subgroup analyses by nb of prior lines
16.2.6.1.2.10.5 QLQ-C30 - Time to first deterioration by 10 pt in emotional functioning according to nb of prior lines (LOCF) - ITT population

	1		>1		
	Kd (N=55)	**IKd (N=79)**	**Kd (N=68)**	**IKd (N=100)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	28 (50.9)	46 (58.2)	32 (47.1)	46 (46.0)	0.5070
Number (%) of patients censored	27 (49.1)	33 (41.8)	36 (52.9)	54 (54.0)	
Kaplan-Meier estimates of Emotional functioning in months					
25% quantile (95% CI)	2.86 (1.117 to 6.472)	3.29 (1.873 to 4.665)	3.12 (1.971 to 4.764)	3.75 (1.873 to 4.797)	
Median (95% CI)	16.00 (6.472 to NC)	9.79 (5.585 to 19.384)	19.35 (5.618 to NC)	NC (8.181 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.4184		0.8727	
Hazard ratio (95% CI) vs Kd	-	1.21 (0.76 to 1.94)		0.96 (0.61 to 1.51)	
P-value	-	0.4191		0.8722	

A higher score represents a better level of quality of life. Clinical meaningful deterioration change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Emotional functioning
16.2.6.1.2.10 Efficacy response data - Subgroup analyses by nb of prior lines
16.2.6.1.2.10.6 QLQ-C30 - Time until permanent improvement by 10 pt in emotional functioning according to nb of prior lines (LOCF) - ITT population

	1		>1		
	Kd (N=55)	**IKd (N=79)**	**Kd (N=68)**	**IKd (N=100)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	9 (16.4)	11 (13.9)	12 (17.6)	23 (23.0)	0.4968
Number (%) of patients censored	46 (83.6)	68 (86.1)	56 (82.4)	77 (77.0)	
Kaplan-Meier estimates of Emotional functioning in months					
25% quantile (95% CI)	22.21 (17.380 to NC)	NC (22.111 to NC)	NC (11.926 to NC)	20.30 (16.657 to NC)	
Median (95% CI)	NC (22.209 to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.8238		0.4735	
Hazard ratio (95% CI) vs Kd	-	0.90 (0.37 to 2.19)		1.29 (0.64 to 2.59)	
P-value	-	0.8239		0.4747	

A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Emotional functioning
16.2.6.1.2.10 Efficacy response data - Subgroup analyses by nb of prior lines
16.2.6.1.2.10.7 QLQ-C30 - Time until permanent deterioration by 10 pt in emotional functioning according to nb of prior lines (LOCF) - ITT population

	1		>1		
	Kd (N=55)	**IKd (N=79)**	**Kd (N=68)**	**IKd (N=100)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	9 (16.4)	15 (19.0)	11 (16.2)	19 (19.0)	0.9760
Number (%) of patients censored	46 (83.6)	64 (81.0)	57 (83.8)	81 (81.0)	
Kaplan-Meier estimates of Emotional functioning in months					
25% quantile (95% CI)	NC (5.684 to NC)	NC (18.431 to NC)	NC (15.376 to NC)	21.82 (15.671 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.7712		0.6997	
Hazard ratio (95% CI) vs Kd	-	1.13 (0.49 to 2.58)		1.16 (0.55 to 2.43)	
P-value	-	0.7713		0.7000	

A higher score represents a better level of quality of life. Clinical meaningful deterioration change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Emotional functioning
16.2.6.1.2.11 Efficacy response data - Subgroup analyses by cytogenetic abnormality
16.2.6.1.2.11.3 QLQ-C30 - Time to first improvement by 10 pt in emotional functioning according to cytogenetic abnormality (LOCF) - ITT population

	At least one		None		
	Kd (N=31)	**IKd (N=42)**	**Kd (N=77)**	**IKd (N=114)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	10 (32.3)	16 (38.1)	33 (42.9)	45 (39.5)	0.6406
Number (%) of patients censored	21 (67.7)	26 (61.9)	44 (57.1)	69 (60.5)	
Kaplan-Meier estimates of Emotional functioning in months					
25% quantile (95% CI)	2.04 (1.051 to NC)	2.00 (1.084 to 17.708)	2.14 (1.906 to 5.651)	2.14 (1.216 to 4.337)	
Median (95% CI)	NC (4.698 to NC)	NC (9.528 to NC)	NC (7.392 to NC)	NC (16.427 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.7292		0.7351	
Hazard ratio (95% CI) vs Kd	-	1.15 (0.52 to 2.53)		0.93 (0.59 to 1.45)	
P-value	-	0.7294		0.7352	

A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Emotional functioning
16.2.6.1.2.11 Efficacy response data - Subgroup analyses by cytogenetic abnormality
16.2.6.1.2.11.4 QLQ-C30 - Time to first deterioration by 10 pt in emotional functioning according to cytogenetic abnormality (LOCF) - ITT population

	At least one		None		
	Kd (N=31)	**IKd (N=42)**	**Kd (N=77)**	**IKd (N=114)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	15 (48.4)	20 (47.6)	40 (51.9)	62 (54.4)	0.6963
Number (%) of patients censored	16 (51.6)	22 (52.4)	37 (48.1)	52 (45.6)	
Kaplan-Meier estimates of Emotional functioning in months					
25% quantile (95% CI)	2.83 (1.643 to 4.830)	3.75 (1.117 to 5.717)	2.96 (1.281 to 4.764)	2.86 (1.873 to 4.665)	
Median (95% CI)	9.72 (4.665 to NC)	NC (5.684 to NC)	16.00 (6.472 to NC)	9.79 (6.571 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.7578		0.7651	
Hazard ratio (95% CI) vs Kd	-	0.90 (0.46 to 1.76)		1.06 (0.71 to 1.58)	
P-value	-	0.7579		0.7664	

A higher score represents a better level of quality of life. Clinical meaningful deterioration change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
PGM=DEVOPS/SAR650984/EFC15246/CIR_RWE/REPORT/PGM/eff_km_subgp_sr_sig_de_i_t.sas OUT=REPORT/OUTPUT/eff_km_c30_emo_detl_cyto_de_i_t_x.rtf (07APR2021 14:24)

16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Emotional functioning
16.2.6.1.2.11 Efficacy response data - Subgroup analyses by cytogenetic abnormality
16.2.6.1.2.11.5 QLQ-C30 - Time until permanent improvement by 10 pt in emotional functioning according to cytogenetic abnormality (LOCF) - ITT population

	At least one		None		
	Kd (N=31)	**IKd (N=42)**	**Kd (N=77)**	**IKd (N=114)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	5 (16.1)	10 (23.8)	13 (16.9)	19 (16.7)	0.4985
Number (%) of patients censored	26 (83.9)	32 (76.2)	64 (83.1)	95 (83.3)	
Kaplan-Meier estimates of Emotional functioning in months					
25% quantile (95% CI)	NC (9.561 to NC)	19.52 (3.680 to NC)	22.21 (17.380 to NC)	NC (19.351 to NC)	
Median (95% CI)	NC (20.632 to NC)	NC (NC to NC)	NC (22.209 to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.4716		0.9188	
Hazard ratio (95% CI) vs Kd	-	1.48 (0.51 to 4.33)		0.96 (0.48 to 1.95)	
P-value	-	0.4745		0.9185	

A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
PGM=DEVOPS/SAR650984/EFC15246/CIR_RWE/REPORT/PGM/eff_km_subgp_sr_sig_de_i_t.sas OUT=REPORT/OUTPUT/eff_km_c30_emo_imppl_cyto_de_i_t_x.rtf (07APR2021 14:24)

16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Emotional functioning
16.2.6.1.2.11 Efficacy response data - Subgroup analyses by cytogenetic abnormality
16.2.6.1.2.11.6 QLQ-C30 - Time until permanent deterioration by 10 pt in emotional functioning according to cytogenetic abnormality (LOCF) - ITT population

	At least one		None		
	Kd (N=31)	**IKd (N=42)**	**Kd (N=77)**	**IKd (N=114)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	6 (19.4)	9 (21.4)	12 (15.6)	22 (19.3)	0.7842
Number (%) of patients censored	25 (80.6)	33 (78.6)	65 (84.4)	92 (80.7)	
Kaplan-Meier estimates of Emotional functioning in months					
25% quantile (95% CI)	NC (1.971 to NC)	NC (7.458 to NC)	NC (20.370 to NC)	NC (18.563 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.9761		0.5692	
Hazard ratio (95% CI) vs Kd	-	1.02 (0.36 to 2.85)		1.23 (0.61 to 2.48)	
P-value	-	0.9762		0.5698	

A higher score represents a better level of quality of life. Clinical meaningful deterioration change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
PGM=DEVOPS/SAR650984/EFC15246/CIR_RWE/REPORT/PGM/eff_km_subgp_sr_sig_de_i_t.sas OUT=REPORT/OUTPUT/eff_km_c30_emo_detpl_cyto_de_i_t_x.rtf (07APR2021 14:24)

16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Emotional functioning
16.2.6.1.2.12 Efficacy response data - Subgroup analyses by MM type at SE
16.2.6.1.2.12.3 QLQ-C30 - Time to first improvement by 10 pt in emotional functioning according to MM type at SE (LOCF) - ITT population

	IgG		Non-IgG		
	Kd (N=85)	**IKd (N=126)**	**Kd (N=38)**	**IKd (N=53)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	37 (43.5)	57 (45.2)	12 (31.6)	15 (28.3)	0.5430
Number (%) of patients censored	48 (56.5)	69 (54.8)	26 (68.4)	38 (71.7)	
Kaplan-Meier estimates of Emotional functioning in months					
25% quantile (95% CI)	2.00 (1.117 to 4.698)	2.00 (1.150 to 2.793)	2.18 (1.216 to NC)	12.98 (1.084 to NC)	
Median (95% CI)	NC (7.425 to NC)	NC (6.472 to NC)	NC (5.914 to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.6955		0.6431	
Hazard ratio (95% CI) vs Kd	-	1.09 (0.72 to 1.64)		0.84 (0.39 to 1.79)	
P-value	-	0.6956		0.6435	

A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
PGM=DEVOPS/SAR650984/EFC15246/CIR_RWE/REPORT/PGM/eff_km_subgp_sr_sig_de_i_t.sas OUT=REPORT/OUTPUT/eff_km_c30_emo_impl_semm_de_i_t_x.rtf (07APR2021 14:24)

16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Emotional functioning
16.2.6.1.2.12 Efficacy response data - Subgroup analyses by MM type at SE
16.2.6.1.2.12.4 QLQ-C30 - Time to first deterioration by 10 pt in emotional functioning according to MM type at SE (LOCF) - ITT population

	IgG		Non-IgG		
	Kd (N=85)	**IKd (N=126)**	**Kd (N=38)**	**IKd (N=53)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	42 (49.4)	62 (49.2)	18 (47.4)	30 (56.6)	0.5465
Number (%) of patients censored	43 (50.6)	64 (50.8)	20 (52.6)	23 (43.4)	
Kaplan-Meier estimates of Emotional functioning in months					
25% quantile (95% CI)	2.83 (1.281 to 4.895)	3.75 (1.873 to 4.797)	3.78 (1.643 to 5.618)	3.19 (1.150 to 4.665)	
Median (95% CI)	19.22 (6.637 to NC)	18.04 (8.181 to NC)	16.00 (4.665 to NC)	8.28 (4.665 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.9948		0.4685	
Hazard ratio (95% CI) vs Kd	-	1.00 (0.67 to 1.48)		1.24 (0.69 to 2.23)	
P-value	-	0.9948		0.4694	

A higher score represents a better level of quality of life. Clinical meaningful deterioration change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
PGM=DEVOPS/SAR650984/EFC15246/CIR_RWE/REPORT/PGM/eff_km_subgp_sr_sig_de_i_t.sas OUT=REPORT/OUTPUT/eff_km_c30_emo_detl_semm_de_i_t_x.rtf (07APR2021 14:24)

16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Emotional functioning
16.2.6.1.2.12 Efficacy response data - Subgroup analyses by MM type at SE
16.2.6.1.2.12.5 QLQ-C30 - Time until permanent improvement by 10 pt in emotional functioning according to MM type at SE (LOCF) - ITT population

	IgG		Non-IgG		
	Kd (N=85)	**IKd (N=126)**	**Kd (N=38)**	**IKd (N=53)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	16 (18.8)	26 (20.6)	5 (13.2)	8 (15.1)	0.8982
Number (%) of patients censored	69 (81.2)	100 (79.4)	33 (86.8)	45 (84.9)	
Kaplan-Meier estimates of Emotional functioning in months					
25% quantile (95% CI)	22.21 (16.296 to NC)	22.11 (18.694 to NC)	NC (9.363 to NC)	NC (16.394 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.6474		0.8842	
Hazard ratio (95% CI) vs Kd	-	1.16 (0.62 to 2.16)		1.09 (0.36 to 3.32)	
P-value	-	0.6477		0.8843	

A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Emotional functioning
16.2.6.1.2.12 Efficacy response data - Subgroup analyses by MM type at SE
16.2.6.1.2.12.6 QLQ-C30 - Time until permanent deterioration by 10 pt in emotional functioning according to MM type at SE (LOCF) - ITT population

	IgG		Non-IgG		
	Kd (N=85)	**IKd (N=126)**	**Kd (N=38)**	**IKd (N=53)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	15 (17.6)	25 (19.8)	5 (13.2)	9 (17.0)	0.9579
Number (%) of patients censored	70 (82.4)	101 (80.2)	33 (86.8)	44 (83.0)	
Kaplan-Meier estimates of Emotional functioning in months					
25% quantile (95% CI)	NC (15.376 to NC)	NC (16.624 to NC)	NC (6.374 to NC)	NC (15.704 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.6833		0.7855	
Hazard ratio (95% CI) vs Kd	-	1.14 (0.60 to 2.17)		1.16 (0.39 to 3.48)	
P-value	-	0.6835		0.7857	

A higher score represents a better level of quality of life. Clinical meaningful deterioration change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Emotional functioning
16.2.6.1.2.13 Efficacy response data - Subgroup analyses by previous autologous stem-cell
16.2.6.1.2.13.3 QLQ-C30 - Time to first improvement by 10 pt in emotional functioning according to previous autologous stem-cell (LOCF) - ITT population

	Yes		No		
	Kd (N=69)	**IKd (N=116)**	**Kd (N=54)**	**IKd (N=63)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	27 (39.1)	41 (35.3)	22 (40.7)	31 (49.2)	0.3437
Number (%) of patients censored	42 (60.9)	75 (64.7)	32 (59.3)	32 (50.8)	
Kaplan-Meier estimates of Emotional functioning in months					
25% quantile (95% CI)	2.92 (1.117 to 7.491)	2.79 (1.971 to 7.721)	2.00 (1.216 to 2.957)	1.97 (1.051 to 2.924)	
Median (95% CI)	NC (7.655 to NC)	NC (NC to NC)	NC (2.957 to NC)	16.43 (2.924 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.6555		0.3881	
Hazard ratio (95% CI) vs Kd	-	0.90 (0.55 to 1.46)		1.27 (0.74 to 2.20)	
P-value	-	0.6556		0.3893	

A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Emotional functioning
16.2.6.1.2.13 Efficacy response data - Subgroup analyses by previous autologous stem-cell
16.2.6.1.2.13.4 QLQ-C30 - Time to first deterioration by 10 pt in emotional functioning according to previous autologous stem-cell (LOCF) - ITT population

	Yes		No		
	Kd (N=69)	**IKd (N=116)**	**Kd (N=54)**	**IKd (N=63)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	34 (49.3)	62 (53.4)	26 (48.1)	30 (47.6)	0.6899
Number (%) of patients censored	35 (50.7)	54 (46.6)	28 (51.9)	33 (52.4)	
Kaplan-Meier estimates of Emotional functioning in months					
25% quantile (95% CI)	3.06 (1.873 to 5.125)	3.06 (1.906 to 4.140)	2.86 (1.150 to 4.830)	3.78 (1.478 to 6.571)	
Median (95% CI)	16.85 (6.472 to NC)	12.68 (5.717 to NC)	19.22 (4.830 to NC)	15.77 (6.571 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.6133		0.9433	
Hazard ratio (95% CI) vs Kd	-	1.11 (0.73 to 1.69)		0.98 (0.58 to 1.66)	
P-value	-	0.6135		0.9433	

A higher score represents a better level of quality of life. Clinical meaningful deterioration change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Emotional functioning
16.2.6.1.2.13 Efficacy response data - Subgroup analyses by previous autologous stem-cell
16.2.6.1.2.13.5 QLQ-C30 - Time until permanent improvement by 10 pt in emotional functioning according to previous autologous stem-cell (LOCF) - ITT population

	Yes		No		
	Kd (N=69)	**IKd (N=116)**	**Kd (N=54)**	**IKd (N=63)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	12 (17.4)	19 (16.4)	9 (16.7)	15 (23.8)	0.4223
Number (%) of patients censored	57 (82.6)	97 (83.6)	45 (83.3)	48 (76.2)	
Kaplan-Meier estimates of Emotional functioning in months					
25% quantile (95% CI)	22.14 (11.926 to NC)	NC (19.351 to NC)	22.21 (15.441 to NC)	19.52 (11.170 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (22.111 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.8904		0.3473	
Hazard ratio (95% CI) vs Kd	-	0.95 (0.46 to 1.96)		1.48 (0.65 to 3.39)	
P-value	-	0.8897		0.3504	

A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Emotional functioning
16.2.6.1.2.13 Efficacy response data - Subgroup analyses by previous autologous stem-cell
16.2.6.1.2.13.6 QLQ-C30 - Time until permanent deterioration by 10 pt in emotional functioning according to previous autologous stem-cell (LOCF) - ITT population

	Yes		No		
	Kd (N=69)	**IKd (N=116)**	**Kd (N=54)**	**IKd (N=63)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	11 (15.9)	25 (21.6)	9 (16.7)	9 (14.3)	0.3809
Number (%) of patients censored	58 (84.1)	91 (78.4)	45 (83.3)	54 (85.7)	
Kaplan-Meier estimates of Emotional functioning in months					
25% quantile (95% CI)	NC (20.370 to NC)	20.76 (15.704 to NC)	NC (8.378 to NC)	NC (18.431 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.3712		0.6790	
Hazard ratio (95% CI) vs Kd	-	1.38 (0.68 to 2.81)		0.82 (0.33 to 2.07)	
P-value	-	0.3733		0.6795	

A higher score represents a better level of quality of life. Clinical meaningful deterioration change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Emotional functioning
16.2.6.1.2.14 Efficacy response data - Subgroup analyses by baseline eGFR (MDRD)
16.2.6.1.2.14.3 QLQ-C30 - Time to first improvement by 10 pt in emotional functioning according to baseline eGFR (MDRD) (LOCF) - ITT population

	>=60 mL/min/1.73m2		<60 mL/min/1.73m2		
	Kd (N=93)	**IKd (N=122)**	**Kd (N=18)**	**IKd (N=43)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	41 (44.1)	47 (38.5)	7 (38.9)	20 (46.5)	0.9825
Number (%) of patients censored	52 (55.9)	75 (61.5)	11 (61.1)	23 (53.5)	
Kaplan-Meier estimates of Emotional functioning in months					
25% quantile (95% CI)	2.02 (1.906 to 3.023)	2.10 (1.117 to 4.337)	1.15 (0.986 to NC)	2.00 (1.150 to 5.815)	
Median (95% CI)	NC (7.392 to NC)	NC (17.708 to NC)	NC (1.051 to NC)	NC (2.891 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.6654		0.7835	
Hazard ratio (95% CI) vs Kd	-	0.91 (0.60 to 1.39)		0.89 (0.37 to 2.10)	
P-value	-	0.6641		0.7836	

A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
PGM=DEVOPS/SAR650984/EFC15246/CIR_RWE/REPORT/PGM/eff_km_subgp_sr_sig_de_i_t.sas OUT=REPORT/OUTPUT/eff_km_c30_emo_impl_crcl_de_i_t_x.rtf (07APR2021 14:24)

16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Emotional functioning
16.2.6.1.2.14 Efficacy response data - Subgroup analyses by baseline eGFR (MDRD)
16.2.6.1.2.14.4 QLQ-C30 - Time to first deterioration by 10 pt in emotional functioning according to baseline eGFR (MDRD) (LOCF) - ITT population

	>=60 mL/min/1.73m2		<60 mL/min/1.73m2		
	Kd (N=93)	**IKd (N=122)**	**Kd (N=18)**	**IKd (N=43)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	46 (49.5)	65 (53.3)	10 (55.6)	20 (46.5)	0.1022
Number (%) of patients censored	47 (50.5)	57 (46.7)	8 (44.4)	23 (53.5)	
Kaplan-Meier estimates of Emotional functioning in months					
25% quantile (95% CI)	3.42 (1.971 to 4.764)	3.29 (1.906 to 4.665)	2.83 (0.920 to 4.830)	3.75 (1.051 to 6.571)	
Median (95% CI)	19.35 (7.556 to NC)	11.50 (5.717 to NC)	4.83 (1.971 to NC)	NC (6.571 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (4.830 to NC)	NC (NC to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.3714		0.2112	
Hazard ratio (95% CI) vs Kd	-	1.19 (0.81 to 1.73)		0.62 (0.29 to 1.32)	
P-value	-	0.3720		0.2156	

A higher score represents a better level of quality of life. Clinical meaningful deterioration change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Emotional functioning
16.2.6.1.2.14 Efficacy response data - Subgroup analyses by baseline eGFR (MDRD)
16.2.6.1.2.14.5 QLQ-C30 - Time until permanent improvement by 10 pt in emotional functioning according to baseline eGFR (MDRD) (LOCF) - ITT population

	>=60 mL/min/1.73m2		<60 mL/min/1.73m2		
	Kd (N=93)	**IKd (N=122)**	**Kd (N=18)**	**IKd (N=43)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	19 (20.4)	20 (16.4)	2 (11.1)	11 (25.6)	0.2909
Number (%) of patients censored	74 (79.6)	102 (83.6)	16 (88.9)	32 (74.4)	
Kaplan-Meier estimates of Emotional functioning in months					
25% quantile (95% CI)	22.14 (16.296 to NC)	NC (19.515 to NC)	NC (0.986 to NC)	18.76 (14.029 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.5700		0.4044	
Hazard ratio (95% CI) vs Kd	-	0.83 (0.44 to 1.56)		1.88 (0.42 to 8.48)	
P-value	-	0.5706		0.4122	

A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Emotional functioning
16.2.6.1.2.14 Efficacy response data - Subgroup analyses by baseline eGFR (MDRD)
16.2.6.1.2.14.6 QLQ-C30 - Time until permanent deterioration by 10 pt in emotional functioning according to baseline eGFR (MDRD) (LOCF) - ITT population

	>=60 mL/min/1.73m2		<60 mL/min/1.73m2		
	Kd (N=93)	**IKd (N=122)**	**Kd (N=18)**	**IKd (N=43)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	13 (14.0)	24 (19.7)	4 (22.2)	9 (20.9)	0.1930
Number (%) of patients censored	80 (86.0)	98 (80.3)	14 (77.8)	34 (79.1)	
Kaplan-Meier estimates of Emotional functioning in months					
25% quantile (95% CI)	NC (20.370 to NC)	NC (15.704 to NC)	5.85 (1.084 to NC)	21.82 (8.181 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (5.848 to NC)	NC (21.815 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.2125		0.4541	
Hazard ratio (95% CI) vs Kd	-	1.53 (0.78 to 3.01)		0.64 (0.19 to 2.09)	
P-value	-	0.2160		0.4578	

A higher score represents a better level of quality of life. Clinical meaningful deterioration change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Emotional functioning
16.2.6.1.2.15 Efficacy response data - Subgroup analyses by previous treatment with PI
16.2.6.1.2.15.3 QLQ-C30 - Time to first improvement by 10 pt in emotional functioning according to previous treatment with PI (LOCF) - ITT population

	Yes		No		
	Kd (N=47)	**IKd (N=81)**	**Kd (N=76)**	**IKd (N=98)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	22 (46.8)	34 (42.0)	27 (35.5)	38 (38.8)	0.4038
Number (%) of patients censored	25 (53.2)	47 (58.0)	49 (64.5)	60 (61.2)	
Kaplan-Meier estimates of Emotional functioning in months					
25% quantile (95% CI)	1.91 (1.051 to 2.136)	2.00 (1.413 to 2.924)	5.13 (1.906 to 17.708)	2.79 (1.084 to 7.326)	
Median (95% CI)	NC (2.037 to NC)	NC (5.815 to NC)	NC (17.971 to NC)	NC (17.643 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.5084		0.6102	
Hazard ratio (95% CI) vs Kd	-	0.83 (0.49 to 1.43)		1.14 (0.69 to 1.86)	
P-value	-	0.5090		0.6104	

A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Emotional functioning
16.2.6.1.2.15 Efficacy response data - Subgroup analyses by previous treatment with PI
16.2.6.1.2.15.4 QLQ-C30 - Time to first deterioration by 10 pt in emotional functioning according to previous treatment with PI (LOCF) - ITT population

	Yes		No		
	Kd (N=47)	**IKd (N=81)**	**Kd (N=76)**	**IKd (N=98)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	17 (36.2)	39 (48.1)	43 (56.6)	53 (54.1)	0.1038
Number (%) of patients censored	30 (63.8)	42 (51.9)	33 (43.4)	45 (45.9)	
Kaplan-Meier estimates of Emotional functioning in months					
25% quantile (95% CI)	6.47 (2.004 to 19.351)	3.42 (1.873 to 5.552)	2.83 (1.150 to 3.778)	3.22 (1.906 to 4.600)	
Median (95% CI)	NC (16.000 to NC)	12.55 (5.717 to NC)	7.79 (4.632 to NC)	12.94 (6.571 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.1234		0.5209	
Hazard ratio (95% CI) vs Kd	-	1.56 (0.88 to 2.76)		0.88 (0.59 to 1.31)	
P-value	-	0.1265		0.5212	

A higher score represents a better level of quality of life. Clinical meaningful deterioration change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Emotional functioning
16.2.6.1.2.15 Efficacy response data - Subgroup analyses by previous treatment with PI
16.2.6.1.2.15.5 QLQ-C30 - Time until permanent improvement by 10 pt in emotional functioning according to previous treatment with PI (LOCF) - ITT population

	Yes		No		
	Kd (N=47)	**IKd (N=81)**	**Kd (N=76)**	**IKd (N=98)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	13 (27.7)	16 (19.8)	8 (10.5)	18 (18.4)	0.1214
Number (%) of patients censored	34 (72.3)	65 (80.2)	68 (89.5)	80 (81.6)	
Kaplan-Meier estimates of Emotional functioning in months					
25% quantile (95% CI)	17.38 (7.655 to NC)	22.11 (14.554 to NC)	NC (22.209 to NC)	NC (18.694 to NC)	
Median (95% CI)	NC (22.144 to NC)	NC (22.111 to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.4213		0.1812	
Hazard ratio (95% CI) vs Kd	-	0.74 (0.35 to 1.54)		1.75 (0.76 to 4.03)	
P-value	-	0.4230		0.1870	

A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Emotional functioning
16.2.6.1.2.15 Efficacy response data - Subgroup analyses by previous treatment with PI
16.2.6.1.2.15.6 QLQ-C30 - Time until permanent deterioration by 10 pt in emotional functioning according to previous treatment with PI (LOCF) - ITT population

	Yes		No		
	Kd (N=47)	**IKd (N=81)**	**Kd (N=76)**	**IKd (N=98)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	6 (12.8)	14 (17.3)	14 (18.4)	20 (20.4)	0.6775
Number (%) of patients censored	41 (87.2)	67 (82.7)	62 (81.6)	78 (79.6)	
Kaplan-Meier estimates of Emotional functioning in months					
25% quantile (95% CI)	NC (14.653 to NC)	21.82 (19.877 to NC)	NC (15.376 to NC)	NC (15.244 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.5093		0.8334	
Hazard ratio (95% CI) vs Kd	-	1.38 (0.53 to 3.59)		1.08 (0.54 to 2.13)	
P-value	-	0.5111		0.8343	

A higher score represents a better level of quality of life. Clinical meaningful deterioration change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Emotional functioning
16.2.6.1.2.16 Efficacy response data - Subgroup analyses by previous treatment with IMiD
16.2.6.1.2.16.3 QLQ-C30 - Time to first improvement by 10 pt in emotional functioning according to previous treatment with IMiD (LOCF) - ITT population

	Yes		No		
	Kd (N=62)	**IKd (N=81)**	**Kd (N=61)**	**IKd (N=98)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	22 (35.5)	30 (37.0)	27 (44.3)	42 (42.9)	0.7214
Number (%) of patients censored	40 (64.5)	51 (63.0)	34 (55.7)	56 (57.1)	
Kaplan-Meier estimates of Emotional functioning in months					
25% quantile (95% CI)	3.78 (1.906 to 7.655)	2.60 (1.051 to 7.754)	1.94 (1.051 to 2.957)	2.00 (1.347 to 2.924)	
Median (95% CI)	NC (17.708 to NC)	NC (17.643 to NC)	NC (2.957 to NC)	NC (9.528 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.8093		0.8116	
Hazard ratio (95% CI) vs Kd	-	1.07 (0.62 to 1.85)		0.94 (0.58 to 1.53)	
P-value	-	0.8102		0.8104	

A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Emotional functioning
16.2.6.1.2.16 Efficacy response data - Subgroup analyses by previous treatment with IMiD
16.2.6.1.2.16.4 QLQ-C30 - Time to first deterioration by 10 pt in emotional functioning according to previous treatment with IMiD (LOCF) - ITT population

	Yes		No		
	Kd (N=62)	**IKd (N=81)**	**Kd (N=61)**	**IKd (N=98)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	32 (51.6)	38 (46.9)	28 (45.9)	54 (55.1)	0.1910
Number (%) of patients censored	30 (48.4)	43 (53.1)	33 (54.1)	44 (44.9)	
Kaplan-Meier estimates of Emotional functioning in months					
25% quantile (95% CI)	3.06 (1.873 to 5.125)	3.94 (1.906 to 5.618)	3.30 (1.248 to 6.374)	3.06 (1.873 to 3.910)	
Median (95% CI)	11.40 (5.125 to NC)	NC (8.279 to NC)	NC (6.374 to NC)	9.79 (5.717 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.4836		0.2511	
Hazard ratio (95% CI) vs Kd	-	0.85 (0.53 to 1.35)		1.31 (0.83 to 2.06)	
P-value	-	0.4841		0.2525	

A higher score represents a better level of quality of life. Clinical meaningful deterioration change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Emotional functioning
16.2.6.1.2.16 Efficacy response data - Subgroup analyses by previous treatment with IMiD
16.2.6.1.2.16.5 QLQ-C30 - Time until permanent improvement by 10 pt in emotional functioning according to previous treatment with IMiD (LOCF) - ITT population

	Yes		No		
	Kd (N=62)	**IKd (N=81)**	**Kd (N=61)**	**IKd (N=98)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	9 (14.5)	16 (19.8)	12 (19.7)	18 (18.4)	0.5096
Number (%) of patients censored	53 (85.5)	65 (80.2)	49 (80.3)	80 (81.6)	
Kaplan-Meier estimates of Emotional functioning in months					
25% quantile (95% CI)	22.21 (20.632 to NC)	20.63 (18.694 to NC)	NC (11.926 to NC)	22.11 (18.168 to NC)	
Median (95% CI)	NC (22.209 to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.4464		0.8448	
Hazard ratio (95% CI) vs Kd	-	1.37 (0.61 to 3.11)		0.93 (0.45 to 1.93)	
P-value	-	0.4483		0.8448	

A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Emotional functioning
16.2.6.1.2.16 Efficacy response data - Subgroup analyses by previous treatment with IMiD
16.2.6.1.2.16.6 QLQ-C30 - Time until permanent deterioration by 10 pt in emotional functioning according to previous treatment with IMiD (LOCF) - ITT population

	Yes		No		
	Kd (N=62)	**IKd (N=81)**	**Kd (N=61)**	**IKd (N=98)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	10 (16.1)	13 (16.0)	10 (16.4)	21 (21.4)	0.5502
Number (%) of patients censored	52 (83.9)	68 (84.0)	51 (83.6)	77 (78.6)	
Kaplan-Meier estimates of Emotional functioning in months					
25% quantile (95% CI)	NC (14.653 to NC)	NC (19.121 to NC)	NC (7.524 to NC)	20.76 (15.671 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.9181		0.4552	
Hazard ratio (95% CI) vs Kd	-	0.96 (0.42 to 2.18)		1.33 (0.63 to 2.83)	
P-value	-	0.9178		0.4568	

A higher score represents a better level of quality of life. Clinical meaningful deterioration change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
PGM=DEVOPS/SAR650984/EFC15246/CIR_RWE/REPORT/PGM/eff_km_subgp_sr_sig_de_i_t.sas OUT=REPORT/OUTPUT/eff_km_c30_emo_detpl_imid_de_i_t_x.rtf (07APR2021 14:24)

16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Emotional functioning
16.2.6.1.2.17 Efficacy response data - Subgroup analyses by previous treatment with PI and IMiD
16.2.6.1.2.17.3 QLQ-C30 - Time to first improvement by 10 pt in emotional functioning according to previous treatment with PI and IMiD (LOCF) - ITT population

	Yes		No		
	Kd (N=17)	**IKd (N=23)**	**Kd (N=106)**	**IKd (N=156)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	4 (23.5)	9 (39.1)	45 (42.5)	63 (40.4)	0.3256
Number (%) of patients censored	13 (76.5)	14 (60.9)	61 (57.5)	93 (59.6)	
Kaplan-Meier estimates of Emotional functioning in months					
25% quantile (95% CI)	5.65 (1.216 to NC)	2.60 (0.986 to NC)	2.04 (1.840 to 3.778)	2.10 (1.347 to 3.943)	
Median (95% CI)	NC (5.651 to NC)	NC (2.595 to NC)	NC (7.491 to NC)	NC (17.708 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.3601		0.7868	
Hazard ratio (95% CI) vs Kd	-	1.72 (0.53 to 5.60)		0.95 (0.65 to 1.39)	
P-value	-	0.3661		0.7858	

A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Emotional functioning
16.2.6.1.2.17 Efficacy response data - Subgroup analyses by previous treatment with PI and IMiD
16.2.6.1.2.17.4 QLQ-C30 - Time to first deterioration by 10 pt in emotional functioning according to previous treatment with PI and IMiD (LOCF) - ITT population

	Yes		No		
	Kd (N=17)	**IKd (N=23)**	**Kd (N=106)**	**IKd (N=156)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	7 (41.2)	10 (43.5)	53 (50.0)	82 (52.6)	0.8505
Number (%) of patients censored	10 (58.8)	13 (56.5)	53 (50.0)	74 (47.4)	
Kaplan-Meier estimates of Emotional functioning in months					
25% quantile (95% CI)	6.47 (2.825 to 16.000)	4.14 (1.117 to 5.552)	2.86 (1.873 to 4.665)	3.19 (1.906 to 4.600)	
Median (95% CI)	NC (3.877 to NC)	NC (4.140 to NC)	16.85 (5.618 to NC)	12.68 (7.655 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.7303		0.7896	
Hazard ratio (95% CI) vs Kd	-	1.19 (0.45 to 3.12)		1.05 (0.74 to 1.48)	
P-value	-	0.7306		0.7905	

A higher score represents a better level of quality of life. Clinical meaningful deterioration change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Emotional functioning
16.2.6.1.2.17 Efficacy response data - Subgroup analyses by previous treatment with PI and IMiD
16.2.6.1.2.17.5 QLQ-C30 - Time until permanent improvement by 10 pt in emotional functioning according to previous treatment with PI and IMiD (LOCF) - ITT population

	Yes		No		
	Kd (N=17)	**IKd (N=23)**	**Kd (N=106)**	**IKd (N=156)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	2 (11.8)	5 (21.7)	19 (17.9)	29 (18.6)	0.4622
Number (%) of patients censored	15 (88.2)	18 (78.3)	87 (82.1)	127 (81.4)	
Kaplan-Meier estimates of Emotional functioning in months					
25% quantile (95% CI)	NC (1.938 to NC)	20.53 (1.413 to NC)	22.21 (17.380 to NC)	22.11 (19.351 to NC)	
Median (95% CI)	NC (22.144 to NC)	NC (20.534 to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (22.144 to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.3532		0.9210	
Hazard ratio (95% CI) vs Kd	-	2.15 (0.41 to 11.27)		1.03 (0.58 to 1.84)	
P-value	-	0.3642		0.9212	

A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Emotional functioning
16.2.6.1.2.17 Efficacy response data - Subgroup analyses by previous treatment with PI and IMiD
16.2.6.1.2.17.6 QLQ-C30 - Time until permanent deterioration by 10 pt in emotional functioning according to previous treatment with PI and IMiD (LOCF) - ITT population

	Yes		No		
	Kd (N=17)	**IKd (N=23)**	**Kd (N=106)**	**IKd (N=156)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	2 (11.8)	4 (17.4)	18 (17.0)	30 (19.2)	0.7903
Number (%) of patients censored	15 (88.2)	19 (82.6)	88 (83.0)	126 (80.8)	
Kaplan-Meier estimates of Emotional functioning in months					
25% quantile (95% CI)	NC (2.825 to NC)	21.82 (1.511 to NC)	NC (20.370 to NC)	NC (18.563 to NC)	
Median (95% CI)	NC (NC to NC)	NC (21.815 to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.6491		0.6997	
Hazard ratio (95% CI) vs Kd	-	1.48 (0.27 to 8.08)		1.12 (0.63 to 2.01)	
P-value	-	0.6513		0.6998	

A higher score represents a better level of quality of life. Clinical meaningful deterioration change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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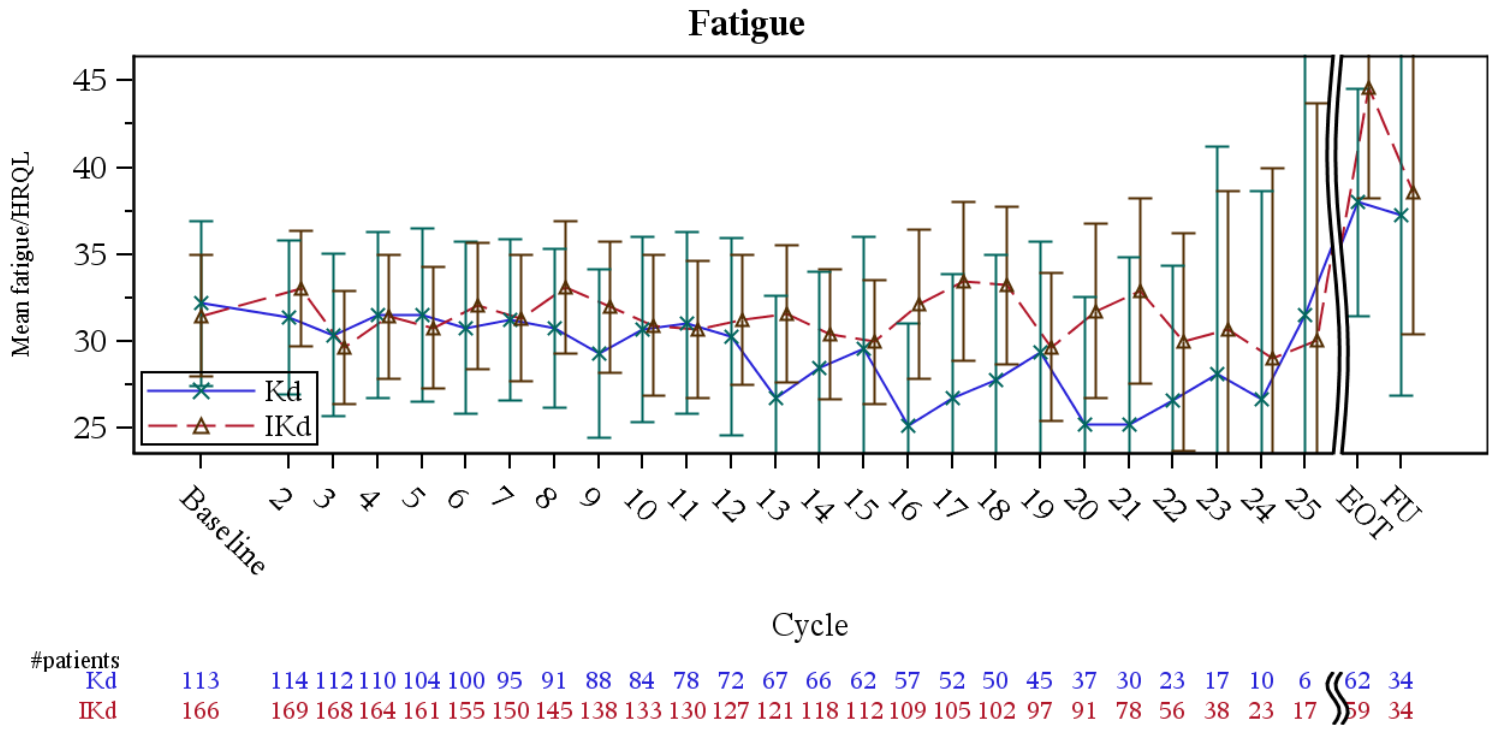
16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Fatigue
16.2.6.1.2.1 Efficacy response data
16.2.6.1.2.1.1 QLQ-C30 - Mean and 95% CI for fatigue score over time (LOCF) - ITT population



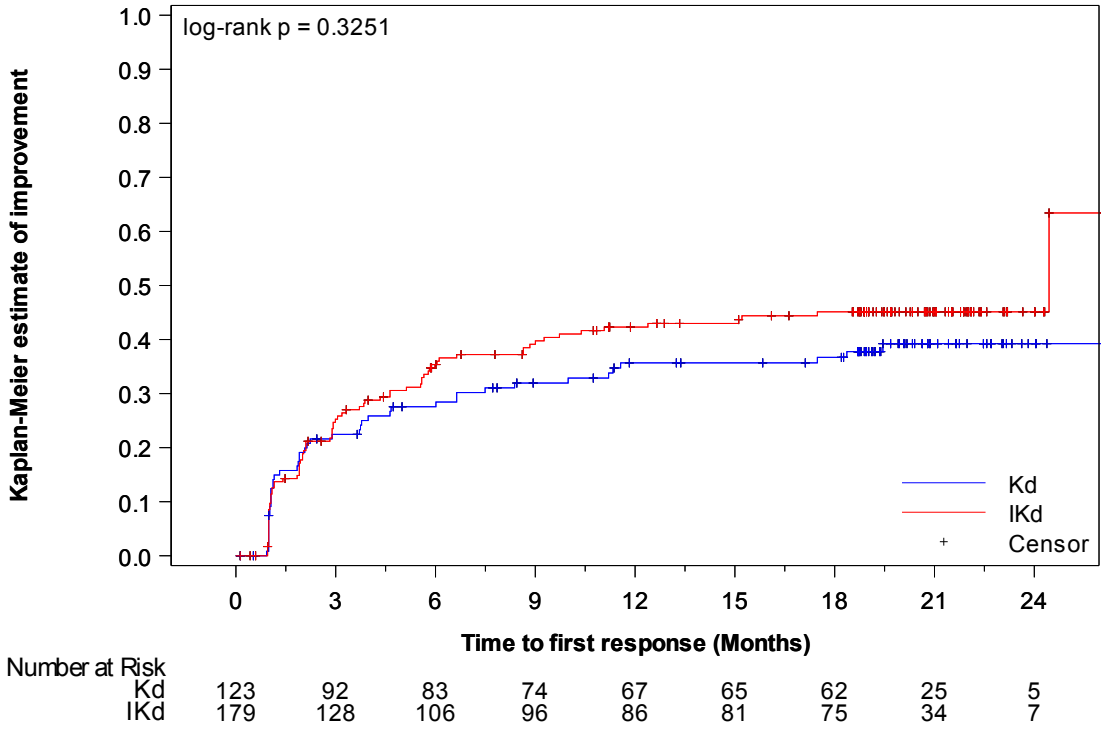
A lower score represents a better level of quality of life. Cycles with less than 20 patients overall are not presented.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
PGM=DEVOPS/SAR650984/EFC15246/CIR_RWE/REPORT/PGM/eff_qlq_line_i_f.sas OUT=REPORT/OUTPUT/eff_qlq_line_c30_fat_de_i_f_x.rtf (12FEB2021 15:16)

16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Fatigue
16.2.6.1.2.1 Efficacy response data
16.2.6.1.2.1.15 QLQ-C30 - Time to first improvement by 15 pt in fatigue (LOCF) - ITT population

First improvement 15 points Fatigue (%)	**Kd (N=123)**	**IKd (N=179)**
Number (%) of events	45 (36.6)	77 (43.0)
Number (%) of patients censored	78 (63.4)	102 (57.0)
Kaplan-Meier estimates of Fatigue in months		
25% quantile (95% CI)	3.78 (1.873 to 9.988)	2.99 (2.004 to 5.552)
Median (95% CI)	NC (NC to NC)	24.44 (11.072 to NC)
75% quantile (95% CI)	NC (NC to NC)	NC (24.444 to NC)
Comparison vs. Kd		
Stratified[a] Log-Rank test p-value[b] vs Kd	-	0.3251
Stratified[a] Hazard ratio (95% CI) vs Kd	-	1.20 (0.83 to 1.74)
P-value	-	0.3258
Improvement probability (95% CI)[c]		
3 Months	0.225 (0.155 to 0.303)	0.253 (0.191 to 0.319)
6 Months	0.276 (0.199 to 0.358)	0.354 (0.283 to 0.425)

A lower score represents a better level of quality of life. Clinical meaningful improvement change from baseline less than or equal to -15 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] Stratified on number of prior lines of therapy (1 vs. >1) and Revised International Staging System (R-ISS) stage (I or II vs. III vs. not classified) according to IRT
[b] One-sided significance level is 0.025
[c] Estimated using the Kaplan-Meier method
NA/NC = Not Applicable / Not Calculable
PGM=DEVOPS/SAR650984/EFC15246/CIR_RWE/REPORT/PGM/eff_km_invhr_sr_i_t.sas OUT=REPORT/OUTPUT/eff_km_c30_fat_imp15l_de_i_t_x.rtf (07APR2021 14:22)

16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Fatigue
16.2.6.1.2.1 Efficacy response data
16.2.6.1.2.1.16 QLQ-C30 - Time to first improvement by 15 pt in fatigue - Kaplan-Meier curve (LOCF) - ITT population



A lower score represents a better level of quality of life. Clinical meaningful improvement change from baseline less than or equal to -15 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.

16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Fatigue
16.2.6.1.2.1 Efficacy response data
16.2.6.1.2.1.17 QLQ-C30 - Time to first deterioration by 15 pt in fatigue (LOCF) - ITT population

First deterioration 15 points Fatigue (%)	**Kd (N=123)**	**IKd (N=179)**
Number (%) of events	65 (52.8)	92 (51.4)
Number (%) of patients censored	58 (47.2)	87 (48.6)
Kaplan-Meier estimates of Fatigue in months		
25% quantile (95% CI)	2.04 (1.248 to 3.811)	2.83 (1.873 to 3.811)
Median (95% CI)	13.54 (5.815 to NC)	12.65 (8.805 to NC)
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)
Comparison vs. Kd		
Stratified[a] Log-Rank test p-value[b] vs Kd	-	0.7232
Stratified[a] Hazard ratio (95% CI) vs Kd	-	0.94 (0.69 to 1.30)
P-value	-	0.7217
Deterioration probability (95% CI)[c]		
3 Months	0.700 (0.609 to 0.773)	0.731 (0.658 to 0.790)
6 Months	0.586 (0.492 to 0.669)	0.619 (0.542 to 0.687)

A lower score represents a better level of quality of life. Clinical meaningful deterioration change from baseline greater than or equal to 15 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] Stratified on number of prior lines of therapy (1 vs. >1) and Revised International Staging System (R-ISS) stage (I or II vs. III vs. not classified) according to IRT
[b] One-sided significance level is 0.025
[c] Estimated using the Kaplan-Meier method
NA/NC = Not Applicable / Not Calculable
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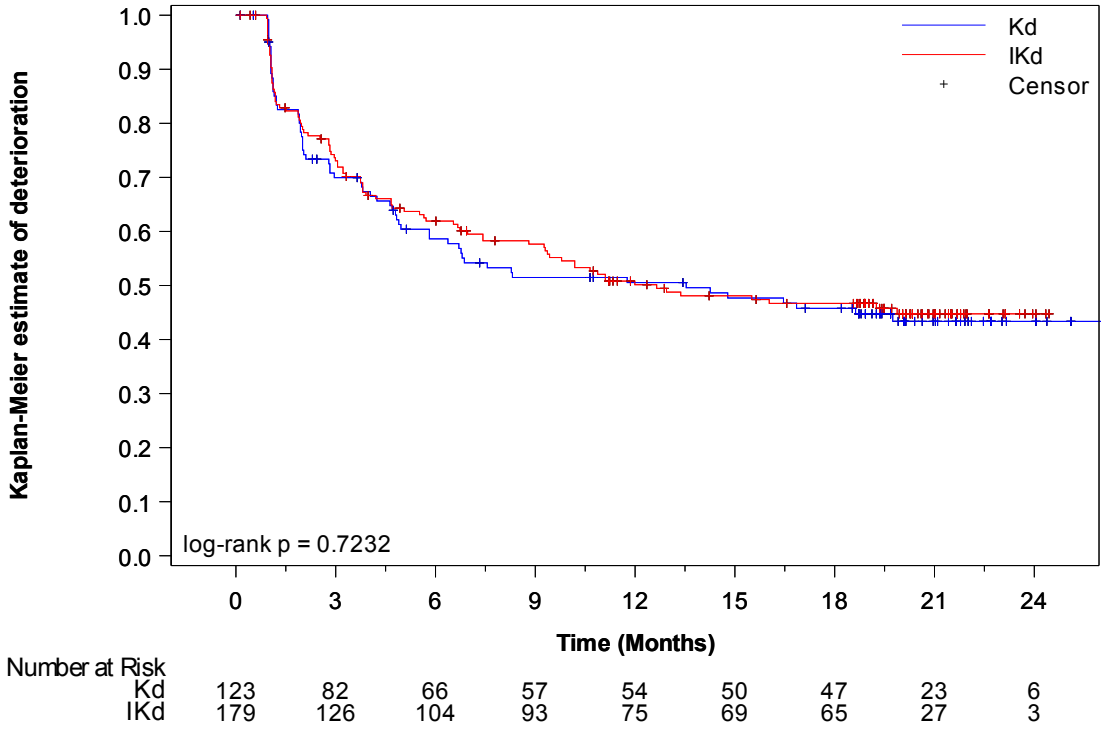
16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Fatigue
16.2.6.1.2.1 Efficacy response data
16.2.6.1.2.1.18 QLQ-C30 - Time to first deterioration by 15 pt in fatigue - Kaplan-Meier curve (LOCF) - ITT population



A lower score represents a better level of quality of life. Clinical meaningful deterioration change from baseline greater than or equal to 15 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
PGM=DEVOPS/SAR650984/EFC15246/CIR_RWE/REPORT/PGM/eff_qlq_km_i_f.sas OUT=REPORT/OUTPUT/eff_km_c30_fat_det15l_de_i_f_x.rtf (07APR2021 14:23)

16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Fatigue
16.2.6.1.2.1 Efficacy response data
16.2.6.1.2.1.19 QLQ-C30 - Time until permanent improvement by 15 pt in fatigue (LOCF) - ITT population

First permanent improvement 15 points Fatigue (%)	**Kd (N=123)**	**IKd (N=179)**
Number (%) of events	15 (12.2)	34 (19.0)
Number (%) of patients censored	108 (87.8)	145 (81.0)
Kaplan-Meier estimates of Fatigue in months		
25% quantile (95% CI)	24.05 (21.947 to NC)	21.72 (19.581 to NC)
Median (95% CI)	NC (24.049 to NC)	24.44 (24.444 to NC)
75% quantile (95% CI)	NC (NC to NC)	NC (24.444 to NC)
Comparison vs. Kd		
Stratified[a] Log-Rank test p-value[b] vs Kd	-	0.1081
Stratified[a] Hazard ratio (95% CI) vs Kd	-	1.65 (0.89 to 3.05)
P-value	-	0.1117
Improvement probability (95% CI)[c]		
3 Months	0.033 (0.011 to 0.077)	0.034 (0.014 to 0.069)
6 Months	0.033 (0.011 to 0.077)	0.040 (0.018 to 0.077)

A lower score represents a better level of quality of life. Clinical meaningful improvement change from baseline less than or equal to -15 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] Stratified on number of prior lines of therapy (1 vs. >1) and Revised International Staging System (R-ISS) stage (I or II vs. III vs. not classified) according to IRT
[b] One-sided significance level is 0.025
[c] Estimated using the Kaplan-Meier method
NA/NC = Not Applicable / Not Calculable
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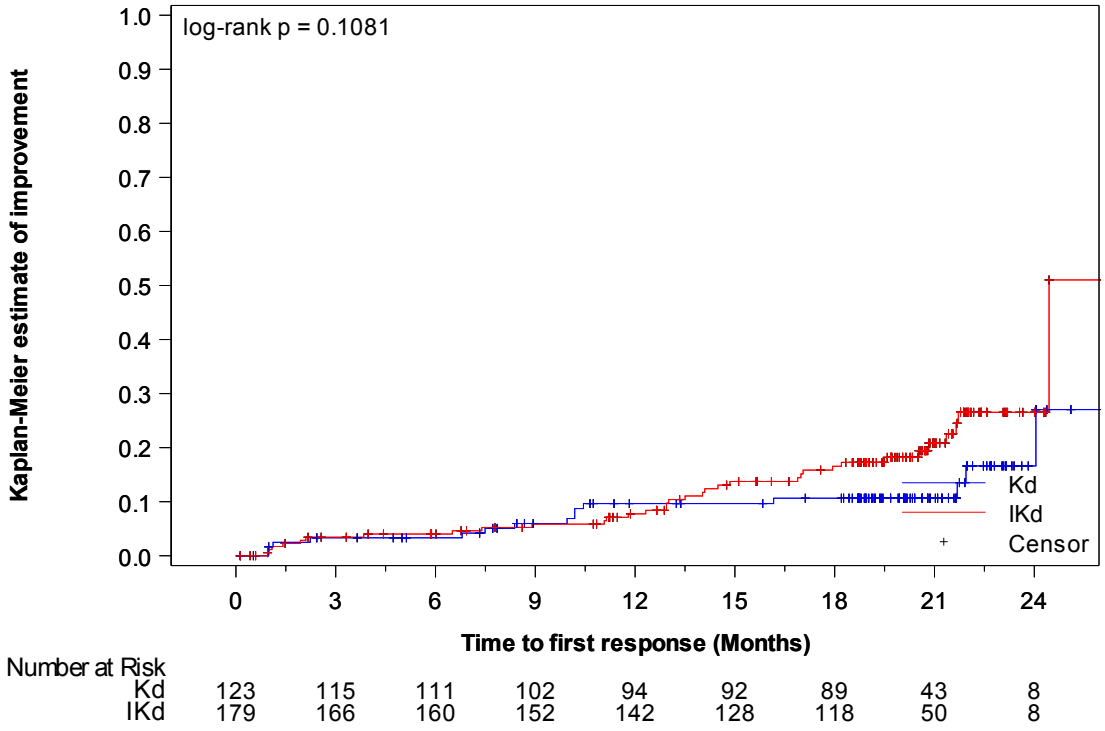
16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Fatigue
16.2.6.1.2.1 Efficacy response data
16.2.6.1.2.1.20 QLQ-C30 - Time until permanent improvement by 15 pt in fatigue - Kaplan-Meier curve (LOCF) - ITT population



A lower score represents a better level of quality of life. Clinical meaningful improvement change from baseline less than or equal to -15 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.

16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Fatigue
16.2.6.1.2.1 Efficacy response data
16.2.6.1.2.1.21 QLQ-C30 - Time until permanent deterioration by 15 pt in fatigue (LOCF) - ITT population

First permanent deterioration 15 points Fatigue (%)	**Kd (N=123)**	**IKd (N=179)**
Number (%) of events	29 (23.6)	44 (24.6)
Number (%) of patients censored	94 (76.4)	135 (75.4)
Kaplan-Meier estimates of Fatigue in months		
25% quantile (95% CI)	20.76 (8.739 to NC)	19.25 (12.156 to NC)
Median (95% CI)	NC (NC to NC)	NC (NC to NC)
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)
Comparison vs. Kd		
Stratified[a] Log-Rank test p-value[b] vs Kd	-	0.9027
Stratified[a] Hazard ratio (95% CI) vs Kd	-	1.03 (0.64 to 1.65)
P-value	-	0.9030
Deterioration probability (95% CI)[c]		
3 Months	0.925 (0.861 to 0.960)	0.931 (0.882 to 0.960)
6 Months	0.881 (0.808 to 0.928)	0.896 (0.840 to 0.933)

A lower score represents a better level of quality of life. Clinical meaningful deterioration change from baseline greater than or equal to 15 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] Stratified on number of prior lines of therapy (1 vs. >1) and Revised International Staging System (R-ISS) stage (I or II vs. III vs. not classified) according to IRT
[b] One-sided significance level is 0.025
[c] Estimated using the Kaplan-Meier method
NA/NC = Not Applicable / Not Calculable
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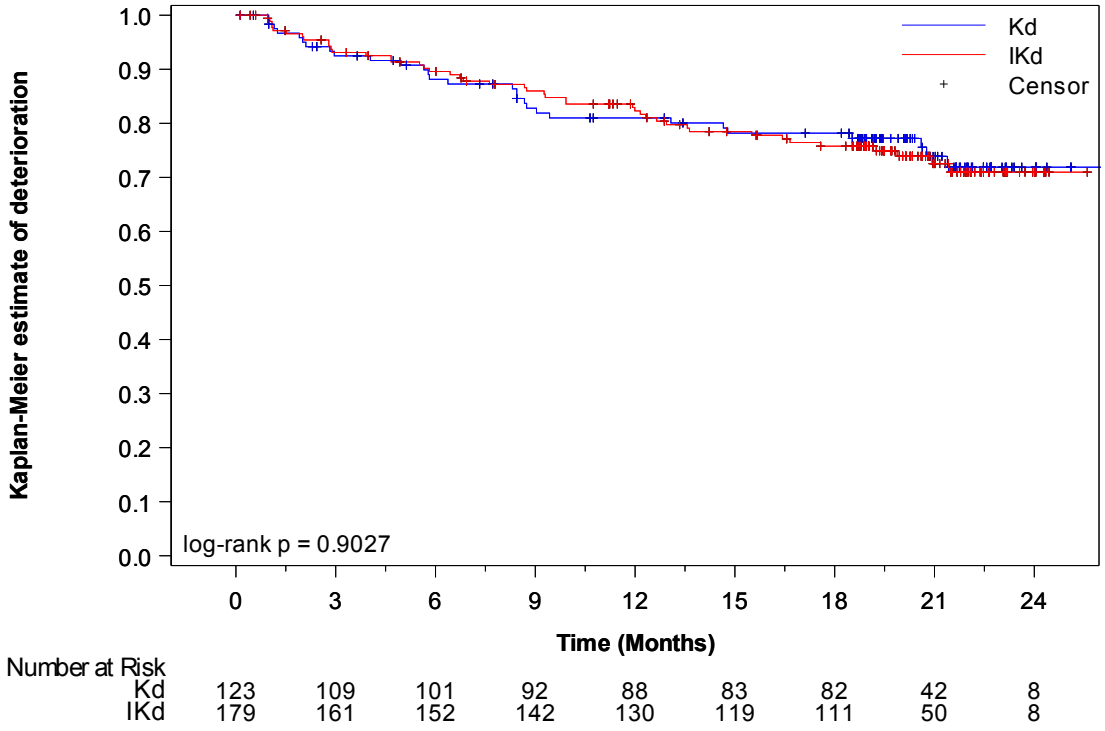
16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Fatigue
16.2.6.1.2.1 Efficacy response data
16.2.6.1.2.1.22 QLQ-C30 - Time until permanent deterioration by 15 pt in fatigue - Kaplan-Meier curve (LOCF) - ITT population



A lower score represents a better level of quality of life. Clinical meaningful deterioration change from baseline greater than or equal to 15 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
PGM=DEVOPS/SAR650984/EFC15246/CIR_RWE/REPORT/PGM/eff_qlq_km_i_f.sas OUT=REPORT/OUTPUT/eff_km_c30_fat_det15pl_de_i_f_x.rtf (07APR2021 14:23)

16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Fatigue
16.2.6.1.2.2 Efficacy response data - Subgroup analyses by age
16.2.6.1.2.2.3 QLQ-C30 - Time to first improvement by 10 pt in fatigue according to age (LOCF) - ITT population

	<65 years		>=65 years		
	Kd (N=66)	**IKd (N=88)**	**Kd (N=57)**	**IKd (N=91)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	36 (54.5)	53 (60.2)	38 (66.7)	56 (61.5)	0.5163
Number (%) of patients censored	30 (45.5)	35 (39.8)	19 (33.3)	35 (38.5)	
Kaplan-Meier estimates of Fatigue in months					
25% quantile (95% CI)	1.05 (0.986 to 1.281)	1.38 (1.018 to 2.004)	1.91 (1.051 to 2.858)	1.15 (1.051 to 2.070)	
Median (95% CI)	9.10 (1.873 to NC)	3.71 (2.136 to 11.072)	3.75 (2.858 to 6.571)	4.67 (2.891 to 11.269)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (6.275 to NC)	NC (12.715 to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.6140		0.6817	
Hazard ratio (95% CI) vs Kd	-	1.12 (0.73 to 1.70)		0.92 (0.61 to 1.39)	
P-value	-	0.6141		0.6818	
Improvement probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful improvement change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
PGM=DEVOPS/SAR650984/EFC15246/CIR_RWE/REPORT/PGM/eff_km_subgp_sr_sig_de_i_t.sas OUT=REPORT/OUTPUT/eff_km_c30_fat_impl_age_de_i_t_x.rtf (07APR2021 14:28)

16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Fatigue
16.2.6.1.2.2 Efficacy response data - Subgroup analyses by age
16.2.6.1.2.2.4 QLQ-C30 - Time to first deterioration by 10 pt in fatigue according to age (LOCF) - ITT population

	<65 years		>=65 years		
	Kd (N=66)	**IKd (N=88)**	**Kd (N=57)**	**IKd (N=91)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	39 (59.1)	65 (73.9)	42 (73.7)	61 (67.0)	0.0834
Number (%) of patients censored	27 (40.9)	23 (26.1)	15 (26.3)	30 (33.0)	
Kaplan-Meier estimates of Fatigue in months					
25% quantile (95% CI)	1.12 (1.051 to 1.971)	1.08 (1.051 to 1.216)	1.22 (0.986 to 2.037)	1.22 (1.051 to 1.971)	
Median (95% CI)	7.26 (2.825 to 19.351)	3.75 (1.906 to 5.224)	3.75 (2.037 to 5.651)	3.75 (2.793 to 6.669)	
75% quantile (95% CI)	NC (19.351 to NC)	13.37 (7.425 to NC)	13.40 (5.618 to NC)	NC (9.133 to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.0579		0.6219	
Hazard ratio (95% CI) vs Kd	-	1.47 (0.98 to 2.18)		0.91 (0.61 to 1.34)	
P-value	-	0.0595		0.6221	
Deterioration probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful deterioration change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Fatigue
16.2.6.1.2.2 Efficacy response data - Subgroup analyses by age
16.2.6.1.2.2.5 QLQ-C30 - Time until permanent improvement by 10 pt in fatigue according to age (LOCF) - ITT population

	<65 years		>=65 years		
	Kd (N=66)	**IKd (N=88)**	**Kd (N=57)**	**IKd (N=91)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	21 (31.8)	28 (31.8)	13 (22.8)	21 (23.1)	0.9091
Number (%) of patients censored	45 (68.2)	60 (68.2)	44 (77.2)	70 (76.9)	
Kaplan-Meier estimates of Fatigue in months					
25% quantile (95% CI)	11.60 (4.698 to NC)	13.73 (8.476 to 19.614)	21.59 (15.047 to NC)	20.80 (13.010 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (21.684 to NC)	24.44 (24.444 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (24.444 to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.9132		0.8924	
Hazard ratio (95% CI) vs Kd	-	0.97 (0.55 to 1.71)		1.05 (0.52 to 2.10)	
P-value	-	0.9130		0.8929	
Improvement probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful improvement change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
PGM=DEVOPS/SAR650984/EFC15246/CIR_RWE/REPORT/PGM/eff_km_subgp_sr_sig_de_i_t.sas OUT=REPORT/OUTPUT/eff_km_c30_fat_imppl_age_de_i_t_x.rtf (07APR2021 14:28)

16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Fatigue
16.2.6.1.2.2 Efficacy response data - Subgroup analyses by age
16.2.6.1.2.2.6 QLQ-C30 - Time until permanent deterioration by 10 pt in fatigue according to age (LOCF) - ITT population

	<65 years		>=65 years		
	Kd (N=66)	**IKd (N=88)**	**Kd (N=57)**	**IKd (N=91)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	24 (36.4)	33 (37.5)	23 (40.4)	36 (39.6)	0.7319
Number (%) of patients censored	42 (63.6)	55 (62.5)	34 (59.6)	55 (60.4)	
Kaplan-Meier estimates of Fatigue in months					
25% quantile (95% CI)	8.74 (4.895 to 21.092)	10.87 (3.745 to 16.657)	9.03 (4.041 to 17.084)	14.00 (8.246 to 18.464)	
Median (95% CI)	22.44 (21.092 to NC)	23.52 (20.501 to NC)	NC (17.084 to NC)	NC (19.253 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (23.524 to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.7881		0.8140	
Hazard ratio (95% CI) vs Kd	-	1.07 (0.63 to 1.82)		0.94 (0.56 to 1.58)	
P-value	-	0.7892		0.8140	
Deterioration probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful deterioration change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Fatigue
16.2.6.1.2.3 Efficacy response data - Subgroup analyses by gender
16.2.6.1.2.3.3 QLQ-C30 - Time to first improvement by 10 pt in fatigue according to gender (LOCF) - ITT population

	Male		Female		
	Kd (N=68)	**IKd (N=101)**	**Kd (N=55)**	**IKd (N=78)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	38 (55.9)	60 (59.4)	36 (65.5)	49 (62.8)	0.8795
Number (%) of patients censored	30 (44.1)	41 (40.6)	19 (34.5)	29 (37.2)	
Kaplan-Meier estimates of Fatigue in months					
25% quantile (95% CI)	1.12 (1.051 to 2.037)	1.97 (1.084 to 2.136)	1.05 (0.986 to 2.858)	1.05 (0.986 to 1.873)	
Median (95% CI)	5.72 (2.070 to NC)	5.13 (2.924 to 11.400)	3.76 (2.858 to 11.203)	3.29 (2.037 to 5.815)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (11.203 to NC)	NC (NC to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.8045		0.9890	
Hazard ratio (95% CI) vs Kd	-	1.05 (0.70 to 1.58)		1.00 (0.65 to 1.54)	
P-value	-	0.8055		0.9890	
Improvement probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful improvement change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Fatigue
16.2.6.1.2.3 Efficacy response data - Subgroup analyses by gender
16.2.6.1.2.3.4 QLQ-C30 - Time to first deterioration by 10 pt in fatigue according to gender (LOCF) - ITT population

	Male		Female		
	Kd (N=68)	**IKd (N=101)**	**Kd (N=55)**	**IKd (N=78)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	44 (64.7)	72 (71.3)	37 (67.3)	54 (69.2)	0.4981
Number (%) of patients censored	24 (35.3)	29 (28.7)	18 (32.7)	24 (30.8)	
Kaplan-Meier estimates of Fatigue in months					
25% quantile (95% CI)	1.91 (1.051 to 2.825)	1.08 (1.018 to 1.314)	1.12 (0.986 to 1.906)	1.18 (1.051 to 1.938)	
Median (95% CI)	4.70 (2.924 to 7.556)	3.22 (1.971 to 4.731)	5.22 (1.906 to 12.189)	3.75 (2.004 to 6.735)	
75% quantile (95% CI)	NC (7.556 to NC)	13.93 (6.899 to NC)	NC (12.189 to NC)	NC (9.199 to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.2198		0.8367	
Hazard ratio (95% CI) vs Kd	-	1.26 (0.87 to 1.84)		1.04 (0.69 to 1.59)	
P-value	-	0.2209		0.8373	
Deterioration probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful deterioration change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Fatigue
16.2.6.1.2.3 Efficacy response data - Subgroup analyses by gender
16.2.6.1.2.3.5 QLQ-C30 - Time until permanent improvement by 10 pt in fatigue according to gender (LOCF) - ITT population

	Male		Female		
	Kd (N=68)	**IKd (N=101)**	**Kd (N=55)**	**IKd (N=78)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	18 (26.5)	25 (24.8)	16 (29.1)	24 (30.8)	0.7191
Number (%) of patients censored	50 (73.5)	76 (75.2)	39 (70.9)	54 (69.2)	
Kaplan-Meier estimates of Fatigue in months					
25% quantile (95% CI)	19.35 (7.425 to NC)	18.89 (12.025 to NC)	16.16 (6.801 to NC)	17.05 (11.138 to 24.444)	
Median (95% CI)	NC (21.684 to NC)	NC (NC to NC)	NC (22.209 to NC)	24.44 (24.444 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (24.444 to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.8215		0.7851	
Hazard ratio (95% CI) vs Kd	-	0.93 (0.51 to 1.71)		1.09 (0.58 to 2.06)	
P-value	-	0.8215		0.7852	
Improvement probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful improvement change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Fatigue
16.2.6.1.2.3 Efficacy response data - Subgroup analyses by gender
16.2.6.1.2.3.6 QLQ-C30 - Time until permanent deterioration by 10 pt in fatigue according to gender (LOCF) - ITT population

	Male		Female		
	Kd (N=68)	**IKd (N=101)**	**Kd (N=55)**	**IKd (N=78)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	24 (35.3)	38 (37.6)	23 (41.8)	31 (39.7)	0.5931
Number (%) of patients censored	44 (64.7)	63 (62.4)	32 (58.2)	47 (60.3)	
Kaplan-Meier estimates of Fatigue in months					
25% quantile (95% CI)	7.56 (3.811 to 21.092)	11.50 (4.600 to 18.694)	9.99 (4.895 to 18.530)	13.57 (7.622 to 18.431)	
Median (95% CI)	NC (21.092 to NC)	23.52 (20.534 to NC)	22.44 (18.530 to NC)	NC (18.464 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.6614		0.7526	
Hazard ratio (95% CI) vs Kd	-	1.12 (0.67 to 1.87)		0.92 (0.53 to 1.57)	
P-value	-	0.6616		0.7527	
Deterioration probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful deterioration change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Fatigue
16.2.6.1.2.4 Efficacy response data - Subgroup analyses by ethnic origin
16.2.6.1.2.4.3 QLQ-C30 - Time to first improvement by 10 pt in fatigue according to ethnic origin (LOCF) - ITT population

	White		Other		
	Kd (N=83)	**IKd (N=131)**	**Kd (N=28)**	**IKd (N=34)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	53 (63.9)	85 (64.9)	17 (60.7)	15 (44.1)	0.3358
Number (%) of patients censored	30 (36.1)	46 (35.1)	11 (39.3)	19 (55.9)	
Kaplan-Meier estimates of Fatigue in months					
25% quantile (95% CI)	1.08 (0.986 to 1.906)	1.08 (1.018 to 1.971)	1.12 (1.018 to 3.745)	1.97 (0.986 to 3.023)	
Median (95% CI)	3.29 (2.825 to 9.101)	3.42 (2.891 to 8.312)	6.01 (1.117 to NC)	NC (1.971 to NC)	
75% quantile (95% CI)	NC (16.624 to NC)	NC (12.715 to NC)	NC (14.522 to NC)	NC (NC to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.8699		0.2937	
Hazard ratio (95% CI) vs Kd	-	1.03 (0.73 to 1.45)		0.69 (0.34 to 1.38)	
P-value	-	0.8703		0.2964	
Improvement probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful improvement change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Fatigue
16.2.6.1.2.4 Efficacy response data - Subgroup analyses by ethnic origin
16.2.6.1.2.4.4 QLQ-C30 - Time to first deterioration by 10 pt in fatigue according to ethnic origin (LOCF) - ITT population

	White		Other		
	Kd (N=83)	**IKd (N=131)**	**Kd (N=28)**	**IKd (N=34)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	54 (65.1)	93 (71.0)	20 (71.4)	27 (79.4)	0.5484
Number (%) of patients censored	29 (34.9)	38 (29.0)	8 (28.6)	7 (20.6)	
Kaplan-Meier estimates of Fatigue in months					
25% quantile (95% CI)	1.12 (1.051 to 1.938)	1.18 (1.051 to 1.873)	1.15 (1.051 to 2.924)	1.05 (0.986 to 1.117)	
Median (95% CI)	4.70 (2.103 to 9.922)	3.22 (2.366 to 4.731)	5.65 (2.037 to 7.556)	2.00 (1.051 to 4.205)	
75% quantile (95% CI)	NC (14.784 to NC)	NC (8.345 to NC)	19.75 (6.702 to NC)	9.23 (3.745 to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.2860		0.1909	
Hazard ratio (95% CI) vs Kd	-	1.20 (0.86 to 1.68)		1.47 (0.82 to 2.62)	
P-value	-	0.2866		0.1936	
Deterioration probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful deterioration change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Fatigue
16.2.6.1.2.4 Efficacy response data - Subgroup analyses by ethnic origin
16.2.6.1.2.4.5 QLQ-C30 - Time until permanent improvement by 10 pt in fatigue according to ethnic origin (LOCF) - ITT population

	White		Other		
	Kd (N=83)	**IKd (N=131)**	**Kd (N=28)**	**IKd (N=34)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	22 (26.5)	33 (25.2)	10 (35.7)	11 (32.4)	0.9574
Number (%) of patients censored	61 (73.5)	98 (74.8)	18 (64.3)	23 (67.6)	
Kaplan-Meier estimates of Fatigue in months					
25% quantile (95% CI)	19.35 (10.448 to NC)	19.58 (12.945 to NC)	14.52 (1.117 to 21.585)	16.89 (3.844 to NC)	
Median (95% CI)	NC (22.209 to NC)	24.44 (24.444 to NC)	NC (14.522 to NC)	NC (17.051 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (24.444 to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.8242		0.7949	
Hazard ratio (95% CI) vs Kd	-	0.94 (0.55 to 1.62)		0.89 (0.38 to 2.10)	
P-value	-	0.8231		0.7950	
Improvement probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful improvement change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Fatigue
16.2.6.1.2.4 Efficacy response data - Subgroup analyses by ethnic origin
16.2.6.1.2.4.6 QLQ-C30 - Time until permanent deterioration by 10 pt in fatigue according to ethnic origin (LOCF) - ITT population

	White		Other		
	Kd (N=83)	**IKd (N=131)**	**Kd (N=28)**	**IKd (N=34)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	33 (39.8)	52 (39.7)	7 (25.0)	14 (41.2)	0.1961
Number (%) of patients censored	50 (60.2)	79 (60.3)	21 (75.0)	20 (58.8)	
Kaplan-Meier estimates of Fatigue in months					
25% quantile (95% CI)	8.74 (3.811 to 18.530)	11.93 (6.834 to 14.850)	21.09 (6.111 to NC)	8.34 (1.117 to 20.501)	
Median (95% CI)	22.44 (20.567 to NC)	23.52 (20.534 to NC)	NC (21.092 to NC)	NC (15.704 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.9824		0.1339	
Hazard ratio (95% CI) vs Kd	-	1.00 (0.65 to 1.55)		1.98 (0.80 to 4.91)	
P-value	-	0.9824		0.1415	
Deterioration probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful deterioration change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Fatigue
16.2.6.1.2.5 Efficacy response data - Subgroup analyses by geographical region
16.2.6.1.2.5.3 QLQ-C30 - Time to first improvement by 10 pt in fatigue according to geographical region (LOCF) - ITT population

	Europe		America		Asia		Other countries		
	Kd (N=60)	**IKd (N=85)**	**Kd (N=20)**	**IKd (N=24)**	**Kd (N=21)**	**IKd (N=25)**	**Kd (N=22)**	**IKd (N=45)**	**p-value of treatment-by-subgroup interaction[c]**
Number (%) of events	34 (56.7)	55 (64.7)	13 (65.0)	13 (54.2)	12 (57.1)	11 (44.0)	15 (68.2)	30 (66.7)	0.6280
Number (%) of patients censored	26 (43.3)	30 (35.3)	7 (35.0)	11 (45.8)	9 (42.9)	14 (56.0)	7 (31.8)	15 (33.3)	
Kaplan-Meier estimates of event in months									
25% quantile (95% CI)	1.12 (0.986 to 2.825)	1.08 (0.986 to 1.971)	1.02 (0.986 to 1.840)	1.91 (0.986 to 2.825)	1.12 (0.986 to 3.975)	1.94 (0.953 to 3.023)	2.00 (1.018 to 3.811)	1.38 (1.018 to 2.891)	
Median (95% CI)	3.75 (2.891 to NC)	3.09 (2.103 to 5.815)	4.71 (0.986 to NC)	5.49 (1.906 to NC)	5.72 (1.117 to NC)	NC (1.971 to NC)	5.11 (2.004 to NC)	3.88 (2.891 to 11.400)	
75% quantile (95% CI)	NC (NC to NC)	NC (11.269 to NC)	NC (6.571 to NC)	NC (5.487 to NC)	NC (15.113 to NC)	NC (NC to NC)	NC (6.012 to NC)	NC (11.072 to NC)	

A lower score represents a better level of quality of life. Clinical meaningful improvement change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Fatigue
16.2.6.1.2.5 Efficacy response data - Subgroup analyses by geographical region
16.2.6.1.2.5.3 QLQ-C30 - Time to first improvement by 10 pt in fatigue according to geographical region (LOCF) - ITT population

	Europe		America		Asia		Other countries		
	Kd (N=60)	**IKd (N=85)**	**Kd (N=20)**	**IKd (N=24)**	**Kd (N=21)**	**IKd (N=25)**	**Kd (N=22)**	**IKd (N=45)**	**p-value of treatment-by-subgroup interaction[c]**
Comparison vs. Kd									
Log-Rank test p-value[a] vs Kd	-	0.3944		0.5465		0.4406		0.9024	
Hazard ratio (95% CI) vs Kd	-	1.20 (0.78 to 1.85)		0.79 (0.37 to 1.71)		0.73 (0.32 to 1.65)		1.04 (0.56 to 1.93)	
P-value	-	0.3951		0.5475		0.4425		0.9030	
Improvement probability (95% CI)[b]									
3 Months	0.429 (0.301 to 0.551)	0.485 (0.373 to 0.587)	0.500 (0.271 to 0.692)	0.448 (0.239 to 0.636)	0.400 (0.193 to 0.600)	0.375 (0.190 to 0.560)	0.409 (0.209 to 0.601)	0.422 (0.278 to 0.560)	

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The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Fatigue
16.2.6.1.2.5 Efficacy response data - Subgroup analyses by geographical region
16.2.6.1.2.5.4 QLQ-C30 - Time to first deterioration by 10 pt in fatigue according to geographical region (LOCF) - ITT population

	Europe		America		Asia		Other countries		
	Kd (N=60)	**IKd (N=85)**	**Kd (N=20)**	**IKd (N=24)**	**Kd (N=21)**	**IKd (N=25)**	**Kd (N=22)**	**IKd (N=45)**	**p-value of treatment-by-subgroup interaction[c]**
Number (%) of events	36 (60.0)	59 (69.4)	15 (75.0)	14 (58.3)	14 (66.7)	21 (84.0)	16 (72.7)	32 (71.1)	0.4911
Number (%) of patients censored	24 (40.0)	26 (30.6)	5 (25.0)	10 (41.7)	7 (33.3)	4 (16.0)	6 (27.3)	13 (28.9)	
Kaplan-Meier estimates of event in months									
25% quantile (95% CI)	1.25 (0.986 to 2.825)	1.48 (1.084 to 2.267)	1.56 (0.953 to 2.004)	1.12 (0.986 to 3.220)	1.13 (1.051 to 2.924)	1.03 (0.920 to 1.117)	1.08 (0.986 to 2.103)	1.08 (1.051 to 1.610)	
Median (95% CI)	5.62 (2.825 to 13.405)	4.40 (2.990 to 5.749)	3.19 (1.216 to 18.628)	3.81 (1.971 to NC)	4.07 (1.117 to 7.556)	1.54 (1.051 to 3.745)	3.50 (1.084 to 19.745)	2.92 (1.314 to 6.998)	
75% quantile (95% CI)	NC (13.405 to NC)	NC (6.899 to NC)	19.35 (3.351 to NC)	NC (9.133 to NC)	NC (6.702 to NC)	8.44 (1.971 to NC)	19.75 (4.041 to NC)	NC (6.669 to NC)	

A lower score represents a better level of quality of life. Clinical meaningful deterioration change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Fatigue
16.2.6.1.2.5 Efficacy response data - Subgroup analyses by geographical region
16.2.6.1.2.5.4 QLQ-C30 - Time to first deterioration by 10 pt in fatigue according to geographical region (LOCF) - ITT population

	Europe		America		Asia		Other countries		
	Kd (N=60)	**IKd (N=85)**	**Kd (N=20)**	**IKd (N=24)**	**Kd (N=21)**	**IKd (N=25)**	**Kd (N=22)**	**IKd (N=45)**	**p-value of treatment-by-subgroup interaction[c]**
Comparison vs. Kd									
Log-Rank test p-value[a] vs Kd	-	0.3237		0.5325		0.1312		0.9313	
Hazard ratio (95% CI) vs Kd	-	1.23 (0.81 to 1.87)		0.79 (0.38 to 1.64)		1.68 (0.85 to 3.31)		1.03 (0.56 to 1.87)	
P-value	-	0.3246		0.5335		0.1354		0.9316	
Deterioration probability (95% CI)[b]									
3 Months	0.621 (0.483 to 0.732)	0.602 (0.488 to 0.698)	0.550 (0.313 to 0.735)	0.601 (0.372 to 0.769)	0.542 (0.303 to 0.730)	0.333 (0.159 to 0.519)	0.500 (0.282 to 0.684)	0.444 (0.297 to 0.582)	
6 Months	0.490 (0.354 to 0.612)	0.388 (0.283 to 0.493)	0.450 (0.231 to 0.647)	0.462 (0.251 to 0.650)	0.488 (0.257 to 0.684)	0.292 (0.130 to 0.476)	0.364 (0.174 to 0.557)	0.398 (0.256 to 0.536)	

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The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Fatigue
16.2.6.1.2.5 Efficacy response data - Subgroup analyses by geographical region
16.2.6.1.2.5.5 QLQ-C30 - Time until permanent improvement by 10 pt in fatigue according to geographical region (LOCF) - ITT population

	Europe		America		Asia		Other countries		
	Kd (N=60)	**IKd (N=85)**	**Kd (N=20)**	**IKd (N=24)**	**Kd (N=21)**	**IKd (N=25)**	**Kd (N=22)**	**IKd (N=45)**	**p-value of treatment-by-subgroup interaction[c]**
Number (%) of events	15 (25.0)	20 (23.5)	7 (35.0)	8 (33.3)	5 (23.8)	8 (32.0)	7 (31.8)	13 (28.9)	0.9160
Number (%) of patients censored	45 (75.0)	65 (76.5)	13 (65.0)	16 (66.7)	16 (76.2)	17 (68.0)	15 (68.2)	32 (71.1)	
Kaplan-Meier estimates of event in months									
25% quantile (95% CI)	19.75 (7.425 to NC)	24.44 (12.945 to 24.444)	10.66 (0.986 to NC)	12.32 (1.051 to NC)	21.59 (1.018 to NC)	17.05 (1.084 to NC)	17.97 (2.037 to NC)	17.51 (8.476 to NC)	
Median (95% CI)	NC (21.684 to NC)	24.44 (NC to NC)	NC (6.801 to NC)	NC (12.320 to NC)	NC (17.643 to NC)	NC (17.051 to NC)	NC (17.971 to NC)	NC (20.797 to NC)	

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The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Fatigue
16.2.6.1.2.5 Efficacy response data - Subgroup analyses by geographical region
16.2.6.1.2.5.5 QLQ-C30 - Time until permanent improvement by 10 pt in fatigue according to geographical region (LOCF) - ITT population

	Europe		America		Asia		Other countries		
	Kd (N=60)	**IKd (N=85)**	**Kd (N=20)**	**IKd (N=24)**	**Kd (N=21)**	**IKd (N=25)**	**Kd (N=22)**	**IKd (N=45)**	**p-value of treatment-by-subgroup interaction[c]**
75% quantile (95% CI)	NC (NC to NC)	24.44 (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (22.209 to NC)	NC (NC to NC)	
Comparison vs. Kd									
Log-Rank test p-value[a] vs Kd	-	0.7171		0.9824		0.5330		0.9098	
Hazard ratio (95% CI) vs Kd	-	0.88 (0.45 to 1.74)		1.01 (0.37 to 2.79)		1.42 (0.47 to 4.36)		0.95 (0.38 to 2.38)	
P-value	-	0.7173		0.9824		0.5352		0.9098	
Improvement probability (95% CI)[b]									

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The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Fatigue
16.2.6.1.2.5 Efficacy response data - Subgroup analyses by geographical region
16.2.6.1.2.5.6 QLQ-C30 - Time until permanent deterioration by 10 pt in fatigue according to geographical region (LOCF) - ITT population

	Europe		America		Asia		Other countries		
	Kd (N=60)	**IKd (N=85)**	**Kd (N=20)**	**IKd (N=24)**	**Kd (N=21)**	**IKd (N=25)**	**Kd (N=22)**	**IKd (N=45)**	**p-value of treatment-by-subgroup interaction[c]**
Number (%) of events	25 (41.7)	32 (37.6)	6 (30.0)	7 (29.2)	7 (33.3)	13 (52.0)	9 (40.9)	17 (37.8)	0.5688
Number (%) of patients censored	35 (58.3)	53 (62.4)	14 (70.0)	17 (70.8)	14 (66.7)	12 (48.0)	13 (59.1)	28 (62.2)	
Kaplan-Meier estimates of event in months									
25% quantile (95% CI)	8.34 (2.825 to 16.887)	14.52 (10.152 to 18.694)	17.38 (1.051 to NC)	12.32 (0.986 to NC)	17.08 (1.150 to NC)	4.63 (1.018 to 18.464)	7.52 (1.018 to NC)	8.25 (2.825 to 14.949)	
Median (95% CI)	22.44 (16.887 to NC)	23.52 (19.877 to NC)	NC (17.380 to NC)	NC (12.320 to NC)	NC (17.084 to NC)	20.50 (4.665 to NC)	NC (7.524 to NC)	NC (12.156 to NC)	

A lower score represents a better level of quality of life. Clinical meaningful deterioration change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Fatigue
16.2.6.1.2.5 Efficacy response data - Subgroup analyses by geographical region
16.2.6.1.2.5.6 QLQ-C30 - Time until permanent deterioration by 10 pt in fatigue according to geographical region (LOCF) - ITT population

	Europe		America		Asia		Other countries		
	Kd (N=60)	**IKd (N=85)**	**Kd (N=20)**	**IKd (N=24)**	**Kd (N=21)**	**IKd (N=25)**	**Kd (N=22)**	**IKd (N=45)**	**p-value of treatment-by-subgroup interaction[c]**
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (20.928 to NC)	NC (21.552 to NC)	NC (20.501 to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Kd									
Log-Rank test p-value[a] vs Kd	-	0.4145		0.8391		0.2459		0.9596	
Hazard ratio (95% CI) vs Kd	-	0.80 (0.48 to 1.36)		1.12 (0.38 to 3.34)		1.71 (0.68 to 4.30)		0.98 (0.44 to 2.20)	
P-value	-	0.4154		0.8395		0.2516		0.9594	
Deterioration probability (95% CI)[b]									

A lower score represents a better level of quality of life. Clinical meaningful deterioration change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Fatigue
16.2.6.1.2.6 Efficacy response data - Subgroup analyses by regulatory region
16.2.6.1.2.6.3 QLQ-C30 - Time to first improvement by 10 pt in fatigue according to regulatory region (LOCF) - ITT population

	Western countries		Other countries		
	Kd (N=55)	**IKd (N=97)**	**Kd (N=68)**	**IKd (N=82)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	32 (58.2)	60 (61.9)	42 (61.8)	49 (59.8)	0.7073
Number (%) of patients censored	23 (41.8)	37 (38.1)	26 (38.2)	33 (40.2)	
Kaplan-Meier estimates of Fatigue in months					
25% quantile (95% CI)	2.07 (1.051 to 3.285)	1.41 (1.051 to 2.825)	1.05 (0.986 to 1.150)	1.08 (1.018 to 1.971)	
Median (95% CI)	6.01 (2.990 to NC)	4.67 (2.957 to 11.400)	3.02 (1.281 to 16.624)	3.29 (2.004 to 8.805)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (17.643 to NC)	NC (NC to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.6538		0.8880	
Hazard ratio (95% CI) vs Kd	-	1.10 (0.72 to 1.69)		0.97 (0.64 to 1.47)	
P-value	-	0.6539		0.8878	
Improvement probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful improvement change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
PGM=DEVOPS/SAR650984/EFC15246/CIR_RWE/REPORT/PGM/eff_km_subgp_sr_sig_de_i_t.sas OUT=REPORT/OUTPUT/eff_km_c30_fat_impl_rreg_de_i_t_x.rtf (07APR2021 14:28)

16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Fatigue
16.2.6.1.2.6 Efficacy response data - Subgroup analyses by regulatory region
16.2.6.1.2.6.4 QLQ-C30 - Time to first deterioration by 10 pt in fatigue according to regulatory region (LOCF) - ITT population

	Western countries		Other countries		
	Kd (N=55)	**IKd (N=97)**	**Kd (N=68)**	**IKd (N=82)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	32 (58.2)	68 (70.1)	49 (72.1)	58 (70.7)	0.8467
Number (%) of patients censored	23 (41.8)	29 (29.9)	19 (27.9)	24 (29.3)	
Kaplan-Meier estimates of Fatigue in months					
25% quantile (95% CI)	1.12 (0.986 to 2.825)	1.18 (1.084 to 2.267)	1.15 (1.051 to 2.037)	1.07 (0.986 to 1.216)	
Median (95% CI)	5.62 (2.037 to 19.745)	3.94 (2.924 to 6.538)	3.75 (2.103 to 7.491)	2.37 (1.873 to 4.205)	
75% quantile (95% CI)	NC (19.745 to NC)	NC (7.425 to NC)	19.35 (9.758 to NC)	15.70 (7.655 to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.3264		0.4472	
Hazard ratio (95% CI) vs Kd	-	1.23 (0.81 to 1.88)		1.16 (0.79 to 1.70)	
P-value	-	0.3273		0.4488	
Deterioration probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful deterioration change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Fatigue
16.2.6.1.2.6 Efficacy response data - Subgroup analyses by regulatory region
16.2.6.1.2.6.5 QLQ-C30 - Time until permanent improvement by 10 pt in fatigue according to regulatory region (LOCF) - ITT population

	Western countries		Other countries		
	Kd (N=55)	**IKd (N=97)**	**Kd (N=68)**	**IKd (N=82)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	17 (30.9)	21 (21.6)	17 (25.0)	28 (34.1)	0.0967
Number (%) of patients censored	38 (69.1)	76 (78.4)	51 (75.0)	54 (65.9)	
Kaplan-Meier estimates of Fatigue in months					
25% quantile (95% CI)	16.16 (6.472 to 22.209)	20.80 (12.945 to NC)	19.35 (7.918 to NC)	13.73 (4.140 to 18.891)	
Median (95% CI)	NC (21.684 to NC)	NC (NC to NC)	NC (NC to NC)	24.44 (19.614 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (24.444 to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.2646		0.2237	
Hazard ratio (95% CI) vs Kd	-	0.70 (0.37 to 1.32)		1.45 (0.79 to 2.65)	
P-value	-	0.2672		0.2264	
Improvement probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful improvement change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Fatigue
16.2.6.1.2.6 Efficacy response data - Subgroup analyses by regulatory region
16.2.6.1.2.6.6 QLQ-C30 - Time until permanent deterioration by 10 pt in fatigue according to regulatory region (LOCF) - ITT population

	Western countries		Other countries		
	Kd (N=55)	**IKd (N=97)**	**Kd (N=68)**	**IKd (N=82)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	22 (40.0)	37 (38.1)	25 (36.8)	32 (39.0)	0.7723
Number (%) of patients censored	33 (60.0)	60 (61.9)	43 (63.2)	50 (61.0)	
Kaplan-Meier estimates of Fatigue in months					
25% quantile (95% CI)	8.34 (4.041 to 19.154)	12.16 (6.735 to 18.004)	12.02 (3.811 to 21.092)	12.32 (4.665 to 18.464)	
Median (95% CI)	22.44 (16.887 to NC)	23.52 (19.253 to NC)	NC (21.092 to NC)	NC (20.501 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (23.524 to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.7844		0.8446	
Hazard ratio (95% CI) vs Kd	-	0.93 (0.55 to 1.58)		1.05 (0.62 to 1.78)	
P-value	-	0.7844		0.8450	
Deterioration probability (95% CI)[b]					

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The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Fatigue
16.2.6.1.2.7 Efficacy response data - Subgroup analyses by baseline ECOG PS
16.2.6.1.2.7.3 QLQ-C30 - Time to first improvement by 10 pt in fatigue according to baseline ECOG PS (LOCF) - ITT population

	0 or 1		>1		
	Kd (N=118)	**IKd (N=168)**	**Kd (N=5)**	**IKd (N=11)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	70 (59.3)	101 (60.1)	4 (80.0)	8 (72.7)	0.9440
Number (%) of patients censored	48 (40.7)	67 (39.9)	1 (20.0)	3 (27.3)	
Kaplan-Meier estimates of Fatigue in months					
25% quantile (95% CI)	1.12 (1.051 to 1.906)	1.31 (1.051 to 2.004)	1.05 (0.986 to 2.070)	1.02 (0.986 to 1.906)	
Median (95% CI)	4.63 (2.957 to 14.522)	3.78 (2.957 to 8.805)	1.94 (0.986 to NC)	1.91 (0.986 to 8.969)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	2.07 (0.986 to NC)	5.13 (1.216 to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.8993		0.9566	
Hazard ratio (95% CI) vs Kd	-	1.02 (0.75 to 1.38)		1.03 (0.31 to 3.47)	
P-value	-	0.8995		0.9568	
Improvement probability (95% CI)[b]					

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The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Fatigue
16.2.6.1.2.7 Efficacy response data - Subgroup analyses by baseline ECOG PS
16.2.6.1.2.7.4 QLQ-C30 - Time to first deterioration by 10 pt in fatigue according to baseline ECOG PS (LOCF) - ITT population

	0 or 1		>1		
	Kd (N=118)	**IKd (N=168)**	**Kd (N=5)**	**IKd (N=11)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	79 (66.9)	123 (73.2)	2 (40.0)	3 (27.3)	0.6879
Number (%) of patients censored	39 (33.1)	45 (26.8)	3 (60.0)	8 (72.7)	
Kaplan-Meier estimates of Fatigue in months					
25% quantile (95% CI)	1.12 (1.051 to 1.938)	1.12 (1.051 to 1.314)	3.81 (3.778 to NC)	2.53 (0.986 to NC)	
Median (95% CI)	4.83 (2.825 to 7.261)	3.22 (2.366 to 4.632)	NC (3.778 to NC)	NC (0.986 to NC)	
75% quantile (95% CI)	NC (13.405 to NC)	14.00 (8.345 to NC)	NC (3.778 to NC)	NC (NC to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.2225		0.9905	
Hazard ratio (95% CI) vs Kd	-	1.19 (0.90 to 1.58)		1.01 (0.17 to 6.07)	
P-value	-	0.2231		0.9906	
Deterioration probability (95% CI)[b]					

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The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Fatigue
16.2.6.1.2.7 Efficacy response data - Subgroup analyses by baseline ECOG PS
16.2.6.1.2.7.5 QLQ-C30 - Time until permanent improvement by 10 pt in fatigue according to baseline ECOG PS (LOCF) - ITT population

	0 or 1		>1		
	Kd (N=118)	**IKd (N=168)**	**Kd (N=5)**	**IKd (N=11)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	31 (26.3)	46 (27.4)	3 (60.0)	3 (27.3)	0.3376
Number (%) of patients censored	87 (73.7)	122 (72.6)	2 (40.0)	8 (72.7)	
Kaplan-Meier estimates of Fatigue in months					
25% quantile (95% CI)	19.35 (13.832 to 22.209)	17.51 (12.945 to NC)	5.62 (1.051 to NC)	6.51 (0.986 to NC)	
Median (95% CI)	NC (22.209 to NC)	24.44 (24.444 to NC)	6.80 (1.051 to NC)	NC (0.986 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (24.444 to NC)	NC (1.051 to NC)	NC (NC to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.8303		0.4710	
Hazard ratio (95% CI) vs Kd	-	1.05 (0.67 to 1.66)		0.56 (0.11 to 2.78)	
P-value	-	0.8310		0.4771	
Improvement probability (95% CI)[b]					

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The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Fatigue
16.2.6.1.2.7 Efficacy response data - Subgroup analyses by baseline ECOG PS
16.2.6.1.2.7.6 QLQ-C30 - Time until permanent deterioration by 10 pt in fatigue according to baseline ECOG PS (LOCF) - ITT population

	0 or 1		>1		
	Kd (N=118)	**IKd (N=168)**	**Kd (N=5)**	**IKd (N=11)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	46 (39.0)	67 (39.9)	1 (20.0)	2 (18.2)	0.8036
Number (%) of patients censored	72 (61.0)	101 (60.1)	4 (80.0)	9 (81.8)	
Kaplan-Meier estimates of Fatigue in months					
25% quantile (95% CI)	8.74 (5.717 to 17.380)	11.93 (6.735 to 14.949)	NC (12.583 to NC)	20.93 (20.534 to NC)	
Median (95% CI)	NC (20.600 to NC)	NC (20.501 to NC)	NC (12.583 to NC)	NC (20.534 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (12.583 to NC)	NC (20.928 to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.8603		0.6485	
Hazard ratio (95% CI) vs Kd	-	1.03 (0.71 to 1.51)		0.57 (0.05 to 6.63)	
P-value	-	0.8607		0.6524	
Deterioration probability (95% CI)[b]					

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CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Fatigue
16.2.6.1.2.8 Efficacy response data - Subgroup analyses by ISS staging at SE
16.2.6.1.2.8.3 QLQ-C30 - Time to first improvement by 10 pt in fatigue according to ISS staging at SE (LOCF) - ITT population

	I		II		III		
	Kd (N=71)	**IKd (N=89)**	**Kd (N=31)**	**IKd (N=63)**	**Kd (N=20)**	**IKd (N=26)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	42 (59.2)	52 (58.4)	20 (64.5)	39 (61.9)	12 (60.0)	17 (65.4)	0.4157
Number (%) of patients censored	29 (40.8)	37 (41.6)	11 (35.5)	24 (38.1)	8 (40.0)	9 (34.6)	
Kaplan-Meier estimates of Fatigue in months							
25% quantile (95% CI)	1.05 (1.018 to 2.037)	1.97 (1.051 to 2.825)	1.08 (0.986 to 2.070)	1.08 (0.986 to 2.004)	1.91 (1.051 to 2.891)	1.05 (0.953 to 1.906)	
Median (95% CI)	6.28 (2.990 to NC)	5.49 (3.023 to NC)	2.89 (1.281 to NC)	3.71 (2.037 to 12.386)	3.37 (1.906 to NC)	1.97 (1.084 to 2.924)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (3.975 to NC)	NC (12.386 to NC)	NC (3.713 to NC)	8.67 (2.103 to NC)	
Comparison vs. Kd							
Log-Rank test p-value[a] vs Kd	-	0.8882		0.6457		0.1716	
Hazard ratio (95% CI) vs Kd	-	0.97 (0.65 to 1.46)		0.88 (0.51 to 1.51)		1.67 (0.79 to 3.54)	
P-value	-	0.8880		0.6459		0.1761	

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The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Fatigue
16.2.6.1.2.8 Efficacy response data - Subgroup analyses by ISS staging at SE
16.2.6.1.2.8.4 QLQ-C30 - Time to first deterioration by 10 pt in fatigue according to ISS staging at SE (LOCF) - ITT population

	I		II		III		
	Kd (N=71)	**IKd (N=89)**	**Kd (N=31)**	**IKd (N=63)**	**Kd (N=20)**	**IKd (N=26)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	48 (67.6)	68 (76.4)	20 (64.5)	49 (77.8)	12 (60.0)	8 (30.8)	0.1405
Number (%) of patients censored	23 (32.4)	21 (23.6)	11 (35.5)	14 (22.2)	8 (40.0)	18 (69.2)	
Kaplan-Meier estimates of Fatigue in months							
25% quantile (95% CI)	1.12 (1.051 to 2.037)	1.15 (1.018 to 1.248)	1.22 (0.986 to 3.811)	1.08 (1.018 to 1.873)	2.00 (1.051 to 7.556)	3.81 (0.986 to NC)	
Median (95% CI)	3.55 (2.037 to 6.801)	3.75 (1.906 to 5.651)	4.90 (1.906 to 18.628)	2.83 (1.938 to 3.778)	9.92 (2.004 to 19.745)	NC (3.811 to NC)	
75% quantile (95% CI)	NC (9.758 to NC)	13.93 (6.899 to NC)	NC (7.228 to NC)	8.38 (4.205 to NC)	19.75 (9.922 to NC)	NC (NC to NC)	
Comparison vs. Kd							
Log-Rank test p-value[a] vs Kd	-	0.3194		0.1770		0.1318	
Hazard ratio (95% CI) vs Kd	-	1.21 (0.83 to 1.75)		1.43 (0.85 to 2.41)		0.51 (0.21 to 1.25)	
P-value	-	0.3201		0.1794		0.1392	

A lower score represents a better level of quality of life. Clinical meaningful deterioration change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Fatigue
16.2.6.1.2.8 Efficacy response data - Subgroup analyses by ISS staging at SE
16.2.6.1.2.8.5 QLQ-C30 - Time until permanent improvement by 10 pt in fatigue according to ISS staging at SE (LOCF) - ITT population

	I		II		III		
	Kd (N=71)	**IKd (N=89)**	**Kd (N=31)**	**IKd (N=63)**	**Kd (N=20)**	**IKd (N=26)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	21 (29.6)	24 (27.0)	6 (19.4)	13 (20.6)	7 (35.0)	12 (46.2)	0.4016
Number (%) of patients censored	50 (70.4)	65 (73.0)	25 (80.6)	50 (79.4)	13 (65.0)	14 (53.8)	
Kaplan-Meier estimates of Fatigue in months							
25% quantile (95% CI)	19.35 (7.918 to 22.209)	18.89 (13.832 to NC)	NC (6.801 to NC)	NC (11.795 to NC)	6.47 (1.051 to 17.971)	1.41 (0.986 to 6.505)	
Median (95% CI)	NC (21.684 to NC)	24.44 (24.444 to NC)	NC (NC to NC)	NC (NC to NC)	NC (5.618 to NC)	12.32 (2.103 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (24.444 to NC)	NC (NC to NC)	NC (NC to NC)	NC (17.971 to NC)	NC (13.240 to NC)	
Comparison vs. Kd							
Log-Rank test p-value[a] vs Kd	-	0.7357		0.9542		0.2473	
Hazard ratio (95% CI) vs Kd	-	0.90 (0.50 to 1.63)		1.03 (0.39 to 2.71)		1.73 (0.68 to 4.41)	
P-value	-	0.7358		0.9544		0.2530	

A lower score represents a better level of quality of life. Clinical meaningful improvement change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
PGM=DEVOPS/SAR650984/EFC15246/CIR_RWE/REPORT/PGM/eff_km_subgp_sr_sig_de_i_t.sas OUT=REPORT/OUTPUT/eff_km_c30_fat_imppl_seiss_de_i_t_x.rtf (07APR2021 14:28)

16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Fatigue
16.2.6.1.2.8 Efficacy response data - Subgroup analyses by ISS staging at SE
16.2.6.1.2.8.6 QLQ-C30 - Time until permanent deterioration by 10 pt in fatigue according to ISS staging at SE (LOCF) - ITT population

	I		II		III		
	Kd (N=71)	**IKd (N=89)**	**Kd (N=31)**	**IKd (N=63)**	**Kd (N=20)**	**IKd (N=26)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	27 (38.0)	38 (42.7)	13 (41.9)	30 (47.6)	6 (30.0)	1 (3.8)	0.1207
Number (%) of patients censored	44 (62.0)	51 (57.3)	18 (58.1)	33 (52.4)	14 (70.0)	25 (96.2)	
Kaplan-Meier estimates of Fatigue in months							
25% quantile (95% CI)	17.08 (5.815 to 20.600)	11.93 (4.665 to 16.657)	8.31 (1.906 to 16.887)	8.25 (1.873 to 13.996)	7.39 (1.051 to NC)	NC (10.152 to NC)	
Median (95% CI)	22.44 (21.092 to NC)	NC (18.464 to NC)	NC (8.739 to NC)	20.93 (14.522 to NC)	NC (5.717 to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (23.524 to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Kd							
Log-Rank test p-value[a] vs Kd	-	0.4402		0.8292		0.0129	
Hazard ratio (95% CI) vs Kd	-	1.21 (0.74 to 1.99)		1.07 (0.56 to 2.06)		0.11 (0.01 to 0.91)	
P-value	-	0.4409		0.8292		0.0407	

A lower score represents a better level of quality of life. Clinical meaningful deterioration change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
PGM=DEVOPS/SAR650984/EFC15246/CIR_RWE/REPORT/PGM/eff_km_subgp_sr_sig_de_i_t.sas OUT=REPORT/OUTPUT/eff_km_c30_fat_detpl_seiss_de_i_t_x.rtf (07APR2021 14:28)

16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Fatigue
16.2.6.1.2.9 Efficacy response data - Subgroup analyses by R-ISS stage at SE
16.2.6.1.2.9.3 QLQ-C30 - Time to first improvement by 10 pt in fatigue according to R-ISS stage at SE (LOCF) - ITT population

	I or II		III		Not classified		
	Kd (N=103)	**IKd (N=155)**	**Kd (N=8)**	**IKd (N=16)**	**Kd (N=12)**	**IKd (N=8)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	60 (58.3)	95 (61.3)	6 (75.0)	10 (62.5)	8 (66.7)	4 (50.0)	1.0000
Number (%) of patients censored	43 (41.7)	60 (38.7)	2 (25.0)	6 (37.5)	4 (33.3)	4 (50.0)	
Kaplan-Meier estimates of Fatigue in months							
25% quantile (95% CI)	1.12 (1.018 to 2.004)	1.15 (1.051 to 2.004)	1.12 (1.051 to 1.906)	1.08 (0.986 to 1.906)	1.05 (0.953 to 4.632)	2.00 (1.018 to 5.125)	
Median (95% CI)	4.21 (2.957 to 14.522)	4.24 (2.990 to 9.002)	1.91 (1.051 to 17.643)	1.91 (1.051 to 2.924)	9.87 (0.986 to NC)	4.06 (1.018 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	17.64 (1.873 to NC)	2.92 (1.906 to NC)	NC (4.632 to NC)	NC (2.004 to NC)	
Comparison vs. Kd							
Log-Rank test p-value[a] vs Kd	-	0.8597		0.9551		0.8821	
Hazard ratio (95% CI) vs Kd	-	1.03 (0.75 to 1.42)		1.03 (0.37 to 2.87)		1.10 (0.32 to 3.71)	
P-value	-	0.8602		0.9552		0.8821	

A lower score represents a better level of quality of life. Clinical meaningful improvement change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Fatigue
16.2.6.1.2.9 Efficacy response data - Subgroup analyses by R-ISS stage at SE
16.2.6.1.2.9.4 QLQ-C30 - Time to first deterioration by 10 pt in fatigue according to R-ISS stage at SE (LOCF) - ITT population

	I or II		III		Not classified		
	Kd (N=103)	**IKd (N=155)**	**Kd (N=8)**	**IKd (N=16)**	**Kd (N=12)**	**IKd (N=8)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	69 (67.0)	121 (78.1)	4 (50.0)	2 (12.5)	8 (66.7)	3 (37.5)	0.0686
Number (%) of patients censored	34 (33.0)	34 (21.9)	4 (50.0)	14 (87.5)	4 (33.3)	5 (62.5)	
Kaplan-Meier estimates of Fatigue in months							
25% quantile (95% CI)	1.15 (1.051 to 2.004)	1.12 (1.051 to 1.183)	1.08 (1.051 to 13.405)	NC (2.825 to NC)	1.51 (0.986 to 3.745)	3.94 (0.986 to NC)	
Median (95% CI)	4.83 (2.825 to 7.261)	2.92 (1.971 to 3.811)	13.40 (1.051 to NC)	NC (9.363 to NC)	3.91 (1.051 to NC)	NC (0.986 to NC)	
75% quantile (95% CI)	NC (12.320 to NC)	10.87 (6.735 to NC)	NC (7.556 to NC)	NC (NC to NC)	NC (3.745 to NC)	NC (3.943 to NC)	
Comparison vs. Kd							
Log-Rank test p-value[a] vs Kd	-	0.0696		0.0346		0.4743	
Hazard ratio (95% CI) vs Kd	-	1.31 (0.98 to 1.77)		0.19 (0.04 to 1.06)		0.62 (0.16 to 2.34)	
P-value	-	0.0705		0.0580		0.4786	

A lower score represents a better level of quality of life. Clinical meaningful deterioration change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
PGM=DEVOPS/SAR650984/EFC15246/CIR_RWE/REPORT/PGM/eff_km_subgp_sr_sig_de_i_t.sas OUT=REPORT/OUTPUT/eff_km_c30_fat_detl_seriss_de_i_t_x.rtf (07APR2021 14:28)

16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Fatigue
16.2.6.1.2.9 Efficacy response data - Subgroup analyses by R-ISS stage at SE
16.2.6.1.2.9.5 QLQ-C30 - Time until permanent improvement by 10 pt in fatigue according to R-ISS stage at SE (LOCF) - ITT population

	I or II		III		Not classified		
	Kd (N=103)	**IKd (N=155)**	**Kd (N=8)**	**IKd (N=16)**	**Kd (N=12)**	**IKd (N=8)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	28 (27.2)	41 (26.5)	4 (50.0)	7 (43.8)	2 (16.7)	1 (12.5)	0.9229
Number (%) of patients censored	75 (72.8)	114 (73.5)	4 (50.0)	9 (56.3)	10 (83.3)	7 (87.5)	
Kaplan-Meier estimates of Fatigue in months							
25% quantile (95% CI)	19.35 (11.598 to 22.209)	18.37 (13.733 to NC)	1.12 (1.051 to 17.643)	1.41 (0.986 to 6.505)	NC (5.585 to NC)	NC (1.018 to NC)	
Median (95% CI)	NC (22.209 to NC)	24.44 (24.444 to NC)	17.64 (1.051 to NC)	6.51 (1.084 to NC)	NC (16.164 to NC)	NC (1.018 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (24.444 to NC)	NC (6.472 to NC)	NC (6.505 to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Kd							
Log-Rank test p-value[a] vs Kd	-	0.7567		0.9566		0.8935	
Hazard ratio (95% CI) vs Kd	-	0.93 (0.57 to 1.50)		1.04 (0.30 to 3.59)		1.18 (0.11 to 13.05)	
P-value	-	0.7567		0.9567		0.8936	

A lower score represents a better level of quality of life. Clinical meaningful improvement change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Fatigue
16.2.6.1.2.9 Efficacy response data - Subgroup analyses by R-ISS stage at SE
16.2.6.1.2.9.6 QLQ-C30 - Time until permanent deterioration by 10 pt in fatigue according to R-ISS stage at SE (LOCF) - ITT population

	I or II		III		Not classified		
	Kd (N=103)	**IKd (N=155)**	**Kd (N=8)**	**IKd (N=16)**	**Kd (N=12)**	**IKd (N=8)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	38 (36.9)	67 (43.2)	2 (25.0)	0 (0.0)	7 (58.3)	2 (25.0)	0.6878
Number (%) of patients censored	65 (63.1)	88 (56.8)	6 (75.0)	16 (100.0)	5 (41.7)	6 (75.0)	
Kaplan-Meier estimates of Fatigue in months							
25% quantile (95% CI)	9.03 (5.717 to 19.154)	11.50 (6.078 to 14.850)	7.56 (3.811 to NC)	NC (NC to NC)	8.69 (1.051 to 21.092)	16.02 (11.499 to NC)	
Median (95% CI)	NC (20.600 to NC)	23.52 (19.877 to NC)	NC (3.811 to NC)	NC (NC to NC)	21.09 (1.873 to NC)	20.53 (11.499 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (7.556 to NC)	NC (NC to NC)	21.55 (21.092 to NC)	NC (11.499 to NC)	
Comparison vs. Kd							
Log-Rank test p-value[a] vs Kd	-	0.4681		0.0398		0.5200	
Hazard ratio (95% CI) vs Kd	-	1.16 (0.78 to 1.73)				0.60 (0.12 to 2.90)	
P-value	-	0.4685		0.9979		0.5245	

A lower score represents a better level of quality of life. Clinical meaningful deterioration change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Fatigue
16.2.6.1.2.10 Efficacy response data - Subgroup analyses by nb of prior lines
16.2.6.1.2.10.3 QLQ-C30 - Time to first improvement by 10 pt in fatigue according to nb of prior lines (LOCF) - ITT population

	1		>1		
	Kd (N=55)	**IKd (N=79)**	**Kd (N=68)**	**IKd (N=100)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	30 (54.5)	44 (55.7)	44 (64.7)	65 (65.0)	0.8916
Number (%) of patients censored	25 (45.5)	35 (44.3)	24 (35.3)	35 (35.0)	
Kaplan-Meier estimates of Fatigue in months					
25% quantile (95% CI)	1.87 (1.051 to 2.990)	1.41 (0.986 to 2.891)	1.05 (0.986 to 1.906)	1.15 (1.051 to 1.971)	
Median (95% CI)	9.10 (2.990 to NC)	5.78 (3.285 to NC)	3.75 (1.906 to 6.571)	2.96 (2.103 to 4.895)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (9.889 to NC)	NC (11.269 to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.8483		0.9705	
Hazard ratio (95% CI) vs Kd	-	1.05 (0.66 to 1.66)		1.01 (0.69 to 1.48)	
P-value	-	0.8489		0.9705	
Improvement probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful improvement change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Fatigue
16.2.6.1.2.10 Efficacy response data - Subgroup analyses by nb of prior lines
16.2.6.1.2.10.4 QLQ-C30 - Time to first deterioration by 10 pt in fatigue according to nb of prior lines (LOCF) - ITT population

	1		>1		
	Kd (N=55)	**IKd (N=79)**	**Kd (N=68)**	**IKd (N=100)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	37 (67.3)	54 (68.4)	44 (64.7)	72 (72.0)	0.7631
Number (%) of patients censored	18 (32.7)	25 (31.6)	24 (35.3)	28 (28.0)	
Kaplan-Meier estimates of Fatigue in months					
25% quantile (95% CI)	1.12 (1.051 to 2.037)	1.12 (0.986 to 1.478)	1.22 (1.051 to 2.825)	1.18 (1.051 to 1.971)	
Median (95% CI)	4.07 (2.037 to 7.491)	3.02 (1.906 to 5.125)	5.55 (2.825 to 13.405)	3.94 (2.530 to 6.538)	
75% quantile (95% CI)	NC (7.491 to NC)	NC (6.669 to NC)	NC (14.784 to NC)	14.00 (8.378 to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.6333		0.2731	
Hazard ratio (95% CI) vs Kd	-	1.11 (0.73 to 1.68)		1.23 (0.85 to 1.80)	
P-value	-	0.6335		0.2739	
Deterioration probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful deterioration change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Fatigue
16.2.6.1.2.10 Efficacy response data - Subgroup analyses by nb of prior lines
16.2.6.1.2.10.5 QLQ-C30 - Time until permanent improvement by 10 pt in fatigue according to nb of prior lines (LOCF) - ITT population

	1		>1		
	Kd (N=55)	**IKd (N=79)**	**Kd (N=68)**	**IKd (N=100)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	13 (23.6)	22 (27.8)	21 (30.9)	27 (27.0)	0.3630
Number (%) of patients censored	42 (76.4)	57 (72.2)	47 (69.1)	73 (73.0)	
Kaplan-Meier estimates of Fatigue in months					
25% quantile (95% CI)	22.21 (14.324 to NC)	18.37 (11.795 to NC)	13.83 (5.618 to 21.684)	17.05 (12.025 to NC)	
Median (95% CI)	NC (22.209 to NC)	24.44 (24.444 to NC)	NC (21.585 to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (24.444 to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.4877		0.5395	
Hazard ratio (95% CI) vs Kd	-	1.27 (0.64 to 2.53)		0.84 (0.47 to 1.48)	
P-value	-	0.4888		0.5400	
Improvement probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful improvement change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Fatigue
16.2.6.1.2.10 Efficacy response data - Subgroup analyses by nb of prior lines
16.2.6.1.2.10.6 QLQ-C30 - Time until permanent deterioration by 10 pt in fatigue according to nb of prior lines (LOCF) - ITT population

	1		>1		
	Kd (N=55)	**IKd (N=79)**	**Kd (N=68)**	**IKd (N=100)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	21 (38.2)	33 (41.8)	26 (38.2)	36 (36.0)	0.4789
Number (%) of patients censored	34 (61.8)	46 (58.2)	42 (61.8)	64 (64.0)	
Kaplan-Meier estimates of Fatigue in months					
25% quantile (95% CI)	16.89 (4.041 to 21.092)	12.68 (4.665 to 18.431)	8.31 (3.811 to 18.530)	12.16 (6.834 to 18.070)	
Median (95% CI)	NC (20.600 to NC)	NC (18.464 to NC)	NC (18.530 to NC)	23.52 (20.698 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (23.524 to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.5379		0.6644	
Hazard ratio (95% CI) vs Kd	-	1.19 (0.69 to 2.05)		0.89 (0.54 to 1.48)	
P-value	-	0.5384		0.6645	
Deterioration probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful deterioration change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
PGM=DEVOPS/SAR650984/EFC15246/CIR_RWE/REPORT/PGM/eff_km_subgp_sr_sig_de_i_t.sas OUT=REPORT/OUTPUT/eff_km_c30_fat_detpl_plne_de_i_t_x.rtf (07APR2021 14:28)

16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Fatigue
16.2.6.1.2.11 Efficacy response data - Subgroup analyses by cytogenetic abnormality
16.2.6.1.2.11.3 QLQ-C30 - Time to first improvement by 10 pt in fatigue according to cytogenetic abnormality (LOCF) - ITT population

	At least one		None		
	Kd (N=31)	**IKd (N=42)**	**Kd (N=77)**	**IKd (N=114)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	20 (64.5)	23 (54.8)	43 (55.8)	74 (64.9)	0.3373
Number (%) of patients censored	11 (35.5)	19 (45.2)	34 (44.2)	40 (35.1)	
Kaplan-Meier estimates of Fatigue in months					
25% quantile (95% CI)	1.15 (1.018 to 2.070)	1.05 (0.986 to 1.971)	1.12 (1.018 to 2.037)	1.31 (1.051 to 2.070)	
Median (95% CI)	3.75 (1.873 to 17.643)	4.14 (1.413 to NC)	6.01 (2.858 to NC)	3.32 (2.891 to 5.782)	
75% quantile (95% CI)	NC (5.717 to NC)	NC (NC to NC)	NC (NC to NC)	NC (12.715 to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.5960		0.3365	
Hazard ratio (95% CI) vs Kd	-	0.85 (0.47 to 1.55)		1.20 (0.83 to 1.75)	
P-value	-	0.5964		0.3372	
Improvement probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful improvement change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
PGM=DEVOPS/SAR650984/EFC15246/CIR_RWE/REPORT/PGM/eff_km_subgp_sr_sig_de_i_t.sas OUT=REPORT/OUTPUT/eff_km_c30_fat_impl_cyto_de_i_t_x.rtf (07APR2021 14:28)

16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Fatigue
16.2.6.1.2.11 Efficacy response data - Subgroup analyses by cytogenetic abnormality
16.2.6.1.2.11.4 QLQ-C30 - Time to first deterioration by 10 pt in fatigue according to cytogenetic abnormality (LOCF) - ITT population

	At least one		None		
	Kd (N=31)	**IKd (N=42)**	**Kd (N=77)**	**IKd (N=114)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	21 (67.7)	26 (61.9)	50 (64.9)	84 (73.7)	0.1556
Number (%) of patients censored	10 (32.3)	16 (38.1)	27 (35.1)	30 (26.3)	
Kaplan-Meier estimates of Fatigue in months					
25% quantile (95% CI)	1.08 (0.986 to 2.037)	1.08 (0.986 to 1.906)	1.22 (1.051 to 2.037)	1.15 (1.051 to 1.478)	
Median (95% CI)	4.25 (1.117 to 7.228)	5.65 (1.150 to NC)	5.65 (2.825 to 12.320)	2.99 (1.971 to 4.402)	
75% quantile (95% CI)	NC (6.374 to NC)	NC (13.996 to NC)	NC (14.784 to NC)	13.37 (6.899 to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.5556		0.0960	
Hazard ratio (95% CI) vs Kd	-	0.84 (0.47 to 1.50)		1.35 (0.95 to 1.91)	
P-value	-	0.5561		0.0972	
Deterioration probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful deterioration change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Fatigue
16.2.6.1.2.11 Efficacy response data - Subgroup analyses by cytogenetic abnormality
16.2.6.1.2.11.5 QLQ-C30 - Time until permanent improvement by 10 pt in fatigue according to cytogenetic abnormality (LOCF) - ITT population

	At least one		None		
	Kd (N=31)	**IKd (N=42)**	**Kd (N=77)**	**IKd (N=114)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	10 (32.3)	13 (31.0)	21 (27.3)	32 (28.1)	0.9017
Number (%) of patients censored	21 (67.7)	29 (69.0)	56 (72.7)	82 (71.9)	
Kaplan-Meier estimates of Fatigue in months					
25% quantile (95% CI)	17.64 (1.117 to NC)	13.37 (1.084 to NC)	17.97 (10.448 to NC)	17.61 (12.320 to 24.444)	
Median (95% CI)	NC (19.745 to NC)	NC (18.366 to NC)	NC (22.209 to NC)	24.44 (24.444 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (24.444 to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.8931		0.9596	
Hazard ratio (95% CI) vs Kd	-	0.94 (0.41 to 2.16)		1.01 (0.58 to 1.76)	
P-value	-	0.8927		0.9597	
Improvement probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful improvement change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Fatigue
16.2.6.1.2.11 Efficacy response data - Subgroup analyses by cytogenetic abnormality
16.2.6.1.2.11.6 QLQ-C30 - Time until permanent deterioration by 10 pt in fatigue according to cytogenetic abnormality (LOCF) - ITT population

	At least one		None		
	Kd (N=31)	**IKd (N=42)**	**Kd (N=77)**	**IKd (N=114)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	13 (41.9)	21 (50.0)	25 (32.5)	37 (32.5)	0.5191
Number (%) of patients censored	18 (58.1)	21 (50.0)	52 (67.5)	77 (67.5)	
Kaplan-Meier estimates of Fatigue in months					
25% quantile (95% CI)	12.58 (1.018 to 20.074)	4.60 (1.051 to 13.996)	9.99 (4.895 to 21.388)	16.66 (10.152 to 19.877)	
Median (95% CI)	22.44 (16.887 to NC)	20.70 (10.875 to NC)	NC (21.388 to NC)	NC (20.928 to NC)	
75% quantile (95% CI)	NC (22.439 to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.4991		0.8780	
Hazard ratio (95% CI) vs Kd	-	1.27 (0.64 to 2.54)		0.96 (0.58 to 1.60)	
P-value	-	0.5001		0.8775	
Deterioration probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful deterioration change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Fatigue
16.2.6.1.2.12 Efficacy response data - Subgroup analyses by MM type at SE
16.2.6.1.2.12.3 QLQ-C30 - Time to first improvement by 10 pt in fatigue according to MM type at SE (LOCF) - ITT population

	IgG		Non-IgG		
	Kd (N=85)	**IKd (N=126)**	**Kd (N=38)**	**IKd (N=53)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	48 (56.5)	77 (61.1)	26 (68.4)	32 (60.4)	0.2116
Number (%) of patients censored	37 (43.5)	49 (38.9)	12 (31.6)	21 (39.6)	
Kaplan-Meier estimates of Fatigue in months					
25% quantile (95% CI)	1.84 (1.051 to 2.825)	1.31 (1.051 to 2.004)	1.05 (0.986 to 1.314)	1.05 (0.986 to 2.037)	
Median (95% CI)	6.57 (2.957 to NC)	3.88 (2.891 to 8.805)	2.99 (1.084 to 4.632)	3.71 (2.004 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (3.745 to NC)	NC (12.715 to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.4164		0.3753	
Hazard ratio (95% CI) vs Kd	-	1.16 (0.81 to 1.67)		0.79 (0.47 to 1.33)	
P-value	-	0.4169		0.3764	
Improvement probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful improvement change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Fatigue
16.2.6.1.2.12 Efficacy response data - Subgroup analyses by MM type at SE
16.2.6.1.2.12.4 QLQ-C30 - Time to first deterioration by 10 pt in fatigue according to MM type at SE (LOCF) - ITT population

	IgG		Non-IgG		
	Kd (N=85)	**IKd (N=126)**	**Kd (N=38)**	**IKd (N=53)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	59 (69.4)	89 (70.6)	22 (57.9)	37 (69.8)	0.3607
Number (%) of patients censored	26 (30.6)	37 (29.4)	16 (42.1)	16 (30.2)	
Kaplan-Meier estimates of Fatigue in months					
25% quantile (95% CI)	1.15 (1.051 to 1.938)	1.15 (1.051 to 1.873)	1.59 (0.986 to 5.618)	1.08 (0.986 to 1.906)	
Median (95% CI)	3.35 (2.037 to 6.702)	3.75 (2.004 to 5.125)	7.49 (4.041 to NC)	3.94 (1.906 to 6.735)	
75% quantile (95% CI)	NC (9.758 to NC)	19.25 (9.199 to NC)	NC (12.320 to NC)	NC (6.735 to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.6985		0.1763	
Hazard ratio (95% CI) vs Kd	-	1.07 (0.77 to 1.48)		1.44 (0.85 to 2.44)	
P-value	-	0.7002		0.1786	
Deterioration probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful deterioration change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Fatigue
16.2.6.1.2.12 Efficacy response data - Subgroup analyses by MM type at SE
16.2.6.1.2.12.5 QLQ-C30 - Time until permanent improvement by 10 pt in fatigue according to MM type at SE (LOCF) - ITT population

	IgG		Non-IgG		
	Kd (N=85)	**IKd (N=126)**	**Kd (N=38)**	**IKd (N=53)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	23 (27.1)	33 (26.2)	11 (28.9)	16 (30.2)	0.7619
Number (%) of patients censored	62 (72.9)	93 (73.8)	27 (71.1)	37 (69.8)	
Kaplan-Meier estimates of Fatigue in months					
25% quantile (95% CI)	19.35 (10.448 to NC)	17.61 (13.010 to NC)	17.38 (6.472 to NC)	13.73 (3.745 to NC)	
Median (95% CI)	NC (22.209 to NC)	24.44 (24.444 to NC)	NC (21.684 to NC)	NC (19.581 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (24.444 to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.8852		0.8340	
Hazard ratio (95% CI) vs Kd	-	0.96 (0.56 to 1.64)		1.09 (0.50 to 2.34)	
P-value	-	0.8848		0.8340	
Improvement probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful improvement change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Fatigue
16.2.6.1.2.12 Efficacy response data - Subgroup analyses by MM type at SE
16.2.6.1.2.12.6 QLQ-C30 - Time until permanent deterioration by 10 pt in fatigue according to MM type at SE (LOCF) - ITT population

	IgG		Non-IgG		
	Kd (N=85)	**IKd (N=126)**	**Kd (N=38)**	**IKd (N=53)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	32 (37.6)	45 (35.7)	15 (39.5)	24 (45.3)	0.7768
Number (%) of patients censored	53 (62.4)	81 (64.3)	23 (60.5)	29 (54.7)	
Kaplan-Meier estimates of Fatigue in months					
25% quantile (95% CI)	12.58 (5.717 to 20.074)	13.27 (9.265 to 18.694)	7.39 (1.051 to 20.567)	6.74 (2.858 to 15.507)	
Median (95% CI)	NC (20.600 to NC)	NC (20.698 to NC)	21.39 (9.035 to NC)	23.52 (13.996 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (23.524 to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.9404		0.7570	
Hazard ratio (95% CI) vs Kd	-	0.98 (0.62 to 1.55)		1.11 (0.58 to 2.12)	
P-value	-	0.9403		0.7571	
Deterioration probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful deterioration change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Fatigue
16.2.6.1.2.13 Efficacy response data - Subgroup analyses by previous autologous stem-cell
16.2.6.1.2.13.3 QLQ-C30 - Time to first improvement by 10 pt in fatigue according to previous autologous stem-cell (LOCF) - ITT population

	Yes		No		
	Kd (N=69)	**IKd (N=116)**	**Kd (N=54)**	**IKd (N=63)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	36 (52.2)	74 (63.8)	38 (70.4)	35 (55.6)	0.0918
Number (%) of patients censored	33 (47.8)	42 (36.2)	16 (29.6)	28 (44.4)	
Kaplan-Meier estimates of Fatigue in months					
25% quantile (95% CI)	1.08 (0.986 to 1.873)	1.38 (1.018 to 2.037)	1.84 (1.018 to 2.825)	1.12 (1.051 to 2.004)	
Median (95% CI)	11.20 (2.004 to NC)	3.71 (2.891 to 5.585)	2.99 (2.825 to 4.632)	5.82 (2.004 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	17.64 (3.975 to NC)	NC (NC to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.2115		0.2404	
Hazard ratio (95% CI) vs Kd	-	1.29 (0.86 to 1.92)		0.76 (0.48 to 1.20)	
P-value	-	0.2127		0.2419	
Improvement probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful improvement change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Fatigue
16.2.6.1.2.13 Efficacy response data - Subgroup analyses by previous autologous stem-cell
16.2.6.1.2.13.4 QLQ-C30 - Time to first deterioration by 10 pt in fatigue according to previous autologous stem-cell (LOCF) - ITT population

	Yes		No		
	Kd (N=69)	**IKd (N=116)**	**Kd (N=54)**	**IKd (N=63)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	44 (63.8)	83 (71.6)	37 (68.5)	43 (68.3)	0.3550
Number (%) of patients censored	25 (36.2)	33 (28.4)	17 (31.5)	20 (31.7)	
Kaplan-Meier estimates of Fatigue in months					
25% quantile (95% CI)	1.12 (1.051 to 1.938)	1.08 (1.051 to 1.183)	1.25 (1.051 to 2.825)	1.61 (1.084 to 2.891)	
Median (95% CI)	5.65 (2.793 to 14.784)	2.92 (1.938 to 4.632)	3.81 (2.037 to 7.228)	4.21 (2.891 to 6.899)	
75% quantile (95% CI)	NC (18.628 to NC)	NC (8.345 to NC)	NC (6.801 to NC)	NC (6.899 to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.1871		0.9928	
Hazard ratio (95% CI) vs Kd	-	1.28 (0.89 to 1.84)		1.00 (0.64 to 1.55)	
P-value	-	0.1882		0.9928	
Deterioration probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful deterioration change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Fatigue
16.2.6.1.2.13 Efficacy response data - Subgroup analyses by previous autologous stem-cell
16.2.6.1.2.13.5 QLQ-C30 - Time until permanent improvement by 10 pt in fatigue according to previous autologous stem-cell (LOCF) - ITT population

	Yes		No		
	Kd (N=69)	**IKd (N=116)**	**Kd (N=54)**	**IKd (N=63)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	18 (26.1)	37 (31.9)	16 (29.6)	12 (19.0)	0.1691
Number (%) of patients censored	51 (73.9)	79 (68.1)	38 (70.4)	51 (81.0)	
Kaplan-Meier estimates of Fatigue in months					
25% quantile (95% CI)	17.97 (7.392 to NC)	16.89 (11.138 to 19.581)	17.64 (7.425 to 22.209)	NC (11.795 to NC)	
Median (95% CI)	NC (NC to NC)	24.44 (NC to NC)	NC (21.585 to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	24.44 (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.4615		0.2594	
Hazard ratio (95% CI) vs Kd	-	1.24 (0.70 to 2.17)		0.65 (0.31 to 1.38)	
P-value	-	0.4624		0.2632	
Improvement probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful improvement change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
PGM=DEVOPS/SAR650984/EFC15246/CIR_RWE/REPORT/PGM/eff_km_subgp_sr_sig_de_i_t.sas OUT=REPORT/OUTPUT/eff_km_c30_fat_imppl_auto_de_i_t_x.rtf (07APR2021 14:28)

16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Fatigue
16.2.6.1.2.13 Efficacy response data - Subgroup analyses by previous autologous stem-cell
16.2.6.1.2.13.6 QLQ-C30 - Time until permanent deterioration by 10 pt in fatigue according to previous autologous stem-cell (LOCF) - ITT population

	Yes		No		
	Kd (N=69)	**IKd (N=116)**	**Kd (N=54)**	**IKd (N=63)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	27 (39.1)	43 (37.1)	20 (37.0)	26 (41.3)	0.6906
Number (%) of patients censored	42 (60.9)	73 (62.9)	34 (63.0)	37 (58.7)	
Kaplan-Meier estimates of Fatigue in months					
25% quantile (95% CI)	7.56 (2.957 to 20.600)	13.27 (6.439 to 18.464)	9.99 (5.717 to 17.380)	11.50 (5.651 to 15.507)	
Median (95% CI)	22.44 (20.600 to NC)	23.52 (20.698 to NC)	NC (16.887 to NC)	NC (15.507 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.9062		0.6884	
Hazard ratio (95% CI) vs Kd	-	0.97 (0.60 to 1.57)		1.13 (0.63 to 2.02)	
P-value	-	0.9058		0.6886	
Deterioration probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful deterioration change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
PGM=DEVOPS/SAR650984/EFC15246/CIR_RWE/REPORT/PGM/eff_km_subgp_sr_sig_de_i_t.sas OUT=REPORT/OUTPUT/eff_km_c30_fat_detpl_auto_de_i_t_x.rtf (07APR2021 14:28)

16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Fatigue
16.2.6.1.2.14 Efficacy response data - Subgroup analyses by baseline eGFR (MDRD)
16.2.6.1.2.14.3 QLQ-C30 - Time to first improvement by 10 pt in fatigue according to baseline eGFR (MDRD) (LOCF) - ITT population

	>=60 mL/min/1.73m2		<60 mL/min/1.73m2		
	Kd (N=93)	**IKd (N=122)**	**Kd (N=18)**	**IKd (N=43)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	58 (62.4)	73 (59.8)	12 (66.7)	27 (62.8)	0.4435
Number (%) of patients censored	35 (37.6)	49 (40.2)	6 (33.3)	16 (37.2)	
Kaplan-Meier estimates of Fatigue in months					
25% quantile (95% CI)	1.10 (1.018 to 1.873)	1.15 (1.018 to 2.037)	1.84 (0.986 to 2.858)	1.08 (0.986 to 2.070)	
Median (95% CI)	4.30 (2.891 to 11.203)	3.75 (2.891 to 11.072)	2.86 (1.150 to 15.113)	5.82 (1.906 to 11.269)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	15.11 (2.858 to NC)	NC (8.969 to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.9654		0.4145	
Hazard ratio (95% CI) vs Kd	-	1.01 (0.71 to 1.42)		0.75 (0.38 to 1.49)	
P-value	-	0.9654		0.4160	
Improvement probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful improvement change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
PGM=DEVOPS/SAR650984/EFC15246/CIR_RWE/REPORT/PGM/eff_km_subgp_sr_sig_de_i_t.sas OUT=REPORT/OUTPUT/eff_km_c30_fat_impl_crcl_de_i_t_x.rtf (07APR2021 14:28)

16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Fatigue
16.2.6.1.2.14 Efficacy response data - Subgroup analyses by baseline eGFR (MDRD)
16.2.6.1.2.14.4 QLQ-C30 - Time to first deterioration by 10 pt in fatigue according to baseline eGFR (MDRD) (LOCF) - ITT population

	>=60 mL/min/1.73m2		<60 mL/min/1.73m2		
	Kd (N=93)	**IKd (N=122)**	**Kd (N=18)**	**IKd (N=43)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	61 (65.6)	92 (75.4)	13 (72.2)	28 (65.1)	0.1484
Number (%) of patients censored	32 (34.4)	30 (24.6)	5 (27.8)	15 (34.9)	
Kaplan-Meier estimates of Fatigue in months					
25% quantile (95% CI)	1.12 (1.051 to 1.938)	1.12 (1.051 to 1.216)	2.83 (0.986 to 4.041)	1.12 (0.986 to 2.530)	
Median (95% CI)	5.16 (2.793 to 8.312)	2.92 (1.938 to 4.205)	4.04 (1.150 to 12.189)	3.22 (1.971 to 13.372)	
75% quantile (95% CI)	NC (19.351 to NC)	10.87 (6.998 to NC)	12.19 (4.041 to NC)	NC (4.632 to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.0470		0.5652	
Hazard ratio (95% CI) vs Kd	-	1.39 (1.00 to 1.92)		0.82 (0.43 to 1.59)	
P-value	-	0.0480		0.5658	
Hazard ratio inverted (95% CI) vs IKd		-		1.21 (0.63 to 2.35)	

A lower score represents a better level of quality of life. Clinical meaningful deterioration change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Fatigue
16.2.6.1.2.14 Efficacy response data - Subgroup analyses by baseline eGFR (MDRD)
16.2.6.1.2.14.5 QLQ-C30 - Time until permanent improvement by 10 pt in fatigue according to baseline eGFR (MDRD) (LOCF) - ITT population

	>=60 mL/min/1.73m2		<60 mL/min/1.73m2		
	Kd (N=93)	**IKd (N=122)**	**Kd (N=18)**	**IKd (N=43)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	32 (34.4)	30 (24.6)	0 (0.0)	14 (32.6)	0.9775
Number (%) of patients censored	61 (65.6)	92 (75.4)	18 (100.0)	29 (67.4)	
Kaplan-Meier estimates of Fatigue in months					
25% quantile (95% CI)	15.05 (7.425 to 21.585)	18.89 (13.733 to NC)	NC (NC to NC)	13.01 (2.103 to 24.444)	
Median (95% CI)	NC (21.585 to NC)	NC (NC to NC)	NC (NC to NC)	24.44 (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	24.44 (NC to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.2191		0.0248	
Hazard ratio (95% CI) vs Kd	-	0.73 (0.45 to 1.21)			
P-value	-	0.2209		0.9924	
Improvement probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful improvement change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Fatigue
16.2.6.1.2.14 Efficacy response data - Subgroup analyses by baseline eGFR (MDRD)
16.2.6.1.2.14.6 QLQ-C30 - Time until permanent deterioration by 10 pt in fatigue according to baseline eGFR (MDRD) (LOCF) - ITT population

	>=60 mL/min/1.73m2		<60 mL/min/1.73m2		
	Kd (N=93)	**IKd (N=122)**	**Kd (N=18)**	**IKd (N=43)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	32 (34.4)	50 (41.0)	8 (44.4)	16 (37.2)	0.0930
Number (%) of patients censored	61 (65.6)	72 (59.0)	10 (55.6)	27 (62.8)	
Kaplan-Meier estimates of Fatigue in months					
25% quantile (95% CI)	16.69 (7.524 to 21.092)	10.87 (4.665 to 13.569)	3.81 (1.051 to 20.074)	18.07 (6.078 to 20.764)	
Median (95% CI)	NC (21.388 to NC)	23.52 (19.253 to NC)	21.55 (3.811 to NC)	NC (19.877 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (20.074 to NC)	NC (NC to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.1822		0.2432	
Hazard ratio (95% CI) vs Kd	-	1.35 (0.87 to 2.11)		0.61 (0.26 to 1.42)	
P-value	-	0.1838		0.2481	
Deterioration probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful deterioration change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Fatigue
16.2.6.1.2.15 Efficacy response data - Subgroup analyses by previous treatment with PI
16.2.6.1.2.15.3 QLQ-C30 - Time to first improvement by 10 pt in fatigue according to previous treatment with PI (LOCF) - ITT population

	Yes		No		
	Kd (N=47)	**IKd (N=81)**	**Kd (N=76)**	**IKd (N=98)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	30 (63.8)	51 (63.0)	44 (57.9)	58 (59.2)	0.8083
Number (%) of patients censored	17 (36.2)	30 (37.0)	32 (42.1)	40 (40.8)	
Kaplan-Meier estimates of Fatigue in months					
25% quantile (95% CI)	1.15 (1.018 to 2.858)	1.08 (1.018 to 1.971)	1.12 (0.986 to 2.004)	1.91 (1.051 to 2.136)	
Median (95% CI)	3.29 (1.906 to 9.889)	2.99 (2.037 to 4.665)	4.63 (2.858 to NC)	5.59 (2.957 to 12.715)	
75% quantile (95% CI)	NC (6.571 to NC)	NC (5.815 to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.7852		0.9886	
Hazard ratio (95% CI) vs Kd	-	1.06 (0.68 to 1.67)		1.00 (0.67 to 1.48)	
P-value	-	0.7852		0.9886	
Improvement probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful improvement change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Fatigue
16.2.6.1.2.15 Efficacy response data - Subgroup analyses by previous treatment with PI
16.2.6.1.2.15.4 QLQ-C30 - Time to first deterioration by 10 pt in fatigue according to previous treatment with PI (LOCF) - ITT population

	Yes		No		
	Kd (N=47)	**IKd (N=81)**	**Kd (N=76)**	**IKd (N=98)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	31 (66.0)	53 (65.4)	50 (65.8)	73 (74.5)	0.3183
Number (%) of patients censored	16 (34.0)	28 (34.6)	26 (34.2)	25 (25.5)	
Kaplan-Meier estimates of Fatigue in months					
25% quantile (95% CI)	1.91 (1.051 to 2.825)	1.91 (1.117 to 2.825)	1.12 (1.051 to 2.004)	1.05 (0.986 to 1.117)	
Median (95% CI)	3.81 (2.037 to 12.320)	4.73 (3.055 to 9.199)	4.90 (2.825 to 9.758)	2.83 (1.216 to 3.811)	
75% quantile (95% CI)	NC (8.312 to NC)	NC (9.363 to NC)	NC (12.189 to NC)	13.37 (5.651 to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.9850		0.1392	
Hazard ratio (95% CI) vs Kd	-	1.00 (0.64 to 1.56)		1.31 (0.91 to 1.88)	
P-value	-	0.9850		0.1404	
Deterioration probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful deterioration change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Fatigue
16.2.6.1.2.15 Efficacy response data - Subgroup analyses by previous treatment with PI
16.2.6.1.2.15.5 QLQ-C30 - Time until permanent improvement by 10 pt in fatigue according to previous treatment with PI (LOCF) - ITT population

	Yes		No		
	Kd (N=47)	**IKd (N=81)**	**Kd (N=76)**	**IKd (N=98)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	11 (23.4)	24 (29.6)	23 (30.3)	25 (25.5)	0.2215
Number (%) of patients censored	36 (76.6)	57 (70.4)	53 (69.7)	73 (74.5)	
Kaplan-Meier estimates of Fatigue in months					
25% quantile (95% CI)	21.59 (7.392 to NC)	13.73 (7.064 to NC)	16.16 (7.425 to 22.209)	19.58 (12.945 to NC)	
Median (95% CI)	NC (21.585 to NC)	NC (NC to NC)	NC (21.684 to NC)	24.44 (24.444 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (24.444 to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.3872		0.4267	
Hazard ratio (95% CI) vs Kd	-	1.37 (0.67 to 2.80)		0.79 (0.45 to 1.40)	
P-value	-	0.3892		0.4277	
Improvement probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful improvement change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Fatigue
16.2.6.1.2.15 Efficacy response data - Subgroup analyses by previous treatment with PI
16.2.6.1.2.15.6 QLQ-C30 - Time until permanent deterioration by 10 pt in fatigue according to previous treatment with PI (LOCF) - ITT population

	Yes		No		
	Kd (N=47)	**IKd (N=81)**	**Kd (N=76)**	**IKd (N=98)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	16 (34.0)	34 (42.0)	31 (40.8)	35 (35.7)	0.2189
Number (%) of patients censored	31 (66.0)	47 (58.0)	45 (59.2)	63 (64.3)	
Kaplan-Meier estimates of Fatigue in months					
25% quantile (95% CI)	12.02 (2.825 to 20.600)	11.50 (6.078 to 16.657)	8.34 (4.041 to 17.380)	12.32 (4.665 to 20.501)	
Median (95% CI)	NC (20.567 to NC)	23.52 (18.431 to NC)	22.44 (20.074 to NC)	NC (20.764 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (23.524 to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.3221		0.4722	
Hazard ratio (95% CI) vs Kd	-	1.35 (0.74 to 2.45)		0.84 (0.52 to 1.36)	
P-value	-	0.3239		0.4728	
Deterioration probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful deterioration change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Fatigue
16.2.6.1.2.16 Efficacy response data - Subgroup analyses by previous treatment with IMiD
16.2.6.1.2.16.3 QLQ-C30 - Time to first improvement by 10 pt in fatigue according to previous treatment with IMiD (LOCF) - ITT population

	Yes		No		
	Kd (N=62)	**IKd (N=81)**	**Kd (N=61)**	**IKd (N=98)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	37 (59.7)	50 (61.7)	37 (60.7)	59 (60.2)	0.7991
Number (%) of patients censored	25 (40.3)	31 (38.3)	24 (39.3)	39 (39.8)	
Kaplan-Meier estimates of Fatigue in months					
25% quantile (95% CI)	1.84 (1.051 to 2.070)	1.97 (1.051 to 2.957)	1.07 (0.986 to 1.906)	1.08 (1.018 to 1.906)	
Median (95% CI)	3.81 (2.070 to 15.113)	4.67 (3.023 to 12.386)	4.63 (1.906 to 17.643)	2.99 (2.004 to 8.805)	
75% quantile (95% CI)	NC (15.113 to NC)	NC (15.639 to NC)	NC (17.643 to NC)	NC (NC to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.9521		0.7962	
Hazard ratio (95% CI) vs Kd	-	0.99 (0.65 to 1.51)		1.06 (0.70 to 1.59)	
P-value	-	0.9520		0.7974	
Improvement probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful improvement change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Fatigue
16.2.6.1.2.16 Efficacy response data - Subgroup analyses by previous treatment with IMiD
16.2.6.1.2.16.4 QLQ-C30 - Time to first deterioration by 10 pt in fatigue according to previous treatment with IMiD (LOCF) - ITT population

	Yes		No		
	Kd (N=62)	**IKd (N=81)**	**Kd (N=61)**	**IKd (N=98)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	41 (66.1)	56 (69.1)	40 (65.6)	70 (71.4)	0.5707
Number (%) of patients censored	21 (33.9)	25 (30.9)	21 (34.4)	28 (28.6)	
Kaplan-Meier estimates of Fatigue in months					
25% quantile (95% CI)	1.12 (1.051 to 2.825)	1.15 (1.084 to 1.906)	1.58 (1.051 to 2.037)	1.12 (1.018 to 1.906)	
Median (95% CI)	4.90 (2.825 to 8.312)	3.78 (2.366 to 5.749)	4.70 (2.037 to 9.922)	3.06 (1.971 to 4.731)	
75% quantile (95% CI)	NC (8.312 to NC)	NC (6.998 to NC)	NC (12.320 to NC)	19.25 (7.655 to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.7510		0.2504	
Hazard ratio (95% CI) vs Kd	-	1.07 (0.71 to 1.60)		1.26 (0.85 to 1.85)	
P-value	-	0.7520		0.2514	
Deterioration probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful deterioration change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Fatigue
16.2.6.1.2.16 Efficacy response data - Subgroup analyses by previous treatment with IMiD
16.2.6.1.2.16.5 QLQ-C30 - Time until permanent improvement by 10 pt in fatigue according to previous treatment with IMiD (LOCF) - ITT population

	Yes		No		
	Kd (N=62)	**IKd (N=81)**	**Kd (N=61)**	**IKd (N=98)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	19 (30.6)	21 (25.9)	15 (24.6)	28 (28.6)	0.3341
Number (%) of patients censored	43 (69.4)	60 (74.1)	46 (75.4)	70 (71.4)	
Kaplan-Meier estimates of Fatigue in months					
25% quantile (95% CI)	14.32 (5.618 to NC)	17.51 (12.945 to NC)	19.75 (11.598 to NC)	14.95 (8.476 to 24.444)	
Median (95% CI)	NC (22.209 to NC)	NC (NC to NC)	NC (21.684 to NC)	24.44 (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	24.44 (NC to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.4838		0.5638	
Hazard ratio (95% CI) vs Kd	-	0.80 (0.43 to 1.49)		1.20 (0.64 to 2.26)	
P-value	-	0.4847		0.5643	
Improvement probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful improvement change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Fatigue
16.2.6.1.2.16 Efficacy response data - Subgroup analyses by previous treatment with IMiD
16.2.6.1.2.16.6 QLQ-C30 - Time until permanent deterioration by 10 pt in fatigue according to previous treatment with IMiD (LOCF) - ITT population

	Yes		No		
	Kd (N=62)	**IKd (N=81)**	**Kd (N=61)**	**IKd (N=98)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	28 (45.2)	27 (33.3)	19 (31.1)	42 (42.9)	0.0438
Number (%) of patients censored	34 (54.8)	54 (66.7)	42 (68.9)	56 (57.1)	
Kaplan-Meier estimates of Fatigue in months					
25% quantile (95% CI)	7.39 (2.957 to 16.690)	12.32 (8.246 to 19.877)	16.89 (6.111 to 21.388)	12.02 (4.665 to 15.507)	
Median (95% CI)	21.55 (16.690 to NC)	NC (20.501 to NC)	NC (20.567 to NC)	20.93 (18.464 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (23.524 to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.1542		0.1461	
Hazard ratio (95% CI) vs Kd	-	0.68 (0.40 to 1.16)		1.49 (0.87 to 2.56)	
P-value	-	0.1567		0.1489	
Deterioration probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful deterioration change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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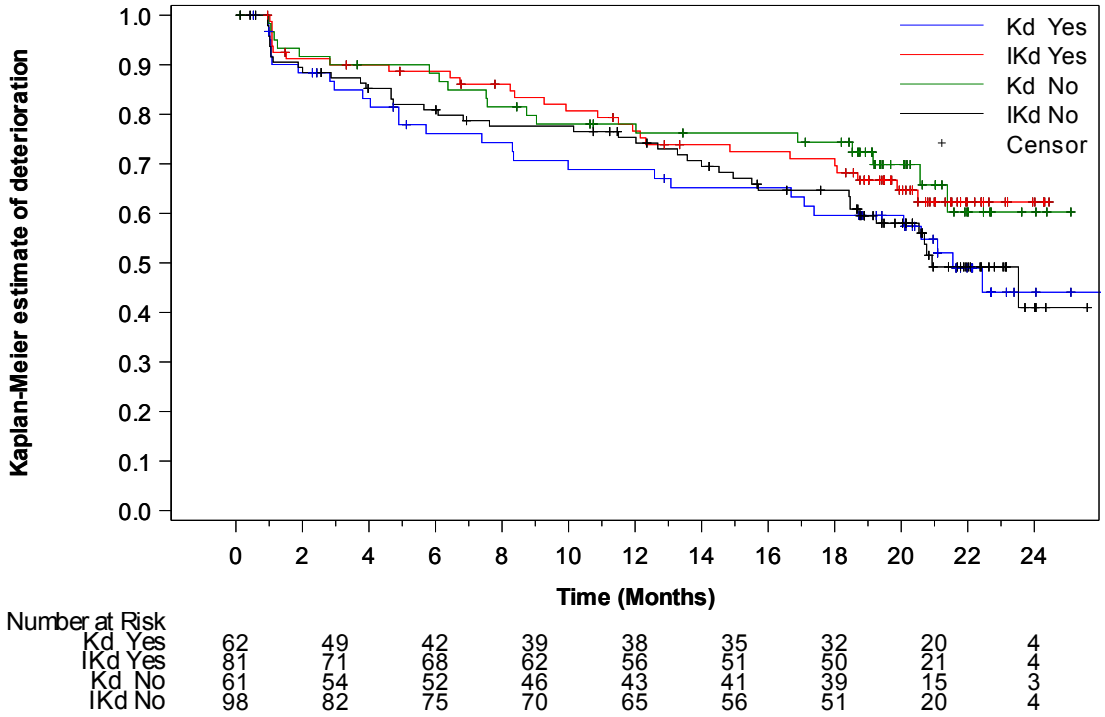
16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Fatigue
16.2.6.1.2.16 Efficacy response data - Subgroup analyses by previous treatment with IMiD
16.2.6.1.2.16.7 QLQ-C30 - Time until permanent deterioration by 10 pt in fatigue according to previous treatment with IMiD- Kaplan-Meier curve (LOCF) - ITT population



A lower score represents a better level of quality of life. Clinical meaningful deterioration change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
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16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Fatigue
16.2.6.1.2.17 Efficacy response data - Subgroup analyses by previous treatment with PI and IMiD
16.2.6.1.2.17.3 QLQ-C30 - Time to first improvement by 10 pt in fatigue according to previous treatment with PI and IMiD (LOCF) - ITT population

	Yes		No		
	Kd (N=17)	**IKd (N=23)**	**Kd (N=106)**	**IKd (N=156)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	10 (58.8)	14 (60.9)	64 (60.4)	95 (60.9)	0.7836
Number (%) of patients censored	7 (41.2)	9 (39.1)	42 (39.6)	61 (39.1)	
Kaplan-Meier estimates of Fatigue in months					
25% quantile (95% CI)	1.46 (0.986 to 2.957)	1.41 (0.986 to 3.285)	1.12 (1.051 to 1.938)	1.15 (1.051 to 1.971)	
Median (95% CI)	2.96 (1.051 to NC)	3.42 (1.906 to NC)	4.63 (2.891 to 15.113)	3.75 (2.891 to 8.969)	
75% quantile (95% CI)	NC (2.957 to NC)	NC (3.778 to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.8299		0.7940	
Hazard ratio (95% CI) vs Kd	-	0.91 (0.41 to 2.06)		1.04 (0.76 to 1.43)	
P-value	-	0.8299		0.7948	
Improvement probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful improvement change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Fatigue
16.2.6.1.2.17 Efficacy response data - Subgroup analyses by previous treatment with PI and IMiD
16.2.6.1.2.17.4 QLQ-C30 - Time to first deterioration by 10 pt in fatigue according to previous treatment with PI and IMiD (LOCF) - ITT population

	Yes		No		
	Kd (N=17)	**IKd (N=23)**	**Kd (N=106)**	**IKd (N=156)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	9 (52.9)	14 (60.9)	72 (67.9)	112 (71.8)	0.9226
Number (%) of patients censored	8 (47.1)	9 (39.1)	34 (32.1)	44 (28.2)	
Kaplan-Meier estimates of Fatigue in months					
25% quantile (95% CI)	2.83 (0.986 to 8.312)	2.83 (0.986 to 4.402)	1.12 (1.051 to 1.938)	1.12 (1.051 to 1.216)	
Median (95% CI)	8.31 (2.825 to NC)	5.62 (3.220 to NC)	4.04 (2.793 to 6.702)	2.96 (2.004 to 4.632)	
75% quantile (95% CI)	NC (8.312 to NC)	NC (5.618 to NC)	NC (12.320 to NC)	19.25 (8.345 to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.6116		0.3433	
Hazard ratio (95% CI) vs Kd	-	1.24 (0.54 to 2.88)		1.15 (0.86 to 1.55)	
P-value	-	0.6123		0.3438	
Deterioration probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful deterioration change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Fatigue
16.2.6.1.2.17 Efficacy response data - Subgroup analyses by previous treatment with PI and IMiD
16.2.6.1.2.17.5 QLQ-C30 - Time until permanent improvement by 10 pt in fatigue according to previous treatment with PI and IMiD (LOCF) - ITT population

	Yes		No		
	Kd (N=17)	**IKd (N=23)**	**Kd (N=106)**	**IKd (N=156)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	5 (29.4)	6 (26.1)	29 (27.4)	43 (27.6)	0.8164
Number (%) of patients censored	12 (70.6)	17 (73.9)	77 (72.6)	113 (72.4)	
Kaplan-Meier estimates of Fatigue in months					
25% quantile (95% CI)	10.45 (1.018 to NC)	17.02 (1.413 to NC)	19.35 (13.240 to 22.209)	17.05 (12.715 to NC)	
Median (95% CI)	NC (10.448 to NC)	NC (17.018 to NC)	NC (22.209 to NC)	24.44 (24.444 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (24.444 to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.7039		0.9266	
Hazard ratio (95% CI) vs Kd	-	0.79 (0.24 to 2.61)		1.02 (0.64 to 1.64)	
P-value	-	0.7045		0.9268	
Improvement probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful improvement change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Fatigue
16.2.6.1.2.17 Efficacy response data - Subgroup analyses by previous treatment with PI and IMiD
16.2.6.1.2.17.6 QLQ-C30 - Time until permanent deterioration by 10 pt in fatigue according to previous treatment with PI and IMiD (LOCF) - ITT population

	Yes		No		
	Kd (N=17)	**IKd (N=23)**	**Kd (N=106)**	**IKd (N=156)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	5 (29.4)	7 (30.4)	42 (39.6)	62 (39.7)	0.9851
Number (%) of patients censored	12 (70.6)	16 (69.6)	64 (60.4)	94 (60.3)	
Kaplan-Meier estimates of Fatigue in months					
25% quantile (95% CI)	12.58 (1.873 to NC)	18.69 (1.511 to NC)	8.74 (4.895 to 17.380)	12.02 (6.735 to 14.949)	
Median (95% CI)	NC (12.583 to NC)	NC (18.694 to NC)	22.44 (20.567 to NC)	23.52 (20.534 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.9956		0.9447	
Hazard ratio (95% CI) vs Kd	-	1.00 (0.32 to 3.14)		1.01 (0.69 to 1.50)	
P-value	-	0.9956		0.9448	
Deterioration probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful deterioration change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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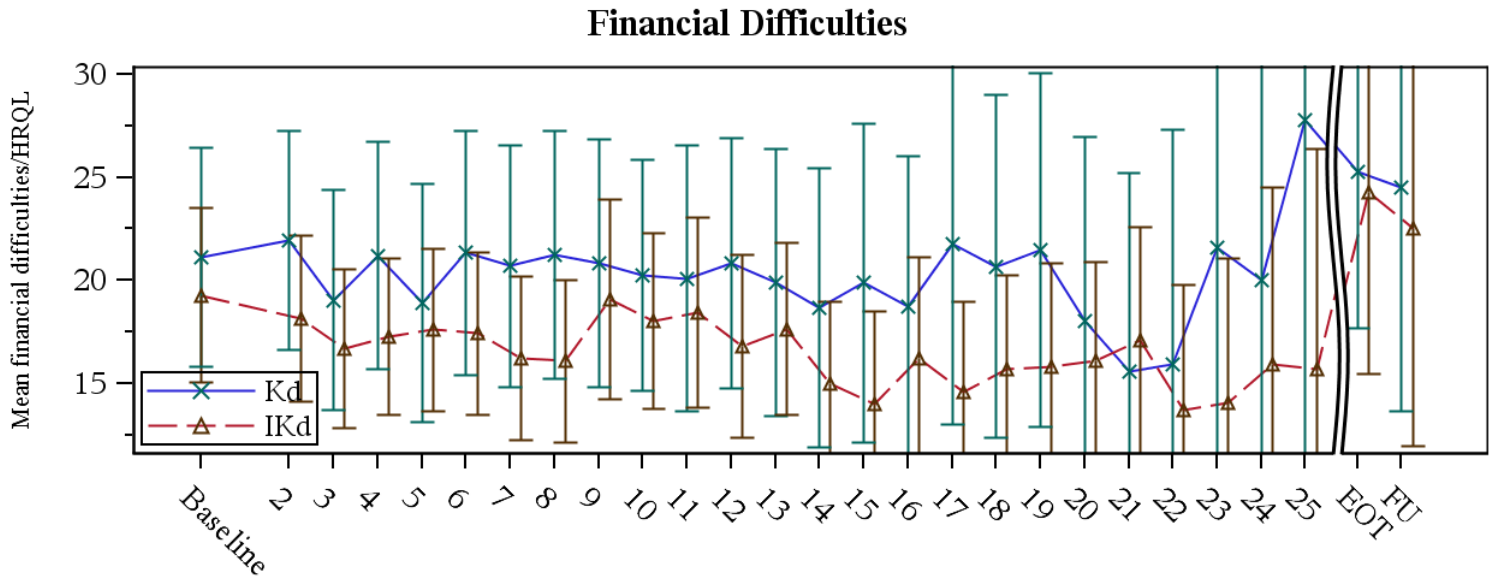
16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Financial difficulties
16.2.6.1.2.1 Efficacy response data
16.2.6.1.2.1.1 QLQ-C30 - Mean and 95% CI for financial difficulties score over time (LOCF) - ITT population



#patients																									
Kd	112	114	112	110	104	100	95	91	88	84	78	72	67	66	62	57	52	50	45	37	30	23	17	10	6	62	34
IKd	166	169	168	164	161	155	150	145	138	133	130	127	121	118	112	109	105	102	97	91	78	56	38	23	17	59	34

A lower score represents a better level of quality of life. Cycles with less than 20 patients overall are not presented.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
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16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Financial difficulties
16.2.6.1.2.1 Efficacy response data
16.2.6.1.2.1.15 QLQ-C30 - Time to first improvement by 15 pt in Financial difficulties (LOCF) - ITT population

First improvement 15 points Financial difficulties (%)	**Kd (N=123)**	**IKd (N=179)**
Number (%) of events	36 (29.3)	51 (28.5)
Number (%) of patients censored	87 (70.7)	128 (71.5)
Kaplan-Meier estimates of Financial difficulties in months		
25% quantile (95% CI)	3.98 (1.873 to NC)	3.71 (2.004 to NC)
Median (95% CI)	NC (NC to NC)	NC (NC to NC)
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)
Comparison vs. Kd		
Stratified[a] Log-Rank test p-value[b] vs Kd	-	0.8341
Stratified[a] Hazard ratio (95% CI) vs Kd	-	0.96 (0.62 to 1.46)
P-value	-	0.8334
Improvement probability (95% CI)[c]		
3 Months	0.233 (0.162 to 0.312)	0.235 (0.175 to 0.300)
6 Months	0.268 (0.192 to 0.350)	0.282 (0.217 to 0.350)

A lower score represents a better level of quality of life. Clinical meaningful improvement change from baseline less than or equal to -15 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] Stratified on number of prior lines of therapy (1 vs. >1) and Revised International Staging System (R-ISS) stage (I or II vs. III vs. not classified) according to IRT
[b] One-sided significance level is 0.025
[c] Estimated using the Kaplan-Meier method
NA/NC = Not Applicable / Not Calculable
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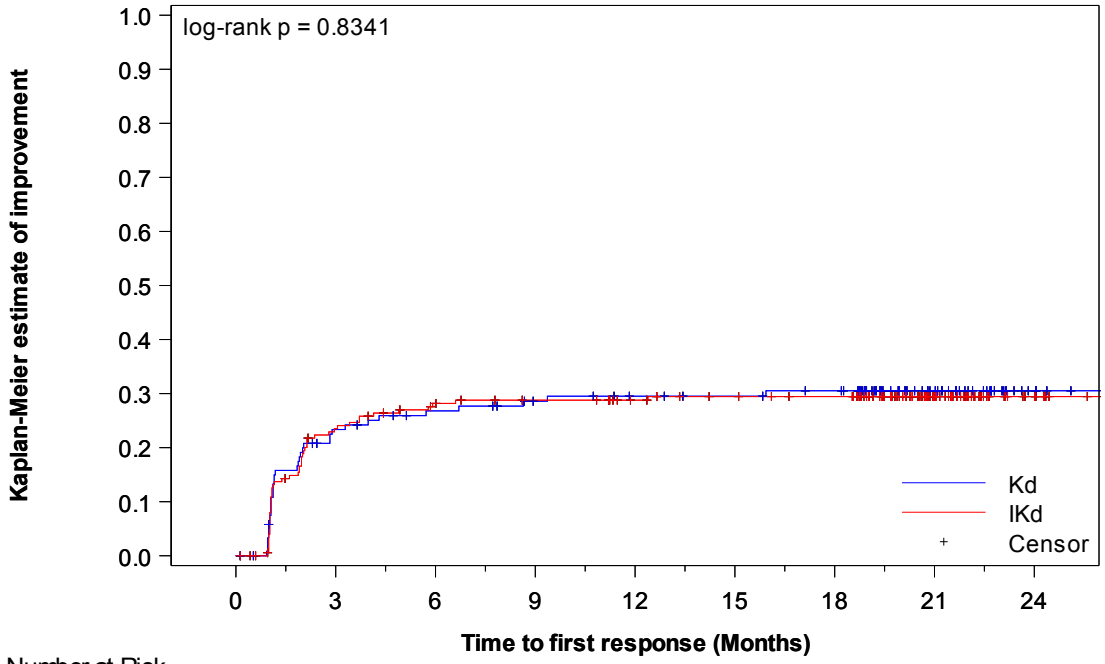
16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Financial difficulties
16.2.6.1.2.1 Efficacy response data
16.2.6.1.2.1.16 QLQ-C30 - Time to first improvement by 15 pt in Financial difficulties - Kaplan-Meier curve (LOCF) - ITT population



Number at Risk

Kd	123	90	83	77	73	71	68	35	5
IKd	179	132	120	115	109	103	100	46	9

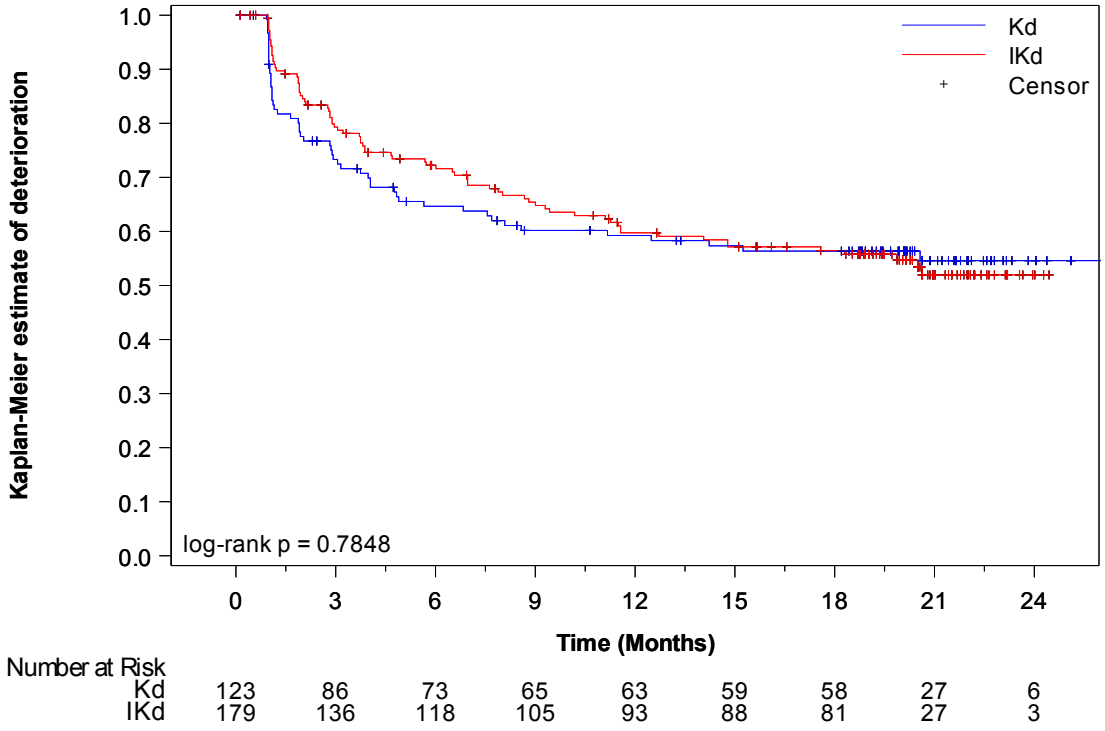
A lower score represents a better level of quality of life. Clinical meaningful improvement change from baseline less than or equal to -15 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
PGM=DEVOPS/SAR650984/EFC15246/CIR_RWE/REPORT/PGM/eff_qlq_km_i_f.sas OUT=REPORT/OUTPUT/eff_km_c30_fin_imp15l_de_i_f_x.rtf (07APR2021 14:24)

16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Financial difficulties
16.2.6.1.2.1 Efficacy response data
16.2.6.1.2.1.17 QLQ-C30 - Time to first deterioration by 15 pt in Financial difficulties (LOCF) - ITT population

First deterioration 15 points Financial difficulties (%)	**Kd (N=123)**	**IKd (N=179)**
Number (%) of events	52 (42.3)	77 (43.0)
Number (%) of patients censored	71 (57.7)	102 (57.0)
Kaplan-Meier estimates of Financial difficulties in months		
25% quantile (95% CI)	2.89 (1.150 to 4.764)	3.88 (2.825 to 6.965)
Median (95% CI)	NC (11.170 to NC)	NC (14.784 to NC)
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)
Comparison vs. Kd		
Stratified[a] Log-Rank test p-value[b] vs Kd	-	0.7848
Stratified[a] Hazard ratio (95% CI) vs Kd	-	0.95 (0.67 to 1.36)
P-value	-	0.7837
Deterioration probability (95% CI)[c]		
3 Months	0.733 (0.644 to 0.803)	0.793 (0.725 to 0.846)
6 Months	0.647 (0.553 to 0.725)	0.722 (0.649 to 0.783)

A lower score represents a better level of quality of life. Clinical meaningful deterioration change from baseline greater than or equal to 15 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] Stratified on number of prior lines of therapy (1 vs. >1) and Revised International Staging System (R-ISS) stage (I or II vs. III vs. not classified) according to IRT
[b] One-sided significance level is 0.025
[c] Estimated using the Kaplan-Meier method
NA/NC = Not Applicable / Not Calculable
PGM=DEVOPS/SAR650984/EFC15246/CIR_RWE/REPORT/PGM/eff_km_invhr_sr_i_t.sas OUT=REPORT/OUTPUT/eff_km_c30_fin_det15l_de_i_t_x.rtf (07APR2021 14:23)

16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Financial difficulties
16.2.6.1.2.1 Efficacy response data
16.2.6.1.2.1.18 QLQ-C30 - Time to first deterioration by 15 pt in Financial difficulties - Kaplan-Meier curve (LOCF) - ITT population



A lower score represents a better level of quality of life. Clinical meaningful deterioration change from baseline greater than or equal to 15 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
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16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Financial difficulties
16.2.6.1.2.1 Efficacy response data
16.2.6.1.2.1.19 QLQ-C30 - Time until permanent improvement by 15 pt in Financial difficulties (LOCF) - ITT population

First permanent improvement 15 points Financial difficulties (%)	**Kd (N=123)**	**IKd (N=179)**
Number (%) of events	19 (15.4)	26 (14.5)
Number (%) of patients censored	104 (84.6)	153 (85.5)
Kaplan-Meier estimates of Financial difficulties in months		
25% quantile (95% CI)	24.34 (21.224 to NC)	NC (22.111 to NC)
Median (95% CI)	NC (24.345 to NC)	NC (NC to NC)
75% quantile (95% CI)	NC (24.345 to NC)	NC (NC to NC)
Comparison vs. Kd		
Stratified[a] Log-Rank test p-value[b] vs Kd	-	0.8795
Stratified[a] Hazard ratio (95% CI) vs Kd	-	0.96 (0.53 to 1.73)
P-value	-	0.8790
Improvement probability (95% CI)[c]		
3 Months	0.083 (0.043 to 0.141)	0.080 (0.046 to 0.126)
6 Months	0.092 (0.049 to 0.152)	0.104 (0.064 to 0.154)

A lower score represents a better level of quality of life. Clinical meaningful improvement change from baseline less than or equal to -15 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] Stratified on number of prior lines of therapy (1 vs. >1) and Revised International Staging System (R-ISS) stage (I or II vs. III vs. not classified) according to IRT
[b] One-sided significance level is 0.025
[c] Estimated using the Kaplan-Meier method
NA/NC = Not Applicable / Not Calculable
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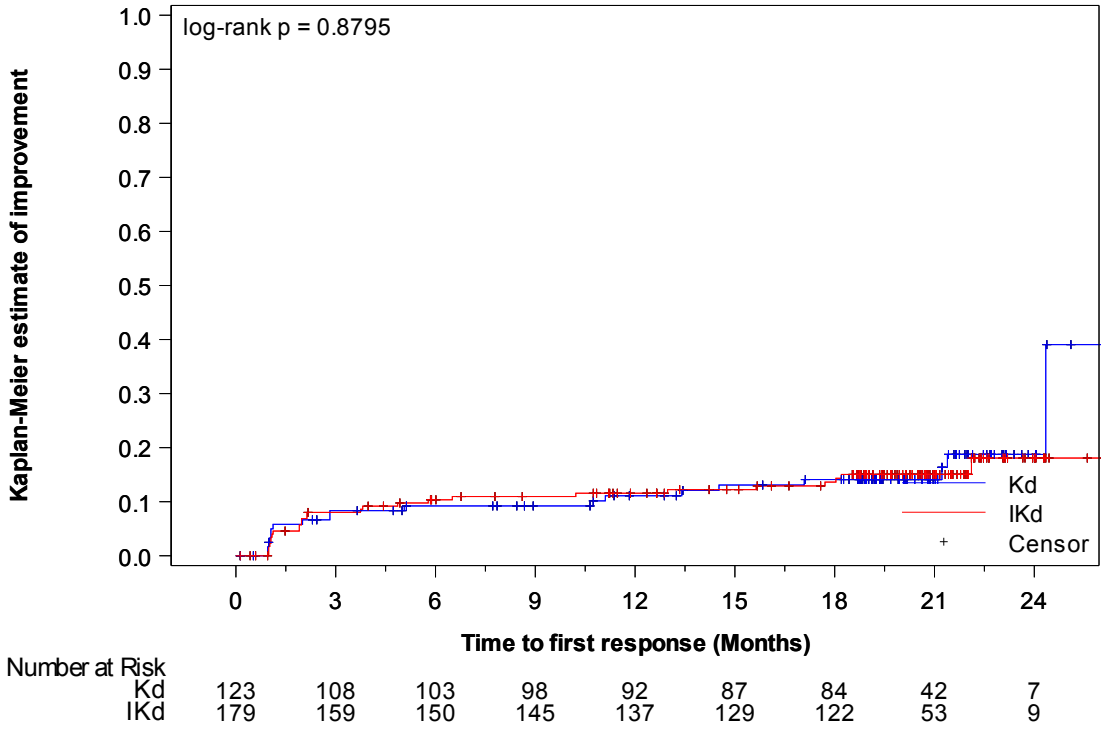
16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Financial difficulties
16.2.6.1.2.1 Efficacy response data
16.2.6.1.2.1.20 QLQ-C30 - Time until permanent improvement by 15 pt in Financial difficulties - Kaplan-Meier curve (LOCF) - ITT population



A lower score represents a better level of quality of life. Clinical meaningful improvement change from baseline less than or equal to -15 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.

16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Financial difficulties
16.2.6.1.2.1 Efficacy response data
16.2.6.1.2.1.21 QLQ-C30 - Time until permanent deterioration by 15 pt in Financial difficulties (LOCF) - ITT population

First permanent deterioration 15 points Financial difficulties (%)	**Kd (N=123)**	**IKd (N=179)**
Number (%) of events	21 (17.1)	26 (14.5)
Number (%) of patients censored	102 (82.9)	153 (85.5)
Kaplan-Meier estimates of Financial difficulties in months		
25% quantile (95% CI)	NC (18.168 to NC)	NC (NC to NC)
Median (95% CI)	NC (NC to NC)	NC (NC to NC)
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)
Comparison vs. Kd		
Stratified[a] Log-Rank test p-value[b] vs Kd	-	0.5322
Stratified[a] Hazard ratio (95% CI) vs Kd	-	0.83 (0.47 to 1.48)
P-value	-	0.5328
Deterioration probability (95% CI)[c]		
3 Months	0.942 (0.882 to 0.972)	0.966 (0.925 to 0.984)
6 Months	0.908 (0.839 to 0.948)	0.948 (0.902 to 0.973)

A lower score represents a better level of quality of life. Clinical meaningful deterioration change from baseline greater than or equal to 15 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] Stratified on number of prior lines of therapy (1 vs. >1) and Revised International Staging System (R-ISS) stage (I or II vs. III vs. not classified) according to IRT
[b] One-sided significance level is 0.025
[c] Estimated using the Kaplan-Meier method
NA/NC = Not Applicable / Not Calculable
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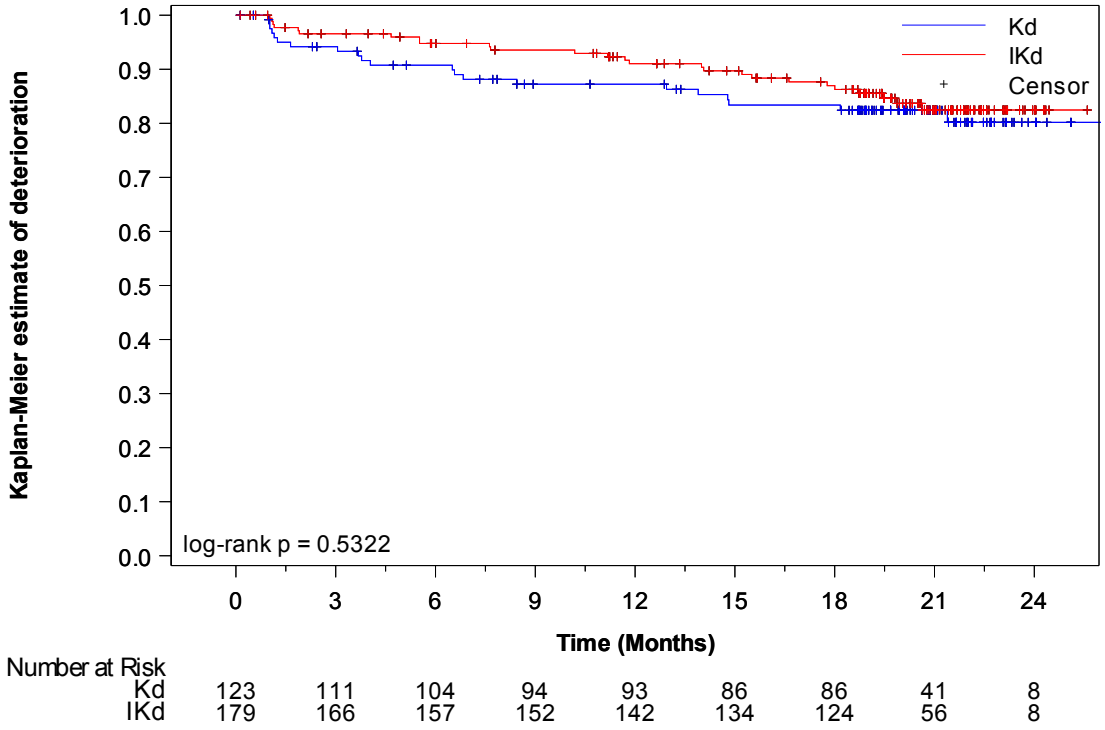
16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Financial difficulties
16.2.6.1.2.1 Efficacy response data
16.2.6.1.2.1.22 QLQ-C30 - Time until permanent deterioration by 15 pt in Financial difficulties - Kaplan-Meier curve (LOCF) - ITT population



A lower score represents a better level of quality of life. Clinical meaningful deterioration change from baseline greater than or equal to 15 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
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16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Financial difficulties
16.2.6.1.2.2 Efficacy response data - Subgroup analyses by age
16.2.6.1.2.2.3 QLQ-C30 - Time to first improvement by 10 pt in financial difficulties according to age (LOCF) - ITT population

	<65 years		>=65 years		
	Kd (N=66)	**IKd (N=88)**	**Kd (N=57)**	**IKd (N=91)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	26 (39.4)	29 (33.0)	10 (17.5)	22 (24.2)	0.2026
Number (%) of patients censored	40 (60.6)	59 (67.0)	47 (82.5)	69 (75.8)	
Kaplan-Meier estimates of Financial difficulties in months					
25% quantile (95% CI)	1.94 (1.051 to 6.702)	2.37 (1.380 to NC)	NC (2.037 to NC)	12.39 (1.971 to NC)	
Median (95% CI)	NC (8.641 to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.3971		0.3419	
Hazard ratio (95% CI) vs Kd	-	0.80 (0.47 to 1.35)		1.43 (0.68 to 3.03)	
P-value	-	0.3982		0.3445	
Improvement probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful improvement change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Financial difficulties
16.2.6.1.2.2 Efficacy response data - Subgroup analyses by age
16.2.6.1.2.2.4 QLQ-C30 - Time to first deterioration by 10 pt in financial difficulties according to age (LOCF) - ITT population

	<65 years		>=65 years		
	Kd (N=66)	**IKd (N=88)**	**Kd (N=57)**	**IKd (N=91)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	26 (39.4)	34 (38.6)	26 (45.6)	43 (47.3)	0.7700
Number (%) of patients censored	40 (60.6)	54 (61.4)	31 (54.4)	48 (52.7)	
Kaplan-Meier estimates of Financial difficulties in months					
25% quantile (95% CI)	2.89 (1.051 to 7.556)	4.67 (2.825 to 11.499)	2.83 (1.150 to 4.830)	3.22 (1.906 to 6.965)	
Median (95% CI)	NC (7.688 to NC)	NC (18.300 to NC)	20.57 (4.830 to NC)	19.88 (8.674 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.6720		0.9989	
Hazard ratio (95% CI) vs Kd	-	0.90 (0.54 to 1.49)		1.00 (0.61 to 1.63)	
P-value	-	0.6721		1.0000	
Deterioration probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful deterioration change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Financial difficulties
16.2.6.1.2.2 Efficacy response data - Subgroup analyses by age
16.2.6.1.2.2.5 QLQ-C30 - Time until permanent improvement by 10 pt in financial difficulties according to age (LOCF) - ITT population

	<65 years		>=65 years		
	Kd (N=66)	**IKd (N=88)**	**Kd (N=57)**	**IKd (N=91)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	15 (22.7)	15 (17.0)	4 (7.0)	11 (12.1)	0.1778
Number (%) of patients censored	51 (77.3)	73 (83.0)	53 (93.0)	80 (87.9)	
Kaplan-Meier estimates of Financial difficulties in months					
25% quantile (95% CI)	21.22 (2.825 to NC)	NC (12.977 to NC)	24.34 (24.345 to NC)	NC (22.111 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (24.345 to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (24.345 to NC)	NC (NC to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.3742		0.2738	
Hazard ratio (95% CI) vs Kd	-	0.72 (0.35 to 1.48)		1.88 (0.60 to 5.91)	
P-value	-	0.3763		0.2816	
Improvement probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful improvement change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Financial difficulties
16.2.6.1.2.2 Efficacy response data - Subgroup analyses by age
16.2.6.1.2.2.6 QLQ-C30 - Time until permanent deterioration by 10 pt in financial difficulties according to age (LOCF) - ITT population

	<65 years		>=65 years		
	Kd (N=66)	**IKd (N=88)**	**Kd (N=57)**	**IKd (N=91)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	11 (16.7)	12 (13.6)	10 (17.5)	14 (15.4)	0.8973
Number (%) of patients censored	55 (83.3)	76 (86.4)	47 (82.5)	77 (84.6)	
Kaplan-Meier estimates of Financial difficulties in months					
25% quantile (95% CI)	NC (12.945 to NC)	NC (19.483 to NC)	NC (6.571 to NC)	NC (19.877 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.5656		0.6951	
Hazard ratio (95% CI) vs Kd	-	0.79 (0.35 to 1.78)		0.85 (0.38 to 1.91)	
P-value	-	0.5665		0.6954	
Deterioration probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful deterioration change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Financial difficulties
16.2.6.1.2.3 Efficacy response data - Subgroup analyses by gender
16.2.6.1.2.3.3 QLQ-C30 - Time to first improvement by 10 pt in financial difficulties according to gender (LOCF) - ITT population

	Male		Female		
	Kd (N=68)	**IKd (N=101)**	**Kd (N=55)**	**IKd (N=78)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	19 (27.9)	27 (26.7)	17 (30.9)	24 (30.8)	0.9802
Number (%) of patients censored	49 (72.1)	74 (73.3)	38 (69.1)	54 (69.2)	
Kaplan-Meier estimates of Financial difficulties in months					
25% quantile (95% CI)	5.72 (1.183 to NC)	5.91 (1.873 to NC)	2.83 (1.051 to NC)	2.79 (1.906 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.8878		0.9170	
Hazard ratio (95% CI) vs Kd	-	0.96 (0.53 to 1.72)		0.97 (0.52 to 1.80)	
P-value	-	0.8874		0.9167	
Improvement probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful improvement change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Financial difficulties
16.2.6.1.2.3 Efficacy response data - Subgroup analyses by gender
16.2.6.1.2.3.4 QLQ-C30 - Time to first deterioration by 10 pt in financial difficulties according to gender (LOCF) - ITT population

	Male		Female		
	Kd (N=68)	**IKd (N=101)**	**Kd (N=55)**	**IKd (N=78)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	29 (42.6)	38 (37.6)	23 (41.8)	39 (50.0)	0.2724
Number (%) of patients censored	39 (57.4)	63 (62.4)	32 (58.2)	39 (50.0)	
Kaplan-Meier estimates of Financial difficulties in months					
25% quantile (95% CI)	3.06 (1.117 to 4.895)	6.97 (2.825 to 11.565)	1.91 (0.986 to 11.170)	3.22 (1.906 to 6.012)	
Median (95% CI)	NC (5.651 to NC)	NC (17.577 to NC)	NC (11.170 to NC)	18.30 (6.965 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.3467		0.5256	
Hazard ratio (95% CI) vs Kd	-	0.79 (0.49 to 1.29)		1.18 (0.71 to 1.98)	
P-value	-	0.3478		0.5261	
Deterioration probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful deterioration change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Financial difficulties
16.2.6.1.2.3 Efficacy response data - Subgroup analyses by gender
16.2.6.1.2.3.5 QLQ-C30 - Time until permanent improvement by 10 pt in financial difficulties according to gender (LOCF) - ITT population

	Male		Female		
	Kd (N=68)	**IKd (N=101)**	**Kd (N=55)**	**IKd (N=78)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	9 (13.2)	12 (11.9)	10 (18.2)	14 (17.9)	0.9134
Number (%) of patients censored	59 (86.8)	89 (88.1)	45 (81.8)	64 (82.1)	
Kaplan-Meier estimates of Financial difficulties in months					
25% quantile (95% CI)	24.34 (24.345 to NC)	NC (22.111 to NC)	21.39 (13.405 to NC)	NC (17.708 to NC)	
Median (95% CI)	24.34 (24.345 to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (24.345 to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.8707		0.9423	
Hazard ratio (95% CI) vs Kd	-	0.93 (0.39 to 2.21)		0.97 (0.43 to 2.18)	
P-value	-	0.8699		0.9422	
Improvement probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful improvement change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Financial difficulties
16.2.6.1.2.3 Efficacy response data - Subgroup analyses by gender
16.2.6.1.2.3.6 QLQ-C30 - Time until permanent deterioration by 10 pt in financial difficulties according to gender (LOCF) - ITT population

	Male		Female		
	Kd (N=68)	**IKd (N=101)**	**Kd (N=55)**	**IKd (N=78)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	11 (16.2)	13 (12.9)	10 (18.2)	13 (16.7)	0.8561
Number (%) of patients censored	57 (83.8)	88 (87.1)	45 (81.8)	65 (83.3)	
Kaplan-Meier estimates of Financial difficulties in months					
25% quantile (95% CI)	NC (14.817 to NC)	NC (20.632 to NC)	NC (8.444 to NC)	NC (17.774 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.5515		0.7366	
Hazard ratio (95% CI) vs Kd	-	0.78 (0.35 to 1.75)		0.87 (0.38 to 1.98)	
P-value	-	0.5525		0.7368	
Deterioration probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful deterioration change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
PGM=DEVOPS/SAR650984/EFC15246/CIR_RWE/REPORT/PGM/eff_km_subgp_sr_sig_de_i_t.sas OUT=REPORT/OUTPUT/eff_km_c30_fin_detpl_sex_de_i_t_x.rtf (07APR2021 14:38)

16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Financial difficulties
16.2.6.1.2.4 Efficacy response data - Subgroup analyses by ethnic origin
16.2.6.1.2.4.3 QLQ-C30 - Time to first improvement by 10 pt in financial difficulties according to ethnic origin (LOCF) - ITT population

	White		Other		
	Kd (N=83)	**IKd (N=131)**	**Kd (N=28)**	**IKd (N=34)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	22 (26.5)	42 (32.1)	13 (46.4)	8 (23.5)	0.0764
Number (%) of patients censored	61 (73.5)	89 (67.9)	15 (53.6)	26 (76.5)	
Kaplan-Meier estimates of Financial difficulties in months					
25% quantile (95% CI)	8.64 (1.840 to NC)	2.96 (1.906 to 12.386)	1.87 (1.117 to 5.717)	NC (1.018 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (2.037 to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.4515		0.1000	
Hazard ratio (95% CI) vs Kd	-	1.22 (0.73 to 2.04)		0.48 (0.20 to 1.17)	
P-value	-	0.4523		0.1074	
Improvement probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful improvement change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
PGM=DEVOPS/SAR650984/EFC15246/CIR_RWE/REPORT/PGM/eff_km_subgp_sr_sig_de_i_t.sas OUT=REPORT/OUTPUT/eff_km_c30_fin_impl_race_de_i_t_x.rtf (07APR2021 14:38)

16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Financial difficulties
16.2.6.1.2.4 Efficacy response data - Subgroup analyses by ethnic origin
16.2.6.1.2.4.4 QLQ-C30 - Time to first deterioration by 10 pt in financial difficulties according to ethnic origin (LOCF) - ITT population

	White		Other		
	Kd (N=83)	**IKd (N=131)**	**Kd (N=28)**	**IKd (N=34)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	40 (48.2)	57 (43.5)	10 (35.7)	17 (50.0)	0.1755
Number (%) of patients censored	43 (51.8)	74 (56.5)	18 (64.3)	17 (50.0)	
Kaplan-Meier estimates of Financial difficulties in months					
25% quantile (95% CI)	1.94 (1.051 to 4.041)	3.88 (2.793 to 6.965)	3.15 (1.018 to NC)	2.89 (1.018 to 9.429)	
Median (95% CI)	NC (4.895 to NC)	NC (11.565 to NC)	NC (6.834 to NC)	14.06 (3.877 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.3295		0.3065	
Hazard ratio (95% CI) vs Kd	-	0.82 (0.55 to 1.23)		1.50 (0.69 to 3.28)	
P-value	-	0.3303		0.3098	
Deterioration probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful deterioration change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Financial difficulties
16.2.6.1.2.4 Efficacy response data - Subgroup analyses by ethnic origin
16.2.6.1.2.4.5 QLQ-C30 - Time until permanent improvement by 10 pt in financial difficulties according to ethnic origin (LOCF) - ITT population

	White		Other		
	Kd (N=83)	**IKd (N=131)**	**Kd (N=28)**	**IKd (N=34)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	12 (14.5)	20 (15.3)	6 (21.4)	5 (14.7)	0.5979
Number (%) of patients censored	71 (85.5)	111 (84.7)	22 (78.6)	29 (85.3)	
Kaplan-Meier estimates of Financial difficulties in months					
25% quantile (95% CI)	NC (21.388 to NC)	NC (22.111 to NC)	24.34 (1.117 to NC)	NC (1.971 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	24.34 (24.345 to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (24.345 to NC)	NC (NC to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.8787		0.6263	
Hazard ratio (95% CI) vs Kd	-	1.06 (0.52 to 2.16)		0.74 (0.23 to 2.46)	
P-value	-	0.8795		0.6275	
Improvement probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful improvement change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Financial difficulties
16.2.6.1.2.4 Efficacy response data - Subgroup analyses by ethnic origin
16.2.6.1.2.4.6 QLQ-C30 - Time until permanent deterioration by 10 pt in financial difficulties according to ethnic origin (LOCF) - ITT population

	White		Other		
	Kd (N=83)	**IKd (N=131)**	**Kd (N=28)**	**IKd (N=34)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	17 (20.5)	18 (13.7)	4 (14.3)	8 (23.5)	0.1657
Number (%) of patients censored	66 (79.5)	113 (86.3)	24 (85.7)	26 (76.5)	
Kaplan-Meier estimates of Financial difficulties in months					
25% quantile (95% CI)	NC (12.945 to NC)	NC (20.632 to NC)	NC (1.084 to NC)	18.73 (5.520 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.1863		0.4009	
Hazard ratio (95% CI) vs Kd	-	0.64 (0.33 to 1.25)		1.66 (0.50 to 5.53)	
P-value	-	0.1899		0.4060	
Deterioration probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful deterioration change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Financial difficulties
16.2.6.1.2.5 Efficacy response data - Subgroup analyses by geographical region
16.2.6.1.2.5.3 QLQ-C30 - Time to first improvement by 10 pt in financial difficulties according to geographical region (LOCF) - ITT population

	Europe		America		Asia		Other countries		
	Kd (N=60)	**IKd (N=85)**	**Kd (N=20)**	**IKd (N=24)**	**Kd (N=21)**	**IKd (N=25)**	**Kd (N=22)**	**IKd (N=45)**	**p-value of treatment-by-subgroup interaction[c]**
Number (%) of events	14 (23.3)	21 (24.7)	6 (30.0)	6 (25.0)	11 (52.4)	6 (24.0)	5 (22.7)	18 (40.0)	0.2168
Number (%) of patients censored	46 (76.7)	64 (75.3)	14 (70.0)	18 (75.0)	10 (47.6)	19 (76.0)	17 (77.3)	27 (60.0)	
Kaplan-Meier estimates of event in months									
25% quantile (95% CI)	NC (1.051 to NC)	5.78 (2.004 to NC)	6.47 (1.840 to NC)	4.14 (1.051 to NC)	1.15 (1.051 to 5.717)	NC (0.986 to NC)	NC (0.953 to NC)	2.14 (1.018 to 6.604)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (4.304 to NC)	NC (4.140 to NC)	6.70 (1.150 to NC)	NC (NC to NC)	NC (NC to NC)	NC (5.914 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (9.363 to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Kd									

A lower score represents a better level of quality of life. Clinical meaningful improvement change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Financial difficulties
16.2.6.1.2.5 Efficacy response data - Subgroup analyses by geographical region
16.2.6.1.2.5.3 QLQ-C30 - Time to first improvement by 10 pt in financial difficulties according to geographical region (LOCF) - ITT population

	Europe		America		Asia		Other countries		
	Kd (N=60)	**IKd (N=85)**	**Kd (N=20)**	**IKd (N=24)**	**Kd (N=21)**	**IKd (N=25)**	**Kd (N=22)**	**IKd (N=45)**	**p-value of treatment-by-subgroup interaction[c]**
Log-Rank test p-value[a] vs Kd	-	0.9611		0.9729		0.0790		0.2163	
Hazard ratio (95% CI) vs Kd	-	1.02 (0.52 to 2.00)		0.98 (0.32 to 3.04)		0.42 (0.15 to 1.14)		1.85 (0.69 to 4.99)	
P-value	-	0.9611		0.9729		0.0884		0.2236	
Improvement probability (95% CI)[b]									
3 Months	0.206 (0.114 to 0.317)	0.205 (0.126 to 0.297)	0.200 (0.062 to 0.393)	0.222 (0.081 to 0.407)	0.350 (0.157 to 0.552)	0.250 (0.102 to 0.431)	0.227 (0.083 to 0.414)	0.289 (0.166 to 0.424)	
6 Months	0.224 (0.127 to 0.337)	0.255 (0.167 to 0.352)	0.250 (0.091 to 0.449)	0.268 (0.109 to 0.457)	0.458 (0.235 to 0.657)	0.250 (0.102 to 0.431)	0.227 (0.083 to 0.414)	0.356 (0.220 to 0.493)	

A lower score represents a better level of quality of life. Clinical meaningful improvement change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Financial difficulties
16.2.6.1.2.5 Efficacy response data - Subgroup analyses by geographical region
16.2.6.1.2.5.4 QLQ-C30 - Time to first deterioration by 10 pt in financial difficulties according to geographical region (LOCF) - ITT population

	Europe		America		Asia		Other countries		
	Kd (N=60)	**IKd (N=85)**	**Kd (N=20)**	**IKd (N=24)**	**Kd (N=21)**	**IKd (N=25)**	**Kd (N=22)**	**IKd (N=45)**	**p-value of treatment-by-subgroup interaction[c]**
Number (%) of events	21 (35.0)	38 (44.7)	14 (70.0)	8 (33.3)	6 (28.6)	13 (52.0)	11 (50.0)	18 (40.0)	0.0171
Number (%) of patients censored	39 (65.0)	47 (55.3)	6 (30.0)	16 (66.7)	15 (71.4)	12 (48.0)	11 (50.0)	27 (60.0)	
Kaplan-Meier estimates of event in months									
25% quantile (95% CI)	3.98 (1.643 to 15.244)	3.22 (1.938 to 6.965)	1.03 (0.920 to 2.858)	8.67 (1.051 to NC)	7.56 (1.018 to NC)	3.42 (1.018 to 9.429)	3.06 (0.953 to 12.485)	7.62 (1.084 to 17.577)	
Median (95% CI)	NC (15.244 to NC)	20.50 (9.298 to NC)	3.04 (1.018 to NC)	NC (8.674 to NC)	NC (7.556 to NC)	14.06 (3.877 to NC)	14.23 (3.055 to NC)	NC (11.269 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (3.154 to NC)	NC (NC to NC)	NC (NC to NC)	NC (14.784 to NC)	NC (NC to NC)	NC (NC to NC)	

A lower score represents a better level of quality of life. Clinical meaningful deterioration change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Financial difficulties
16.2.6.1.2.5 Efficacy response data - Subgroup analyses by geographical region
16.2.6.1.2.5.4 QLQ-C30 - Time to first deterioration by 10 pt in financial difficulties according to geographical region (LOCF) - ITT population

	Europe		America		Asia		Other countries		
	Kd (N=60)	**IKd (N=85)**	**Kd (N=20)**	**IKd (N=24)**	**Kd (N=21)**	**IKd (N=25)**	**Kd (N=22)**	**IKd (N=45)**	**p-value of treatment-by-subgroup interaction[c]**
Comparison vs. Kd									
Log-Rank test p-value[a] vs Kd	-	0.3412		0.0101		0.1718		0.4048	
Hazard ratio (95% CI) vs Kd	-	1.29 (0.76 to 2.21)		0.33 (0.14 to 0.80)		1.94 (0.74 to 5.14)		0.73 (0.34 to 1.54)	
P-value	-	0.3425		0.0141		0.1796		0.4067	
Deterioration probability (95% CI)[b]									
3 Months	0.776 (0.646 to 0.864)	0.770 (0.663 to 0.846)	0.500 (0.271 to 0.692)	0.822 (0.592 to 0.929)	0.800 (0.551 to 0.920)	0.750 (0.526 to 0.879)	0.773 (0.537 to 0.898)	0.844 (0.701 to 0.923)	
6 Months	0.722 (0.587 to 0.820)	0.681 (0.568 to 0.771)	0.350 (0.157 to 0.552)	0.776 (0.543 to 0.900)	0.800 (0.551 to 0.920)	0.667 (0.443 to 0.817)	0.591 (0.361 to 0.762)	0.799 (0.649 to 0.890)	

A lower score represents a better level of quality of life. Clinical meaningful deterioration change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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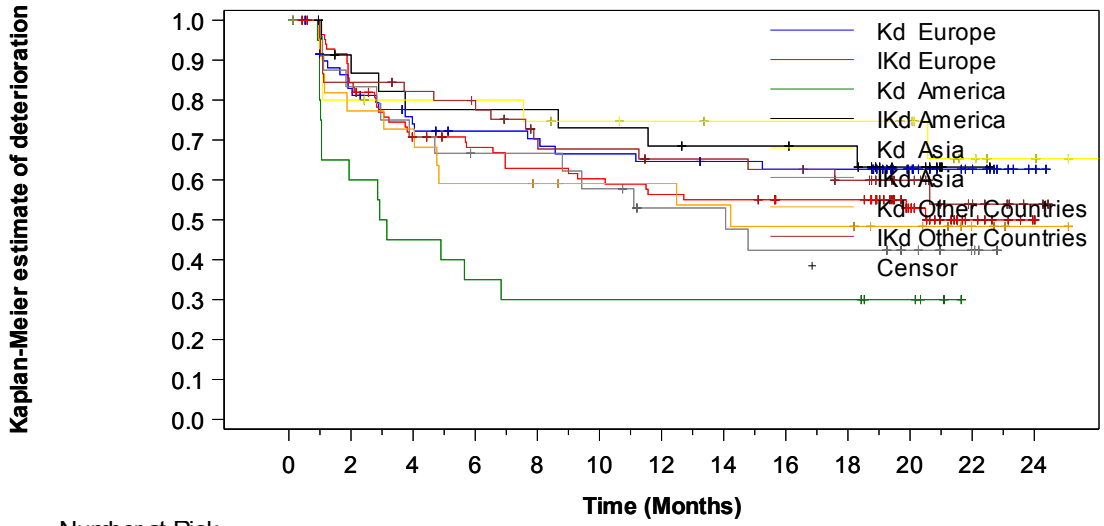
16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Financial difficulties
16.2.6.1.2.5 Efficacy response data - Subgroup analyses by geographical region
16.2.6.1.2.5.5 QLQ-C30 - Time to first deterioration by 10 pt in financial difficulties according to geographical region - Kaplan-Meier curve (LOCF) - ITT population



Number at Risk									
Kd Europe	60	44	38	35	34	33	32	12	2
IKd Europe	85	62	52	48	43	42	39	13	1
Kd America	20	10	7	6	6	6	6	2	0
IKd America	24	18	17	16	15	14	13	2	0
Kd Asia	21	15	15	13	12	11	11	7	3
IKd Asia	25	18	15	14	10	8	8	4	0
Kd Other Countries	22	17	13	11	11	9	9	6	1
IKd Other Countries	45	38	34	27	25	24	21	8	2

A lower score represents a better level of quality of life. Clinical meaningful deterioration change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
PGM=DEVOPS/SAR650984/EFC15246/CIR_RWE/REPORT/PGM/eff_qlq_km_subgp_de_i_f.sas OUT=REPORT/OUTPUT/eff_km_c30_fin_detl_greg_de_i_f_x.rtf (07APR2021 14:33)

16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Financial difficulties
16.2.6.1.2.5 Efficacy response data - Subgroup analyses by geographical region
16.2.6.1.2.5.6 QLQ-C30 - Time until permanent improvement by 10 pt in financial difficulties according to geographical region (LOCF) - ITT population

	Europe		America		Asia		Other countries		
	Kd (N=60)	**IKd (N=85)**	**Kd (N=20)**	**IKd (N=24)**	**Kd (N=21)**	**IKd (N=25)**	**Kd (N=22)**	**IKd (N=45)**	**p-value of treatment-by-subgroup interaction[c]**
Number (%) of events	9 (15.0)	11 (12.9)	3 (15.0)	4 (16.7)	5 (23.8)	4 (16.0)	2 (9.1)	7 (15.6)	0.7662
Number (%) of patients censored	51 (85.0)	74 (87.1)	17 (85.0)	20 (83.3)	16 (76.2)	21 (84.0)	20 (90.9)	38 (84.4)	
Kaplan-Meier estimates of event in months									
25% quantile (95% CI)	NC (17.084 to NC)	NC (NC to NC)	21.39 (2.825 to NC)	NC (1.051 to NC)	24.34 (1.051 to NC)	NC (0.986 to NC)	NC (0.953 to NC)	22.11 (3.745 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	21.39 (21.388 to NC)	NC (NC to NC)	24.34 (24.345 to NC)	NC (NC to NC)	NC (NC to NC)	NC (22.111 to NC)	

A lower score represents a better level of quality of life. Clinical meaningful improvement change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Financial difficulties
16.2.6.1.2.5 Efficacy response data - Subgroup analyses by geographical region
16.2.6.1.2.5.6 QLQ-C30 - Time until permanent improvement by 10 pt in financial difficulties according to geographical region (LOCF) - ITT population

	Europe		America		Asia		Other countries		
	Kd (N=60)	**IKd (N=85)**	**Kd (N=20)**	**IKd (N=24)**	**Kd (N=21)**	**IKd (N=25)**	**Kd (N=22)**	**IKd (N=45)**	**p-value of treatment-by-subgroup interaction[c]**
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (21.388 to NC)	NC (NC to NC)	NC (24.345 to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Kd									
Log-Rank test p-value[a] vs Kd	-	0.6806		0.7152		0.6109		0.4256	
Hazard ratio (95% CI) vs Kd	-	0.83 (0.34 to 2.01)		1.32 (0.30 to 5.90)		0.71 (0.19 to 2.67)		1.88 (0.39 to 9.14)	
P-value	-	0.6811		0.7161		0.6126		0.4330	
Improvement probability (95% CI)[b]									

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The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Financial difficulties
16.2.6.1.2.5 Efficacy response data - Subgroup analyses by geographical region
16.2.6.1.2.5.7 QLQ-C30 - Time until permanent deterioration by 10 pt in financial difficulties according to geographical region (LOCF) - ITT population

	Europe		America		Asia		Other countries		
	Kd (N=60)	**IKd (N=85)**	**Kd (N=20)**	**IKd (N=24)**	**Kd (N=21)**	**IKd (N=25)**	**Kd (N=22)**	**IKd (N=45)**	**p-value of treatment-by-subgroup interaction[c]**
Number (%) of events	7 (11.7)	9 (10.6)	7 (35.0)	4 (16.7)	2 (9.5)	5 (20.0)	5 (22.7)	8 (17.8)	0.5747
Number (%) of patients censored	53 (88.3)	76 (89.4)	13 (65.0)	20 (83.3)	19 (90.5)	20 (80.0)	17 (77.3)	37 (82.2)	
Kaplan-Meier estimates of event in months									
25% quantile (95% CI)	NC (21.388 to NC)	NC (NC to NC)	12.94 (1.018 to NC)	NC (5.520 to NC)	NC (1.018 to NC)	NC (1.117 to NC)	NC (0.986 to NC)	NC (10.185 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (12.945 to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	

A lower score represents a better level of quality of life. Clinical meaningful deterioration change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Financial difficulties
16.2.6.1.2.5 Efficacy response data - Subgroup analyses by geographical region
16.2.6.1.2.5.7 QLQ-C30 - Time until permanent deterioration by 10 pt in financial difficulties according to geographical region (LOCF) - ITT population

	Europe		America		Asia		Other countries		
	Kd (N=60)	**IKd (N=85)**	**Kd (N=20)**	**IKd (N=24)**	**Kd (N=21)**	**IKd (N=25)**	**Kd (N=22)**	**IKd (N=45)**	**p-value of treatment-by-subgroup interaction[c]**
Comparison vs. Kd									
Log-Rank test p-value[a] vs Kd	-	0.7889		0.2192		0.4192		0.6363	
Hazard ratio (95% CI) vs Kd	-	0.87 (0.33 to 2.35)		0.47 (0.14 to 1.61)		1.94 (0.38 to 10.01)		0.76 (0.25 to 2.34)	
P-value	-	0.7891		0.2300		0.4276		0.6373	
Deterioration probability (95% CI)[b]									
3 Months	0.966 (0.869 to 0.991)	0.964 (0.892 to 0.988)	0.950 (0.695 to 0.993)	1.000 (1.000 to 1.000)	0.900 (0.656 to 0.974)	0.958 (0.739 to 0.994)	0.909 (0.683 to 0.976)	0.956 (0.834 to 0.989)	

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CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Financial difficulties
16.2.6.1.2.6 Efficacy response data - Subgroup analyses by regulatory region
16.2.6.1.2.6.3 QLQ-C30 - Time to first improvement by 10 pt in financial difficulties according to regulatory region (LOCF) - ITT population

	Western countries		Other countries		
	Kd (N=55)	**IKd (N=97)**	**Kd (N=68)**	**IKd (N=82)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	11 (20.0)	26 (26.8)	25 (36.8)	25 (30.5)	0.3538
Number (%) of patients censored	44 (80.0)	71 (73.2)	43 (63.2)	57 (69.5)	
Kaplan-Meier estimates of Financial difficulties in months					
25% quantile (95% CI)	NC (1.051 to NC)	5.91 (2.037 to NC)	2.83 (1.150 to 8.641)	2.14 (1.084 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (9.363 to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.4556		0.5769	
Hazard ratio (95% CI) vs Kd	-	1.31 (0.65 to 2.65)		0.85 (0.49 to 1.49)	
P-value	-	0.4570		0.5773	
Improvement probability (95% CI)[b]					

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CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Financial difficulties
16.2.6.1.2.6 Efficacy response data - Subgroup analyses by regulatory region
16.2.6.1.2.6.4 QLQ-C30 - Time to first deterioration by 10 pt in financial difficulties according to regulatory region (LOCF) - ITT population

	Western countries		Other countries		
	Kd (N=55)	**IKd (N=97)**	**Kd (N=68)**	**IKd (N=82)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	17 (30.9)	30 (30.9)	35 (51.5)	47 (57.3)	0.6320
Number (%) of patients censored	38 (69.1)	67 (69.1)	33 (48.5)	35 (42.7)	
Kaplan-Meier estimates of Financial difficulties in months					
25% quantile (95% CI)	8.57 (1.084 to NC)	9.30 (3.745 to 20.632)	1.87 (1.051 to 3.154)	2.79 (1.873 to 3.877)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	12.48 (3.745 to NC)	10.18 (4.698 to 14.784)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.8321		0.6576	
Hazard ratio (95% CI) vs Kd	-	0.94 (0.52 to 1.70)		1.10 (0.71 to 1.71)	
P-value	-	0.8321		0.6578	
Deterioration probability (95% CI)[b]					

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CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Financial difficulties
16.2.6.1.2.6 Efficacy response data - Subgroup analyses by regulatory region
16.2.6.1.2.6.5 QLQ-C30 - Time until permanent improvement by 10 pt in financial difficulties according to regulatory region (LOCF) - ITT population

	Western countries		Other countries		
	Kd (N=55)	**IKd (N=97)**	**Kd (N=68)**	**IKd (N=82)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	7 (12.7)	13 (13.4)	12 (17.6)	13 (15.9)	0.7659
Number (%) of patients censored	48 (87.3)	84 (86.6)	56 (82.4)	69 (84.1)	
Kaplan-Meier estimates of Financial difficulties in months					
25% quantile (95% CI)	NC (21.224 to NC)	NC (NC to NC)	24.34 (11.105 to NC)	NC (18.037 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (24.345 to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (24.345 to NC)	NC (NC to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.9048		0.7759	
Hazard ratio (95% CI) vs Kd	-	1.06 (0.42 to 2.65)		0.89 (0.41 to 1.96)	
P-value	-	0.9056		0.7760	
Improvement probability (95% CI)[b]					

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CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Financial difficulties
16.2.6.1.2.6 Efficacy response data - Subgroup analyses by regulatory region
16.2.6.1.2.6.6 QLQ-C30 - Time until permanent deterioration by 10 pt in financial difficulties according to regulatory region (LOCF) - ITT population

	Western countries		Other countries		
	Kd (N=55)	**IKd (N=97)**	**Kd (N=68)**	**IKd (N=82)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	4 (7.3)	11 (11.3)	17 (25.0)	15 (18.3)	0.2455
Number (%) of patients censored	51 (92.7)	86 (88.7)	51 (75.0)	67 (81.7)	
Kaplan-Meier estimates of Financial difficulties in months					
25% quantile (95% CI)	NC (NC to NC)	NC (20.632 to NC)	21.39 (4.041 to NC)	NC (15.211 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.4381		0.3144	
Hazard ratio (95% CI) vs Kd	-	1.57 (0.50 to 4.92)		0.70 (0.35 to 1.40)	
P-value	-	0.4421		0.3170	
Deterioration probability (95% CI)[b]					

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CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Financial difficulties
16.2.6.1.2.7 Efficacy response data - Subgroup analyses by baseline ECOG PS
16.2.6.1.2.7.3 QLQ-C30 - Time to first improvement by 10 pt in financial difficulties according to baseline ECOG PS (LOCF) - ITT population

	0 or 1		>1		
	Kd (N=118)	**IKd (N=168)**	**Kd (N=5)**	**IKd (N=11)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	36 (30.5)	47 (28.0)	0 (0.0)	4 (36.4)	0.9788
Number (%) of patients censored	82 (69.5)	121 (72.0)	5 (100.0)	7 (63.6)	
Kaplan-Meier estimates of Financial difficulties in months					
25% quantile (95% CI)	3.29 (1.840 to NC)	4.14 (2.070 to NC)	NC (NC to NC)	1.91 (1.018 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (1.018 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (1.971 to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.5931		0.0992	
Hazard ratio (95% CI) vs Kd	-	0.89 (0.58 to 1.37)			
P-value	-	0.5933		0.9969	
Improvement probability (95% CI)[b]					

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The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Financial difficulties
16.2.6.1.2.7 Efficacy response data - Subgroup analyses by baseline ECOG PS
16.2.6.1.2.7.4 QLQ-C30 - Time to first deterioration by 10 pt in financial difficulties according to baseline ECOG PS (LOCF) - ITT population

	0 or 1		>1		
	Kd (N=118)	**IKd (N=168)**	**Kd (N=5)**	**IKd (N=11)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	50 (42.4)	74 (44.0)	2 (40.0)	3 (27.3)	0.5507
Number (%) of patients censored	68 (57.6)	94 (56.0)	3 (60.0)	8 (72.7)	
Kaplan-Meier estimates of Financial difficulties in months					
25% quantile (95% CI)	2.89 (1.248 to 4.830)	3.88 (2.825 to 7.622)	0.99 (0.986 to NC)	6.97 (1.216 to NC)	
Median (95% CI)	NC (11.170 to NC)	NC (14.062 to NC)	NC (0.986 to NC)	NC (1.216 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (0.986 to NC)	NC (NC to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.9099		0.5920	
Hazard ratio (95% CI) vs Kd	-	0.98 (0.68 to 1.40)		0.61 (0.10 to 3.73)	
P-value	-	0.9097		0.5953	
Deterioration probability (95% CI)[b]					

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The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Financial difficulties
16.2.6.1.2.7 Efficacy response data - Subgroup analyses by baseline ECOG PS
16.2.6.1.2.7.5 QLQ-C30 - Time until permanent improvement by 10 pt in financial difficulties according to baseline ECOG PS (LOCF) - ITT population

	0 or 1		>1		
	Kd (N=118)	**IKd (N=168)**	**Kd (N=5)**	**IKd (N=11)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	19 (16.1)	22 (13.1)	0 (0.0)	4 (36.4)	0.9889
Number (%) of patients censored	99 (83.9)	146 (86.9)	5 (100.0)	7 (63.6)	
Kaplan-Meier estimates of Financial difficulties in months					
25% quantile (95% CI)	24.34 (21.224 to NC)	NC (22.111 to NC)	NC (NC to NC)	1.97 (1.018 to NC)	
Median (95% CI)	NC (24.345 to NC)	NC (NC to NC)	NC (NC to NC)	NC (1.018 to NC)	
75% quantile (95% CI)	NC (24.345 to NC)	NC (NC to NC)	NC (NC to NC)	NC (15.639 to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.4971		0.1308	
Hazard ratio (95% CI) vs Kd	-	0.81 (0.44 to 1.49)			
P-value	-	0.4979		0.9970	
Improvement probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful improvement change from baseline less than or equal to -10 pt.
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CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Financial difficulties
16.2.6.1.2.7 Efficacy response data - Subgroup analyses by baseline ECOG PS
16.2.6.1.2.7.6 QLQ-C30 - Time until permanent deterioration by 10 pt in financial difficulties according to baseline ECOG PS (LOCF) - ITT population

	0 or 1		>1		
	Kd (N=118)	**IKd (N=168)**	**Kd (N=5)**	**IKd (N=11)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	20 (16.9)	26 (15.5)	1 (20.0)	0 (0.0)	0.9868
Number (%) of patients censored	98 (83.1)	142 (84.5)	4 (80.0)	11 (100.0)	
Kaplan-Meier estimates of Financial difficulties in months					
25% quantile (95% CI)	NC (18.168 to NC)	NC (20.632 to NC)	NC (3.778 to NC)	NC (NC to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (3.778 to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (3.778 to NC)	NC (NC to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.6843		0.1797	
Hazard ratio (95% CI) vs Kd	-	0.89 (0.49 to 1.59)			
P-value	-	0.6845		0.9985	
Deterioration probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful deterioration change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
PGM=DEVOPS/SAR650984/EFC15246/CIR_RWE/REPORT/PGM/eff_km_subgp_sr_sig_de_i_t.sas OUT=REPORT/OUTPUT/eff_km_c30_fin_detpl_ecog_de_i_t_x.rtf (07APR2021 14:38)

16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Financial difficulties
16.2.6.1.2.8 Efficacy response data - Subgroup analyses by ISS staging at SE
16.2.6.1.2.8.3 QLQ-C30 - Time to first improvement by 10 pt in financial difficulties according to ISS staging at SE (LOCF) - ITT population

	I		II		III		
	Kd (N=71)	**IKd (N=89)**	**Kd (N=31)**	**IKd (N=63)**	**Kd (N=20)**	**IKd (N=26)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	20 (28.2)	21 (23.6)	10 (32.3)	20 (31.7)	6 (30.0)	10 (38.5)	0.6529
Number (%) of patients censored	51 (71.8)	68 (76.4)	21 (67.7)	43 (68.3)	14 (70.0)	16 (61.5)	
Kaplan-Meier estimates of Financial difficulties in months							
25% quantile (95% CI)	5.72 (1.840 to NC)	NC (2.004 to NC)	3.98 (1.051 to NC)	2.37 (1.084 to NC)	2.89 (0.953 to NC)	2.14 (0.986 to 6.604)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (15.934 to NC)	NC (NC to NC)	NC (2.891 to NC)	NC (3.055 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Kd							
Log-Rank test p-value[a] vs Kd	-	0.4941		0.9440		0.5065	
Hazard ratio (95% CI) vs Kd	-	0.81 (0.44 to 1.49)		0.97 (0.46 to 2.08)		1.41 (0.51 to 3.87)	
P-value	-	0.4950		0.9438		0.5085	

A lower score represents a better level of quality of life. Clinical meaningful improvement change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
PGM=DEVOPS/SAR650984/EFC15246/CIR_RWE/REPORT/PGM/eff_km_subgp_sr_sig_de_i_t.sas OUT=REPORT/OUTPUT/eff_km_c30_fin_impl_seiss_de_i_t_x.rtf (07APR2021 14:38)

16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Financial difficulties
16.2.6.1.2.8 Efficacy response data - Subgroup analyses by ISS staging at SE
16.2.6.1.2.8.4 QLQ-C30 - Time to first deterioration by 10 pt in financial difficulties according to ISS staging at SE (LOCF) - ITT population

	I		II		III		
	Kd (N=71)	**IKd (N=89)**	**Kd (N=31)**	**IKd (N=63)**	**Kd (N=20)**	**IKd (N=26)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	30 (42.3)	43 (48.3)	11 (35.5)	27 (42.9)	10 (50.0)	7 (26.9)	0.2165
Number (%) of patients censored	41 (57.7)	46 (51.7)	20 (64.5)	36 (57.1)	10 (50.0)	19 (73.1)	
Kaplan-Meier estimates of Financial difficulties in months							
25% quantile (95% CI)	3.06 (1.084 to 6.834)	3.78 (2.103 to 7.622)	3.15 (1.248 to NC)	4.70 (1.906 to 11.565)	1.05 (0.953 to 4.041)	6.57 (0.953 to NC)	
Median (95% CI)	NC (11.170 to NC)	20.50 (9.429 to NC)	NC (8.575 to NC)	NC (14.062 to NC)	7.56 (1.051 to NC)	NC (6.571 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (7.556 to NC)	NC (NC to NC)	
Comparison vs. Kd							
Log-Rank test p-value[a] vs Kd	-	0.6543		0.6507		0.1110	
Hazard ratio (95% CI) vs Kd	-	1.11 (0.70 to 1.77)		1.18 (0.58 to 2.37)		0.46 (0.18 to 1.22)	
P-value	-	0.6544		0.6511		0.1198	

A lower score represents a better level of quality of life. Clinical meaningful deterioration change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
PGM=DEVOPS/SAR650984/EFC15246/CIR_RWE/REPORT/PGM/eff_km_subgp_sr_sig_de_i_t.sas OUT=REPORT/OUTPUT/eff_km_c30_fin_detl_seiss_de_i_t_x.rtf (07APR2021 14:38)

16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Financial difficulties
16.2.6.1.2.8 Efficacy response data - Subgroup analyses by ISS staging at SE
16.2.6.1.2.8.5 QLQ-C30 - Time until permanent improvement by 10 pt in financial difficulties according to ISS staging at SE (LOCF) - ITT population

	I		II		III		
	Kd (N=71)	**IKd (N=89)**	**Kd (N=31)**	**IKd (N=63)**	**Kd (N=20)**	**IKd (N=26)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	10 (14.1)	9 (10.1)	5 (16.1)	11 (17.5)	4 (20.0)	6 (23.1)	0.7396
Number (%) of patients censored	61 (85.9)	80 (89.9)	26 (83.9)	52 (82.5)	16 (80.0)	20 (76.9)	
Kaplan-Meier estimates of Financial difficulties in months							
25% quantile (95% CI)	24.34 (21.224 to NC)	NC (NC to NC)	NC (1.051 to NC)	NC (12.977 to NC)	13.40 (0.953 to NC)	4.86 (0.986 to NC)	
Median (95% CI)	NC (24.345 to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (13.405 to NC)	NC (4.862 to NC)	
75% quantile (95% CI)	NC (24.345 to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Kd							
Log-Rank test p-value[a] vs Kd	-	0.5208		0.9209		0.7069	
Hazard ratio (95% CI) vs Kd	-	0.75 (0.30 to 1.84)		1.06 (0.37 to 3.04)		1.27 (0.36 to 4.52)	
P-value	-	0.5223		0.9209		0.7076	

A lower score represents a better level of quality of life. Clinical meaningful improvement change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
PGM=DEVOPS/SAR650984/EFC15246/CIR_RWE/REPORT/PGM/eff_km_subgp_sr_sig_de_i_t.sas OUT=REPORT/OUTPUT/eff_km_c30_fin_imppl_seiss_de_i_t_x.rtf (07APR2021 14:39)

16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Financial difficulties
16.2.6.1.2.8 Efficacy response data - Subgroup analyses by ISS staging at SE
16.2.6.1.2.8.6 QLQ-C30 - Time until permanent deterioration by 10 pt in financial difficulties according to ISS staging at SE (LOCF) - ITT population

	I		II		III		
	Kd (N=71)	**IKd (N=89)**	**Kd (N=31)**	**IKd (N=63)**	**Kd (N=20)**	**IKd (N=26)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	13 (18.3)	15 (16.9)	3 (9.7)	10 (15.9)	4 (20.0)	1 (3.8)	0.2784
Number (%) of patients censored	58 (81.7)	74 (83.1)	28 (90.3)	53 (84.1)	16 (80.0)	25 (96.2)	
Kaplan-Meier estimates of Financial difficulties in months							
25% quantile (95% CI)	NC (13.897 to NC)	NC (16.624 to NC)	NC (3.778 to NC)	NC (18.727 to NC)	14.82 (1.018 to NC)	NC (11.170 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (14.817 to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Kd							
Log-Rank test p-value[a] vs Kd	-	0.8519		0.5313		0.0884	
Hazard ratio (95% CI) vs Kd	-	0.93 (0.44 to 1.96)		1.51 (0.41 to 5.47)		0.18 (0.02 to 1.64)	
P-value	-	0.8514		0.5344		0.1295	

A lower score represents a better level of quality of life. Clinical meaningful deterioration change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Financial difficulties
16.2.6.1.2.9 Efficacy response data - Subgroup analyses by R-ISS stage at SE
16.2.6.1.2.9.3 QLQ-C30 - Time to first improvement by 10 pt in financial difficulties according to R-ISS stage at SE (LOCF) - ITT population

	I or II		III		Not classified		
	Kd (N=103)	**IKd (N=155)**	**Kd (N=8)**	**IKd (N=16)**	**Kd (N=12)**	**IKd (N=8)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	28 (27.2)	43 (27.7)	5 (62.5)	5 (31.3)	3 (25.0)	3 (37.5)	0.2136
Number (%) of patients censored	75 (72.8)	112 (72.3)	3 (37.5)	11 (68.8)	9 (75.0)	5 (62.5)	
Kaplan-Meier estimates of Financial difficulties in months							
25% quantile (95% CI)	6.70 (1.873 to NC)	3.71 (1.971 to NC)	1.12 (0.953 to 2.891)	4.14 (1.018 to NC)	NC (0.953 to NC)	1.08 (1.018 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	2.89 (0.953 to NC)	NC (3.055 to NC)	NC (1.117 to NC)	NC (1.018 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	9.36 (1.906 to NC)	NC (NC to NC)	NC (NC to NC)	NC (1.084 to NC)	
Comparison vs. Kd							
Log-Rank test p-value[a] vs Kd	-	0.9954		0.1050		0.3299	
Hazard ratio (95% CI) vs Kd	-	1.00 (0.62 to 1.61)		0.37 (0.11 to 1.29)		2.18 (0.44 to 10.85)	
P-value	-	0.9954		0.1190		0.3418	

A lower score represents a better level of quality of life. Clinical meaningful improvement change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
PGM=DEVOPS/SAR650984/EFC15246/CIR_RWE/REPORT/PGM/eff_km_subgp_sr_sig_de_i_t.sas OUT=REPORT/OUTPUT/eff_km_c30_fin_impl_seriss_de_i_t_x.rtf (07APR2021 14:38)

16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Financial difficulties
16.2.6.1.2.9 Efficacy response data - Subgroup analyses by R-ISS stage at SE
16.2.6.1.2.9.4 QLQ-C30 - Time to first deterioration by 10 pt in financial difficulties according to R-ISS stage at SE (LOCF) - ITT population

	I or II		III		Not classified		
	Kd (N=103)	**IKd (N=155)**	**Kd (N=8)**	**IKd (N=16)**	**Kd (N=12)**	**IKd (N=8)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	41 (39.8)	72 (46.5)	3 (37.5)	3 (18.8)	8 (66.7)	2 (25.0)	0.2445
Number (%) of patients censored	62 (60.2)	83 (53.5)	5 (62.5)	13 (81.3)	4 (33.3)	6 (75.0)	
Kaplan-Meier estimates of Financial difficulties in months							
25% quantile (95% CI)	2.92 (1.248 to 6.834)	3.81 (2.760 to 6.965)	4.04 (1.084 to NC)	NC (1.084 to NC)	1.12 (0.953 to 3.745)	11.50 (6.965 to NC)	
Median (95% CI)	NC (14.226 to NC)	20.63 (11.565 to NC)	NC (1.084 to NC)	NC (2.825 to NC)	4.70 (0.986 to NC)	NC (6.965 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (7.556 to NC)	NC (NC to NC)	NC (3.745 to NC)	NC (6.965 to NC)	
Comparison vs. Kd							
Log-Rank test p-value[a] vs Kd	-	0.6192		0.3956		0.1833	
Hazard ratio (95% CI) vs Kd	-	1.10 (0.75 to 1.62)		0.51 (0.10 to 2.51)		0.36 (0.08 to 1.72)	
P-value	-	0.6193		0.4047		0.2016	

A lower score represents a better level of quality of life. Clinical meaningful deterioration change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Financial difficulties
16.2.6.1.2.9 Efficacy response data - Subgroup analyses by R-ISS stage at SE
16.2.6.1.2.9.5 QLQ-C30 - Time until permanent improvement by 10 pt in financial difficulties according to R-ISS stage at SE (LOCF) - ITT population

	I or II		III		Not classified		
	Kd (N=103)	**IKd (N=155)**	**Kd (N=8)**	**IKd (N=16)**	**Kd (N=12)**	**IKd (N=8)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	15 (14.6)	22 (14.2)	3 (37.5)	3 (18.8)	1 (8.3)	1 (12.5)	0.5767
Number (%) of patients censored	88 (85.4)	133 (85.8)	5 (62.5)	13 (81.3)	11 (91.7)	7 (87.5)	
Kaplan-Meier estimates of Financial difficulties in months							
25% quantile (95% CI)	24.34 (21.224 to NC)	NC (22.111 to NC)	1.12 (0.953 to NC)	NC (1.018 to NC)	NC (5.060 to NC)	NC (2.136 to NC)	
Median (95% CI)	NC (24.345 to NC)	NC (NC to NC)	13.40 (0.953 to NC)	NC (4.862 to NC)	NC (NC to NC)	NC (2.136 to NC)	
75% quantile (95% CI)	NC (24.345 to NC)	NC (NC to NC)	NC (13.405 to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Kd							
Log-Rank test p-value[a] vs Kd	-	0.9025		0.3436		0.5699	
Hazard ratio (95% CI) vs Kd	-	0.96 (0.50 to 1.85)		0.47 (0.09 to 2.33)		2.19 (0.14 to 35.12)	
P-value	-	0.9021		0.3550		0.5796	

A lower score represents a better level of quality of life. Clinical meaningful improvement change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
PGM=DEVOPS/SAR650984/EFC15246/CIR_RWE/REPORT/PGM/eff_km_subgp_sr_sig_de_i_t.sas OUT=REPORT/OUTPUT/eff_km_c30_fin_imppl_seriss_de_i_t_x.rtf (07APR2021 14:39)

16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Financial difficulties
16.2.6.1.2.9 Efficacy response data - Subgroup analyses by R-ISS stage at SE
16.2.6.1.2.9.6 QLQ-C30 - Time until permanent deterioration by 10 pt in financial difficulties according to R-ISS stage at SE (LOCF) - ITT population

	I or II		III		Not classified		
	Kd (N=103)	**IKd (N=155)**	**Kd (N=8)**	**IKd (N=16)**	**Kd (N=12)**	**IKd (N=8)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	16 (15.5)	26 (16.8)	1 (12.5)	0 (0.0)	4 (33.3)	0 (0.0)	0.9998
Number (%) of patients censored	87 (84.5)	129 (83.2)	7 (87.5)	16 (100.0)	8 (66.7)	8 (100.0)	
Kaplan-Meier estimates of Financial difficulties in months							
25% quantile (95% CI)	NC (21.388 to NC)	NC (19.877 to NC)	NC (4.041 to NC)	NC (NC to NC)	13.42 (1.084 to NC)	NC (NC to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (4.041 to NC)	NC (NC to NC)	NC (1.150 to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Kd							
Log-Rank test p-value[a] vs Kd	-	0.9519		0.1730		0.1695	
Hazard ratio (95% CI) vs Kd	-	1.02 (0.55 to 1.90)					
P-value	-	0.9520		0.9985		0.9971	

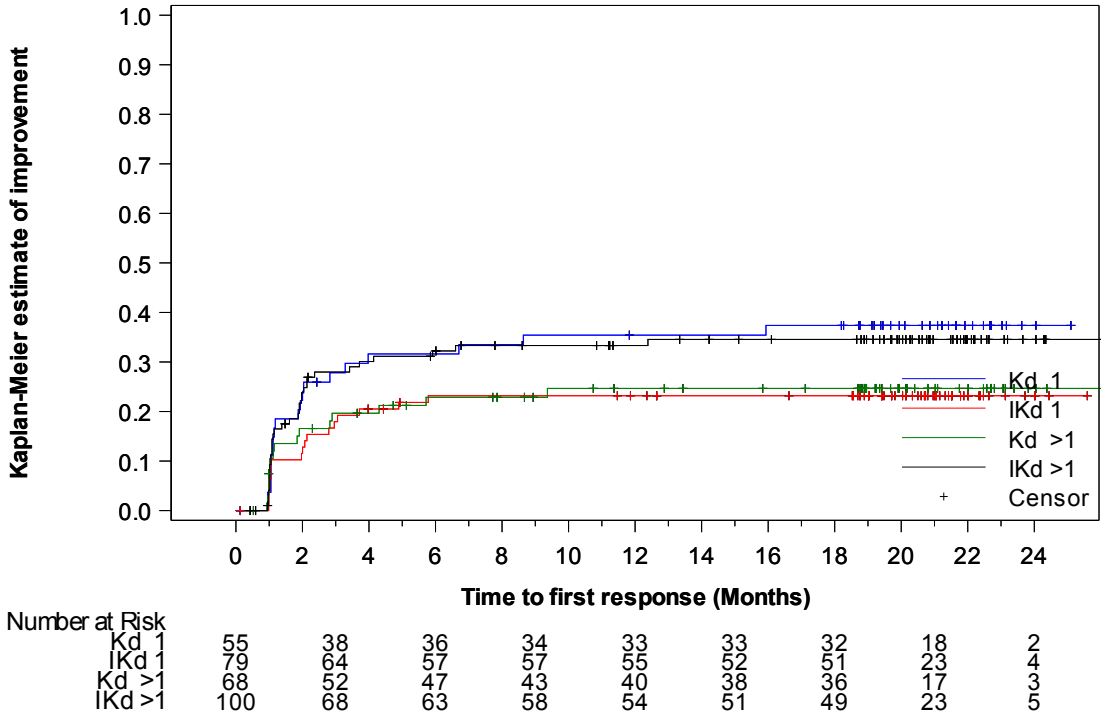
A lower score represents a better level of quality of life. Clinical meaningful deterioration change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
PGM=DEVOPS/SAR650984/EFC15246/CIR_RWE/REPORT/PGM/eff_km_subgp_sr_sig_de_i_t.sas OUT=REPORT/OUTPUT/eff_km_c30_fin_detpl_seriss_de_i_t_x.rtf (07APR2021 14:38)

16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Financial difficulties
16.2.6.1.2.10 Efficacy response data - Subgroup analyses by nb of prior lines
16.2.6.1.2.10.3 QLQ-C30 - Time to first improvement by 10 pt in financial difficulties according to nb of prior lines (LOCF) - ITT population

	1		>1		
	Kd (N=55)	**IKd (N=79)**	**Kd (N=68)**	**IKd (N=100)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	20 (36.4)	18 (22.8)	16 (23.5)	33 (33.0)	0.0359
Number (%) of patients censored	35 (63.6)	61 (77.2)	52 (76.5)	67 (67.0)	
Kaplan-Meier estimates of Financial difficulties in months					
25% quantile (95% CI)	2.04 (1.117 to 15.934)	NC (2.136 to NC)	NC (1.840 to NC)	2.14 (1.150 to 12.386)	
Median (95% CI)	NC (15.934 to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.0893		0.2063	
Hazard ratio (95% CI) vs Kd	-	0.58 (0.31 to 1.10)		1.47 (0.81 to 2.66)	
P-value	-	0.0933		0.2091	
Improvement probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful improvement change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
PGM=DEVOPS/SAR650984/EFC15246/CIR_RWE/REPORT/PGM/eff_km_subgp_sr_sig_de_i_t.sas OUT=REPORT/OUTPUT/eff_km_c30_fin_impl_plne_de_i_t_x.rtf (07APR2021 14:38)

16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Financial difficulties
16.2.6.1.2.10 Efficacy response data - Subgroup analyses by nb of prior lines
16.2.6.1.2.10.4 QLQ-C30 - Time to first improvement by 10 pt in financial difficulties according to nb of prior lines - Kaplan-Meier curve (LOCF) - ITT population



A lower score represents a better level of quality of life. Clinical meaningful improvement change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
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16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Financial difficulties
16.2.6.1.2.10 Efficacy response data - Subgroup analyses by nb of prior lines
16.2.6.1.2.10.5 QLQ-C30 - Time to first deterioration by 10 pt in financial difficulties according to nb of prior lines (LOCF) - ITT population

	1		>1		
	Kd (N=55)	**IKd (N=79)**	**Kd (N=68)**	**IKd (N=100)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	19 (34.5)	33 (41.8)	33 (48.5)	44 (44.0)	0.1760
Number (%) of patients censored	36 (65.5)	46 (58.2)	35 (51.5)	56 (56.0)	
Kaplan-Meier estimates of Financial difficulties in months					
25% quantile (95% CI)	7.56 (1.248 to NC)	5.68 (2.103 to 9.002)	1.87 (1.018 to 2.924)	3.75 (1.938 to 8.674)	
Median (95% CI)	NC (15.244 to NC)	NC (11.105 to NC)	20.57 (3.055 to NC)	NC (11.565 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.4040		0.2750	
Hazard ratio (95% CI) vs Kd	-	1.27 (0.72 to 2.24)		0.78 (0.50 to 1.22)	
P-value	-	0.4052		0.2763	
Deterioration probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful deterioration change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
PGM=DEVOPS/SAR650984/EFC15246/CIR_RWE/REPORT/PGM/eff_km_subgp_sr_sig_de_i_t.sas OUT=REPORT/OUTPUT/eff_km_c30_fin_detl_plne_de_i_t_x.rtf (07APR2021 14:38)

16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Financial difficulties
16.2.6.1.2.10 Efficacy response data - Subgroup analyses by nb of prior lines
16.2.6.1.2.10.6 QLQ-C30 - Time until permanent improvement by 10 pt in financial difficulties according to nb of prior lines (LOCF) - ITT population

	1		>1		
	Kd (N=55)	**IKd (N=79)**	**Kd (N=68)**	**IKd (N=100)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	10 (18.2)	8 (10.1)	9 (13.2)	18 (18.0)	0.1061
Number (%) of patients censored	45 (81.8)	71 (89.9)	59 (86.8)	82 (82.0)	
Kaplan-Meier estimates of Financial difficulties in months					
25% quantile (95% CI)	NC (2.825 to NC)	NC (NC to NC)	24.34 (21.224 to NC)	NC (15.639 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (24.345 to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (24.345 to NC)	NC (NC to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.1641		0.3463	
Hazard ratio (95% CI) vs Kd	-	0.52 (0.21 to 1.32)		1.47 (0.66 to 3.27)	
P-value	-	0.1715		0.3492	
Improvement probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful improvement change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
PGM=DEVOPS/SAR650984/EFC15246/CIR_RWE/REPORT/PGM/eff_km_subgp_sr_sig_de_i_t.sas OUT=REPORT/OUTPUT/eff_km_c30_fin_imppl_plne_de_i_t_x.rtf (07APR2021 14:38)

16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Financial difficulties
16.2.6.1.2.10 Efficacy response data - Subgroup analyses by nb of prior lines
16.2.6.1.2.10.7 QLQ-C30 - Time until permanent deterioration by 10 pt in financial difficulties according to nb of prior lines (LOCF) - ITT population

	1		>1		
	Kd (N=55)	**IKd (N=79)**	**Kd (N=68)**	**IKd (N=100)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	6 (10.9)	11 (13.9)	15 (22.1)	15 (15.0)	0.2631
Number (%) of patients censored	49 (89.1)	68 (86.1)	53 (77.9)	85 (85.0)	
Kaplan-Meier estimates of Financial difficulties in months					
25% quantile (95% CI)	NC (21.388 to NC)	NC (19.483 to NC)	NC (6.571 to NC)	NC (18.727 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.6165		0.2158	
Hazard ratio (95% CI) vs Kd	-	1.29 (0.48 to 3.49)		0.64 (0.31 to 1.31)	
P-value	-	0.6175		0.2196	
Deterioration probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful deterioration change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Financial difficulties
16.2.6.1.2.11 Efficacy response data - Subgroup analyses by cytogenetic abnormality
16.2.6.1.2.11.3 QLQ-C30 - Time to first improvement by 10 pt in financial difficulties according to cytogenetic abnormality (LOCF) - ITT population

	At least one		None		
	Kd (N=31)	**IKd (N=42)**	**Kd (N=77)**	**IKd (N=114)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	10 (32.3)	14 (33.3)	23 (29.9)	28 (24.6)	0.5414
Number (%) of patients censored	21 (67.7)	28 (66.7)	54 (70.1)	86 (75.4)	
Kaplan-Meier estimates of Financial difficulties in months					
25% quantile (95% CI)	6.70 (1.018 to NC)	2.04 (1.117 to NC)	2.83 (1.183 to NC)	12.39 (2.366 to NC)	
Median (95% CI)	NC (9.363 to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.8981		0.3769	
Hazard ratio (95% CI) vs Kd	-	1.05 (0.47 to 2.38)		0.78 (0.45 to 1.35)	
P-value	-	0.8986		0.3781	
Improvement probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful improvement change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Financial difficulties
16.2.6.1.2.11 Efficacy response data - Subgroup analyses by cytogenetic abnormality
16.2.6.1.2.11.4 QLQ-C30 - Time to first deterioration by 10 pt in financial difficulties according to cytogenetic abnormality (LOCF) - ITT population

	At least one		None		
	Kd (N=31)	**IKd (N=42)**	**Kd (N=77)**	**IKd (N=114)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	12 (38.7)	20 (47.6)	31 (40.3)	49 (43.0)	0.7420
Number (%) of patients censored	19 (61.3)	22 (52.4)	46 (59.7)	65 (57.0)	
Kaplan-Meier estimates of Financial difficulties in months					
25% quantile (95% CI)	4.04 (1.018 to 12.485)	3.88 (1.906 to 9.298)	2.92 (1.084 to 6.834)	3.81 (2.070 to 7.622)	
Median (95% CI)	NC (7.688 to NC)	14.78 (7.885 to NC)	NC (8.082 to NC)	NC (14.784 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.6663		0.8923	
Hazard ratio (95% CI) vs Kd	-	1.17 (0.57 to 2.40)		1.03 (0.66 to 1.62)	
P-value	-	0.6666		0.8927	
Deterioration probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful deterioration change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Financial difficulties
16.2.6.1.2.11 Efficacy response data - Subgroup analyses by cytogenetic abnormality
16.2.6.1.2.11.5 QLQ-C30 - Time until permanent improvement by 10 pt in financial difficulties according to cytogenetic abnormality (LOCF) - ITT population

	At least one		None		
	Kd (N=31)	**IKd (N=42)**	**Kd (N=77)**	**IKd (N=114)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	3 (9.7)	7 (16.7)	15 (19.5)	14 (12.3)	0.2076
Number (%) of patients censored	28 (90.3)	35 (83.3)	62 (80.5)	100 (87.7)	
Kaplan-Meier estimates of Financial difficulties in months					
25% quantile (95% CI)	NC (1.117 to NC)	22.11 (1.971 to NC)	24.34 (14.522 to NC)	NC (NC to NC)	
Median (95% CI)	NC (NC to NC)	NC (22.111 to NC)	NC (24.345 to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (24.345 to NC)	NC (NC to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.4304		0.1948	
Hazard ratio (95% CI) vs Kd	-	1.71 (0.44 to 6.65)		0.62 (0.30 to 1.29)	
P-value	-	0.4360		0.1990	
Improvement probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful improvement change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Financial difficulties
16.2.6.1.2.11 Efficacy response data - Subgroup analyses by cytogenetic abnormality
16.2.6.1.2.11.6 QLQ-C30 - Time until permanent deterioration by 10 pt in financial difficulties according to cytogenetic abnormality (LOCF) - ITT population

	At least one		None		
	Kd (N=31)	**IKd (N=42)**	**Kd (N=77)**	**IKd (N=114)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	7 (22.6)	9 (21.4)	10 (13.0)	15 (13.2)	0.8940
Number (%) of patients censored	24 (77.4)	33 (78.6)	67 (87.0)	99 (86.8)	
Kaplan-Meier estimates of Financial difficulties in months					
25% quantile (95% CI)	NC (3.680 to NC)	NC (11.696 to NC)	NC (21.388 to NC)	NC (20.632 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.7873		0.9434	
Hazard ratio (95% CI) vs Kd	-	0.87 (0.33 to 2.34)		0.97 (0.44 to 2.16)	
P-value	-	0.7875		0.9432	
Deterioration probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful deterioration change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Financial difficulties
16.2.6.1.2.12 Efficacy response data - Subgroup analyses by MM type at SE
16.2.6.1.2.12.3 QLQ-C30 - Time to first improvement by 10 pt in financial difficulties according to MM type at SE (LOCF) - ITT population

	IgG		Non-IgG		
	Kd (N=85)	**IKd (N=126)**	**Kd (N=38)**	**IKd (N=53)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	24 (28.2)	34 (27.0)	12 (31.6)	17 (32.1)	0.9518
Number (%) of patients censored	61 (71.8)	92 (73.0)	26 (68.4)	36 (67.9)	
Kaplan-Meier estimates of Financial difficulties in months					
25% quantile (95% CI)	4.30 (1.183 to NC)	4.90 (2.070 to NC)	3.29 (1.018 to NC)	2.04 (1.051 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (9.363 to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.8753		0.9544	
Hazard ratio (95% CI) vs Kd	-	0.96 (0.57 to 1.62)		0.98 (0.47 to 2.05)	
P-value	-	0.8748		0.9543	
Improvement probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful improvement change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Financial difficulties
16.2.6.1.2.12 Efficacy response data - Subgroup analyses by MM type at SE
16.2.6.1.2.12.4 QLQ-C30 - Time to first deterioration by 10 pt in financial difficulties according to MM type at SE (LOCF) - ITT population

	IgG		Non-IgG		
	Kd (N=85)	**IKd (N=126)**	**Kd (N=38)**	**IKd (N=53)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	39 (45.9)	56 (44.4)	13 (34.2)	21 (39.6)	0.7742
Number (%) of patients censored	46 (54.1)	70 (55.6)	25 (65.8)	32 (60.4)	
Kaplan-Meier estimates of Financial difficulties in months					
25% quantile (95% CI)	2.92 (1.084 to 4.895)	4.70 (2.760 to 7.885)	1.97 (0.986 to NC)	3.88 (1.938 to 12.715)	
Median (95% CI)	NC (7.688 to NC)	20.63 (11.565 to NC)	NC (4.041 to NC)	NC (11.105 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.7175		0.9209	
Hazard ratio (95% CI) vs Kd	-	0.93 (0.62 to 1.40)		1.04 (0.52 to 2.07)	
P-value	-	0.7176		0.9212	
Deterioration probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful deterioration change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Financial difficulties
16.2.6.1.2.12 Efficacy response data - Subgroup analyses by MM type at SE
16.2.6.1.2.12.5 QLQ-C30 - Time until permanent improvement by 10 pt in financial difficulties according to MM type at SE (LOCF) - ITT population

	IgG		Non-IgG		
	Kd (N=85)	**IKd (N=126)**	**Kd (N=38)**	**IKd (N=53)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	14 (16.5)	13 (10.3)	5 (13.2)	13 (24.5)	0.0956
Number (%) of patients censored	71 (83.5)	113 (89.7)	33 (86.8)	40 (75.5)	
Kaplan-Meier estimates of Financial difficulties in months					
25% quantile (95% CI)	24.34 (21.224 to NC)	NC (NC to NC)	NC (2.825 to NC)	22.11 (1.906 to NC)	
Median (95% CI)	NC (24.345 to NC)	NC (NC to NC)	NC (NC to NC)	NC (22.111 to NC)	
75% quantile (95% CI)	NC (24.345 to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.2303		0.2645	
Hazard ratio (95% CI) vs Kd	-	0.63 (0.30 to 1.35)		1.78 (0.64 to 5.01)	
P-value	-	0.2344		0.2714	
Improvement probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful improvement change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Financial difficulties
16.2.6.1.2.12 Efficacy response data - Subgroup analyses by MM type at SE
16.2.6.1.2.12.6 QLQ-C30 - Time until permanent deterioration by 10 pt in financial difficulties according to MM type at SE (LOCF) - ITT population

	IgG		Non-IgG		
	Kd (N=85)	**IKd (N=126)**	**Kd (N=38)**	**IKd (N=53)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	15 (17.6)	17 (13.5)	6 (15.8)	9 (17.0)	0.5661
Number (%) of patients censored	70 (82.4)	109 (86.5)	32 (84.2)	44 (83.0)	
Kaplan-Meier estimates of Financial difficulties in months					
25% quantile (95% CI)	NC (13.897 to NC)	NC (20.632 to NC)	NC (6.834 to NC)	NC (13.996 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (21.388 to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.3848		0.9457	
Hazard ratio (95% CI) vs Kd	-	0.74 (0.37 to 1.47)		1.04 (0.37 to 2.91)	
P-value	-	0.3867		0.9459	
Deterioration probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful deterioration change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Financial difficulties
16.2.6.1.2.13 Efficacy response data - Subgroup analyses by previous autologous stem-cell
16.2.6.1.2.13.3 QLQ-C30 - Time to first improvement by 10 pt in financial difficulties according to previous autologous stem-cell (LOCF) - ITT population

	Yes		No		
	Kd (N=69)	**IKd (N=116)**	**Kd (N=54)**	**IKd (N=63)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	23 (33.3)	34 (29.3)	13 (24.1)	17 (27.0)	0.3954
Number (%) of patients censored	46 (66.7)	82 (70.7)	41 (75.9)	46 (73.0)	
Kaplan-Meier estimates of Financial difficulties in months					
25% quantile (95% CI)	1.92 (1.051 to NC)	3.71 (1.971 to NC)	15.93 (2.037 to NC)	4.60 (1.084 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.4671		0.6096	
Hazard ratio (95% CI) vs Kd	-	0.82 (0.48 to 1.40)		1.21 (0.59 to 2.48)	
P-value	-	0.4678		0.6101	
Improvement probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful improvement change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Financial difficulties
16.2.6.1.2.13 Efficacy response data - Subgroup analyses by previous autologous stem-cell
16.2.6.1.2.13.4 QLQ-C30 - Time to first deterioration by 10 pt in financial difficulties according to previous autologous stem-cell (LOCF) - ITT population

	Yes		No		
	Kd (N=69)	**IKd (N=116)**	**Kd (N=54)**	**IKd (N=63)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	26 (37.7)	45 (38.8)	26 (48.1)	32 (50.8)	0.9663
Number (%) of patients censored	43 (62.3)	71 (61.2)	28 (51.9)	31 (49.2)	
Kaplan-Meier estimates of Financial difficulties in months					
25% quantile (95% CI)	4.04 (1.117 to 12.485)	5.72 (3.055 to 9.002)	1.91 (1.018 to 3.055)	2.89 (1.840 to 7.622)	
Median (95% CI)	NC (15.244 to NC)	NC (20.501 to NC)	14.23 (3.055 to NC)	14.78 (7.622 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.9763		0.9333	
Hazard ratio (95% CI) vs Kd	-	0.99 (0.61 to 1.61)		0.98 (0.58 to 1.64)	
P-value	-	0.9762		0.9332	
Deterioration probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful deterioration change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Financial difficulties
16.2.6.1.2.13 Efficacy response data - Subgroup analyses by previous autologous stem-cell
16.2.6.1.2.13.5 QLQ-C30 - Time until permanent improvement by 10 pt in financial difficulties according to previous autologous stem-cell (LOCF) - ITT population

	Yes		No		
	Kd (N=69)	**IKd (N=116)**	**Kd (N=54)**	**IKd (N=63)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	13 (18.8)	19 (16.4)	6 (11.1)	7 (11.1)	0.8462
Number (%) of patients censored	56 (81.2)	97 (83.6)	48 (88.9)	56 (88.9)	
Kaplan-Meier estimates of Financial difficulties in months					
25% quantile (95% CI)	NC (13.405 to NC)	NC (18.201 to NC)	24.34 (21.388 to NC)	NC (NC to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	24.34 (24.345 to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (24.345 to NC)	NC (NC to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.6956		0.9851	
Hazard ratio (95% CI) vs Kd	-	0.87 (0.43 to 1.76)		0.99 (0.33 to 2.95)	
P-value	-	0.6958		0.9851	
Improvement probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful improvement change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Financial difficulties
16.2.6.1.2.13 Efficacy response data - Subgroup analyses by previous autologous stem-cell
16.2.6.1.2.13.6 QLQ-C30 - Time until permanent deterioration by 10 pt in financial difficulties according to previous autologous stem-cell (LOCF) - ITT population

	Yes		No		
	Kd (N=69)	**IKd (N=116)**	**Kd (N=54)**	**IKd (N=63)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	10 (14.5)	14 (12.1)	11 (20.4)	12 (19.0)	0.8515
Number (%) of patients censored	59 (85.5)	102 (87.9)	43 (79.6)	51 (81.0)	
Kaplan-Meier estimates of Financial difficulties in months					
25% quantile (95% CI)	NC (14.817 to NC)	NC (NC to NC)	NC (4.041 to NC)	NC (14.062 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.6258		0.8181	
Hazard ratio (95% CI) vs Kd	-	0.82 (0.36 to 1.84)		0.91 (0.40 to 2.06)	
P-value	-	0.6264		0.8175	
Deterioration probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful deterioration change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Financial difficulties
16.2.6.1.2.14 Efficacy response data - Subgroup analyses by baseline eGFR (MDRD)
16.2.6.1.2.14.3 QLQ-C30 - Time to first improvement by 10 pt in financial difficulties according to baseline eGFR (MDRD) (LOCF) - ITT population

	>=60 mL/min/1.73m2		<60 mL/min/1.73m2		
	Kd (N=93)	**IKd (N=122)**	**Kd (N=18)**	**IKd (N=43)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	29 (31.2)	35 (28.7)	6 (33.3)	15 (34.9)	0.9630
Number (%) of patients censored	64 (68.8)	87 (71.3)	12 (66.7)	28 (65.1)	
Kaplan-Meier estimates of Financial difficulties in months					
25% quantile (95% CI)	4.14 (1.150 to NC)	3.71 (1.971 to NC)	2.37 (1.051 to NC)	1.97 (1.018 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (1.906 to NC)	NC (5.914 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.7740		0.9348	
Hazard ratio (95% CI) vs Kd	-	0.93 (0.57 to 1.52)		0.96 (0.37 to 2.48)	
P-value	-	0.7731		0.9342	
Improvement probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful improvement change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Financial difficulties
16.2.6.1.2.14 Efficacy response data - Subgroup analyses by baseline eGFR (MDRD)
16.2.6.1.2.14.4 QLQ-C30 - Time to first deterioration by 10 pt in financial difficulties according to baseline eGFR (MDRD) (LOCF) - ITT population

	>=60 mL/min/1.73m2		<60 mL/min/1.73m2		
	Kd (N=93)	**IKd (N=122)**	**Kd (N=18)**	**IKd (N=43)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	38 (40.9)	56 (45.9)	12 (66.7)	18 (41.9)	0.0110
Number (%) of patients censored	55 (59.1)	66 (54.1)	6 (33.3)	25 (58.1)	
Kaplan-Meier estimates of Financial difficulties in months					
25% quantile (95% CI)	2.87 (1.084 to 6.834)	4.70 (2.825 to 8.016)	1.15 (0.920 to 4.041)	2.07 (1.478 to 7.622)	
Median (95% CI)	NC (14.226 to NC)	20.63 (11.269 to NC)	4.04 (1.084 to 12.485)	NC (6.571 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	12.48 (4.041 to NC)	NC (NC to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.5524		0.0142	
Hazard ratio (95% CI) vs Kd	-	1.13 (0.75 to 1.71)		0.41 (0.20 to 0.86)	
P-value	-	0.5527		0.0176	
Deterioration probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful deterioration change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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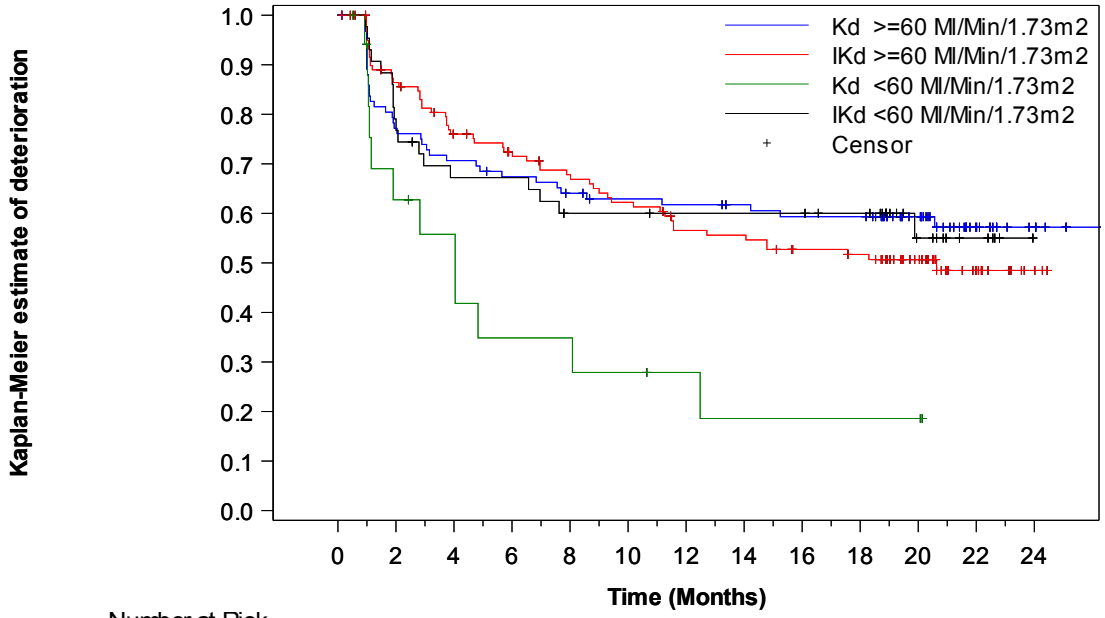
16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Financial difficulties
16.2.6.1.2.14 Efficacy response data - Subgroup analyses by baseline eGFR (MDRD)
16.2.6.1.2.14.5 QLQ-C30 - Time to first deterioration by 10 pt in financial difficulties according to baseline eGFR (MDRD) - Kaplan-Meier curve (LOCF) - ITT population



Number at Risk

Kd >=60 Ml/Min/1.73m2	93	68	61	54	53	50	49	24	6
lKd >=60 Ml/Min/1.73m2	122	94	79	70	59	55	50	16	3
Kd <60 Ml/Min/1.73m2	18	8	5	4	3	2	2	0	0
lKd <60 Ml/Min/1.73m2	43	29	28	24	23	23	21	6	0

A lower score represents a better level of quality of life. Clinical meaningful deterioration change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
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16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Financial difficulties
16.2.6.1.2.14 Efficacy response data - Subgroup analyses by baseline eGFR (MDRD)
16.2.6.1.2.14.6 QLQ-C30 - Time until permanent improvement by 10 pt in financial difficulties according to baseline eGFR (MDRD) (LOCF) - ITT population

	>=60 mL/min/1.73m2		<60 mL/min/1.73m2		
	Kd (N=93)	**IKd (N=122)**	**Kd (N=18)**	**IKd (N=43)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	15 (16.1)	15 (12.3)	3 (16.7)	10 (23.3)	0.5471
Number (%) of patients censored	78 (83.9)	107 (87.7)	15 (83.3)	33 (76.7)	
Kaplan-Meier estimates of Financial difficulties in months					
25% quantile (95% CI)	24.34 (17.084 to NC)	NC (NC to NC)	21.39 (2.825 to NC)	22.11 (1.084 to NC)	
Median (95% CI)	NC (24.345 to NC)	NC (NC to NC)	NC (21.388 to NC)	NC (22.111 to NC)	
75% quantile (95% CI)	NC (24.345 to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.5092		0.7289	
Hazard ratio (95% CI) vs Kd	-	0.79 (0.38 to 1.61)		1.26 (0.35 to 4.56)	
P-value	-	0.5102		0.7295	
Improvement probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful improvement change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
PGM=DEVOPS/SAR650984/EFC15246/CIR_RWE/REPORT/PGM/eff_km_subgp_sr_sig_de_i_t.sas OUT=REPORT/OUTPUT/eff_km_c30_fin_imppl_crcl_de_i_t_x.rtf (07APR2021 14:38)

16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Financial difficulties
16.2.6.1.2.14 Efficacy response data - Subgroup analyses by baseline eGFR (MDRD)
16.2.6.1.2.14.7 QLQ-C30 - Time until permanent deterioration by 10 pt in financial difficulties according to baseline eGFR (MDRD) (LOCF) - ITT population

	>=60 mL/min/1.73m2		<60 mL/min/1.73m2		
	Kd (N=93)	**IKd (N=122)**	**Kd (N=18)**	**IKd (N=43)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	16 (17.2)	19 (15.6)	5 (27.8)	7 (16.3)	0.2053
Number (%) of patients censored	77 (82.8)	103 (84.4)	13 (72.2)	36 (83.7)	
Kaplan-Meier estimates of Financial difficulties in months					
25% quantile (95% CI)	NC (14.817 to NC)	NC (19.483 to NC)	4.04 (1.018 to NC)	NC (7.655 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (4.041 to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.8570		0.1360	
Hazard ratio (95% CI) vs Kd	-	0.94 (0.48 to 1.83)		0.43 (0.14 to 1.35)	
P-value	-	0.8565		0.1477	
Deterioration probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful deterioration change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Financial difficulties
16.2.6.1.2.15 Efficacy response data - Subgroup analyses by previous treatment with PI
16.2.6.1.2.15.3 QLQ-C30 - Time to first improvement by 10 pt in financial difficulties according to previous treatment with PI (LOCF) - ITT population

	Yes		No		
	Kd (N=47)	**IKd (N=81)**	**Kd (N=76)**	**IKd (N=98)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	14 (29.8)	22 (27.2)	22 (28.9)	29 (29.6)	0.7520
Number (%) of patients censored	33 (70.2)	59 (72.8)	54 (71.1)	69 (70.4)	
Kaplan-Meier estimates of Financial difficulties in months					
25% quantile (95% CI)	3.98 (1.051 to NC)	3.42 (1.971 to NC)	4.30 (1.840 to NC)	3.71 (1.380 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.7488		0.9322	
Hazard ratio (95% CI) vs Kd	-	0.90 (0.46 to 1.75)		1.02 (0.59 to 1.78)	
P-value	-	0.7490		0.9323	
Improvement probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful improvement change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Financial difficulties
16.2.6.1.2.15 Efficacy response data - Subgroup analyses by previous treatment with PI
16.2.6.1.2.15.4 QLQ-C30 - Time to first deterioration by 10 pt in financial difficulties according to previous treatment with PI (LOCF) - ITT population

	Yes		No		
	Kd (N=47)	**IKd (N=81)**	**Kd (N=76)**	**IKd (N=98)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	16 (34.0)	37 (45.7)	36 (47.4)	40 (40.8)	0.0743
Number (%) of patients censored	31 (66.0)	44 (54.3)	40 (52.6)	58 (59.2)	
Kaplan-Meier estimates of Financial difficulties in months					
25% quantile (95% CI)	2.83 (1.051 to NC)	2.89 (1.873 to 6.012)	2.89 (1.084 to 4.764)	6.57 (3.220 to 10.185)	
Median (95% CI)	NC (11.170 to NC)	20.50 (8.805 to NC)	20.57 (5.651 to NC)	NC (14.062 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.2478		0.1753	
Hazard ratio (95% CI) vs Kd	-	1.41 (0.78 to 2.54)		0.73 (0.47 to 1.15)	
P-value	-	0.2502		0.1770	
Deterioration probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful deterioration change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Financial difficulties
16.2.6.1.2.15 Efficacy response data - Subgroup analyses by previous treatment with PI
16.2.6.1.2.15.5 QLQ-C30 - Time until permanent improvement by 10 pt in financial difficulties according to previous treatment with PI (LOCF) - ITT population

	Yes		No		
	Kd (N=47)	**IKd (N=81)**	**Kd (N=76)**	**IKd (N=98)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	7 (14.9)	11 (13.6)	12 (15.8)	15 (15.3)	0.9997
Number (%) of patients censored	40 (85.1)	70 (86.4)	64 (84.2)	83 (84.7)	
Kaplan-Meier estimates of Financial difficulties in months					
25% quantile (95% CI)	24.34 (2.825 to NC)	NC (18.201 to NC)	NC (17.084 to NC)	NC (22.111 to NC)	
Median (95% CI)	24.34 (24.345 to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (24.345 to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.9319		0.9169	
Hazard ratio (95% CI) vs Kd	-	1.04 (0.39 to 2.82)		0.96 (0.45 to 2.05)	
P-value	-	0.9323		0.9167	
Improvement probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful improvement change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Financial difficulties
16.2.6.1.2.15 Efficacy response data - Subgroup analyses by previous treatment with PI
16.2.6.1.2.15.6 QLQ-C30 - Time until permanent deterioration by 10 pt in financial difficulties according to previous treatment with PI (LOCF) - ITT population

	Yes		No		
	Kd (N=47)	**IKd (N=81)**	**Kd (N=76)**	**IKd (N=98)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	8 (17.0)	13 (16.0)	13 (17.1)	13 (13.3)	0.6372
Number (%) of patients censored	39 (83.0)	68 (84.0)	63 (82.9)	85 (86.7)	
Kaplan-Meier estimates of Financial difficulties in months					
25% quantile (95% CI)	NC (13.897 to NC)	NC (15.507 to NC)	NC (12.945 to NC)	NC (20.632 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.9111		0.4031	
Hazard ratio (95% CI) vs Kd	-	0.95 (0.39 to 2.29)		0.72 (0.33 to 1.56)	
P-value	-	0.9105		0.4051	
Deterioration probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful deterioration change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Financial difficulties
16.2.6.1.2.16 Efficacy response data - Subgroup analyses by previous treatment with IMiD
16.2.6.1.2.16.3 QLQ-C30 - Time to first improvement by 10 pt in financial difficulties according to previous treatment with IMiD (LOCF) - ITT population

	Yes		No		
	Kd (N=62)	**IKd (N=81)**	**Kd (N=61)**	**IKd (N=98)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	17 (27.4)	21 (25.9)	19 (31.1)	30 (30.6)	0.7509
Number (%) of patients censored	45 (72.6)	60 (74.1)	42 (68.9)	68 (69.4)	
Kaplan-Meier estimates of Financial difficulties in months					
25% quantile (95% CI)	2.89 (1.117 to NC)	5.91 (2.004 to NC)	5.72 (1.150 to NC)	2.14 (1.610 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.7256		0.9354	
Hazard ratio (95% CI) vs Kd	-	0.89 (0.47 to 1.69)		1.02 (0.58 to 1.82)	
P-value	-	0.7258		0.9356	
Improvement probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful improvement change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Financial difficulties
16.2.6.1.2.16 Efficacy response data - Subgroup analyses by previous treatment with IMiD
16.2.6.1.2.16.4 QLQ-C30 - Time to first deterioration by 10 pt in financial difficulties according to previous treatment with IMiD (LOCF) - ITT population

	Yes		No		
	Kd (N=62)	**IKd (N=81)**	**Kd (N=61)**	**IKd (N=98)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	25 (40.3)	31 (38.3)	27 (44.3)	46 (46.9)	0.5403
Number (%) of patients censored	37 (59.7)	50 (61.7)	34 (55.7)	52 (53.1)	
Kaplan-Meier estimates of Financial difficulties in months					
25% quantile (95% CI)	3.06 (1.150 to 8.575)	8.67 (2.825 to 17.577)	1.91 (1.051 to 6.834)	2.96 (2.004 to 5.717)	
Median (95% CI)	NC (8.575 to NC)	NC (19.877 to NC)	NC (6.834 to NC)	14.78 (6.965 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.5306		0.8750	
Hazard ratio (95% CI) vs Kd	-	0.84 (0.50 to 1.43)		1.04 (0.65 to 1.67)	
P-value	-	0.5311		0.8755	
Deterioration probability (95% CI)[b]					

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The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Financial difficulties
16.2.6.1.2.16 Efficacy response data - Subgroup analyses by previous treatment with IMiD
16.2.6.1.2.16.5 QLQ-C30 - Time until permanent improvement by 10 pt in financial difficulties according to previous treatment with IMiD (LOCF) - ITT population

	Yes		No		
	Kd (N=62)	**IKd (N=81)**	**Kd (N=61)**	**IKd (N=98)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	10 (16.1)	8 (9.9)	9 (14.8)	18 (18.4)	0.1757
Number (%) of patients censored	52 (83.9)	73 (90.1)	52 (85.2)	80 (81.6)	
Kaplan-Meier estimates of Financial difficulties in months					
25% quantile (95% CI)	NC (14.522 to NC)	NC (22.111 to NC)	24.34 (21.224 to NC)	NC (10.218 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	24.34 (24.345 to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (24.345 to NC)	NC (NC to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.2311		0.4718	
Hazard ratio (95% CI) vs Kd	-	0.57 (0.23 to 1.45)		1.34 (0.60 to 2.99)	
P-value	-	0.2372		0.4734	
Improvement probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful improvement change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Financial difficulties
16.2.6.1.2.16 Efficacy response data - Subgroup analyses by previous treatment with IMiD
16.2.6.1.2.16.6 QLQ-C30 - Time until permanent deterioration by 10 pt in financial difficulties according to previous treatment with IMiD (LOCF) - ITT population

	Yes		No		
	Kd (N=62)	**IKd (N=81)**	**Kd (N=61)**	**IKd (N=98)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	8 (12.9)	10 (12.3)	13 (21.3)	16 (16.3)	0.7685
Number (%) of patients censored	54 (87.1)	71 (87.7)	48 (78.7)	82 (83.7)	
Kaplan-Meier estimates of Financial difficulties in months					
25% quantile (95% CI)	NC (14.784 to NC)	NC (20.632 to NC)	21.39 (8.444 to NC)	NC (15.507 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.8507		0.4510	
Hazard ratio (95% CI) vs Kd	-	0.91 (0.36 to 2.32)		0.76 (0.36 to 1.57)	
P-value	-	0.8508		0.4525	
Deterioration probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful deterioration change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Financial difficulties
16.2.6.1.2.17 Efficacy response data - Subgroup analyses by previous treatment with PI and IMiD
16.2.6.1.2.17.3 QLQ-C30 - Time to first improvement by 10 pt in financial difficulties according to previous treatment with PI and IMiD (LOCF) - ITT population

	Yes		No		
	Kd (N=17)	**IKd (N=23)**	**Kd (N=106)**	**IKd (N=156)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	4 (23.5)	3 (13.0)	32 (30.2)	48 (30.8)	0.3266
Number (%) of patients censored	13 (76.5)	20 (87.0)	74 (69.8)	108 (69.2)	
Kaplan-Meier estimates of Financial difficulties in months					
25% quantile (95% CI)	3.98 (0.953 to NC)	NC (1.051 to NC)	3.29 (1.873 to NC)	2.96 (1.906 to NC)	
Median (95% CI)	NC (3.975 to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.3254		0.8825	
Hazard ratio (95% CI) vs Kd	-	0.48 (0.11 to 2.14)		1.03 (0.66 to 1.62)	
P-value	-	0.3363		0.8829	
Improvement probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful improvement change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Financial difficulties
16.2.6.1.2.17 Efficacy response data - Subgroup analyses by previous treatment with PI and IMiD
16.2.6.1.2.17.4 QLQ-C30 - Time to first deterioration by 10 pt in financial difficulties according to previous treatment with PI and IMiD (LOCF) - ITT population

	Yes		No		
	Kd (N=17)	**IKd (N=23)**	**Kd (N=106)**	**IKd (N=156)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	3 (17.6)	8 (34.8)	49 (46.2)	69 (44.2)	0.2467
Number (%) of patients censored	14 (82.4)	15 (65.2)	57 (53.8)	87 (55.8)	
Kaplan-Meier estimates of Financial difficulties in months					
25% quantile (95% CI)	NC (0.986 to NC)	14.78 (0.986 to NC)	2.86 (1.084 to 4.041)	3.75 (2.793 to 6.965)	
Median (95% CI)	NC (NC to NC)	NC (14.784 to NC)	NC (7.688 to NC)	NC (11.565 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.2859		0.5075	
Hazard ratio (95% CI) vs Kd	-	2.03 (0.54 to 7.67)		0.88 (0.61 to 1.27)	
P-value	-	0.2959		0.5078	
Deterioration probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful deterioration change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Financial difficulties
16.2.6.1.2.17 Efficacy response data - Subgroup analyses by previous treatment with PI and IMiD
16.2.6.1.2.17.5 QLQ-C30 - Time until permanent improvement by 10 pt in financial difficulties according to previous treatment with PI and IMiD (LOCF) - ITT population

	Yes		No		
	Kd (N=17)	**IKd (N=23)**	**Kd (N=106)**	**IKd (N=156)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	3 (17.6)	0 (0.0)	16 (15.1)	26 (16.7)	0.9873
Number (%) of patients censored	14 (82.4)	23 (100.0)	90 (84.9)	130 (83.3)	
Kaplan-Meier estimates of Financial difficulties in months					
25% quantile (95% CI)	NC (0.953 to NC)	NC (NC to NC)	24.34 (21.224 to NC)	NC (22.111 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (24.345 to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (24.345 to NC)	NC (NC to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.0318		0.6573	
Hazard ratio (95% CI) vs Kd	-			1.15 (0.62 to 2.15)	
P-value	-	0.9972		0.6576	
Improvement probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful improvement change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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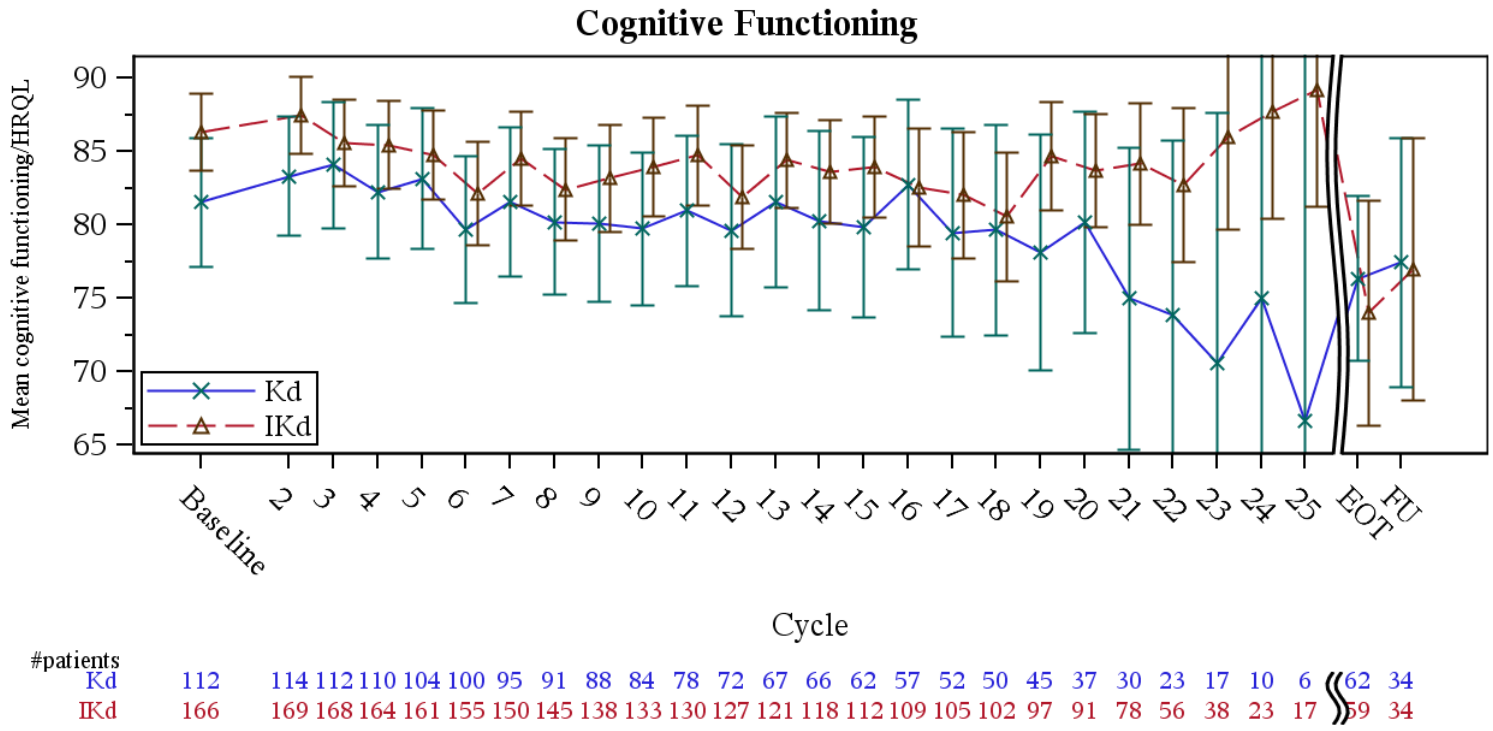
16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Financial difficulties
16.2.6.1.2.17 Efficacy response data - Subgroup analyses by previous treatment with PI and IMiD
16.2.6.1.2.17.6 QLQ-C30 - Time until permanent deterioration by 10 pt in financial difficulties according to previous treatment with PI and IMiD (LOCF) - ITT population

	Yes		No		
	Kd (N=17)	**IKd (N=23)**	**Kd (N=106)**	**IKd (N=156)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	1 (5.9)	1 (4.3)	20 (18.9)	25 (16.0)	0.9239
Number (%) of patients censored	16 (94.1)	22 (95.7)	86 (81.1)	131 (84.0)	
Kaplan-Meier estimates of Financial difficulties in months					
25% quantile (95% CI)	NC (0.986 to NC)	NC (19.877 to NC)	NC (14.784 to NC)	NC (19.483 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.8244		0.5045	
Hazard ratio (95% CI) vs Kd	-	0.73 (0.05 to 11.71)		0.82 (0.45 to 1.47)	
P-value	-	0.8251		0.5052	
Deterioration probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful deterioration change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
PGM=DEVOPS/SAR650984/EFC15246/CIR_RWE/REPORT/PGM/eff_km_subgp_sr_sig_de_i_t.sas OUT=REPORT/OUTPUT/eff_km_c30_fin_detpl_piimid_de_i_t_x.rtf (07APR2021 14:38)

16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Cognitive functioning
16.2.6.1.2.1 Efficacy response data
16.2.6.1.2.1.1 QLQ-C30 - Mean and 95% CI for cognitive functioning score over time (LOCF) - ITT population



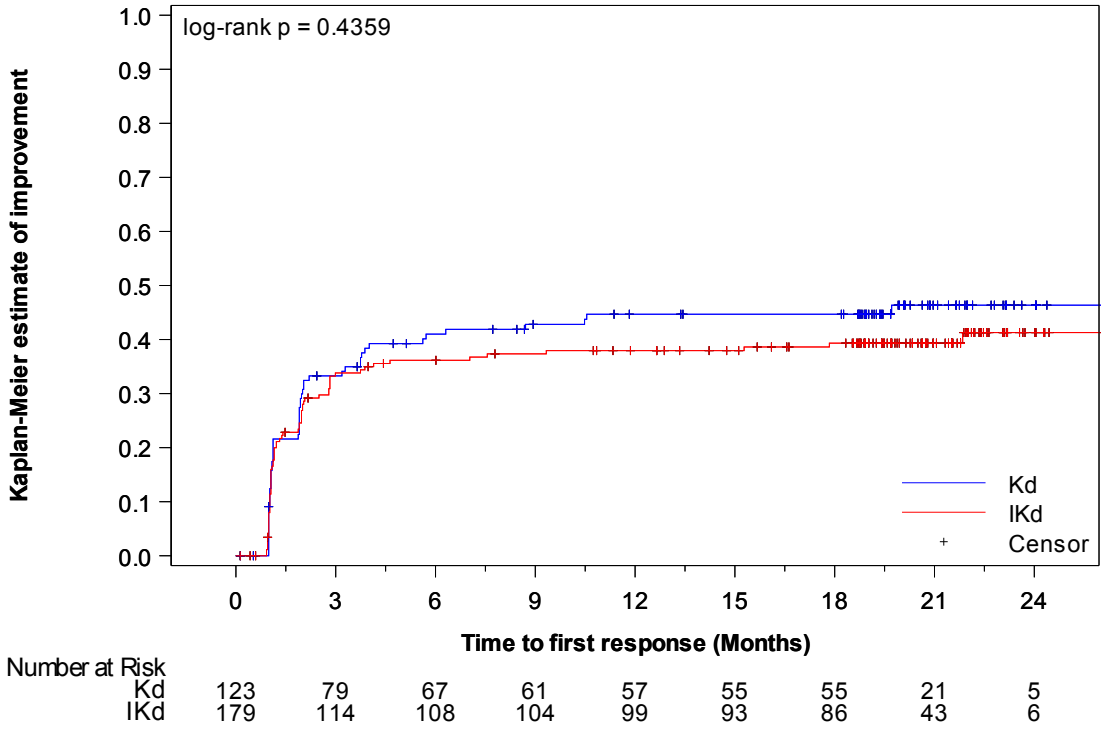
A higher score represents a better level of quality of life. Cycles with less than 20 patients overall are not presented.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
PGM=DEVOPS/SAR650984/EFC15246/CIR_RWE/REPORT/PGM/eff_qlq_line_i_f.sas OUT=REPORT/OUTPUT/eff_qlq_line_c30_cog_de_i_f_x.rtf (12FEB2021 15:16)

16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Cognitive functioning
16.2.6.1.2.1 Efficacy response data
16.2.6.1.2.1.15 QLQ-C30 - Time to first improvement by 15 pt in Cognitive functioning (LOCF) - ITT population

First improvement 15 points Cognitive functioning (%)	**Kd (N=123)**	**IKd (N=179)**
Number (%) of events	54 (43.9)	69 (38.5)
Number (%) of patients censored	69 (56.1)	110 (61.5)
Kaplan-Meier estimates of Cognitive functioning in months		
25% quantile (95% CI)	1.91 (1.084 to 2.201)	1.97 (1.150 to 2.825)
Median (95% CI)	NC (5.717 to NC)	NC (NC to NC)
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)
Comparison vs. Kd		
Stratified[a] Log-Rank test p-value[b] vs Kd	-	0.4359
Stratified[a] Hazard ratio (95% CI) vs Kd	-	0.87 (0.61 to 1.24)
P-value	-	0.4363
Improvement probability (95% CI)[c]		
3 Months	0.333 (0.250 to 0.417)	0.338 (0.269 to 0.409)
6 Months	0.410 (0.321 to 0.497)	0.362 (0.291 to 0.433)

A lower score represents a better level of quality of life. Clinical meaningful improvement change from baseline less than or equal to -15 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] Stratified on number of prior lines of therapy (1 vs. >1) and Revised International Staging System (R-ISS) stage (I or II vs. III vs. not classified) according to IRT
[b] One-sided significance level is 0.025
[c] Estimated using the Kaplan-Meier method
NA/NC = Not Applicable / Not Calculable
PGM=DEVOPS/SAR650984/EFC15246/CIR_RWE/REPORT/PGM/eff_km_invhr_sr_i_t.sas OUT=REPORT/OUTPUT/eff_km_c30_cog_imp15l_de_i_t_x.rtf (07APR2021 14:22)

16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Cognitive functioning
16.2.6.1.2.1 Efficacy response data
16.2.6.1.2.1.16 QLQ-C30 - Time to first improvement by 15 pt in Cognitive functioning - Kaplan-Meier curve (LOCF) - ITT population



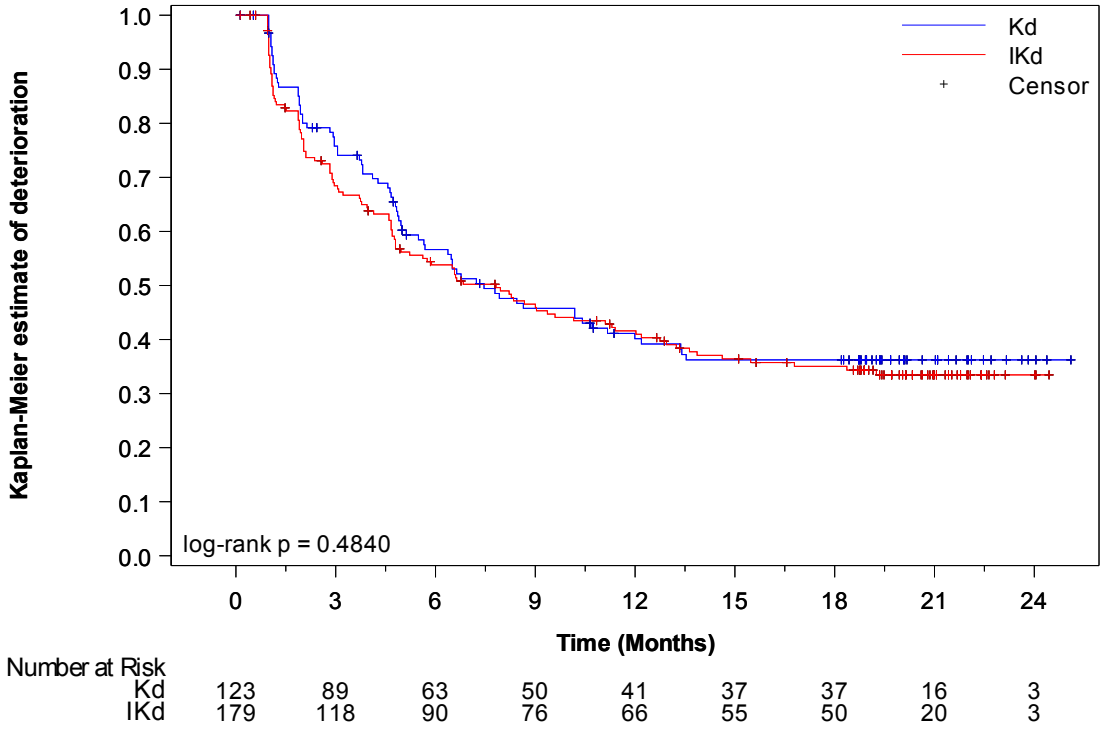
A lower score represents a better level of quality of life. Clinical meaningful improvement change from baseline less than or equal to -15 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
PGM=DEVOPS/SAR650984/EFC15246/CIR_RWE/REPORT/PGM/eff_qlq_km_i_f.sas OUT=REPORT/OUTPUT/eff_km_c30_cog_imp15l_de_i_f_x.rtf (07APR2021 14:23)

16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Cognitive functioning
16.2.6.1.2.1 Efficacy response data
16.2.6.1.2.1.17 QLQ-C30 - Time to first deterioration by 15 pt in Cognitive functioning (LOCF) - ITT population

First deterioration 15 points Cognitive functioning (%)	**Kd (N=123)**	**IKd (N=179)**
Number (%) of events	73 (59.3)	112 (62.6)
Number (%) of patients censored	50 (40.7)	67 (37.4)
Kaplan-Meier estimates of Cognitive functioning in months		
25% quantile (95% CI)	3.06 (1.938 to 4.632)	2.04 (1.873 to 2.957)
Median (95% CI)	7.46 (5.125 to 11.992)	7.82 (4.797 to 11.302)
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)
Comparison vs. Kd		
Stratified[a] Log-Rank test p-value[b] vs Kd	-	0.4840
Stratified[a] Hazard ratio (95% CI) vs Kd	-	1.11 (0.82 to 1.50)
P-value	-	0.4842
Deterioration probability (95% CI)[c]		
3 Months	0.758 (0.671 to 0.825)	0.684 (0.610 to 0.748)
6 Months	0.566 (0.472 to 0.651)	0.538 (0.461 to 0.609)

A lower score represents a better level of quality of life. Clinical meaningful deterioration change from baseline greater than or equal to 15 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] Stratified on number of prior lines of therapy (1 vs. >1) and Revised International Staging System (R-ISS) stage (I or II vs. III vs. not classified) according to IRT
[b] One-sided significance level is 0.025
[c] Estimated using the Kaplan-Meier method
NA/NC = Not Applicable / Not Calculable
PGM=DEVOPS/SAR650984/EFC15246/CIR_RWE/REPORT/PGM/eff_km_invhr_sr_i_t.sas OUT=REPORT/OUTPUT/eff_km_c30_cog_det15l_de_i_t_x.rtf (07APR2021 14:22)

16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Cognitive functioning
16.2.6.1.2.1 Efficacy response data
16.2.6.1.2.1.18 QLQ-C30 - Time to first deterioration by 15 pt in Cognitive functioning - Kaplan-Meier curve (LOCF) - ITT population



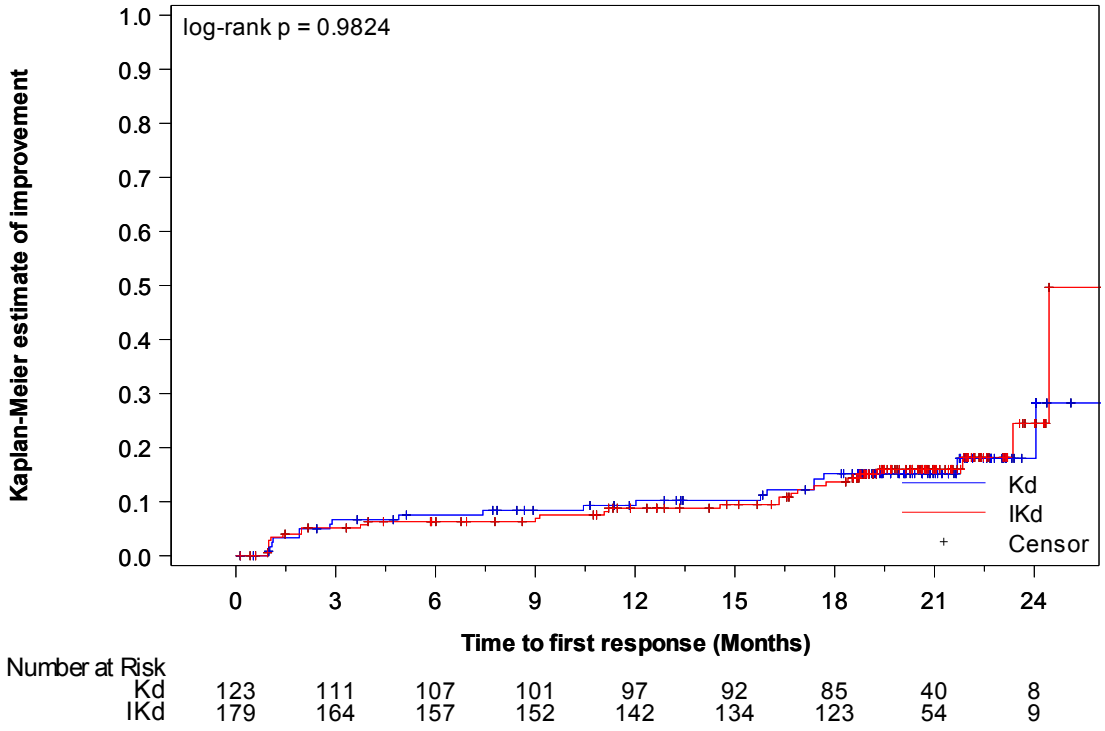
A lower score represents a better level of quality of life. Clinical meaningful deterioration change from baseline greater than or equal to 15 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
PGM=DEVOPS/SAR650984/EFC15246/CIR_RWE/REPORT/PGM/eff_qlq_km_i_f.sas OUT=REPORT/OUTPUT/eff_km_c30_cog_det15l_de_i_f_x.rtf (07APR2021 14:23)

16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Cognitive functioning
16.2.6.1.2.1 Efficacy response data
16.2.6.1.2.1.19 QLQ-C30 - Time until permanent improvement by 15 pt in Cognitive functioning (LOCF) - ITT population

First permanent improvement 15 points Cognitive functioning (%)	Kd (N=123)	IKd (N=179)
Number (%) of events	19 (15.4)	28 (15.6)
Number (%) of patients censored	104 (84.6)	151 (84.4)
Kaplan-Meier estimates of Cognitive functioning in months		
25% quantile (95% CI)	24.05 (21.684 to NC)	24.44 (21.848 to NC)
Median (95% CI)	NC (24.049 to NC)	NC (24.444 to NC)
75% quantile (95% CI)	NC (NC to NC)	NC (24.444 to NC)
Comparison vs. Kd		
Stratified[a] Log-Rank test p-value[b] vs Kd	-	0.9824
Stratified[a] Hazard ratio (95% CI) vs Kd	-	1.01 (0.56 to 1.82)
P-value	-	0.9824
Improvement probability (95% CI)[c]		
3 Months	0.067 (0.031 to 0.121)	0.051 (0.025 to 0.091)
6 Months	0.075 (0.037 to 0.132)	0.063 (0.033 to 0.106)

A lower score represents a better level of quality of life. Clinical meaningful improvement change from baseline less than or equal to -15 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] Stratified on number of prior lines of therapy (1 vs. >1) and Revised International Staging System (R-ISS) stage (I or II vs. III vs. not classified) according to IRT
[b] One-sided significance level is 0.025
[c] Estimated using the Kaplan-Meier method
NA/NC = Not Applicable / Not Calculable
PGM=DEVOPS/SAR650984/EFC15246/CIR_RWE/REPORT/PGM/eff_km_invhr_sr_i_t.sas OUT=REPORT/OUTPUT/eff_km_c30_cog_imp15pl_de_i_t_x.rtf (07APR2021 14:22)

16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Cognitive functioning
16.2.6.1.2.1 Efficacy response data
16.2.6.1.2.1.20 QLQ-C30 - Time until permanent improvement by 15 pt in Cognitive functioning - Kaplan-Meier curve (LOCF) - ITT population



A lower score represents a better level of quality of life. Clinical meaningful improvement change from baseline less than or equal to -15 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
PGM=DEVOPS/SAR650984/EFC15246/CIR_RWE/REPORT/PGM/eff_qlq_km_i_f.sas OUT=REPORT/OUTPUT/eff_km_c30_cog_imp15pl_de_i_f_x.rtf (07APR2021 14:24)

16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Cognitive functioning
16.2.6.1.2.1 Efficacy response data
16.2.6.1.2.1.21 QLQ-C30 - Time until permanent deterioration by 15 pt in Cognitive functioning (LOCF) - ITT population

First permanent deterioration 15 points Cognitive functioning (%)	Kd (N=123)	IKd (N=179)
Number (%) of events	38 (30.9)	59 (33.0)
Number (%) of patients censored	85 (69.1)	120 (67.0)
Kaplan-Meier estimates of Cognitive functioning in months		
25% quantile (95% CI)	16.82 (8.444 to 20.600)	13.14 (10.185 to 18.070)
Median (95% CI)	NC (21.520 to NC)	NC (23.097 to NC)
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)
Comparison vs. Kd		
Stratified[a] Log-Rank test p-value[b] vs Kd	-	0.5598
Stratified[a] Hazard ratio (95% CI) vs Kd	-	1.13 (0.75 to 1.71)
P-value	-	0.5600
Deterioration probability (95% CI)[c]		
3 Months	0.933 (0.871 to 0.966)	0.908 (0.855 to 0.943)
6 Months	0.890 (0.818 to 0.935)	0.879 (0.821 to 0.920)

A lower score represents a better level of quality of life. Clinical meaningful deterioration change from baseline greater than or equal to 15 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] Stratified on number of prior lines of therapy (1 vs. >1) and Revised International Staging System (R-ISS) stage (I or II vs. III vs. not classified) according to IRT
[b] One-sided significance level is 0.025
[c] Estimated using the Kaplan-Meier method
NA/NC = Not Applicable / Not Calculable
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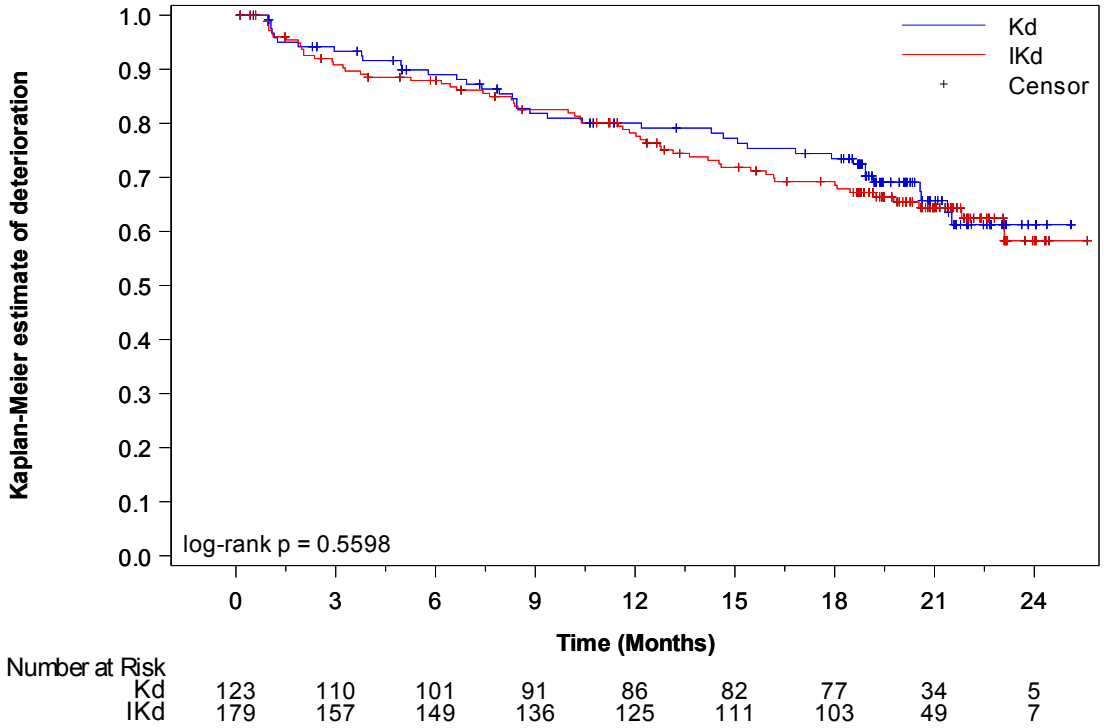
16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Cognitive functioning
16.2.6.1.2.1 Efficacy response data
16.2.6.1.2.1.22 QLQ-C30 - Time until permanent deterioration by 15 pt in Cognitive functioning - Kaplan-Meier curve (LOCF) - ITT population



A lower score represents a better level of quality of life. Clinical meaningful deterioration change from baseline greater than or equal to 15 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
PGM=DEVOPS/SAR650984/EFC15246/CIR_RWE/REPORT/PGM/eff_qlq_km_i_f.sas OUT=REPORT/OUTPUT/eff_km_c30_cog_det15pl_de_i_f_x.rtf (07APR2021 14:24)

16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Cognitive functioning
16.2.6.1.2.2 Efficacy response data - Subgroup analyses by age
16.2.6.1.2.2.3 QLQ-C30 - Time to first improvement by 10 pt in cognitive functioning according to age (LOCF) - ITT population

	<65 years		>=65 years		
	Kd (N=66)	**IKd (N=88)**	**Kd (N=57)**	**IKd (N=91)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	27 (40.9)	31 (35.2)	27 (47.4)	38 (41.8)	0.8939
Number (%) of patients censored	39 (59.1)	57 (64.8)	30 (52.6)	53 (58.2)	
Kaplan-Meier estimates of Cognitive functioning in months					
25% quantile (95% CI)	1.91 (1.018 to 4.008)	1.91 (1.051 to 17.840)	1.91 (1.084 to 3.187)	1.97 (1.150 to 2.825)	
Median (95% CI)	NC (8.706 to NC)	NC (21.848 to NC)	NC (3.187 to NC)	NC (3.877 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.4678		0.5701	
Hazard ratio (95% CI) vs Kd	-	0.83 (0.49 to 1.38)		0.87 (0.53 to 1.42)	
P-value	-	0.4685		0.5705	
Improvement probability (95% CI)[b]					

A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Cognitive functioning
16.2.6.1.2.2 Efficacy response data - Subgroup analyses by age
16.2.6.1.2.2.4 QLQ-C30 - Time to first deterioration by 10 pt in cognitive functioning according to age (LOCF) - ITT population

	<65 years		>=65 years		
	Kd (N=66)	**IKd (N=88)**	**Kd (N=57)**	**IKd (N=91)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	34 (51.5)	48 (54.5)	39 (68.4)	64 (70.3)	0.9577
Number (%) of patients censored	32 (48.5)	40 (45.5)	18 (31.6)	27 (29.7)	
Kaplan-Meier estimates of Cognitive functioning in months					
25% quantile (95% CI)	3.06 (1.906 to 4.731)	2.10 (1.084 to 3.745)	3.06 (1.248 to 4.830)	2.04 (1.216 to 3.220)	
Median (95% CI)	6.77 (4.862 to NC)	11.10 (4.698 to NC)	7.46 (4.830 to 10.710)	6.57 (4.665 to 9.002)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (10.710 to NC)	19.25 (11.302 to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.7091		0.6974	
Hazard ratio (95% CI) vs Kd	-	1.09 (0.70 to 1.69)		1.08 (0.73 to 1.61)	
P-value	-	0.7092		0.6974	
Deterioration probability (95% CI)[b]					

A higher score represents a better level of quality of life. Clinical meaningful deterioration change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Cognitive functioning
16.2.6.1.2.2 Efficacy response data - Subgroup analyses by age
16.2.6.1.2.2.5 QLQ-C30 - Time until permanent improvement by 10 pt in cognitive functioning according to age (LOCF) - ITT population

	<65 years		>=65 years		
	Kd (N=66)	**IKd (N=88)**	**Kd (N=57)**	**IKd (N=91)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	10 (15.2)	16 (18.2)	9 (15.8)	12 (13.2)	0.5187
Number (%) of patients censored	56 (84.8)	72 (81.8)	48 (84.2)	79 (86.8)	
Kaplan-Meier estimates of Cognitive functioning in months					
25% quantile (95% CI)	NC (17.380 to NC)	21.85 (17.741 to NC)	24.05 (17.676 to NC)	24.44 (23.359 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (24.049 to NC)	NC (23.359 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (24.049 to NC)	NC (24.444 to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.6253		0.7407	
Hazard ratio (95% CI) vs Kd	-	1.22 (0.55 to 2.68)		0.86 (0.36 to 2.05)	
P-value	-	0.6259		0.7409	
Improvement probability (95% CI)[b]					

A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
PGM=DEVOPS/SAR650984/EFC15246/CIR_RWE/REPORT/PGM/eff_km_subgp_sr_sig_de_i_t.sas OUT=REPORT/OUTPUT/eff_km_c30_cog_imppl_age_de_i_t_x.rtf (07APR2021 14:26)

16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Cognitive functioning
16.2.6.1.2.2 Efficacy response data - Subgroup analyses by age
16.2.6.1.2.2.6 QLQ-C30 - Time until permanent deterioration by 10 pt in cognitive functioning according to age (LOCF) - ITT population

	<65 years		>=65 years		
	Kd (N=66)	**IKd (N=88)**	**Kd (N=57)**	**IKd (N=91)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	19 (28.8)	26 (29.5)	19 (33.3)	33 (36.3)	0.9297
Number (%) of patients censored	47 (71.2)	62 (70.5)	38 (66.7)	58 (63.7)	
Kaplan-Meier estimates of Cognitive functioning in months					
25% quantile (95% CI)	18.92 (8.838 to 21.520)	12.32 (6.637 to NC)	14.29 (6.932 to 20.567)	14.52 (8.476 to 19.253)	
Median (95% CI)	NC (21.388 to NC)	NC (NC to NC)	NC (20.567 to NC)	23.10 (20.534 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.7876		0.8631	
Hazard ratio (95% CI) vs Kd	-	1.08 (0.60 to 1.96)		1.05 (0.60 to 1.85)	
P-value	-	0.7887		0.8640	
Deterioration probability (95% CI)[b]					

A higher score represents a better level of quality of life. Clinical meaningful deterioration change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Cognitive functioning
16.2.6.1.2.3 Efficacy response data - Subgroup analyses by gender
16.2.6.1.2.3.3 QLQ-C30 - Time to first improvement by 10 pt in cognitive functioning according to gender (LOCF) - ITT population

	Male		Female		
	Kd (N=68)	**IKd (N=101)**	**Kd (N=55)**	**IKd (N=78)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	26 (38.2)	39 (38.6)	28 (50.9)	30 (38.5)	0.3565
Number (%) of patients censored	42 (61.8)	62 (61.4)	27 (49.1)	48 (61.5)	
Kaplan-Meier estimates of Cognitive functioning in months					
25% quantile (95% CI)	1.97 (1.084 to 8.706)	2.00 (1.216 to 3.745)	1.87 (1.018 to 2.037)	1.15 (1.051 to 2.825)	
Median (95% CI)	NC (10.480 to NC)	NC (21.848 to NC)	8.08 (2.037 to NC)	NC (15.277 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.9918		0.2218	
Hazard ratio (95% CI) vs Kd	-	1.00 (0.61 to 1.65)		0.73 (0.43 to 1.22)	
P-value	-	0.9918		0.2238	
Improvement probability (95% CI)[b]					

A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Cognitive functioning
16.2.6.1.2.3 Efficacy response data - Subgroup analyses by gender
16.2.6.1.2.3.4 QLQ-C30 - Time to first deterioration by 10 pt in cognitive functioning according to gender (LOCF) - ITT population

	Male		Female		
	Kd (N=68)	**IKd (N=101)**	**Kd (N=55)**	**IKd (N=78)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	38 (55.9)	56 (55.4)	35 (63.6)	56 (71.8)	0.5564
Number (%) of patients censored	30 (44.1)	45 (44.6)	20 (36.4)	22 (28.2)	
Kaplan-Meier estimates of Cognitive functioning in months					
25% quantile (95% CI)	4.63 (2.136 to 4.961)	2.04 (1.511 to 4.600)	2.00 (1.216 to 3.811)	2.10 (1.150 to 3.055)	
Median (95% CI)	7.23 (4.994 to NC)	9.36 (5.618 to 19.253)	7.46 (3.811 to 13.372)	4.96 (3.713 to 9.035)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (11.992 to NC)	NC (11.302 to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.9958		0.4075	
Hazard ratio (95% CI) vs Kd	-	1.00 (0.66 to 1.51)		1.20 (0.78 to 1.82)	
P-value	-	0.9958		0.4081	
Deterioration probability (95% CI)[b]					

A higher score represents a better level of quality of life. Clinical meaningful deterioration change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Cognitive functioning
16.2.6.1.2.3 Efficacy response data - Subgroup analyses by gender
16.2.6.1.2.3.5 QLQ-C30 - Time until permanent improvement by 10 pt in cognitive functioning according to gender (LOCF) - ITT population

	Male		Female		
	Kd (N=68)	**IKd (N=101)**	**Kd (N=55)**	**IKd (N=78)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	9 (13.2)	15 (14.9)	10 (18.2)	13 (16.7)	0.7101
Number (%) of patients censored	59 (86.8)	86 (85.1)	45 (81.8)	65 (83.3)	
Kaplan-Meier estimates of Cognitive functioning in months					
25% quantile (95% CI)	NC (21.684 to NC)	NC (18.760 to NC)	24.05 (17.380 to NC)	23.36 (19.285 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (24.049 to NC)	24.44 (23.359 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (24.049 to NC)	NC (24.444 to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.7878		0.8607	
Hazard ratio (95% CI) vs Kd	-	1.12 (0.49 to 2.56)		0.93 (0.41 to 2.12)	
P-value	-	0.7879		0.8607	
Improvement probability (95% CI)[b]					

A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Cognitive functioning
16.2.6.1.2.3 Efficacy response data - Subgroup analyses by gender
16.2.6.1.2.3.6 QLQ-C30 - Time until permanent deterioration by 10 pt in cognitive functioning according to gender (LOCF) - ITT population

	Male		Female		
	Kd (N=68)	**IKd (N=101)**	**Kd (N=55)**	**IKd (N=78)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	17 (25.0)	31 (30.7)	21 (38.2)	28 (35.9)	0.4025
Number (%) of patients censored	51 (75.0)	70 (69.3)	34 (61.8)	50 (64.1)	
Kaplan-Meier estimates of Cognitive functioning in months					
25% quantile (95% CI)	18.56 (9.363 to NC)	13.14 (10.349 to 19.778)	15.08 (3.811 to 19.154)	12.78 (7.425 to 18.464)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (19.154 to NC)	NC (21.815 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.3948		0.7589	
Hazard ratio (95% CI) vs Kd	-	1.29 (0.71 to 2.33)		0.92 (0.52 to 1.61)	
P-value	-	0.3961		0.7590	
Deterioration probability (95% CI)[b]					

A higher score represents a better level of quality of life. Clinical meaningful deterioration change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Cognitive functioning
16.2.6.1.2.4 Efficacy response data - Subgroup analyses by ethnic origin
16.2.6.1.2.4.3 QLQ-C30 - Time to first improvement by 10 pt in cognitive functioning according to ethnic origin (LOCF) - ITT population

	White		Other		
	Kd (N=83)	**IKd (N=131)**	**Kd (N=28)**	**IKd (N=34)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	39 (47.0)	51 (38.9)	13 (46.4)	12 (35.3)	0.8628
Number (%) of patients censored	44 (53.0)	80 (61.1)	15 (53.6)	22 (64.7)	
Kaplan-Meier estimates of Cognitive functioning in months					
25% quantile (95% CI)	1.91 (1.051 to 2.004)	1.91 (1.051 to 2.825)	1.91 (1.018 to 6.308)	4.14 (0.986 to 21.848)	
Median (95% CI)	NC (3.745 to NC)	NC (NC to NC)	19.71 (2.037 to NC)	NC (9.331 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.3033		0.3645	
Hazard ratio (95% CI) vs Kd	-	0.80 (0.53 to 1.22)		0.70 (0.32 to 1.53)	
P-value	-	0.3042		0.3671	
Improvement probability (95% CI)[b]					

A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Cognitive functioning
16.2.6.1.2.4 Efficacy response data - Subgroup analyses by ethnic origin
16.2.6.1.2.4.4 QLQ-C30 - Time to first deterioration by 10 pt in cognitive functioning according to ethnic origin (LOCF) - ITT population

	White		Other		
	Kd (N=83)	**IKd (N=131)**	**Kd (N=28)**	**IKd (N=34)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	50 (60.2)	83 (63.4)	17 (60.7)	24 (70.6)	0.6511
Number (%) of patients censored	33 (39.8)	48 (36.6)	11 (39.3)	10 (29.4)	
Kaplan-Meier estimates of Cognitive functioning in months					
25% quantile (95% CI)	3.06 (1.906 to 4.632)	2.37 (1.873 to 3.713)	2.92 (1.084 to 4.731)	1.15 (0.986 to 2.825)	
Median (95% CI)	7.46 (4.895 to 13.405)	6.60 (4.797 to 11.302)	6.51 (2.957 to NC)	6.64 (1.873 to 8.345)	
75% quantile (95% CI)	NC (NC to NC)	NC (19.253 to NC)	NC (7.228 to NC)	18.37 (8.214 to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.5986		0.3899	
Hazard ratio (95% CI) vs Kd	-	1.10 (0.77 to 1.56)		1.31 (0.70 to 2.44)	
P-value	-	0.5987		0.3914	
Deterioration probability (95% CI)[b]					

A higher score represents a better level of quality of life. Clinical meaningful deterioration change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Cognitive functioning
16.2.6.1.2.4 Efficacy response data - Subgroup analyses by ethnic origin
16.2.6.1.2.4.5 QLQ-C30 - Time until permanent improvement by 10 pt in cognitive functioning according to ethnic origin (LOCF) - ITT population

	White		Other		
	Kd (N=83)	**IKd (N=131)**	**Kd (N=28)**	**IKd (N=34)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	14 (16.9)	17 (13.0)	4 (14.3)	7 (20.6)	0.2918
Number (%) of patients censored	69 (83.1)	114 (87.0)	24 (85.7)	27 (79.4)	
Kaplan-Meier estimates of Cognitive functioning in months					
25% quantile (95% CI)	24.05 (17.380 to NC)	24.44 (23.359 to NC)	NC (1.117 to NC)	21.85 (16.690 to NC)	
Median (95% CI)	NC (24.049 to NC)	24.44 (24.444 to NC)	NC (NC to NC)	NC (21.848 to NC)	
75% quantile (95% CI)	NC (24.049 to NC)	NC (24.444 to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.4046		0.5211	
Hazard ratio (95% CI) vs Kd	-	0.74 (0.36 to 1.51)		1.49 (0.44 to 5.10)	
P-value	-	0.4064		0.5239	
Improvement probability (95% CI)[b]					

A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Cognitive functioning
16.2.6.1.2.4 Efficacy response data - Subgroup analyses by ethnic origin
16.2.6.1.2.4.6 QLQ-C30 - Time until permanent deterioration by 10 pt in cognitive functioning according to ethnic origin (LOCF) - ITT population

	White		Other		
	Kd (N=83)	**IKd (N=131)**	**Kd (N=28)**	**IKd (N=34)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	23 (27.7)	45 (34.4)	10 (35.7)	12 (35.3)	0.6661
Number (%) of patients censored	60 (72.3)	86 (65.6)	18 (64.3)	22 (64.7)	
Kaplan-Meier estimates of Cognitive functioning in months					
25% quantile (95% CI)	18.92 (8.444 to NC)	12.78 (8.279 to 18.464)	15.38 (2.957 to 21.520)	12.75 (2.037 to 16.164)	
Median (95% CI)	NC (NC to NC)	NC (21.815 to NC)	NC (17.906 to NC)	NC (13.634 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.3139		0.8447	
Hazard ratio (95% CI) vs Kd	-	1.29 (0.78 to 2.14)		1.09 (0.47 to 2.52)	
P-value	-	0.3153		0.8451	
Deterioration probability (95% CI)[b]					

A higher score represents a better level of quality of life. Clinical meaningful deterioration change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Cognitive functioning
16.2.6.1.2.5 Efficacy response data - Subgroup analyses by geographical region
16.2.6.1.2.5.3 QLQ-C30 - Time to first improvement by 10 pt in cognitive functioning according to geographical region (LOCF) - ITT population

	Europe		America		Asia		Other countries		
	Kd (N=60)	**IKd (N=85)**	**Kd (N=20)**	**IKd (N=24)**	**Kd (N=21)**	**IKd (N=25)**	**Kd (N=22)**	**IKd (N=45)**	**p-value of treatment-by-subgroup interaction[c]**
Number (%) of events	21 (35.0)	31 (36.5)	11 (55.0)	7 (29.2)	11 (52.4)	9 (36.0)	11 (50.0)	22 (48.9)	0.3377
Number (%) of patients censored	39 (65.0)	54 (63.5)	9 (45.0)	17 (70.8)	10 (47.6)	16 (64.0)	11 (50.0)	23 (51.1)	
Kaplan-Meier estimates of event in months									
25% quantile (95% CI)	1.91 (1.051 to 10.546)	1.97 (1.084 to 4.632)	1.46 (0.986 to 1.938)	4.14 (0.986 to NC)	1.58 (0.986 to 6.308)	1.99 (0.920 to NC)	2.04 (0.986 to 5.618)	1.15 (1.018 to 2.004)	
Median (95% CI)	NC (10.546 to NC)	NC (NC to NC)	2.09 (1.051 to NC)	NC (4.140 to NC)	8.71 (1.117 to NC)	NC (2.004 to NC)	NC (2.037 to NC)	NC (1.971 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (2.201 to NC)	NC (NC to NC)	NC (8.706 to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	

A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Cognitive functioning
16.2.6.1.2.5 Efficacy response data - Subgroup analyses by geographical region
16.2.6.1.2.5.3 QLQ-C30 - Time to first improvement by 10 pt in cognitive functioning according to geographical region (LOCF) - ITT population

	Europe		America		Asia		Other countries		
	Kd (N=60)	**IKd (N=85)**	**Kd (N=20)**	**IKd (N=24)**	**Kd (N=21)**	**IKd (N=25)**	**Kd (N=22)**	**IKd (N=45)**	**p-value of treatment-by-subgroup interaction[c]**
Comparison vs. Kd									
Log-Rank test p-value[a] vs Kd	-	0.8745		0.0688		0.2549		0.8196	
Hazard ratio (95% CI) vs Kd	-	1.05 (0.60 to 1.82)		0.42 (0.16 to 1.10)		0.60 (0.25 to 1.46)		1.09 (0.53 to 2.24)	
P-value	-	0.8750		0.0773		0.2598		0.8197	
Improvement probability (95% CI)[b]									
3 Months	0.292 (0.182 to 0.411)	0.338 (0.239 to 0.440)	0.550 (0.313 to 0.735)	0.224 (0.081 to 0.410)	0.300 (0.123 to 0.501)	0.292 (0.130 to 0.476)	0.273 (0.111 to 0.464)	0.422 (0.278 to 0.560)	

A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Cognitive functioning
16.2.6.1.2.5 Efficacy response data - Subgroup analyses by geographical region
16.2.6.1.2.5.4 QLQ-C30 - Time to first deterioration by 10 pt in cognitive functioning according to geographical region (LOCF) - ITT population

	Europe		America		Asia		Other countries		
	Kd (N=60)	**IKd (N=85)**	**Kd (N=20)**	**IKd (N=24)**	**Kd (N=21)**	**IKd (N=25)**	**Kd (N=22)**	**IKd (N=45)**	**p-value of treatment-by-subgroup interaction[c]**
Number (%) of events	31 (51.7)	49 (57.6)	12 (60.0)	13 (54.2)	11 (52.4)	18 (72.0)	19 (86.4)	32 (71.1)	0.4940
Number (%) of patients censored	29 (48.3)	36 (42.4)	8 (40.0)	11 (45.8)	10 (47.6)	7 (28.0)	3 (13.6)	13 (28.9)	
Kaplan-Meier estimates of event in months									
25% quantile (95% CI)	4.67 (1.873 to 6.505)	3.22 (1.906 to 4.961)	4.42 (1.281 to 4.895)	1.97 (0.953 to 2.891)	2.53 (1.051 to 4.731)	1.51 (0.986 to 2.825)	1.94 (0.986 to 3.055)	1.87 (1.051 to 3.088)	
Median (95% CI)	11.99 (6.505 to NC)	11.40 (6.505 to 19.253)	6.55 (4.271 to NC)	5.88 (1.971 to NC)	7.23 (2.136 to NC)	5.67 (1.873 to 13.864)	3.94 (1.938 to 8.641)	4.80 (2.891 to 9.363)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (7.458 to NC)	NC (5.881 to NC)	NC (7.786 to NC)	18.37 (6.834 to NC)	10.41 (4.830 to NC)	NC (9.035 to NC)	

A higher score represents a better level of quality of life. Clinical meaningful deterioration change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
PGM=DEVOPS/SAR650984/EFC15246/CIR_RWE/REPORT/PGM/eff_km_subgp_sr_sig_de_i_t.sas OUT=REPORT/OUTPUT/eff_km_c30_cog_detl_greg_de_i_t_x.rtf (07APR2021 14:25)

16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Cognitive functioning
16.2.6.1.2.5 Efficacy response data - Subgroup analyses by geographical region
16.2.6.1.2.5.4 QLQ-C30 - Time to first deterioration by 10 pt in cognitive functioning according to geographical region (LOCF) - ITT population

	Europe		America		Asia		Other countries		
	Kd (N=60)	**IKd (N=85)**	**Kd (N=20)**	**IKd (N=24)**	**Kd (N=21)**	**IKd (N=25)**	**Kd (N=22)**	**IKd (N=45)**	**p-value of treatment-by-subgroup interaction[c]**
Comparison vs. Kd									
Log-Rank test p-value[a] vs Kd	-	0.7006		0.6163		0.2941		0.3554	
Hazard ratio (95% CI) vs Kd	-	1.09 (0.70 to 1.71)		1.22 (0.56 to 2.69)		1.49 (0.70 to 3.16)		0.77 (0.43 to 1.35)	
P-value	-	0.7007		0.6169		0.2973		0.3568	
Deterioration probability (95% CI)[b]									
3 Months	0.811 (0.685 to 0.891)	0.771 (0.664 to 0.847)	0.900 (0.656 to 0.974)	0.552 (0.327 to 0.729)	0.643 (0.393 to 0.812)	0.583 (0.364 to 0.750)	0.591 (0.361 to 0.762)	0.644 (0.487 to 0.765)	

A higher score represents a better level of quality of life. Clinical meaningful deterioration change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Cognitive functioning
16.2.6.1.2.5 Efficacy response data - Subgroup analyses by geographical region
16.2.6.1.2.5.5 QLQ-C30 - Time until permanent improvement by 10 pt in cognitive functioning according to geographical region (LOCF) - ITT population

	Europe		America		Asia		Other countries		
	Kd (N=60)	**IKd (N=85)**	**Kd (N=20)**	**IKd (N=24)**	**Kd (N=21)**	**IKd (N=25)**	**Kd (N=22)**	**IKd (N=45)**	**p-value of treatment-by-subgroup interaction[c]**
Number (%) of events	9 (15.0)	14 (16.5)	5 (25.0)	4 (16.7)	3 (14.3)	5 (20.0)	2 (9.1)	5 (11.1)	0.8771
Number (%) of patients censored	51 (85.0)	71 (83.5)	15 (75.0)	20 (83.3)	18 (85.7)	20 (80.0)	20 (90.9)	40 (88.9)	
Kaplan-Meier estimates of event in months									
25% quantile (95% CI)	NC (10.448 to NC)	23.36 (18.760 to 24.444)	17.38 (4.895 to NC)	NC (0.986 to NC)	NC (1.018 to NC)	21.85 (1.971 to NC)	24.05 (15.967 to 24.049)	NC (16.329 to NC)	
Median (95% CI)	NC (NC to NC)	24.44 (23.359 to 24.444)	NC (17.380 to NC)	NC (NC to NC)	NC (NC to NC)	NC (19.285 to NC)	24.05 (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	24.44 (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	24.05 (NC to NC)	NC (NC to NC)	

A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Cognitive functioning
16.2.6.1.2.5 Efficacy response data - Subgroup analyses by geographical region
16.2.6.1.2.5.5 QLQ-C30 - Time until permanent improvement by 10 pt in cognitive functioning according to geographical region (LOCF) - ITT population

	Europe		America		Asia		Other countries		
	Kd (N=60)	**IKd (N=85)**	**Kd (N=20)**	**IKd (N=24)**	**Kd (N=21)**	**IKd (N=25)**	**Kd (N=22)**	**IKd (N=45)**	**p-value of treatment-by-subgroup interaction[c]**
Comparison vs. Kd									
Log-Rank test p-value[a] vs Kd	-	0.9802		0.6713		0.6206		0.7357	
Hazard ratio (95% CI) vs Kd	-	0.99 (0.42 to 2.31)		0.75 (0.20 to 2.81)		1.43 (0.34 to 6.00)		1.33 (0.26 to 6.83)	
P-value	-	0.9802		0.6723		0.6225		0.7366	
Improvement probability (95% CI)[b]									
3 Months	0.103 (0.042 to 0.197)	0.072 (0.030 to 0.141)		0.043 (0.003 to 0.182)	0.100 (0.017 to 0.272)	0.042 (0.003 to 0.176)		0.022 (0.002 to 0.101)	

A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Cognitive functioning
16.2.6.1.2.5 Efficacy response data - Subgroup analyses by geographical region
16.2.6.1.2.5.6 QLQ-C30 - Time until permanent deterioration by 10 pt in cognitive functioning according to geographical region (LOCF) - ITT population

	Europe		**America**		**Asia**		**Other countries**		
	Kd (N=60)	**IKd (N=85)**	**Kd (N=20)**	**IKd (N=24)**	**Kd (N=21)**	**IKd (N=25)**	**Kd (N=22)**	**IKd (N=45)**	**p-value of treatment-by-subgroup interaction[c]**
Number (%) of events	18 (30.0)	23 (27.1)	5 (25.0)	8 (33.3)	8 (38.1)	9 (36.0)	7 (31.8)	19 (42.2)	0.5584
Number (%) of patients censored	42 (70.0)	62 (72.9)	15 (75.0)	16 (66.7)	13 (61.9)	16 (64.0)	15 (68.2)	26 (57.8)	
Kaplan-Meier estimates of event in months									
25% quantile (95% CI)	18.92 (8.312 to 21.388)	19.25 (12.780 to NC)	18.92 (3.778 to NC)	6.44 (0.986 to NC)	10.41 (1.051 to 21.520)	10.18 (0.986 to NC)	8.44 (1.084 to NC)	10.38 (3.745 to 18.070)	
Median (95% CI)	NC (20.600 to NC)	NC (NC to NC)	NC (18.924 to NC)	NC (6.439 to NC)	NC (10.415 to NC)	NC (11.828 to NC)	NC (8.444 to NC)	23.10 (14.587 to NC)	

A higher score represents a better level of quality of life. Clinical meaningful deterioration change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Cognitive functioning
16.2.6.1.2.5 Efficacy response data - Subgroup analyses by geographical region
16.2.6.1.2.5.6 QLQ-C30 - Time until permanent deterioration by 10 pt in cognitive functioning according to geographical region (LOCF) - ITT population

	Europe		America		Asia		Other countries		
	Kd (N=60)	**IKd (N=85)**	**Kd (N=20)**	**IKd (N=24)**	**Kd (N=21)**	**IKd (N=25)**	**Kd (N=22)**	**IKd (N=45)**	**p-value of treatment-by-subgroup interaction[c]**
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (21.520 to NC)	NC (NC to NC)	NC (NC to NC)	NC (23.097 to NC)	
Comparison vs. Kd									
Log-Rank test p-value[a] vs Kd	-	0.5478		0.2569		0.9301		0.4961	
Hazard ratio (95% CI) vs Kd	-	0.83 (0.45 to 1.53)		1.89 (0.62 to 5.83)		0.96 (0.37 to 2.48)		1.35 (0.57 to 3.21)	
P-value	-	0.5484		0.2648		0.9300		0.4978	
Deterioration probability (95% CI)[b]									

A higher score represents a better level of quality of life. Clinical meaningful deterioration change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Cognitive functioning
16.2.6.1.2.6 Efficacy response data - Subgroup analyses by regulatory region
16.2.6.1.2.6.3 QLQ-C30 - Time to first improvement by 10 pt in cognitive functioning according to regulatory region (LOCF) - ITT population

	Western countries		Other countries		
	Kd (N=55)	**IKd (N=97)**	**Kd (N=68)**	**IKd (N=82)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	24 (43.6)	38 (39.2)	30 (44.1)	31 (37.8)	0.9708
Number (%) of patients censored	31 (56.4)	59 (60.8)	38 (55.9)	51 (62.2)	
Kaplan-Meier estimates of Cognitive functioning in months					
25% quantile (95% CI)	1.91 (1.051 to 3.778)	1.97 (1.216 to 2.825)	1.91 (1.051 to 2.201)	1.26 (1.018 to 4.632)	
Median (95% CI)	NC (3.745 to NC)	NC (15.277 to NC)	NC (3.187 to NC)	NC (21.848 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.5537		0.5764	
Hazard ratio (95% CI) vs Kd	-	0.86 (0.51 to 1.43)		0.87 (0.52 to 1.43)	
P-value	-	0.5541		0.5767	
Improvement probability (95% CI)[b]					

A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Cognitive functioning
16.2.6.1.2.6 Efficacy response data - Subgroup analyses by regulatory region
16.2.6.1.2.6.4 QLQ-C30 - Time to first deterioration by 10 pt in cognitive functioning according to regulatory region (LOCF) - ITT population

	Western countries		Other countries		
	Kd (N=55)	**IKd (N=97)**	**Kd (N=68)**	**IKd (N=82)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	32 (58.2)	54 (55.7)	41 (60.3)	58 (70.7)	0.1653
Number (%) of patients censored	23 (41.8)	43 (44.3)	27 (39.7)	24 (29.3)	
Kaplan-Meier estimates of Cognitive functioning in months					
25% quantile (95% CI)	3.71 (1.117 to 5.684)	2.96 (2.037 to 4.665)	3.06 (1.906 to 4.632)	1.51 (1.084 to 2.366)	
Median (95% CI)	10.18 (5.684 to 13.536)	9.59 (5.749 to NC)	6.77 (4.665 to 11.992)	4.80 (2.825 to 8.279)	
75% quantile (95% CI)	NC (13.405 to NC)	NC (NC to NC)	NC (NC to NC)	18.37 (11.302 to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.6485		0.1183	
Hazard ratio (95% CI) vs Kd	-	0.90 (0.58 to 1.40)		1.37 (0.92 to 2.05)	
P-value	-	0.6486		0.1198	
Deterioration probability (95% CI)[b]					

A higher score represents a better level of quality of life. Clinical meaningful deterioration change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Cognitive functioning
16.2.6.1.2.6 Efficacy response data - Subgroup analyses by regulatory region
16.2.6.1.2.6.5 QLQ-C30 - Time until permanent improvement by 10 pt in cognitive functioning according to regulatory region (LOCF) - ITT population

	Western countries		Other countries		
	Kd (N=55)	**IKd (N=97)**	**Kd (N=68)**	**IKd (N=82)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	7 (12.7)	12 (12.4)	12 (17.6)	16 (19.5)	0.7565
Number (%) of patients censored	48 (87.3)	85 (87.6)	56 (82.4)	66 (80.5)	
Kaplan-Meier estimates of Cognitive functioning in months					
25% quantile (95% CI)	24.05 (21.684 to 24.049)	NC (NC to NC)	NC (15.967 to NC)	23.36 (17.741 to 24.444)	
Median (95% CI)	24.05 (NC to NC)	NC (NC to NC)	NC (NC to NC)	24.44 (23.359 to NC)	
75% quantile (95% CI)	24.05 (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (24.444 to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.9354		0.7198	
Hazard ratio (95% CI) vs Kd	-	0.96 (0.38 to 2.44)		1.15 (0.54 to 2.43)	
P-value	-	0.9351		0.7200	
Improvement probability (95% CI)[b]					

A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Cognitive functioning
16.2.6.1.2.6 Efficacy response data - Subgroup analyses by regulatory region
16.2.6.1.2.6.6 QLQ-C30 - Time until permanent deterioration by 10 pt in cognitive functioning according to regulatory region (LOCF) - ITT population

	Western countries		Other countries		
	Kd (N=55)	**IKd (N=97)**	**Kd (N=68)**	**IKd (N=82)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	17 (30.9)	28 (28.9)	21 (30.9)	31 (37.8)	0.3896
Number (%) of patients censored	38 (69.1)	69 (71.1)	47 (69.1)	51 (62.2)	
Kaplan-Meier estimates of Cognitive functioning in months					
25% quantile (95% CI)	14.65 (7.392 to NC)	18.00 (9.988 to NC)	16.82 (8.444 to 21.520)	11.83 (3.745 to 14.522)	
Median (95% CI)	NC (20.567 to NC)	NC (23.097 to NC)	NC (21.388 to NC)	NC (16.164 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.7476		0.3450	
Hazard ratio (95% CI) vs Kd	-	0.91 (0.50 to 1.66)		1.31 (0.75 to 2.27)	
P-value	-	0.7477		0.3464	
Deterioration probability (95% CI)[b]					

A higher score represents a better level of quality of life. Clinical meaningful deterioration change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Cognitive functioning
16.2.6.1.2.7 Efficacy response data - Subgroup analyses by baseline ECOG PS
16.2.6.1.2.7.3 QLQ-C30 - Time to first improvement by 10 pt in cognitive functioning according to baseline ECOG PS (LOCF) - ITT population

	0 or 1		>1		
	Kd (N=118)	**IKd (N=168)**	**Kd (N=5)**	**IKd (N=11)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	53 (44.9)	67 (39.9)	1 (20.0)	2 (18.2)	0.8266
Number (%) of patients censored	65 (55.1)	101 (60.1)	4 (80.0)	9 (81.8)	
Kaplan-Meier estimates of Cognitive functioning in months					
25% quantile (95% CI)	1.91 (1.084 to 2.037)	1.91 (1.117 to 2.793)	NC (3.778 to NC)	NC (1.971 to NC)	
Median (95% CI)	NC (5.618 to NC)	NC (21.848 to NC)	NC (3.778 to NC)	NC (1.971 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (3.778 to NC)	NC (NC to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.4065		0.8508	
Hazard ratio (95% CI) vs Kd	-	0.86 (0.60 to 1.23)		1.26 (0.11 to 13.92)	
P-value	-	0.4069		0.8511	
Improvement probability (95% CI)[b]					

A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
PGM=DEVOPS/SAR650984/EFC15246/CIR_RWE/REPORT/PGM/eff_km_subgp_sr_sig_de_i_t.sas OUT=REPORT/OUTPUT/eff_km_c30_cog_impl_ecog_de_i_t_x.rtf (07APR2021 14:25)

16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Cognitive functioning
16.2.6.1.2.7 Efficacy response data - Subgroup analyses by baseline ECOG PS
16.2.6.1.2.7.4 QLQ-C30 - Time to first deterioration by 10 pt in cognitive functioning according to baseline ECOG PS (LOCF) - ITT population

	0 or 1		>1		
	Kd (N=118)	**IKd (N=168)**	**Kd (N=5)**	**IKd (N=11)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	70 (59.3)	109 (64.9)	3 (60.0)	3 (27.3)	0.1691
Number (%) of patients censored	48 (40.7)	59 (35.1)	2 (40.0)	8 (72.7)	
Kaplan-Meier estimates of Cognitive functioning in months					
25% quantile (95% CI)	3.06 (1.938 to 4.665)	2.04 (1.873 to 2.924)	3.78 (0.986 to 6.637)	4.80 (1.216 to NC)	
Median (95% CI)	7.79 (5.125 to 11.992)	6.64 (4.764 to 10.152)	6.64 (0.986 to NC)	NC (1.216 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (19.253 to NC)	NC (0.986 to NC)	NC (NC to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.3774		0.2937	
Hazard ratio (95% CI) vs Kd	-	1.14 (0.85 to 1.55)		0.43 (0.09 to 2.16)	
P-value	-	0.3778		0.3075	
Deterioration probability (95% CI)[b]					

A higher score represents a better level of quality of life. Clinical meaningful deterioration change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Cognitive functioning
16.2.6.1.2.7 Efficacy response data - Subgroup analyses by baseline ECOG PS
16.2.6.1.2.7.5 QLQ-C30 - Time until permanent improvement by 10 pt in cognitive functioning according to baseline ECOG PS (LOCF) - ITT population

	0 or 1		>1		
	Kd (N=118)	**IKd (N=168)**	**Kd (N=5)**	**IKd (N=11)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	19 (16.1)	26 (15.5)	0 (0.0)	2 (18.2)	0.9872
Number (%) of patients censored	99 (83.9)	142 (84.5)	5 (100.0)	9 (81.8)	
Kaplan-Meier estimates of Cognitive functioning in months					
25% quantile (95% CI)	24.05 (21.684 to NC)	24.44 (21.848 to NC)	NC (NC to NC)	NC (1.971 to NC)	
Median (95% CI)	NC (24.049 to NC)	NC (24.444 to NC)	NC (NC to NC)	NC (1.971 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (24.444 to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.9358		0.3611	
Hazard ratio (95% CI) vs Kd	-	0.98 (0.54 to 1.76)			
P-value	-	0.9357		0.9981	
Improvement probability (95% CI)[b]					

A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Cognitive functioning
16.2.6.1.2.7 Efficacy response data - Subgroup analyses by baseline ECOG PS
16.2.6.1.2.7.6 QLQ-C30 - Time until permanent deterioration by 10 pt in cognitive functioning according to baseline ECOG PS (LOCF) - ITT population

	0 or 1		>1		
	Kd (N=118)	**IKd (N=168)**	**Kd (N=5)**	**IKd (N=11)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	35 (29.7)	56 (33.3)	3 (60.0)	3 (27.3)	0.1102
Number (%) of patients censored	83 (70.3)	112 (66.7)	2 (40.0)	8 (72.7)	
Kaplan-Meier estimates of Cognitive functioning in months					
25% quantile (95% CI)	18.56 (8.838 to 21.388)	12.75 (8.476 to 16.197)	7.39 (3.778 to 14.653)	20.53 (9.988 to NC)	
Median (95% CI)	NC (NC to NC)	NC (23.097 to NC)	14.65 (3.778 to NC)	21.82 (9.988 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (3.778 to NC)	NC (21.815 to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.4939		0.0425	
Hazard ratio (95% CI) vs Kd	-	1.16 (0.76 to 1.77)		0.18 (0.03 to 1.13)	
P-value	-	0.4943		0.0679	
Deterioration probability (95% CI)[b]					

A higher score represents a better level of quality of life. Clinical meaningful deterioration change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
PGM=DEVOPS/SAR650984/EFC15246/CIR_RWE/REPORT/PGM/eff_km_subgp_sr_sig_de_i_t.sas OUT=REPORT/OUTPUT/eff_km_c30_cog_detpl_ecog_de_i_t_x.rtf (07APR2021 14:26)

16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Cognitive functioning
16.2.6.1.2.8 Efficacy response data - Subgroup analyses by ISS staging at SE
16.2.6.1.2.8.3 QLQ-C30 - Time to first improvement by 10 pt in cognitive functioning according to ISS staging at SE (LOCF) - ITT population

	I		II		III		
	Kd (N=71)	**IKd (N=89)**	**Kd (N=31)**	**IKd (N=63)**	**Kd (N=20)**	**IKd (N=26)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	39 (54.9)	35 (39.3)	10 (32.3)	24 (38.1)	5 (25.0)	9 (34.6)	0.1942
Number (%) of patients censored	32 (45.1)	54 (60.7)	21 (67.7)	39 (61.9)	15 (75.0)	17 (65.4)	
Kaplan-Meier estimates of Cognitive functioning in months							
25% quantile (95% CI)	1.12 (1.018 to 1.906)	1.31 (1.084 to 2.825)	3.88 (0.986 to NC)	1.97 (1.051 to 7.556)	3.78 (1.051 to NC)	2.83 (0.986 to 17.840)	
Median (95% CI)	5.72 (2.004 to NC)	NC (21.848 to NC)	NC (6.308 to NC)	NC (7.556 to NC)	NC (3.778 to NC)	NC (2.825 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Kd							
Log-Rank test p-value[a] vs Kd	-	0.0734		0.5682		0.4860	
Hazard ratio (95% CI) vs Kd	-	0.66 (0.42 to 1.04)		1.24 (0.59 to 2.59)		1.47 (0.49 to 4.40)	
P-value	-	0.0755		0.5690		0.4887	

A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Cognitive functioning
16.2.6.1.2.8 Efficacy response data - Subgroup analyses by ISS staging at SE
16.2.6.1.2.8.4 QLQ-C30 - Time to first deterioration by 10 pt in cognitive functioning according to ISS staging at SE (LOCF) - ITT population

	I		II		III		
	Kd (N=71)	**IKd (N=89)**	**Kd (N=31)**	**IKd (N=63)**	**Kd (N=20)**	**IKd (N=26)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	42 (59.2)	56 (62.9)	20 (64.5)	45 (71.4)	10 (50.0)	11 (42.3)	0.6212
Number (%) of patients censored	29 (40.8)	33 (37.1)	11 (35.5)	18 (28.6)	10 (50.0)	15 (57.7)	
Kaplan-Meier estimates of Cognitive functioning in months							
25% quantile (95% CI)	3.81 (2.004 to 4.895)	2.10 (1.183 to 3.778)	2.14 (1.117 to 4.731)	1.87 (1.051 to 2.595)	2.92 (0.986 to 7.458)	6.64 (0.953 to 9.363)	
Median (95% CI)	10.18 (5.651 to NC)	8.21 (4.665 to 15.474)	5.49 (3.778 to 12.189)	4.80 (2.825 to 9.002)	7.92 (2.924 to NC)	10.15 (6.637 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (19.253 to NC)	NC (6.505 to NC)	NC (9.035 to NC)	NC (7.918 to NC)	NC (14.620 to NC)	
Comparison vs. Kd							
Log-Rank test p-value[a] vs Kd	-	0.4970		0.6479		0.4022	
Hazard ratio (95% CI) vs Kd	-	1.15 (0.77 to 1.71)		1.13 (0.67 to 1.92)		0.69 (0.29 to 1.64)	
P-value	-	0.4973		0.6481		0.4047	

A higher score represents a better level of quality of life. Clinical meaningful deterioration change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Cognitive functioning
16.2.6.1.2.8 Efficacy response data - Subgroup analyses by ISS staging at SE
16.2.6.1.2.8.5 QLQ-C30 - Time until permanent improvement by 10 pt in cognitive functioning according to ISS staging at SE (LOCF) - ITT population

	I		II		III		
	Kd (N=71)	**IKd (N=89)**	**Kd (N=31)**	**IKd (N=63)**	**Kd (N=20)**	**IKd (N=26)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	13 (18.3)	13 (14.6)	4 (12.9)	8 (12.7)	2 (10.0)	6 (23.1)	0.4387
Number (%) of patients censored	58 (81.7)	76 (85.4)	27 (87.1)	55 (87.3)	18 (90.0)	20 (76.9)	
Kaplan-Meier estimates of Cognitive functioning in months							
25% quantile (95% CI)	24.05 (17.380 to NC)	24.44 (21.848 to NC)	NC (1.906 to NC)	23.36 (23.359 to NC)	NC (1.117 to NC)	17.38 (0.986 to NC)	
Median (95% CI)	NC (24.049 to NC)	NC (24.444 to NC)	NC (NC to NC)	NC (23.359 to NC)	NC (NC to NC)	NC (17.380 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (24.444 to NC)	NC (NC to NC)	NC (23.359 to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Kd							
Log-Rank test p-value[a] vs Kd	-	0.6418		0.8765		0.2358	
Hazard ratio (95% CI) vs Kd	-	0.83 (0.39 to 1.80)		0.91 (0.27 to 3.02)		2.55 (0.51 to 12.63)	
P-value	-	0.6423		0.8765		0.2527	

A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Cognitive functioning
16.2.6.1.2.8 Efficacy response data - Subgroup analyses by ISS staging at SE
16.2.6.1.2.8.6 QLQ-C30 - Time until permanent deterioration by 10 pt in cognitive functioning according to ISS staging at SE (LOCF) - ITT population

	I		II		III		
	Kd (N=71)	**IKd (N=89)**	**Kd (N=31)**	**IKd (N=63)**	**Kd (N=20)**	**IKd (N=26)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	17 (23.9)	28 (31.5)	11 (35.5)	28 (44.4)	9 (45.0)	3 (11.5)	0.0340
Number (%) of patients censored	54 (76.1)	61 (68.5)	20 (64.5)	35 (55.6)	11 (55.0)	23 (88.5)	
Kaplan-Meier estimates of Cognitive functioning in months							
25% quantile (95% CI)	20.60 (15.080 to NC)	15.93 (10.349 to 23.097)	14.65 (3.778 to 21.520)	8.48 (3.220 to 14.522)	7.92 (0.986 to 14.292)	NC (3.745 to NC)	
Median (95% CI)	NC (NC to NC)	NC (23.097 to NC)	NC (15.376 to NC)	NC (14.522 to NC)	14.29 (7.392 to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (14.292 to NC)	NC (NC to NC)	
Comparison vs. Kd							
Log-Rank test p-value[a] vs Kd	-	0.2560		0.5621		0.0106	
Hazard ratio (95% CI) vs Kd	-	1.42 (0.77 to 2.59)		1.23 (0.61 to 2.47)		0.21 (0.06 to 0.79)	
P-value	-	0.2584		0.5628		0.0203	

A higher score represents a better level of quality of life. Clinical meaningful deterioration change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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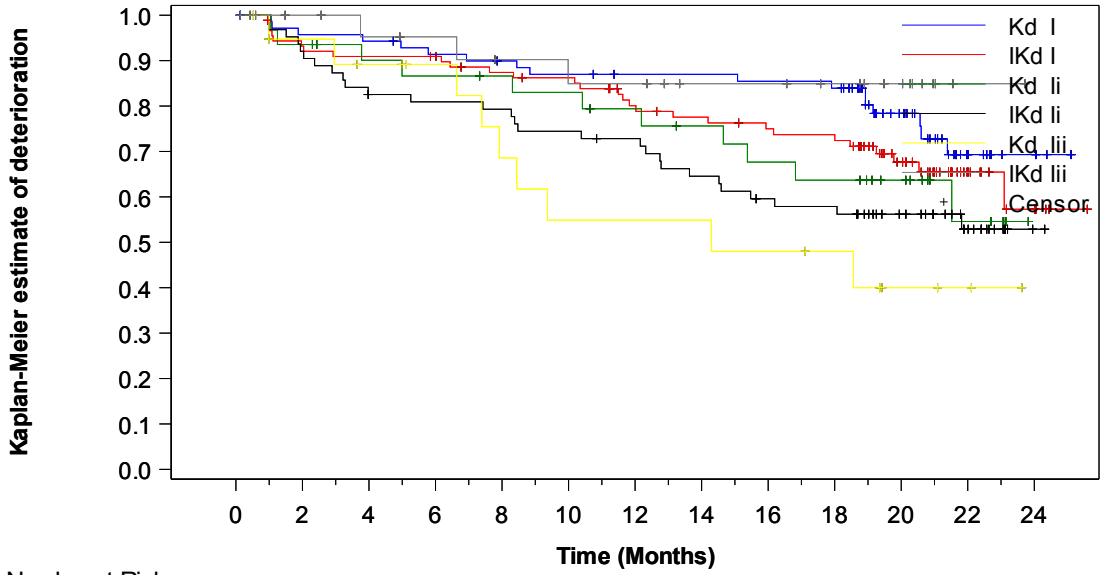
16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Cognitive functioning
16.2.6.1.2.8 Efficacy response data - Subgroup analyses by ISS staging at SE
16.2.6.1.2.8.7 QLQ-C30 - Time until permanent deterioration by 10 pt in cognitive functioning according to ISS staging at SE - Kaplan-Meier curve (LOCF) - ITT population



Number at Risk

Kd I	71	67	63	59	57	57	55	24	5
IKd I	89	80	79	72	64	60	57	25	6
Kd Ii	31	27	25	23	21	18	16	7	0
IKd Ii	63	55	50	46	44	37	34	20	1
Kd Iii	20	16	13	9	8	7	6	3	0
IKd Iii	26	21	19	17	16	13	11	3	0

A higher score represents a better level of quality of life. Clinical meaningful deterioration change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
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16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Cognitive functioning
16.2.6.1.2.9 Efficacy response data - Subgroup analyses by R-ISS stage at SE
16.2.6.1.2.9.2 QLQ-C30 - Time to first improvement by 10 pt in cognitive functioning according to R-ISS stage at SE (LOCF) - ITT population

	I or II		III		Not classified		
	Kd (N=103)	**IKd (N=155)**	**Kd (N=8)**	**IKd (N=16)**	**Kd (N=12)**	**IKd (N=8)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	47 (45.6)	61 (39.4)	2 (25.0)	5 (31.3)	5 (41.7)	3 (37.5)	0.7171
Number (%) of patients censored	56 (54.4)	94 (60.6)	6 (75.0)	11 (68.8)	7 (58.3)	5 (62.5)	
Kaplan-Meier estimates of Cognitive functioning in months							
25% quantile (95% CI)	1.91 (1.051 to 2.201)	1.91 (1.117 to 2.825)	1.12 (1.051 to NC)	2.83 (1.413 to NC)	1.91 (0.986 to NC)	1.08 (1.018 to NC)	
Median (95% CI)	NC (3.877 to NC)	NC (NC to NC)	NC (1.051 to NC)	NC (2.004 to NC)	NC (1.117 to NC)	NC (1.018 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (19.713 to NC)	NC (1.084 to NC)	
Comparison vs. Kd							
Log-Rank test p-value[a] vs Kd	-	0.3088		0.8744		0.5887	
Hazard ratio (95% CI) vs Kd	-	0.82 (0.56 to 1.20)		1.14 (0.22 to 5.90)		1.49 (0.35 to 6.33)	
P-value	-	0.3096		0.8745		0.5909	

A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Cognitive functioning
16.2.6.1.2.9 Efficacy response data - Subgroup analyses by R-ISS stage at SE
16.2.6.1.2.9.3 QLQ-C30 - Time to first deterioration by 10 pt in cognitive functioning according to R-ISS stage at SE (LOCF) - ITT population

	I or II		III		Not classified		
	Kd (N=103)	**IKd (N=155)**	**Kd (N=8)**	**IKd (N=16)**	**Kd (N=12)**	**IKd (N=8)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	61 (59.2)	102 (65.8)	3 (37.5)	6 (37.5)	9 (75.0)	4 (50.0)	0.7128
Number (%) of patients censored	42 (40.8)	53 (34.2)	5 (62.5)	10 (62.5)	3 (25.0)	4 (50.0)	
Kaplan-Meier estimates of Cognitive functioning in months							
25% quantile (95% CI)	3.78 (1.938 to 4.731)	2.04 (1.478 to 2.891)	1.12 (0.986 to NC)	8.67 (0.953 to 14.620)	2.79 (1.084 to 6.472)	3.98 (3.745 to 8.345)	
Median (95% CI)	7.46 (4.994 to 13.372)	6.57 (4.665 to 11.105)	NC (0.986 to NC)	14.62 (6.637 to NC)	7.20 (1.150 to NC)	6.78 (3.745 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (19.253 to NC)	NC (2.924 to NC)	NC (14.620 to NC)	NC (6.472 to NC)	NC (3.975 to NC)	
Comparison vs. Kd							
Log-Rank test p-value[a] vs Kd	-	0.3414		0.7216		0.7663	
Hazard ratio (95% CI) vs Kd	-	1.17 (0.85 to 1.60)		0.78 (0.19 to 3.16)		0.84 (0.26 to 2.73)	

A higher score represents a better level of quality of life. Clinical meaningful deterioration change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
PGM=DEVOPS/SAR650984/EFC15246/CIR_RWE/REPORT/PGM/eff_km_subgp_sr_sig_de_i_t.sas OUT=REPORT/OUTPUT/eff_km_c30_cog_detl_seriss_de_i_t_x.rtf (07APR2021 14:25)

16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Cognitive functioning
16.2.6.1.2.9 Efficacy response data - Subgroup analyses by R-ISS stage at SE
16.2.6.1.2.9.4 QLQ-C30 - Time until permanent improvement by 10 pt in cognitive functioning according to R-ISS stage at SE (LOCF) - ITT population

	I or II		III		Not classified		
	Kd (N=103)	**IKd (N=155)**	**Kd (N=8)**	**IKd (N=16)**	**Kd (N=12)**	**IKd (N=8)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	16 (15.5)	22 (14.2)	2 (25.0)	5 (31.3)	1 (8.3)	1 (12.5)	0.6703
Number (%) of patients censored	87 (84.5)	133 (85.8)	6 (75.0)	11 (68.8)	11 (91.7)	7 (87.5)	
Kaplan-Meier estimates of Cognitive functioning in months							
25% quantile (95% CI)	24.05 (21.684 to NC)	24.44 (23.359 to NC)	2.89 (1.117 to NC)	14.55 (1.413 to 18.398)	NC (12.025 to NC)	NC (16.329 to NC)	
Median (95% CI)	NC (24.049 to NC)	NC (24.444 to NC)	NC (1.117 to NC)	18.40 (14.554 to NC)	NC (NC to NC)	NC (16.329 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (24.444 to NC)	NC (NC to NC)	NC (17.380 to NC)	NC (NC to NC)	NC (16.329 to NC)	
Comparison vs. Kd							
Log-Rank test p-value[a] vs Kd	-	0.7404		0.6665		0.4348	
Hazard ratio (95% CI) vs Kd	-	0.90 (0.47 to 1.71)		1.44 (0.27 to 7.55)		2.87 (0.18 to 45.95)	
P-value	-	0.7406		0.6682		0.4557	

A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Cognitive functioning
16.2.6.1.2.9 Efficacy response data - Subgroup analyses by R-ISS stage at SE
16.2.6.1.2.9.5 QLQ-C30 - Time until permanent deterioration by 10 pt in cognitive functioning according to R-ISS stage at SE (LOCF) - ITT population

	I or II		III		Not classified		
	Kd (N=103)	**IKd (N=155)**	**Kd (N=8)**	**IKd (N=16)**	**Kd (N=12)**	**IKd (N=8)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	31 (30.1)	53 (34.2)	3 (37.5)	2 (12.5)	4 (33.3)	4 (50.0)	0.1749
Number (%) of patients censored	72 (69.9)	102 (65.8)	5 (62.5)	14 (87.5)	8 (66.7)	4 (50.0)	
Kaplan-Meier estimates of Cognitive functioning in months							
25% quantile (95% CI)	17.91 (8.838 to 21.388)	13.14 (10.185 to 18.070)	6.64 (0.986 to NC)	NC (6.637 to NC)	11.50 (1.150 to NC)	8.34 (3.745 to 20.534)	
Median (95% CI)	NC (21.520 to NC)	NC (23.097 to NC)	18.56 (0.986 to NC)	NC (9.988 to NC)	NC (6.932 to NC)	16.02 (3.745 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (6.637 to NC)	NC (NC to NC)	NC (NC to NC)	NC (8.345 to NC)	
Comparison vs. Kd							
Log-Rank test p-value[a] vs Kd	-	0.5716		0.1170		0.2635	
Hazard ratio (95% CI) vs Kd	-	1.14 (0.73 to 1.77)		0.26 (0.04 to 1.58)		2.17 (0.54 to 8.71)	
P-value	-	0.5719		0.1442		0.2752	

A higher score represents a better level of quality of life. Clinical meaningful deterioration change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Cognitive functioning
16.2.6.1.2.10 Efficacy response data - Subgroup analyses by nb of prior lines
16.2.6.1.2.10.3 QLQ-C30 - Time to first improvement by 10 pt in cognitive functioning according to nb of prior lines (LOCF) - ITT population

	1		>1		
	Kd (N=55)	**IKd (N=79)**	**Kd (N=68)**	**IKd (N=100)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	22 (40.0)	30 (38.0)	32 (47.1)	39 (39.0)	0.6222
Number (%) of patients censored	33 (60.0)	49 (62.0)	36 (52.9)	61 (61.0)	
Kaplan-Meier estimates of Cognitive functioning in months					
25% quantile (95% CI)	2.04 (1.084 to 5.717)	1.97 (1.117 to 4.632)	1.91 (1.018 to 2.004)	1.91 (1.051 to 2.825)	
Median (95% CI)	NC (5.717 to NC)	NC (15.277 to NC)	NC (3.187 to NC)	NC (17.840 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.8382		0.3440	
Hazard ratio (95% CI) vs Kd	-	0.94 (0.54 to 1.64)		0.80 (0.50 to 1.27)	
P-value	-	0.8374		0.3450	
Improvement probability (95% CI)[b]					

A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Cognitive functioning
16.2.6.1.2.10 Efficacy response data - Subgroup analyses by nb of prior lines
16.2.6.1.2.10.4 QLQ-C30 - Time to first deterioration by 10 pt in cognitive functioning according to nb of prior lines (LOCF) - ITT population

	1		>1		
	Kd (N=55)	**IKd (N=79)**	**Kd (N=68)**	**IKd (N=100)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	33 (60.0)	50 (63.3)	40 (58.8)	62 (62.0)	0.6641
Number (%) of patients censored	22 (40.0)	29 (36.7)	28 (41.2)	38 (38.0)	
Kaplan-Meier estimates of Cognitive functioning in months					
25% quantile (95% CI)	4.27 (1.248 to 4.961)	1.97 (1.117 to 2.891)	2.92 (1.873 to 4.665)	2.83 (1.216 to 4.665)	
Median (95% CI)	10.18 (4.961 to NC)	7.95 (3.220 to 13.864)	6.77 (4.797 to 11.992)	6.83 (4.764 to 11.302)	
75% quantile (95% CI)	NC (NC to NC)	NC (18.366 to NC)	NC (13.372 to NC)	NC (15.474 to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.5096		0.9068	
Hazard ratio (95% CI) vs Kd	-	1.16 (0.75 to 1.80)		1.02 (0.69 to 1.52)	
P-value	-	0.5100		0.9070	
Deterioration probability (95% CI)[b]					

A higher score represents a better level of quality of life. Clinical meaningful deterioration change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Cognitive functioning
16.2.6.1.2.10 Efficacy response data - Subgroup analyses by nb of prior lines
16.2.6.1.2.10.5 QLQ-C30 - Time until permanent improvement by 10 pt in cognitive functioning according to nb of prior lines (LOCF) - ITT population

	1		>1		
	Kd (N=55)	**IKd (N=79)**	**Kd (N=68)**	**IKd (N=100)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	7 (12.7)	13 (16.5)	12 (17.6)	15 (15.0)	0.4491
Number (%) of patients censored	48 (87.3)	66 (83.5)	56 (82.4)	85 (85.0)	
Kaplan-Meier estimates of Cognitive functioning in months					
25% quantile (95% CI)	24.05 (24.049 to NC)	23.36 (19.285 to NC)	NC (12.025 to NC)	NC (18.398 to NC)	
Median (95% CI)	NC (24.049 to NC)	24.44 (23.359 to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (24.049 to NC)	NC (24.444 to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.4731		0.6328	
Hazard ratio (95% CI) vs Kd	-	1.40 (0.56 to 3.54)		0.83 (0.39 to 1.78)	
P-value	-	0.4752		0.6332	
Improvement probability (95% CI)[b]					

A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Cognitive functioning
16.2.6.1.2.10 Efficacy response data - Subgroup analyses by nb of prior lines
16.2.6.1.2.10.6 QLQ-C30 - Time until permanent deterioration by 10 pt in cognitive functioning according to nb of prior lines (LOCF) - ITT population

	1		>1		
	Kd (N=55)	**IKd (N=79)**	**Kd (N=68)**	**IKd (N=100)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	15 (27.3)	26 (32.9)	23 (33.8)	33 (33.0)	0.4856
Number (%) of patients censored	40 (72.7)	53 (67.1)	45 (66.2)	67 (67.0)	
Kaplan-Meier estimates of Cognitive functioning in months					
25% quantile (95% CI)	20.60 (6.637 to NC)	13.14 (6.177 to 20.534)	15.08 (7.918 to 18.924)	12.75 (10.185 to 19.253)	
Median (95% CI)	NC (21.388 to NC)	NC (NC to NC)	NC (18.924 to NC)	NC (21.815 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.4630		0.8655	
Hazard ratio (95% CI) vs Kd	-	1.27 (0.67 to 2.39)		0.95 (0.56 to 1.63)	
P-value	-	0.4641		0.8649	
Deterioration probability (95% CI)[b]					

A higher score represents a better level of quality of life. Clinical meaningful deterioration change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Cognitive functioning
16.2.6.1.2.11 Efficacy response data - Subgroup analyses by cytogenetic abnormality
16.2.6.1.2.11.3 QLQ-C30 - Time to first improvement by 10 pt in cognitive functioning according to cytogenetic abnormality (LOCF) - ITT population

	At least one		None		
	Kd (N=31)	**IKd (N=42)**	**Kd (N=77)**	**IKd (N=114)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	14 (45.2)	18 (42.9)	32 (41.6)	42 (36.8)	0.7493
Number (%) of patients censored	17 (54.8)	24 (57.1)	45 (58.4)	72 (63.2)	
Kaplan-Meier estimates of Cognitive functioning in months					
25% quantile (95% CI)	1.91 (1.018 to 6.308)	1.41 (1.018 to 3.877)	1.91 (1.051 to 3.187)	2.00 (1.117 to 4.140)	
Median (95% CI)	NC (3.877 to NC)	21.85 (2.037 to NC)	NC (3.745 to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (21.848 to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.9021		0.4792	
Hazard ratio (95% CI) vs Kd	-	0.96 (0.48 to 1.92)		0.85 (0.53 to 1.34)	
P-value	-	0.9018		0.4797	
Improvement probability (95% CI)[b]					

A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Cognitive functioning
16.2.6.1.2.11 Efficacy response data - Subgroup analyses by cytogenetic abnormality
16.2.6.1.2.11.4 QLQ-C30 - Time to first deterioration by 10 pt in cognitive functioning according to cytogenetic abnormality (LOCF) - ITT population

	At least one		None		
	Kd (N=31)	**IKd (N=42)**	**Kd (N=77)**	**IKd (N=114)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	16 (51.6)	25 (59.5)	47 (61.0)	74 (64.9)	0.8079
Number (%) of patients censored	15 (48.4)	17 (40.5)	30 (39.0)	40 (35.1)	
Kaplan-Meier estimates of Cognitive functioning in months					
25% quantile (95% CI)	4.83 (2.825 to 6.637)	1.97 (0.986 to 6.637)	2.96 (1.281 to 4.632)	2.04 (1.216 to 2.891)	
Median (95% CI)	10.18 (6.505 to NC)	12.19 (4.797 to NC)	6.47 (4.797 to 13.372)	6.51 (4.600 to 10.152)	
75% quantile (95% CI)	NC (11.170 to NC)	NC (14.620 to NC)	NC (13.536 to NC)	NC (16.789 to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.6125		0.5600	
Hazard ratio (95% CI) vs Kd	-	1.18 (0.63 to 2.21)		1.11 (0.77 to 1.61)	
P-value	-	0.6129		0.5602	
Deterioration probability (95% CI)[b]					

A higher score represents a better level of quality of life. Clinical meaningful deterioration change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Cognitive functioning
16.2.6.1.2.11 Efficacy response data - Subgroup analyses by cytogenetic abnormality
16.2.6.1.2.11.5 QLQ-C30 - Time until permanent improvement by 10 pt in cognitive functioning according to cytogenetic abnormality (LOCF) - ITT population

	At least one		None		
	Kd (N=31)	**IKd (N=42)**	**Kd (N=77)**	**IKd (N=114)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	5 (16.1)	10 (23.8)	11 (14.3)	13 (11.4)	0.4706
Number (%) of patients censored	26 (83.9)	32 (76.2)	66 (85.7)	101 (88.6)	
Kaplan-Meier estimates of Cognitive functioning in months					
25% quantile (95% CI)	NC (2.891 to NC)	21.85 (16.329 to 23.359)	24.05 (17.676 to NC)	24.44 (24.444 to NC)	
Median (95% CI)	NC (21.684 to NC)	23.36 (21.848 to NC)	NC (24.049 to NC)	24.44 (24.444 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (23.359 to NC)	NC (NC to NC)	NC (24.444 to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.5374		0.6641	
Hazard ratio (95% CI) vs Kd	-	1.40 (0.48 to 4.11)		0.84 (0.37 to 1.87)	
P-value	-	0.5393		0.6645	
Improvement probability (95% CI)[b]					

A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Cognitive functioning
16.2.6.1.2.11 Efficacy response data - Subgroup analyses by cytogenetic abnormality
16.2.6.1.2.11.6 QLQ-C30 - Time until permanent deterioration by 10 pt in cognitive functioning according to cytogenetic abnormality (LOCF) - ITT population

	At least one		None		
	Kd (N=31)	**IKd (N=42)**	**Kd (N=77)**	**IKd (N=114)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	8 (25.8)	10 (23.8)	24 (31.2)	39 (34.2)	0.7745
Number (%) of patients censored	23 (74.2)	32 (76.2)	53 (68.8)	75 (65.8)	
Kaplan-Meier estimates of Cognitive functioning in months					
25% quantile (95% CI)	18.56 (4.994 to NC)	NC (1.084 to NC)	16.82 (8.444 to 21.388)	13.14 (10.382 to 18.464)	
Median (95% CI)	NC (18.924 to NC)	NC (NC to NC)	NC (21.388 to NC)	NC (21.815 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.8798		0.7653	
Hazard ratio (95% CI) vs Kd	-	0.93 (0.37 to 2.36)		1.08 (0.65 to 1.80)	
P-value	-	0.8793		0.7653	
Deterioration probability (95% CI)[b]					

A higher score represents a better level of quality of life. Clinical meaningful deterioration change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Cognitive functioning
16.2.6.1.2.12 Efficacy response data - Subgroup analyses by MM type at SE
16.2.6.1.2.12.3 QLQ-C30 - Time to first improvement by 10 pt in cognitive functioning according to MM type at SE (LOCF) - ITT population

	IgG		Non-IgG		
	Kd (N=85)	**IKd (N=126)**	**Kd (N=38)**	**IKd (N=53)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	41 (48.2)	47 (37.3)	13 (34.2)	22 (41.5)	0.2262
Number (%) of patients censored	44 (51.8)	79 (62.7)	25 (65.8)	31 (58.5)	
Kaplan-Meier estimates of Cognitive functioning in months					
25% quantile (95% CI)	1.91 (1.051 to 2.037)	1.97 (1.117 to 4.140)	1.94 (1.051 to NC)	1.91 (1.018 to 2.793)	
Median (95% CI)	19.71 (3.745 to NC)	NC (21.848 to NC)	NC (4.008 to NC)	NC (2.070 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.1585		0.5784	
Hazard ratio (95% CI) vs Kd	-	0.74 (0.49 to 1.13)		1.21 (0.61 to 2.41)	
P-value	-	0.1601		0.5790	
Improvement probability (95% CI)[b]					

A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Cognitive functioning
16.2.6.1.2.12 Efficacy response data - Subgroup analyses by MM type at SE
16.2.6.1.2.12.4 QLQ-C30 - Time to first deterioration by 10 pt in cognitive functioning according to MM type at SE (LOCF) - ITT population

	IgG		Non-IgG		
	Kd (N=85)	**IKd (N=126)**	**Kd (N=38)**	**IKd (N=53)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	54 (63.5)	78 (61.9)	19 (50.0)	34 (64.2)	0.2133
Number (%) of patients censored	31 (36.5)	48 (38.1)	19 (50.0)	19 (35.8)	
Kaplan-Meier estimates of Cognitive functioning in months					
25% quantile (95% CI)	2.96 (1.281 to 4.632)	2.89 (1.906 to 4.600)	3.78 (1.938 to 5.487)	1.87 (1.018 to 2.825)	
Median (95% CI)	6.77 (4.862 to 11.170)	7.95 (5.224 to 12.025)	10.18 (4.961 to NC)	4.70 (2.825 to 15.474)	
75% quantile (95% CI)	NC (13.372 to NC)	NC (NC to NC)	NC (NC to NC)	NC (14.620 to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.8390		0.1658	
Hazard ratio (95% CI) vs Kd	-	0.96 (0.68 to 1.36)		1.48 (0.85 to 2.60)	
P-value	-	0.8384		0.1685	
Deterioration probability (95% CI)[b]					

A higher score represents a better level of quality of life. Clinical meaningful deterioration change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Cognitive functioning
16.2.6.1.2.12 Efficacy response data - Subgroup analyses by MM type at SE
16.2.6.1.2.12.5 QLQ-C30 - Time until permanent improvement by 10 pt in cognitive functioning according to MM type at SE (LOCF) - ITT population

	IgG		Non-IgG		
	Kd (N=85)	**IKd (N=126)**	**Kd (N=38)**	**IKd (N=53)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	12 (14.1)	18 (14.3)	7 (18.4)	10 (18.9)	0.9747
Number (%) of patients censored	73 (85.9)	108 (85.7)	31 (81.6)	43 (81.1)	
Kaplan-Meier estimates of Cognitive functioning in months					
25% quantile (95% CI)	24.05 (24.049 to NC)	24.44 (21.848 to NC)	21.68 (2.825 to NC)	NC (16.329 to NC)	
Median (95% CI)	NC (24.049 to NC)	NC (24.444 to NC)	NC (21.684 to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (24.444 to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.9314		0.9404	
Hazard ratio (95% CI) vs Kd	-	1.03 (0.50 to 2.14)		0.96 (0.37 to 2.53)	
P-value	-	0.9316		0.9402	
Improvement probability (95% CI)[b]					

A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Cognitive functioning
16.2.6.1.2.12 Efficacy response data - Subgroup analyses by MM type at SE
16.2.6.1.2.12.6 QLQ-C30 - Time until permanent deterioration by 10 pt in cognitive functioning according to MM type at SE (LOCF) - ITT population

	IgG		Non-IgG		
	Kd (N=85)	**IKd (N=126)**	**Kd (N=38)**	**IKd (N=53)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	23 (27.1)	45 (35.7)	15 (39.5)	14 (26.4)	0.0741
Number (%) of patients censored	62 (72.9)	81 (64.3)	23 (60.5)	39 (73.6)	
Kaplan-Meier estimates of Cognitive functioning in months					
25% quantile (95% CI)	18.92 (8.444 to NC)	12.78 (8.476 to 18.070)	10.41 (5.782 to 20.567)	14.59 (3.745 to NC)	
Median (95% CI)	NC (NC to NC)	NC (21.815 to NC)	21.39 (18.563 to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (21.388 to NC)	NC (NC to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.1981		0.1739	
Hazard ratio (95% CI) vs Kd	-	1.39 (0.84 to 2.30)		0.61 (0.29 to 1.26)	
P-value	-	0.2002		0.1783	
Deterioration probability (95% CI)[b]					

A higher score represents a better level of quality of life. Clinical meaningful deterioration change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Cognitive functioning
16.2.6.1.2.13 Efficacy response data - Subgroup analyses by previous autologous stem-cell
16.2.6.1.2.13.3 QLQ-C30 - Time to first improvement by 10 pt in cognitive functioning according to previous autologous stem-cell (LOCF) - ITT population

	Yes		No		
	Kd (N=69)	**IKd (N=116)**	**Kd (N=54)**	**IKd (N=63)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	30 (43.5)	45 (38.8)	24 (44.4)	24 (38.1)	0.8995
Number (%) of patients censored	39 (56.5)	71 (61.2)	30 (55.6)	39 (61.9)	
Kaplan-Meier estimates of Cognitive functioning in months					
25% quantile (95% CI)	1.91 (1.051 to 3.745)	1.91 (1.117 to 2.825)	1.91 (1.051 to 3.285)	1.97 (1.051 to 7.031)	
Median (95% CI)	NC (4.008 to NC)	NC (21.848 to NC)	NC (3.285 to NC)	NC (7.031 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.5756		0.5238	
Hazard ratio (95% CI) vs Kd	-	0.88 (0.55 to 1.39)		0.83 (0.47 to 1.47)	
P-value	-	0.5758		0.5244	
Improvement probability (95% CI)[b]					

A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Cognitive functioning
16.2.6.1.2.13 Efficacy response data - Subgroup analyses by previous autologous stem-cell
16.2.6.1.2.13.4 QLQ-C30 - Time to first deterioration by 10 pt in cognitive functioning according to previous autologous stem-cell (LOCF) - ITT population

	Yes		No		
	Kd (N=69)	**IKd (N=116)**	**Kd (N=54)**	**IKd (N=63)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	36 (52.2)	69 (59.5)	37 (68.5)	43 (68.3)	0.5511
Number (%) of patients censored	33 (47.8)	47 (40.5)	17 (31.5)	20 (31.7)	
Kaplan-Meier estimates of Cognitive functioning in months					
25% quantile (95% CI)	2.96 (1.906 to 4.895)	2.04 (1.117 to 2.957)	3.06 (1.248 to 4.731)	2.35 (1.478 to 4.797)	
Median (95% CI)	8.64 (4.961 to NC)	8.21 (4.665 to 16.789)	6.64 (4.731 to 10.185)	6.57 (4.797 to 9.593)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	13.54 (10.185 to NC)	15.47 (9.593 to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.3451		0.9904	
Hazard ratio (95% CI) vs Kd	-	1.21 (0.81 to 1.82)		1.00 (0.64 to 1.55)	
P-value	-	0.3459		0.9904	
Deterioration probability (95% CI)[b]					

A higher score represents a better level of quality of life. Clinical meaningful deterioration change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Cognitive functioning
16.2.6.1.2.13 Efficacy response data - Subgroup analyses by previous autologous stem-cell
16.2.6.1.2.13.5 QLQ-C30 - Time until permanent improvement by 10 pt in cognitive functioning according to previous autologous stem-cell (LOCF) - ITT population

	Yes		No		
	Kd (N=69)	**IKd (N=116)**	**Kd (N=54)**	**IKd (N=63)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	7 (10.1)	19 (16.4)	12 (22.2)	9 (14.3)	0.1227
Number (%) of patients censored	62 (89.9)	97 (83.6)	42 (77.8)	54 (85.7)	
Kaplan-Meier estimates of Cognitive functioning in months					
25% quantile (95% CI)	NC (21.684 to NC)	24.44 (19.285 to 24.444)	24.05 (15.770 to NC)	23.36 (17.380 to NC)	
Median (95% CI)	NC (NC to NC)	24.44 (NC to NC)	NC (24.049 to NC)	NC (23.359 to NC)	
75% quantile (95% CI)	NC (NC to NC)	24.44 (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.2253		0.3339	
Hazard ratio (95% CI) vs Kd	-	1.70 (0.71 to 4.05)		0.65 (0.28 to 1.56)	
P-value	-	0.2310		0.3378	
Improvement probability (95% CI)[b]					

A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Cognitive functioning
16.2.6.1.2.13 Efficacy response data - Subgroup analyses by previous autologous stem-cell
16.2.6.1.2.13.6 QLQ-C30 - Time until permanent deterioration by 10 pt in cognitive functioning according to previous autologous stem-cell (LOCF) - ITT population

	Yes		No		
	Kd (N=69)	**IKd (N=116)**	**Kd (N=54)**	**IKd (N=63)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	19 (27.5)	38 (32.8)	19 (35.2)	21 (33.3)	0.5450
Number (%) of patients censored	50 (72.5)	78 (67.2)	35 (64.8)	42 (66.7)	
Kaplan-Meier estimates of Cognitive functioning in months					
25% quantile (95% CI)	18.92 (8.838 to NC)	14.19 (8.279 to 19.253)	12.19 (6.932 to 20.567)	12.32 (8.345 to 21.815)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (18.924 to NC)	NC (21.815 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.4700		0.8114	
Hazard ratio (95% CI) vs Kd	-	1.22 (0.71 to 2.12)		0.93 (0.50 to 1.73)	
P-value	-	0.4708		0.8109	
Deterioration probability (95% CI)[b]					

A higher score represents a better level of quality of life. Clinical meaningful deterioration change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Cognitive functioning
16.2.6.1.2.14 Efficacy response data - Subgroup analyses by baseline eGFR (MDRD)
16.2.6.1.2.14.3 QLQ-C30 - Time to first improvement by 10 pt in cognitive functioning according to baseline eGFR (MDRD) (LOCF) - ITT population

	>=60 mL/min/1.73m2		<60 mL/min/1.73m2		
	Kd (N=93)	**IKd (N=122)**	**Kd (N=18)**	**IKd (N=43)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	45 (48.4)	50 (41.0)	7 (38.9)	13 (30.2)	0.7124
Number (%) of patients censored	48 (51.6)	72 (59.0)	11 (61.1)	30 (69.8)	
Kaplan-Meier estimates of Cognitive functioning in months					
25% quantile (95% CI)	1.89 (1.051 to 2.004)	1.91 (1.051 to 2.825)	3.88 (0.986 to NC)	2.83 (0.986 to NC)	
Median (95% CI)	NC (3.745 to NC)	NC (9.331 to NC)	NC (1.971 to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.4174		0.4464	
Hazard ratio (95% CI) vs Kd	-	0.85 (0.57 to 1.27)		0.70 (0.28 to 1.76)	
P-value	-	0.4180		0.4487	
Improvement probability (95% CI)[b]					

A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Cognitive functioning
16.2.6.1.2.14 Efficacy response data - Subgroup analyses by baseline eGFR (MDRD)
16.2.6.1.2.14.4 QLQ-C30 - Time to first deterioration by 10 pt in cognitive functioning according to baseline eGFR (MDRD) (LOCF) - ITT population

	>=60 mL/min/1.73m2		<60 mL/min/1.73m2		
	Kd (N=93)	**IKd (N=122)**	**Kd (N=18)**	**IKd (N=43)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	57 (61.3)	82 (67.2)	10 (55.6)	25 (58.1)	0.1657
Number (%) of patients censored	36 (38.7)	40 (32.8)	8 (44.4)	18 (41.9)	
Kaplan-Meier estimates of Cognitive functioning in months					
25% quantile (95% CI)	2.96 (1.906 to 4.271)	1.97 (1.117 to 2.891)	2.83 (0.986 to 4.961)	2.60 (1.084 to 6.571)	
Median (95% CI)	6.77 (4.895 to 12.189)	5.22 (3.975 to 9.035)	4.96 (2.825 to NC)	10.15 (5.749 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (12.945 to NC)	NC (4.961 to NC)	NC (NC to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.1596		0.3360	
Hazard ratio (95% CI) vs Kd	-	1.27 (0.91 to 1.79)		0.70 (0.33 to 1.46)	
P-value	-	0.1606		0.3382	
Deterioration probability (95% CI)[b]					

A higher score represents a better level of quality of life. Clinical meaningful deterioration change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
PGM=DEVOPS/SAR650984/EFC15246/CIR_RWE/REPORT/PGM/eff_km_subgp_sr_sig_de_i_t.sas OUT=REPORT/OUTPUT/eff_km_c30_cog_detl_crcl_de_i_t_x.rtf (07APR2021 14:25)

16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Cognitive functioning
16.2.6.1.2.14 Efficacy response data - Subgroup analyses by baseline eGFR (MDRD)
16.2.6.1.2.14.5 QLQ-C30 - Time until permanent improvement by 10 pt in cognitive functioning according to baseline eGFR (MDRD) (LOCF) - ITT population

	>=60 mL/min/1.73m2		<60 mL/min/1.73m2		
	Kd (N=93)	**IKd (N=122)**	**Kd (N=18)**	**IKd (N=43)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	16 (17.2)	16 (13.1)	2 (11.1)	8 (18.6)	0.5512
Number (%) of patients censored	77 (82.8)	106 (86.9)	16 (88.9)	35 (81.4)	
Kaplan-Meier estimates of Cognitive functioning in months					
25% quantile (95% CI)	24.05 (17.676 to NC)	NC (21.848 to NC)	NC (2.825 to NC)	23.36 (14.554 to 24.444)	
Median (95% CI)	NC (24.049 to NC)	NC (NC to NC)	NC (NC to NC)	24.44 (23.359 to 24.444)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	24.44 (23.359 to 24.444)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.5465		0.7782	
Hazard ratio (95% CI) vs Kd	-	0.81 (0.40 to 1.62)		1.25 (0.26 to 6.04)	
P-value	-	0.5472		0.7787	
Improvement probability (95% CI)[b]					

A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Cognitive functioning
16.2.6.1.2.14 Efficacy response data - Subgroup analyses by baseline eGFR (MDRD)
16.2.6.1.2.14.6 QLQ-C30 - Time until permanent deterioration by 10 pt in cognitive functioning according to baseline eGFR (MDRD) (LOCF) - ITT population

	>=60 mL/min/1.73m2		<60 mL/min/1.73m2		
	Kd (N=93)	**IKd (N=122)**	**Kd (N=18)**	**IKd (N=43)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	29 (31.2)	41 (33.6)	4 (22.2)	16 (37.2)	0.9521
Number (%) of patients censored	64 (68.8)	81 (66.4)	14 (77.8)	27 (62.8)	
Kaplan-Meier estimates of Cognitive functioning in months					
25% quantile (95% CI)	18.56 (8.838 to 21.388)	12.75 (8.378 to 18.464)	9.36 (0.986 to NC)	12.78 (6.439 to 21.815)	
Median (95% CI)	NC (21.520 to NC)	NC (23.097 to NC)	NC (9.363 to NC)	NC (16.197 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.4376		0.6822	
Hazard ratio (95% CI) vs Kd	-	1.21 (0.75 to 1.94)		1.26 (0.42 to 3.77)	
P-value	-	0.4383		0.6829	
Deterioration probability (95% CI)[b]					

A higher score represents a better level of quality of life. Clinical meaningful deterioration change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Cognitive functioning
16.2.6.1.2.15 Efficacy response data - Subgroup analyses by previous treatment with PI
16.2.6.1.2.15.3 QLQ-C30 - Time to first improvement by 10 pt in cognitive functioning according to previous treatment with PI (LOCF) - ITT population

	Yes		No		
	Kd (N=47)	**IKd (N=81)**	**Kd (N=76)**	**IKd (N=98)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	22 (46.8)	32 (39.5)	32 (42.1)	37 (37.8)	0.9084
Number (%) of patients censored	25 (53.2)	49 (60.5)	44 (57.9)	61 (62.2)	
Kaplan-Meier estimates of Cognitive functioning in months					
25% quantile (95% CI)	1.91 (1.051 to 3.877)	1.97 (1.084 to 2.825)	1.91 (1.051 to 3.187)	1.91 (1.051 to 3.877)	
Median (95% CI)	NC (3.285 to NC)	NC (9.331 to NC)	NC (4.008 to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.4834		0.5823	
Hazard ratio (95% CI) vs Kd	-	0.82 (0.48 to 1.42)		0.88 (0.55 to 1.41)	
P-value	-	0.4841		0.5826	
Improvement probability (95% CI)[b]					

A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Cognitive functioning
16.2.6.1.2.15 Efficacy response data - Subgroup analyses by previous treatment with PI
16.2.6.1.2.15.4 QLQ-C30 - Time to first deterioration by 10 pt in cognitive functioning according to previous treatment with PI (LOCF) - ITT population

	Yes		No		
	Kd (N=47)	**IKd (N=81)**	**Kd (N=76)**	**IKd (N=98)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	27 (57.4)	51 (63.0)	46 (60.5)	61 (62.2)	0.4527
Number (%) of patients censored	20 (42.6)	30 (37.0)	30 (39.5)	37 (37.8)	
Kaplan-Meier estimates of Cognitive functioning in months					
25% quantile (95% CI)	3.81 (1.216 to 4.994)	1.97 (1.117 to 3.055)	3.06 (1.906 to 4.567)	2.37 (1.873 to 3.943)	
Median (95% CI)	10.18 (4.830 to NC)	6.57 (4.140 to 11.302)	6.51 (4.862 to 10.710)	8.28 (4.764 to 13.240)	
75% quantile (95% CI)	NC (13.536 to NC)	NC (13.864 to NC)	NC (12.189 to NC)	NC (18.366 to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.3545		0.9504	
Hazard ratio (95% CI) vs Kd	-	1.25 (0.78 to 1.99)		0.99 (0.67 to 1.45)	
P-value	-	0.3555		0.9503	
Deterioration probability (95% CI)[b]					

A higher score represents a better level of quality of life. Clinical meaningful deterioration change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Cognitive functioning
16.2.6.1.2.15 Efficacy response data - Subgroup analyses by previous treatment with PI
16.2.6.1.2.15.5 QLQ-C30 - Time until permanent improvement by 10 pt in cognitive functioning according to previous treatment with PI (LOCF) - ITT population

	Yes		No		
	Kd (N=47)	**IKd (N=81)**	**Kd (N=76)**	**IKd (N=98)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	8 (17.0)	15 (18.5)	11 (14.5)	13 (13.3)	0.5412
Number (%) of patients censored	39 (83.0)	66 (81.5)	65 (85.5)	85 (86.7)	
Kaplan-Meier estimates of Cognitive functioning in months					
25% quantile (95% CI)	NC (10.448 to NC)	23.36 (14.554 to NC)	24.05 (21.684 to NC)	24.44 (24.444 to NC)	
Median (95% CI)	NC (NC to NC)	NC (23.359 to NC)	NC (24.049 to NC)	NC (24.444 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (23.359 to NC)	NC (24.049 to NC)	NC (24.444 to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.7278		0.6939	
Hazard ratio (95% CI) vs Kd	-	1.17 (0.49 to 2.76)		0.85 (0.38 to 1.90)	
P-value	-	0.7280		0.6942	
Improvement probability (95% CI)[b]					

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The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Cognitive functioning
16.2.6.1.2.15 Efficacy response data - Subgroup analyses by previous treatment with PI
16.2.6.1.2.15.6 QLQ-C30 - Time until permanent deterioration by 10 pt in cognitive functioning according to previous treatment with PI (LOCF) - ITT population

	Yes		No		
	Kd (N=47)	**IKd (N=81)**	**Kd (N=76)**	**IKd (N=98)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	10 (21.3)	30 (37.0)	28 (36.8)	29 (29.6)	0.0183
Number (%) of patients censored	37 (78.7)	51 (63.0)	48 (63.2)	69 (70.4)	
Kaplan-Meier estimates of Cognitive functioning in months					
25% quantile (95% CI)	20.60 (14.653 to NC)	8.48 (6.439 to 16.164)	9.36 (6.637 to 18.924)	15.47 (12.025 to NC)	
Median (95% CI)	NC (21.520 to NC)	23.10 (19.253 to NC)	NC (18.924 to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (23.097 to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.0383		0.2374	
Hazard ratio (95% CI) vs Kd	-	2.10 (1.02 to 4.30)		0.73 (0.44 to 1.23)	
P-value	-	0.0428		0.2393	
Hazard ratio inverted (95% CI) vs IKd		-		1.37 (0.81 to 2.30)	

A higher score represents a better level of quality of life. Clinical meaningful deterioration change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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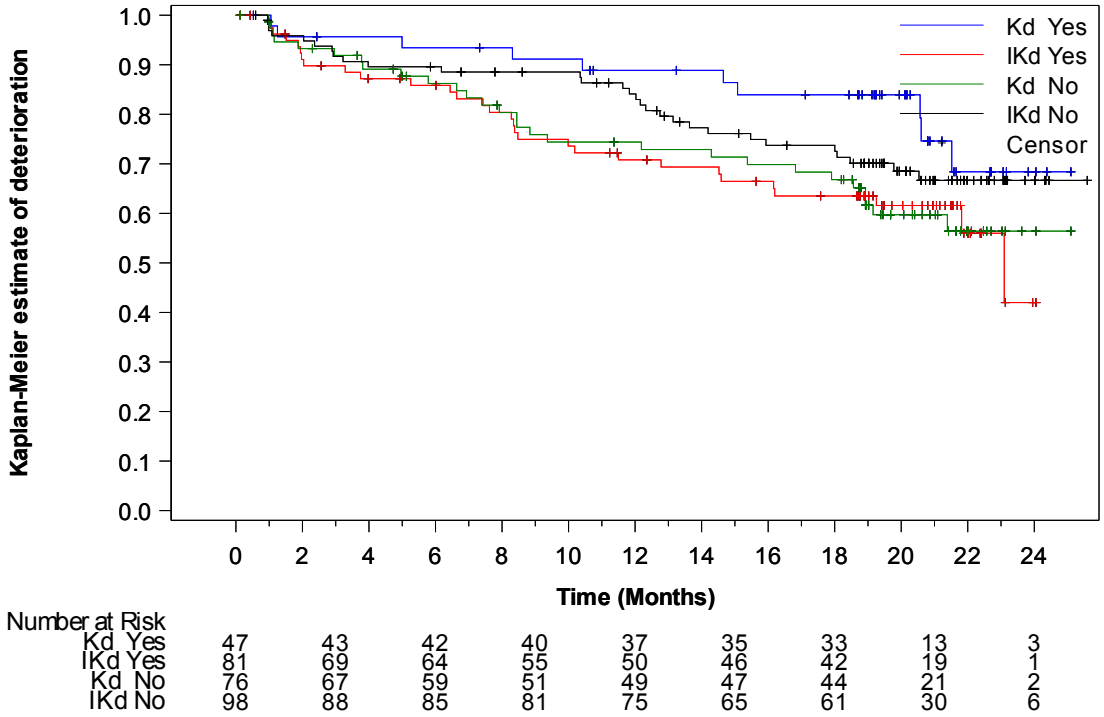
16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Cognitive functioning
16.2.6.1.2.15 Efficacy response data - Subgroup analyses by previous treatment with PI
16.2.6.1.2.15.7 QLQ-C30 - Time until permanent deterioration by 10 pt in cognitive functioning according to previous treatment with PI - Kaplan-Meier curve (LOCF) - ITT population



A higher score represents a better level of quality of life. Clinical meaningful deterioration change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
PGM=DEVOPS/SAR650984/EFC15246/CIR_RWE/REPORT/PGM/eff_qlq_km_subgp_de_i_f.sas OUT=REPORT/OUTPUT/eff_km_c30_cog_detpl_pi_de_i_f_x.rtf (07APR2021 15:00)

16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Cognitive functioning
16.2.6.1.2.16 Efficacy response data - Subgroup analyses by previous treatment with IMiD
16.2.6.1.2.16.3 QLQ-C30 - Time to first improvement by 10 pt in cognitive functioning according to previous treatment with IMiD (LOCF) - ITT population

	Yes		No		
	Kd (N=62)	**IKd (N=81)**	**Kd (N=61)**	**IKd (N=98)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	27 (43.5)	30 (37.0)	27 (44.3)	39 (39.8)	0.8813
Number (%) of patients censored	35 (56.5)	51 (63.0)	34 (55.7)	59 (60.2)	
Kaplan-Meier estimates of Cognitive functioning in months					
25% quantile (95% CI)	2.04 (1.051 to 4.008)	2.07 (1.150 to 7.556)	1.51 (1.051 to 1.938)	1.22 (1.051 to 2.825)	
Median (95% CI)	NC (4.008 to NC)	NC (17.840 to NC)	NC (1.938 to NC)	NC (9.331 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.4674		0.6153	
Hazard ratio (95% CI) vs Kd	-	0.82 (0.49 to 1.39)		0.88 (0.54 to 1.44)	
P-value	-	0.4680		0.6155	
Improvement probability (95% CI)[b]					

A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Cognitive functioning
16.2.6.1.2.16 Efficacy response data - Subgroup analyses by previous treatment with IMiD
16.2.6.1.2.16.4 QLQ-C30 - Time to first deterioration by 10 pt in cognitive functioning according to previous treatment with IMiD (LOCF) - ITT population

	Yes		No		
	Kd (N=62)	**IKd (N=81)**	**Kd (N=61)**	**IKd (N=98)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	38 (61.3)	47 (58.0)	35 (57.4)	65 (66.3)	0.2144
Number (%) of patients censored	24 (38.7)	34 (42.0)	26 (42.6)	33 (33.7)	
Kaplan-Meier estimates of Cognitive functioning in months					
25% quantile (95% CI)	2.83 (1.873 to 4.665)	2.04 (1.511 to 3.943)	3.78 (1.873 to 4.994)	2.04 (1.117 to 3.713)	
Median (95% CI)	6.47 (4.665 to 10.185)	6.83 (4.665 to NC)	10.41 (4.994 to NC)	8.21 (4.665 to 12.025)	
75% quantile (95% CI)	NC (10.185 to NC)	NC (NC to NC)	NC (NC to NC)	NC (13.864 to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.6350		0.2093	
Hazard ratio (95% CI) vs Kd	-	0.90 (0.59 to 1.38)		1.30 (0.86 to 1.96)	
P-value	-	0.6352		0.2107	
Deterioration probability (95% CI)[b]					

A higher score represents a better level of quality of life. Clinical meaningful deterioration change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Cognitive functioning
16.2.6.1.2.16 Efficacy response data - Subgroup analyses by previous treatment with IMiD
16.2.6.1.2.16.5 QLQ-C30 - Time until permanent improvement by 10 pt in cognitive functioning according to previous treatment with IMiD (LOCF) - ITT population

	Yes		No		
	Kd (N=62)	**IKd (N=81)**	**Kd (N=61)**	**IKd (N=98)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	9 (14.5)	9 (11.1)	10 (16.4)	19 (19.4)	0.4476
Number (%) of patients censored	53 (85.5)	72 (88.9)	51 (83.6)	79 (80.6)	
Kaplan-Meier estimates of Cognitive functioning in months					
25% quantile (95% CI)	24.05 (17.676 to NC)	NC (23.359 to NC)	NC (15.770 to NC)	24.44 (17.380 to 24.444)	
Median (95% CI)	NC (24.049 to NC)	NC (23.359 to NC)	NC (NC to NC)	24.44 (NC to NC)	
75% quantile (95% CI)	NC (24.049 to NC)	NC (NC to NC)	NC (NC to NC)	24.44 (NC to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.5754		0.6247	
Hazard ratio (95% CI) vs Kd	-	0.77 (0.30 to 1.94)		1.21 (0.56 to 2.61)	
P-value	-	0.5765		0.6252	
Improvement probability (95% CI)[b]					

A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Cognitive functioning
16.2.6.1.2.16 Efficacy response data - Subgroup analyses by previous treatment with IMiD
16.2.6.1.2.16.6 QLQ-C30 - Time until permanent deterioration by 10 pt in cognitive functioning according to previous treatment with IMiD (LOCF) - ITT population

	Yes		No		
	Kd (N=62)	**IKd (N=81)**	**Kd (N=61)**	**IKd (N=98)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	20 (32.3)	30 (37.0)	18 (29.5)	29 (29.6)	0.8147
Number (%) of patients censored	42 (67.7)	51 (63.0)	43 (70.5)	69 (70.4)	
Kaplan-Meier estimates of Cognitive functioning in months					
25% quantile (95% CI)	14.65 (8.312 to 21.520)	12.16 (7.425 to 18.004)	18.92 (4.994 to NC)	14.52 (8.279 to NC)	
Median (95% CI)	NC (20.600 to NC)	NC (19.778 to NC)	NC (21.388 to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.6656		0.9138	
Hazard ratio (95% CI) vs Kd	-	1.13 (0.64 to 2.00)		1.03 (0.57 to 1.86)	
P-value	-	0.6658		0.9141	
Deterioration probability (95% CI)[b]					

A higher score represents a better level of quality of life. Clinical meaningful deterioration change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Cognitive functioning
16.2.6.1.2.17 Efficacy response data - Subgroup analyses by previous treatment with PI and IMiD
16.2.6.1.2.17.3 QLQ-C30 - Time to first improvement by 10 pt in cognitive functioning according to previous treatment with PI and IMiD (LOCF) - ITT population

	Yes		No		
	Kd (N=17)	**IKd (N=23)**	**Kd (N=106)**	**IKd (N=156)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	4 (23.5)	6 (26.1)	50 (47.2)	63 (40.4)	0.6214
Number (%) of patients censored	13 (76.5)	17 (73.9)	56 (52.8)	93 (59.6)	
Kaplan-Meier estimates of Cognitive functioning in months					
25% quantile (95% CI)	10.48 (1.018 to NC)	15.28 (1.018 to NC)	1.91 (1.051 to 1.971)	1.91 (1.117 to 2.793)	
Median (95% CI)	NC (10.480 to NC)	NC (15.277 to NC)	NC (3.745 to NC)	NC (21.848 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.8504		0.3211	
Hazard ratio (95% CI) vs Kd	-	1.13 (0.32 to 4.01)		0.83 (0.57 to 1.20)	
P-value	-	0.8505		0.3218	
Improvement probability (95% CI)[b]					

A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Cognitive functioning
16.2.6.1.2.17 Efficacy response data - Subgroup analyses by previous treatment with PI and IMiD
16.2.6.1.2.17.4 QLQ-C30 - Time to first deterioration by 10 pt in cognitive functioning according to previous treatment with PI and IMiD (LOCF) - ITT population

	Yes		No		
	Kd (N=17)	**IKd (N=23)**	**Kd (N=106)**	**IKd (N=156)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	10 (58.8)	13 (56.5)	63 (59.4)	99 (63.5)	0.6407
Number (%) of patients censored	7 (41.2)	10 (43.5)	43 (40.6)	57 (36.5)	
Kaplan-Meier estimates of Cognitive functioning in months					
25% quantile (95% CI)	2.04 (0.986 to 6.472)	2.60 (0.986 to 4.665)	3.06 (1.938 to 4.797)	2.04 (1.873 to 3.055)	
Median (95% CI)	6.47 (1.938 to NC)	4.80 (2.825 to NC)	7.92 (5.125 to 12.189)	8.21 (4.961 to 11.400)	
75% quantile (95% CI)	NC (6.472 to NC)	NC (4.797 to NC)	NC (NC to NC)	NC (19.253 to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.8367		0.4943	
Hazard ratio (95% CI) vs Kd	-	0.92 (0.40 to 2.09)		1.12 (0.81 to 1.53)	
P-value	-	0.8368		0.4946	
Deterioration probability (95% CI)[b]					

A higher score represents a better level of quality of life. Clinical meaningful deterioration change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Cognitive functioning
16.2.6.1.2.17 Efficacy response data - Subgroup analyses by previous treatment with PI and IMiD
16.2.6.1.2.17.5 QLQ-C30 - Time until permanent improvement by 10 pt in cognitive functioning according to previous treatment with PI and IMiD (LOCF) - ITT population

	Yes		No		
	Kd (N=17)	**IKd (N=23)**	**Kd (N=106)**	**IKd (N=156)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	1 (5.9)	3 (13.0)	18 (17.0)	25 (16.0)	0.4035
Number (%) of patients censored	16 (94.1)	20 (87.0)	88 (83.0)	131 (84.0)	
Kaplan-Meier estimates of Cognitive functioning in months					
25% quantile (95% CI)	NC (10.448 to NC)	23.36 (1.051 to NC)	24.05 (17.676 to NC)	24.44 (21.848 to NC)	
Median (95% CI)	NC (NC to NC)	23.36 (23.359 to NC)	NC (24.049 to NC)	NC (24.444 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (23.359 to NC)	NC (NC to NC)	NC (24.444 to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.4357		0.8544	
Hazard ratio (95% CI) vs Kd	-	2.40 (0.25 to 23.14)		0.94 (0.52 to 1.73)	
P-value	-	0.4500		0.8537	

A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
PGM=DEVOPS/SAR650984/EFC15246/CIR_RWE/REPORT/PGM/eff_km_subgp_sr_sig_de_i_t.sas OUT=REPORT/OUTPUT/eff_km_c30_cog_imppl_piimid_de_i_t_x.rtf (07APR2021 14:26)

16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Cognitive functioning
16.2.6.1.2.17 Efficacy response data - Subgroup analyses by previous treatment with PI and IMiD
16.2.6.1.2.17.6 QLQ-C30 - Time until permanent deterioration by 10 pt in cognitive functioning according to previous treatment with PI and IMiD (LOCF) - ITT population

	Yes		No		
	Kd (N=17)	**IKd (N=23)**	**Kd (N=106)**	**IKd (N=156)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	5 (29.4)	11 (47.8)	33 (31.1)	48 (30.8)	0.2634
Number (%) of patients censored	12 (70.6)	12 (52.2)	73 (68.9)	108 (69.2)	
Kaplan-Meier estimates of Cognitive functioning in months					
25% quantile (95% CI)	20.60 (8.312 to NC)	8.38 (1.511 to 21.815)	15.38 (7.918 to 20.567)	14.19 (11.499 to 19.253)	
Median (95% CI)	NC (14.653 to NC)	21.82 (8.378 to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (21.520 to NC)	23.10 (21.815 to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.2424		0.9555	
Hazard ratio (95% CI) vs Kd	-	1.86 (0.65 to 5.38)		0.99 (0.63 to 1.54)	
P-value	-	0.2500		0.9555	
Deterioration probability (95% CI)[b]					

A higher score represents a better level of quality of life. Clinical meaningful deterioration change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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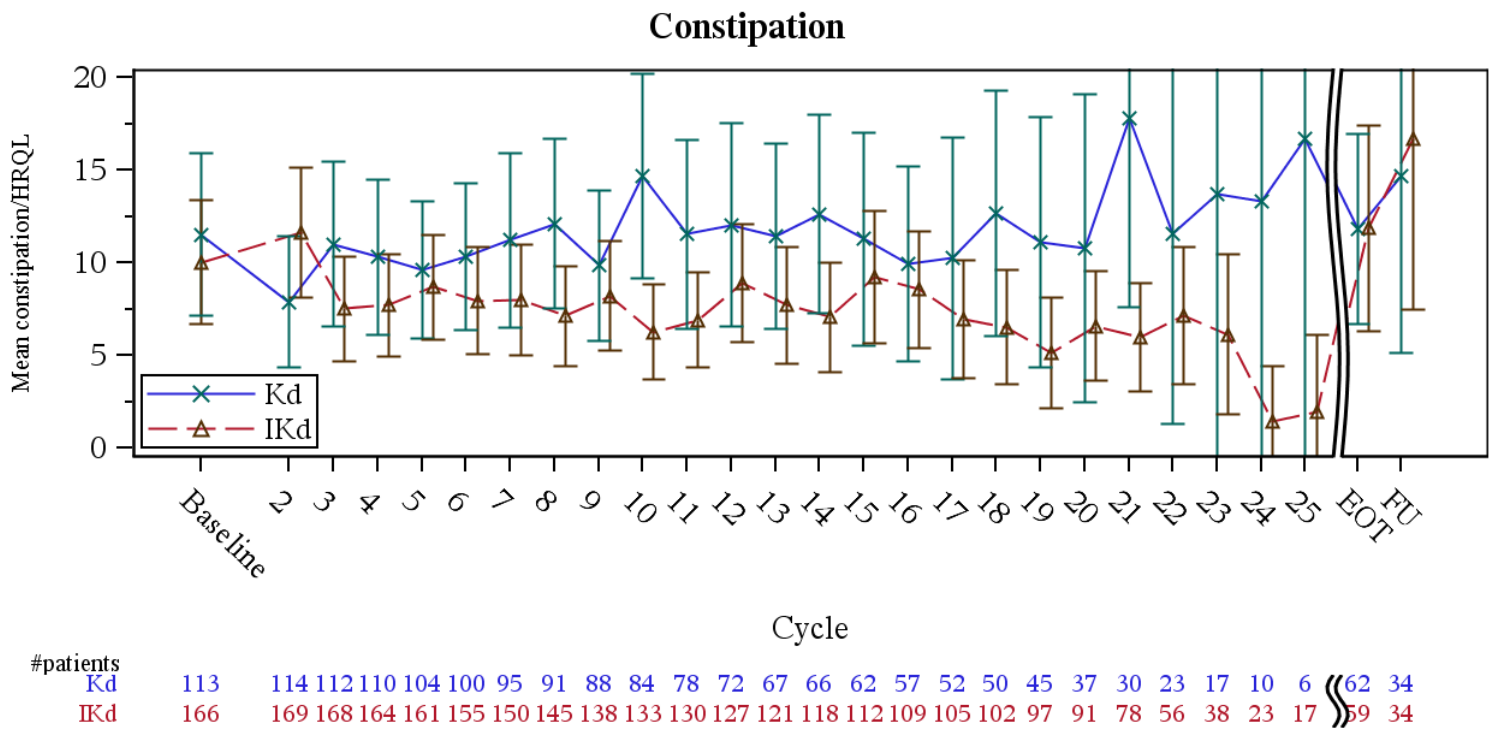
16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Constipation
16.2.6.1.2.1 Efficacy response data
16.2.6.1.2.1.1 QLQ-C30 - Mean and 95% CI for constipation score over time (LOCF) - ITT population



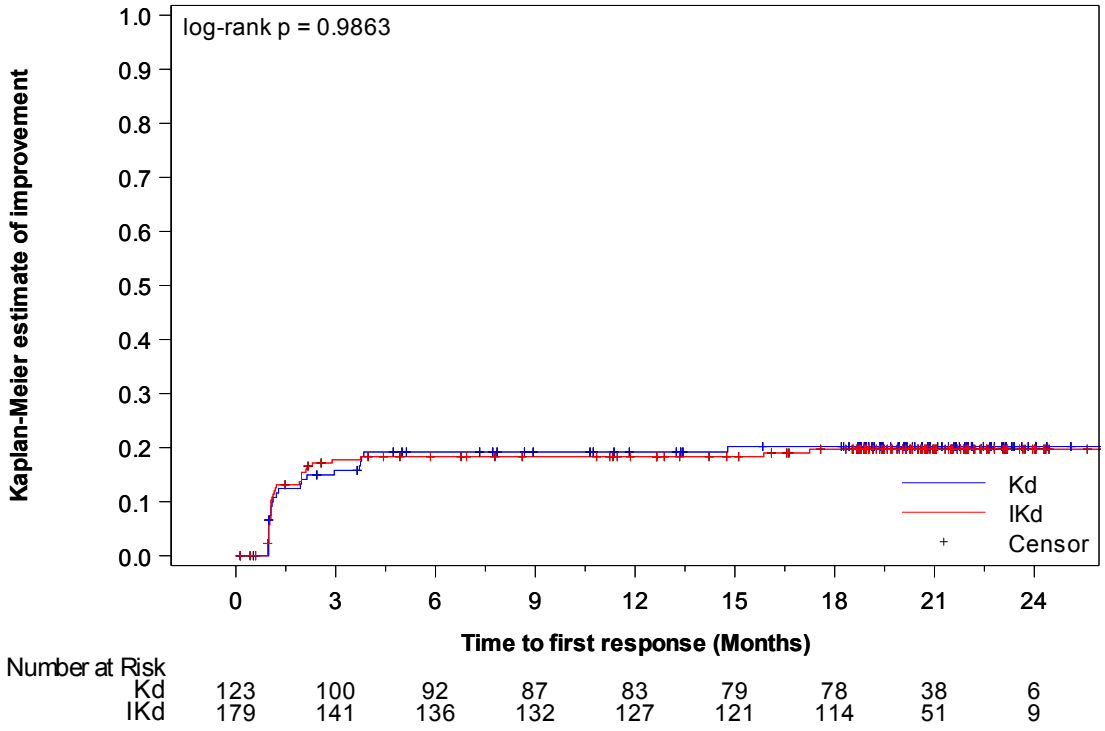
A lower score represents a better level of quality of life. Cycles with less than 20 patients overall are not presented.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
PGM=DEVOPS/SAR650984/EFC15246/CIR_RWE/REPORT/PGM/eff_qlq_line_i_f.sas OUT=REPORT/OUTPUT/eff_qlq_line_c30_con_de_i_f_x.rtf (12FEB2021 15:16)

16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Constipation
16.2.6.1.2.1 Efficacy response data
16.2.6.1.2.1.15 QLQ-C30 - Time to first improvement by 15 pt in Constipation (LOCF) - ITT population

First improvement 15 points Constipation (%)	**Kd (N=123)**	**IKd (N=179)**
Number (%) of events	24 (19.5)	34 (19.0)
Number (%) of patients censored	99 (80.5)	145 (81.0)
Kaplan-Meier estimates of Constipation in months		
25% quantile (95% CI)	NC (3.745 to NC)	NC (15.869 to NC)
Median (95% CI)	NC (NC to NC)	NC (NC to NC)
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)
Comparison vs. Kd		
Stratified[a] Log-Rank test p-value[b] vs Kd	-	0.9863
Stratified[a] Hazard ratio (95% CI) vs Kd	-	1.00 (0.59 to 1.70)
P-value	-	0.9863
Improvement probability (95% CI)[c]		
3 Months	0.158 (0.099 to 0.229)	0.177 (0.125 to 0.238)
6 Months	0.192 (0.127 to 0.267)	0.183 (0.130 to 0.244)

A lower score represents a better level of quality of life. Clinical meaningful improvement change from baseline less than or equal to -15 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] Stratified on number of prior lines of therapy (1 vs. >1) and Revised International Staging System (R-ISS) stage (I or II vs. III vs. not classified) according to IRT
[b] One-sided significance level is 0.025
[c] Estimated using the Kaplan-Meier method
NA/NC = Not Applicable / Not Calculable
PGM=DEVOPS/SAR650984/EFC15246/CIR_RWE/REPORT/PGM/eff_km_invhr_sr_i_t.sas OUT=REPORT/OUTPUT/eff_km_c30_con_imp15l_de_i_t_x.rtf (07APR2021 14:23)

16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Constipation
16.2.6.1.2.1 Efficacy response data
16.2.6.1.2.1.16 QLQ-C30 - Time to first improvement by 15 pt in Constipation - Kaplan-Meier curve (LOCF) - ITT population



A lower score represents a better level of quality of life. Clinical meaningful improvement change from baseline less than or equal to -15 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
PGM=DEVOPS/SAR650984/EFC15246/CIR_RWE/REPORT/PGM/eff_qlq_km_i_f.sas OUT=REPORT/OUTPUT/eff_km_c30_con_imp15l_de_i_f_x.rtf (07APR2021 14:24)

16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Constipation
16.2.6.1.2.1 Efficacy response data
16.2.6.1.2.1.17 QLQ-C30 - Time to first deterioration by 15 pt in Constipation (LOCF) - ITT population

First deterioration 15 points Constipation (%)	**Kd (N=123)**	**IKd (N=179)**
Number (%) of events	48 (39.0)	76 (42.5)
Number (%) of patients censored	75 (61.0)	103 (57.5)
Kaplan-Meier estimates of Constipation in months		
25% quantile (95% CI)	5.55 (2.858 to 11.039)	4.67 (2.530 to 5.848)
Median (95% CI)	NC (16.986 to NC)	NC (14.160 to NC)
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)
Comparison vs. Kd		
Stratified[a] Log-Rank test p-value[b] vs Kd	-	0.5366
Stratified[a] Hazard ratio (95% CI) vs Kd	-	1.12 (0.78 to 1.61)
P-value	-	0.5368
Deterioration probability (95% CI)[c]		
3 Months	0.816 (0.734 to 0.875)	0.799 (0.732 to 0.852)
6 Months	0.747 (0.658 to 0.816)	0.686 (0.611 to 0.750)

A lower score represents a better level of quality of life. Clinical meaningful deterioration change from baseline greater than or equal to 15 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] Stratified on number of prior lines of therapy (1 vs. >1) and Revised International Staging System (R-ISS) stage (I or II vs. III vs. not classified) according to IRT
[b] One-sided significance level is 0.025
[c] Estimated using the Kaplan-Meier method
NA/NC = Not Applicable / Not Calculable
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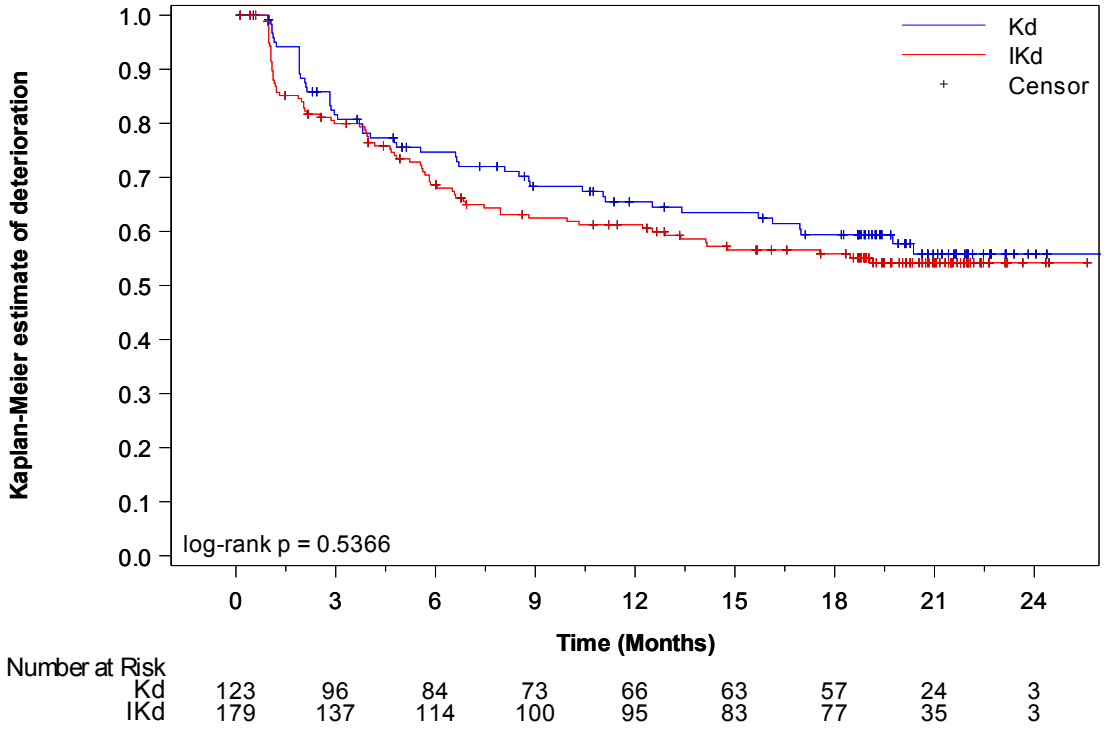
16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Constipation
16.2.6.1.2.1 Efficacy response data
16.2.6.1.2.1.18 QLQ-C30 - Time to first deterioration by 15 pt in Constipation - Kaplan-Meier curve (LOCF) - ITT population



A lower score represents a better level of quality of life. Clinical meaningful deterioration change from baseline greater than or equal to 15 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
PGM=DEVOPS/SAR650984/EFC15246/CIR_RWE/REPORT/PGM/eff_qlq_km_i_f.sas OUT=REPORT/OUTPUT/eff_km_c30_con_det15l_de_i_f_x.rtf (07APR2021 14:24)

16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Constipation
16.2.6.1.2.1 Efficacy response data
16.2.6.1.2.1.19 QLQ-C30 - Time until permanent improvement by 15 pt in Constipation (LOCF) - ITT population

First permanent improvement 15 points Constipation (%)	**Kd (N=123)**	**IKd (N=179)**
Number (%) of events	14 (11.4)	28 (15.6)
Number (%) of patients censored	109 (88.6)	151 (84.4)
Kaplan-Meier estimates of Constipation in months		
25% quantile (95% CI)	NC (22.439 to NC)	NC (20.698 to NC)
Median (95% CI)	NC (NC to NC)	NC (NC to NC)
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)
Comparison vs. Kd		
Stratified[a] Log-Rank test p-value[b] vs Kd	-	0.2732
Stratified[a] Hazard ratio (95% CI) vs Kd	-	1.43 (0.75 to 2.72)
P-value	-	0.2757
Improvement probability (95% CI)[c]		
3 Months	0.050 (0.020 to 0.099)	0.097 (0.059 to 0.147)
6 Months	0.076 (0.037 to 0.132)	0.109 (0.068 to 0.160)

A lower score represents a better level of quality of life. Clinical meaningful improvement change from baseline less than or equal to -15 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] Stratified on number of prior lines of therapy (1 vs. >1) and Revised International Staging System (R-ISS) stage (I or II vs. III vs. not classified) according to IRT
[b] One-sided significance level is 0.025
[c] Estimated using the Kaplan-Meier method
NA/NC = Not Applicable / Not Calculable
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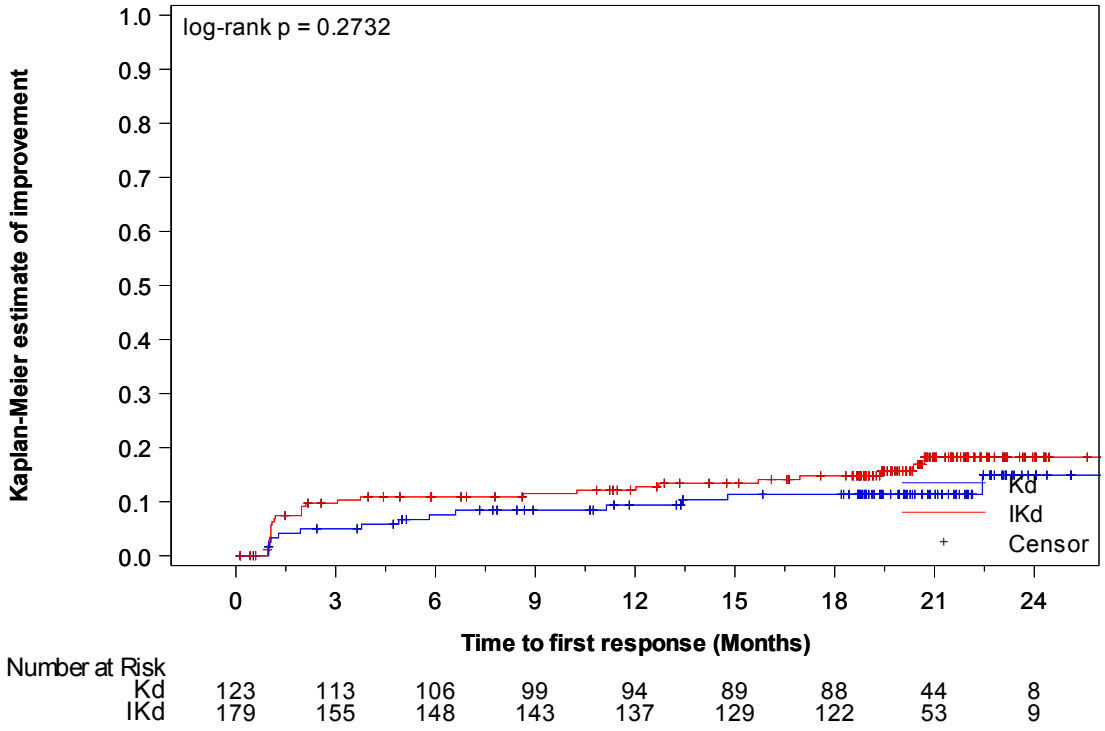
16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Constipation
16.2.6.1.2.1 Efficacy response data
16.2.6.1.2.1.20 QLQ-C30 - Time until permanent improvement by 15 pt in Constipation - Kaplan-Meier curve (LOCF) - ITT population



A lower score represents a better level of quality of life. Clinical meaningful improvement change from baseline less than or equal to -15 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.

16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Constipation
16.2.6.1.2.1 Efficacy response data
16.2.6.1.2.1.21 QLQ-C30 - Time until permanent deterioration by 15 pt in Constipation (LOCF) - ITT population

First permanent deterioration 15 points Constipation (%)	**Kd (N=123)**	**IKd (N=179)**
Number (%) of events	15 (12.2)	24 (13.4)
Number (%) of patients censored	108 (87.8)	155 (86.6)
Kaplan-Meier estimates of Constipation in months		
25% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)
Median (95% CI)	NC (NC to NC)	NC (NC to NC)
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)
Comparison vs. Kd		
Stratified[a] Log-Rank test p-value[b] vs Kd	-	0.8780
Stratified[a] Hazard ratio (95% CI) vs Kd	-	1.05 (0.55 to 2.01)
P-value	-	0.8787
Deterioration probability (95% CI)[c]		
3 Months	0.983 (0.935 to 0.996)	0.966 (0.925 to 0.984)
6 Months	0.966 (0.911 to 0.987)	0.948 (0.902 to 0.972)

A lower score represents a better level of quality of life. Clinical meaningful deterioration change from baseline greater than or equal to 15 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] Stratified on number of prior lines of therapy (1 vs. >1) and Revised International Staging System (R-ISS) stage (I or II vs. III vs. not classified) according to IRT
[b] One-sided significance level is 0.025
[c] Estimated using the Kaplan-Meier method
NA/NC = Not Applicable / Not Calculable
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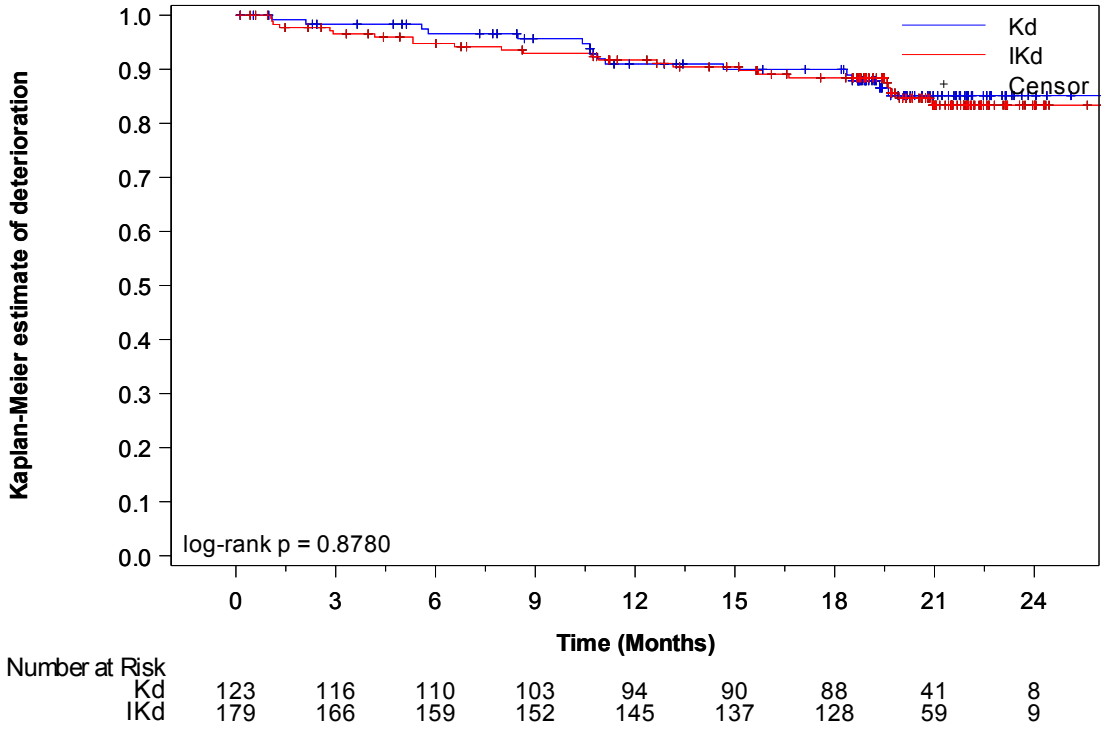
16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Constipation
16.2.6.1.2.1 Efficacy response data
16.2.6.1.2.1.22 QLQ-C30 - Time until permanent deterioration by 15 pt in Constipation - Kaplan-Meier curve (LOCF) - ITT population



A lower score represents a better level of quality of life. Clinical meaningful deterioration change from baseline greater than or equal to 15 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
PGM=DEVOPS/SAR650984/EFC15246/CIR_RWE/REPORT/PGM/eff_qlq_km_i_f.sas OUT=REPORT/OUTPUT/eff_km_c30_con_det15pl_de_i_f_x.rtf (07APR2021 14:24)

16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Constipation
16.2.6.1.2.2 Efficacy response data - Subgroup analyses by age
16.2.6.1.2.2.3 QLQ-C30 - Time to first improvement by 10 pt in constipation according to age (LOCF) - ITT population

	<65 years		>=65 years		
	Kd (N=66)	**IKd (N=88)**	**Kd (N=57)**	**IKd (N=91)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	15 (22.7)	13 (14.8)	9 (15.8)	21 (23.1)	0.1047
Number (%) of patients censored	51 (77.3)	75 (85.2)	48 (84.2)	70 (76.9)	
Kaplan-Meier estimates of Constipation in months					
25% quantile (95% CI)	NC (1.281 to NC)	NC (NC to NC)	NC (3.745 to NC)	NC (1.183 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.2251		0.2827	
Hazard ratio (95% CI) vs Kd	-	0.63 (0.30 to 1.33)		1.53 (0.70 to 3.34)	
P-value	-	0.2292		0.2864	
Improvement probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful improvement change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
PGM=DEVOPS/SAR650984/EFC15246/CIR_RWE/REPORT/PGM/eff_km_subgp_sr_sig_de_i_t.sas OUT=REPORT/OUTPUT/eff_km_c30_con_impl_age_de_i_t_x.rtf (07APR2021 14:35)

16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Constipation
16.2.6.1.2.2 Efficacy response data - Subgroup analyses by age
16.2.6.1.2.2.4 QLQ-C30 - Time to first deterioration by 10 pt in constipation according to age (LOCF) - ITT population

	<65 years		>=65 years		
	Kd (N=66)	**IKd (N=88)**	**Kd (N=57)**	**IKd (N=91)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	26 (39.4)	35 (39.8)	22 (38.6)	41 (45.1)	0.5484
Number (%) of patients censored	40 (60.6)	53 (60.2)	35 (61.4)	50 (54.9)	
Kaplan-Meier estimates of Constipation in months					
25% quantile (95% CI)	4.04 (2.136 to 11.039)	4.76 (2.037 to 7.458)	8.08 (2.825 to 15.704)	4.17 (1.314 to 6.834)	
Median (95% CI)	NC (11.105 to NC)	NC (14.127 to NC)	NC (15.704 to NC)	NC (8.805 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.9212		0.3397	
Hazard ratio (95% CI) vs Kd	-	1.03 (0.62 to 1.70)		1.29 (0.77 to 2.16)	
P-value	-	0.9213		0.3410	
Deterioration probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful deterioration change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Constipation
16.2.6.1.2.2 Efficacy response data - Subgroup analyses by age
16.2.6.1.2.2.5 QLQ-C30 - Time until permanent improvement by 10 pt in constipation according to age (LOCF) - ITT population

	<65 years		>=65 years		
	Kd (N=66)	**IKd (N=88)**	**Kd (N=57)**	**IKd (N=91)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	8 (12.1)	10 (11.4)	6 (10.5)	18 (19.8)	0.2592
Number (%) of patients censored	58 (87.9)	78 (88.6)	51 (89.5)	73 (80.2)	
Kaplan-Meier estimates of Constipation in months					
25% quantile (95% CI)	NC (22.439 to NC)	NC (NC to NC)	NC (NC to NC)	NC (15.704 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.9115		0.1413	
Hazard ratio (95% CI) vs Kd	-	0.95 (0.37 to 2.40)		1.97 (0.78 to 4.98)	
P-value	-	0.9112		0.1490	
Improvement probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful improvement change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Constipation
16.2.6.1.2.2 Efficacy response data - Subgroup analyses by age
16.2.6.1.2.2.6 QLQ-C30 - Time until permanent deterioration by 10 pt in constipation according to age (LOCF) - ITT population

	<65 years		>=65 years		
	Kd (N=66)	**IKd (N=88)**	**Kd (N=57)**	**IKd (N=91)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	9 (13.6)	13 (14.8)	6 (10.5)	11 (12.1)	0.9206
Number (%) of patients censored	57 (86.4)	75 (85.2)	51 (89.5)	80 (87.9)	
Kaplan-Meier estimates of Constipation in months					
25% quantile (95% CI)	NC (18.366 to NC)	NC (19.680 to NC)	NC (19.351 to NC)	NC (19.877 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.8859		0.8088	
Hazard ratio (95% CI) vs Kd	-	1.06 (0.45 to 2.49)		1.13 (0.42 to 3.06)	
P-value	-	0.8865		0.8090	
Deterioration probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful deterioration change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Constipation
16.2.6.1.2.3 Efficacy response data - Subgroup analyses by gender
16.2.6.1.2.3.3 QLQ-C30 - Time to first improvement by 10 pt in constipation according to gender (LOCF) - ITT population

	Male		Female		
	Kd (N=68)	**IKd (N=101)**	**Kd (N=55)**	**IKd (N=78)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	9 (13.2)	16 (15.8)	15 (27.3)	18 (23.1)	0.5491
Number (%) of patients censored	59 (86.8)	85 (84.2)	40 (72.7)	60 (76.9)	
Kaplan-Meier estimates of Constipation in months					
25% quantile (95% CI)	NC (NC to NC)	NC (17.248 to NC)	3.84 (1.051 to NC)	NC (1.051 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.6606		0.6775	
Hazard ratio (95% CI) vs Kd	-	1.20 (0.53 to 2.72)		0.86 (0.44 to 1.72)	
P-value	-	0.6611		0.6777	
Improvement probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful improvement change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Constipation
16.2.6.1.2.3 Efficacy response data - Subgroup analyses by gender
16.2.6.1.2.3.4 QLQ-C30 - Time to first deterioration by 10 pt in constipation according to gender (LOCF) - ITT population

	Male		Female		
	Kd (N=68)	**IKd (N=101)**	**Kd (N=55)**	**IKd (N=78)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	22 (32.4)	45 (44.6)	26 (47.3)	31 (39.7)	0.0559
Number (%) of patients censored	46 (67.6)	56 (55.4)	29 (52.7)	47 (60.3)	
Kaplan-Meier estimates of Constipation in months					
25% quantile (95% CI)	8.84 (2.957 to 16.953)	3.88 (1.216 to 5.815)	3.71 (1.906 to 6.702)	5.82 (2.070 to 12.912)	
Median (95% CI)	NC (16.953 to NC)	NC (6.899 to NC)	20.37 (6.702 to NC)	NC (14.160 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.0665		0.3588	
Hazard ratio (95% CI) vs Kd	-	1.61 (0.96 to 2.67)		0.78 (0.47 to 1.32)	
P-value	-	0.0691		0.3599	
Deterioration probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful deterioration change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Constipation
16.2.6.1.2.3 Efficacy response data - Subgroup analyses by gender
16.2.6.1.2.3.5 QLQ-C30 - Time until permanent improvement by 10 pt in constipation according to gender (LOCF) - ITT population

	Male		Female		
	Kd (N=68)	**IKd (N=101)**	**Kd (N=55)**	**IKd (N=78)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	7 (10.3)	14 (13.9)	7 (12.7)	14 (17.9)	0.9233
Number (%) of patients censored	61 (89.7)	87 (86.1)	48 (87.3)	64 (82.1)	
Kaplan-Meier estimates of Constipation in months					
25% quantile (95% CI)	NC (NC to NC)	NC (20.370 to NC)	NC (22.439 to NC)	NC (8.641 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.4725		0.3858	
Hazard ratio (95% CI) vs Kd	-	1.39 (0.56 to 3.45)		1.49 (0.60 to 3.70)	
P-value	-	0.4746		0.3890	
Improvement probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful improvement change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Constipation
16.2.6.1.2.3 Efficacy response data - Subgroup analyses by gender
16.2.6.1.2.3.6 QLQ-C30 - Time until permanent deterioration by 10 pt in constipation according to gender (LOCF) - ITT population

	Male		Female		
	Kd (N=68)	**IKd (N=101)**	**Kd (N=55)**	**IKd (N=78)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	7 (10.3)	13 (12.9)	8 (14.5)	11 (14.1)	0.5929
Number (%) of patients censored	61 (89.7)	88 (87.1)	47 (85.5)	67 (85.9)	
Kaplan-Meier estimates of Constipation in months					
25% quantile (95% CI)	NC (19.614 to NC)	NC (NC to NC)	NC (18.366 to NC)	NC (19.877 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.6069		0.7958	
Hazard ratio (95% CI) vs Kd	-	1.27 (0.51 to 3.19)		0.89 (0.36 to 2.21)	
P-value	-	0.6078		0.7960	
Deterioration probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful deterioration change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Constipation
16.2.6.1.2.4 Efficacy response data - Subgroup analyses by ethnic origin
16.2.6.1.2.4.3 QLQ-C30 - Time to first improvement by 10 pt in constipation according to ethnic origin (LOCF) - ITT population

	White		Other		
	Kd (N=83)	**IKd (N=131)**	**Kd (N=28)**	**IKd (N=34)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	17 (20.5)	29 (22.1)	5 (17.9)	5 (14.7)	0.6874
Number (%) of patients censored	66 (79.5)	102 (77.9)	23 (82.1)	29 (85.3)	
Kaplan-Meier estimates of Constipation in months					
25% quantile (95% CI)	NC (3.713 to NC)	NC (1.971 to NC)	NC (1.051 to NC)	NC (1.051 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.7347		0.7731	
Hazard ratio (95% CI) vs Kd	-	1.11 (0.61 to 2.02)		0.83 (0.24 to 2.88)	
P-value	-	0.7348		0.7734	
Improvement probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful improvement change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Constipation
16.2.6.1.2.4 Efficacy response data - Subgroup analyses by ethnic origin
16.2.6.1.2.4.4 QLQ-C30 - Time to first deterioration by 10 pt in constipation according to ethnic origin (LOCF) - ITT population

	White		Other		
	Kd (N=83)	**IKd (N=131)**	**Kd (N=28)**	**IKd (N=34)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	29 (34.9)	52 (39.7)	14 (50.0)	18 (52.9)	0.9066
Number (%) of patients censored	54 (65.1)	79 (60.3)	14 (50.0)	16 (47.1)	
Kaplan-Meier estimates of Constipation in months					
25% quantile (95% CI)	8.80 (2.858 to 16.131)	5.55 (3.713 to 6.834)	5.55 (1.084 to 10.415)	3.43 (1.051 to 6.045)	
Median (95% CI)	NC (20.370 to NC)	NC (18.464 to NC)	16.95 (6.604 to NC)	12.52 (3.943 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (16.986 to NC)	NC (14.784 to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.3552		0.6138	
Hazard ratio (95% CI) vs Kd	-	1.24 (0.79 to 1.95)		1.20 (0.59 to 2.41)	
P-value	-	0.3561		0.6142	
Deterioration probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful deterioration change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Constipation
16.2.6.1.2.4 Efficacy response data - Subgroup analyses by ethnic origin
16.2.6.1.2.4.5 QLQ-C30 - Time until permanent improvement by 10 pt in constipation according to ethnic origin (LOCF) - ITT population

	White		Other		
	Kd (N=83)	**IKd (N=131)**	**Kd (N=28)**	**IKd (N=34)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	10 (12.0)	23 (17.6)	2 (7.1)	5 (14.7)	0.6858
Number (%) of patients censored	73 (88.0)	108 (82.4)	26 (92.9)	29 (85.3)	
Kaplan-Meier estimates of Constipation in months					
25% quantile (95% CI)	NC (22.439 to NC)	NC (19.384 to NC)	NC (11.138 to NC)	NC (1.971 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.2484		0.3463	
Hazard ratio (95% CI) vs Kd	-	1.54 (0.73 to 3.24)		2.16 (0.42 to 11.12)	
P-value	-	0.2523		0.3581	
Improvement probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful improvement change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
PGM=DEVOPS/SAR650984/EFC15246/CIR_RWE/REPORT/PGM/eff_km_subgp_sr_sig_de_i_t.sas OUT=REPORT/OUTPUT/eff_km_c30_con_imppl_race_de_i_t_x.rtf (07APR2021 14:36)

16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Constipation
16.2.6.1.2.4 Efficacy response data - Subgroup analyses by ethnic origin
16.2.6.1.2.4.6 QLQ-C30 - Time until permanent deterioration by 10 pt in constipation according to ethnic origin (LOCF) - ITT population

	White		Other		
	Kd (N=83)	**IKd (N=131)**	**Kd (N=28)**	**IKd (N=34)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	10 (12.0)	14 (10.7)	3 (10.7)	6 (17.6)	0.4572
Number (%) of patients censored	73 (88.0)	117 (89.3)	25 (89.3)	28 (82.4)	
Kaplan-Meier estimates of Constipation in months					
25% quantile (95% CI)	NC (19.614 to NC)	NC (NC to NC)	NC (8.476 to NC)	NC (13.142 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.7709		0.5064	
Hazard ratio (95% CI) vs Kd	-	0.89 (0.39 to 2.00)		1.59 (0.40 to 6.38)	
P-value	-	0.7711		0.5103	
Deterioration probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful deterioration change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
PGM=DEVOPS/SAR650984/EFC15246/CIR_RWE/REPORT/PGM/eff_km_subgp_sr_sig_de_i_t.sas OUT=REPORT/OUTPUT/eff_km_c30_con_detpl_race_de_i_t_x.rtf (07APR2021 14:36)

16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Constipation
16.2.6.1.2.5 Efficacy response data - Subgroup analyses by geographical region
16.2.6.1.2.5.3 QLQ-C30 - Time to first improvement by 10 pt in constipation according to geographical region (LOCF) - ITT population

	Europe		America		Asia		Other countries		
	Kd (N=60)	**IKd (N=85)**	**Kd (N=20)**	**IKd (N=24)**	**Kd (N=21)**	**IKd (N=25)**	**Kd (N=22)**	**IKd (N=45)**	**p-value of treatment-by-subgroup interaction[c]**
Number (%) of events	11 (18.3)	18 (21.2)	7 (35.0)	3 (12.5)	4 (19.0)	3 (12.0)	2 (9.1)	10 (22.2)	0.1761
Number (%) of patients censored	49 (81.7)	67 (78.8)	13 (65.0)	21 (87.5)	17 (81.0)	22 (88.0)	20 (90.9)	35 (77.8)	
Kaplan-Meier estimates of event in months									
25% quantile (95% CI)	NC (1.971 to NC)	NC (1.971 to NC)	1.25 (0.986 to NC)	NC (0.953 to NC)	NC (0.986 to NC)	NC (1.018 to NC)	NC (0.986 to NC)	NC (1.051 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (1.216 to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Kd									

A lower score represents a better level of quality of life. Clinical meaningful improvement change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Constipation
16.2.6.1.2.5 Efficacy response data - Subgroup analyses by geographical region
16.2.6.1.2.5.3 QLQ-C30 - Time to first improvement by 10 pt in constipation according to geographical region (LOCF) - ITT population

	Europe		America		Asia		Other countries		
	Kd (N=60)	**IKd (N=85)**	**Kd (N=20)**	**IKd (N=24)**	**Kd (N=21)**	**IKd (N=25)**	**Kd (N=22)**	**IKd (N=45)**	**p-value of treatment-by-subgroup interaction[c]**
Log-Rank test p-value[a] vs Kd	-	0.6678		0.1028		0.4757		0.1937	
Hazard ratio (95% CI) vs Kd	-	1.18 (0.56 to 2.49)		0.34 (0.09 to 1.32)		0.58 (0.13 to 2.61)		2.63 (0.58 to 12.03)	
P-value	-	0.6682		0.1198		0.4809		0.2112	
Improvement probability (95% CI)[b]									
3 Months	0.137 (0.064 to 0.238)	0.193 (0.116 to 0.284)	0.300 (0.123 to 0.501)	0.131 (0.033 to 0.299)	0.203 (0.063 to 0.399)	0.083 (0.014 to 0.233)	0.045 (0.003 to 0.189)	0.222 (0.115 to 0.351)	
6 Months	0.172 (0.089 to 0.279)	0.193 (0.116 to 0.284)	0.350 (0.157 to 0.552)	0.131 (0.033 to 0.299)	0.203 (0.063 to 0.399)	0.125 (0.031 to 0.287)	0.091 (0.016 to 0.251)	0.222 (0.115 to 0.351)	

A lower score represents a better level of quality of life. Clinical meaningful improvement change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Constipation
16.2.6.1.2.5 Efficacy response data - Subgroup analyses by geographical region
16.2.6.1.2.5.4 QLQ-C30 - Time to first deterioration by 10 pt in constipation according to geographical region (LOCF) - ITT population

	Europe		America		Asia		Other countries		
	Kd (N=60)	**IKd (N=85)**	**Kd (N=20)**	**IKd (N=24)**	**Kd (N=21)**	**IKd (N=25)**	**Kd (N=22)**	**IKd (N=45)**	**p-value of treatment-by-subgroup interaction[c]**
Number (%) of events	19 (31.7)	33 (38.8)	8 (40.0)	12 (50.0)	12 (57.1)	17 (68.0)	9 (40.9)	14 (31.1)	0.5383
Number (%) of patients censored	41 (68.3)	52 (61.2)	12 (60.0)	12 (50.0)	9 (42.9)	8 (32.0)	13 (59.1)	31 (68.9)	
Kaplan-Meier estimates of event in months									
25% quantile (95% CI)	8.51 (2.825 to NC)	5.22 (1.314 to 6.899)	7.18 (1.906 to NC)	2.53 (1.051 to 13.372)	4.04 (1.051 to 10.415)	2.50 (0.986 to 3.943)	3.06 (1.084 to 20.370)	7.46 (3.713 to NC)	
Median (95% CI)	NC (19.745 to NC)	NC (10.316 to NC)	NC (5.552 to NC)	14.16 (3.975 to NC)	13.40 (4.041 to NC)	7.24 (2.858 to 14.127)	NC (3.055 to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (18.464 to NC)	NC (13.405 to NC)	14.78 (12.222 to NC)	NC (NC to NC)	NC (NC to NC)	

A lower score represents a better level of quality of life. Clinical meaningful deterioration change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Constipation
16.2.6.1.2.5 Efficacy response data - Subgroup analyses by geographical region
16.2.6.1.2.5.4 QLQ-C30 - Time to first deterioration by 10 pt in constipation according to geographical region (LOCF) - ITT population

	Europe		America		Asia		Other countries		
	Kd (N=60)	**IKd (N=85)**	**Kd (N=20)**	**IKd (N=24)**	**Kd (N=21)**	**IKd (N=25)**	**Kd (N=22)**	**IKd (N=45)**	**p-value of treatment-by-subgroup interaction[c]**
Comparison vs. Kd									
Log-Rank test p-value[a] vs Kd	-	0.3498		0.3121		0.3097		0.4145	
Hazard ratio (95% CI) vs Kd	-	1.31 (0.74 to 2.30)		1.58 (0.65 to 3.87)		1.47 (0.70 to 3.08)		0.71 (0.31 to 1.63)	
P-value	-	0.3513		0.3163		0.3126		0.4168	
Deterioration probability (95% CI)[b]									
3 Months	0.809 (0.682 to 0.890)	0.807 (0.705 to 0.877)	0.900 (0.656 to 0.974)	0.734 (0.501 to 0.871)	0.797 (0.545 to 0.919)	0.667 (0.443 to 0.817)	0.773 (0.537 to 0.898)	0.889 (0.753 to 0.952)	

A lower score represents a better level of quality of life. Clinical meaningful deterioration change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Constipation
16.2.6.1.2.5 Efficacy response data - Subgroup analyses by geographical region
16.2.6.1.2.5.5 QLQ-C30 - Time until permanent improvement by 10 pt in constipation according to geographical region (LOCF) - ITT population

	Europe		America		Asia		Other countries		
	Kd (N=60)	**IKd (N=85)**	**Kd (N=20)**	**IKd (N=24)**	**Kd (N=21)**	**IKd (N=25)**	**Kd (N=22)**	**IKd (N=45)**	**p-value of treatment-by-subgroup interaction[c]**
Number (%) of events	7 (11.7)	14 (16.5)	5 (25.0)	3 (12.5)	1 (4.8)	3 (12.0)	1 (4.5)	8 (17.8)	0.3318
Number (%) of patients censored	53 (88.3)	71 (83.5)	15 (75.0)	21 (87.5)	20 (95.2)	22 (88.0)	21 (95.5)	37 (82.2)	
Kaplan-Meier estimates of event in months									
25% quantile (95% CI)	NC (22.439 to NC)	NC (19.384 to NC)	NC (1.051 to NC)	NC (0.953 to NC)	NC (11.138 to NC)	NC (1.018 to NC)	NC (14.784 to NC)	NC (15.704 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (5.815 to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	

A lower score represents a better level of quality of life. Clinical meaningful improvement change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
PGM=DEVOPS/SAR650984/EFC15246/CIR_RWE/REPORT/PGM/eff_km_subgp_sr_sig_de_i_t.sas OUT=REPORT/OUTPUT/eff_km_c30_con_imppl_greg_de_i_t_x.rtf (07APR2021 14:36)

16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Constipation
16.2.6.1.2.5 Efficacy response data - Subgroup analyses by geographical region
16.2.6.1.2.5.5 QLQ-C30 - Time until permanent improvement by 10 pt in constipation according to geographical region (LOCF) - ITT population

	Europe		America		Asia		Other countries		
	Kd (N=60)	**IKd (N=85)**	**Kd (N=20)**	**IKd (N=24)**	**Kd (N=21)**	**IKd (N=25)**	**Kd (N=22)**	**IKd (N=45)**	**p-value of treatment-by-subgroup interaction[c]**
Comparison vs. Kd									
Log-Rank test p-value[a] vs Kd	-	0.3952		0.3153		0.4079		0.1216	
Hazard ratio (95% CI) vs Kd	-	1.48 (0.60 to 3.68)		0.49 (0.12 to 2.04)		2.52 (0.26 to 24.20)		4.49 (0.56 to 35.97)	
P-value	-	0.3982		0.3256		0.4243		0.1576	
Improvement probability (95% CI)[b]									
3 Months	0.068 (0.022 to 0.152)	0.108 (0.053 to 0.186)	0.100 (0.017 to 0.272)	0.042 (0.003 to 0.176)		0.083 (0.014 to 0.233)		0.111 (0.041 to 0.221)	

A lower score represents a better level of quality of life. Clinical meaningful improvement change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Constipation
16.2.6.1.2.5 Efficacy response data - Subgroup analyses by geographical region
16.2.6.1.2.5.6 QLQ-C30 - Time until permanent deterioration by 10 pt in constipation according to geographical region (LOCF) - ITT population

	Europe		America		Asia		Other countries		
	Kd (N=60)	**IKd (N=85)**	**Kd (N=20)**	**IKd (N=24)**	**Kd (N=21)**	**IKd (N=25)**	**Kd (N=22)**	**IKd (N=45)**	**p-value of treatment-by-subgroup interaction[c]**
Number (%) of events	5 (8.3)	9 (10.6)	4 (20.0)	3 (12.5)	3 (14.3)	6 (24.0)	3 (13.6)	6 (13.3)	0.9099
Number (%) of patients censored	55 (91.7)	76 (89.4)	16 (80.0)	21 (87.5)	18 (85.7)	19 (76.0)	19 (86.4)	39 (86.7)	
Kaplan-Meier estimates of event in months									
25% quantile (95% CI)	NC (NC to NC)	NC (20.928 to NC)	NC (5.585 to NC)	NC (1.051 to NC)	NC (1.084 to NC)	19.68 (2.924 to NC)	NC (5.782 to NC)	NC (6.571 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (18.530 to NC)	NC (NC to NC)	NC (NC to NC)	NC (19.680 to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	

A lower score represents a better level of quality of life. Clinical meaningful deterioration change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Constipation
16.2.6.1.2.5 Efficacy response data - Subgroup analyses by geographical region
16.2.6.1.2.5.6 QLQ-C30 - Time until permanent deterioration by 10 pt in constipation according to geographical region (LOCF) - ITT population

	Europe		America		Asia		Other countries		
	Kd (N=60)	**IKd (N=85)**	**Kd (N=20)**	**IKd (N=24)**	**Kd (N=21)**	**IKd (N=25)**	**Kd (N=22)**	**IKd (N=45)**	**p-value of treatment-by-subgroup interaction[c]**
Comparison vs. Kd									
Log-Rank test p-value[a] vs Kd	-	0.8027		0.6767		0.5714		0.9598	
Hazard ratio (95% CI) vs Kd	-	1.15 (0.38 to 3.43)		0.73 (0.16 to 3.26)		1.49 (0.37 to 5.96)		1.04 (0.26 to 4.14)	
P-value	-	0.8029		0.6780		0.5739		0.9600	
Deterioration probability (95% CI)[b]									
3 Months	0.983 (0.884 to 0.998)	0.976 (0.906 to 0.994)	1.000 (1.000 to 1.000)	0.957 (0.729 to 0.994)	0.950 (0.695 to 0.993)	0.958 (0.739 to 0.994)	1.000 (1.000 to 1.000)	0.956 (0.834 to 0.989)	
6 Months	0.983 (0.884 to 0.998)	0.976 (0.906 to 0.994)	0.950 (0.695 to 0.993)	0.911 (0.688 to 0.977)	0.950 (0.695 to 0.993)	0.958 (0.739 to 0.994)	0.955 (0.719 to 0.993)	0.910 (0.778 to 0.965)	

A lower score represents a better level of quality of life. Clinical meaningful deterioration change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Constipation
16.2.6.1.2.6 Efficacy response data - Subgroup analyses by regulatory region
16.2.6.1.2.6.3 QLQ-C30 - Time to first improvement by 10 pt in constipation according to regulatory region (LOCF) - ITT population

	Western countries		Other countries		
	Kd (N=55)	**IKd (N=97)**	**Kd (N=68)**	**IKd (N=82)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	8 (14.5)	20 (20.6)	16 (23.5)	14 (17.1)	0.2284
Number (%) of patients censored	47 (85.5)	77 (79.4)	52 (76.5)	68 (82.9)	
Kaplan-Meier estimates of Constipation in months					
25% quantile (95% CI)	NC (3.745 to NC)	NC (1.971 to NC)	NC (1.281 to NC)	NC (2.891 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.3911		0.4073	
Hazard ratio (95% CI) vs Kd	-	1.43 (0.63 to 3.24)		0.74 (0.36 to 1.51)	
P-value	-	0.3937		0.4091	
Improvement probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful improvement change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
PGM=DEVOPS/SAR650984/EFC15246/CIR_RWE/REPORT/PGM/eff_km_subgp_sr_sig_de_i_t.sas OUT=REPORT/OUTPUT/eff_km_c30_con_impl_rreg_de_i_t_x.rtf (07APR2021 14:35)

16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Constipation
16.2.6.1.2.6 Efficacy response data - Subgroup analyses by regulatory region
16.2.6.1.2.6.4 QLQ-C30 - Time to first deterioration by 10 pt in constipation according to regulatory region (LOCF) - ITT population

	Western countries		Other countries		
	Kd (N=55)	**IKd (N=97)**	**Kd (N=68)**	**IKd (N=82)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	19 (34.5)	34 (35.1)	29 (42.6)	42 (51.2)	0.3024
Number (%) of patients censored	36 (65.5)	63 (64.9)	39 (57.4)	40 (48.8)	
Kaplan-Meier estimates of Constipation in months					
25% quantile (95% CI)	3.71 (1.938 to 20.370)	5.62 (3.713 to 10.316)	6.70 (3.055 to 11.105)	2.96 (1.084 to 5.684)	
Median (95% CI)	NC (19.745 to NC)	NC (NC to NC)	NC (12.517 to NC)	14.78 (6.505 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.9013		0.1405	
Hazard ratio (95% CI) vs Kd	-	0.96 (0.55 to 1.69)		1.43 (0.89 to 2.29)	
P-value	-	0.9008		0.1426	
Deterioration probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful deterioration change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
PGM=DEVOPS/SAR650984/EFC15246/CIR_RWE/REPORT/PGM/eff_km_subgp_sr_sig_de_i_t.sas OUT=REPORT/OUTPUT/eff_km_c30_con_detl_rreg_de_i_t_x.rtf (07APR2021 14:35)

16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Constipation
16.2.6.1.2.6 Efficacy response data - Subgroup analyses by regulatory region
16.2.6.1.2.6.5 QLQ-C30 - Time until permanent improvement by 10 pt in constipation according to regulatory region (LOCF) - ITT population

	Western countries		Other countries		
	Kd (N=55)	**IKd (N=97)**	**Kd (N=68)**	**IKd (N=82)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	6 (10.9)	17 (17.5)	8 (11.8)	11 (13.4)	0.5886
Number (%) of patients censored	49 (89.1)	80 (82.5)	60 (88.2)	71 (86.6)	
Kaplan-Meier estimates of Constipation in months					
25% quantile (95% CI)	NC (22.439 to NC)	NC (19.384 to NC)	NC (NC to NC)	NC (NC to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.2321		0.7149	
Hazard ratio (95% CI) vs Kd	-	1.76 (0.69 to 4.48)		1.18 (0.48 to 2.95)	
P-value	-	0.2380		0.7152	
Improvement probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful improvement change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Constipation
16.2.6.1.2.6 Efficacy response data - Subgroup analyses by regulatory region
16.2.6.1.2.6.6 QLQ-C30 - Time until permanent deterioration by 10 pt in constipation according to regulatory region (LOCF) - ITT population

	Western countries		Other countries		
	Kd (N=55)	**IKd (N=97)**	**Kd (N=68)**	**IKd (N=82)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	5 (9.1)	10 (10.3)	10 (14.7)	14 (17.1)	0.9966
Number (%) of patients censored	50 (90.9)	87 (89.7)	58 (85.3)	68 (82.9)	
Kaplan-Meier estimates of Constipation in months					
25% quantile (95% CI)	NC (19.614 to NC)	NC (NC to NC)	NC (18.530 to NC)	NC (19.581 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.8269		0.7792	
Hazard ratio (95% CI) vs Kd	-	1.13 (0.39 to 3.30)		1.12 (0.50 to 2.53)	
P-value	-	0.8270		0.7793	
Deterioration probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful deterioration change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
PGM=DEVOPS/SAR650984/EFC15246/CIR_RWE/REPORT/PGM/eff_km_subgp_sr_sig_de_i_t.sas OUT=REPORT/OUTPUT/eff_km_c30_con_detpl_rreg_de_i_t_x.rtf (07APR2021 14:36)

16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Constipation
16.2.6.1.2.7 Efficacy response data - Subgroup analyses by baseline ECOG PS
16.2.6.1.2.7.3 QLQ-C30 - Time to first improvement by 10 pt in constipation according to baseline ECOG PS (LOCF) - ITT population

	0 or 1		>1		
	Kd (N=118)	**IKd (N=168)**	**Kd (N=5)**	**IKd (N=11)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	23 (19.5)	32 (19.0)	1 (20.0)	2 (18.2)	0.9614
Number (%) of patients censored	95 (80.5)	136 (81.0)	4 (80.0)	9 (81.8)	
Kaplan-Meier estimates of Constipation in months					
25% quantile (95% CI)	NC (3.745 to NC)	NC (15.869 to NC)	NC (0.986 to NC)	NC (0.986 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (0.986 to NC)	NC (0.986 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (0.986 to NC)	NC (NC to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.9346		0.9540	
Hazard ratio (95% CI) vs Kd	-	0.98 (0.57 to 1.67)		1.07 (0.10 to 11.84)	
P-value	-	0.9345		0.9540	
Improvement probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful improvement change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
PGM=DEVOPS/SAR650984/EFC15246/CIR_RWE/REPORT/PGM/eff_km_subgp_sr_sig_de_i_t.sas OUT=REPORT/OUTPUT/eff_km_c30_con_impl_ecog_de_i_t_x.rtf (07APR2021 14:35)

16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Constipation
16.2.6.1.2.7 Efficacy response data - Subgroup analyses by baseline ECOG PS
16.2.6.1.2.7.4 QLQ-C30 - Time to first deterioration by 10 pt in constipation according to baseline ECOG PS (LOCF) - ITT population

	0 or 1		>1		
	Kd (N=118)	**IKd (N=168)**	**Kd (N=5)**	**IKd (N=11)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	46 (39.0)	71 (42.3)	2 (40.0)	5 (45.5)	0.9922
Number (%) of patients censored	72 (61.0)	97 (57.7)	3 (60.0)	6 (54.5)	
Kaplan-Meier estimates of Constipation in months					
25% quantile (95% CI)	5.55 (2.858 to 11.039)	4.67 (2.136 to 5.848)	8.80 (2.070 to NC)	13.37 (1.216 to 19.055)	
Median (95% CI)	NC (16.986 to NC)	NC (14.127 to NC)	NC (2.070 to NC)	19.06 (1.216 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (2.070 to NC)	NC (17.544 to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.4737		0.9072	
Hazard ratio (95% CI) vs Kd	-	1.15 (0.79 to 1.66)		0.90 (0.17 to 4.86)	
P-value	-	0.4740		0.9072	
Deterioration probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful deterioration change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Constipation
16.2.6.1.2.7 Efficacy response data - Subgroup analyses by baseline ECOG PS
16.2.6.1.2.7.5 QLQ-C30 - Time until permanent improvement by 10 pt in constipation according to baseline ECOG PS (LOCF) - ITT population

	0 or 1		>1		
	Kd (N=118)	**IKd (N=168)**	**Kd (N=5)**	**IKd (N=11)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	13 (11.0)	26 (15.5)	1 (20.0)	2 (18.2)	0.7779
Number (%) of patients censored	105 (89.0)	142 (84.5)	4 (80.0)	9 (81.8)	
Kaplan-Meier estimates of Constipation in months					
25% quantile (95% CI)	NC (22.439 to NC)	NC (20.698 to NC)	NC (0.986 to NC)	NC (0.986 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (0.986 to NC)	NC (0.986 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (0.986 to NC)	NC (NC to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.2689		0.9540	
Hazard ratio (95% CI) vs Kd	-	1.45 (0.75 to 2.83)		1.07 (0.10 to 11.84)	
P-value	-	0.2717		0.9540	
Improvement probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful improvement change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Constipation
16.2.6.1.2.7 Efficacy response data - Subgroup analyses by baseline ECOG PS
16.2.6.1.2.7.6 QLQ-C30 - Time until permanent deterioration by 10 pt in constipation according to baseline ECOG PS (LOCF) - ITT population

	0 or 1		>1		
	Kd (N=118)	**IKd (N=168)**	**Kd (N=5)**	**IKd (N=11)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	14 (11.9)	23 (13.7)	1 (20.0)	1 (9.1)	0.4376
Number (%) of patients censored	104 (88.1)	145 (86.3)	4 (80.0)	10 (90.9)	
Kaplan-Meier estimates of Constipation in months					
25% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	14.65 (14.653 to NC)	NC (10.908 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (14.653 to NC)	NC (10.908 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (14.653 to NC)	NC (NC to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.7014		0.4202	
Hazard ratio (95% CI) vs Kd	-	1.14 (0.59 to 2.21)		0.33 (0.02 to 5.48)	
P-value	-	0.7016		0.4420	
Deterioration probability (95% CI)[b]					

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The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Constipation
16.2.6.1.2.8 Efficacy response data - Subgroup analyses by ISS staging at SE
16.2.6.1.2.8.3 QLQ-C30 - Time to first improvement by 10 pt in constipation according to ISS staging at SE (LOCF) - ITT population

	I		II		III		
	Kd (N=71)	**IKd (N=89)**	**Kd (N=31)**	**IKd (N=63)**	**Kd (N=20)**	**IKd (N=26)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	16 (22.5)	18 (20.2)	6 (19.4)	12 (19.0)	2 (10.0)	4 (15.4)	0.7678
Number (%) of patients censored	55 (77.5)	71 (79.8)	25 (80.6)	51 (81.0)	18 (90.0)	22 (84.6)	
Kaplan-Meier estimates of Constipation in months							
25% quantile (95% CI)	NC (1.938 to NC)	NC (2.136 to NC)	NC (1.084 to NC)	NC (1.906 to NC)	NC (0.986 to NC)	NC (0.953 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Kd							
Log-Rank test p-value[a] vs Kd	-	0.7440		0.9835		0.5211	
Hazard ratio (95% CI) vs Kd	-	0.89 (0.46 to 1.75)		0.99 (0.37 to 2.64)		1.73 (0.32 to 9.46)	
P-value	-	0.7442		0.9835		0.5263	

A lower score represents a better level of quality of life. Clinical meaningful improvement change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Constipation
16.2.6.1.2.8 Efficacy response data - Subgroup analyses by ISS staging at SE
16.2.6.1.2.8.4 QLQ-C30 - Time to first deterioration by 10 pt in constipation according to ISS staging at SE (LOCF) - ITT population

	I		II		III		
	Kd (N=71)	**IKd (N=89)**	**Kd (N=31)**	**IKd (N=63)**	**Kd (N=20)**	**IKd (N=26)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	30 (42.3)	38 (42.7)	11 (35.5)	29 (46.0)	6 (30.0)	8 (30.8)	0.9144
Number (%) of patients censored	41 (57.7)	51 (57.3)	20 (64.5)	34 (54.0)	14 (70.0)	18 (69.2)	
Kaplan-Meier estimates of Constipation in months							
25% quantile (95% CI)	6.64 (2.858 to 15.704)	4.67 (1.216 to 6.899)	4.76 (1.906 to NC)	5.22 (1.971 to 6.604)	6.60 (1.084 to NC)	6.57 (1.051 to NC)	
Median (95% CI)	NC (16.131 to NC)	NC (12.912 to NC)	NC (8.805 to NC)	NC (6.834 to NC)	NC (6.604 to NC)	NC (6.571 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Kd							
Log-Rank test p-value[a] vs Kd	-	0.7175		0.4144		0.8414	
Hazard ratio (95% CI) vs Kd	-	1.09 (0.68 to 1.76)		1.33 (0.67 to 2.67)		1.11 (0.39 to 3.21)	
P-value	-	0.7187		0.4161		0.8415	

A lower score represents a better level of quality of life. Clinical meaningful deterioration change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Constipation
16.2.6.1.2.8 Efficacy response data - Subgroup analyses by ISS staging at SE
16.2.6.1.2.8.5 QLQ-C30 - Time until permanent improvement by 10 pt in constipation according to ISS staging at SE (LOCF) - ITT population

	I		II		III		
	Kd (N=71)	**IKd (N=89)**	**Kd (N=31)**	**IKd (N=63)**	**Kd (N=20)**	**IKd (N=26)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	8 (11.3)	14 (15.7)	4 (12.9)	10 (15.9)	2 (10.0)	4 (15.4)	0.9342
Number (%) of patients censored	63 (88.7)	75 (84.3)	27 (87.1)	53 (84.1)	18 (90.0)	22 (84.6)	
Kaplan-Meier estimates of Constipation in months							
25% quantile (95% CI)	NC (22.439 to NC)	NC (20.698 to NC)	NC (6.604 to NC)	NC (19.384 to NC)	NC (0.986 to NC)	NC (0.953 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Kd							
Log-Rank test p-value[a] vs Kd	-	0.3723		0.7766		0.5369	
Hazard ratio (95% CI) vs Kd	-	1.48 (0.62 to 3.54)		1.18 (0.37 to 3.77)		1.70 (0.31 to 9.26)	
P-value	-	0.3753		0.7769		0.5416	

A lower score represents a better level of quality of life. Clinical meaningful improvement change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
PGM=DEVOPS/SAR650984/EFC15246/CIR_RWE/REPORT/PGM/eff_km_subgp_sr_sig_de_i_t.sas OUT=REPORT/OUTPUT/eff_km_c30_con_imppl_seiss_de_i_t_x.rtf (07APR2021 14:36)

16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Constipation
16.2.6.1.2.8 Efficacy response data - Subgroup analyses by ISS staging at SE
16.2.6.1.2.8.6 QLQ-C30 - Time until permanent deterioration by 10 pt in constipation according to ISS staging at SE (LOCF) - ITT population

	I		II		III		
	Kd (N=71)	**IKd (N=89)**	**Kd (N=31)**	**IKd (N=63)**	**Kd (N=20)**	**IKd (N=26)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	7 (9.9)	12 (13.5)	4 (12.9)	8 (12.7)	4 (20.0)	3 (11.5)	0.5245
Number (%) of patients censored	64 (90.1)	77 (86.5)	27 (87.1)	55 (87.3)	16 (80.0)	23 (88.5)	
Kaplan-Meier estimates of Constipation in months							
25% quantile (95% CI)	NC (NC to NC)	NC (19.614 to NC)	NC (10.875 to NC)	NC (19.877 to NC)	10.74 (1.084 to NC)	NC (1.084 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (10.743 to NC)	NC (19.680 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Kd							
Log-Rank test p-value[a] vs Kd	-	0.4587		0.8106		0.3695	
Hazard ratio (95% CI) vs Kd	-	1.42 (0.56 to 3.61)		0.86 (0.26 to 2.87)		0.51 (0.11 to 2.28)	
P-value	-	0.4610		0.8108		0.3784	

A lower score represents a better level of quality of life. Clinical meaningful deterioration change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
PGM=DEVOPS/SAR650984/EFC15246/CIR_RWE/REPORT/PGM/eff_km_subgp_sr_sig_de_i_t.sas OUT=REPORT/OUTPUT/eff_km_c30_con_detpl_seiss_de_i_t_x.rtf (07APR2021 14:36)

16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Constipation
16.2.6.1.2.9 Efficacy response data - Subgroup analyses by R-ISS stage at SE
16.2.6.1.2.9.3 QLQ-C30 - Time to first improvement by 10 pt in constipation according to R-ISS stage at SE (LOCF) - ITT population

	I or II		III		Not classified		
	Kd (N=103)	**IKd (N=155)**	**Kd (N=8)**	**IKd (N=16)**	**Kd (N=12)**	**IKd (N=8)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	21 (20.4)	29 (18.7)	0 (0.0)	3 (18.8)	3 (25.0)	2 (25.0)	0.8900
Number (%) of patients censored	82 (79.6)	126 (81.3)	8 (100.0)	13 (81.3)	9 (75.0)	6 (75.0)	
Kaplan-Meier estimates of Constipation in months							
25% quantile (95% CI)	NC (2.957 to NC)	NC (15.869 to NC)	NC (NC to NC)	NC (0.953 to NC)	NC (0.986 to NC)	1.08 (1.018 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (2.103 to NC)	NC (0.986 to NC)	NC (1.018 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (1.084 to NC)	
Comparison vs. Kd							
Log-Rank test p-value[a] vs Kd	-	0.6968		0.1770		0.7469	
Hazard ratio (95% CI) vs Kd	-	0.89 (0.51 to 1.57)				1.34 (0.22 to 8.06)	
P-value	-	0.6969		0.9974		0.7477	

A lower score represents a better level of quality of life. Clinical meaningful improvement change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Constipation
16.2.6.1.2.9 Efficacy response data - Subgroup analyses by R-ISS stage at SE
16.2.6.1.2.9.4 QLQ-C30 - Time to first deterioration by 10 pt in constipation according to R-ISS stage at SE (LOCF) - ITT population

	I or II		III		Not classified		
	Kd (N=103)	**IKd (N=155)**	**Kd (N=8)**	**IKd (N=16)**	**Kd (N=12)**	**IKd (N=8)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	39 (37.9)	69 (44.5)	4 (50.0)	5 (31.3)	5 (41.7)	2 (25.0)	0.2839
Number (%) of patients censored	64 (62.1)	86 (55.5)	4 (50.0)	11 (68.8)	7 (58.3)	6 (75.0)	
Kaplan-Meier estimates of Constipation in months							
25% quantile (95% CI)	6.60 (2.825 to 11.039)	4.63 (2.037 to 5.815)	1.91 (1.084 to 4.041)	7.95 (1.084 to NC)	13.40 (1.150 to NC)	17.54 (2.070 to NC)	
Median (95% CI)	NC (19.745 to NC)	NC (12.517 to NC)	4.04 (1.084 to NC)	NC (2.957 to NC)	NC (3.713 to NC)	NC (2.070 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (2.957 to NC)	NC (NC to NC)	NC (NC to NC)	NC (17.544 to NC)	
Comparison vs. Kd							
Log-Rank test p-value[a] vs Kd	-	0.2878		0.2440		0.9652	
Hazard ratio (95% CI) vs Kd	-	1.24 (0.84 to 1.83)		0.45 (0.12 to 1.77)		0.96 (0.19 to 5.00)	
P-value	-	0.2887		0.2549		0.9655	

A lower score represents a better level of quality of life. Clinical meaningful deterioration change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Constipation
16.2.6.1.2.9 Efficacy response data - Subgroup analyses by R-ISS stage at SE
16.2.6.1.2.9.5 QLQ-C30 - Time until permanent improvement by 10 pt in constipation according to R-ISS stage at SE (LOCF) - ITT population

	I or II		III		Not classified		
	Kd (N=103)	**IKd (N=155)**	**Kd (N=8)**	**IKd (N=16)**	**Kd (N=12)**	**IKd (N=8)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	13 (12.6)	23 (14.8)	0 (0.0)	3 (18.8)	1 (8.3)	2 (25.0)	0.4486
Number (%) of patients censored	90 (87.4)	132 (85.2)	8 (100.0)	13 (81.3)	11 (91.7)	6 (75.0)	
Kaplan-Meier estimates of Constipation in months							
25% quantile (95% CI)	NC (22.439 to NC)	NC (NC to NC)	NC (NC to NC)	NC (0.953 to NC)	NC (14.784 to NC)	1.08 (1.018 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (2.103 to NC)	NC (NC to NC)	NC (1.018 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (1.084 to NC)	
Comparison vs. Kd							
Log-Rank test p-value[a] vs Kd	-	0.6776		0.1770		0.1268	
Hazard ratio (95% CI) vs Kd	-	1.16 (0.58 to 2.28)				5.43 (0.48 to 61.32)	
P-value	-	0.6779		0.9974		0.1714	

A lower score represents a better level of quality of life. Clinical meaningful improvement change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Constipation
16.2.6.1.2.9 Efficacy response data - Subgroup analyses by R-ISS stage at SE
16.2.6.1.2.9.6 QLQ-C30 - Time until permanent deterioration by 10 pt in constipation according to R-ISS stage at SE (LOCF) - ITT population

	I or II		III		Not classified		
	Kd (N=103)	**IKd (N=155)**	**Kd (N=8)**	**IKd (N=16)**	**Kd (N=12)**	**IKd (N=8)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	11 (10.7)	21 (13.5)	3 (37.5)	2 (12.5)	1 (8.3)	1 (12.5)	0.1888
Number (%) of patients censored	92 (89.3)	134 (86.5)	5 (62.5)	14 (87.5)	11 (91.7)	7 (87.5)	
Kaplan-Meier estimates of Constipation in months							
25% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	8.48 (1.084 to NC)	NC (1.084 to NC)	NC (11.105 to NC)	20.93 (20.928 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	10.64 (1.084 to NC)	NC (NC to NC)	NC (NC to NC)	NC (20.928 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (8.476 to NC)	NC (NC to NC)	NC (NC to NC)	NC (20.928 to NC)	
Comparison vs. Kd							
Log-Rank test p-value[a] vs Kd	-	0.5999		0.0796		0.4581	
Hazard ratio (95% CI) vs Kd	-	1.22 (0.59 to 2.52)		0.22 (0.04 to 1.38)		2.74 (0.17 to 43.91)	
P-value	-	0.6005		0.1069		0.4767	

A lower score represents a better level of quality of life. Clinical meaningful deterioration change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Constipation
16.2.6.1.2.10 Efficacy response data - Subgroup analyses by nb of prior lines
16.2.6.1.2.10.3 QLQ-C30 - Time to first improvement by 10 pt in constipation according to nb of prior lines (LOCF) - ITT population

	1		>1		
	Kd (N=55)	**IKd (N=79)**	**Kd (N=68)**	**IKd (N=100)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	7 (12.7)	16 (20.3)	17 (25.0)	18 (18.0)	0.1197
Number (%) of patients censored	48 (87.3)	63 (79.7)	51 (75.0)	82 (82.0)	
Kaplan-Meier estimates of Constipation in months					
25% quantile (95% CI)	NC (3.844 to NC)	NC (1.971 to NC)	14.78 (1.216 to NC)	NC (3.745 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.2514		0.2876	
Hazard ratio (95% CI) vs Kd	-	1.67 (0.69 to 4.06)		0.70 (0.36 to 1.36)	
P-value	-	0.2568		0.2902	
Improvement probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful improvement change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Constipation
16.2.6.1.2.10 Efficacy response data - Subgroup analyses by nb of prior lines
16.2.6.1.2.10.4 QLQ-C30 - Time to first deterioration by 10 pt in constipation according to nb of prior lines (LOCF) - ITT population

	1		>1		
	Kd (N=55)	**IKd (N=79)**	**Kd (N=68)**	**IKd (N=100)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	24 (43.6)	34 (43.0)	24 (35.3)	42 (42.0)	0.7559
Number (%) of patients censored	31 (56.4)	45 (57.0)	44 (64.7)	58 (58.0)	
Kaplan-Meier estimates of Constipation in months					
25% quantile (95% CI)	6.64 (3.713 to 13.405)	4.83 (3.713 to 6.571)	3.06 (1.906 to 16.986)	3.94 (1.216 to 6.834)	
Median (95% CI)	NC (11.039 to NC)	NC (7.951 to NC)	NC (16.986 to NC)	NC (12.517 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.7401		0.4156	
Hazard ratio (95% CI) vs Kd	-	1.09 (0.65 to 1.84)		1.23 (0.75 to 2.03)	
P-value	-	0.7402		0.4165	
Deterioration probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful deterioration change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Constipation
16.2.6.1.2.10 Efficacy response data - Subgroup analyses by nb of prior lines
16.2.6.1.2.10.5 QLQ-C30 - Time until permanent improvement by 10 pt in constipation according to nb of prior lines (LOCF) - ITT population

	1		>1		
	Kd (N=55)	**IKd (N=79)**	**Kd (N=68)**	**IKd (N=100)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	3 (5.5)	13 (16.5)	11 (16.2)	15 (15.0)	0.0929
Number (%) of patients censored	52 (94.5)	66 (83.5)	57 (83.8)	85 (85.0)	
Kaplan-Meier estimates of Constipation in months					
25% quantile (95% CI)	NC (NC to NC)	NC (12.025 to NC)	NC (13.405 to NC)	NC (20.370 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.0541		0.8600	
Hazard ratio (95% CI) vs Kd	-	3.21 (0.91 to 11.27)		0.93 (0.43 to 2.03)	
P-value	-	0.0686		0.8592	
Improvement probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful improvement change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Constipation
16.2.6.1.2.10 Efficacy response data - Subgroup analyses by nb of prior lines
16.2.6.1.2.10.6 QLQ-C30 - Time until permanent deterioration by 10 pt in constipation according to nb of prior lines (LOCF) - ITT population

	1		>1		
	Kd (N=55)	**IKd (N=79)**	**Kd (N=68)**	**IKd (N=100)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	7 (12.7)	11 (13.9)	8 (11.8)	13 (13.0)	0.8896
Number (%) of patients censored	48 (87.3)	68 (86.1)	60 (88.2)	87 (87.0)	
Kaplan-Meier estimates of Constipation in months					
25% quantile (95% CI)	NC (19.351 to NC)	NC (19.614 to NC)	NC (18.530 to NC)	NC (20.928 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.7897		0.9357	
Hazard ratio (95% CI) vs Kd	-	1.14 (0.44 to 2.93)		1.04 (0.43 to 2.50)	
P-value	-	0.7899		0.9359	
Deterioration probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful deterioration change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Constipation
16.2.6.1.2.11 Efficacy response data - Subgroup analyses by cytogenetic abnormality
16.2.6.1.2.11.3 QLQ-C30 - Time to first improvement by 10 pt in constipation according to cytogenetic abnormality (LOCF) - ITT population

	At least one		None		
	Kd (N=31)	**IKd (N=42)**	**Kd (N=77)**	**IKd (N=114)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	4 (12.9)	12 (28.6)	16 (20.8)	17 (14.9)	0.0704
Number (%) of patients censored	27 (87.1)	30 (71.4)	61 (79.2)	97 (85.1)	
Kaplan-Meier estimates of Constipation in months					
25% quantile (95% CI)	NC (1.117 to NC)	2.10 (0.986 to NC)	NC (2.136 to NC)	NC (NC to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.1302		0.3080	
Hazard ratio (95% CI) vs Kd	-	2.34 (0.75 to 7.25)		0.70 (0.35 to 1.39)	
P-value	-	0.1418		0.3105	
Improvement probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful improvement change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Constipation
16.2.6.1.2.11 Efficacy response data - Subgroup analyses by cytogenetic abnormality
16.2.6.1.2.11.4 QLQ-C30 - Time to first deterioration by 10 pt in constipation according to cytogenetic abnormality (LOCF) - ITT population

	At least one		None		
	Kd (N=31)	**IKd (N=42)**	**Kd (N=77)**	**IKd (N=114)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	13 (41.9)	18 (42.9)	32 (41.6)	47 (41.2)	0.9878
Number (%) of patients censored	18 (58.1)	24 (57.1)	45 (58.4)	67 (58.8)	
Kaplan-Meier estimates of Constipation in months					
25% quantile (95% CI)	3.81 (2.103 to 13.405)	3.91 (1.051 to 8.805)	4.76 (1.906 to 8.838)	4.76 (2.530 to 6.604)	
Median (95% CI)	NC (4.830 to NC)	NC (7.951 to NC)	NC (11.039 to NC)	NC (14.127 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.9854		0.9713	
Hazard ratio (95% CI) vs Kd	-	1.01 (0.49 to 2.06)		1.01 (0.64 to 1.58)	
P-value	-	0.9854		0.9714	
Deterioration probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful deterioration change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
PGM=DEVOPS/SAR650984/EFC15246/CIR_RWE/REPORT/PGM/eff_km_subgp_sr_sig_de_i_t.sas OUT=REPORT/OUTPUT/eff_km_c30_con_detl_cyto_de_i_t_x.rtf (07APR2021 14:35)

16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Constipation
16.2.6.1.2.11 Efficacy response data - Subgroup analyses by cytogenetic abnormality
16.2.6.1.2.11.5 QLQ-C30 - Time until permanent improvement by 10 pt in constipation according to cytogenetic abnormality (LOCF) - ITT population

	At least one		None		
	Kd (N=31)	**IKd (N=42)**	**Kd (N=77)**	**IKd (N=114)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	2 (6.5)	10 (23.8)	10 (13.0)	14 (12.3)	0.0858
Number (%) of patients censored	29 (93.5)	32 (76.2)	67 (87.0)	100 (87.7)	
Kaplan-Meier estimates of Constipation in months					
25% quantile (95% CI)	NC (11.138 to NC)	20.37 (1.971 to NC)	NC (NC to NC)	NC (NC to NC)	
Median (95% CI)	NC (22.439 to NC)	NC (20.370 to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.0290		0.8473	
Hazard ratio (95% CI) vs Kd	-	4.78 (1.03 to 22.25)		0.92 (0.41 to 2.08)	
P-value	-	0.0463		0.8474	
Hazard ratio inverted (95% CI) vs IKd		-		1.08 (0.48 to 2.44)	

A lower score represents a better level of quality of life. Clinical meaningful improvement change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
PGM=DEVOPS/SAR650984/EFC15246/CIR_RWE/REPORT/PGM/eff_km_subgp_sr_sig_de_i_t.sas OUT=REPORT/OUTPUT/eff_km_c30_con_imppl_cyto_de_i_t_x.rtf (07APR2021 14:36)

16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Constipation
16.2.6.1.2.11 Efficacy response data - Subgroup analyses by cytogenetic abnormality
16.2.6.1.2.11.6 QLQ-C30 - Time until permanent deterioration by 10 pt in constipation according to cytogenetic abnormality (LOCF) - ITT population

	At least one		None		
	Kd (N=31)	**IKd (N=42)**	**Kd (N=77)**	**IKd (N=114)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	6 (19.4)	7 (16.7)	8 (10.4)	15 (13.2)	0.4565
Number (%) of patients censored	25 (80.6)	35 (83.3)	69 (89.6)	99 (86.8)	
Kaplan-Meier estimates of Constipation in months					
25% quantile (95% CI)	NC (5.782 to NC)	NC (10.678 to NC)	NC (NC to NC)	NC (19.877 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.6340		0.5930	
Hazard ratio (95% CI) vs Kd	-	0.77 (0.26 to 2.29)		1.26 (0.54 to 2.98)	
P-value	-	0.6349		0.5939	
Deterioration probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful deterioration change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
PGM=DEVOPS/SAR650984/EFC15246/CIR_RWE/REPORT/PGM/eff_km_subgp_sr_sig_de_i_t.sas OUT=REPORT/OUTPUT/eff_km_c30_con_detpl_cyto_de_i_t_x.rtf (07APR2021 14:36)

16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Constipation
16.2.6.1.2.12 Efficacy response data - Subgroup analyses by MM type at SE
16.2.6.1.2.12.3 QLQ-C30 - Time to first improvement by 10 pt in constipation according to MM type at SE (LOCF) - ITT population

	IgG		Non-IgG		
	Kd (N=85)	**IKd (N=126)**	**Kd (N=38)**	**IKd (N=53)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	18 (21.2)	25 (19.8)	6 (15.8)	9 (17.0)	0.8736
Number (%) of patients censored	67 (78.8)	101 (80.2)	32 (84.2)	44 (83.0)	
Kaplan-Meier estimates of Constipation in months					
25% quantile (95% CI)	NC (1.938 to NC)	NC (2.136 to NC)	NC (2.136 to NC)	NC (1.906 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.8906		0.9191	
Hazard ratio (95% CI) vs Kd	-	0.96 (0.52 to 1.76)		1.05 (0.38 to 2.96)	
P-value	-	0.8902		0.9195	
Improvement probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful improvement change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
PGM=DEVOPS/SAR650984/EFC15246/CIR_RWE/REPORT/PGM/eff_km_subgp_sr_sig_de_i_t.sas OUT=REPORT/OUTPUT/eff_km_c30_con_impl_semm_de_i_t_x.rtf (07APR2021 14:35)

16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Constipation
16.2.6.1.2.12 Efficacy response data - Subgroup analyses by MM type at SE
16.2.6.1.2.12.4 QLQ-C30 - Time to first deterioration by 10 pt in constipation according to MM type at SE (LOCF) - ITT population

	IgG		Non-IgG		
	Kd (N=85)	**IKd (N=126)**	**Kd (N=38)**	**IKd (N=53)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	37 (43.5)	54 (42.9)	11 (28.9)	22 (41.5)	0.2572
Number (%) of patients censored	48 (56.5)	72 (57.1)	27 (71.1)	31 (58.5)	
Kaplan-Meier estimates of Constipation in months					
25% quantile (95% CI)	4.04 (2.070 to 11.105)	5.62 (2.858 to 6.899)	8.80 (2.858 to NC)	3.94 (1.084 to 5.585)	
Median (95% CI)	NC (15.704 to NC)	NC (13.372 to NC)	NC (11.039 to NC)	NC (5.585 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.9588		0.1857	
Hazard ratio (95% CI) vs Kd	-	1.01 (0.67 to 1.54)		1.62 (0.79 to 3.35)	
P-value	-	0.9588		0.1901	
Deterioration probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful deterioration change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Constipation
16.2.6.1.2.12 Efficacy response data - Subgroup analyses by MM type at SE
16.2.6.1.2.12.5 QLQ-C30 - Time until permanent improvement by 10 pt in constipation according to MM type at SE (LOCF) - ITT population

	IgG		Non-IgG		
	Kd (N=85)	**IKd (N=126)**	**Kd (N=38)**	**IKd (N=53)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	11 (12.9)	21 (16.7)	3 (7.9)	7 (13.2)	0.8053
Number (%) of patients censored	74 (87.1)	105 (83.3)	35 (92.1)	46 (86.8)	
Kaplan-Meier estimates of Constipation in months					
25% quantile (95% CI)	NC (22.439 to NC)	NC (20.370 to NC)	NC (11.138 to NC)	NC (19.384 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.3939		0.4646	
Hazard ratio (95% CI) vs Kd	-	1.37 (0.66 to 2.85)		1.65 (0.43 to 6.37)	
P-value	-	0.3959		0.4693	
Improvement probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful improvement change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Constipation
16.2.6.1.2.12 Efficacy response data - Subgroup analyses by MM type at SE
16.2.6.1.2.12.6 QLQ-C30 - Time until permanent deterioration by 10 pt in constipation according to MM type at SE (LOCF) - ITT population

	IgG		Non-IgG		
	Kd (N=85)	**IKd (N=126)**	**Kd (N=38)**	**IKd (N=53)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	11 (12.9)	16 (12.7)	4 (10.5)	8 (15.1)	0.6883
Number (%) of patients censored	74 (87.1)	110 (87.3)	34 (89.5)	45 (84.9)	
Kaplan-Meier estimates of Constipation in months					
25% quantile (95% CI)	NC (19.614 to NC)	NC (NC to NC)	NC (10.875 to NC)	NC (15.146 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.9701		0.6528	
Hazard ratio (95% CI) vs Kd	-	0.99 (0.46 to 2.12)		1.32 (0.40 to 4.38)	
P-value	-	0.9700		0.6538	
Deterioration probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful deterioration change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Constipation
16.2.6.1.2.13 Efficacy response data - Subgroup analyses by previous autologous stem-cell
16.2.6.1.2.13.3 QLQ-C30 - Time to first improvement by 10 pt in constipation according to previous autologous stem-cell (LOCF) - ITT population

	Yes		No		
	Kd (N=69)	**IKd (N=116)**	**Kd (N=54)**	**IKd (N=63)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	13 (18.8)	17 (14.7)	11 (20.4)	17 (27.0)	0.2447
Number (%) of patients censored	56 (81.2)	99 (85.3)	43 (79.6)	46 (73.0)	
Kaplan-Meier estimates of Constipation in months					
25% quantile (95% CI)	NC (1.938 to NC)	NC (NC to NC)	NC (1.971 to NC)	2.89 (1.084 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.4662		0.3647	
Hazard ratio (95% CI) vs Kd	-	0.77 (0.37 to 1.58)		1.42 (0.66 to 3.03)	
P-value	-	0.4676		0.3671	
Improvement probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful improvement change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Constipation
16.2.6.1.2.13 Efficacy response data - Subgroup analyses by previous autologous stem-cell
16.2.6.1.2.13.4 QLQ-C30 - Time to first deterioration by 10 pt in constipation according to previous autologous stem-cell (LOCF) - ITT population

	Yes		No		
	Kd (N=69)	**IKd (N=116)**	**Kd (N=54)**	**IKd (N=63)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	29 (42.0)	49 (42.2)	19 (35.2)	27 (42.9)	0.6448
Number (%) of patients censored	40 (58.0)	67 (57.8)	35 (64.8)	36 (57.1)	
Kaplan-Meier estimates of Constipation in months					
25% quantile (95% CI)	4.76 (2.136 to 11.105)	3.98 (2.037 to 5.815)	6.64 (2.103 to 20.370)	5.68 (1.971 to 7.951)	
Median (95% CI)	NC (13.405 to NC)	NC (12.222 to NC)	NC (15.704 to NC)	NC (12.912 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.7772		0.4118	
Hazard ratio (95% CI) vs Kd	-	1.07 (0.68 to 1.69)		1.28 (0.71 to 2.30)	
P-value	-	0.7773		0.4130	
Deterioration probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful deterioration change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
PGM=DEVOPS/SAR650984/EFC15246/CIR_RWE/REPORT/PGM/eff_km_subgp_sr_sig_de_i_t.sas OUT=REPORT/OUTPUT/eff_km_c30_con_detl_auto_de_i_t_x.rtf (07APR2021 14:35)

16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Constipation
16.2.6.1.2.13 Efficacy response data - Subgroup analyses by previous autologous stem-cell
16.2.6.1.2.13.5 QLQ-C30 - Time until permanent improvement by 10 pt in constipation according to previous autologous stem-cell (LOCF) - ITT population

	Yes		No		
	Kd (N=69)	**IKd (N=116)**	**Kd (N=54)**	**IKd (N=63)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	7 (10.1)	12 (10.3)	7 (13.0)	16 (25.4)	0.2696
Number (%) of patients censored	62 (89.9)	104 (89.7)	47 (87.0)	47 (74.6)	
Kaplan-Meier estimates of Constipation in months					
25% quantile (95% CI)	NC (22.439 to NC)	NC (NC to NC)	NC (14.784 to NC)	20.37 (2.103 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.9278		0.0907	
Hazard ratio (95% CI) vs Kd	-	1.04 (0.41 to 2.65)		2.11 (0.87 to 5.14)	
P-value	-	0.9282		0.0985	
Improvement probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful improvement change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
PGM=DEVOPS/SAR650984/EFC15246/CIR_RWE/REPORT/PGM/eff_km_subgp_sr_sig_de_i_t.sas OUT=REPORT/OUTPUT/eff_km_c30_con_imppl_auto_de_i_t_x.rtf (07APR2021 14:36)

16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Constipation
16.2.6.1.2.13 Efficacy response data - Subgroup analyses by previous autologous stem-cell
16.2.6.1.2.13.6 QLQ-C30 - Time until permanent deterioration by 10 pt in constipation according to previous autologous stem-cell (LOCF) - ITT population

	Yes		No		
	Kd (N=69)	**IKd (N=116)**	**Kd (N=54)**	**IKd (N=63)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	9 (13.0)	14 (12.1)	6 (11.1)	10 (15.9)	0.5171
Number (%) of patients censored	60 (87.0)	102 (87.9)	48 (88.9)	53 (84.1)	
Kaplan-Meier estimates of Constipation in months					
25% quantile (95% CI)	NC (19.351 to NC)	NC (NC to NC)	NC (18.366 to NC)	NC (16.624 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.8275		0.5016	
Hazard ratio (95% CI) vs Kd	-	0.91 (0.39 to 2.11)		1.41 (0.51 to 3.89)	
P-value	-	0.8276		0.5038	
Deterioration probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful deterioration change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
PGM=DEVOPS/SAR650984/EFC15246/CIR_RWE/REPORT/PGM/eff_km_subgp_sr_sig_de_i_t.sas OUT=REPORT/OUTPUT/eff_km_c30_con_detpl_auto_de_i_t_x.rtf (07APR2021 14:35)

16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Constipation
16.2.6.1.2.14 Efficacy response data - Subgroup analyses by baseline eGFR (MDRD)
16.2.6.1.2.14.3 QLQ-C30 - Time to first improvement by 10 pt in constipation according to baseline eGFR (MDRD) (LOCF) - ITT population

	>=60 mL/min/1.73m2		<60 mL/min/1.73m2		
	Kd (N=93)	**IKd (N=122)**	**Kd (N=18)**	**IKd (N=43)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	20 (21.5)	29 (23.8)	2 (11.1)	5 (11.6)	0.7693
Number (%) of patients censored	73 (78.5)	93 (76.2)	16 (88.9)	38 (88.4)	
Kaplan-Meier estimates of Constipation in months					
25% quantile (95% CI)	NC (2.136 to NC)	NC (1.216 to NC)	NC (0.986 to NC)	NC (15.869 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.5571		0.8730	
Hazard ratio (95% CI) vs Kd	-	1.19 (0.67 to 2.10)		0.87 (0.17 to 4.52)	
P-value	-	0.5576		0.8731	
Improvement probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful improvement change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
PGM=DEVOPS/SAR650984/EFC15246/CIR_RWE/REPORT/PGM/eff_km_subgp_sr_sig_de_i_t.sas OUT=REPORT/OUTPUT/eff_km_c30_con_impl_crcl_de_i_t_x.rtf (07APR2021 14:35)

16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Constipation
16.2.6.1.2.14 Efficacy response data - Subgroup analyses by baseline eGFR (MDRD)
16.2.6.1.2.14.4 QLQ-C30 - Time to first deterioration by 10 pt in constipation according to baseline eGFR (MDRD) (LOCF) - ITT population

	>=60 mL/min/1.73m2		<60 mL/min/1.73m2		
	Kd (N=93)	**IKd (N=122)**	**Kd (N=18)**	**IKd (N=43)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	38 (40.9)	48 (39.3)	5 (27.8)	22 (51.2)	0.3022
Number (%) of patients censored	55 (59.1)	74 (60.7)	13 (72.2)	21 (48.8)	
Kaplan-Meier estimates of Constipation in months					
25% quantile (95% CI)	6.60 (2.858 to 11.105)	5.59 (3.910 to 7.458)	8.08 (1.150 to NC)	1.97 (1.051 to 6.571)	
Median (95% CI)	NC (16.986 to NC)	NC (14.160 to NC)	NC (8.082 to NC)	18.46 (5.224 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.8082		0.2181	
Hazard ratio (95% CI) vs Kd	-	1.05 (0.69 to 1.61)		1.82 (0.69 to 4.82)	
P-value	-	0.8087		0.2250	
Deterioration probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful deterioration change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Constipation
16.2.6.1.2.14 Efficacy response data - Subgroup analyses by baseline eGFR (MDRD)
16.2.6.1.2.14.5 QLQ-C30 - Time until permanent improvement by 10 pt in constipation according to baseline eGFR (MDRD) (LOCF) - ITT population

	>=60 mL/min/1.73m2		<60 mL/min/1.73m2		
	Kd (N=93)	**IKd (N=122)**	**Kd (N=18)**	**IKd (N=43)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	10 (10.8)	23 (18.9)	2 (11.1)	5 (11.6)	0.3808
Number (%) of patients censored	83 (89.2)	99 (81.1)	16 (88.9)	38 (88.4)	
Kaplan-Meier estimates of Constipation in months					
25% quantile (95% CI)	NC (22.439 to NC)	NC (12.715 to NC)	NC (3.778 to NC)	NC (19.384 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.0688		0.8648	
Hazard ratio (95% CI) vs Kd	-	1.97 (0.94 to 4.14)		0.87 (0.17 to 4.48)	
P-value	-	0.0742		0.8649	
Improvement probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful improvement change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Constipation
16.2.6.1.2.14 Efficacy response data - Subgroup analyses by baseline eGFR (MDRD)
16.2.6.1.2.14.6 QLQ-C30 - Time until permanent deterioration by 10 pt in constipation according to baseline eGFR (MDRD) (LOCF) - ITT population

	>=60 mL/min/1.73m2		<60 mL/min/1.73m2		
	Kd (N=93)	**IKd (N=122)**	**Kd (N=18)**	**IKd (N=43)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	12 (12.9)	13 (10.7)	1 (5.6)	7 (16.3)	0.3804
Number (%) of patients censored	81 (87.1)	109 (89.3)	17 (94.4)	36 (83.7)	
Kaplan-Meier estimates of Constipation in months					
25% quantile (95% CI)	NC (19.614 to NC)	NC (NC to NC)	NC (10.645 to NC)	NC (15.146 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.7169		0.3905	
Hazard ratio (95% CI) vs Kd	-	0.86 (0.39 to 1.90)		2.43 (0.30 to 19.77)	
P-value	-	0.7172		0.4059	
Deterioration probability (95% CI)[b]					

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The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Constipation
16.2.6.1.2.15 Efficacy response data - Subgroup analyses by previous treatment with PI
16.2.6.1.2.15.3 QLQ-C30 - Time to first improvement by 10 pt in constipation according to previous treatment with PI (LOCF) - ITT population

	Yes		No		
	Kd (N=47)	**IKd (N=81)**	**Kd (N=76)**	**IKd (N=98)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	11 (23.4)	19 (23.5)	13 (17.1)	15 (15.3)	0.7086
Number (%) of patients censored	36 (76.6)	62 (76.5)	63 (82.9)	83 (84.7)	
Kaplan-Meier estimates of Constipation in months					
25% quantile (95% CI)	NC (1.971 to NC)	NC (1.084 to NC)	NC (1.281 to NC)	NC (NC to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.8764		0.7318	
Hazard ratio (95% CI) vs Kd	-	1.06 (0.50 to 2.23)		0.88 (0.42 to 1.85)	
P-value	-	0.8773		0.7320	
Improvement probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful improvement change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Constipation
16.2.6.1.2.15 Efficacy response data - Subgroup analyses by previous treatment with PI
16.2.6.1.2.15.4 QLQ-C30 - Time to first deterioration by 10 pt in constipation according to previous treatment with PI (LOCF) - ITT population

	Yes		No		
	Kd (N=47)	**IKd (N=81)**	**Kd (N=76)**	**IKd (N=98)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	14 (29.8)	28 (34.6)	34 (44.7)	48 (49.0)	0.8590
Number (%) of patients censored	33 (70.2)	53 (65.4)	42 (55.3)	50 (51.0)	
Kaplan-Meier estimates of Constipation in months					
25% quantile (95% CI)	10.41 (2.858 to NC)	7.46 (1.971 to 13.372)	5.55 (2.103 to 8.805)	3.94 (1.314 to 5.618)	
Median (95% CI)	NC (NC to NC)	NC (19.055 to NC)	20.37 (11.039 to NC)	17.54 (6.571 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.5148		0.5064	
Hazard ratio (95% CI) vs Kd	-	1.24 (0.65 to 2.35)		1.16 (0.75 to 1.80)	
P-value	-	0.5156		0.5068	
Deterioration probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful deterioration change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Constipation
16.2.6.1.2.15 Efficacy response data - Subgroup analyses by previous treatment with PI
16.2.6.1.2.15.5 QLQ-C30 - Time until permanent improvement by 10 pt in constipation according to previous treatment with PI (LOCF) - ITT population

	Yes		No		
	Kd (N=47)	**IKd (N=81)**	**Kd (N=76)**	**IKd (N=98)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	6 (12.8)	16 (19.8)	8 (10.5)	12 (12.2)	0.5096
Number (%) of patients censored	41 (87.2)	65 (80.2)	68 (89.5)	86 (87.8)	
Kaplan-Meier estimates of Constipation in months					
25% quantile (95% CI)	NC (11.138 to NC)	NC (2.103 to NC)	NC (22.439 to NC)	NC (20.698 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.2699		0.7730	
Hazard ratio (95% CI) vs Kd	-	1.69 (0.66 to 4.31)		1.14 (0.47 to 2.79)	
P-value	-	0.2756		0.7732	
Improvement probability (95% CI)[b]					

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The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Constipation
16.2.6.1.2.15 Efficacy response data - Subgroup analyses by previous treatment with PI
16.2.6.1.2.15.6 QLQ-C30 - Time until permanent deterioration by 10 pt in constipation according to previous treatment with PI (LOCF) - ITT population

	Yes		No		
	Kd (N=47)	**IKd (N=81)**	**Kd (N=76)**	**IKd (N=98)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	5 (10.6)	10 (12.3)	10 (13.2)	14 (14.3)	0.8435
Number (%) of patients censored	42 (89.4)	71 (87.7)	66 (86.8)	84 (85.7)	
Kaplan-Meier estimates of Constipation in months					
25% quantile (95% CI)	NC (18.530 to NC)	NC (19.877 to NC)	NC (19.351 to NC)	NC (20.928 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.7464		0.9185	
Hazard ratio (95% CI) vs Kd	-	1.19 (0.41 to 3.49)		1.04 (0.46 to 2.35)	
P-value	-	0.7467		0.9187	
Deterioration probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful deterioration change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Constipation
16.2.6.1.2.16 Efficacy response data - Subgroup analyses by previous treatment with IMiD
16.2.6.1.2.16.3 QLQ-C30 - Time to first improvement by 10 pt in constipation according to previous treatment with IMiD (LOCF) - ITT population

	Yes		No		
	Kd (N=62)	**IKd (N=81)**	**Kd (N=61)**	**IKd (N=98)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	13 (21.0)	9 (11.1)	11 (18.0)	25 (25.5)	0.0498
Number (%) of patients censored	49 (79.0)	72 (88.9)	50 (82.0)	73 (74.5)	
Kaplan-Meier estimates of Constipation in months					
25% quantile (95% CI)	NC (1.281 to NC)	NC (NC to NC)	NC (3.713 to NC)	3.75 (1.216 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.1074		0.2416	
Hazard ratio (95% CI) vs Kd	-	0.50 (0.22 to 1.18)		1.52 (0.75 to 3.10)	
P-value	-	0.1144		0.2452	
Improvement probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful improvement change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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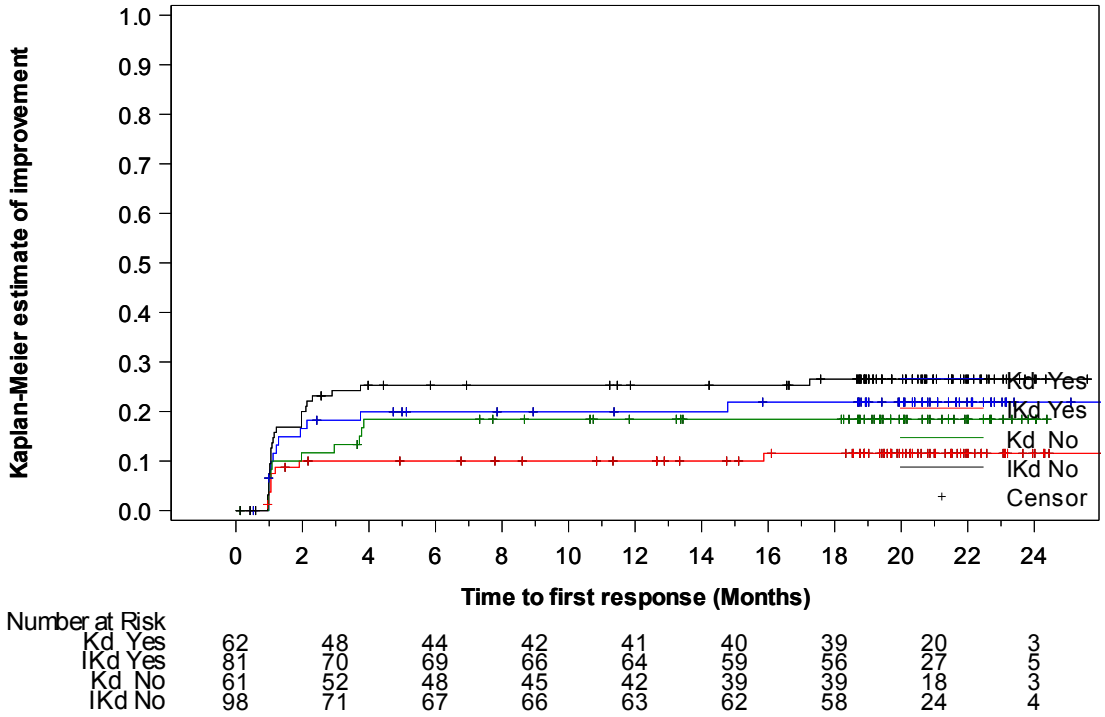
16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Constipation
16.2.6.1.2.16 Efficacy response data - Subgroup analyses by previous treatment with IMiD
16.2.6.1.2.16.4 QLQ-C30 - Time to first improvement by 10 pt in constipation according to previous treatment with IMiD - Kaplan-Meier curve (LOCF) - ITT population



Number at Risk

Kd Yes	62	48	44	42	41	40	39	20	3
IKd Yes	81	70	69	66	64	59	56	27	5
Kd No	61	52	48	45	42	39	39	18	3
IKd No	98	71	67	66	63	62	58	24	4

A lower score represents a better level of quality of life. Clinical meaningful improvement change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
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16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Constipation
16.2.6.1.2.16 Efficacy response data - Subgroup analyses by previous treatment with IMiD
16.2.6.1.2.16.5 QLQ-C30 - Time to first deterioration by 10 pt in constipation according to previous treatment with IMiD (LOCF) - ITT population

	Yes		No		
	Kd (N=62)	**IKd (N=81)**	**Kd (N=61)**	**IKd (N=98)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	21 (33.9)	39 (48.1)	27 (44.3)	37 (37.8)	0.0887
Number (%) of patients censored	41 (66.1)	42 (51.9)	34 (55.7)	61 (62.2)	
Kaplan-Meier estimates of Constipation in months					
25% quantile (95% CI)	8.84 (2.825 to 19.745)	3.94 (1.216 to 6.604)	3.81 (1.906 to 8.805)	5.55 (2.136 to 7.951)	
Median (95% CI)	NC (19.745 to NC)	18.46 (7.458 to NC)	NC (8.805 to NC)	NC (17.544 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.0777		0.5597	
Hazard ratio (95% CI) vs Kd	-	1.61 (0.94 to 2.73)		0.86 (0.53 to 1.42)	
P-value	-	0.0805		0.5600	
Deterioration probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful deterioration change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Constipation
16.2.6.1.2.16 Efficacy response data - Subgroup analyses by previous treatment with IMiD
16.2.6.1.2.16.6 QLQ-C30 - Time until permanent improvement by 10 pt in constipation according to previous treatment with IMiD (LOCF) - ITT population

	Yes		No		
	Kd (N=62)	**IKd (N=81)**	**Kd (N=61)**	**IKd (N=98)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	10 (16.1)	9 (11.1)	4 (6.6)	19 (19.4)	0.0257
Number (%) of patients censored	52 (83.9)	72 (88.9)	57 (93.4)	79 (80.6)	
Kaplan-Meier estimates of Constipation in months					
25% quantile (95% CI)	NC (11.138 to NC)	NC (20.698 to NC)	NC (NC to NC)	NC (10.251 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.3938		0.0224	
Hazard ratio (95% CI) vs Kd	-	0.68 (0.27 to 1.67)		3.27 (1.11 to 9.62)	
P-value	-	0.3968		0.0312	
Hazard ratio inverted (95% CI) vs IKd		-		0.31 (0.10 to 0.90)	

A lower score represents a better level of quality of life. Clinical meaningful improvement change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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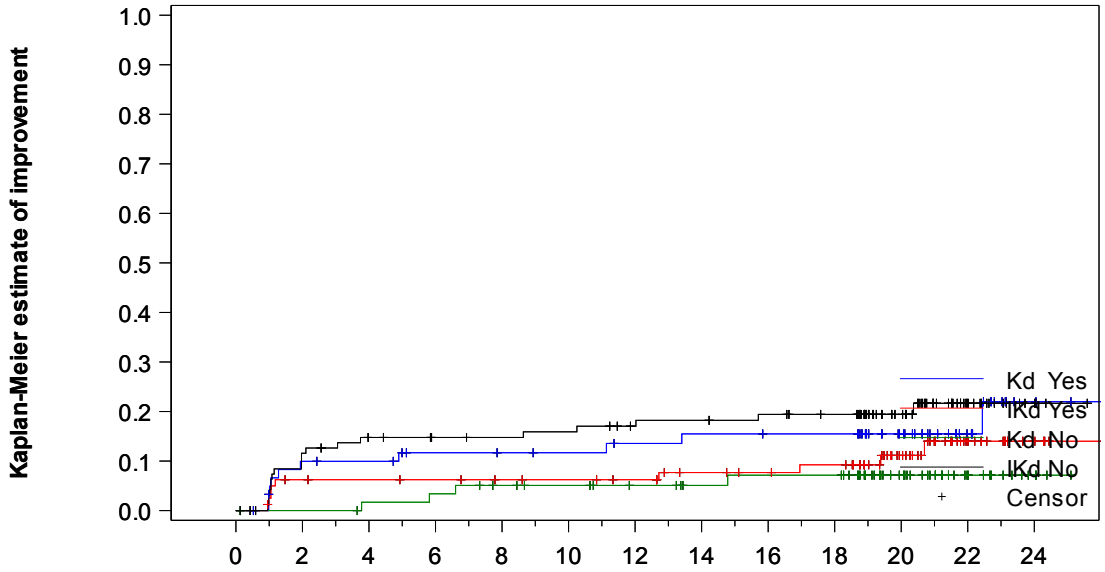
16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Constipation
16.2.6.1.2.16 Efficacy response data - Subgroup analyses by previous treatment with IMiD
16.2.6.1.2.16.7 QLQ-C30 - Time until permanent improvement by 10 pt in constipation according to previous treatment with IMiD - Kaplan-Meier curve (LOCF) - ITT population



Number at Risk

Kd Yes	62	53	49	47	45	44	43	22	4
IKd Yes	81	73	72	69	67	61	58	27	5
Kd No	61	60	57	52	49	45	45	22	4
IKd No	98	82	76	74	70	68	64	26	4

A lower score represents a better level of quality of life. Clinical meaningful improvement change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
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16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Constipation
16.2.6.1.2.16 Efficacy response data - Subgroup analyses by previous treatment with IMiD
16.2.6.1.2.16.8 QLQ-C30 - Time until permanent deterioration by 10 pt in constipation according to previous treatment with IMiD (LOCF) - ITT population

	Yes		No		
	Kd (N=62)	**IKd (N=81)**	**Kd (N=61)**	**IKd (N=98)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	4 (6.5)	12 (14.8)	11 (18.0)	12 (12.2)	0.0682
Number (%) of patients censored	58 (93.5)	69 (85.2)	50 (82.0)	86 (87.8)	
Kaplan-Meier estimates of Constipation in months					
25% quantile (95% CI)	NC (NC to NC)	NC (19.680 to NC)	NC (11.105 to NC)	NC (19.877 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.1301		0.2759	
Hazard ratio (95% CI) vs Kd	-	2.34 (0.75 to 7.24)		0.64 (0.28 to 1.44)	
P-value	-	0.1418		0.2799	
Deterioration probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful deterioration change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Constipation
16.2.6.1.2.17 Efficacy response data - Subgroup analyses by previous treatment with PI and IMiD
16.2.6.1.2.17.3 QLQ-C30 - Time to first improvement by 10 pt in constipation according to previous treatment with PI and IMiD (LOCF) - ITT population

	Yes		No		
	Kd (N=17)	**IKd (N=23)**	**Kd (N=106)**	**IKd (N=156)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	5 (29.4)	2 (8.7)	19 (17.9)	32 (20.5)	0.0911
Number (%) of patients censored	12 (70.6)	21 (91.3)	87 (82.1)	124 (79.5)	
Kaplan-Meier estimates of Constipation in months					
25% quantile (95% CI)	8.46 (0.986 to NC)	NC (0.986 to NC)	NC (3.778 to NC)	NC (2.300 to NC)	
Median (95% CI)	NC (2.136 to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.0943		0.5684	
Hazard ratio (95% CI) vs Kd	-	0.27 (0.05 to 1.40)		1.18 (0.67 to 2.08)	
P-value	-	0.1187		0.5688	
Improvement probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful improvement change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Constipation
16.2.6.1.2.17 Efficacy response data - Subgroup analyses by previous treatment with PI and IMiD
16.2.6.1.2.17.4 QLQ-C30 - Time to first deterioration by 10 pt in constipation according to previous treatment with PI and IMiD (LOCF) - ITT population

	Yes		No		
	Kd (N=17)	**IKd (N=23)**	**Kd (N=106)**	**IKd (N=156)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	5 (29.4)	7 (30.4)	43 (40.6)	69 (44.2)	0.7992
Number (%) of patients censored	12 (70.6)	16 (69.6)	63 (59.4)	87 (55.8)	
Kaplan-Meier estimates of Constipation in months					
25% quantile (95% CI)	3.71 (1.906 to NC)	12.91 (0.986 to NC)	5.55 (2.825 to 11.039)	3.98 (2.070 to 5.684)	
Median (95% CI)	NC (3.713 to NC)	NC (12.912 to NC)	NC (16.131 to NC)	NC (12.222 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.9795		0.4218	
Hazard ratio (95% CI) vs Kd	-	1.02 (0.32 to 3.20)		1.17 (0.80 to 1.71)	
P-value	-	0.9795		0.4222	
Deterioration probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful deterioration change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Constipation
16.2.6.1.2.17 Efficacy response data - Subgroup analyses by previous treatment with PI and IMiD
16.2.6.1.2.17.5 QLQ-C30 - Time until permanent improvement by 10 pt in constipation according to previous treatment with PI and IMiD (LOCF) - ITT population

	Yes		No		
	Kd (N=17)	**IKd (N=23)**	**Kd (N=106)**	**IKd (N=156)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	3 (17.6)	2 (8.7)	11 (10.4)	26 (16.7)	0.1982
Number (%) of patients censored	14 (82.4)	21 (91.3)	95 (89.6)	130 (83.3)	
Kaplan-Meier estimates of Constipation in months					
25% quantile (95% CI)	NC (1.018 to NC)	NC (1.051 to NC)	NC (22.439 to NC)	NC (20.370 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.3759		0.1384	
Hazard ratio (95% CI) vs Kd	-	0.45 (0.08 to 2.72)		1.69 (0.84 to 3.43)	
P-value	-	0.3881		0.1432	

A lower score represents a better level of quality of life. Clinical meaningful improvement change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Constipation
16.2.6.1.2.17 Efficacy response data - Subgroup analyses by previous treatment with PI and IMiD
16.2.6.1.2.17.6 QLQ-C30 - Time until permanent deterioration by 10 pt in constipation according to previous treatment with PI and IMiD (LOCF) - ITT population

	Yes		No		
	Kd (N=17)	**IKd (N=23)**	**Kd (N=106)**	**IKd (N=156)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	2 (11.8)	2 (8.7)	13 (12.3)	22 (14.1)	0.6890
Number (%) of patients censored	15 (88.2)	21 (91.3)	93 (87.7)	134 (85.9)	
Kaplan-Meier estimates of Constipation in months					
25% quantile (95% CI)	NC (14.653 to NC)	NC (10.908 to NC)	NC (NC to NC)	NC (20.928 to NC)	
Median (95% CI)	NC (19.614 to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.7804		0.7326	
Hazard ratio (95% CI) vs Kd	-	0.76 (0.11 to 5.38)		1.13 (0.57 to 2.24)	
P-value	-	0.7811		0.7327	
Deterioration probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful deterioration change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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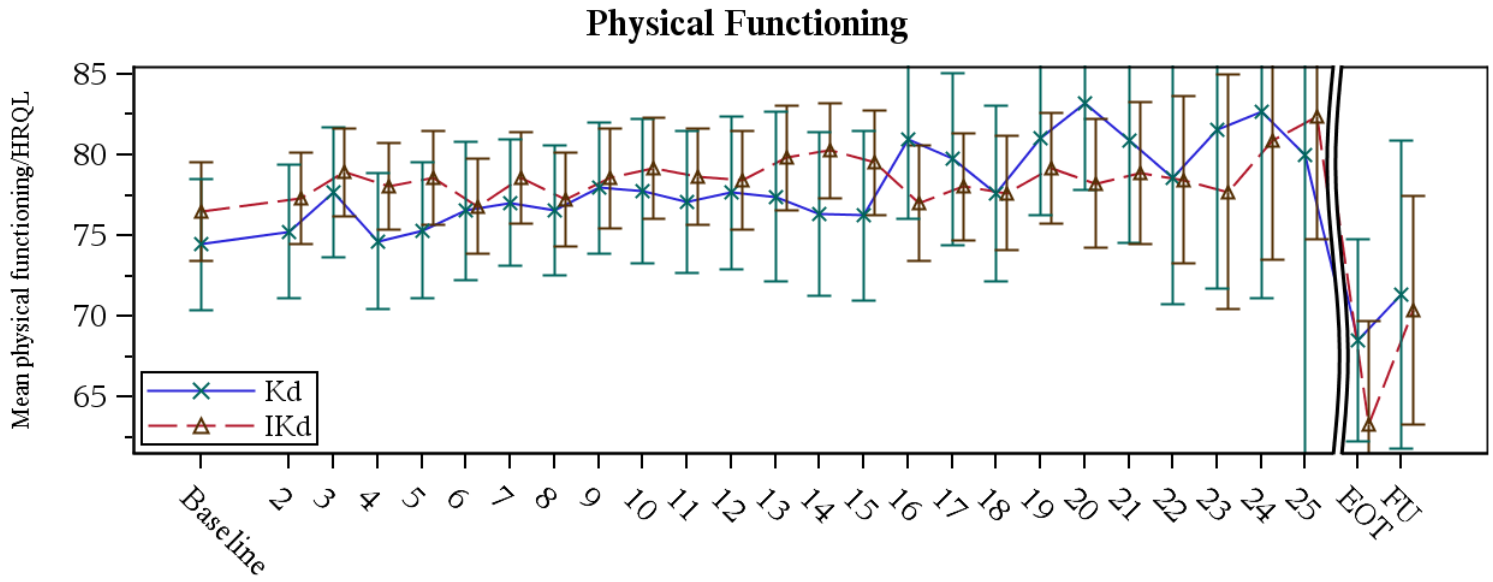
16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Physical functioning
16.2.6.1.2.1 Efficacy response data
16.2.6.1.2.1.1 QLQ-C30 - Mean and 95% CI for physical functioning score over time (LOCF) - ITT population



#patients																									
Kd	113	114	112	110	104	100	95	91	88	84	78	72	67	66	62	57	52	50	45	37	30	23	17	10	6	62	34
IKd	166	169	168	164	161	155	150	145	138	133	130	127	121	118	112	109	105	102	97	91	78	56	38	23	17	59	34

A higher score represents a better level of quality of life. Cycles with less than 20 patients overall are not presented.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
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16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Physical functioning
16.2.6.1.2.1 Efficacy response data
16.2.6.1.2.1.15 QLQ-C30 - Time to first improvement by 15 pt in physical functioning (LOCF) - ITT population

First improvement 15 points Physical functioning (%)	**Kd (N=123)**	**IKd (N=179)**
Number (%) of events	35 (28.5)	56 (31.3)
Number (%) of patients censored	88 (71.5)	123 (68.7)
Kaplan-Meier estimates of Physical functioning in months		
25% quantile (95% CI)	6.57 (2.234 to NC)	5.72 (2.103 to 13.700)
Median (95% CI)	NC (NC to NC)	NC (NC to NC)
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)
Comparison vs. Kd		
Stratified[a] Log-Rank test p-value[b] vs Kd	-	0.5475
Stratified[a] Hazard ratio (95% CI) vs Kd	-	1.14 (0.74 to 1.74)
P-value	-	0.5478
Improvement probability (95% CI)[c]		
3 Months	0.192 (0.127 to 0.267)	0.224 (0.165 to 0.288)
6 Months	0.226 (0.156 to 0.305)	0.254 (0.192 to 0.320)

A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 15 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] Stratified on number of prior lines of therapy (1 vs. >1) and Revised International Staging System (R-ISS) stage (I or II vs. III vs. not classified) according to IRT
[b] One-sided significance level is 0.025
[c] Estimated using the Kaplan-Meier method
NA/NC = Not Applicable / Not Calculable
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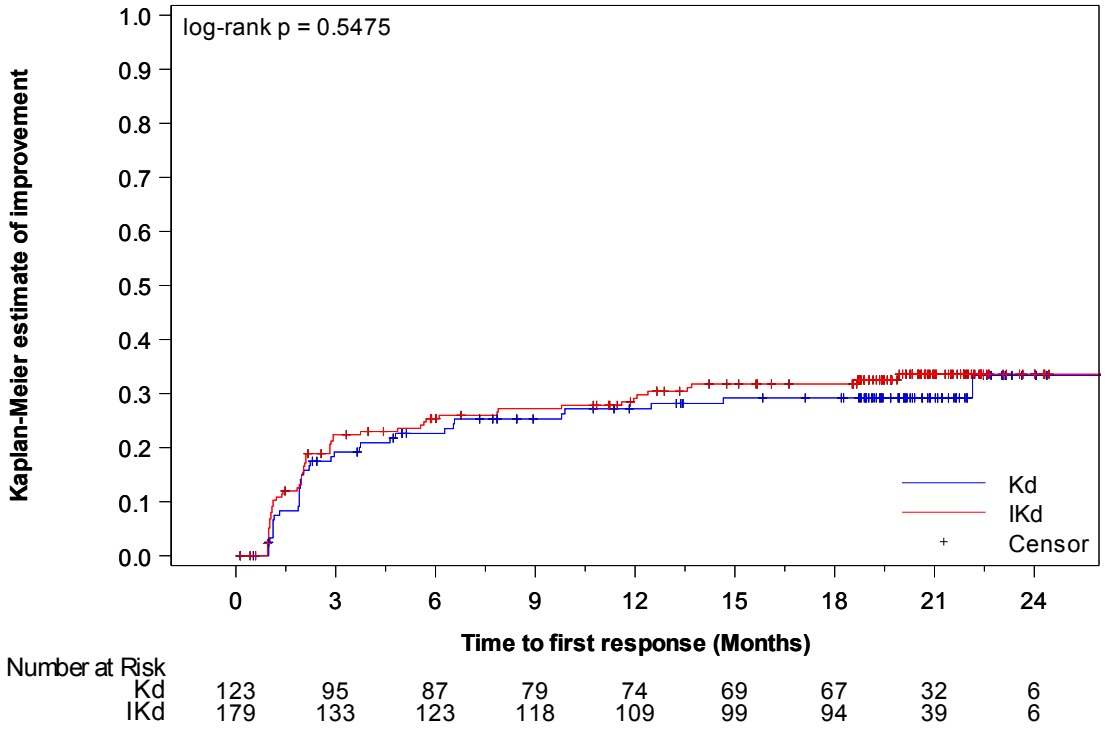
16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Physical functioning
16.2.6.1.2.1 Efficacy response data
16.2.6.1.2.1.16 QLQ-C30 - Time to first improvement by 15 pt in physical functioning - Kaplan-Meier curve (LOCF) - ITT population



A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 15 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
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16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Physical functioning
16.2.6.1.2.1 Efficacy response data
16.2.6.1.2.1.17 QLQ-C30 - Time to first deterioration by 15 pt in physical functioning (LOCF) - ITT population

First deterioration 15 points Physical functioning (%)	**Kd (N=123)**	**IKd (N=179)**
Number (%) of events	49 (39.8)	78 (43.6)
Number (%) of patients censored	74 (60.2)	101 (56.4)
Kaplan-Meier estimates of Physical functioning in months		
25% quantile (95% CI)	5.62 (2.957 to 7.458)	6.01 (3.877 to 9.363)
Median (95% CI)	NC (15.507 to NC)	NC (15.474 to NC)
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)
Comparison vs. Kd		
Stratified[a] Log-Rank test p-value[b] vs Kd	-	0.7484
Stratified[a] Hazard ratio (95% CI) vs Kd	-	1.06 (0.74 to 1.52)
P-value	-	0.7498
Deterioration probability (95% CI)[c]		
3 Months	0.825 (0.744 to 0.882)	0.845 (0.782 to 0.891)
6 Months	0.712 (0.621 to 0.785)	0.752 (0.680 to 0.810)

A higher score represents a better level of quality of life. Clinical meaningful deterioration change from baseline less than or equal to -15 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] Stratified on number of prior lines of therapy (1 vs. >1) and Revised International Staging System (R-ISS) stage (I or II vs. III vs. not classified) according to IRT
[b] One-sided significance level is 0.025
[c] Estimated using the Kaplan-Meier method
NA/NC = Not Applicable / Not Calculable
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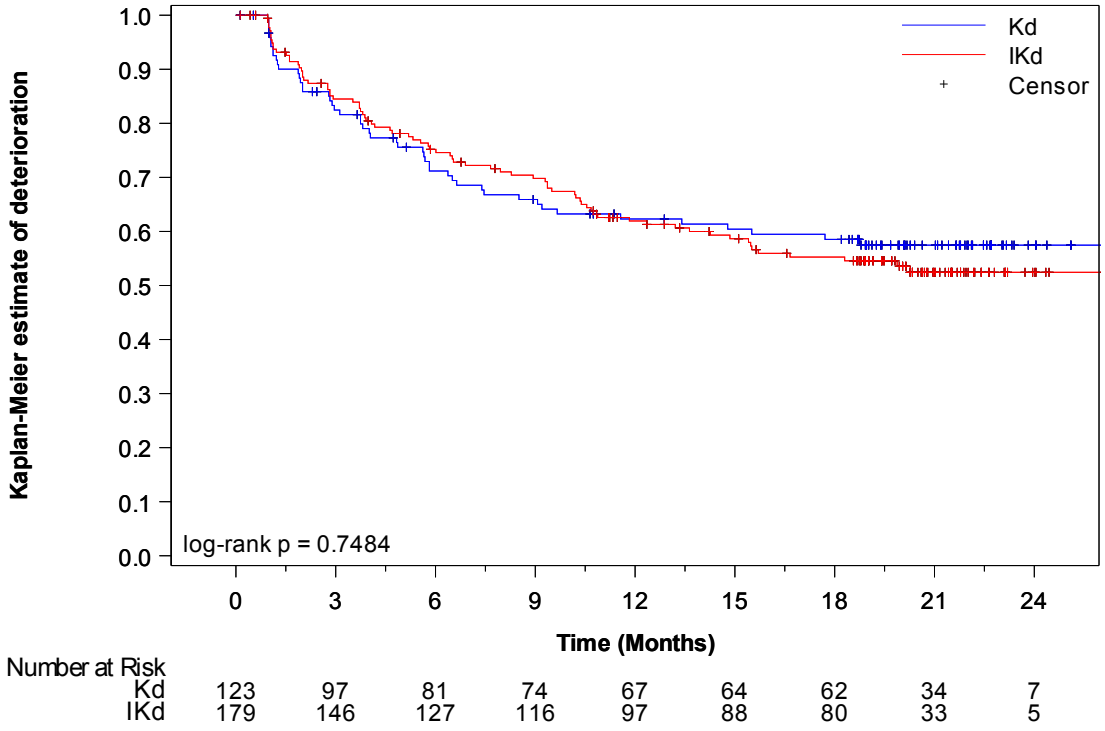
16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Physical functioning
16.2.6.1.2.1 Efficacy response data
16.2.6.1.2.1.18 QLQ-C30 - Time to first deterioration by 15 pt in physical functioning - Kaplan-Meier curve (LOCF) - ITT population



A higher score represents a better level of quality of life. Clinical meaningful deterioration change from baseline less than or equal to -15 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
PGM=DEVOPS/SAR650984/EFC15246/CIR_RWE/REPORT/PGM/eff_qlq_km_i_f.sas OUT=REPORT/OUTPUT/eff_km_c30_phy_det15l_de_i_f_x.rtf (07APR2021 14:23)

16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Physical functioning
16.2.6.1.2.1 Efficacy response data
16.2.6.1.2.1.19 QLQ-C30 - Time until permanent improvement by 15 pt in physical functioning (LOCF) - ITT population

First permanent improvement 15 points Physical functioning (%)	**Kd (N=123)**	**IKd (N=179)**
Number (%) of events	18 (14.6)	25 (14.0)
Number (%) of patients censored	105 (85.4)	154 (86.0)
Kaplan-Meier estimates of Physical functioning in months		
25% quantile (95% CI)	NC (21.684 to NC)	23.36 (22.801 to NC)
Median (95% CI)	NC (NC to NC)	24.44 (24.444 to NC)
75% quantile (95% CI)	NC (NC to NC)	NC (24.444 to NC)
Comparison vs. Kd		
Stratified[a] Log-Rank test p-value[b] vs Kd	-	0.8074
Stratified[a] Hazard ratio (95% CI) vs Kd	-	0.93 (0.50 to 1.72)
P-value	-	0.8075
Improvement probability (95% CI)[c]		
3 Months	0.033 (0.011 to 0.077)	0.046 (0.021 to 0.084)
6 Months	0.051 (0.021 to 0.101)	0.052 (0.025 to 0.092)

A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 15 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] Stratified on number of prior lines of therapy (1 vs. >1) and Revised International Staging System (R-ISS) stage (I or II vs. III vs. not classified) according to IRT
[b] One-sided significance level is 0.025
[c] Estimated using the Kaplan-Meier method
NA/NC = Not Applicable / Not Calculable
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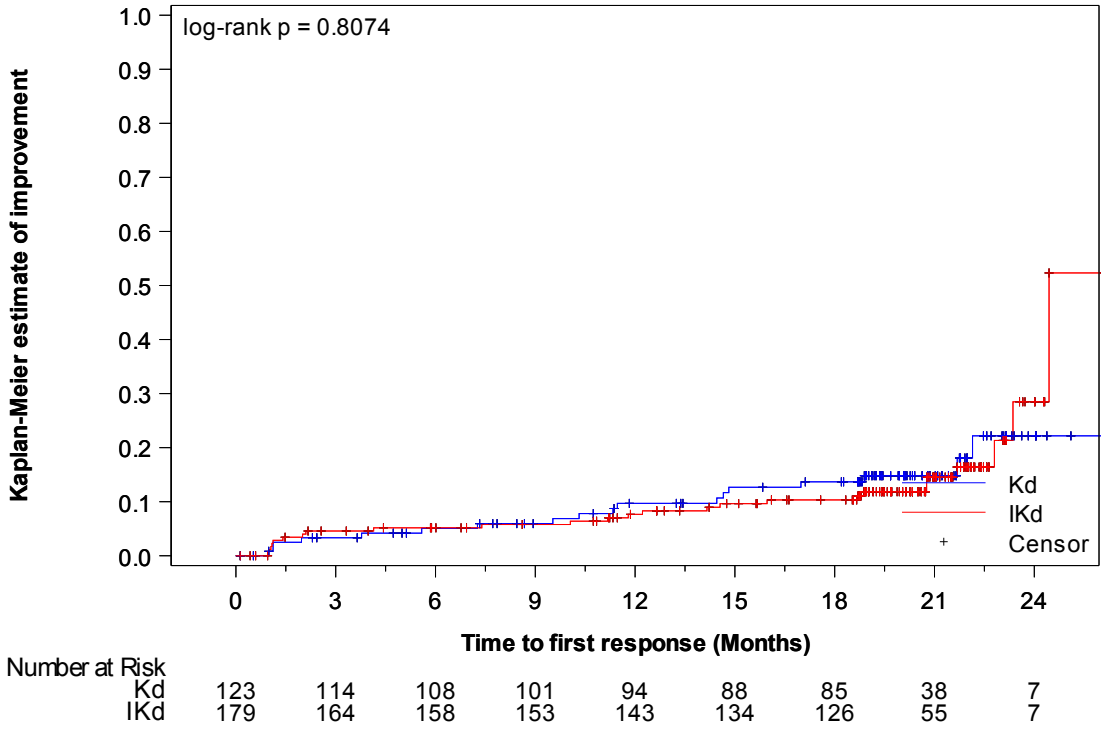
16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Physical functioning
16.2.6.1.2.1 Efficacy response data
16.2.6.1.2.1.20 QLQ-C30 - Time until permanent improvement by 15 pt in physical functioning - Kaplan-Meier curve (LOCF) - ITT population



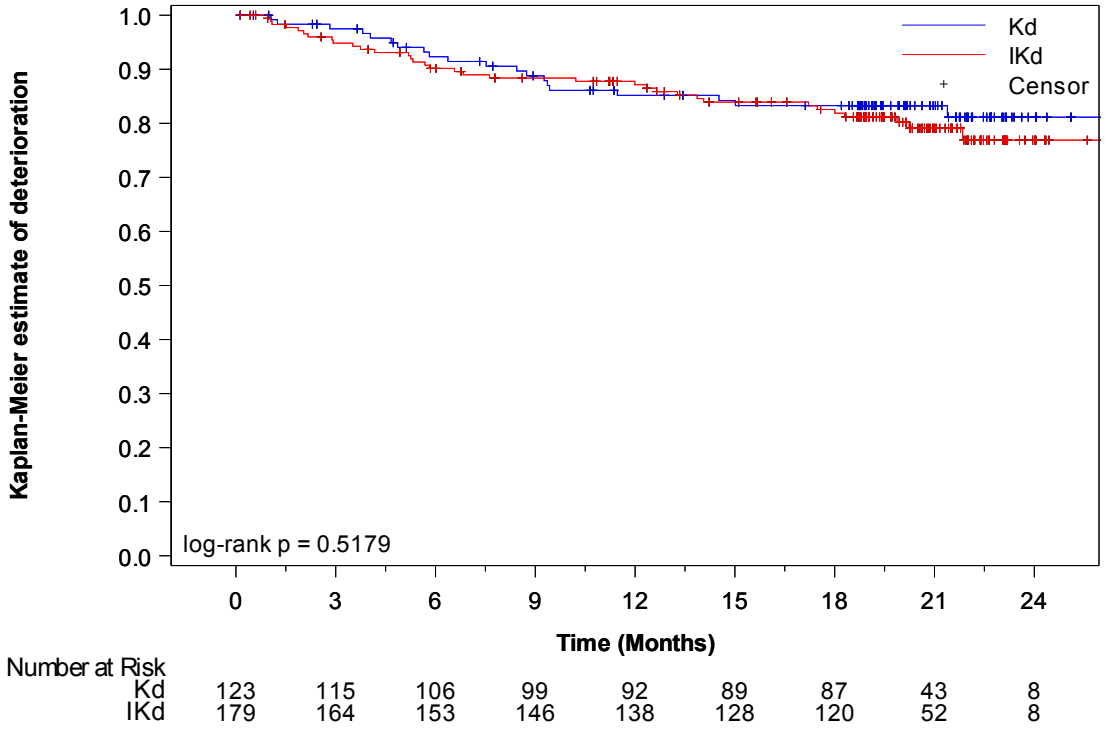
A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 15 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.

16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Physical functioning
16.2.6.1.2.1 Efficacy response data
16.2.6.1.2.1.21 QLQ-C30 - Time until permanent deterioration by 15 pt in physical functioning (LOCF) - ITT population

First permanent deterioration 15 points Physical functioning (%)	**Kd (N=123)**	**IKd (N=179)**
Number (%) of events	20 (16.3)	34 (19.0)
Number (%) of patients censored	103 (83.7)	145 (81.0)
Kaplan-Meier estimates of Physical functioning in months		
25% quantile (95% CI)	NC (21.388 to NC)	NC (18.300 to NC)
Median (95% CI)	NC (NC to NC)	NC (NC to NC)
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)
Comparison vs. Kd		
Stratified[a] Log-Rank test p-value[b] vs Kd	-	0.5179
Stratified[a] Hazard ratio (95% CI) vs Kd	-	1.20 (0.69 to 2.09)
P-value	-	0.5185
Deterioration probability (95% CI)[c]		
3 Months	0.975 (0.924 to 0.992)	0.948 (0.903 to 0.973)
6 Months	0.923 (0.857 to 0.959)	0.902 (0.847 to 0.938)

A higher score represents a better level of quality of life. Clinical meaningful deterioration change from baseline less than or equal to -15 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] Stratified on number of prior lines of therapy (1 vs. >1) and Revised International Staging System (R-ISS) stage (I or II vs. III vs. not classified) according to IRT
[b] One-sided significance level is 0.025
[c] Estimated using the Kaplan-Meier method
NA/NC = Not Applicable / Not Calculable
PGM=DEVOPS/SAR650984/EFC15246/CIR_RWE/REPORT/PGM/eff_km_invhr_sr_i_t.sas OUT=REPORT/OUTPUT/eff_km_c30_phy_det15pl_de_i_t_x.rtf (07APR2021 14:22)

16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Physical functioning
16.2.6.1.2.1 Efficacy response data
16.2.6.1.2.1.22 QLQ-C30 - Time until permanent deterioration by 15 pt in physical functioning - Kaplan-Meier curve (LOCF) - ITT population



A higher score represents a better level of quality of life. Clinical meaningful deterioration change from baseline less than or equal to -15 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
PGM=DEVOPS/SAR650984/EFC15246/CIR_RWE/REPORT/PGM/eff_qlq_km_i_f.sas OUT=REPORT/OUTPUT/eff_km_c30_phy_det15pl_de_i_f_x.rtf (07APR2021 14:23)

16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Physical functioning
16.2.6.1.2.2 Efficacy response data - Subgroup analyses by age
16.2.6.1.2.2.3 QLQ-C30 - Time to first improvement by 10 pt in physical functioning according to age (LOCF) - ITT population

	<65 years		>=65 years		
	Kd (N=66)	**IKd (N=88)**	**Kd (N=57)**	**IKd (N=91)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	23 (34.8)	42 (47.7)	30 (52.6)	42 (46.2)	0.1126
Number (%) of patients censored	43 (65.2)	46 (52.3)	27 (47.4)	49 (53.8)	
Kaplan-Meier estimates of Physical functioning in months					
25% quantile (95% CI)	2.23 (1.117 to 17.643)	2.10 (1.051 to 3.877)	1.91 (1.117 to 2.037)	2.05 (1.577 to 2.924)	
Median (95% CI)	NC (NC to NC)	18.66 (5.782 to NC)	7.03 (2.037 to NC)	NC (4.402 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.1668		0.3762	
Hazard ratio (95% CI) vs Kd	-	1.43 (0.86 to 2.38)		0.81 (0.51 to 1.29)	
P-value	-	0.1690		0.3771	
Improvement probability (95% CI)[b]					

A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
PGM=DEVOPS/SAR650984/EFC15246/CIR_RWE/REPORT/PGM/eff_km_subgp_sr_sig_de_i_t.sas OUT=REPORT/OUTPUT/eff_km_c30_phy_impl_age_de_i_t_x.rtf (07APR2021 14:22)

16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Physical functioning
16.2.6.1.2.2 Efficacy response data - Subgroup analyses by age
16.2.6.1.2.2.4 QLQ-C30 - Time to first deterioration by 10 pt in physical functioning according to age (LOCF) - ITT population

	<65 years		>=65 years		
	Kd (N=66)	**IKd (N=88)**	**Kd (N=57)**	**IKd (N=91)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	35 (53.0)	47 (53.4)	30 (52.6)	55 (60.4)	0.2878
Number (%) of patients censored	31 (47.0)	41 (46.6)	27 (47.4)	36 (39.6)	
Kaplan-Meier estimates of Physical functioning in months					
25% quantile (95% CI)	2.00 (1.051 to 3.713)	2.83 (1.511 to 3.877)	3.75 (1.873 to 6.505)	2.76 (1.610 to 3.187)	
Median (95% CI)	9.20 (3.745 to NC)	13.63 (6.505 to NC)	11.56 (6.505 to NC)	9.40 (4.632 to 16.657)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (19.877 to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.6969		0.2561	
Hazard ratio (95% CI) vs Kd	-	0.92 (0.59 to 1.42)		1.29 (0.83 to 2.02)	
P-value	-	0.6970		0.2574	
Deterioration probability (95% CI)[b]					

A higher score represents a better level of quality of life. Clinical meaningful deterioration change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
PGM=DEVOPS/SAR650984/EFC15246/CIR_RWE/REPORT/PGM/eff_km_subgp_sr_sig_de_i_t.sas OUT=REPORT/OUTPUT/eff_km_c30_phy_detl_age_de_i_t_x.rtf (07APR2021 14:21)

16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Physical functioning
16.2.6.1.2.2 Efficacy response data - Subgroup analyses by age
16.2.6.1.2.2.5 QLQ-C30 - Time until permanent improvement by 10 pt in physical functioning according to age (LOCF) - ITT population

	<65 years		>=65 years		
	Kd (N=66)	**IKd (N=88)**	**Kd (N=57)**	**IKd (N=91)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	15 (22.7)	22 (25.0)	14 (24.6)	16 (17.6)	0.3014
Number (%) of patients censored	51 (77.3)	66 (75.0)	43 (75.4)	75 (82.4)	
Kaplan-Meier estimates of Physical functioning in months					
25% quantile (95% CI)	22.14 (10.316 to NC)	18.20 (5.815 to NC)	21.68 (10.316 to NC)	21.68 (20.304 to NC)	
Median (95% CI)	NC (22.144 to NC)	NC (NC to NC)	NC (23.129 to NC)	24.44 (24.444 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (24.444 to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.7788		0.2257	
Hazard ratio (95% CI) vs Kd	-	1.10 (0.57 to 2.12)		0.64 (0.31 to 1.32)	
P-value	-	0.7788		0.2294	
Improvement probability (95% CI)[b]					

A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Physical functioning
16.2.6.1.2.2 Efficacy response data - Subgroup analyses by age
16.2.6.1.2.2.6 QLQ-C30 - Time until permanent deterioration by 10 pt in physical functioning according to age (LOCF) - ITT population

	<65 years		>=65 years		
	Kd (N=66)	**IKd (N=88)**	**Kd (N=57)**	**IKd (N=91)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	19 (28.8)	27 (30.7)	13 (22.8)	26 (28.6)	0.6231
Number (%) of patients censored	47 (71.2)	61 (69.3)	44 (77.2)	65 (71.4)	
Kaplan-Meier estimates of Physical functioning in months					
25% quantile (95% CI)	10.55 (3.811 to NC)	18.30 (12.156 to 20.698)	NC (5.815 to NC)	17.22 (9.922 to NC)	
Median (95% CI)	NC (21.388 to NC)	NC (21.520 to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.8713		0.4648	
Hazard ratio (95% CI) vs Kd	-	1.05 (0.58 to 1.89)		1.28 (0.66 to 2.49)	
P-value	-	0.8718		0.4659	
Deterioration probability (95% CI)[b]					

A higher score represents a better level of quality of life. Clinical meaningful deterioration change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
PGM=DEVOPS/SAR650984/EFC15246/CIR_RWE/REPORT/PGM/eff_km_subgp_sr_sig_de_i_t.sas OUT=REPORT/OUTPUT/eff_km_c30_phy_detpl_age_de_i_t_x.rtf (07APR2021 14:22)

16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Physical functioning
16.2.6.1.2.3 Efficacy response data - Subgroup analyses by gender
16.2.6.1.2.3.3 QLQ-C30 - Time to first improvement by 10 pt in physical functioning according to gender (LOCF) - ITT population

	Male		Female		
	Kd (N=68)	**IKd (N=101)**	**Kd (N=55)**	**IKd (N=78)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	26 (38.2)	42 (41.6)	27 (49.1)	42 (53.8)	0.8825
Number (%) of patients censored	42 (61.8)	59 (58.4)	28 (50.9)	36 (46.2)	
Kaplan-Meier estimates of Physical functioning in months					
25% quantile (95% CI)	1.91 (1.084 to 4.632)	2.14 (1.840 to 3.745)	1.94 (1.117 to 3.285)	2.04 (1.117 to 2.891)	
Median (95% CI)	NC (13.634 to NC)	NC (5.815 to NC)	9.89 (3.285 to NC)	12.06 (4.402 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.8238		0.6618	
Hazard ratio (95% CI) vs Kd	-	1.06 (0.65 to 1.72)		1.11 (0.69 to 1.81)	
P-value	-	0.8248		0.6620	
Improvement probability (95% CI)[b]					

A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Physical functioning
16.2.6.1.2.3 Efficacy response data - Subgroup analyses by gender
16.2.6.1.2.3.4 QLQ-C30 - Time to first deterioration by 10 pt in physical functioning according to gender (LOCF) - ITT population

	Male		Female		
	Kd (N=68)	**IKd (N=101)**	**Kd (N=55)**	**IKd (N=78)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	38 (55.9)	55 (54.5)	27 (49.1)	47 (60.3)	0.3122
Number (%) of patients censored	30 (44.1)	46 (45.5)	28 (50.9)	31 (39.7)	
Kaplan-Meier estimates of Physical functioning in months					
25% quantile (95% CI)	2.83 (1.216 to 3.844)	2.83 (1.873 to 3.877)	2.00 (1.051 to 6.505)	2.27 (1.248 to 3.713)	
Median (95% CI)	8.51 (4.041 to NC)	9.26 (5.585 to NC)	17.71 (6.505 to NC)	10.87 (3.811 to 19.680)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.7230		0.2947	
Hazard ratio (95% CI) vs Kd	-	0.93 (0.61 to 1.40)		1.29 (0.80 to 2.07)	
P-value	-	0.7230		0.2959	
Deterioration probability (95% CI)[b]					

A higher score represents a better level of quality of life. Clinical meaningful deterioration change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
PGM=DEVOPS/SAR650984/EFC15246/CIR_RWE/REPORT/PGM/eff_km_subgp_sr_sig_de_i_t.sas OUT=REPORT/OUTPUT/eff_km_c30_phy_detl_sex_de_i_t_x.rtf (07APR2021 14:22)

16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Physical functioning
16.2.6.1.2.3 Efficacy response data - Subgroup analyses by gender
16.2.6.1.2.3.5 QLQ-C30 - Time until permanent improvement by 10 pt in physical functioning according to gender (LOCF) - ITT population

	Male		Female		
	Kd (N=68)	**IKd (N=101)**	**Kd (N=55)**	**IKd (N=78)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	15 (22.1)	20 (19.8)	14 (25.5)	18 (23.1)	0.9966
Number (%) of patients censored	53 (77.9)	81 (80.2)	41 (74.5)	60 (76.9)	
Kaplan-Meier estimates of Physical functioning in months					
25% quantile (95% CI)	21.68 (11.335 to NC)	21.65 (14.554 to NC)	18.46 (3.778 to NC)	21.42 (16.000 to NC)	
Median (95% CI)	NC (21.684 to NC)	NC (NC to NC)	NC (23.129 to NC)	24.44 (24.444 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (24.444 to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.6147		0.6495	
Hazard ratio (95% CI) vs Kd	-	0.84 (0.43 to 1.65)		0.85 (0.42 to 1.71)	
P-value	-	0.6152		0.6498	
Improvement probability (95% CI)[b]					

A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
PGM=DEVOPS/SAR650984/EFC15246/CIR_RWE/REPORT/PGM/eff_km_subgp_sr_sig_de_i_t.sas OUT=REPORT/OUTPUT/eff_km_c30_phy_imppl_sex_de_i_t_x.rtf (07APR2021 14:22)

16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Physical functioning
16.2.6.1.2.3 Efficacy response data - Subgroup analyses by gender
16.2.6.1.2.3.6 QLQ-C30 - Time until permanent deterioration by 10 pt in physical functioning according to gender (LOCF) - ITT population

	Male		Female		
	Kd (N=68)	**IKd (N=101)**	**Kd (N=55)**	**IKd (N=78)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	19 (27.9)	29 (28.7)	13 (23.6)	24 (30.8)	0.5029
Number (%) of patients censored	49 (72.1)	72 (71.3)	42 (76.4)	54 (69.2)	
Kaplan-Meier estimates of Physical functioning in months					
25% quantile (95% CI)	10.55 (4.041 to NC)	16.85 (12.649 to 21.520)	21.39 (5.815 to NC)	17.22 (7.622 to NC)	
Median (95% CI)	NC (NC to NC)	NC (21.520 to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.9816		0.3880	
Hazard ratio (95% CI) vs Kd	-	0.99 (0.56 to 1.77)		1.34 (0.68 to 2.64)	
P-value	-	0.9816		0.3897	
Deterioration probability (95% CI)[b]					

A higher score represents a better level of quality of life. Clinical meaningful deterioration change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
PGM=DEVOPS/SAR650984/EFC15246/CIR_RWE/REPORT/PGM/eff_km_subgp_sr_sig_de_i_t.sas OUT=REPORT/OUTPUT/eff_km_c30_phy_detpl_sex_de_i_t_x.rtf (07APR2021 14:22)

16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Physical functioning
16.2.6.1.2.4 Efficacy response data - Subgroup analyses by ethnic origin
16.2.6.1.2.4.3 QLQ-C30 - Time to first improvement by 10 pt in physical functioning according to ethnic origin (LOCF) - ITT population

	White		Other		
	Kd (N=83)	**IKd (N=131)**	**Kd (N=28)**	**IKd (N=34)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	38 (45.8)	62 (47.3)	12 (42.9)	17 (50.0)	0.6354
Number (%) of patients censored	45 (54.2)	69 (52.7)	16 (57.1)	17 (50.0)	
Kaplan-Meier estimates of Physical functioning in months					
25% quantile (95% CI)	1.91 (1.117 to 2.858)	2.79 (1.577 to 3.713)	1.15 (1.051 to 3.975)	1.91 (1.018 to 2.004)	
Median (95% CI)	NC (3.778 to NC)	18.66 (5.782 to NC)	NC (1.906 to NC)	9.26 (1.938 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.9341		0.5700	
Hazard ratio (95% CI) vs Kd	-	1.02 (0.68 to 1.52)		1.24 (0.59 to 2.59)	
P-value	-	0.9342		0.5708	
Improvement probability (95% CI)[b]					

A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
PGM=DEVOPS/SAR650984/EFC15246/CIR_RWE/REPORT/PGM/eff_km_subgp_sr_sig_de_i_t.sas OUT=REPORT/OUTPUT/eff_km_c30_phy_impl_race_de_i_t_x.rtf (07APR2021 14:22)

16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Physical functioning
16.2.6.1.2.4 Efficacy response data - Subgroup analyses by ethnic origin
16.2.6.1.2.4.4 QLQ-C30 - Time to first deterioration by 10 pt in physical functioning according to ethnic origin (LOCF) - ITT population

	White		Other		
	Kd (N=83)	**IKd (N=131)**	**Kd (N=28)**	**IKd (N=34)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	48 (57.8)	79 (60.3)	14 (50.0)	19 (55.9)	0.8350
Number (%) of patients censored	35 (42.2)	52 (39.7)	14 (50.0)	15 (44.1)	
Kaplan-Meier estimates of Physical functioning in months					
25% quantile (95% CI)	2.00 (1.051 to 3.745)	2.76 (1.873 to 3.088)	2.00 (1.051 to 4.074)	2.79 (1.018 to 4.961)	
Median (95% CI)	9.20 (4.830 to NC)	8.18 (4.665 to 13.634)	9.07 (2.957 to NC)	13.21 (2.825 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (15.507 to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.7478		0.6931	
Hazard ratio (95% CI) vs Kd	-	1.06 (0.74 to 1.52)		1.15 (0.58 to 2.29)	
P-value	-	0.7494		0.6934	
Deterioration probability (95% CI)[b]					

A higher score represents a better level of quality of life. Clinical meaningful deterioration change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Physical functioning
16.2.6.1.2.4 Efficacy response data - Subgroup analyses by ethnic origin
16.2.6.1.2.4.5 QLQ-C30 - Time until permanent improvement by 10 pt in physical functioning according to ethnic origin (LOCF) - ITT population

	White		Other		
	Kd (N=83)	**IKd (N=131)**	**Kd (N=28)**	**IKd (N=34)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	19 (22.9)	26 (19.8)	9 (32.1)	10 (29.4)	0.9223
Number (%) of patients censored	64 (77.1)	105 (80.2)	19 (67.9)	24 (70.6)	
Kaplan-Meier estimates of Physical functioning in months					
25% quantile (95% CI)	21.68 (11.335 to NC)	21.68 (18.891 to NC)	13.17 (1.051 to NC)	14.13 (3.023 to NC)	
Median (95% CI)	NC (22.144 to NC)	24.44 (24.444 to NC)	NC (14.456 to NC)	NC (17.051 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (24.444 to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.4768		0.7557	
Hazard ratio (95% CI) vs Kd	-	0.81 (0.44 to 1.46)		0.87 (0.35 to 2.13)	
P-value	-	0.4777		0.7559	
Improvement probability (95% CI)[b]					

A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Physical functioning
16.2.6.1.2.4 Efficacy response data - Subgroup analyses by ethnic origin
16.2.6.1.2.4.6 QLQ-C30 - Time until permanent deterioration by 10 pt in physical functioning according to ethnic origin (LOCF) - ITT population

	White		Other		
	Kd (N=83)	**IKd (N=131)**	**Kd (N=28)**	**IKd (N=34)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	25 (30.1)	44 (33.6)	7 (25.0)	8 (23.5)	0.7348
Number (%) of patients censored	58 (69.9)	87 (66.4)	21 (75.0)	26 (76.5)	
Kaplan-Meier estimates of Physical functioning in months					
25% quantile (95% CI)	15.08 (4.665 to NC)	15.51 (10.218 to 19.844)	12.68 (1.314 to NC)	20.24 (6.407 to NC)	
Median (95% CI)	NC (NC to NC)	NC (21.520 to NC)	NC (NC to NC)	NC (20.698 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.6163		0.8609	
Hazard ratio (95% CI) vs Kd	-	1.13 (0.69 to 1.85)		0.91 (0.33 to 2.52)	
P-value	-	0.6165		0.8609	
Deterioration probability (95% CI)[b]					

A higher score represents a better level of quality of life. Clinical meaningful deterioration change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Physical functioning
16.2.6.1.2.5 Efficacy response data - Subgroup analyses by geographical region
16.2.6.1.2.5.3 QLQ-C30 - Time to first improvement by 10 pt in physical functioning according to geographical region (LOCF) - ITT population

	Europe		America		Asia		Other countries		
	Kd (N=60)	**IKd (N=85)**	**Kd (N=20)**	**IKd (N=24)**	**Kd (N=21)**	**IKd (N=25)**	**Kd (N=22)**	**IKd (N=45)**	**p-value of treatment-by-subgroup interaction[c]**
Number (%) of events	23 (38.3)	40 (47.1)	12 (60.0)	13 (54.2)	8 (38.1)	14 (56.0)	10 (45.5)	17 (37.8)	0.5725
Number (%) of patients censored	37 (61.7)	45 (52.9)	8 (40.0)	11 (45.8)	13 (61.9)	11 (44.0)	12 (54.5)	28 (62.2)	
Kaplan-Meier estimates of event in months									
25% quantile (95% CI)	2.00 (1.117 to 3.811)	2.14 (1.150 to 3.811)	1.10 (0.986 to 2.201)	1.58 (0.953 to 4.764)	1.59 (1.051 to NC)	1.92 (0.953 to 2.004)	2.04 (0.953 to 13.634)	3.71 (1.380 to 16.591)	
Median (95% CI)	NC (3.811 to NC)	NC (4.402 to NC)	2.53 (1.084 to NC)	10.51 (1.971 to NC)	NC (1.150 to NC)	4.81 (1.938 to NC)	NC (2.037 to NC)	NC (8.312 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (2.825 to NC)	NC (10.513 to NC)	NC (NC to NC)	NC (9.265 to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Kd									

A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Physical functioning
16.2.6.1.2.5 Efficacy response data - Subgroup analyses by geographical region
16.2.6.1.2.5.3 QLQ-C30 - Time to first improvement by 10 pt in physical functioning according to geographical region (LOCF) - ITT population

	Europe		America		Asia		Other countries		
	Kd (N=60)	**IKd (N=85)**	**Kd (N=20)**	**IKd (N=24)**	**Kd (N=21)**	**IKd (N=25)**	**Kd (N=22)**	**IKd (N=45)**	**p-value of treatment-by-subgroup interaction[c]**
Log-Rank test p-value[a] vs Kd	-	0.4030		0.6622		0.2842		0.6199	
Hazard ratio (95% CI) vs Kd	-	1.24 (0.74 to 2.08)		0.84 (0.38 to 1.84)		1.60 (0.67 to 3.82)		0.82 (0.38 to 1.79)	
P-value	-	0.4039		0.6626		0.2886		0.6204	
Improvement probability (95% CI)[b]									
3 Months	0.293 (0.183 to 0.412)	0.340 (0.240 to 0.442)	0.550 (0.313 to 0.735)	0.354 (0.169 to 0.546)	0.300 (0.123 to 0.501)	0.417 (0.222 to 0.601)	0.273 (0.111 to 0.464)	0.244 (0.132 to 0.376)	
6 Months	0.383 (0.259 to 0.506)	0.455 (0.344 to 0.559)	0.600 (0.357 to 0.776)	0.447 (0.239 to 0.635)	0.354 (0.158 to 0.557)	0.542 (0.327 to 0.714)	0.273 (0.111 to 0.464)	0.290 (0.167 to 0.426)	

A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Physical functioning
16.2.6.1.2.5 Efficacy response data - Subgroup analyses by geographical region
16.2.6.1.2.5.4 QLQ-C30 - Time to first deterioration by 10 pt in physical functioning according to geographical region (LOCF) - ITT population

	Europe		America		Asia		Other countries		
	Kd (N=60)	**IKd (N=85)**	**Kd (N=20)**	**IKd (N=24)**	**Kd (N=21)**	**IKd (N=25)**	**Kd (N=22)**	**IKd (N=45)**	**p-value of treatment-by-subgroup interaction[c]**
Number (%) of events	27 (45.0)	42 (49.4)	12 (60.0)	8 (33.3)	11 (52.4)	17 (68.0)	15 (68.2)	35 (77.8)	0.1868
Number (%) of patients censored	33 (55.0)	43 (50.6)	8 (40.0)	16 (66.7)	10 (47.6)	8 (32.0)	7 (31.8)	10 (22.2)	
Kaplan-Meier estimates of event in months									
25% quantile (95% CI)	2.83 (1.051 to 6.505)	2.99 (1.873 to 4.665)	1.92 (0.953 to 3.745)	6.51 (1.051 to NC)	2.48 (1.051 to 4.074)	2.45 (0.986 to 2.825)	2.96 (0.986 to 6.374)	1.97 (1.084 to 2.793)	
Median (95% CI)	NC (6.505 to NC)	18.46 (6.834 to NC)	5.19 (1.906 to NC)	NC (6.505 to NC)	7.51 (2.004 to NC)	5.75 (2.760 to 14.226)	7.18 (2.957 to NC)	3.75 (2.793 to 9.363)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (6.571 to NC)	NC (NC to NC)	NC (9.068 to NC)	NC (11.105 to NC)	NC (7.721 to NC)	15.51 (7.951 to NC)	
Comparison vs. Kd									

A higher score represents a better level of quality of life. Clinical meaningful deterioration change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Physical functioning
16.2.6.1.2.5 Efficacy response data - Subgroup analyses by geographical region
16.2.6.1.2.5.4 QLQ-C30 - Time to first deterioration by 10 pt in physical functioning according to geographical region (LOCF) - ITT population

	Europe		America		Asia		Other countries		
	Kd (N=60)	**IKd (N=85)**	**Kd (N=20)**	**IKd (N=24)**	**Kd (N=21)**	**IKd (N=25)**	**Kd (N=22)**	**IKd (N=45)**	**p-value of treatment-by-subgroup interaction[c]**
Log-Rank test p-value[a] vs Kd	-	0.8153		0.0810		0.3924		0.2720	
Hazard ratio (95% CI) vs Kd	-	1.06 (0.65 to 1.72)		0.46 (0.19 to 1.13)		1.39 (0.65 to 2.97)		1.40 (0.76 to 2.57)	
P-value	-	0.8164		0.0887		0.3945		0.2743	
Deterioration probability (95% CI)[b]									
3 Months	0.742 (0.609 to 0.836)	0.746 (0.638 to 0.826)	0.650 (0.403 to 0.815)	0.865 (0.638 to 0.955)	0.700 (0.451 to 0.853)	0.583 (0.364 to 0.750)	0.727 (0.491 to 0.867)	0.578 (0.421 to 0.706)	
6 Months	0.669 (0.531 to 0.775)	0.648 (0.535 to 0.740)	0.500 (0.271 to 0.692)	0.865 (0.638 to 0.955)	0.500 (0.271 to 0.692)	0.500 (0.291 to 0.678)	0.591 (0.361 to 0.762)	0.422 (0.278 to 0.560)	

A higher score represents a better level of quality of life. Clinical meaningful deterioration change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Physical functioning
16.2.6.1.2.5 Efficacy response data - Subgroup analyses by geographical region
16.2.6.1.2.5.5 QLQ-C30 - Time until permanent improvement by 10 pt in physical functioning according to geographical region (LOCF) - ITT population

	Europe		America		Asia		Other countries		
	Kd (N=60)	**IKd (N=85)**	**Kd (N=20)**	**IKd (N=24)**	**Kd (N=21)**	**IKd (N=25)**	**Kd (N=22)**	**IKd (N=45)**	**p-value of treatment-by-subgroup interaction[c]**
Number (%) of events	13 (21.7)	20 (23.5)	4 (20.0)	6 (25.0)	6 (28.6)	7 (28.0)	6 (27.3)	5 (11.1)	0.5194
Number (%) of patients censored	47 (78.3)	65 (76.5)	16 (80.0)	18 (75.0)	15 (71.4)	18 (72.0)	16 (72.7)	40 (88.9)	
Kaplan-Meier estimates of event in months									
25% quantile (95% CI)	21.68 (11.105 to NC)	21.65 (15.179 to 24.444)	NC (0.986 to NC)	16.85 (0.953 to NC)	13.17 (1.051 to NC)	17.05 (2.004 to NC)	22.14 (0.953 to 23.129)	NC (21.421 to NC)	
Median (95% CI)	NC (21.684 to NC)	24.44 (NC to NC)	NC (NC to NC)	NC (16.854 to NC)	NC (13.175 to NC)	NC (17.051 to NC)	23.13 (22.144 to NC)	NC (NC to NC)	

A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Physical functioning
16.2.6.1.2.5 Efficacy response data - Subgroup analyses by geographical region
16.2.6.1.2.5.5 QLQ-C30 - Time until permanent improvement by 10 pt in physical functioning according to geographical region (LOCF) - ITT population

	Europe		America		Asia		Other countries		
	Kd (N=60)	**IKd (N=85)**	**Kd (N=20)**	**IKd (N=24)**	**Kd (N=21)**	**IKd (N=25)**	**Kd (N=22)**	**IKd (N=45)**	**p-value of treatment-by-subgroup interaction[c]**
75% quantile (95% CI)	NC (NC to NC)	24.44 (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (23.129 to NC)	NC (NC to NC)	
Comparison vs. Kd									
Log-Rank test p-value[a] vs Kd	-	0.8931		0.6326		0.8238		0.1525	
Hazard ratio (95% CI) vs Kd	-	0.95 (0.47 to 1.93)		1.36 (0.38 to 4.82)		0.88 (0.30 to 2.63)		0.43 (0.13 to 1.41)	
P-value	-	0.8926		0.6340		0.8239		0.1647	
Improvement probability (95% CI)[b]									

A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Physical functioning
16.2.6.1.2.5 Efficacy response data - Subgroup analyses by geographical region
16.2.6.1.2.5.6 QLQ-C30 - Time until permanent deterioration by 10 pt in physical functioning according to geographical region (LOCF) - ITT population

	Europe		America		Asia		Other countries		
	Kd (N=60)	**IKd (N=85)**	**Kd (N=20)**	**IKd (N=24)**	**Kd (N=21)**	**IKd (N=25)**	**Kd (N=22)**	**IKd (N=45)**	**p-value of treatment-by-subgroup interaction[c]**
Number (%) of events	15 (25.0)	22 (25.9)	7 (35.0)	4 (16.7)	6 (28.6)	7 (28.0)	4 (18.2)	20 (44.4)	0.1591
Number (%) of patients censored	45 (75.0)	63 (74.1)	13 (65.0)	20 (83.3)	15 (71.4)	18 (72.0)	18 (81.8)	25 (55.6)	
Kaplan-Meier estimates of event in months									
25% quantile (95% CI)	18.92 (4.665 to NC)	18.79 (12.649 to NC)	9.36 (2.858 to NC)	19.84 (1.051 to NC)	8.59 (1.051 to NC)	16.85 (1.117 to NC)	NC (2.957 to NC)	10.22 (3.745 to 15.869)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	21.39 (9.363 to NC)	NC (19.844 to NC)	NC (6.637 to NC)	NC (16.854 to NC)	NC (NC to NC)	21.52 (15.671 to NC)	

A higher score represents a better level of quality of life. Clinical meaningful deterioration change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Physical functioning
16.2.6.1.2.5 Efficacy response data - Subgroup analyses by geographical region
16.2.6.1.2.5.6 QLQ-C30 - Time until permanent deterioration by 10 pt in physical functioning according to geographical region (LOCF) - ITT population

	Europe		America		Asia		Other countries		
	Kd (N=60)	**IKd (N=85)**	**Kd (N=20)**	**IKd (N=24)**	**Kd (N=21)**	**IKd (N=25)**	**Kd (N=22)**	**IKd (N=45)**	**p-value of treatment-by-subgroup interaction[c]**
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (21.388 to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Kd									
Log-Rank test p-value[a] vs Kd	-	0.9637		0.3231		0.8439		0.0376	
Hazard ratio (95% CI) vs Kd	-	0.98 (0.51 to 1.90)		0.54 (0.16 to 1.86)		0.90 (0.30 to 2.67)		2.97 (1.01 to 8.71)	
P-value	-	0.9637		0.3305		0.8440		0.0475	
Hazard ratio inverted (95% CI) vs IKd		-		1.85 (0.54 to 6.36)		1.12 (0.37 to 3.32)		0.34 (0.11 to 0.99)	
Deterioration probability (95% CI)[b]									

A higher score represents a better level of quality of life. Clinical meaningful deterioration change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Physical functioning
16.2.6.1.2.6 Efficacy response data - Subgroup analyses by regulatory region
16.2.6.1.2.6.3 QLQ-C30 - Time to first improvement by 10 pt in physical functioning according to regulatory region (LOCF) - ITT population

	Western countries		Other countries		
	Kd (N=55)	**IKd (N=97)**	**Kd (N=68)**	**IKd (N=82)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	24 (43.6)	35 (36.1)	29 (42.6)	49 (59.8)	0.0273
Number (%) of patients censored	31 (56.4)	62 (63.9)	39 (57.4)	33 (40.2)	
Kaplan-Meier estimates of Physical functioning in months					
25% quantile (95% CI)	1.94 (1.051 to 4.632)	2.89 (2.103 to 5.815)	1.91 (1.117 to 2.858)	1.61 (1.051 to 1.971)	
Median (95% CI)	NC (3.811 to NC)	NC (NC to NC)	NC (3.713 to NC)	5.22 (2.924 to 13.569)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (18.661 to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.2394		0.0435	
Hazard ratio (95% CI) vs Kd	-	0.73 (0.44 to 1.23)		1.60 (1.01 to 2.53)	
P-value	-	0.2413		0.0455	
Hazard ratio inverted (95% CI) vs IKd		-		0.63 (0.40 to 0.99)	

A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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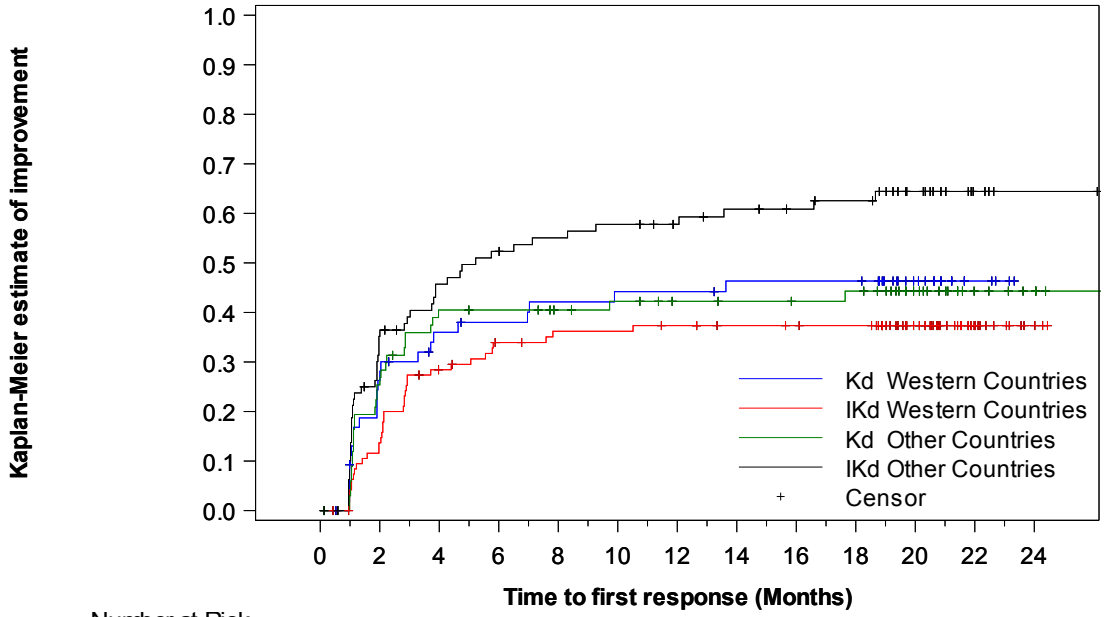
16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Physical functioning
16.2.6.1.2.6 Efficacy response data - Subgroup analyses by regulatory region
16.2.6.1.2.6.4 QLQ-C30 - Time to first improvement by 10 pt in physical functioning according to regulatory region- Kaplan-Meier curve (LOCF) - ITT population



Number at Risk									
Kd Western Countries	55	36	30	28	27	25	25	8	0
IKd Western Countries	97	69	59	56	54	51	49	22	3
Kd Other Countries	68	42	38	34	30	29	27	14	4
IKd Other Countries	82	46	36	32	28	24	21	8	1

A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
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16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Physical functioning
16.2.6.1.2.6 Efficacy response data - Subgroup analyses by regulatory region
16.2.6.1.2.6.5 QLQ-C30 - Time to first deterioration by 10 pt in physical functioning according to regulatory region (LOCF) - ITT population

	Western countries		Other countries		
	Kd (N=55)	**IKd (N=97)**	**Kd (N=68)**	**IKd (N=82)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	20 (36.4)	53 (54.6)	45 (66.2)	49 (59.8)	0.0575
Number (%) of patients censored	35 (63.6)	44 (45.4)	23 (33.8)	33 (40.2)	
Kaplan-Meier estimates of Physical functioning in months					
25% quantile (95% CI)	6.37 (1.216 to 11.236)	2.83 (1.873 to 3.745)	1.91 (1.117 to 2.957)	2.53 (1.610 to 3.745)	
Median (95% CI)	NC (11.236 to NC)	10.87 (6.505 to NC)	5.62 (3.121 to 11.565)	7.95 (4.665 to 16.000)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (14.784 to NC)	NC (NC to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.0682		0.4585	
Hazard ratio (95% CI) vs Kd	-	1.61 (0.96 to 2.69)		0.86 (0.57 to 1.29)	
P-value	-	0.0710		0.4589	
Deterioration probability (95% CI)[b]					

A higher score represents a better level of quality of life. Clinical meaningful deterioration change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Physical functioning
16.2.6.1.2.6 Efficacy response data - Subgroup analyses by regulatory region
16.2.6.1.2.6.6 QLQ-C30 - Time until permanent improvement by 10 pt in physical functioning according to regulatory region (LOCF) - ITT population

	Western countries		Other countries		
	Kd (N=55)	**IKd (N=97)**	**Kd (N=68)**	**IKd (N=82)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	16 (29.1)	14 (14.4)	13 (19.1)	24 (29.3)	0.0115
Number (%) of patients censored	39 (70.9)	83 (85.6)	55 (80.9)	58 (70.7)	
Kaplan-Meier estimates of Physical functioning in months					
25% quantile (95% CI)	18.89 (1.906 to 23.129)	NC (21.651 to NC)	NC (13.175 to NC)	17.05 (9.133 to 24.444)	
Median (95% CI)	23.13 (21.684 to NC)	NC (NC to NC)	NC (NC to NC)	24.44 (21.421 to NC)	
75% quantile (95% CI)	NC (23.129 to NC)	NC (NC to NC)	NC (NC to NC)	NC (24.444 to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.0244		0.1868	
Hazard ratio (95% CI) vs Kd	-	0.45 (0.22 to 0.92)		1.57 (0.80 to 3.09)	
P-value	-	0.0284		0.1906	
Improvement probability (95% CI)[b]					

A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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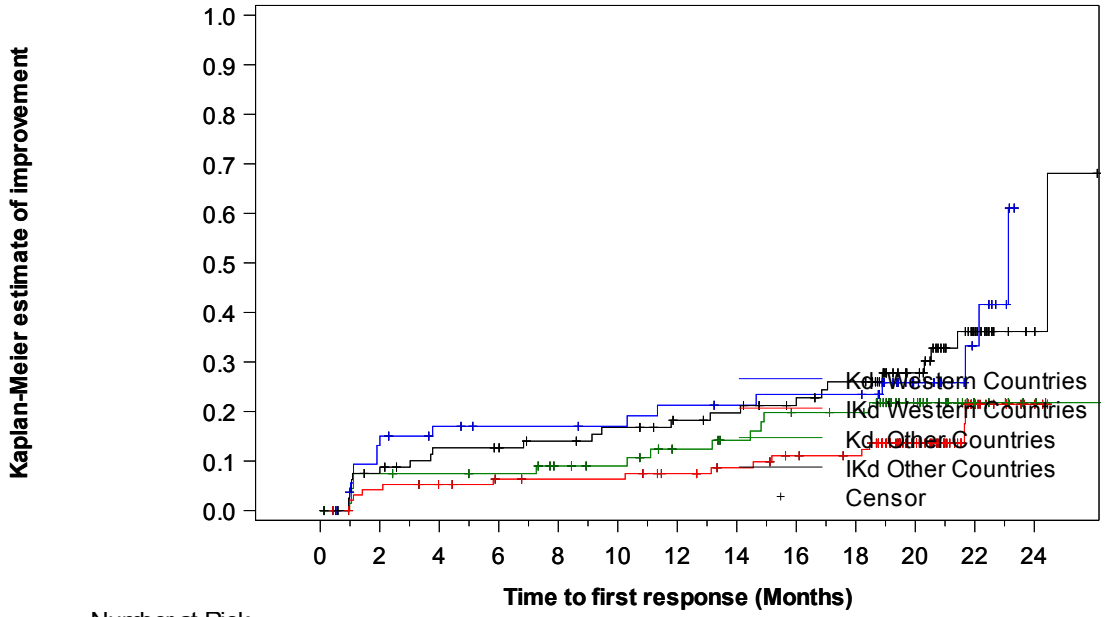
16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Physical functioning
16.2.6.1.2.6 Efficacy response data - Subgroup analyses by regulatory region
16.2.6.1.2.6.7 QLQ-C30 - Time until permanent improvement by 10 pt in physical functioning according to regulatory region- Kaplan-Meier curve (LOCF) - ITT population



Number at Risk									
Kd Western Countries	55	44	40	39	37	35	35	14	0
IKd Western Countries	97	90	85	84	80	75	70	28	3
Kd Other Countries	68	61	60	54	49	43	41	19	4
IKd Other Countries	82	70	66	62	56	51	46	21	3

A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
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16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Physical functioning
16.2.6.1.2.6 Efficacy response data - Subgroup analyses by regulatory region
16.2.6.1.2.6.8 QLQ-C30 - Time until permanent deterioration by 10 pt in physical functioning according to regulatory region (LOCF) - ITT population

	Western countries		Other countries		
	Kd (N=55)	**IKd (N=97)**	**Kd (N=68)**	**IKd (N=82)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	9 (16.4)	28 (28.9)	23 (33.8)	25 (30.5)	0.0909
Number (%) of patients censored	46 (83.6)	69 (71.1)	45 (66.2)	57 (69.5)	
Kaplan-Meier estimates of Physical functioning in months					
25% quantile (95% CI)	NC (12.682 to NC)	18.00 (12.156 to 20.534)	7.43 (3.680 to 21.388)	17.22 (9.922 to 21.520)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (21.388 to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.0856		0.5699	
Hazard ratio (95% CI) vs Kd	-	1.91 (0.90 to 4.06)		0.85 (0.48 to 1.50)	
P-value	-	0.0911		0.5704	
Deterioration probability (95% CI)[b]					

A higher score represents a better level of quality of life. Clinical meaningful deterioration change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Physical functioning
16.2.6.1.2.7 Efficacy response data - Subgroup analyses by baseline ECOG PS
16.2.6.1.2.7.3 QLQ-C30 - Time to first improvement by 10 pt in physical functioning according to baseline ECOG PS (LOCF) - ITT population

	0 or 1		>1		
	Kd (N=118)	**IKd (N=168)**	**Kd (N=5)**	**IKd (N=11)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	49 (41.5)	76 (45.2)	4 (80.0)	8 (72.7)	0.5987
Number (%) of patients censored	69 (58.5)	92 (54.8)	1 (20.0)	3 (27.3)	
Kaplan-Meier estimates of Physical functioning in months					
25% quantile (95% CI)	1.91 (1.150 to 3.285)	2.14 (1.906 to 3.023)	1.94 (1.051 to 3.811)	0.99 (0.986 to 1.971)	
Median (95% CI)	NC (9.725 to NC)	NC (7.819 to NC)	2.83 (1.051 to NC)	1.97 (0.986 to 7.129)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	3.81 (1.051 to NC)	3.88 (1.018 to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.7700		0.6516	
Hazard ratio (95% CI) vs Kd	-	1.05 (0.74 to 1.51)		1.32 (0.39 to 4.44)	
P-value	-	0.7712		0.6526	
Improvement probability (95% CI)[b]					

A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Physical functioning
16.2.6.1.2.7 Efficacy response data - Subgroup analyses by baseline ECOG PS
16.2.6.1.2.7.4 QLQ-C30 - Time to first deterioration by 10 pt in physical functioning according to baseline ECOG PS (LOCF) - ITT population

	0 or 1		>1		
	Kd (N=118)	**IKd (N=168)**	**Kd (N=5)**	**IKd (N=11)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	63 (53.4)	98 (58.3)	2 (40.0)	4 (36.4)	0.7371
Number (%) of patients censored	55 (46.6)	70 (41.7)	3 (60.0)	7 (63.6)	
Kaplan-Meier estimates of Physical functioning in months					
25% quantile (95% CI)	2.83 (1.281 to 3.811)	2.79 (1.906 to 3.088)	2.07 (0.986 to NC)	4.96 (1.610 to NC)	
Median (95% CI)	11.24 (6.374 to NC)	9.40 (6.505 to 15.507)	NC (0.986 to NC)	NC (1.610 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (0.986 to NC)	NC (18.464 to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.5627		0.9023	
Hazard ratio (95% CI) vs Kd	-	1.10 (0.80 to 1.51)		0.90 (0.16 to 4.97)	
P-value	-	0.5628		0.9023	
Deterioration probability (95% CI)[b]					

A higher score represents a better level of quality of life. Clinical meaningful deterioration change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Physical functioning
16.2.6.1.2.7 Efficacy response data - Subgroup analyses by baseline ECOG PS
16.2.6.1.2.7.5 QLQ-C30 - Time until permanent improvement by 10 pt in physical functioning according to baseline ECOG PS (LOCF) - ITT population

	0 or 1		>1		
	Kd (N=118)	**IKd (N=168)**	**Kd (N=5)**	**IKd (N=11)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	27 (22.9)	34 (20.2)	2 (40.0)	4 (36.4)	0.9695
Number (%) of patients censored	91 (77.1)	134 (79.8)	3 (60.0)	7 (63.6)	
Kaplan-Meier estimates of Physical functioning in months					
25% quantile (95% CI)	21.68 (13.175 to NC)	21.68 (18.464 to NC)	14.65 (3.778 to NC)	14.55 (0.986 to NC)	
Median (95% CI)	NC (23.129 to NC)	24.44 (24.444 to NC)	14.65 (3.778 to NC)	NC (0.986 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (24.444 to NC)	NC (3.778 to NC)	NC (20.534 to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.4793		0.8775	
Hazard ratio (95% CI) vs Kd	-	0.83 (0.50 to 1.38)		0.87 (0.16 to 4.90)	
P-value	-	0.4799		0.8775	
Improvement probability (95% CI)[b]					

A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Physical functioning
16.2.6.1.2.7 Efficacy response data - Subgroup analyses by baseline ECOG PS
16.2.6.1.2.7.6 QLQ-C30 - Time until permanent deterioration by 10 pt in physical functioning according to baseline ECOG PS (LOCF) - ITT population

	0 or 1		>1		
	Kd (N=118)	**IKd (N=168)**	**Kd (N=5)**	**IKd (N=11)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	31 (26.3)	51 (30.4)	1 (20.0)	2 (18.2)	0.8322
Number (%) of patients censored	87 (73.7)	117 (69.6)	4 (80.0)	9 (81.8)	
Kaplan-Meier estimates of Physical functioning in months					
25% quantile (95% CI)	18.92 (7.425 to NC)	16.85 (12.649 to 20.304)	NC (3.778 to NC)	17.22 (4.961 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (3.778 to NC)	NC (4.961 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (3.778 to NC)	NC (NC to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.5248		0.9146	
Hazard ratio (95% CI) vs Kd	-	1.16 (0.74 to 1.81)		0.88 (0.08 to 9.78)	
P-value	-	0.5251		0.9146	
Deterioration probability (95% CI)[b]					

A higher score represents a better level of quality of life. Clinical meaningful deterioration change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Physical functioning
16.2.6.1.2.8 Efficacy response data - Subgroup analyses by ISS staging at SE
16.2.6.1.2.8.3 QLQ-C30 - Time to first improvement by 10 pt in physical functioning according to ISS staging at SE (LOCF) - ITT population

	I		II		III		
	Kd (N=71)	**IKd (N=89)**	**Kd (N=31)**	**IKd (N=63)**	**Kd (N=20)**	**IKd (N=26)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	28 (39.4)	36 (40.4)	15 (48.4)	31 (49.2)	9 (45.0)	16 (61.5)	0.2648
Number (%) of patients censored	43 (60.6)	53 (59.6)	16 (51.6)	32 (50.8)	11 (55.0)	10 (38.5)	
Kaplan-Meier estimates of Physical functioning in months							
25% quantile (95% CI)	2.04 (1.117 to 4.632)	2.83 (1.840 to 5.815)	1.91 (1.117 to 3.975)	2.83 (1.906 to 4.698)	1.91 (0.953 to 3.778)	1.05 (0.953 to 1.413)	
Median (95% CI)	NC (9.725 to NC)	NC (16.591 to NC)	13.63 (2.234 to NC)	12.06 (4.698 to NC)	17.64 (1.906 to NC)	2.10 (1.051 to 3.877)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (17.643 to NC)	NC (2.103 to NC)	
Comparison vs. Kd							
Log-Rank test p-value[a] vs Kd	-	0.9564		0.8393		0.1118	
Hazard ratio (95% CI) vs Kd	-	0.99 (0.60 to 1.62)		0.94 (0.51 to 1.74)		1.93 (0.85 to 4.38)	
P-value	-	0.9564		0.8393		0.1181	

A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Physical functioning
16.2.6.1.2.8 Efficacy response data - Subgroup analyses by ISS staging at SE
16.2.6.1.2.8.4 QLQ-C30 - Time to first deterioration by 10 pt in physical functioning according to ISS staging at SE (LOCF) - ITT population

	I		II		III		
	Kd (N=71)	**IKd (N=89)**	**Kd (N=31)**	**IKd (N=63)**	**Kd (N=20)**	**IKd (N=26)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	36 (50.7)	54 (60.7)	18 (58.1)	41 (65.1)	10 (50.0)	7 (26.9)	0.1272
Number (%) of patients censored	35 (49.3)	35 (39.3)	13 (41.9)	22 (34.9)	10 (50.0)	19 (73.1)	
Kaplan-Meier estimates of Physical functioning in months							
25% quantile (95% CI)	3.75 (1.938 to 5.618)	2.83 (2.004 to 3.713)	1.25 (0.986 to 2.825)	1.87 (1.051 to 3.351)	2.00 (0.953 to 3.811)	6.57 (1.084 to NC)	
Median (95% CI)	15.93 (6.472 to NC)	9.26 (4.665 to 18.464)	8.51 (1.314 to NC)	8.18 (3.713 to 15.507)	6.57 (2.004 to NC)	NC (6.571 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (11.565 to NC)	NC (16.000 to NC)	NC (6.571 to NC)	NC (NC to NC)	
Comparison vs. Kd							
Log-Rank test p-value[a] vs Kd	-	0.2226		0.8610		0.0918	
Hazard ratio (95% CI) vs Kd	-	1.30 (0.85 to 1.98)		1.05 (0.60 to 1.83)		0.44 (0.17 to 1.17)	
P-value	-	0.2239		0.8611		0.1007	

A higher score represents a better level of quality of life. Clinical meaningful deterioration change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Physical functioning
16.2.6.1.2.8 Efficacy response data - Subgroup analyses by ISS staging at SE
16.2.6.1.2.8.5 QLQ-C30 - Time until permanent improvement by 10 pt in physical functioning according to ISS staging at SE (LOCF) - ITT population

	I		II		III		
	Kd (N=71)	**IKd (N=89)**	**Kd (N=31)**	**IKd (N=63)**	**Kd (N=20)**	**IKd (N=26)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	15 (21.1)	18 (20.2)	11 (35.5)	10 (15.9)	3 (15.0)	10 (38.5)	0.0159
Number (%) of patients censored	56 (78.9)	71 (79.8)	20 (64.5)	53 (84.1)	17 (85.0)	16 (61.5)	
Kaplan-Meier estimates of Physical functioning in months							
25% quantile (95% CI)	23.13 (10.316 to NC)	24.44 (17.051 to NC)	14.46 (1.906 to 22.144)	NC (20.304 to NC)	NC (0.953 to NC)	2.10 (0.953 to 14.554)	
Median (95% CI)	NC (23.129 to NC)	NC (24.444 to NC)	22.14 (14.456 to NC)	NC (NC to NC)	NC (NC to NC)	NC (3.778 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (24.444 to NC)	NC (22.144 to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Kd							
Log-Rank test p-value[a] vs Kd	-	0.8253		0.0088		0.0745	
Hazard ratio (95% CI) vs Kd	-	0.93 (0.47 to 1.84)		0.33 (0.14 to 0.79)		3.06 (0.84 to 11.15)	
P-value	-	0.8246		0.0125		0.0900	

A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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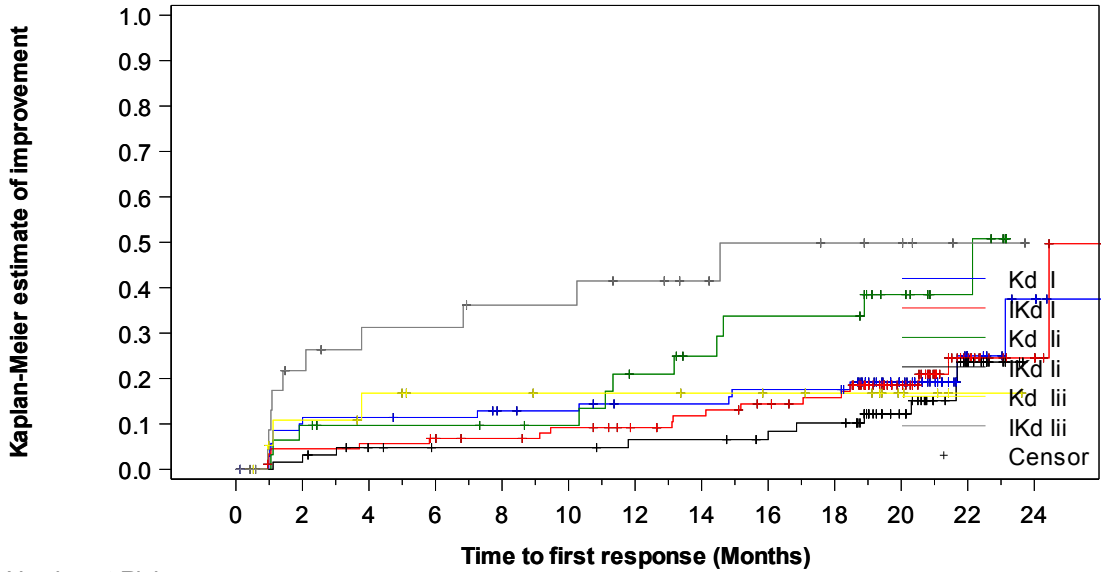
16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Physical functioning
16.2.6.1.2.8 Efficacy response data - Subgroup analyses by ISS staging at SE
16.2.6.1.2.8.6 QLQ-C30 - Time until permanent improvement by 10 pt in physical functioning according to ISS staging at SE- Kaplan-Meier curve (LOCF) - ITT population



Number at Risk

Kd I	71	62	61	57	54	52	52	24	4
IKd I	89	84	81	78	72	67	61	25	6
Kd Ii	31	26	26	24	20	15	15	5	0
IKd Ii	63	60	55	55	53	52	49	21	0
Kd Iii	20	16	12	11	11	10	8	3	0
IKd Iii	26	15	14	12	10	6	5	2	0

A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
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16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Physical functioning
16.2.6.1.2.8 Efficacy response data - Subgroup analyses by ISS staging at SE
16.2.6.1.2.8.7 QLQ-C30 - Time until permanent deterioration by 10 pt in physical functioning according to ISS staging at SE (LOCF) - ITT population

	I		II		III		
	Kd (N=71)	**IKd (N=89)**	**Kd (N=31)**	**IKd (N=63)**	**Kd (N=20)**	**IKd (N=26)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	17 (23.9)	28 (31.5)	9 (29.0)	22 (34.9)	6 (30.0)	3 (11.5)	0.2203
Number (%) of patients censored	54 (76.1)	61 (68.5)	22 (71.0)	41 (65.1)	14 (70.0)	23 (88.5)	
Kaplan-Meier estimates of Physical functioning in months							
25% quantile (95% CI)	21.39 (8.444 to NC)	16.85 (9.922 to 20.698)	8.74 (1.248 to NC)	15.51 (5.815 to 20.304)	6.64 (1.051 to NC)	NC (3.745 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (20.304 to NC)	NC (5.815 to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Kd							
Log-Rank test p-value[a] vs Kd	-	0.2818		0.7366		0.0989	
Hazard ratio (95% CI) vs Kd	-	1.39 (0.76 to 2.54)		1.14 (0.53 to 2.48)		0.33 (0.08 to 1.32)	
P-value	-	0.2840		0.7368		0.1165	

A higher score represents a better level of quality of life. Clinical meaningful deterioration change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Physical functioning
16.2.6.1.2.9 Efficacy response data - Subgroup analyses by R-ISS stage at SE
16.2.6.1.2.9.3 QLQ-C30 - Time to first improvement by 10 pt in physical functioning according to R-ISS stage at SE (LOCF) - ITT population

	I or II		III		Not classified		
	Kd (N=103)	**IKd (N=155)**	**Kd (N=8)**	**IKd (N=16)**	**Kd (N=12)**	**IKd (N=8)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	42 (40.8)	69 (44.5)	4 (50.0)	11 (68.8)	7 (58.3)	4 (50.0)	0.3733
Number (%) of patients censored	61 (59.2)	86 (55.5)	4 (50.0)	5 (31.3)	5 (41.7)	4 (50.0)	
Kaplan-Meier estimates of Physical functioning in months							
25% quantile (95% CI)	2.00 (1.117 to 2.858)	2.83 (1.971 to 3.877)	1.12 (1.051 to 17.643)	1.02 (0.953 to 1.971)	2.81 (1.084 to 4.632)	1.02 (0.986 to 5.060)	
Median (95% CI)	NC (7.031 to NC)	NC (9.265 to NC)	17.64 (1.051 to NC)	1.97 (0.986 to 2.924)	7.18 (1.150 to NC)	3.07 (0.986 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (1.906 to NC)	2.92 (1.971 to NC)	NC (4.632 to NC)	NC (1.018 to NC)	
Comparison vs. Kd							
Log-Rank test p-value[a] vs Kd	-	0.9341		0.1900		0.4759	
Hazard ratio (95% CI) vs Kd	-	1.02 (0.69 to 1.49)		2.15 (0.67 to 6.95)		1.56 (0.45 to 5.36)	
P-value	-	0.9342		0.1995		0.4792	

A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Physical functioning
16.2.6.1.2.9 Efficacy response data - Subgroup analyses by R-ISS stage at SE
16.2.6.1.2.9.4 QLQ-C30 - Time to first deterioration by 10 pt in physical functioning according to R-ISS stage at SE (LOCF) - ITT population

	I or II		III		Not classified		
	Kd (N=103)	**IKd (N=155)**	**Kd (N=8)**	**IKd (N=16)**	**Kd (N=12)**	**IKd (N=8)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	52 (50.5)	98 (63.2)	5 (62.5)	2 (12.5)	8 (66.7)	2 (25.0)	0.0018
Number (%) of patients censored	51 (49.5)	57 (36.8)	3 (37.5)	14 (87.5)	4 (33.3)	6 (75.0)	
Kaplan-Meier estimates of Physical functioning in months							
25% quantile (95% CI)	2.86 (1.281 to 4.830)	2.53 (1.873 to 2.891)	1.02 (0.953 to 2.004)	NC (1.084 to NC)	3.75 (1.873 to 4.074)	18.46 (3.745 to NC)	
Median (95% CI)	14.78 (6.505 to NC)	6.90 (4.665 to 13.207)	1.12 (0.953 to NC)	NC (9.363 to NC)	5.90 (3.713 to NC)	NC (3.745 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (1.051 to NC)	NC (NC to NC)	NC (4.074 to NC)	NC (18.464 to NC)	
Comparison vs. Kd							
Log-Rank test p-value[a] vs Kd	-	0.1123		0.0032		0.1921	
Hazard ratio (95% CI) vs Kd	-	1.31 (0.94 to 1.84)		0.11 (0.02 to 0.62)		0.37 (0.08 to 1.75)	
P-value	-	0.1135		0.0121		0.2101	

A higher score represents a better level of quality of life. Clinical meaningful deterioration change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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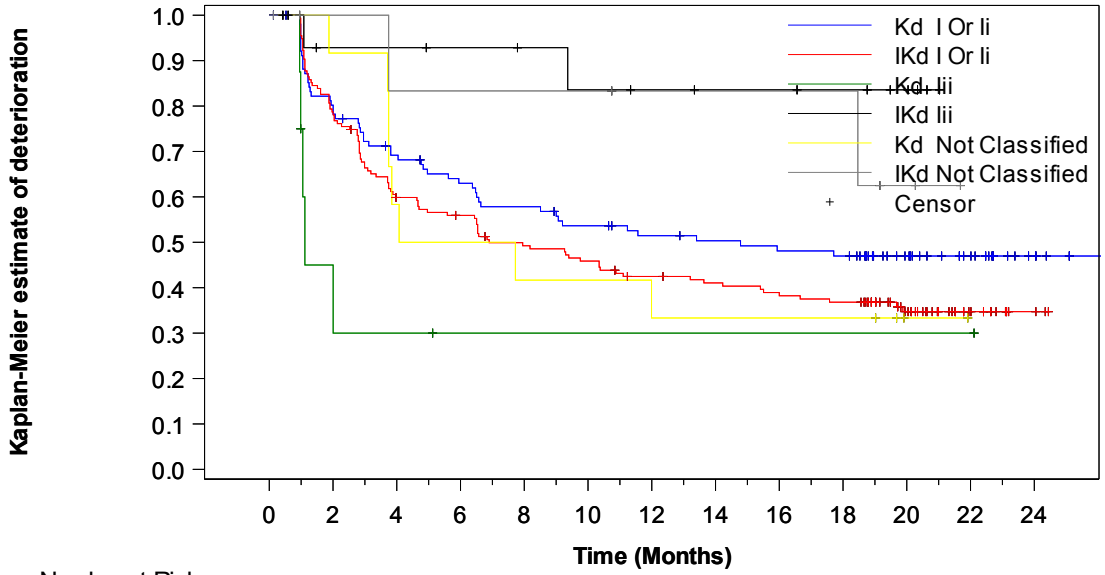
16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Physical functioning
16.2.6.1.2.9 Efficacy response data - Subgroup analyses by R-ISS stage at SE
16.2.6.1.2.9.5 QLQ-C30 - Time to first deterioration by 10 pt in physical functioning according to R-ISS stage at SE- Kaplan-Meier curve (LOCF) - ITT population



Number at Risk									
Kd I Or Ii	103	72	61	54	47	44	42	22	6
IKd I Or Ii	155	102	84	72	61	57	52	20	3
Kd Iii	8	2	1	1	1	1	1	1	0
IKd Iii	16	12	11	10	8	7	6	1	0
Kd Not Classified	12	11	6	5	4	4	4	1	0
IKd Not Classified	8	6	5	5	4	4	4	1	0

A higher score represents a better level of quality of life. Clinical meaningful deterioration change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
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16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Physical functioning
16.2.6.1.2.9 Efficacy response data - Subgroup analyses by R-ISS stage at SE
16.2.6.1.2.9.6 QLQ-C30 - Time until permanent improvement by 10 pt in physical functioning according to R-ISS stage at SE (LOCF) - ITT population

	I or II		III		Not classified		
	Kd (N=103)	**IKd (N=155)**	**Kd (N=8)**	**IKd (N=16)**	**Kd (N=12)**	**IKd (N=8)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	27 (26.2)	29 (18.7)	1 (12.5)	7 (43.8)	1 (8.3)	2 (25.0)	0.0392
Number (%) of patients censored	76 (73.8)	126 (81.3)	7 (87.5)	9 (56.3)	11 (91.7)	6 (75.0)	
Kaplan-Meier estimates of Physical functioning in months							
25% quantile (95% CI)	18.89 (10.316 to 23.129)	24.44 (20.304 to NC)	NC (1.117 to NC)	1.41 (0.953 to 14.554)	NC (18.464 to NC)	16.82 (13.109 to NC)	
Median (95% CI)	NC (22.144 to NC)	NC (24.444 to NC)	NC (1.117 to NC)	14.55 (1.084 to NC)	NC (NC to NC)	20.53 (13.109 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (24.444 to NC)	NC (NC to NC)	NC (14.554 to NC)	NC (NC to NC)	NC (13.109 to NC)	
Comparison vs. Kd							
Log-Rank test p-value[a] vs Kd	-	0.0689		0.1133		0.0657	
Hazard ratio (95% CI) vs Kd	-	0.62 (0.36 to 1.04)		4.67 (0.57 to 38.16)		6.97 (0.63 to 77.13)	
P-value	-	0.0716		0.1501		0.1135	

A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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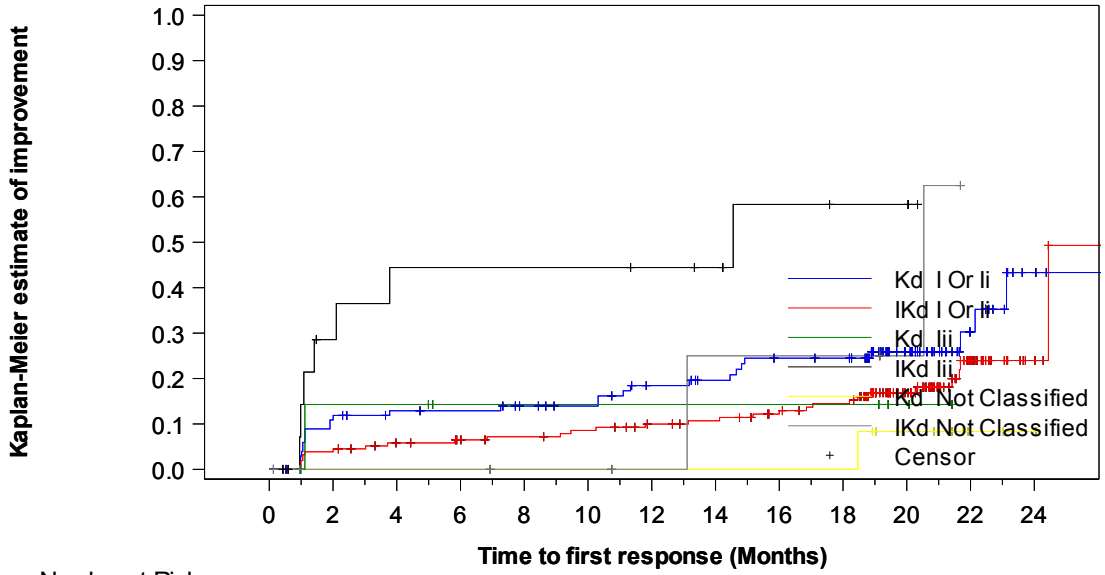
16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Physical functioning
16.2.6.1.2.9 Efficacy response data - Subgroup analyses by R-ISS stage at SE
16.2.6.1.2.9.7 QLQ-C30 - Time until permanent improvement by 10 pt in physical functioning according to R-ISS stage at SE- Kaplan-Meier curve (LOCF) - ITT population



Number at Risk									
Kd I Or Ii	103	87	84	77	70	62	60	26	3
IKd I Or Ii	155	146	138	134	126	120	111	48	6
Kd Iii	8	6	4	4	4	4	4	1	0
IKd Iii	16	8	7	7	6	3	2	0	0
Kd Not Classified	12	12	12	12	12	12	12	6	1
IKd Not Classified	8	6	6	5	4	3	3	1	0

A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
PGM=DEVOPS/SAR650984/EFC15246/CIR_RWE/REPORT/PGM/eff_qlq_km_subgp_de_i_f.sas OUT=REPORT/OUTPUT/eff_km_c30_phy_imppl_seriss_de_i_f_x.rtf (07APR2021 15:13)

16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Physical functioning
16.2.6.1.2.9 Efficacy response data - Subgroup analyses by R-ISS stage at SE
16.2.6.1.2.9.8 QLQ-C30 - Time until permanent deterioration by 10 pt in physical functioning according to R-ISS stage at SE (LOCF) - ITT population

	I or II		III		Not classified		
	Kd (N=103)	**IKd (N=155)**	**Kd (N=8)**	**IKd (N=16)**	**Kd (N=12)**	**IKd (N=8)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	27 (26.2)	52 (33.5)	3 (37.5)	0 (0.0)	2 (16.7)	1 (12.5)	0.9983
Number (%) of patients censored	76 (73.8)	103 (66.5)	5 (62.5)	16 (100.0)	10 (83.3)	7 (87.5)	
Kaplan-Meier estimates of Physical functioning in months							
25% quantile (95% CI)	18.92 (6.374 to NC)	15.70 (12.025 to 19.877)	5.82 (1.051 to NC)	NC (NC to NC)	NC (12.025 to NC)	NC (3.745 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (1.051 to NC)	NC (NC to NC)	NC (15.080 to NC)	NC (3.745 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (5.815 to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Kd							
Log-Rank test p-value[a] vs Kd	-	0.3524		0.0069		0.8471	
Hazard ratio (95% CI) vs Kd	-	1.25 (0.78 to 1.98)				1.27 (0.11 to 14.09)	
P-value	-	0.3533		0.9976		0.8474	

A higher score represents a better level of quality of life. Clinical meaningful deterioration change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
PGM=DEVOPS/SAR650984/EFC15246/CIR_RWE/REPORT/PGM/eff_km_subgp_sr_sig_de_i_t.sas OUT=REPORT/OUTPUT/eff_km_c30_phy_detpl_seriss_de_i_t_x.rtf (07APR2021 14:22)

16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Physical functioning
16.2.6.1.2.10 Efficacy response data - Subgroup analyses by nb of prior lines
16.2.6.1.2.10.3 QLQ-C30 - Time to first improvement by 10 pt in physical functioning according to nb of prior lines (LOCF) - ITT population

	1		>1		
	Kd (N=55)	**IKd (N=79)**	**Kd (N=68)**	**IKd (N=100)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	18 (32.7)	33 (41.8)	35 (51.5)	51 (51.0)	0.3228
Number (%) of patients censored	37 (67.3)	46 (58.2)	33 (48.5)	49 (49.0)	
Kaplan-Meier estimates of Physical functioning in months					
25% quantile (95% CI)	3.29 (1.117 to NC)	2.83 (1.216 to 5.749)	1.84 (1.084 to 2.234)	1.97 (1.150 to 2.858)	
Median (95% CI)	NC (NC to NC)	NC (7.819 to NC)	9.72 (2.825 to NC)	8.31 (3.023 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.3213		0.7405	
Hazard ratio (95% CI) vs Kd	-	1.34 (0.75 to 2.37)		0.93 (0.60 to 1.43)	
P-value	-	0.3230		0.7405	
Improvement probability (95% CI)[b]					

A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
PGM=DEVOPS/SAR650984/EFC15246/CIR_RWE/REPORT/PGM/eff_km_subgp_sr_sig_de_i_t.sas OUT=REPORT/OUTPUT/eff_km_c30_phy_impl_plne_de_i_t_x.rtf (07APR2021 14:22)

16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Physical functioning
16.2.6.1.2.10 Efficacy response data - Subgroup analyses by nb of prior lines
16.2.6.1.2.10.4 QLQ-C30 - Time to first deterioration by 10 pt in physical functioning according to nb of prior lines (LOCF) - ITT population

	1		>1		
	Kd (N=55)	**IKd (N=79)**	**Kd (N=68)**	**IKd (N=100)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	31 (56.4)	43 (54.4)	34 (50.0)	59 (59.0)	0.5020
Number (%) of patients censored	24 (43.6)	36 (45.6)	34 (50.0)	41 (41.0)	
Kaplan-Meier estimates of Physical functioning in months					
25% quantile (95% CI)	2.96 (1.117 to 4.074)	2.76 (1.216 to 3.745)	2.00 (1.117 to 5.947)	2.83 (1.873 to 3.745)	
Median (95% CI)	9.10 (4.074 to NC)	15.41 (4.665 to NC)	11.99 (6.374 to NC)	8.18 (4.698 to 14.226)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.8773		0.4216	
Hazard ratio (95% CI) vs Kd	-	0.96 (0.61 to 1.53)		1.19 (0.78 to 1.81)	
P-value	-	0.8769		0.4222	
Deterioration probability (95% CI)[b]					

A higher score represents a better level of quality of life. Clinical meaningful deterioration change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Physical functioning
16.2.6.1.2.10 Efficacy response data - Subgroup analyses by nb of prior lines
16.2.6.1.2.10.5 QLQ-C30 - Time until permanent improvement by 10 pt in physical functioning according to nb of prior lines (LOCF) - ITT population

	1		>1		
	Kd (N=55)	**IKd (N=79)**	**Kd (N=68)**	**IKd (N=100)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	13 (23.6)	18 (22.8)	16 (23.5)	20 (20.0)	0.7755
Number (%) of patients censored	42 (76.4)	61 (77.2)	52 (76.5)	80 (80.0)	
Kaplan-Meier estimates of Physical functioning in months					
25% quantile (95% CI)	22.14 (7.261 to NC)	24.44 (14.554 to NC)	18.89 (10.316 to NC)	21.65 (16.854 to NC)	
Median (95% CI)	NC (22.144 to NC)	24.44 (24.444 to NC)	NC (21.684 to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (23.129 to NC)	NC (24.444 to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.7488		0.4542	
Hazard ratio (95% CI) vs Kd	-	0.89 (0.43 to 1.83)		0.78 (0.40 to 1.50)	
P-value	-	0.7489		0.4553	
Improvement probability (95% CI)[b]					

A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
PGM=DEVOPS/SAR650984/EFC15246/CIR_RWE/REPORT/PGM/eff_km_subgp_sr_sig_de_i_t.sas OUT=REPORT/OUTPUT/eff_km_c30_phy_imppl_plne_de_i_t_x.rtf (07APR2021 14:22)

16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Physical functioning
16.2.6.1.2.10 Efficacy response data - Subgroup analyses by nb of prior lines
16.2.6.1.2.10.6 QLQ-C30 - Time until permanent deterioration by 10 pt in physical functioning according to nb of prior lines (LOCF) - ITT population

	1		>1		
	Kd (N=55)	**IKd (N=79)**	**Kd (N=68)**	**IKd (N=100)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	14 (25.5)	22 (27.8)	18 (26.5)	31 (31.0)	0.9790
Number (%) of patients censored	41 (74.5)	57 (72.2)	50 (73.5)	69 (69.0)	
Kaplan-Meier estimates of Physical functioning in months					
25% quantile (95% CI)	21.39 (5.717 to NC)	18.00 (9.922 to NC)	15.08 (4.665 to NC)	15.67 (11.072 to 20.304)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (20.698 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.6914		0.6760	
Hazard ratio (95% CI) vs Kd	-	1.15 (0.59 to 2.24)		1.13 (0.63 to 2.02)	
P-value	-	0.6916		0.6762	
Deterioration probability (95% CI)[b]					

A higher score represents a better level of quality of life. Clinical meaningful deterioration change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
PGM=DEVOPS/SAR650984/EFC15246/CIR_RWE/REPORT/PGM/eff_km_subgp_sr_sig_de_i_t.sas OUT=REPORT/OUTPUT/eff_km_c30_phy_detpl_plne_de_i_t_x.rtf (07APR2021 14:22)

16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Physical functioning
16.2.6.1.2.11 Efficacy response data - Subgroup analyses by cytogenetic abnormality
16.2.6.1.2.11.3 QLQ-C30 - Time to first improvement by 10 pt in physical functioning according to cytogenetic abnormality (LOCF) - ITT population

	At least one		None		
	Kd (N=31)	**IKd (N=42)**	**Kd (N=77)**	**IKd (N=114)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	11 (35.5)	23 (54.8)	34 (44.2)	53 (46.5)	0.2799
Number (%) of patients censored	20 (64.5)	19 (45.2)	43 (55.8)	61 (53.5)	
Kaplan-Meier estimates of Physical functioning in months					
25% quantile (95% CI)	1.91 (1.051 to NC)	1.97 (1.084 to 2.858)	1.94 (1.117 to 2.825)	2.14 (1.216 to 3.713)	
Median (95% CI)	NC (3.811 to NC)	7.82 (2.103 to NC)	NC (3.778 to NC)	NC (5.782 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.2022		0.9400	
Hazard ratio (95% CI) vs Kd	-	1.59 (0.77 to 3.27)		1.02 (0.66 to 1.56)	
P-value	-	0.2062		0.9401	
Improvement probability (95% CI)[b]					

A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
PGM=DEVOPS/SAR650984/EFC15246/CIR_RWE/REPORT/PGM/eff_km_subgp_sr_sig_de_i_t.sas OUT=REPORT/OUTPUT/eff_km_c30_phy_impl_cyto_de_i_t_x.rtf (07APR2021 14:22)

16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Physical functioning
16.2.6.1.2.11 Efficacy response data - Subgroup analyses by cytogenetic abnormality
16.2.6.1.2.11.4 QLQ-C30 - Time to first deterioration by 10 pt in physical functioning according to cytogenetic abnormality (LOCF) - ITT population

	At least one		None		
	Kd (N=31)	**IKd (N=42)**	**Kd (N=77)**	**IKd (N=114)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	17 (54.8)	26 (61.9)	40 (51.9)	65 (57.0)	0.8150
Number (%) of patients censored	14 (45.2)	16 (38.1)	37 (48.1)	49 (43.0)	
Kaplan-Meier estimates of Physical functioning in months					
25% quantile (95% CI)	1.94 (0.986 to 4.830)	2.79 (1.084 to 4.632)	2.83 (1.216 to 4.041)	2.53 (1.610 to 3.187)	
Median (95% CI)	6.51 (2.070 to NC)	10.35 (3.713 to 19.680)	13.40 (6.472 to NC)	8.18 (5.585 to 19.877)	
75% quantile (95% CI)	NC (11.565 to NC)	NC (15.409 to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.9051		0.5506	
Hazard ratio (95% CI) vs Kd	-	1.04 (0.56 to 1.91)		1.13 (0.76 to 1.67)	
P-value	-	0.9054		0.5509	
Deterioration probability (95% CI)[b]					

A higher score represents a better level of quality of life. Clinical meaningful deterioration change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
PGM=DEVOPS/SAR650984/EFC15246/CIR_RWE/REPORT/PGM/eff_km_subgp_sr_sig_de_i_t.sas OUT=REPORT/OUTPUT/eff_km_c30_phy_detl_cyto_de_i_t_x.rtf (07APR2021 14:22)

16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Physical functioning
16.2.6.1.2.11 Efficacy response data - Subgroup analyses by cytogenetic abnormality
16.2.6.1.2.11.5 QLQ-C30 - Time until permanent improvement by 10 pt in physical functioning according to cytogenetic abnormality (LOCF) - ITT population

	At least one		None		
	Kd (N=31)	**IKd (N=42)**	**Kd (N=77)**	**IKd (N=114)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	7 (22.6)	9 (21.4)	19 (24.7)	25 (21.9)	0.9391
Number (%) of patients censored	24 (77.4)	33 (78.6)	58 (75.3)	89 (78.1)	
Kaplan-Meier estimates of Physical functioning in months					
25% quantile (95% CI)	21.68 (1.906 to NC)	NC (1.413 to NC)	22.14 (10.316 to NC)	21.65 (16.854 to NC)	
Median (95% CI)	NC (21.684 to NC)	NC (NC to NC)	NC (22.144 to NC)	24.44 (24.444 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (24.444 to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.8119		0.5390	
Hazard ratio (95% CI) vs Kd	-	0.89 (0.33 to 2.39)		0.83 (0.46 to 1.51)	
P-value	-	0.8120		0.5395	
Improvement probability (95% CI)[b]					

A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
PGM=DEVOPS/SAR650984/EFC15246/CIR_RWE/REPORT/PGM/eff_km_subgp_sr_sig_de_i_t.sas OUT=REPORT/OUTPUT/eff_km_c30_phy_imppl_cyto_de_i_t_x.rtf (07APR2021 14:22)

16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Physical functioning
16.2.6.1.2.11 Efficacy response data - Subgroup analyses by cytogenetic abnormality
16.2.6.1.2.11.6 QLQ-C30 - Time until permanent deterioration by 10 pt in physical functioning according to cytogenetic abnormality (LOCF) - ITT population

	At least one		None		
	Kd (N=31)	**IKd (N=42)**	**Kd (N=77)**	**IKd (N=114)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	8 (25.8)	14 (33.3)	21 (27.3)	34 (29.8)	0.6493
Number (%) of patients censored	23 (74.2)	28 (66.7)	56 (72.7)	80 (70.2)	
Kaplan-Meier estimates of Physical functioning in months					
25% quantile (95% CI)	18.92 (3.680 to NC)	15.51 (4.665 to NC)	12.68 (4.665 to NC)	18.46 (12.156 to 20.534)	
Median (95% CI)	NC (NC to NC)	NC (15.869 to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.5357		0.8410	
Hazard ratio (95% CI) vs Kd	-	1.32 (0.55 to 3.14)		1.06 (0.61 to 1.82)	
P-value	-	0.5370		0.8419	
Deterioration probability (95% CI)[b]					

A higher score represents a better level of quality of life. Clinical meaningful deterioration change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
PGM=DEVOPS/SAR650984/EFC15246/CIR_RWE/REPORT/PGM/eff_km_subgp_sr_sig_de_i_t.sas OUT=REPORT/OUTPUT/eff_km_c30_phy_detpl_cyto_de_i_t_x.rtf (07APR2021 14:22)

16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Physical functioning
16.2.6.1.2.12 Efficacy response data - Subgroup analyses by MM type at SE
16.2.6.1.2.12.3 QLQ-C30 - Time to first improvement by 10 pt in physical functioning according to MM type at SE (LOCF) - ITT population

	IgG		Non-IgG		
	Kd (N=85)	**IKd (N=126)**	**Kd (N=38)**	**IKd (N=53)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	35 (41.2)	60 (47.6)	18 (47.4)	24 (45.3)	0.3773
Number (%) of patients censored	50 (58.8)	66 (52.4)	20 (52.6)	29 (54.7)	
Kaplan-Meier estimates of Physical functioning in months					
25% quantile (95% CI)	1.91 (1.117 to 2.858)	1.97 (1.150 to 2.891)	2.41 (1.051 to 3.975)	2.83 (1.216 to 5.552)	
Median (95% CI)	NC (7.031 to NC)	13.57 (4.698 to NC)	17.64 (3.285 to NC)	NC (5.552 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.4112		0.6171	
Hazard ratio (95% CI) vs Kd	-	1.19 (0.78 to 1.81)		0.86 (0.46 to 1.58)	
P-value	-	0.4118		0.6175	
Improvement probability (95% CI)[b]					

A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Physical functioning
16.2.6.1.2.12 Efficacy response data - Subgroup analyses by MM type at SE
16.2.6.1.2.12.4 QLQ-C30 - Time to first deterioration by 10 pt in physical functioning according to MM type at SE (LOCF) - ITT population

	IgG		Non-IgG		
	Kd (N=85)	**IKd (N=126)**	**Kd (N=38)**	**IKd (N=53)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	44 (51.8)	73 (57.9)	21 (55.3)	29 (54.7)	0.6985
Number (%) of patients censored	41 (48.2)	53 (42.1)	17 (44.7)	24 (45.3)	
Kaplan-Meier estimates of Physical functioning in months					
25% quantile (95% CI)	2.83 (1.281 to 3.811)	2.83 (1.873 to 3.811)	2.56 (0.986 to 6.374)	2.79 (1.084 to 3.713)	
Median (95% CI)	11.99 (4.830 to NC)	10.38 (6.571 to 17.577)	9.07 (4.764 to NC)	6.54 (2.891 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (14.784 to NC)	NC (NC to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.5218		0.9901	
Hazard ratio (95% CI) vs Kd	-	1.13 (0.78 to 1.64)		1.00 (0.57 to 1.75)	
P-value	-	0.5221		0.9901	
Deterioration probability (95% CI)[b]					

A higher score represents a better level of quality of life. Clinical meaningful deterioration change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Physical functioning
16.2.6.1.2.12 Efficacy response data - Subgroup analyses by MM type at SE
16.2.6.1.2.12.5 QLQ-C30 - Time until permanent improvement by 10 pt in physical functioning according to MM type at SE (LOCF) - ITT population

	IgG		Non-IgG		
	Kd (N=85)	**IKd (N=126)**	**Kd (N=38)**	**IKd (N=53)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	23 (27.1)	30 (23.8)	6 (15.8)	8 (15.1)	0.9841
Number (%) of patients censored	62 (72.9)	96 (76.2)	32 (84.2)	45 (84.9)	
Kaplan-Meier estimates of Physical functioning in months					
25% quantile (95% CI)	18.46 (10.316 to NC)	21.42 (16.000 to 24.444)	21.68 (11.105 to NC)	NC (15.179 to NC)	
Median (95% CI)	NC (23.129 to NC)	24.44 (24.444 to NC)	NC (21.684 to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (24.444 to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.5595		0.8077	
Hazard ratio (95% CI) vs Kd	-	0.85 (0.49 to 1.47)		0.88 (0.30 to 2.53)	
P-value	-	0.5599		0.8078	
Improvement probability (95% CI)[b]					

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The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Physical functioning
16.2.6.1.2.12 Efficacy response data - Subgroup analyses by MM type at SE
16.2.6.1.2.12.6 QLQ-C30 - Time until permanent deterioration by 10 pt in physical functioning according to MM type at SE (LOCF) - ITT population

	IgG		Non-IgG		
	Kd (N=85)	**IKd (N=126)**	**Kd (N=38)**	**IKd (N=53)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	22 (25.9)	37 (29.4)	10 (26.3)	16 (30.2)	0.8617
Number (%) of patients censored	63 (74.1)	89 (70.6)	28 (73.7)	37 (69.8)	
Kaplan-Meier estimates of Physical functioning in months					
25% quantile (95% CI)	18.30 (6.637 to NC)	18.30 (12.025 to 20.698)	18.92 (3.778 to NC)	15.70 (10.218 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (21.388 to NC)	NC (20.304 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.5643		0.8560	
Hazard ratio (95% CI) vs Kd	-	1.17 (0.69 to 1.98)		1.08 (0.49 to 2.37)	
P-value	-	0.5647		0.8560	
Deterioration probability (95% CI)[b]					

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The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Physical functioning
16.2.6.1.2.13 Efficacy response data - Subgroup analyses by previous autologous stem-cell
16.2.6.1.2.13.3 QLQ-C30 - Time to first improvement by 10 pt in physical functioning according to previous autologous stem-cell (LOCF) - ITT population

	Yes		No		
	Kd (N=69)	**IKd (N=116)**	**Kd (N=54)**	**IKd (N=63)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	17 (24.6)	53 (45.7)	36 (66.7)	31 (49.2)	0.0026
Number (%) of patients censored	52 (75.4)	63 (54.3)	18 (33.3)	32 (50.8)	
Kaplan-Meier estimates of Physical functioning in months					
25% quantile (95% CI)	13.63 (1.906 to NC)	2.83 (1.906 to 4.698)	1.31 (1.051 to 1.938)	1.97 (1.117 to 2.825)	
Median (95% CI)	NC (NC to NC)	NC (7.819 to NC)	3.29 (1.938 to 7.031)	5.22 (2.825 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (6.965 to NC)	NC (NC to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.0108		0.0821	
Hazard ratio (95% CI) vs Kd	-	2.01 (1.16 to 3.47)		0.65 (0.40 to 1.06)	
P-value	-	0.0125		0.0843	
Hazard ratio inverted (95% CI) vs IKd		-		1.53 (0.94 to 2.47)	

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The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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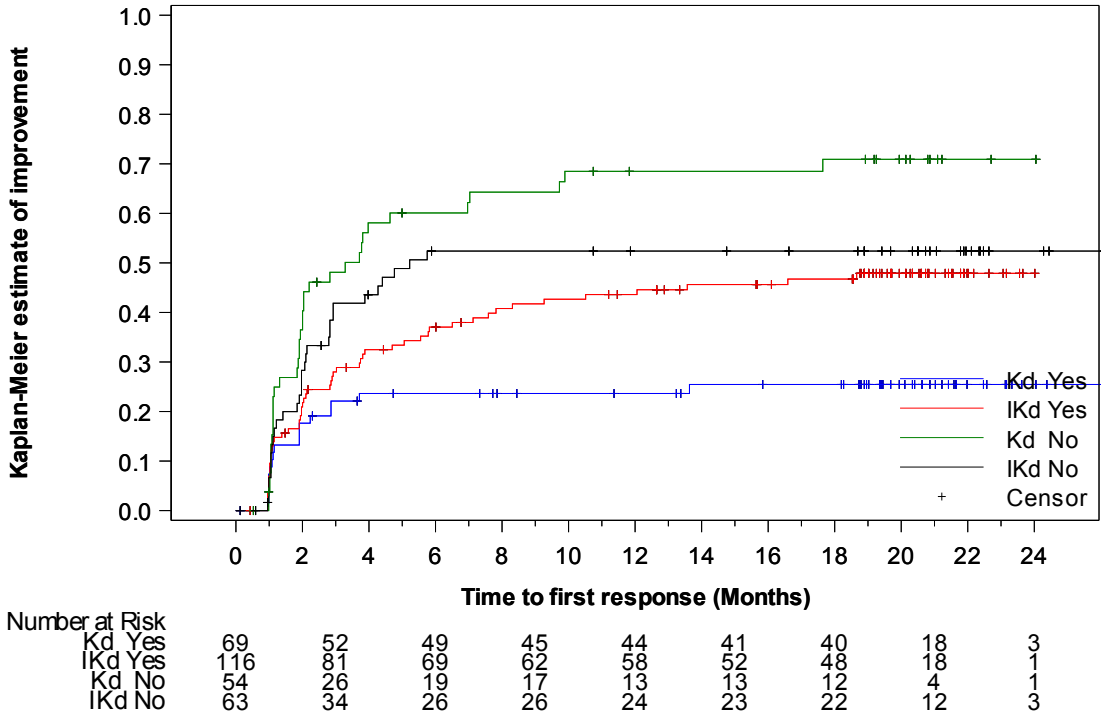
16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Physical functioning
16.2.6.1.2.13 Efficacy response data - Subgroup analyses by previous autologous stem-cell
16.2.6.1.2.13.4 QLQ-C30 - Time to first improvement by 10 pt in physical functioning according to previous autologous stem-cell- Kaplan-Meier curve (LOCF) - ITT population



A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
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16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Physical functioning
16.2.6.1.2.13 Efficacy response data - Subgroup analyses by previous autologous stem-cell
16.2.6.1.2.13.5 QLQ-C30 - Time to first deterioration by 10 pt in physical functioning according to previous autologous stem-cell (LOCF) - ITT population

	Yes		No		
	Kd (N=69)	**IKd (N=116)**	**Kd (N=54)**	**IKd (N=63)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	41 (59.4)	70 (60.3)	24 (44.4)	32 (50.8)	0.6656
Number (%) of patients censored	28 (40.6)	46 (39.7)	30 (55.6)	31 (49.2)	
Kaplan-Meier estimates of Physical functioning in months					
25% quantile (95% CI)	2.00 (1.051 to 3.745)	2.04 (1.347 to 2.858)	3.75 (1.248 to 6.571)	3.81 (2.760 to 9.363)	
Median (95% CI)	6.64 (3.811 to 15.934)	6.83 (3.745 to 15.409)	NC (6.571 to NC)	16.00 (9.363 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.9778		0.5828	
Hazard ratio (95% CI) vs Kd	-	0.99 (0.68 to 1.46)		1.16 (0.68 to 1.97)	
P-value	-	0.9778		0.5831	
Deterioration probability (95% CI)[b]					

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The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Physical functioning
16.2.6.1.2.13 Efficacy response data - Subgroup analyses by previous autologous stem-cell
16.2.6.1.2.13.6 QLQ-C30 - Time until permanent improvement by 10 pt in physical functioning according to previous autologous stem-cell (LOCF) - ITT population

	Yes		No		
	Kd (N=69)	**IKd (N=116)**	**Kd (N=54)**	**IKd (N=63)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	12 (17.4)	24 (20.7)	17 (31.5)	14 (22.2)	0.1534
Number (%) of patients censored	57 (82.6)	92 (79.3)	37 (68.5)	49 (77.8)	
Kaplan-Meier estimates of Physical functioning in months					
25% quantile (95% CI)	22.14 (14.817 to NC)	21.42 (17.051 to 24.444)	13.17 (2.004 to 23.129)	21.65 (13.142 to NC)	
Median (95% CI)	NC (22.144 to NC)	24.44 (NC to NC)	23.13 (23.129 to NC)	NC (21.684 to NC)	
75% quantile (95% CI)	NC (NC to NC)	24.44 (NC to NC)	NC (23.129 to NC)	NC (NC to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.5688		0.1591	
Hazard ratio (95% CI) vs Kd	-	1.22 (0.61 to 2.45)		0.60 (0.30 to 1.23)	
P-value	-	0.5695		0.1635	
Improvement probability (95% CI)[b]					

A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Physical functioning
16.2.6.1.2.13 Efficacy response data - Subgroup analyses by previous autologous stem-cell
16.2.6.1.2.13.7 QLQ-C30 - Time until permanent deterioration by 10 pt in physical functioning according to previous autologous stem-cell (LOCF) - ITT population

	Yes		No		
	Kd (N=69)	**IKd (N=116)**	**Kd (N=54)**	**IKd (N=63)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	20 (29.0)	33 (28.4)	12 (22.2)	20 (31.7)	0.3065
Number (%) of patients censored	49 (71.0)	83 (71.6)	42 (77.8)	43 (68.3)	
Kaplan-Meier estimates of Physical functioning in months					
25% quantile (95% CI)	10.55 (5.717 to NC)	18.79 (12.649 to 21.520)	21.39 (4.665 to NC)	15.87 (6.407 to 19.877)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (19.877 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.8541		0.2373	
Hazard ratio (95% CI) vs Kd	-	0.95 (0.54 to 1.65)		1.54 (0.75 to 3.14)	
P-value	-	0.8531		0.2409	
Deterioration probability (95% CI)[b]					

A higher score represents a better level of quality of life. Clinical meaningful deterioration change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Physical functioning
16.2.6.1.2.14 Efficacy response data - Subgroup analyses by baseline eGFR (MDRD)
16.2.6.1.2.14.3 QLQ-C30 - Time to first improvement by 10 pt in physical functioning according to baseline eGFR (MDRD) (LOCF) - ITT population

	>=60 mL/min/1.73m2		<60 mL/min/1.73m2		
	Kd (N=93)	**IKd (N=122)**	**Kd (N=18)**	**IKd (N=43)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	44 (47.3)	54 (44.3)	6 (33.3)	25 (58.1)	0.3655
Number (%) of patients censored	49 (52.7)	68 (55.7)	12 (66.7)	18 (41.9)	
Kaplan-Meier estimates of Physical functioning in months					
25% quantile (95% CI)	1.91 (1.117 to 2.234)	1.97 (1.216 to 2.858)	1.87 (1.084 to NC)	2.79 (1.051 to 4.402)	
Median (95% CI)	NC (3.975 to NC)	NC (5.782 to NC)	NC (1.840 to NC)	8.31 (4.271 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.8429		0.3710	
Hazard ratio (95% CI) vs Kd	-	0.96 (0.65 to 1.43)		1.50 (0.61 to 3.65)	
P-value	-	0.8426		0.3747	
Improvement probability (95% CI)[b]					

A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Physical functioning
16.2.6.1.2.14 Efficacy response data - Subgroup analyses by baseline eGFR (MDRD)
16.2.6.1.2.14.4 QLQ-C30 - Time to first deterioration by 10 pt in physical functioning according to baseline eGFR (MDRD) (LOCF) - ITT population

	>=60 mL/min/1.73m2		<60 mL/min/1.73m2		
	Kd (N=93)	**IKd (N=122)**	**Kd (N=18)**	**IKd (N=43)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	47 (50.5)	74 (60.7)	15 (83.3)	24 (55.8)	0.0060
Number (%) of patients censored	46 (49.5)	48 (39.3)	3 (16.7)	19 (44.2)	
Kaplan-Meier estimates of Physical functioning in months					
25% quantile (95% CI)	2.00 (1.216 to 3.811)	2.76 (1.511 to 2.891)	2.83 (0.986 to 4.041)	1.97 (1.084 to 6.505)	
Median (95% CI)	14.78 (5.947 to NC)	7.95 (3.975 to 15.409)	4.83 (1.314 to 9.002)	10.38 (4.632 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	9.07 (4.041 to 17.708)	NC (19.877 to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.1532		0.0087	
Hazard ratio (95% CI) vs Kd	-	1.30 (0.90 to 1.88)		0.42 (0.22 to 0.82)	
P-value	-	0.1544		0.0108	
Deterioration probability (95% CI)[b]					

A higher score represents a better level of quality of life. Clinical meaningful deterioration change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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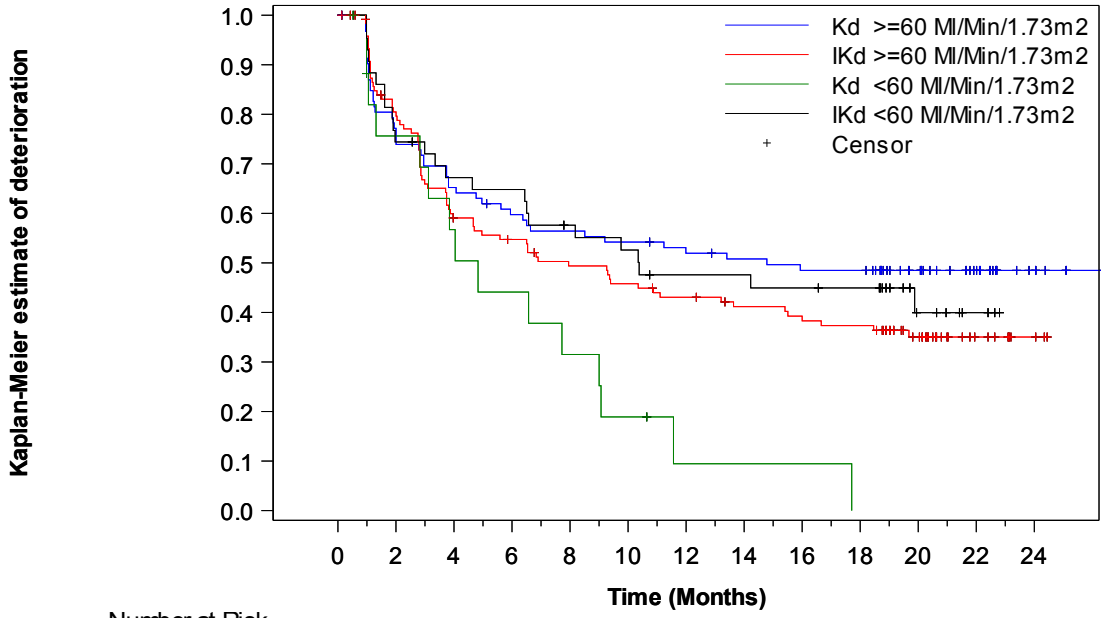
16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Physical functioning
16.2.6.1.2.14 Efficacy response data - Subgroup analyses by baseline eGFR (MDRD)
16.2.6.1.2.14.5 QLQ-C30 - Time to first deterioration by 10 pt in physical functioning according to baseline eGFR (MDRD)- Kaplan-Meier curve (LOCF) - ITT population



Number at Risk

Kd >=60 Ml/Min/1.73m2	93	64	54	50	46	43	42	23	6
lKd >=60 Ml/Min/1.73m2	122	77	62	55	47	43	39	13	3
Kd <60 Ml/Min/1.73m2	18	11	7	5	1	1	0	0	0
lKd <60 Ml/Min/1.73m2	43	30	27	22	18	17	16	5	0

A higher score represents a better level of quality of life. Clinical meaningful deterioration change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
PGM=DEVOPS/SAR650984/EFC15246/CIR_RWE/REPORT/PGM/eff_qlq_km_subgp_de_i_f.sas OUT=REPORT/OUTPUT/eff_km_c30_phy_detl_crcl_de_i_f_x.rtf (07APR2021 14:48)

16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Physical functioning
16.2.6.1.2.14 Efficacy response data - Subgroup analyses by baseline eGFR (MDRD)
16.2.6.1.2.14.6 QLQ-C30 - Time until permanent improvement by 10 pt in physical functioning according to baseline eGFR (MDRD) (LOCF) - ITT population

	>=60 mL/min/1.73m2		<60 mL/min/1.73m2		
	Kd (N=93)	**IKd (N=122)**	**Kd (N=18)**	**IKd (N=43)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	27 (29.0)	24 (19.7)	1 (5.6)	12 (27.9)	0.0717
Number (%) of patients censored	66 (71.0)	98 (80.3)	17 (94.4)	31 (72.1)	
Kaplan-Meier estimates of Physical functioning in months					
25% quantile (95% CI)	18.46 (7.261 to 23.129)	21.42 (18.201 to NC)	NC (10.316 to NC)	21.65 (3.778 to 24.444)	
Median (95% CI)	23.13 (22.144 to NC)	NC (NC to NC)	NC (NC to NC)	24.44 (21.651 to 24.444)	
75% quantile (95% CI)	NC (23.129 to NC)	NC (NC to NC)	NC (NC to NC)	24.44 (NC to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.1347		0.1420	
Hazard ratio (95% CI) vs Kd	-	0.66 (0.38 to 1.14)		4.11 (0.53 to 31.84)	
P-value	-	0.1375		0.1761	
Improvement probability (95% CI)[b]					

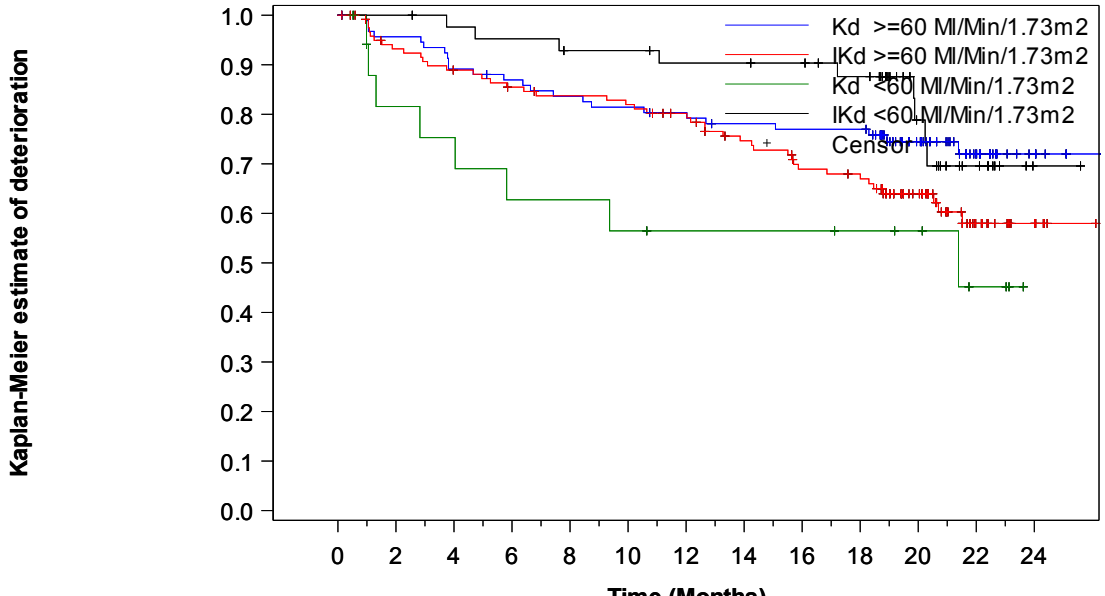
A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
PGM=DEVOPS/SAR650984/EFC15246/CIR_RWE/REPORT/PGM/eff_km_subgp_sr_sig_de_i_t.sas OUT=REPORT/OUTPUT/eff_km_c30_phy_imppl_crcl_de_i_t_x.rtf (07APR2021 14:22)

16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Physical functioning
16.2.6.1.2.14 Efficacy response data - Subgroup analyses by baseline eGFR (MDRD)
16.2.6.1.2.14.7 QLQ-C30 - Time until permanent deterioration by 10 pt in physical functioning according to baseline eGFR (MDRD) (LOCF) - ITT population

	>=60 mL/min/1.73m2		<60 mL/min/1.73m2		
	Kd (N=93)	**IKd (N=122)**	**Kd (N=18)**	**IKd (N=43)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	24 (25.8)	43 (35.2)	8 (44.4)	9 (20.9)	0.0039
Number (%) of patients censored	69 (74.2)	79 (64.8)	10 (55.6)	34 (79.1)	
Kaplan-Meier estimates of Physical functioning in months					
25% quantile (95% CI)	18.92 (7.425 to NC)	13.86 (9.265 to 18.004)	4.04 (0.986 to 21.388)	20.24 (17.216 to NC)	
Median (95% CI)	NC (NC to NC)	NC (20.698 to NC)	21.39 (2.825 to NC)	NC (20.304 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (21.388 to NC)	NC (NC to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.1029		0.0180	
Hazard ratio (95% CI) vs Kd	-	1.51 (0.92 to 2.49)		0.33 (0.13 to 0.87)	
P-value	-	0.1054		0.0243	
Deterioration probability (95% CI)[b]					

A higher score represents a better level of quality of life. Clinical meaningful deterioration change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
PGM=DEVOPS/SAR650984/EFC15246/CIR_RWE/REPORT/PGM/eff_km_subgp_sr_sig_de_i_t.sas OUT=REPORT/OUTPUT/eff_km_c30_phy_detpl_crcl_de_i_t_x.rtf (07APR2021 14:22)

16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Physical functioning
16.2.6.1.2.14 Efficacy response data - Subgroup analyses by baseline eGFR (MDRD)
16.2.6.1.2.14.8 QLQ-C30 - Time until permanent deterioration by 10 pt in physical functioning according to baseline eGFR (MDRD)- Kaplan-Meier curve (LOCF) - ITT population



Number at Risk

Kd >=60 Ml/Min/1.73m2	93	86	79	74	72	69	68	33	7
lKd >=60 Ml/Min/1.73m2	122	106	98	95	88	77	69	28	7
Kd <60 Ml/Min/1.73m2	18	12	10	10	8	8	7	5	0
lKd <60 Ml/Min/1.73m2	43	42	40	38	36	35	32	11	1

A higher score represents a better level of quality of life. Clinical meaningful deterioration change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
PGM=DEVOPS/SAR650984/EFC15246/CIR_RWE/REPORT/PGM/eff_qlq_km_subgp_de_i_f.sas OUT=REPORT/OUTPUT/eff_km_c30_phy_detpl_crcl_de_i_f_x.rtf (07APR2021 14:48)

16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Physical functioning
16.2.6.1.2.15 Efficacy response data - Subgroup analyses by previous treatment with PI
16.2.6.1.2.15.3 QLQ-C30 - Time to first improvement by 10 pt in physical functioning according to previous treatment with PI (LOCF) - ITT population

	Yes		No		
	Kd (N=47)	**IKd (N=81)**	**Kd (N=76)**	**IKd (N=98)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	22 (46.8)	41 (50.6)	31 (40.8)	43 (43.9)	0.7281
Number (%) of patients censored	25 (53.2)	40 (49.4)	45 (59.2)	55 (56.1)	
Kaplan-Meier estimates of Physical functioning in months					
25% quantile (95% CI)	2.00 (1.117 to 3.811)	2.04 (1.117 to 2.924)	1.91 (1.084 to 2.825)	2.14 (1.577 to 3.811)	
Median (95% CI)	NC (3.778 to NC)	7.59 (3.877 to NC)	NC (4.632 to NC)	NC (7.819 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.5931		0.9323	
Hazard ratio (95% CI) vs Kd	-	1.15 (0.69 to 1.93)		1.02 (0.64 to 1.62)	
P-value	-	0.5934		0.9324	
Improvement probability (95% CI)[b]					

A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
PGM=DEVOPS/SAR650984/EFC15246/CIR_RWE/REPORT/PGM/eff_km_subgp_sr_sig_de_i_t.sas OUT=REPORT/OUTPUT/eff_km_c30_phy_impl_pi_de_i_t_x.rtf (07APR2021 14:22)

16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Physical functioning
16.2.6.1.2.15 Efficacy response data - Subgroup analyses by previous treatment with PI
16.2.6.1.2.15.4 QLQ-C30 - Time to first deterioration by 10 pt in physical functioning according to previous treatment with PI (LOCF) - ITT population

	Yes		No		
	Kd (N=47)	**IKd (N=81)**	**Kd (N=76)**	**IKd (N=98)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	29 (61.7)	46 (56.8)	36 (47.4)	56 (57.1)	0.3619
Number (%) of patients censored	18 (38.3)	35 (43.2)	40 (52.6)	42 (42.9)	
Kaplan-Meier estimates of Physical functioning in months					
25% quantile (95% CI)	1.94 (1.051 to 3.811)	2.76 (1.248 to 3.713)	2.96 (1.216 to 5.947)	2.83 (1.906 to 3.877)	
Median (95% CI)	6.47 (3.713 to 14.784)	10.35 (3.811 to 19.877)	17.71 (6.505 to NC)	9.40 (6.505 to NC)	
75% quantile (95% CI)	NC (13.405 to NC)	NC (19.877 to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.7012		0.3733	
Hazard ratio (95% CI) vs Kd	-	0.91 (0.57 to 1.45)		1.21 (0.80 to 1.84)	
P-value	-	0.7013		0.3740	
Deterioration probability (95% CI)[b]					

A higher score represents a better level of quality of life. Clinical meaningful deterioration change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Physical functioning
16.2.6.1.2.15 Efficacy response data - Subgroup analyses by previous treatment with PI
16.2.6.1.2.15.5 QLQ-C30 - Time until permanent improvement by 10 pt in physical functioning according to previous treatment with PI (LOCF) - ITT population

	Yes		No		
	Kd (N=47)	**IKd (N=81)**	**Kd (N=76)**	**IKd (N=98)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	12 (25.5)	18 (22.2)	17 (22.4)	20 (20.4)	0.9649
Number (%) of patients censored	35 (74.5)	63 (77.8)	59 (77.6)	78 (79.6)	
Kaplan-Meier estimates of Physical functioning in months					
25% quantile (95% CI)	18.46 (1.117 to NC)	21.42 (14.554 to NC)	21.68 (11.335 to NC)	21.68 (16.854 to NC)	
Median (95% CI)	NC (22.144 to NC)	NC (NC to NC)	NC (23.129 to NC)	24.44 (24.444 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (24.444 to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.6478		0.6198	
Hazard ratio (95% CI) vs Kd	-	0.84 (0.41 to 1.75)		0.85 (0.44 to 1.62)	
P-value	-	0.6482		0.6202	
Improvement probability (95% CI)[b]					

A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Physical functioning
16.2.6.1.2.15 Efficacy response data - Subgroup analyses by previous treatment with PI
16.2.6.1.2.15.6 QLQ-C30 - Time until permanent deterioration by 10 pt in physical functioning according to previous treatment with PI (LOCF) - ITT population

	Yes		No		
	Kd (N=47)	**IKd (N=81)**	**Kd (N=76)**	**IKd (N=98)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	12 (25.5)	28 (34.6)	20 (26.3)	25 (25.5)	0.2915
Number (%) of patients censored	35 (74.5)	53 (65.4)	56 (73.7)	73 (74.5)	
Kaplan-Meier estimates of Physical functioning in months					
25% quantile (95% CI)	15.08 (3.811 to NC)	14.26 (5.257 to 19.877)	18.92 (5.815 to NC)	19.84 (12.649 to NC)	
Median (95% CI)	NC (NC to NC)	NC (20.238 to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.2656		0.7584	
Hazard ratio (95% CI) vs Kd	-	1.47 (0.74 to 2.89)		0.91 (0.51 to 1.64)	
P-value	-	0.2686		0.7584	
Deterioration probability (95% CI)[b]					

A higher score represents a better level of quality of life. Clinical meaningful deterioration change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
PGM=DEVOPS/SAR650984/EFC15246/CIR_RWE/REPORT/PGM/eff_km_subgp_sr_sig_de_i_t.sas OUT=REPORT/OUTPUT/eff_km_c30_phy_detpl_pi_de_i_t_x.rtf (07APR2021 14:22)

16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Physical functioning
16.2.6.1.2.16 Efficacy response data - Subgroup analyses by previous treatment with IMiD
16.2.6.1.2.16.3 QLQ-C30 - Time to first improvement by 10 pt in physical functioning according to previous treatment with IMiD (LOCF) - ITT population

	Yes		No		
	Kd (N=62)	**IKd (N=81)**	**Kd (N=61)**	**IKd (N=98)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	28 (45.2)	35 (43.2)	25 (41.0)	49 (50.0)	0.1717
Number (%) of patients censored	34 (54.8)	46 (56.8)	36 (59.0)	49 (50.0)	
Kaplan-Meier estimates of Physical functioning in months					
25% quantile (95% CI)	1.91 (1.084 to 2.234)	2.83 (1.971 to 4.402)	2.41 (1.150 to 6.965)	1.91 (1.051 to 2.825)	
Median (95% CI)	NC (2.234 to NC)	NC (5.782 to NC)	NC (6.965 to NC)	13.57 (4.698 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.4646		0.2173	
Hazard ratio (95% CI) vs Kd	-	0.83 (0.51 to 1.37)		1.35 (0.84 to 2.19)	
P-value	-	0.4652		0.2191	
Improvement probability (95% CI)[b]					

A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Physical functioning
16.2.6.1.2.16 Efficacy response data - Subgroup analyses by previous treatment with IMiD
16.2.6.1.2.16.4 QLQ-C30 - Time to first deterioration by 10 pt in physical functioning according to previous treatment with IMiD (LOCF) - ITT population

	Yes		No		
	Kd (N=62)	**IKd (N=81)**	**Kd (N=61)**	**IKd (N=98)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	27 (43.5)	47 (58.0)	38 (62.3)	55 (56.1)	0.0970
Number (%) of patients censored	35 (56.5)	34 (42.0)	23 (37.7)	43 (43.9)	
Kaplan-Meier estimates of Physical functioning in months					
25% quantile (95% CI)	3.71 (1.314 to 6.637)	2.53 (1.511 to 3.877)	1.92 (1.051 to 3.745)	2.83 (1.873 to 3.713)	
Median (95% CI)	NC (6.637 to NC)	10.35 (4.698 to 19.877)	6.47 (3.745 to 13.405)	9.76 (4.961 to 19.680)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (13.405 to NC)	NC (NC to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.1436		0.4079	
Hazard ratio (95% CI) vs Kd	-	1.42 (0.89 to 2.28)		0.84 (0.56 to 1.27)	
P-value	-	0.1456		0.4085	
Deterioration probability (95% CI)[b]					

A higher score represents a better level of quality of life. Clinical meaningful deterioration change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
PGM=DEVOPS/SAR650984/EFC15246/CIR_RWE/REPORT/PGM/eff_km_subgp_sr_sig_de_i_t.sas OUT=REPORT/OUTPUT/eff_km_c30_phy_detl_imid_de_i_t_x.rtf (07APR2021 14:22)

16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Physical functioning
16.2.6.1.2.16 Efficacy response data - Subgroup analyses by previous treatment with IMiD
16.2.6.1.2.16.5 QLQ-C30 - Time until permanent improvement by 10 pt in physical functioning according to previous treatment with IMiD (LOCF) - ITT population

	Yes		No		
	Kd (N=62)	**IKd (N=81)**	**Kd (N=61)**	**IKd (N=98)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	18 (29.0)	14 (17.3)	11 (18.0)	24 (24.5)	0.0538
Number (%) of patients censored	44 (71.0)	67 (82.7)	50 (82.0)	74 (75.5)	
Kaplan-Meier estimates of Physical functioning in months					
25% quantile (95% CI)	14.65 (7.261 to 23.129)	21.68 (20.304 to NC)	21.68 (14.817 to NC)	18.89 (11.795 to 24.444)	
Median (95% CI)	23.13 (22.144 to NC)	NC (NC to NC)	NC (NC to NC)	24.44 (NC to NC)	
75% quantile (95% CI)	NC (23.129 to NC)	NC (NC to NC)	NC (NC to NC)	24.44 (NC to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.0619		0.4264	
Hazard ratio (95% CI) vs Kd	-	0.52 (0.26 to 1.05)		1.34 (0.65 to 2.74)	
P-value	-	0.0666		0.4280	
Improvement probability (95% CI)[b]					

A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
PGM=DEVOPS/SAR650984/EFC15246/CIR_RWE/REPORT/PGM/eff_km_subgp_sr_sig_de_i_t.sas OUT=REPORT/OUTPUT/eff_km_c30_phy_imppl_imid_de_i_t_x.rtf (07APR2021 14:22)

16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Physical functioning
16.2.6.1.2.16 Efficacy response data - Subgroup analyses by previous treatment with IMiD
16.2.6.1.2.16.6 QLQ-C30 - Time until permanent deterioration by 10 pt in physical functioning according to previous treatment with IMiD (LOCF) - ITT population

	Yes		No		
	Kd (N=62)	**IKd (N=81)**	**Kd (N=61)**	**IKd (N=98)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	11 (17.7)	24 (29.6)	21 (34.4)	29 (29.6)	0.0967
Number (%) of patients censored	51 (82.3)	57 (70.4)	40 (65.6)	69 (70.4)	
Kaplan-Meier estimates of Physical functioning in months					
25% quantile (95% CI)	NC (9.363 to NC)	17.22 (9.922 to NC)	8.44 (3.811 to 21.388)	18.46 (13.864 to 20.698)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (21.388 to NC)	NC (21.520 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.1237		0.4823	
Hazard ratio (95% CI) vs Kd	-	1.74 (0.85 to 3.56)		0.82 (0.47 to 1.43)	
P-value	-	0.1286		0.4831	
Deterioration probability (95% CI)[b]					

A higher score represents a better level of quality of life. Clinical meaningful deterioration change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Physical functioning
16.2.6.1.2.17 Efficacy response data - Subgroup analyses by previous treatment with PI and IMiD
16.2.6.1.2.17.3 QLQ-C30 - Time to first improvement by 10 pt in physical functioning according to previous treatment with PI and IMiD (LOCF) - ITT population

	Yes		No		
	Kd (N=17)	**IKd (N=23)**	**Kd (N=106)**	**IKd (N=156)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	7 (41.2)	10 (43.5)	46 (43.4)	74 (47.4)	0.7507
Number (%) of patients censored	10 (58.8)	13 (56.5)	60 (56.6)	82 (52.6)	
Kaplan-Meier estimates of Physical functioning in months					
25% quantile (95% CI)	2.86 (1.018 to NC)	4.27 (1.413 to 9.265)	1.91 (1.150 to 2.825)	1.97 (1.216 to 2.825)	
Median (95% CI)	NC (2.858 to NC)	NC (4.271 to NC)	NC (6.965 to NC)	NC (5.749 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.8638		0.6005	
Hazard ratio (95% CI) vs Kd	-	0.92 (0.35 to 2.42)		1.10 (0.76 to 1.59)	
P-value	-	0.8638		0.6006	
Improvement probability (95% CI)[b]					

A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Physical functioning
16.2.6.1.2.17 Efficacy response data - Subgroup analyses by previous treatment with PI and IMiD
16.2.6.1.2.17.4 QLQ-C30 - Time to first deterioration by 10 pt in physical functioning according to previous treatment with PI and IMiD (LOCF) - ITT population

	Yes		No		
	Kd (N=17)	**IKd (N=23)**	**Kd (N=106)**	**IKd (N=156)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	9 (52.9)	13 (56.5)	56 (52.8)	89 (57.1)	0.9320
Number (%) of patients censored	8 (47.1)	10 (43.5)	50 (47.2)	67 (42.9)	
Kaplan-Meier estimates of Physical functioning in months					
25% quantile (95% CI)	2.45 (0.953 to 9.068)	1.51 (0.986 to 6.439)	2.86 (1.248 to 3.844)	2.83 (2.004 to 3.713)	
Median (95% CI)	11.93 (2.070 to NC)	6.54 (1.906 to NC)	11.24 (6.374 to NC)	10.35 (6.538 to 16.000)	
75% quantile (95% CI)	NC (9.068 to NC)	NC (17.577 to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.8287		0.6753	
Hazard ratio (95% CI) vs Kd	-	1.10 (0.47 to 2.57)		1.07 (0.77 to 1.50)	
P-value	-	0.8287		0.6754	
Deterioration probability (95% CI)[b]					

A higher score represents a better level of quality of life. Clinical meaningful deterioration change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Physical functioning
16.2.6.1.2.17 Efficacy response data - Subgroup analyses by previous treatment with PI and IMiD
16.2.6.1.2.17.5 QLQ-C30 - Time until permanent improvement by 10 pt in physical functioning according to previous treatment with PI and IMiD (LOCF) - ITT population

	Yes		No		
	Kd (N=17)	**IKd (N=23)**	**Kd (N=106)**	**IKd (N=156)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	6 (35.3)	4 (17.4)	23 (21.7)	34 (21.8)	0.2036
Number (%) of patients censored	11 (64.7)	19 (82.6)	83 (78.3)	122 (78.2)	
Kaplan-Meier estimates of Physical functioning in months					
25% quantile (95% CI)	13.17 (1.018 to 22.144)	NC (1.413 to NC)	21.68 (14.456 to NC)	21.65 (17.051 to NC)	
Median (95% CI)	22.14 (13.175 to NC)	NC (21.421 to NC)	NC (23.129 to NC)	24.44 (24.444 to NC)	
75% quantile (95% CI)	NC (22.144 to NC)	NC (NC to NC)	NC (NC to NC)	NC (24.444 to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.1259		0.9059	
Hazard ratio (95% CI) vs Kd	-	0.38 (0.11 to 1.37)		0.97 (0.57 to 1.64)	
P-value	-	0.1403		0.9056	

A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Physical functioning
16.2.6.1.2.17 Efficacy response data - Subgroup analyses by previous treatment with PI and IMiD
16.2.6.1.2.17.6 QLQ-C30 - Time until permanent deterioration by 10 pt in physical functioning according to previous treatment with PI and IMiD (LOCF) - ITT population

	Yes		No		
	Kd (N=17)	**IKd (N=23)**	**Kd (N=106)**	**IKd (N=156)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	2 (11.8)	7 (30.4)	30 (28.3)	46 (29.5)	0.2075
Number (%) of patients censored	15 (88.2)	16 (69.6)	76 (71.7)	110 (70.5)	
Kaplan-Meier estimates of Physical functioning in months					
25% quantile (95% CI)	NC (1.314 to NC)	17.22 (1.248 to NC)	15.08 (6.374 to NC)	18.00 (12.649 to 20.534)	
Median (95% CI)	NC (NC to NC)	NC (17.216 to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.1809		0.9196	
Hazard ratio (95% CI) vs Kd	-	2.80 (0.58 to 13.50)		1.02 (0.65 to 1.62)	
P-value	-	0.2001		0.9198	
Deterioration probability (95% CI)[b]					

A higher score represents a better level of quality of life. Clinical meaningful deterioration change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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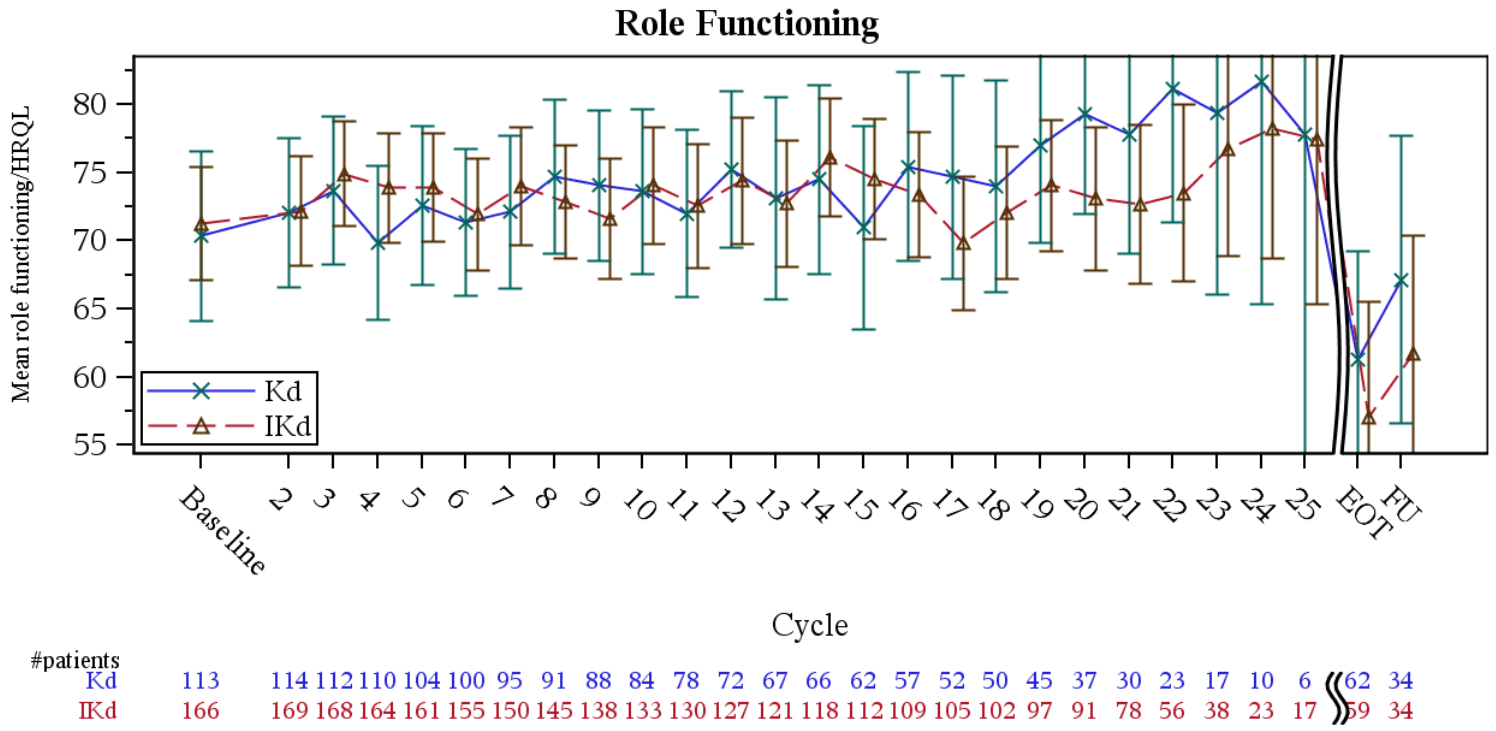
16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Role functioning
16.2.6.1.2.1 Efficacy response data
16.2.6.1.2.1.1 QLQ-C30 - Mean and 95% CI for role functioning score over time (LOCF) - ITT population



#patients																									
Kd	113	114	112	110	104	100	95	91	88	84	78	72	67	66	62	57	52	50	45	37	30	23	17	10	6	62	34
IKd	166	169	168	164	161	155	150	145	138	133	130	127	121	118	112	109	105	102	97	91	78	56	38	23	17	59	34

A higher score represents a better level of quality of life. Cycles with less than 20 patients overall are not presented.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
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16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Role functioning
16.2.6.1.2.1 Efficacy response data
16.2.6.1.2.1.15 QLQ-C30 - Time to first improvement by 15 pt in Role functioning (LOCF) - ITT population

First improvement 15 points Role functioning (%)	Kd (N=123)	IKd (N=179)
Number (%) of events	53 (43.1)	91 (50.8)
Number (%) of patients censored	70 (56.9)	88 (49.2)
Kaplan-Meier estimates of Role functioning in months		
25% quantile (95% CI)	1.91 (1.084 to 2.037)	1.15 (1.051 to 1.971)
Median (95% CI)	NC (6.012 to NC)	6.70 (2.891 to NC)
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)
Comparison vs. Kd		
Stratified[a] Log-Rank test p-value[b] vs Kd	-	0.2373
Stratified[a] Hazard ratio (95% CI) vs Kd	-	1.23 (0.87 to 1.72)
P-value	-	0.2381
Improvement probability (95% CI)[c]		
3 Months	0.375 (0.289 to 0.461)	0.437 (0.362 to 0.509)
6 Months	0.401 (0.313 to 0.488)	0.484 (0.408 to 0.556)

A lower score represents a better level of quality of life. Clinical meaningful improvement change from baseline less than or equal to -15 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] Stratified on number of prior lines of therapy (1 vs. >1) and Revised International Staging System (R-ISS) stage (I or II vs. III vs. not classified) according to IRT
[b] One-sided significance level is 0.025
[c] Estimated using the Kaplan-Meier method
NA/NC = Not Applicable / Not Calculable
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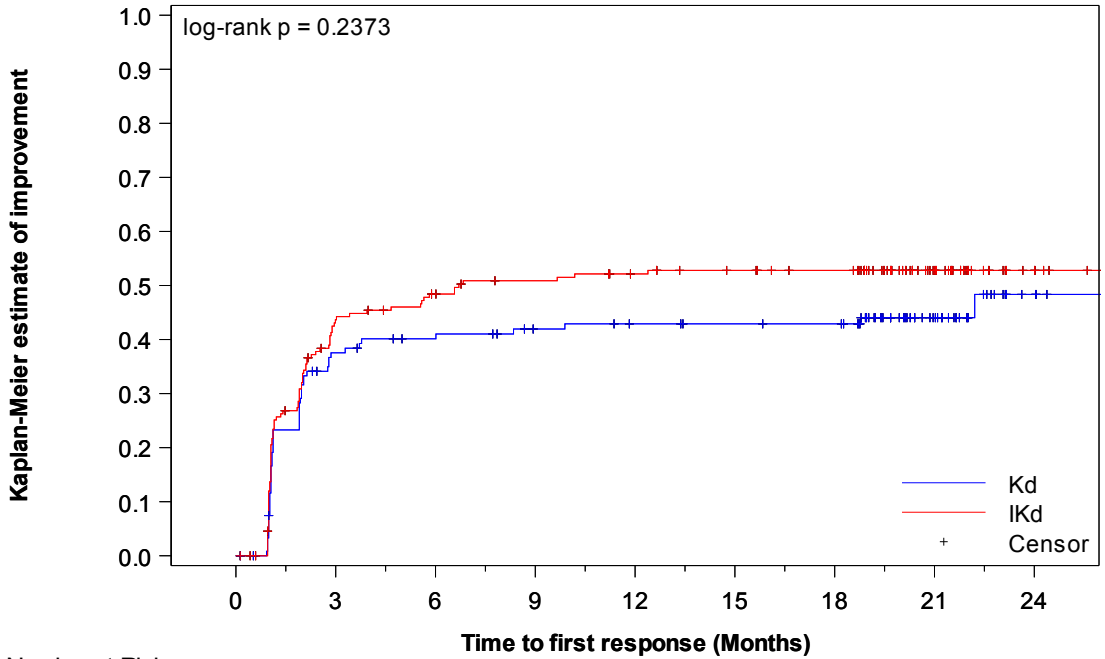
16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Role functioning
16.2.6.1.2.1 Efficacy response data
16.2.6.1.2.1.16 QLQ-C30 - Time to first improvement by 15 pt in Role functioning - Kaplan-Meier curve (LOCF) - ITT population



Number at Risk

Kd	123	73	67	61	58	56	55	26	4
IKd	179	96	85	78	73	68	64	31	6

A lower score represents a better level of quality of life. Clinical meaningful improvement change from baseline less than or equal to -15 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
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16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Role functioning
16.2.6.1.2.1 Efficacy response data
16.2.6.1.2.1.17 QLQ-C30 - Time to first deterioration by 15 pt in Role functioning (LOCF) - ITT population

First deterioration 15 points Role functioning (%)	Kd (N=123)	IKd (N=179)
Number (%) of events	69 (56.1)	111 (62.0)
Number (%) of patients censored	54 (43.9)	68 (38.0)
Kaplan-Meier estimates of Role functioning in months		
25% quantile (95% CI)	2.00 (1.216 to 2.825)	1.91 (1.150 to 2.595)
Median (95% CI)	5.82 (3.943 to 21.454)	5.75 (3.778 to 10.218)
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)
Comparison vs. Kd		
Stratified[a] Log-Rank test p-value[b] vs Kd	-	0.2610
Stratified[a] Hazard ratio (95% CI) vs Kd	-	1.19 (0.88 to 1.61)
P-value	-	0.2616
Deterioration probability (95% CI)[c]		
3 Months	0.658 (0.566 to 0.736)	0.616 (0.540 to 0.684)
6 Months	0.494 (0.401 to 0.580)	0.493 (0.416 to 0.565)

A lower score represents a better level of quality of life. Clinical meaningful deterioration change from baseline greater than or equal to 15 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] Stratified on number of prior lines of therapy (1 vs. >1) and Revised International Staging System (R-ISS) stage (I or II vs. III vs. not classified) according to IRT
[b] One-sided significance level is 0.025
[c] Estimated using the Kaplan-Meier method
NA/NC = Not Applicable / Not Calculable
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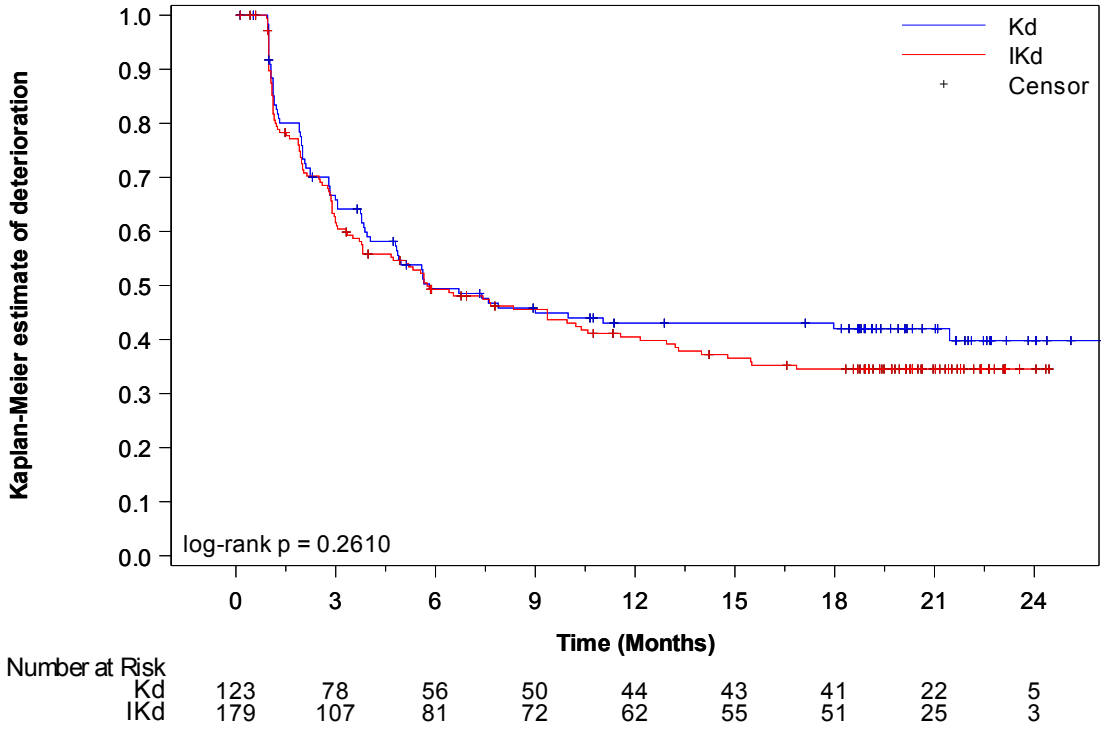
16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Role functioning
16.2.6.1.2.1 Efficacy response data
16.2.6.1.2.1.18 QLQ-C30 - Time to first deterioration by 15 pt in Role functioning - Kaplan-Meier curve (LOCF) - ITT population



A lower score represents a better level of quality of life. Clinical meaningful deterioration change from baseline greater than or equal to 15 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
PGM=DEVOPS/SAR650984/EFC15246/CIR_RWE/REPORT/PGM/eff_qlq_km_i_f.sas OUT=REPORT/OUTPUT/eff_km_c30_rol_det15l_de_i_f_x.rtf (07APR2021 14:23)

16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Role functioning
16.2.6.1.2.1 Efficacy response data
16.2.6.1.2.1.19 QLQ-C30 - Time until permanent improvement by 15 pt in Role functioning (LOCF) - ITT population

First permanent improvement 15 points Role functioning (%)	Kd (N=123)	IKd (N=179)
Number (%) of events	28 (22.8)	43 (24.0)
Number (%) of patients censored	95 (77.2)	136 (76.0)
Kaplan-Meier estimates of Role functioning in months		
25% quantile (95% CI)	22.14 (9.561 to NC)	19.38 (13.634 to NC)
Median (95% CI)	NC (NC to NC)	NC (NC to NC)
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)
Comparison vs. Kd		
Stratified[a] Log-Rank test p-value[b] vs Kd	-	0.9203
Stratified[a] Hazard ratio (95% CI) vs Kd	-	1.02 (0.63 to 1.65)
P-value	-	0.9205
Improvement probability (95% CI)[c]		
3 Months	0.134 (0.080 to 0.201)	0.086 (0.050 to 0.133)
6 Months	0.160 (0.100 to 0.231)	0.098 (0.059 to 0.147)

A lower score represents a better level of quality of life. Clinical meaningful improvement change from baseline less than or equal to -15 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] Stratified on number of prior lines of therapy (1 vs. >1) and Revised International Staging System (R-ISS) stage (I or II vs. III vs. not classified) according to IRT
[b] One-sided significance level is 0.025
[c] Estimated using the Kaplan-Meier method
NA/NC = Not Applicable / Not Calculable
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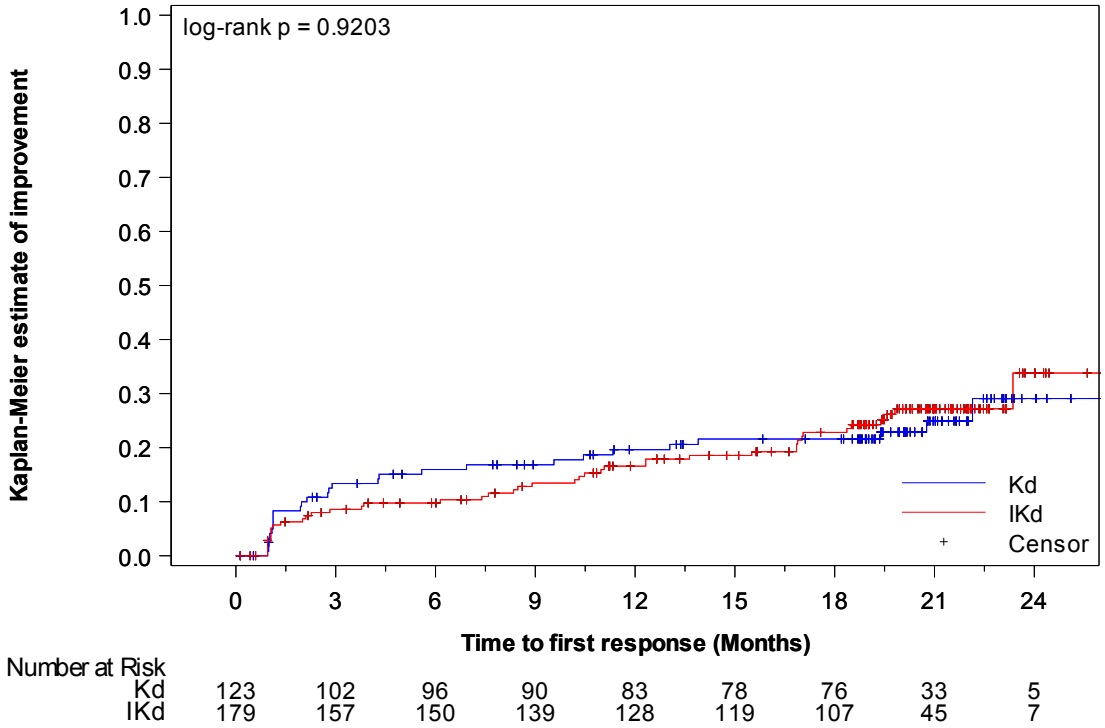
16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Role functioning
16.2.6.1.2.1 Efficacy response data
16.2.6.1.2.1.20 QLQ-C30 - Time until permanent improvement by 15 pt in Role functioning - Kaplan-Meier curve (LOCF) - ITT population



A lower score represents a better level of quality of life. Clinical meaningful improvement change from baseline less than or equal to -15 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
PGM=DEVOPS/SAR650984/EFC15246/CIR_RWE/REPORT/PGM/eff_qlq_km_i_f.sas OUT=REPORT/OUTPUT/eff_km_c30_rol_imp15pl_de_i_f_x.rtf (07APR2021 14:23)

16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Role functioning
16.2.6.1.2.1 Efficacy response data
16.2.6.1.2.1.21 QLQ-C30 - Time until permanent deterioration by 15 pt in Role functioning (LOCF) - ITT population

First permanent deterioration 15 points Role functioning (%)	**Kd (N=123)**	**IKd (N=179)**
Number (%) of events	41 (33.3)	59 (33.0)
Number (%) of patients censored	82 (66.7)	120 (67.0)
Kaplan-Meier estimates of Role functioning in months		
25% quantile (95% CI)	11.50 (6.374 to 19.450)	14.00 (7.951 to 18.464)
Median (95% CI)	NC (23.129 to NC)	NC (22.669 to NC)
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)
Comparison vs. Kd		
Stratified[a] Log-Rank test p-value[b] vs Kd	-	0.9314
Stratified[a] Hazard ratio (95% CI) vs Kd	-	1.02 (0.68 to 1.52)
P-value	-	0.9315
Deterioration probability (95% CI)[c]		
3 Months	0.909 (0.841 to 0.948)	0.897 (0.841 to 0.934)
6 Months	0.832 (0.751 to 0.888)	0.839 (0.775 to 0.886)

A lower score represents a better level of quality of life. Clinical meaningful deterioration change from baseline greater than or equal to 15 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] Stratified on number of prior lines of therapy (1 vs. >1) and Revised International Staging System (R-ISS) stage (I or II vs. III vs. not classified) according to IRT
[b] One-sided significance level is 0.025
[c] Estimated using the Kaplan-Meier method
NA/NC = Not Applicable / Not Calculable
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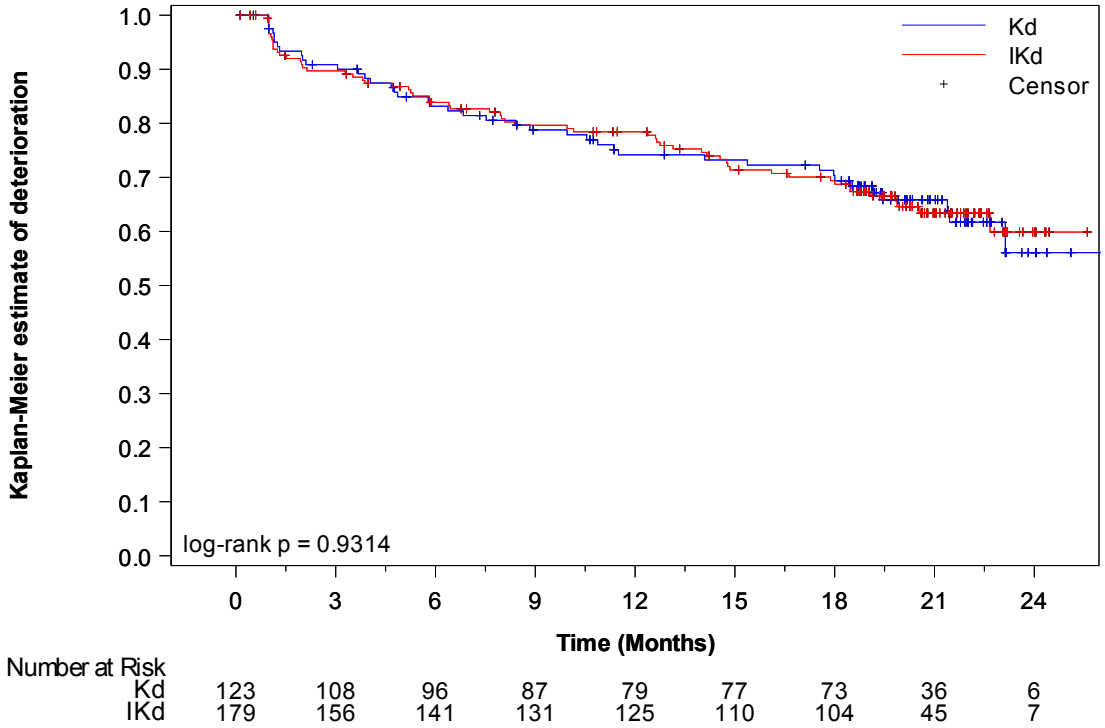
16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Role functioning
16.2.6.1.2.1 Efficacy response data
16.2.6.1.2.1.22 QLQ-C30 - Time until permanent deterioration by 15 pt in Role functioning - Kaplan-Meier curve (LOCF) - ITT population



A lower score represents a better level of quality of life. Clinical meaningful deterioration change from baseline greater than or equal to 15 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
PGM=DEVOPS/SAR650984/EFC15246/CIR_RWE/REPORT/PGM/eff_qlq_km_i_f.sas OUT=REPORT/OUTPUT/eff_km_c30_rol_det15pl_de_i_f_x.rtf (07APR2021 14:23)

16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Role functioning
16.2.6.1.2.2 Efficacy response data - Subgroup analyses by age
16.2.6.1.2.2.3 QLQ-C30 - Time to first improvement by 10 pt in role functioning according to age (LOCF) - ITT population

	<65 years		>=65 years		
	Kd (N=66)	**IKd (N=88)**	**Kd (N=57)**	**IKd (N=91)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	28 (42.4)	45 (51.1)	25 (43.9)	46 (50.5)	0.6434
Number (%) of patients censored	38 (57.6)	43 (48.9)	32 (56.1)	45 (49.5)	
Kaplan-Meier estimates of Role functioning in months					
25% quantile (95% CI)	1.91 (1.051 to 2.793)	1.05 (1.018 to 2.004)	1.12 (1.018 to 2.037)	1.63 (1.117 to 2.037)	
Median (95% CI)	NC (3.713 to NC)	5.55 (2.793 to NC)	22.21 (2.037 to NC)	9.66 (2.825 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.2373		0.5854	
Hazard ratio (95% CI) vs Kd	-	1.33 (0.83 to 2.13)		1.15 (0.70 to 1.86)	
P-value	-	0.2389		0.5857	
Improvement probability (95% CI)[b]					

A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
PGM=DEVOPS/SAR650984/EFC15246/CIR_RWE/REPORT/PGM/eff_km_subgp_sr_sig_de_i_t.sas OUT=REPORT/OUTPUT/eff_km_c30_rol_impl_age_de_i_t_x.rtf (07APR2021 14:23)

16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Role functioning
16.2.6.1.2.2 Efficacy response data - Subgroup analyses by age
16.2.6.1.2.2.4 QLQ-C30 - Time to first deterioration by 10 pt in role functioning according to age (LOCF) - ITT population

	<65 years		>=65 years		
	Kd (N=66)	**IKd (N=88)**	**Kd (N=57)**	**IKd (N=91)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	35 (53.0)	51 (58.0)	34 (59.6)	60 (65.9)	0.5243
Number (%) of patients censored	31 (47.0)	37 (42.0)	23 (40.4)	31 (34.1)	
Kaplan-Meier estimates of Role functioning in months					
25% quantile (95% CI)	2.00 (1.117 to 3.055)	2.53 (1.216 to 3.713)	2.00 (1.150 to 3.055)	1.20 (1.051 to 1.971)	
Median (95% CI)	7.39 (3.778 to NC)	10.22 (3.811 to 16.854)	5.59 (3.055 to NC)	5.13 (2.858 to 8.345)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (17.971 to NC)	NC (10.579 to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.8742		0.3039	
Hazard ratio (95% CI) vs Kd	-	1.04 (0.67 to 1.59)		1.25 (0.82 to 1.90)	
P-value	-	0.8746		0.3049	
Deterioration probability (95% CI)[b]					

A higher score represents a better level of quality of life. Clinical meaningful deterioration change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
PGM=DEVOPS/SAR650984/EFC15246/CIR_RWE/REPORT/PGM/eff_km_subgp_sr_sig_de_i_t.sas OUT=REPORT/OUTPUT/eff_km_c30_rol_detl_age_de_i_t_x.rtf (07APR2021 14:23)

16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Role functioning
16.2.6.1.2.2 Efficacy response data - Subgroup analyses by age
16.2.6.1.2.2.5 QLQ-C30 - Time until permanent improvement by 10 pt in role functioning according to age (LOCF) - ITT population

	<65 years		>=65 years		
	Kd (N=66)	**IKd (N=88)**	**Kd (N=57)**	**IKd (N=91)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	16 (24.2)	24 (27.3)	12 (21.1)	19 (20.9)	0.6898
Number (%) of patients censored	50 (75.8)	64 (72.7)	45 (78.9)	72 (79.1)	
Kaplan-Meier estimates of Role functioning in months					
25% quantile (95% CI)	20.76 (4.271 to NC)	16.89 (8.345 to NC)	NC (1.938 to NC)	23.36 (13.634 to NC)	
Median (95% CI)	NC (22.144 to NC)	NC (NC to NC)	NC (NC to NC)	NC (23.359 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.6508		0.8703	
Hazard ratio (95% CI) vs Kd	-	1.16 (0.61 to 2.18)		0.94 (0.46 to 1.94)	
P-value	-	0.6511		0.8703	
Improvement probability (95% CI)[b]					

A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
PGM=DEVOPS/SAR650984/EFC15246/CIR_RWE/REPORT/PGM/eff_km_subgp_sr_sig_de_i_t.sas OUT=REPORT/OUTPUT/eff_km_c30_rol_imppl_age_de_i_t_x.rtf (07APR2021 14:23)

16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Role functioning
16.2.6.1.2.2 Efficacy response data - Subgroup analyses by age
16.2.6.1.2.2.6 QLQ-C30 - Time until permanent deterioration by 10 pt in role functioning according to age (LOCF) - ITT population

	<65 years		>=65 years		
	Kd (N=66)	**IKd (N=88)**	**Kd (N=57)**	**IKd (N=91)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	20 (30.3)	26 (29.5)	21 (36.8)	33 (36.3)	0.8971
Number (%) of patients censored	46 (69.7)	62 (70.5)	36 (63.2)	58 (63.7)	
Kaplan-Meier estimates of Role functioning in months					
25% quantile (95% CI)	15.38 (7.524 to 21.454)	14.16 (4.731 to NC)	6.37 (3.055 to 19.450)	14.00 (7.622 to 18.464)	
Median (95% CI)	NC (21.388 to NC)	NC (NC to NC)	23.13 (19.450 to NC)	NC (20.534 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (23.129 to NC)	NC (NC to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.9782		0.8840	
Hazard ratio (95% CI) vs Kd	-	1.01 (0.56 to 1.81)		0.96 (0.56 to 1.66)	
P-value	-	0.9783		0.8835	
Deterioration probability (95% CI)[b]					

A higher score represents a better level of quality of life. Clinical meaningful deterioration change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Role functioning
16.2.6.1.2.3 Efficacy response data - Subgroup analyses by gender
16.2.6.1.2.3.3 QLQ-C30 - Time to first improvement by 10 pt in role functioning according to gender (LOCF) - ITT population

	Male		Female		
	Kd (N=68)	**IKd (N=101)**	**Kd (N=55)**	**IKd (N=78)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	23 (33.8)	48 (47.5)	30 (54.5)	43 (55.1)	0.1602
Number (%) of patients censored	45 (66.2)	53 (52.5)	25 (45.5)	35 (44.9)	
Kaplan-Meier estimates of Role functioning in months					
25% quantile (95% CI)	1.97 (1.117 to 18.793)	1.41 (1.051 to 2.004)	1.05 (0.986 to 1.971)	1.15 (1.018 to 2.037)	
Median (95% CI)	NC (NC to NC)	12.39 (2.825 to NC)	3.75 (1.971 to NC)	5.82 (2.398 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (22.209 to NC)	NC (NC to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.0728		0.9093	
Hazard ratio (95% CI) vs Kd	-	1.57 (0.96 to 2.58)		0.97 (0.61 to 1.55)	
P-value	-	0.0753		0.9091	
Improvement probability (95% CI)[b]					

A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
PGM=DEVOPS/SAR650984/EFC15246/CIR_RWE/REPORT/PGM/eff_km_subgp_sr_sig_de_i_t.sas OUT=REPORT/OUTPUT/eff_km_c30_rol_impl_sex_de_i_t_x.rtf (07APR2021 14:23)

16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Role functioning
16.2.6.1.2.3 Efficacy response data - Subgroup analyses by gender
16.2.6.1.2.3.4 QLQ-C30 - Time to first deterioration by 10 pt in role functioning according to gender (LOCF) - ITT population

	Male		Female		
	Kd (N=68)	**IKd (N=101)**	**Kd (N=55)**	**IKd (N=78)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	41 (60.3)	62 (61.4)	28 (50.9)	49 (62.8)	0.4517
Number (%) of patients censored	27 (39.7)	39 (38.6)	27 (49.1)	29 (37.2)	
Kaplan-Meier estimates of Role functioning in months					
25% quantile (95% CI)	2.00 (1.150 to 3.055)	1.87 (1.117 to 2.793)	2.00 (1.051 to 3.778)	1.97 (1.051 to 2.990)	
Median (95% CI)	4.96 (3.745 to 17.971)	5.65 (2.957 to 12.156)	7.59 (3.778 to NC)	7.66 (3.318 to 13.207)	
75% quantile (95% CI)	NC (21.454 to NC)	NC (16.854 to NC)	NC (NC to NC)	NC (13.996 to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.9012		0.2818	
Hazard ratio (95% CI) vs Kd	-	1.03 (0.69 to 1.52)		1.29 (0.81 to 2.05)	
P-value	-	0.9015		0.2831	
Deterioration probability (95% CI)[b]					

A higher score represents a better level of quality of life. Clinical meaningful deterioration change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
PGM=DEVOPS/SAR650984/EFC15246/CIR_RWE/REPORT/PGM/eff_km_subgp_sr_sig_de_i_t.sas OUT=REPORT/OUTPUT/eff_km_c30_rol_detl_sex_de_i_t_x.rtf (07APR2021 14:23)

16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Role functioning
16.2.6.1.2.3 Efficacy response data - Subgroup analyses by gender
16.2.6.1.2.3.5 QLQ-C30 - Time until permanent improvement by 10 pt in role functioning according to gender (LOCF) - ITT population

	Male		Female		
	Kd (N=68)	**IKd (N=101)**	**Kd (N=55)**	**IKd (N=78)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	13 (19.1)	23 (22.8)	15 (27.3)	20 (25.6)	0.4283
Number (%) of patients censored	55 (80.9)	78 (77.2)	40 (72.7)	58 (74.4)	
Kaplan-Meier estimates of Role functioning in months					
25% quantile (95% CI)	22.14 (6.932 to NC)	19.81 (10.316 to NC)	13.90 (1.938 to NC)	19.38 (12.320 to NC)	
Median (95% CI)	NC (22.144 to NC)	NC (NC to NC)	NC (NC to NC)	NC (23.359 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.5192		0.6102	
Hazard ratio (95% CI) vs Kd	-	1.25 (0.63 to 2.47)		0.84 (0.43 to 1.64)	
P-value	-	0.5201		0.6106	
Improvement probability (95% CI)[b]					

A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
PGM=DEVOPS/SAR650984/EFC15246/CIR_RWE/REPORT/PGM/eff_km_subgp_sr_sig_de_i_t.sas OUT=REPORT/OUTPUT/eff_km_c30_rol_imppl_sex_de_i_t_x.rtf (07APR2021 14:23)

16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Role functioning
16.2.6.1.2.3 Efficacy response data - Subgroup analyses by gender
16.2.6.1.2.3.6 QLQ-C30 - Time until permanent deterioration by 10 pt in role functioning according to gender (LOCF) - ITT population

	Male		Female		
	Kd (N=68)	**IKd (N=101)**	**Kd (N=55)**	**IKd (N=78)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	23 (33.8)	34 (33.7)	18 (32.7)	25 (32.1)	0.7770
Number (%) of patients censored	45 (66.2)	67 (66.3)	37 (67.3)	53 (67.9)	
Kaplan-Meier estimates of Role functioning in months					
25% quantile (95% CI)	11.37 (4.764 to 21.388)	12.65 (5.322 to 17.873)	17.54 (3.877 to 23.129)	14.78 (7.622 to 20.534)	
Median (95% CI)	NC (21.388 to NC)	NC (22.669 to NC)	NC (23.129 to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.8880		0.7860	
Hazard ratio (95% CI) vs Kd	-	1.04 (0.61 to 1.76)		0.92 (0.50 to 1.69)	
P-value	-	0.8884		0.7861	
Deterioration probability (95% CI)[b]					

A higher score represents a better level of quality of life. Clinical meaningful deterioration change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
PGM=DEVOPS/SAR650984/EFC15246/CIR_RWE/REPORT/PGM/eff_km_subgp_sr_sig_de_i_t.sas OUT=REPORT/OUTPUT/eff_km_c30_rol_detpl_sex_de_i_t_x.rtf (07APR2021 14:23)

16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Role functioning
16.2.6.1.2.4 Efficacy response data - Subgroup analyses by ethnic origin
16.2.6.1.2.4.3 QLQ-C30 - Time to first improvement by 10 pt in role functioning according to ethnic origin (LOCF) - ITT population

	White		Other		
	Kd (N=83)	**IKd (N=131)**	**Kd (N=28)**	**IKd (N=34)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	36 (43.4)	68 (51.9)	13 (46.4)	18 (52.9)	0.8531
Number (%) of patients censored	47 (56.6)	63 (48.1)	15 (53.6)	16 (47.1)	
Kaplan-Meier estimates of Role functioning in months					
25% quantile (95% CI)	1.91 (1.051 to 1.971)	1.35 (1.051 to 2.103)	1.12 (0.986 to 2.136)	1.05 (0.953 to 1.906)	
Median (95% CI)	NC (3.285 to NC)	6.70 (2.891 to NC)	NC (1.971 to NC)	2.96 (1.051 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.2686		0.4148	
Hazard ratio (95% CI) vs Kd	-	1.26 (0.84 to 1.88)		1.34 (0.66 to 2.75)	
P-value	-	0.2697		0.4165	
Improvement probability (95% CI)[b]					

A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
PGM=DEVOPS/SAR650984/EFC15246/CIR_RWE/REPORT/PGM/eff_km_subgp_sr_sig_de_i_t.sas OUT=REPORT/OUTPUT/eff_km_c30_rol_impl_race_de_i_t_x.rtf (07APR2021 14:23)

16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Role functioning
16.2.6.1.2.4 Efficacy response data - Subgroup analyses by ethnic origin
16.2.6.1.2.4.4 QLQ-C30 - Time to first deterioration by 10 pt in role functioning according to ethnic origin (LOCF) - ITT population

	White		Other		
	Kd (N=83)	**IKd (N=131)**	**Kd (N=28)**	**IKd (N=34)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	48 (57.8)	84 (64.1)	16 (57.1)	21 (61.8)	0.9345
Number (%) of patients censored	35 (42.2)	47 (35.9)	12 (42.9)	13 (38.2)	
Kaplan-Meier estimates of Role functioning in months					
25% quantile (95% CI)	2.00 (1.051 to 2.825)	1.87 (1.117 to 2.595)	1.28 (1.117 to 3.844)	1.54 (0.986 to 2.858)	
Median (95% CI)	5.59 (3.778 to 21.454)	5.65 (3.351 to 9.955)	6.70 (1.314 to NC)	5.80 (1.938 to 15.507)	
75% quantile (95% CI)	NC (NC to NC)	NC (15.474 to NC)	NC (17.971 to NC)	NC (13.207 to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.4352		0.5980	
Hazard ratio (95% CI) vs Kd	-	1.15 (0.81 to 1.64)		1.19 (0.62 to 2.28)	
P-value	-	0.4356		0.5984	
Deterioration probability (95% CI)[b]					

A higher score represents a better level of quality of life. Clinical meaningful deterioration change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
PGM=DEVOPS/SAR650984/EFC15246/CIR_RWE/REPORT/PGM/eff_km_subgp_sr_sig_de_i_t.sas OUT=REPORT/OUTPUT/eff_km_c30_rol_detl_race_de_i_t_x.rtf (07APR2021 14:23)

16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Role functioning
16.2.6.1.2.4 Efficacy response data - Subgroup analyses by ethnic origin
16.2.6.1.2.4.5 QLQ-C30 - Time until permanent improvement by 10 pt in role functioning according to ethnic origin (LOCF) - ITT population

	White		Other		
	Kd (N=83)	**IKd (N=131)**	**Kd (N=28)**	**IKd (N=34)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	19 (22.9)	30 (22.9)	7 (25.0)	11 (32.4)	0.5755
Number (%) of patients censored	64 (77.1)	101 (77.1)	21 (75.0)	23 (67.6)	
Kaplan-Meier estimates of Role functioning in months					
25% quantile (95% CI)	22.14 (4.304 to NC)	19.81 (12.320 to NC)	13.04 (1.117 to NC)	13.63 (0.953 to NC)	
Median (95% CI)	NC (NC to NC)	NC (23.359 to NC)	NC (13.043 to NC)	NC (16.887 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.9527		0.6013	
Hazard ratio (95% CI) vs Kd	-	0.98 (0.55 to 1.75)		1.29 (0.50 to 3.32)	
P-value	-	0.9526		0.6023	
Improvement probability (95% CI)[b]					

A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Role functioning
16.2.6.1.2.4 Efficacy response data - Subgroup analyses by ethnic origin
16.2.6.1.2.4.6 QLQ-C30 - Time until permanent deterioration by 10 pt in role functioning according to ethnic origin (LOCF) - ITT population

	White		Other		
	Kd (N=83)	**IKd (N=131)**	**Kd (N=28)**	**IKd (N=34)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	29 (34.9)	44 (33.6)	8 (28.6)	12 (35.3)	0.4719
Number (%) of patients censored	54 (65.1)	87 (66.4)	20 (71.4)	22 (64.7)	
Kaplan-Meier estimates of Role functioning in months					
25% quantile (95% CI)	11.37 (5.782 to 21.388)	14.55 (7.951 to 19.088)	15.38 (1.150 to NC)	6.41 (0.986 to NC)	
Median (95% CI)	NC (21.454 to NC)	NC (22.669 to NC)	NC (15.376 to NC)	NC (12.747 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.8920		0.5092	
Hazard ratio (95% CI) vs Kd	-	0.97 (0.61 to 1.55)		1.35 (0.55 to 3.30)	
P-value	-	0.8916		0.5108	
Deterioration probability (95% CI)[b]					

A higher score represents a better level of quality of life. Clinical meaningful deterioration change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Role functioning
16.2.6.1.2.5 Efficacy response data - Subgroup analyses by geographical region
16.2.6.1.2.5.3 QLQ-C30 - Time to first improvement by 10 pt in role functioning according to geographical region (LOCF) - ITT population

	Europe		America		Asia		Other countries		
	Kd (N=60)	**IKd (N=85)**	**Kd (N=20)**	**IKd (N=24)**	**Kd (N=21)**	**IKd (N=25)**	**Kd (N=22)**	**IKd (N=45)**	**p-value of treatment-by-subgroup interaction[c]**
Number (%) of events	26 (43.3)	42 (49.4)	9 (45.0)	14 (58.3)	11 (52.4)	15 (60.0)	7 (31.8)	20 (44.4)	0.8474
Number (%) of patients censored	34 (56.7)	43 (50.6)	11 (55.0)	10 (41.7)	10 (47.6)	10 (40.0)	15 (68.2)	25 (55.6)	
Kaplan-Meier estimates of event in months									
25% quantile (95% CI)	1.91 (1.018 to 2.793)	1.41 (1.051 to 2.398)	1.48 (0.953 to 2.858)	1.05 (0.953 to 1.051)	1.10 (0.986 to 2.037)	1.05 (0.953 to 1.906)	8.34 (1.018 to NC)	2.14 (1.051 to 5.585)	
Median (95% CI)	NC (2.793 to NC)	9.66 (2.858 to NC)	NC (1.051 to NC)	2.00 (1.051 to NC)	10.46 (1.084 to NC)	1.99 (1.051 to NC)	22.21 (8.345 to NC)	NC (3.417 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (2.530 to NC)	NC (18.793 to NC)	NC (2.957 to NC)	NC (22.209 to NC)	NC (NC to NC)	

A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Role functioning
16.2.6.1.2.5 Efficacy response data - Subgroup analyses by geographical region
16.2.6.1.2.5.3 QLQ-C30 - Time to first improvement by 10 pt in role functioning according to geographical region (LOCF) - ITT population

	Europe		America		Asia		Other countries		
	Kd (N=60)	**IKd (N=85)**	**Kd (N=20)**	**IKd (N=24)**	**Kd (N=21)**	**IKd (N=25)**	**Kd (N=22)**	**IKd (N=45)**	**p-value of treatment-by-subgroup interaction[c]**
Comparison vs. Kd									
Log-Rank test p-value[a] vs Kd	-	0.6091		0.2967		0.5005		0.3026	
Hazard ratio (95% CI) vs Kd	-	1.14 (0.70 to 1.85)		1.56 (0.67 to 3.61)		1.31 (0.60 to 2.85)		1.57 (0.66 to 3.71)	
P-value	-	0.6093		0.3006		0.5017		0.3069	
Improvement probability (95% CI)[b]									
3 Months	0.379 (0.256 to 0.502)	0.425 (0.317 to 0.528)	0.450 (0.231 to 0.647)	0.575 (0.348 to 0.749)	0.500 (0.271 to 0.692)	0.583 (0.364 to 0.750)	0.182 (0.057 to 0.363)	0.311 (0.184 to 0.447)	

A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Role functioning
16.2.6.1.2.5 Efficacy response data - Subgroup analyses by geographical region
16.2.6.1.2.5.4 QLQ-C30 - Time to first deterioration by 10 pt in role functioning according to geographical region (LOCF) - ITT population

	Europe		America		Asia		Other countries		
	Kd (N=60)	**IKd (N=85)**	**Kd (N=20)**	**IKd (N=24)**	**Kd (N=21)**	**IKd (N=25)**	**Kd (N=22)**	**IKd (N=45)**	**p-value of treatment-by-subgroup interaction[c]**
Number (%) of events	29 (48.3)	51 (60.0)	11 (55.0)	14 (58.3)	11 (52.4)	15 (60.0)	18 (81.8)	31 (68.9)	0.6585
Number (%) of patients censored	31 (51.7)	34 (40.0)	9 (45.0)	10 (41.7)	10 (47.6)	10 (40.0)	4 (18.2)	14 (31.1)	
Kaplan-Meier estimates of event in months									
25% quantile (95% CI)	2.23 (1.051 to 4.895)	2.00 (1.150 to 2.957)	1.59 (0.986 to 3.778)	1.61 (1.051 to 3.778)	1.13 (1.051 to 3.844)	1.12 (0.986 to 2.825)	2.23 (0.986 to 3.877)	1.94 (1.117 to 3.713)	
Median (95% CI)	9.00 (4.895 to NC)	5.65 (3.055 to 15.474)	6.19 (1.281 to NC)	7.43 (2.037 to NC)	8.34 (1.117 to NC)	5.80 (1.117 to NC)	3.99 (2.234 to 5.651)	7.62 (2.891 to 9.955)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (7.589 to NC)	NC (7.425 to NC)	NC (9.988 to NC)	NC (13.207 to NC)	17.97 (4.041 to NC)	NC (9.363 to NC)	

A higher score represents a better level of quality of life. Clinical meaningful deterioration change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Role functioning
16.2.6.1.2.5 Efficacy response data - Subgroup analyses by geographical region
16.2.6.1.2.5.4 QLQ-C30 - Time to first deterioration by 10 pt in role functioning according to geographical region (LOCF) - ITT population

	Europe		America		Asia		Other countries		
	Kd (N=60)	**IKd (N=85)**	**Kd (N=20)**	**IKd (N=24)**	**Kd (N=21)**	**IKd (N=25)**	**Kd (N=22)**	**IKd (N=45)**	**p-value of treatment-by-subgroup interaction[c]**
Comparison vs. Kd									
Log-Rank test p-value[a] vs Kd	-	0.2756		0.7844		0.5688		0.4189	
Hazard ratio (95% CI) vs Kd	-	1.29 (0.82 to 2.03)		1.12 (0.51 to 2.46)		1.25 (0.58 to 2.73)		0.79 (0.44 to 1.41)	
P-value	-	0.2769		0.7845		0.5696		0.4200	
Deterioration probability (95% CI)[b]									
3 Months	0.690 (0.554 to 0.792)	0.627 (0.513 to 0.721)	0.600 (0.357 to 0.776)	0.598 (0.369 to 0.768)	0.600 (0.357 to 0.776)	0.542 (0.327 to 0.714)	0.682 (0.446 to 0.834)	0.644 (0.487 to 0.765)	
6 Months	0.558 (0.419 to 0.677)	0.479 (0.368 to 0.582)	0.500 (0.271 to 0.692)	0.506 (0.288 to 0.690)	0.550 (0.313 to 0.735)	0.500 (0.291 to 0.678)	0.273 (0.111 to 0.464)	0.506 (0.352 to 0.642)	

A higher score represents a better level of quality of life. Clinical meaningful deterioration change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Role functioning
16.2.6.1.2.5 Efficacy response data - Subgroup analyses by geographical region
16.2.6.1.2.5.5 QLQ-C30 - Time until permanent improvement by 10 pt in role functioning according to geographical region (LOCF) - ITT population

	Europe		America		Asia		Other countries		
	Kd (N=60)	**IKd (N=85)**	**Kd (N=20)**	**IKd (N=24)**	**Kd (N=21)**	**IKd (N=25)**	**Kd (N=22)**	**IKd (N=45)**	**p-value of treatment-by-subgroup interaction[c]**
Number (%) of events	14 (23.3)	18 (21.2)	4 (20.0)	10 (41.7)	6 (28.6)	8 (32.0)	4 (18.2)	7 (15.6)	0.4522
Number (%) of patients censored	46 (76.7)	67 (78.8)	16 (80.0)	14 (58.3)	15 (71.4)	17 (68.0)	18 (81.8)	38 (84.4)	
Kaplan-Meier estimates of event in months									
25% quantile (95% CI)	20.76 (4.304 to NC)	23.36 (16.854 to NC)	NC (0.953 to NC)	8.90 (0.953 to 18.366)	9.56 (1.117 to NC)	15.51 (0.953 to NC)	22.14 (1.018 to NC)	NC (10.480 to NC)	
Median (95% CI)	NC (NC to NC)	NC (23.359 to NC)	NC (NC to NC)	NC (8.903 to NC)	NC (9.561 to NC)	NC (15.507 to NC)	NC (22.144 to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	

A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Role functioning
16.2.6.1.2.5 Efficacy response data - Subgroup analyses by geographical region
16.2.6.1.2.5.5 QLQ-C30 - Time until permanent improvement by 10 pt in role functioning according to geographical region (LOCF) - ITT population

	Europe		America		Asia		Other countries		
	Kd (N=60)	**IKd (N=85)**	**Kd (N=20)**	**IKd (N=24)**	**Kd (N=21)**	**IKd (N=25)**	**Kd (N=22)**	**IKd (N=45)**	**p-value of treatment-by-subgroup interaction[c]**
Comparison vs. Kd									
Log-Rank test p-value[a] vs Kd	-	0.6384		0.1243		0.9139		0.8624	
Hazard ratio (95% CI) vs Kd	-	0.85 (0.42 to 1.70)		2.42 (0.76 to 7.74)		1.06 (0.37 to 3.06)		0.90 (0.26 to 3.09)	
P-value	-	0.6388		0.1365		0.9142		0.8625	
Improvement probability (95% CI)[b]									
3 Months	0.121 (0.053 to 0.219)	0.061 (0.022 to 0.126)	0.150 (0.037 to 0.335)	0.172 (0.054 to 0.347)	0.153 (0.038 to 0.340)	0.167 (0.052 to 0.337)	0.136 (0.034 to 0.309)	0.044 (0.008 to 0.133)	

A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Role functioning
16.2.6.1.2.5 Efficacy response data - Subgroup analyses by geographical region
16.2.6.1.2.5.6 QLQ-C30 - Time until permanent deterioration by 10 pt in role functioning according to geographical region (LOCF) - ITT population

	Europe		America		Asia		Other countries		
	Kd (N=60)	**IKd (N=85)**	**Kd (N=20)**	**IKd (N=24)**	**Kd (N=21)**	**IKd (N=25)**	**Kd (N=22)**	**IKd (N=45)**	**p-value of treatment-by-subgroup interaction[c]**
Number (%) of events	16 (26.7)	27 (31.8)	7 (35.0)	4 (16.7)	6 (28.6)	11 (44.0)	12 (54.5)	17 (37.8)	0.3626
Number (%) of patients censored	44 (73.3)	58 (68.2)	13 (65.0)	20 (83.3)	15 (71.4)	14 (56.0)	10 (45.5)	28 (62.2)	
Kaplan-Meier estimates of event in months									
25% quantile (95% CI)	18.46 (4.665 to NC)	14.85 (8.082 to 22.669)	15.38 (0.986 to NC)	NC (1.117 to NC)	10.55 (1.117 to NC)	3.56 (0.986 to 14.784)	6.37 (1.150 to 17.971)	7.95 (3.877 to 19.088)	
Median (95% CI)	NC (NC to NC)	NC (22.669 to NC)	NC (15.376 to NC)	NC (19.844 to NC)	NC (10.546 to NC)	NC (5.191 to NC)	21.45 (6.374 to NC)	NC (17.873 to NC)	

A higher score represents a better level of quality of life. Clinical meaningful deterioration change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Role functioning
16.2.6.1.2.5 Efficacy response data - Subgroup analyses by geographical region
16.2.6.1.2.5.6 QLQ-C30 - Time until permanent deterioration by 10 pt in role functioning according to geographical region (LOCF) - ITT population

	Europe		America		Asia		Other countries		
	Kd (N=60)	**IKd (N=85)**	**Kd (N=20)**	**IKd (N=24)**	**Kd (N=21)**	**IKd (N=25)**	**Kd (N=22)**	**IKd (N=45)**	**p-value of treatment-by-subgroup interaction[c]**
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	23.13 (21.454 to NC)	NC (NC to NC)	
Comparison vs. Kd									
Log-Rank test p-value[a] vs Kd	-	0.6969		0.2894		0.3278		0.3843	
Hazard ratio (95% CI) vs Kd	-	1.13 (0.61 to 2.10)		0.52 (0.15 to 1.78)		1.64 (0.60 to 4.43)		0.72 (0.34 to 1.51)	
P-value	-	0.6971		0.2979		0.3326		0.3864	
Deterioration probability (95% CI)[b]									

A higher score represents a better level of quality of life. Clinical meaningful deterioration change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Role functioning
16.2.6.1.2.6 Efficacy response data - Subgroup analyses by regulatory region
16.2.6.1.2.6.3 QLQ-C30 - Time to first improvement by 10 pt in role functioning according to regulatory region (LOCF) - ITT population

	Western countries		Other countries		
	Kd (N=55)	**IKd (N=97)**	**Kd (N=68)**	**IKd (N=82)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	27 (49.1)	46 (47.4)	26 (38.2)	45 (54.9)	0.0642
Number (%) of patients censored	28 (50.9)	51 (52.6)	42 (61.8)	37 (45.1)	
Kaplan-Meier estimates of Role functioning in months					
25% quantile (95% CI)	1.91 (1.051 to 2.793)	1.91 (1.150 to 2.825)	1.91 (1.051 to 2.136)	1.05 (0.986 to 1.840)	
Median (95% CI)	9.89 (2.793 to NC)	NC (5.552 to NC)	NC (2.858 to NC)	2.89 (1.971 to NC)	
75% quantile (95% CI)	NC (22.209 to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.6902		0.0370	
Hazard ratio (95% CI) vs Kd	-	0.91 (0.56 to 1.46)		1.66 (1.03 to 2.70)	
P-value	-	0.6903		0.0390	
Hazard ratio inverted (95% CI) vs IKd		-		0.60 (0.37 to 0.97)	

A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Role functioning
16.2.6.1.2.6 Efficacy response data - Subgroup analyses by regulatory region
16.2.6.1.2.6.4 QLQ-C30 - Time to first deterioration by 10 pt in role functioning according to regulatory region (LOCF) - ITT population

	Western countries		Other countries		
	Kd (N=55)	**IKd (N=97)**	**Kd (N=68)**	**IKd (N=82)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	26 (47.3)	59 (60.8)	43 (63.2)	52 (63.4)	0.3649
Number (%) of patients censored	29 (52.7)	38 (39.2)	25 (36.8)	30 (36.6)	
Kaplan-Meier estimates of Role functioning in months					
25% quantile (95% CI)	2.83 (2.004 to 5.618)	2.14 (1.314 to 2.891)	1.25 (1.117 to 2.234)	1.13 (0.986 to 2.037)	
Median (95% CI)	17.97 (4.961 to NC)	7.62 (3.515 to 13.996)	4.80 (2.793 to 9.988)	5.13 (2.858 to 11.565)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (21.454 to NC)	NC (13.306 to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.1770		0.8883	
Hazard ratio (95% CI) vs Kd	-	1.37 (0.86 to 2.18)		1.03 (0.69 to 1.54)	
P-value	-	0.1789		0.8884	
Deterioration probability (95% CI)[b]					

A higher score represents a better level of quality of life. Clinical meaningful deterioration change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Role functioning
16.2.6.1.2.6 Efficacy response data - Subgroup analyses by regulatory region
16.2.6.1.2.6.5 QLQ-C30 - Time until permanent improvement by 10 pt in role functioning according to regulatory region (LOCF) - ITT population

	Western countries		Other countries		
	Kd (N=55)	**IKd (N=97)**	**Kd (N=68)**	**IKd (N=82)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	17 (30.9)	18 (18.6)	11 (16.2)	25 (30.5)	0.0077
Number (%) of patients censored	38 (69.1)	79 (81.4)	57 (83.8)	57 (69.5)	
Kaplan-Meier estimates of Role functioning in months					
25% quantile (95% CI)	10.45 (1.117 to 22.144)	NC (12.320 to NC)	NC (13.043 to NC)	16.85 (3.844 to 23.359)	
Median (95% CI)	NC (22.144 to NC)	NC (NC to NC)	NC (NC to NC)	NC (23.359 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.0675		0.0486	
Hazard ratio (95% CI) vs Kd	-	0.54 (0.28 to 1.06)		2.01 (0.99 to 4.09)	
P-value	-	0.0717		0.0534	
Improvement probability (95% CI)[b]					

A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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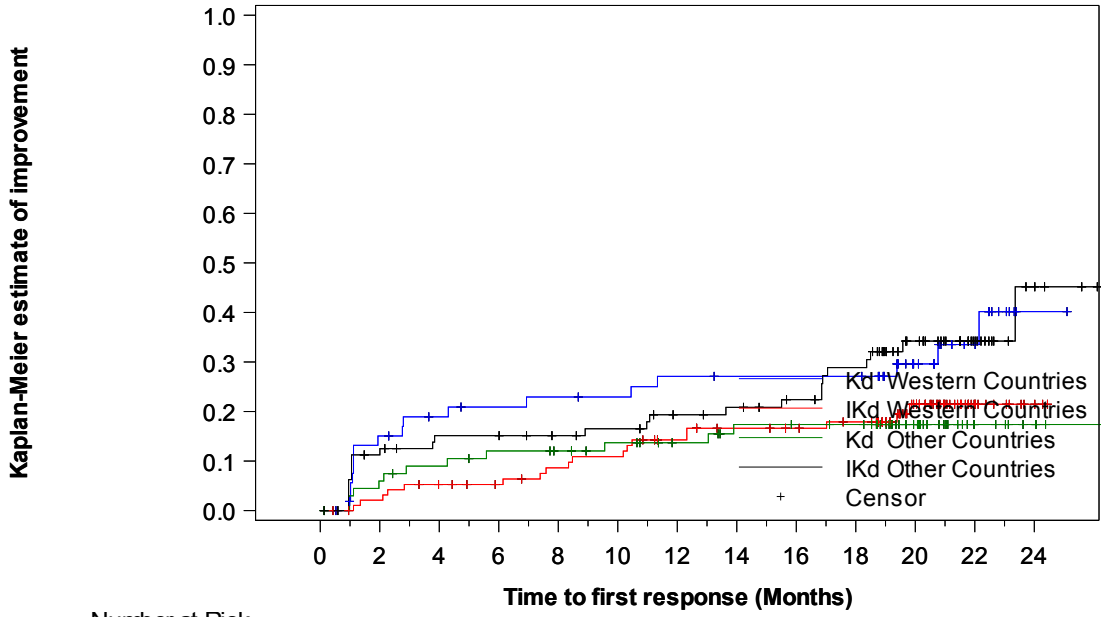
16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Role functioning
16.2.6.1.2.6 Efficacy response data - Subgroup analyses by regulatory region
16.2.6.1.2.6.6 QLQ-C30 - Time until permanent improvement by 10 pt in role functioning according to regulatory region- Kaplan-Meier curve (LOCF) - ITT population



Number at Risk									
Kd Western Countries	55	42	39	37	35	34	34	15	1
IKd Western Countries	97	90	85	79	73	68	63	23	3
Kd Other Countries	68	60	57	53	48	44	42	18	4
IKd Other Countries	82	67	65	60	55	51	44	22	4

A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
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16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Role functioning
16.2.6.1.2.6 Efficacy response data - Subgroup analyses by regulatory region
16.2.6.1.2.6.7 QLQ-C30 - Time until permanent deterioration by 10 pt in role functioning according to regulatory region (LOCF) - ITT population

	Western countries		Other countries		
	Kd (N=55)	**IKd (N=97)**	**Kd (N=68)**	**IKd (N=82)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	14 (25.5)	31 (32.0)	27 (39.7)	28 (34.1)	0.3072
Number (%) of patients censored	41 (74.5)	66 (68.0)	41 (60.3)	54 (65.9)	
Kaplan-Meier estimates of Role functioning in months					
25% quantile (95% CI)	19.15 (5.815 to NC)	14.75 (6.439 to 19.877)	9.95 (3.680 to 18.004)	12.62 (5.191 to 19.844)	
Median (95% CI)	23.13 (23.129 to NC)	NC (NC to NC)	NC (18.464 to NC)	NC (22.669 to NC)	
75% quantile (95% CI)	NC (23.129 to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.4288		0.5196	
Hazard ratio (95% CI) vs Kd	-	1.29 (0.69 to 2.42)		0.84 (0.50 to 1.43)	
P-value	-	0.4300		0.5201	
Deterioration probability (95% CI)[b]					

A higher score represents a better level of quality of life. Clinical meaningful deterioration change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Role functioning
16.2.6.1.2.7 Efficacy response data - Subgroup analyses by baseline ECOG PS
16.2.6.1.2.7.3 QLQ-C30 - Time to first improvement by 10 pt in role functioning according to baseline ECOG PS (LOCF) - ITT population

	0 or 1		>1		
	Kd (N=118)	**IKd (N=168)**	**Kd (N=5)**	**IKd (N=11)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	51 (43.2)	85 (50.6)	2 (40.0)	6 (54.5)	0.4482
Number (%) of patients censored	67 (56.8)	83 (49.4)	3 (60.0)	5 (45.5)	
Kaplan-Meier estimates of Role functioning in months					
25% quantile (95% CI)	1.91 (1.051 to 2.037)	1.15 (1.051 to 2.004)	2.79 (1.938 to NC)	1.22 (0.986 to 2.530)	
Median (95% CI)	NC (6.012 to NC)	6.83 (2.990 to NC)	NC (1.938 to NC)	2.53 (0.986 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (1.938 to NC)	NC (1.971 to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.3002		0.3196	
Hazard ratio (95% CI) vs Kd	-	1.20 (0.85 to 1.70)		2.21 (0.44 to 11.01)	
P-value	-	0.3009		0.3320	
Improvement probability (95% CI)[b]					

A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Role functioning
16.2.6.1.2.7 Efficacy response data - Subgroup analyses by baseline ECOG PS
16.2.6.1.2.7.4 QLQ-C30 - Time to first deterioration by 10 pt in role functioning according to baseline ECOG PS (LOCF) - ITT population

	0 or 1		>1		
	Kd (N=118)	**IKd (N=168)**	**Kd (N=5)**	**IKd (N=11)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	67 (56.8)	107 (63.7)	2 (40.0)	4 (36.4)	0.8682
Number (%) of patients censored	51 (43.2)	61 (36.3)	3 (60.0)	7 (63.6)	
Kaplan-Meier estimates of Role functioning in months					
25% quantile (95% CI)	2.00 (1.216 to 2.825)	1.94 (1.150 to 2.760)	2.07 (0.986 to NC)	1.61 (0.986 to NC)	
Median (95% CI)	5.65 (3.943 to 21.454)	5.75 (3.713 to 9.955)	NC (0.986 to NC)	NC (0.986 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (0.986 to NC)	NC (5.191 to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.3606		0.9416	
Hazard ratio (95% CI) vs Kd	-	1.15 (0.85 to 1.56)		1.07 (0.19 to 5.86)	
P-value	-	0.3610		0.9416	
Deterioration probability (95% CI)[b]					

A higher score represents a better level of quality of life. Clinical meaningful deterioration change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Role functioning
16.2.6.1.2.7 Efficacy response data - Subgroup analyses by baseline ECOG PS
16.2.6.1.2.7.5 QLQ-C30 - Time until permanent improvement by 10 pt in role functioning according to baseline ECOG PS (LOCF) - ITT population

	0 or 1		>1		
	Kd (N=118)	**IKd (N=168)**	**Kd (N=5)**	**IKd (N=11)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	26 (22.0)	39 (23.2)	2 (40.0)	4 (36.4)	0.9720
Number (%) of patients censored	92 (78.0)	129 (76.8)	3 (60.0)	7 (63.6)	
Kaplan-Meier estimates of Role functioning in months					
25% quantile (95% CI)	22.14 (9.561 to NC)	19.81 (15.507 to NC)	2.79 (1.938 to NC)	10.18 (2.825 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (1.938 to NC)	NC (2.825 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (1.938 to NC)	NC (18.366 to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.9138		0.8388	
Hazard ratio (95% CI) vs Kd	-	1.03 (0.63 to 1.69)		0.84 (0.15 to 4.60)	
P-value	-	0.9140		0.8390	
Improvement probability (95% CI)[b]					

A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Role functioning
16.2.6.1.2.7 Efficacy response data - Subgroup analyses by baseline ECOG PS
16.2.6.1.2.7.6 QLQ-C30 - Time until permanent deterioration by 10 pt in role functioning according to baseline ECOG PS (LOCF) - ITT population

	0 or 1		>1		
	Kd (N=118)	**IKd (N=168)**	**Kd (N=5)**	**IKd (N=11)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	39 (33.1)	56 (33.3)	2 (40.0)	3 (27.3)	0.4445
Number (%) of patients censored	79 (66.9)	112 (66.7)	3 (60.0)	8 (72.7)	
Kaplan-Meier estimates of Role functioning in months					
25% quantile (95% CI)	11.50 (6.834 to 19.450)	14.00 (7.622 to 18.464)	4.76 (0.986 to NC)	16.62 (5.191 to NC)	
Median (95% CI)	NC (23.129 to NC)	NC (22.669 to NC)	NC (0.986 to NC)	NC (5.191 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (0.986 to NC)	NC (16.624 to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.9274		0.4212	
Hazard ratio (95% CI) vs Kd	-	1.02 (0.68 to 1.53)		0.48 (0.08 to 2.97)	
P-value	-	0.9275		0.4306	
Deterioration probability (95% CI)[b]					

A higher score represents a better level of quality of life. Clinical meaningful deterioration change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Role functioning
16.2.6.1.2.8 Efficacy response data - Subgroup analyses by ISS staging at SE
16.2.6.1.2.8.3 QLQ-C30 - Time to first improvement by 10 pt in role functioning according to ISS staging at SE (LOCF) - ITT population

	I		II		III		
	Kd (N=71)	**IKd (N=89)**	**Kd (N=31)**	**IKd (N=63)**	**Kd (N=20)**	**IKd (N=26)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	30 (42.3)	38 (42.7)	15 (48.4)	37 (58.7)	8 (40.0)	15 (57.7)	0.3981
Number (%) of patients censored	41 (57.7)	51 (57.3)	16 (51.6)	26 (41.3)	12 (60.0)	11 (42.3)	
Kaplan-Meier estimates of Role functioning in months							
25% quantile (95% CI)	1.91 (1.051 to 3.285)	1.91 (1.051 to 2.891)	1.12 (1.018 to 2.136)	1.12 (1.018 to 2.004)	1.97 (0.953 to 6.012)	1.05 (0.953 to 2.004)	
Median (95% CI)	NC (3.778 to NC)	NC (5.815 to NC)	NC (1.906 to NC)	5.55 (2.037 to NC)	NC (1.971 to NC)	2.14 (1.051 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (2.825 to NC)	
Comparison vs. Kd							
Log-Rank test p-value[a] vs Kd	-	0.9870		0.4865		0.1103	
Hazard ratio (95% CI) vs Kd	-	1.00 (0.62 to 1.62)		1.24 (0.68 to 2.25)		1.99 (0.84 to 4.72)	
P-value	-	0.9870		0.4873		0.1173	

A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Role functioning
16.2.6.1.2.8 Efficacy response data - Subgroup analyses by ISS staging at SE
16.2.6.1.2.8.4 QLQ-C30 - Time to first deterioration by 10 pt in role functioning according to ISS staging at SE (LOCF) - ITT population

	I		II		III		
	Kd (N=71)	**IKd (N=89)**	**Kd (N=31)**	**IKd (N=63)**	**Kd (N=20)**	**IKd (N=26)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	42 (59.2)	62 (69.7)	17 (54.8)	40 (63.5)	9 (45.0)	9 (34.6)	0.5212
Number (%) of patients censored	29 (40.8)	27 (30.3)	14 (45.2)	23 (36.5)	11 (55.0)	17 (65.4)	
Kaplan-Meier estimates of Role functioning in months							
25% quantile (95% CI)	2.79 (1.906 to 3.778)	1.91 (1.117 to 2.760)	1.31 (0.986 to 2.825)	1.87 (1.051 to 2.891)	1.15 (0.953 to 9.002)	2.53 (0.953 to NC)	
Median (95% CI)	5.62 (3.877 to 21.454)	5.55 (2.990 to 7.622)	5.82 (2.070 to NC)	9.36 (3.318 to 13.996)	17.97 (1.150 to NC)	NC (2.891 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (10.579 to NC)	NC (NC to NC)	NC (13.996 to NC)	NC (17.971 to NC)	NC (NC to NC)	
Comparison vs. Kd							
Log-Rank test p-value[a] vs Kd	-	0.1801		0.6702		0.5113	
Hazard ratio (95% CI) vs Kd	-	1.31 (0.88 to 1.93)		1.13 (0.64 to 2.00)		0.73 (0.29 to 1.85)	
P-value	-	0.1814		0.6704		0.5130	

A higher score represents a better level of quality of life. Clinical meaningful deterioration change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
PGM=DEVOPS/SAR650984/EFC15246/CIR_RWE/REPORT/PGM/eff_km_subgp_sr_sig_de_i_t.sas OUT=REPORT/OUTPUT/eff_km_c30_rol_detl_seiss_de_i_t_x.rtf (07APR2021 14:23)

16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Role functioning
16.2.6.1.2.8 Efficacy response data - Subgroup analyses by ISS staging at SE
16.2.6.1.2.8.5 QLQ-C30 - Time until permanent improvement by 10 pt in role functioning according to ISS staging at SE (LOCF) - ITT population

	I		II		III		
	Kd (N=71)	**IKd (N=89)**	**Kd (N=31)**	**IKd (N=63)**	**Kd (N=20)**	**IKd (N=26)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	15 (21.1)	16 (18.0)	9 (29.0)	19 (30.2)	4 (20.0)	8 (30.8)	0.4124
Number (%) of patients censored	56 (78.9)	73 (82.0)	22 (71.0)	44 (69.8)	16 (80.0)	18 (69.2)	
Kaplan-Meier estimates of Role functioning in months							
25% quantile (95% CI)	NC (6.932 to NC)	NC (16.887 to NC)	11.33 (1.117 to NC)	18.37 (8.903 to NC)	NC (1.938 to NC)	3.84 (0.953 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (22.144 to NC)	23.36 (23.359 to NC)	NC (13.043 to NC)	NC (3.844 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (23.359 to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Kd							
Log-Rank test p-value[a] vs Kd	-	0.5614		0.8102		0.2684	
Hazard ratio (95% CI) vs Kd	-	0.81 (0.40 to 1.64)		0.91 (0.41 to 2.02)		1.95 (0.58 to 6.50)	
P-value	-	0.5621		0.8103		0.2772	

A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Role functioning
16.2.6.1.2.8 Efficacy response data - Subgroup analyses by ISS staging at SE
16.2.6.1.2.8.6 QLQ-C30 - Time until permanent deterioration by 10 pt in role functioning according to ISS staging at SE (LOCF) - ITT population

	I		II		III		
	Kd (N=71)	**IKd (N=89)**	**Kd (N=31)**	**IKd (N=63)**	**Kd (N=20)**	**IKd (N=26)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	21 (29.6)	35 (39.3)	12 (38.7)	20 (31.7)	7 (35.0)	4 (15.4)	0.0856
Number (%) of patients censored	50 (70.4)	54 (60.7)	19 (61.3)	43 (68.3)	13 (65.0)	22 (84.6)	
Kaplan-Meier estimates of Role functioning in months							
25% quantile (95% CI)	19.15 (8.838 to 23.129)	8.38 (3.877 to 16.099)	6.37 (1.314 to 15.376)	14.55 (7.951 to NC)	6.83 (0.986 to NC)	22.67 (0.986 to 22.669)	
Median (95% CI)	NC (23.129 to NC)	NC (19.844 to NC)	NC (11.499 to NC)	NC (NC to NC)	NC (6.834 to NC)	22.67 (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	22.67 (NC to NC)	
Comparison vs. Kd							
Log-Rank test p-value[a] vs Kd	-	0.1511		0.3654		0.1519	
Hazard ratio (95% CI) vs Kd	-	1.48 (0.86 to 2.55)		0.72 (0.35 to 1.47)		0.42 (0.12 to 1.43)	
P-value	-	0.1538		0.3675		0.1648	

A higher score represents a better level of quality of life. Clinical meaningful deterioration change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Role functioning
16.2.6.1.2.9 Efficacy response data - Subgroup analyses by R-ISS stage at SE
16.2.6.1.2.9.3 QLQ-C30 - Time to first improvement by 10 pt in role functioning according to R-ISS stage at SE (LOCF) - ITT population

	I or II		III		Not classified		
	Kd (N=103)	**IKd (N=155)**	**Kd (N=8)**	**IKd (N=16)**	**Kd (N=12)**	**IKd (N=8)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	44 (42.7)	78 (50.3)	3 (37.5)	9 (56.3)	6 (50.0)	4 (50.0)	0.7403
Number (%) of patients censored	59 (57.3)	77 (49.7)	5 (62.5)	7 (43.8)	6 (50.0)	4 (50.0)	
Kaplan-Meier estimates of Role functioning in months							
25% quantile (95% CI)	1.91 (1.051 to 2.037)	1.15 (1.051 to 2.004)	1.97 (1.084 to NC)	1.22 (0.953 to 2.103)	1.91 (0.953 to 18.793)	1.91 (1.084 to 3.943)	
Median (95% CI)	NC (3.778 to NC)	10.18 (3.023 to NC)	NC (1.084 to NC)	2.10 (1.018 to NC)	NC (0.953 to NC)	3.04 (1.084 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (2.793 to NC)	NC (2.103 to NC)	NC (18.793 to NC)	NC (1.906 to NC)	
Comparison vs. Kd							
Log-Rank test p-value[a] vs Kd	-	0.3419		0.2984		0.6060	
Hazard ratio (95% CI) vs Kd	-	1.20 (0.83 to 1.73)		1.98 (0.53 to 7.32)		1.40 (0.39 to 4.98)	
P-value	-	0.3426		0.3076		0.6075	

A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Role functioning
16.2.6.1.2.9 Efficacy response data - Subgroup analyses by R-ISS stage at SE
16.2.6.1.2.9.4 QLQ-C30 - Time to first deterioration by 10 pt in role functioning according to R-ISS stage at SE (LOCF) - ITT population

	I or II		III		Not classified		
	Kd (N=103)	**IKd (N=155)**	**Kd (N=8)**	**IKd (N=16)**	**Kd (N=12)**	**IKd (N=8)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	57 (55.3)	107 (69.0)	4 (50.0)	3 (18.8)	8 (66.7)	1 (12.5)	0.0182
Number (%) of patients censored	46 (44.7)	48 (31.0)	4 (50.0)	13 (81.3)	4 (33.3)	7 (87.5)	
Kaplan-Meier estimates of Role functioning in months							
25% quantile (95% CI)	2.00 (1.248 to 2.825)	1.61 (1.117 to 2.136)	1.05 (0.953 to NC)	NC (1.906 to NC)	3.37 (0.986 to 3.844)	NC (0.986 to NC)	
Median (95% CI)	6.70 (4.041 to NC)	5.19 (3.023 to 7.622)	1.97 (0.953 to NC)	NC (9.363 to NC)	4.37 (1.150 to NC)	NC (0.986 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (14.784 to NC)	NC (1.117 to NC)	NC (NC to NC)	NC (3.844 to NC)	NC (NC to NC)	
Comparison vs. Kd							
Log-Rank test p-value[a] vs Kd	-	0.0785		0.0590		0.1008	
Hazard ratio (95% CI) vs Kd	-	1.33 (0.97 to 1.84)		0.26 (0.06 to 1.17)		0.21 (0.03 to 1.66)	
P-value	-	0.0796		0.0785		0.1376	

A higher score represents a better level of quality of life. Clinical meaningful deterioration change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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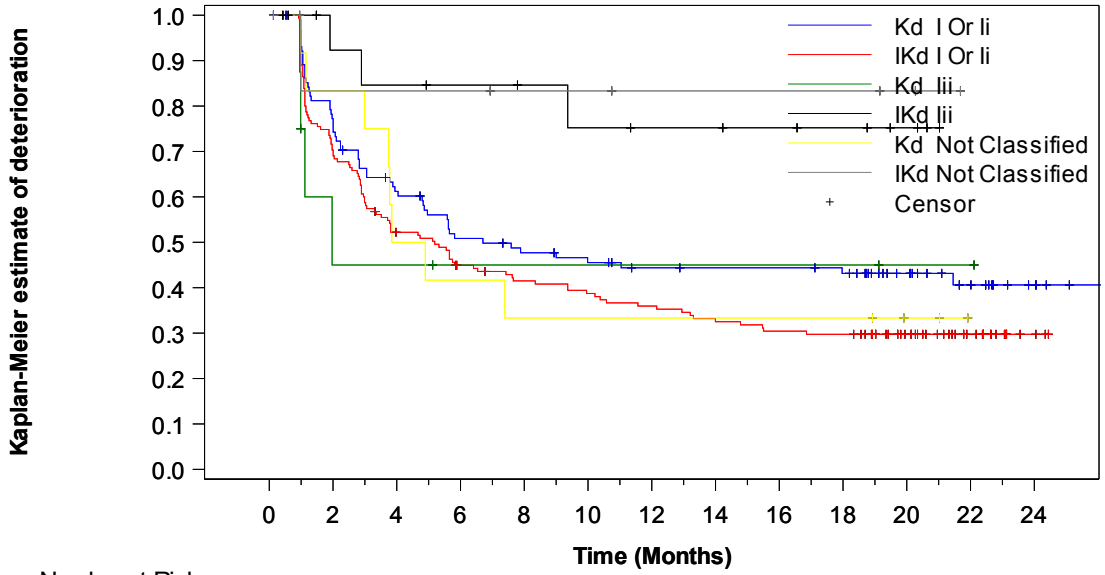
16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Role functioning
16.2.6.1.2.9 Efficacy response data - Subgroup analyses by R-ISS stage at SE
16.2.6.1.2.9.5 QLQ-C30 - Time to first deterioration by 10 pt in role functioning according to R-ISS stage at SE- Kaplan-Meier curve (LOCF) - ITT population



Number at Risk									
Kd I Or Ii	103	66	49	44	38	37	35	19	5
IKd I Or Ii	155	91	66	59	52	46	43	23	3
Kd Iii	8	3	2	2	2	2	2	1	0
IKd Iii	16	11	10	9	7	6	5	1	0
Kd Not Classified	12	9	5	4	4	4	4	2	0
IKd Not Classified	8	5	5	4	3	3	3	1	0

A higher score represents a better level of quality of life. Clinical meaningful deterioration change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
PGM=DEVOPS/SAR650984/EFC15246/CIR_RWE/REPORT/PGM/eff_qlq_km_subgp_de_i_f.sas OUT=REPORT/OUTPUT/eff_km_c30_rol_detl_seriss_de_i_f_x.rtf (07APR2021 15:13)

16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Role functioning
16.2.6.1.2.9 Efficacy response data - Subgroup analyses by R-ISS stage at SE
16.2.6.1.2.9.6 QLQ-C30 - Time until permanent improvement by 10 pt in role functioning according to R-ISS stage at SE (LOCF) - ITT population

	I or II		III		Not classified		
	Kd (N=103)	**IKd (N=155)**	**Kd (N=8)**	**IKd (N=16)**	**Kd (N=12)**	**IKd (N=8)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	22 (21.4)	38 (24.5)	3 (37.5)	5 (31.3)	3 (25.0)	0 (0.0)	0.9990
Number (%) of patients censored	81 (78.6)	117 (75.5)	5 (62.5)	11 (68.8)	9 (75.0)	8 (100.0)	
Kaplan-Meier estimates of Role functioning in months							
25% quantile (95% CI)	22.14 (4.304 to NC)	19.58 (15.507 to NC)	9.56 (2.793 to NC)	3.78 (0.953 to NC)	20.76 (6.932 to NC)	NC (NC to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (2.793 to NC)	NC (2.825 to NC)	NC (13.897 to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (9.561 to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Kd							
Log-Rank test p-value[a] vs Kd	-	0.8079		0.9572		0.2746	
Hazard ratio (95% CI) vs Kd	-	1.07 (0.63 to 1.80)		1.04 (0.25 to 4.36)			
P-value	-	0.8079		0.9574		0.9976	

A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
PGM=DEVOPS/SAR650984/EFC15246/CIR_RWE/REPORT/PGM/eff_km_subgp_sr_sig_de_i_t.sas OUT=REPORT/OUTPUT/eff_km_c30_rol_imppl_seriss_de_i_t_x.rtf (07APR2021 14:23)

16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Role functioning
16.2.6.1.2.9 Efficacy response data - Subgroup analyses by R-ISS stage at SE
16.2.6.1.2.9.7 QLQ-C30 - Time until permanent deterioration by 10 pt in role functioning according to R-ISS stage at SE (LOCF) - ITT population

	I or II		III		Not classified		
	Kd (N=103)	**IKd (N=155)**	**Kd (N=8)**	**IKd (N=16)**	**Kd (N=12)**	**IKd (N=8)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	34 (33.0)	58 (37.4)	3 (37.5)	0 (0.0)	4 (33.3)	1 (12.5)	0.8174
Number (%) of patients censored	69 (67.0)	97 (62.6)	5 (62.5)	16 (100.0)	8 (66.7)	7 (87.5)	
Kaplan-Meier estimates of Role functioning in months							
25% quantile (95% CI)	11.50 (6.374 to 21.388)	12.62 (5.815 to 16.099)	1.12 (0.986 to NC)	NC (NC to NC)	18.00 (1.150 to NC)	NC (16.624 to NC)	
Median (95% CI)	NC (21.454 to NC)	NC (22.669 to NC)	NC (0.986 to NC)	NC (NC to NC)	NC (11.368 to NC)	NC (16.624 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (1.971 to NC)	NC (NC to NC)	NC (NC to NC)	NC (16.624 to NC)	
Comparison vs. Kd							
Log-Rank test p-value[a] vs Kd	-	0.5910		0.0102		0.7122	
Hazard ratio (95% CI) vs Kd	-	1.12 (0.74 to 1.72)				0.66 (0.07 to 5.97)	
P-value	-	0.5912		0.9975		0.7141	

A higher score represents a better level of quality of life. Clinical meaningful deterioration change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Role functioning
16.2.6.1.2.10 Efficacy response data - Subgroup analyses by nb of prior lines
16.2.6.1.2.10.3 QLQ-C30 - Time to first improvement by 10 pt in role functioning according to nb of prior lines (LOCF) - ITT population

	1		>1		
	Kd (N=55)	**IKd (N=79)**	**Kd (N=68)**	**IKd (N=100)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	25 (45.5)	35 (44.3)	28 (41.2)	56 (56.0)	0.1477
Number (%) of patients censored	30 (54.5)	44 (55.7)	40 (58.8)	44 (44.0)	
Kaplan-Meier estimates of Role functioning in months					
25% quantile (95% CI)	1.12 (1.051 to 2.136)	1.97 (1.051 to 2.891)	1.91 (1.018 to 2.858)	1.08 (1.051 to 1.873)	
Median (95% CI)	22.21 (2.136 to NC)	NC (3.417 to NC)	NC (3.713 to NC)	3.94 (2.004 to NC)	
75% quantile (95% CI)	NC (22.209 to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.7973		0.0652	
Hazard ratio (95% CI) vs Kd	-	0.93 (0.56 to 1.56)		1.53 (0.97 to 2.41)	
P-value	-	0.7961		0.0672	
Improvement probability (95% CI)[b]					

A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Role functioning
16.2.6.1.2.10 Efficacy response data - Subgroup analyses by nb of prior lines
16.2.6.1.2.10.4 QLQ-C30 - Time to first deterioration by 10 pt in role functioning according to nb of prior lines (LOCF) - ITT population

	1		>1		
	Kd (N=55)	**IKd (N=79)**	**Kd (N=68)**	**IKd (N=100)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	34 (61.8)	52 (65.8)	35 (51.5)	59 (59.0)	0.9114
Number (%) of patients censored	21 (38.2)	27 (34.2)	33 (48.5)	41 (41.0)	
Kaplan-Meier estimates of Role functioning in months					
25% quantile (95% CI)	2.00 (1.051 to 2.990)	1.15 (1.051 to 2.595)	1.97 (1.150 to 3.778)	2.00 (1.248 to 3.515)	
Median (95% CI)	4.93 (2.990 to 21.454)	3.35 (2.858 to 7.622)	9.99 (3.943 to NC)	9.36 (4.731 to 14.784)	
75% quantile (95% CI)	NC (21.454 to NC)	NC (12.945 to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.4925		0.5586	
Hazard ratio (95% CI) vs Kd	-	1.16 (0.75 to 1.79)		1.13 (0.75 to 1.72)	
P-value	-	0.4929		0.5589	
Deterioration probability (95% CI)[b]					

A higher score represents a better level of quality of life. Clinical meaningful deterioration change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Role functioning
16.2.6.1.2.10 Efficacy response data - Subgroup analyses by nb of prior lines
16.2.6.1.2.10.5 QLQ-C30 - Time until permanent improvement by 10 pt in role functioning according to nb of prior lines (LOCF) - ITT population

	1		>1		
	Kd (N=55)	**IKd (N=79)**	**Kd (N=68)**	**IKd (N=100)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	15 (27.3)	16 (20.3)	13 (19.1)	27 (27.0)	0.1062
Number (%) of patients censored	40 (72.7)	63 (79.7)	55 (80.9)	73 (73.0)	
Kaplan-Meier estimates of Role functioning in months					
25% quantile (95% CI)	20.76 (2.136 to NC)	23.36 (16.854 to NC)	NC (10.448 to NC)	16.85 (8.903 to NC)	
Median (95% CI)	NC (22.144 to NC)	NC (23.359 to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.2511		0.2487	
Hazard ratio (95% CI) vs Kd	-	0.66 (0.33 to 1.34)		1.47 (0.76 to 2.85)	
P-value	-	0.2544		0.2517	
Improvement probability (95% CI)[b]					

A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
PGM=DEVOPS/SAR650984/EFC15246/CIR_RWE/REPORT/PGM/eff_km_subgp_sr_sig_de_i_t.sas OUT=REPORT/OUTPUT/eff_km_c30_rol_imppl_plne_de_i_t_x.rtf (07APR2021 14:23)

16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Role functioning
16.2.6.1.2.10 Efficacy response data - Subgroup analyses by nb of prior lines
16.2.6.1.2.10.6 QLQ-C30 - Time until permanent deterioration by 10 pt in role functioning according to nb of prior lines (LOCF) - ITT population

	1		>1		
	Kd (N=55)	**IKd (N=79)**	**Kd (N=68)**	**IKd (N=100)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	17 (30.9)	27 (34.2)	24 (35.3)	32 (32.0)	0.4546
Number (%) of patients censored	38 (69.1)	52 (65.8)	44 (64.7)	68 (68.0)	
Kaplan-Meier estimates of Role functioning in months					
25% quantile (95% CI)	18.46 (3.680 to 23.129)	13.14 (5.815 to 19.877)	10.55 (5.815 to 18.004)	14.00 (6.407 to 19.844)	
Median (95% CI)	NC (21.454 to NC)	NC (22.669 to NC)	NC (18.004 to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.5822		0.5695	
Hazard ratio (95% CI) vs Kd	-	1.19 (0.65 to 2.18)		0.86 (0.51 to 1.46)	
P-value	-	0.5826		0.5699	
Deterioration probability (95% CI)[b]					

A higher score represents a better level of quality of life. Clinical meaningful deterioration change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
PGM=DEVOPS/SAR650984/EFC15246/CIR_RWE/REPORT/PGM/eff_km_subgp_sr_sig_de_i_t.sas OUT=REPORT/OUTPUT/eff_km_c30_rol_detpl_plne_de_i_t_x.rtf (07APR2021 14:23)

16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Role functioning
16.2.6.1.2.11 Efficacy response data - Subgroup analyses by cytogenetic abnormality
16.2.6.1.2.11.3 QLQ-C30 - Time to first improvement by 10 pt in role functioning according to cytogenetic abnormality (LOCF) - ITT population

	At least one		None		
	Kd (N=31)	**IKd (N=42)**	**Kd (N=77)**	**IKd (N=114)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	10 (32.3)	25 (59.5)	36 (46.8)	55 (48.2)	0.1057
Number (%) of patients censored	21 (67.7)	17 (40.5)	41 (53.2)	59 (51.8)	
Kaplan-Meier estimates of Role functioning in months					
25% quantile (95% CI)	1.97 (1.018 to NC)	1.15 (0.986 to 1.906)	1.91 (1.051 to 2.037)	1.12 (1.051 to 2.267)	
Median (95% CI)	NC (2.793 to NC)	2.84 (1.906 to NC)	22.21 (2.858 to NC)	12.39 (3.023 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.0537		0.8242	
Hazard ratio (95% CI) vs Kd	-	2.03 (0.97 to 4.23)		1.05 (0.69 to 1.60)	
P-value	-	0.0588		0.8250	
Improvement probability (95% CI)[b]					

A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
PGM=DEVOPS/SAR650984/EFC15246/CIR_RWE/REPORT/PGM/eff_km_subgp_sr_sig_de_i_t.sas OUT=REPORT/OUTPUT/eff_km_c30_rol_impl_cyto_de_i_t_x.rtf (07APR2021 14:23)

16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Role functioning
16.2.6.1.2.11 Efficacy response data - Subgroup analyses by cytogenetic abnormality
16.2.6.1.2.11.4 QLQ-C30 - Time to first deterioration by 10 pt in role functioning according to cytogenetic abnormality (LOCF) - ITT population

	At least one		None		
	Kd (N=31)	**IKd (N=42)**	**Kd (N=77)**	**IKd (N=114)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	18 (58.1)	24 (57.1)	43 (55.8)	78 (68.4)	0.3359
Number (%) of patients censored	13 (41.9)	18 (42.9)	34 (44.2)	36 (31.6)	
Kaplan-Meier estimates of Role functioning in months					
25% quantile (95% CI)	2.07 (1.018 to 2.825)	2.00 (1.051 to 3.351)	1.91 (1.117 to 2.793)	1.87 (1.117 to 2.497)	
Median (95% CI)	5.62 (2.234 to NC)	6.41 (3.023 to NC)	7.39 (3.877 to NC)	4.73 (2.891 to 9.363)	
75% quantile (95% CI)	NC (9.988 to NC)	NC (NC to NC)	NC (NC to NC)	NC (12.945 to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.7786		0.1424	
Hazard ratio (95% CI) vs Kd	-	0.92 (0.50 to 1.69)		1.32 (0.91 to 1.92)	
P-value	-	0.7786		0.1437	
Deterioration probability (95% CI)[b]					

A higher score represents a better level of quality of life. Clinical meaningful deterioration change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Role functioning
16.2.6.1.2.11 Efficacy response data - Subgroup analyses by cytogenetic abnormality
16.2.6.1.2.11.5 QLQ-C30 - Time until permanent improvement by 10 pt in role functioning according to cytogenetic abnormality (LOCF) - ITT population

	At least one		None		
	Kd (N=31)	**IKd (N=42)**	**Kd (N=77)**	**IKd (N=114)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	5 (16.1)	10 (23.8)	19 (24.7)	30 (26.3)	0.5228
Number (%) of patients censored	26 (83.9)	32 (76.2)	58 (75.3)	84 (73.7)	
Kaplan-Meier estimates of Role functioning in months					
25% quantile (95% CI)	NC (5.585 to NC)	23.36 (2.103 to NC)	20.76 (2.891 to NC)	18.37 (10.480 to NC)	
Median (95% CI)	NC (NC to NC)	23.36 (23.359 to NC)	NC (22.144 to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (23.359 to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.5057		0.9477	
Hazard ratio (95% CI) vs Kd	-	1.44 (0.49 to 4.21)		1.02 (0.57 to 1.81)	
P-value	-	0.5081		0.9478	
Improvement probability (95% CI)[b]					

A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Role functioning
16.2.6.1.2.11 Efficacy response data - Subgroup analyses by cytogenetic abnormality
16.2.6.1.2.11.6 QLQ-C30 - Time until permanent deterioration by 10 pt in role functioning according to cytogenetic abnormality (LOCF) - ITT population

	At least one		None		
	Kd (N=31)	**IKd (N=42)**	**Kd (N=77)**	**IKd (N=114)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	11 (35.5)	15 (35.7)	26 (33.8)	37 (32.5)	0.9582
Number (%) of patients censored	20 (64.5)	27 (64.3)	51 (66.2)	77 (67.5)	
Kaplan-Meier estimates of Role functioning in months					
25% quantile (95% CI)	10.55 (3.680 to 19.450)	14.00 (1.117 to 19.088)	10.87 (4.665 to 21.454)	14.16 (7.951 to 19.877)	
Median (95% CI)	NC (11.499 to NC)	NC (18.464 to NC)	NC (21.454 to NC)	NC (22.669 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.8612		0.8460	
Hazard ratio (95% CI) vs Kd	-	0.93 (0.43 to 2.03)		0.95 (0.58 to 1.57)	
P-value	-	0.8612		0.8452	
Deterioration probability (95% CI)[b]					

A higher score represents a better level of quality of life. Clinical meaningful deterioration change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Role functioning
16.2.6.1.2.12 Efficacy response data - Subgroup analyses by MM type at SE
16.2.6.1.2.12.3 QLQ-C30 - Time to first improvement by 10 pt in role functioning according to MM type at SE (LOCF) - ITT population

	IgG		Non-IgG		
	Kd (N=85)	**IKd (N=126)**	**Kd (N=38)**	**IKd (N=53)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	36 (42.4)	66 (52.4)	17 (44.7)	25 (47.2)	0.1980
Number (%) of patients censored	49 (57.6)	60 (47.6)	21 (55.3)	28 (52.8)	
Kaplan-Meier estimates of Role functioning in months					
25% quantile (95% CI)	1.91 (1.084 to 2.793)	1.05 (1.051 to 1.873)	1.08 (0.986 to 2.136)	2.00 (1.150 to 3.417)	
Median (95% CI)	NC (6.012 to NC)	5.82 (2.398 to NC)	NC (1.117 to NC)	NC (2.990 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.0835		0.7070	
Hazard ratio (95% CI) vs Kd	-	1.43 (0.95 to 2.15)		0.89 (0.48 to 1.65)	
P-value	-	0.0852		0.7071	
Improvement probability (95% CI)[b]					

A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Role functioning
16.2.6.1.2.12 Efficacy response data - Subgroup analyses by MM type at SE
16.2.6.1.2.12.4 QLQ-C30 - Time to first deterioration by 10 pt in role functioning according to MM type at SE (LOCF) - ITT population

	IgG		Non-IgG		
	Kd (N=85)	**IKd (N=126)**	**Kd (N=38)**	**IKd (N=53)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	52 (61.2)	80 (63.5)	17 (44.7)	31 (58.5)	0.4897
Number (%) of patients censored	33 (38.8)	46 (36.5)	21 (55.3)	22 (41.5)	
Kaplan-Meier estimates of Role functioning in months					
25% quantile (95% CI)	1.94 (1.117 to 2.793)	1.91 (1.117 to 2.595)	3.06 (0.986 to 5.618)	1.94 (0.986 to 3.713)	
Median (95% CI)	4.90 (2.990 to 17.971)	5.55 (2.990 to 9.363)	NC (4.041 to NC)	10.38 (3.055 to NC)	
75% quantile (95% CI)	NC (21.454 to NC)	NC (16.854 to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.7124		0.3261	
Hazard ratio (95% CI) vs Kd	-	1.07 (0.75 to 1.51)		1.34 (0.74 to 2.43)	
P-value	-	0.7141		0.3279	
Deterioration probability (95% CI)[b]					

A higher score represents a better level of quality of life. Clinical meaningful deterioration change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Role functioning
16.2.6.1.2.12 Efficacy response data - Subgroup analyses by MM type at SE
16.2.6.1.2.12.5 QLQ-C30 - Time until permanent improvement by 10 pt in role functioning according to MM type at SE (LOCF) - ITT population

	IgG		Non-IgG		
	Kd (N=85)	**IKd (N=126)**	**Kd (N=38)**	**IKd (N=53)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	20 (23.5)	32 (25.4)	8 (21.1)	11 (20.8)	0.8086
Number (%) of patients censored	65 (76.5)	94 (74.6)	30 (78.9)	42 (79.2)	
Kaplan-Meier estimates of Role functioning in months					
25% quantile (95% CI)	20.76 (5.585 to NC)	18.50 (12.320 to NC)	NC (2.136 to NC)	NC (8.903 to NC)	
Median (95% CI)	NC (NC to NC)	NC (23.359 to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.7957		0.8954	
Hazard ratio (95% CI) vs Kd	-	1.08 (0.62 to 1.88)		0.94 (0.38 to 2.34)	
P-value	-	0.7957		0.8949	
Improvement probability (95% CI)[b]					

A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Role functioning
16.2.6.1.2.12 Efficacy response data - Subgroup analyses by MM type at SE
16.2.6.1.2.12.6 QLQ-C30 - Time until permanent deterioration by 10 pt in role functioning according to MM type at SE (LOCF) - ITT population

	IgG		Non-IgG		
	Kd (N=85)	**IKd (N=126)**	**Kd (N=38)**	**IKd (N=53)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	29 (34.1)	44 (34.9)	12 (31.6)	15 (28.3)	0.5453
Number (%) of patients censored	56 (65.9)	82 (65.1)	26 (68.4)	38 (71.7)	
Kaplan-Meier estimates of Role functioning in months					
25% quantile (95% CI)	15.38 (4.862 to 19.450)	13.14 (7.622 to 18.004)	9.95 (4.041 to NC)	14.00 (3.811 to NC)	
Median (95% CI)	NC (21.454 to NC)	NC (22.669 to NC)	NC (11.499 to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.7557		0.5937	
Hazard ratio (95% CI) vs Kd	-	1.08 (0.67 to 1.72)		0.81 (0.38 to 1.74)	
P-value	-	0.7557		0.5944	
Deterioration probability (95% CI)[b]					

A higher score represents a better level of quality of life. Clinical meaningful deterioration change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Role functioning
16.2.6.1.2.13 Efficacy response data - Subgroup analyses by previous autologous stem-cell
16.2.6.1.2.13.3 QLQ-C30 - Time to first improvement by 10 pt in role functioning according to previous autologous stem-cell (LOCF) - ITT population

	Yes		No		
	Kd (N=69)	**IKd (N=116)**	**Kd (N=54)**	**IKd (N=63)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	25 (36.2)	57 (49.1)	28 (51.9)	34 (54.0)	0.2520
Number (%) of patients censored	44 (63.8)	59 (50.9)	26 (48.1)	29 (46.0)	
Kaplan-Meier estimates of Role functioning in months					
25% quantile (95% CI)	2.00 (1.117 to 8.345)	1.35 (1.051 to 2.136)	1.08 (1.018 to 1.938)	1.15 (1.051 to 2.004)	
Median (95% CI)	NC (18.793 to NC)	12.39 (2.891 to NC)	3.29 (1.906 to NC)	5.82 (2.004 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (22.209 to NC)	NC (NC to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.0837		0.9590	
Hazard ratio (95% CI) vs Kd	-	1.51 (0.94 to 2.42)		1.01 (0.61 to 1.67)	
P-value	-	0.0860		0.9590	
Improvement probability (95% CI)[b]					

A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Role functioning
16.2.6.1.2.13 Efficacy response data - Subgroup analyses by previous autologous stem-cell
16.2.6.1.2.13.4 QLQ-C30 - Time to first deterioration by 10 pt in role functioning according to previous autologous stem-cell (LOCF) - ITT population

	Yes		No		
	Kd (N=69)	**IKd (N=116)**	**Kd (N=54)**	**IKd (N=63)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	42 (60.9)	73 (62.9)	27 (50.0)	38 (60.3)	0.4539
Number (%) of patients censored	27 (39.1)	43 (37.1)	27 (50.0)	25 (39.7)	
Kaplan-Meier estimates of Role functioning in months					
25% quantile (95% CI)	1.95 (1.117 to 2.825)	1.61 (1.117 to 2.136)	2.10 (1.150 to 3.877)	2.68 (1.117 to 3.055)	
Median (95% CI)	5.62 (3.055 to 17.971)	6.54 (3.023 to 12.156)	9.99 (3.877 to NC)	5.65 (3.055 to 13.306)	
75% quantile (95% CI)	NC (21.454 to NC)	NC (NC to NC)	NC (NC to NC)	NC (13.306 to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.8841		0.2995	
Hazard ratio (95% CI) vs Kd	-	1.03 (0.70 to 1.50)		1.30 (0.79 to 2.13)	
P-value	-	0.8845		0.3009	
Deterioration probability (95% CI)[b]					

A higher score represents a better level of quality of life. Clinical meaningful deterioration change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Role functioning
16.2.6.1.2.13 Efficacy response data - Subgroup analyses by previous autologous stem-cell
16.2.6.1.2.13.5 QLQ-C30 - Time until permanent improvement by 10 pt in role functioning according to previous autologous stem-cell (LOCF) - ITT population

	Yes		No		
	Kd (N=69)	**IKd (N=116)**	**Kd (N=54)**	**IKd (N=63)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	11 (15.9)	29 (25.0)	17 (31.5)	14 (22.2)	0.0406
Number (%) of patients censored	58 (84.1)	87 (75.0)	37 (68.5)	49 (77.8)	
Kaplan-Meier estimates of Role functioning in months					
25% quantile (95% CI)	NC (19.384 to NC)	17.05 (10.973 to NC)	2.89 (1.117 to NC)	19.81 (10.480 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (23.359 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.1249		0.1660	
Hazard ratio (95% CI) vs Kd	-	1.71 (0.85 to 3.43)		0.61 (0.30 to 1.24)	
P-value	-	0.1297		0.1703	
Improvement probability (95% CI)[b]					

A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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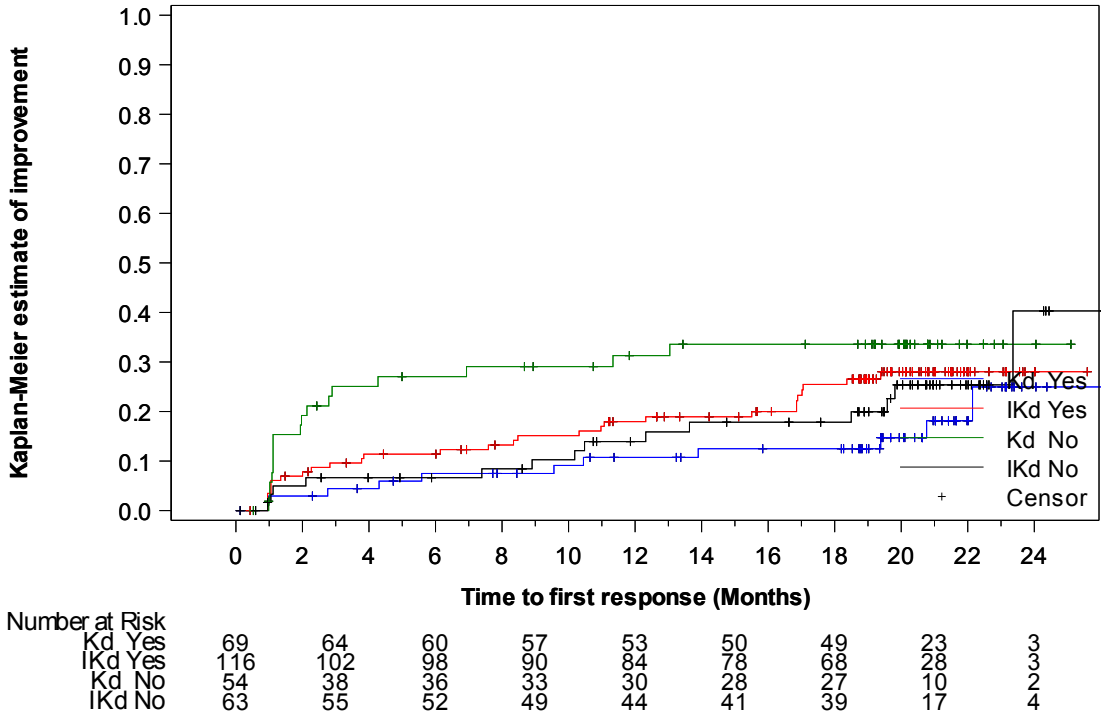
16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Role functioning
16.2.6.1.2.13 Efficacy response data - Subgroup analyses by previous autologous stem-cell
16.2.6.1.2.13.6 QLQ-C30 - Time until permanent improvement by 10 pt in role functioning according to previous autologous stem-cell- Kaplan-Meier curve (LOCF) - ITT population



A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
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16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Role functioning
16.2.6.1.2.13 Efficacy response data - Subgroup analyses by previous autologous stem-cell
16.2.6.1.2.13.7 QLQ-C30 - Time until permanent deterioration by 10 pt in role functioning according to previous autologous stem-cell (LOCF) - ITT population

	Yes		No		
	Kd (N=69)	**IKd (N=116)**	**Kd (N=54)**	**IKd (N=63)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	24 (34.8)	39 (33.6)	17 (31.5)	20 (31.7)	0.9586
Number (%) of patients censored	45 (65.2)	77 (66.4)	37 (68.5)	43 (68.3)	
Kaplan-Meier estimates of Role functioning in months					
25% quantile (95% CI)	11.37 (5.815 to 21.388)	14.00 (5.815 to 19.088)	11.50 (2.103 to NC)	14.16 (5.257 to 19.877)	
Median (95% CI)	NC (21.388 to NC)	NC (22.669 to NC)	NC (23.129 to NC)	NC (19.877 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (23.129 to NC)	NC (NC to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.9488		0.9912	
Hazard ratio (95% CI) vs Kd	-	0.98 (0.59 to 1.64)		1.00 (0.52 to 1.90)	
P-value	-	0.9487		0.9911	
Deterioration probability (95% CI)[b]					

A higher score represents a better level of quality of life. Clinical meaningful deterioration change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Role functioning
16.2.6.1.2.14 Efficacy response data - Subgroup analyses by baseline eGFR (MDRD)
16.2.6.1.2.14.3 QLQ-C30 - Time to first improvement by 10 pt in role functioning according to baseline eGFR (MDRD) (LOCF) - ITT population

	>=60 mL/min/1.73m2		<60 mL/min/1.73m2		
	Kd (N=93)	**IKd (N=122)**	**Kd (N=18)**	**IKd (N=43)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	43 (46.2)	62 (50.8)	6 (33.3)	24 (55.8)	0.4665
Number (%) of patients censored	50 (53.8)	60 (49.2)	12 (66.7)	19 (44.2)	
Kaplan-Meier estimates of Role functioning in months					
25% quantile (95% CI)	1.51 (1.051 to 1.971)	1.12 (1.051 to 1.971)	2.86 (0.986 to NC)	1.12 (0.986 to 2.398)	
Median (95% CI)	22.21 (2.793 to NC)	6.83 (2.825 to NC)	NC (2.037 to NC)	5.55 (2.004 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.3908		0.2464	
Hazard ratio (95% CI) vs Kd	-	1.19 (0.80 to 1.75)		1.69 (0.69 to 4.13)	
P-value	-	0.3913		0.2518	
Improvement probability (95% CI)[b]					

A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Role functioning
16.2.6.1.2.14 Efficacy response data - Subgroup analyses by baseline eGFR (MDRD)
16.2.6.1.2.14.4 QLQ-C30 - Time to first deterioration by 10 pt in role functioning according to baseline eGFR (MDRD) (LOCF) - ITT population

	>=60 mL/min/1.73m2		<60 mL/min/1.73m2		
	Kd (N=93)	**IKd (N=122)**	**Kd (N=18)**	**IKd (N=43)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	51 (54.8)	80 (65.6)	13 (72.2)	25 (58.1)	0.0619
Number (%) of patients censored	42 (45.2)	42 (34.4)	5 (27.8)	18 (41.9)	
Kaplan-Meier estimates of Role functioning in months					
25% quantile (95% CI)	1.95 (1.117 to 2.825)	1.91 (1.117 to 2.760)	1.97 (0.986 to 4.041)	1.31 (0.986 to 2.990)	
Median (95% CI)	5.65 (3.778 to NC)	5.55 (3.055 to 9.363)	4.83 (1.314 to 9.002)	7.62 (2.595 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (13.207 to NC)	9.00 (4.041 to NC)	NC (NC to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.1133		0.1965	
Hazard ratio (95% CI) vs Kd	-	1.33 (0.93 to 1.89)		0.64 (0.32 to 1.27)	
P-value	-	0.1145		0.1998	
Deterioration probability (95% CI)[b]					

A higher score represents a better level of quality of life. Clinical meaningful deterioration change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Role functioning
16.2.6.1.2.14 Efficacy response data - Subgroup analyses by baseline eGFR (MDRD)
16.2.6.1.2.14.5 QLQ-C30 - Time until permanent improvement by 10 pt in role functioning according to baseline eGFR (MDRD) (LOCF) - ITT population

	>=60 mL/min/1.73m2		<60 mL/min/1.73m2		
	Kd (N=93)	**IKd (N=122)**	**Kd (N=18)**	**IKd (N=43)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	25 (26.9)	25 (20.5)	1 (5.6)	16 (37.2)	0.0501
Number (%) of patients censored	68 (73.1)	97 (79.5)	17 (94.4)	27 (62.8)	
Kaplan-Meier estimates of Role functioning in months					
25% quantile (95% CI)	13.90 (4.271 to NC)	NC (12.320 to NC)	NC (0.986 to NC)	18.37 (2.103 to 19.811)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	23.36 (19.384 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (23.359 to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.3358		0.0418	
Hazard ratio (95% CI) vs Kd	-	0.76 (0.44 to 1.33)		6.25 (0.83 to 47.15)	
P-value	-	0.3372		0.0755	
Improvement probability (95% CI)[b]					

A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Role functioning
16.2.6.1.2.14 Efficacy response data - Subgroup analyses by baseline eGFR (MDRD)
16.2.6.1.2.14.6 QLQ-C30 - Time until permanent deterioration by 10 pt in role functioning according to baseline eGFR (MDRD) (LOCF) - ITT population

	>=60 mL/min/1.73m2		<60 mL/min/1.73m2		
	Kd (N=93)	**IKd (N=122)**	**Kd (N=18)**	**IKd (N=43)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	30 (32.3)	42 (34.4)	7 (38.9)	14 (32.6)	0.1712
Number (%) of patients censored	63 (67.7)	80 (65.6)	11 (61.1)	29 (67.4)	
Kaplan-Meier estimates of Role functioning in months					
25% quantile (95% CI)	17.54 (8.411 to 21.454)	12.65 (5.322 to 16.624)	4.04 (0.986 to NC)	18.46 (6.439 to 22.669)	
Median (95% CI)	NC (23.129 to NC)	NC (NC to NC)	NC (1.971 to NC)	NC (19.877 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (22.669 to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.4609		0.2769	
Hazard ratio (95% CI) vs Kd	-	1.19 (0.75 to 1.91)		0.61 (0.24 to 1.51)	
P-value	-	0.4615		0.2818	
Deterioration probability (95% CI)[b]					

A higher score represents a better level of quality of life. Clinical meaningful deterioration change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Role functioning
16.2.6.1.2.15 Efficacy response data - Subgroup analyses by previous treatment with PI
16.2.6.1.2.15.3 QLQ-C30 - Time to first improvement by 10 pt in role functioning according to previous treatment with PI (LOCF) - ITT population

	Yes		No		
	Kd (N=47)	**IKd (N=81)**	**Kd (N=76)**	**IKd (N=98)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	24 (51.1)	39 (48.1)	29 (38.2)	52 (53.1)	0.1130
Number (%) of patients censored	23 (48.9)	42 (51.9)	47 (61.8)	46 (46.9)	
Kaplan-Meier estimates of Role functioning in months					
25% quantile (95% CI)	1.12 (1.018 to 2.760)	1.97 (1.150 to 2.398)	1.91 (1.051 to 3.713)	1.05 (0.986 to 1.347)	
Median (95% CI)	8.34 (2.037 to NC)	10.18 (2.957 to NC)	NC (18.793 to NC)	5.59 (2.136 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.6725		0.0616	
Hazard ratio (95% CI) vs Kd	-	0.90 (0.54 to 1.49)		1.54 (0.98 to 2.42)	
P-value	-	0.6726		0.0636	
Improvement probability (95% CI)[b]					

A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Role functioning
16.2.6.1.2.15 Efficacy response data - Subgroup analyses by previous treatment with PI
16.2.6.1.2.15.4 QLQ-C30 - Time to first deterioration by 10 pt in role functioning according to previous treatment with PI (LOCF) - ITT population

	Yes		No		
	Kd (N=47)	**IKd (N=81)**	**Kd (N=76)**	**IKd (N=98)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	25 (53.2)	52 (64.2)	44 (57.9)	59 (60.2)	0.2527
Number (%) of patients censored	22 (46.8)	29 (35.8)	32 (42.1)	39 (39.8)	
Kaplan-Meier estimates of Role functioning in months					
25% quantile (95% CI)	2.00 (1.051 to 3.943)	1.51 (1.084 to 2.595)	2.00 (1.117 to 2.825)	2.00 (1.117 to 2.990)	
Median (95% CI)	6.51 (3.778 to NC)	3.81 (2.858 to 8.345)	5.82 (3.055 to 21.454)	9.36 (4.665 to 14.784)	
75% quantile (95% CI)	NC (NC to NC)	NC (13.306 to NC)	NC (21.454 to NC)	NC (NC to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.1743		0.9213	
Hazard ratio (95% CI) vs Kd	-	1.39 (0.86 to 2.24)		0.98 (0.66 to 1.45)	
P-value	-	0.1763		0.9212	
Deterioration probability (95% CI)[b]					

A higher score represents a better level of quality of life. Clinical meaningful deterioration change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
PGM=DEVOPS/SAR650984/EFC15246/CIR_RWE/REPORT/PGM/eff_km_subgp_sr_sig_de_i_t.sas OUT=REPORT/OUTPUT/eff_km_c30_rol_detl_pi_de_i_t_x.rtf (07APR2021 14:23)

16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Role functioning
16.2.6.1.2.15 Efficacy response data - Subgroup analyses by previous treatment with PI
16.2.6.1.2.15.5 QLQ-C30 - Time until permanent improvement by 10 pt in role functioning according to previous treatment with PI (LOCF) - ITT population

	Yes		No		
	Kd (N=47)	**IKd (N=81)**	**Kd (N=76)**	**IKd (N=98)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	13 (27.7)	16 (19.8)	15 (19.7)	27 (27.6)	0.1427
Number (%) of patients censored	34 (72.3)	65 (80.2)	61 (80.3)	71 (72.4)	
Kaplan-Meier estimates of Role functioning in months					
25% quantile (95% CI)	20.76 (1.971 to NC)	23.36 (12.320 to NC)	NC (6.932 to NC)	16.85 (10.316 to NC)	
Median (95% CI)	NC (22.144 to NC)	NC (23.359 to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (23.359 to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.3252		0.2939	
Hazard ratio (95% CI) vs Kd	-	0.69 (0.33 to 1.44)		1.40 (0.74 to 2.63)	
P-value	-	0.3279		0.2962	
Improvement probability (95% CI)[b]					

A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Role functioning
16.2.6.1.2.15 Efficacy response data - Subgroup analyses by previous treatment with PI
16.2.6.1.2.15.6 QLQ-C30 - Time until permanent deterioration by 10 pt in role functioning according to previous treatment with PI (LOCF) - ITT population

	Yes		No		
	Kd (N=47)	**IKd (N=81)**	**Kd (N=76)**	**IKd (N=98)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	14 (29.8)	30 (37.0)	27 (35.5)	29 (29.6)	0.1394
Number (%) of patients censored	33 (70.2)	51 (63.0)	49 (64.5)	69 (70.4)	
Kaplan-Meier estimates of Role functioning in months					
25% quantile (95% CI)	17.54 (6.374 to NC)	8.38 (5.191 to 14.752)	8.84 (4.041 to 21.388)	18.00 (9.955 to 22.669)	
Median (95% CI)	NC (19.450 to NC)	NC (16.099 to NC)	23.13 (21.388 to NC)	NC (22.669 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (23.129 to NC)	NC (NC to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.3139		0.3185	
Hazard ratio (95% CI) vs Kd	-	1.38 (0.73 to 2.61)		0.77 (0.45 to 1.29)	
P-value	-	0.3161		0.3199	
Deterioration probability (95% CI)[b]					

A higher score represents a better level of quality of life. Clinical meaningful deterioration change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Role functioning
16.2.6.1.2.16 Efficacy response data - Subgroup analyses by previous treatment with IMiD
16.2.6.1.2.16.3 QLQ-C30 - Time to first improvement by 10 pt in role functioning according to previous treatment with IMiD (LOCF) - ITT population

	Yes		No		
	Kd (N=62)	**IKd (N=81)**	**Kd (N=61)**	**IKd (N=98)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	29 (46.8)	36 (44.4)	24 (39.3)	55 (56.1)	0.0962
Number (%) of patients censored	33 (53.2)	45 (55.6)	37 (60.7)	43 (43.9)	
Kaplan-Meier estimates of Role functioning in months					
25% quantile (95% CI)	1.12 (1.018 to 2.136)	1.15 (1.051 to 2.825)	1.91 (1.084 to 3.285)	1.35 (1.051 to 2.004)	
Median (95% CI)	22.21 (2.136 to NC)	NC (3.943 to NC)	NC (3.285 to NC)	3.42 (2.136 to NC)	
75% quantile (95% CI)	NC (22.209 to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.7153		0.0455	
Hazard ratio (95% CI) vs Kd	-	0.91 (0.56 to 1.49)		1.62 (1.01 to 2.62)	
P-value	-	0.7154		0.0477	
Hazard ratio inverted (95% CI) vs IKd		-		0.62 (0.38 to 1.00)	

A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Role functioning
16.2.6.1.2.16 Efficacy response data - Subgroup analyses by previous treatment with IMiD
16.2.6.1.2.16.4 QLQ-C30 - Time to first deterioration by 10 pt in role functioning according to previous treatment with IMiD (LOCF) - ITT population

	Yes		No		
	Kd (N=62)	**IKd (N=81)**	**Kd (N=61)**	**IKd (N=98)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	34 (54.8)	53 (65.4)	35 (57.4)	58 (59.2)	0.4096
Number (%) of patients censored	28 (45.2)	28 (34.6)	26 (42.6)	40 (40.8)	
Kaplan-Meier estimates of Role functioning in months					
25% quantile (95% CI)	2.99 (1.281 to 4.041)	1.91 (1.117 to 2.858)	1.91 (1.051 to 2.234)	1.94 (1.084 to 2.891)	
Median (95% CI)	7.59 (4.041 to NC)	5.75 (2.957 to 10.579)	4.83 (2.234 to NC)	6.54 (3.318 to 13.306)	
75% quantile (95% CI)	NC (NC to NC)	NC (13.207 to NC)	NC (21.454 to NC)	NC (NC to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.2279		0.9636	
Hazard ratio (95% CI) vs Kd	-	1.30 (0.85 to 2.00)		1.01 (0.66 to 1.54)	
P-value	-	0.2292		0.9637	
Deterioration probability (95% CI)[b]					

A higher score represents a better level of quality of life. Clinical meaningful deterioration change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Role functioning
16.2.6.1.2.16 Efficacy response data - Subgroup analyses by previous treatment with IMiD
16.2.6.1.2.16.5 QLQ-C30 - Time until permanent improvement by 10 pt in role functioning according to previous treatment with IMiD (LOCF) - ITT population

	Yes		No		
	Kd (N=62)	**IKd (N=81)**	**Kd (N=61)**	**IKd (N=98)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	19 (30.6)	16 (19.8)	9 (14.8)	27 (27.6)	0.0157
Number (%) of patients censored	43 (69.4)	65 (80.2)	52 (85.2)	71 (72.4)	
Kaplan-Meier estimates of Role functioning in months					
25% quantile (95% CI)	10.45 (2.136 to 22.144)	23.36 (15.507 to NC)	NC (13.043 to NC)	17.05 (8.903 to NC)	
Median (95% CI)	NC (22.144 to NC)	NC (23.359 to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.1043		0.0706	
Hazard ratio (95% CI) vs Kd	-	0.58 (0.30 to 1.13)		1.98 (0.93 to 4.21)	
P-value	-	0.1086		0.0761	
Improvement probability (95% CI)[b]					

A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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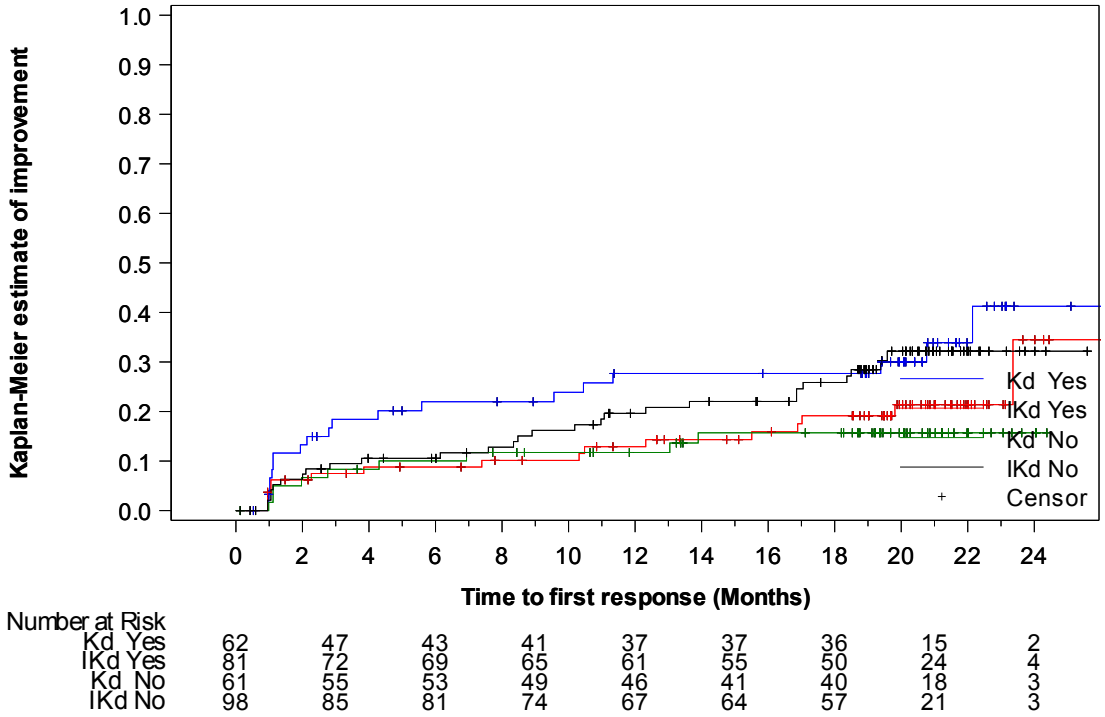
16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Role functioning
16.2.6.1.2.16 Efficacy response data - Subgroup analyses by previous treatment with IMiD
16.2.6.1.2.16.6 QLQ-C30 - Time until permanent improvement by 10 pt in role functioning according to previous treatment with IMiD- Kaplan-Meier curve (LOCF) - ITT population



Number at Risk

Kd Yes	62	47	43	41	37	37	36	15	2
IKd Yes	81	72	69	65	61	55	50	24	4
Kd No	61	55	53	49	46	41	40	18	3
IKd No	98	85	81	74	67	64	57	21	3

A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
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16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Role functioning
16.2.6.1.2.16 Efficacy response data - Subgroup analyses by previous treatment with IMiD
16.2.6.1.2.16.7 QLQ-C30 - Time until permanent deterioration by 10 pt in role functioning according to previous treatment with IMiD (LOCF) - ITT population

	Yes		No		
	Kd (N=62)	**IKd (N=81)**	**Kd (N=61)**	**IKd (N=98)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	18 (29.0)	26 (32.1)	23 (37.7)	33 (33.7)	0.5376
Number (%) of patients censored	44 (71.0)	55 (67.9)	38 (62.3)	65 (66.3)	
Kaplan-Meier estimates of Role functioning in months					
25% quantile (95% CI)	11.50 (4.764 to NC)	13.14 (5.257 to 19.877)	10.87 (4.665 to 19.450)	14.55 (7.951 to 19.088)	
Median (95% CI)	NC (23.129 to NC)	NC (NC to NC)	NC (19.154 to NC)	NC (22.669 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.7298		0.6244	
Hazard ratio (95% CI) vs Kd	-	1.11 (0.61 to 2.03)		0.88 (0.51 to 1.49)	
P-value	-	0.7299		0.6246	
Deterioration probability (95% CI)[b]					

A higher score represents a better level of quality of life. Clinical meaningful deterioration change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Role functioning
16.2.6.1.2.17 Efficacy response data - Subgroup analyses by previous treatment with PI and IMiD
16.2.6.1.2.17.3 QLQ-C30 - Time to first improvement by 10 pt in role functioning according to previous treatment with PI and IMiD (LOCF) - ITT population

	Yes		No		
	Kd (N=17)	**IKd (N=23)**	**Kd (N=106)**	**IKd (N=156)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	9 (52.9)	7 (30.4)	44 (41.5)	84 (53.8)	0.0264
Number (%) of patients censored	8 (47.1)	16 (69.6)	62 (58.5)	72 (46.2)	
Kaplan-Meier estimates of Role functioning in months					
25% quantile (95% CI)	1.08 (0.986 to 3.778)	4.67 (1.051 to NC)	1.91 (1.084 to 2.037)	1.12 (1.051 to 1.906)	
Median (95% CI)	3.78 (1.051 to NC)	NC (4.665 to NC)	NC (9.889 to NC)	5.59 (2.530 to NC)	
75% quantile (95% CI)	NC (3.778 to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.0712		0.0546	
Hazard ratio (95% CI) vs Kd	-	0.41 (0.15 to 1.11)		1.43 (0.99 to 2.06)	
P-value	-	0.0806		0.0559	
Improvement probability (95% CI)[b]					

A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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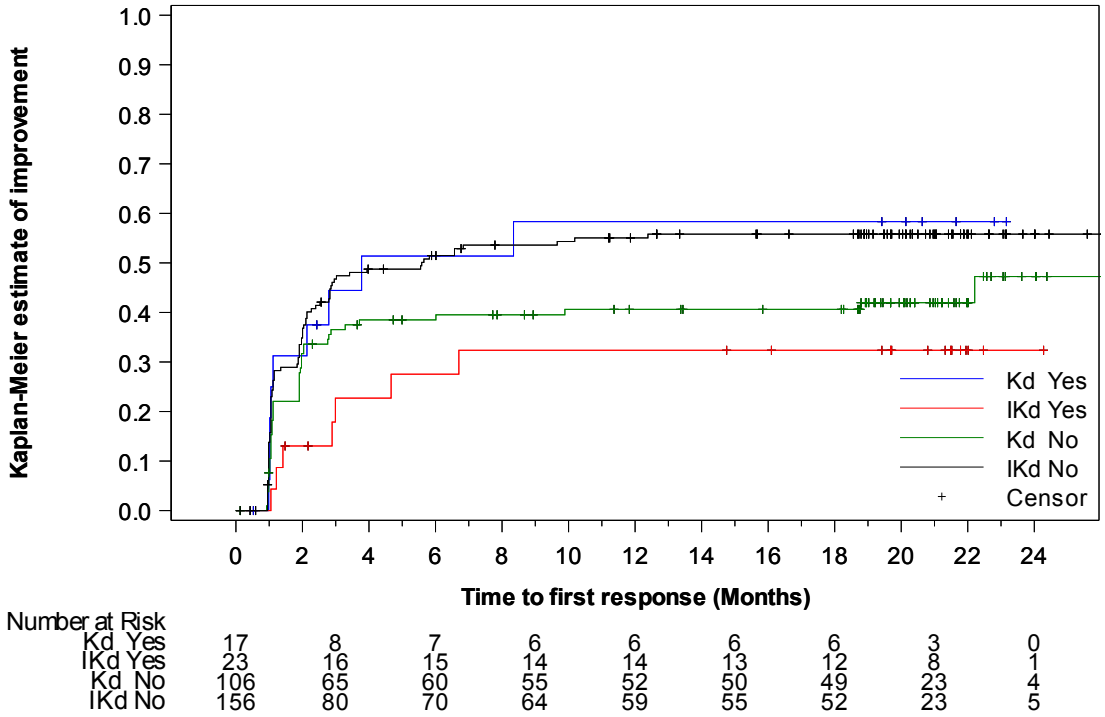
16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Role functioning
16.2.6.1.2.17 Efficacy response data - Subgroup analyses by previous treatment with PI and IMiD
16.2.6.1.2.17.4 QLQ-C30 - Time to first improvement by 10 pt in role functioning according to previous treatment with PI and IMiD- Kaplan-Meier curve (LOCF) - ITT population



A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
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16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Role functioning
16.2.6.1.2.17 Efficacy response data - Subgroup analyses by previous treatment with PI and IMiD
16.2.6.1.2.17.5 QLQ-C30 - Time to first deterioration by 10 pt in role functioning according to previous treatment with PI and IMiD (LOCF) - ITT population

	Yes		No		
	Kd (N=17)	**IKd (N=23)**	**Kd (N=106)**	**IKd (N=156)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	9 (52.9)	17 (73.9)	60 (56.6)	94 (60.3)	0.1497
Number (%) of patients censored	8 (47.1)	6 (26.1)	46 (43.4)	62 (39.7)	
Kaplan-Meier estimates of Role functioning in months					
25% quantile (95% CI)	2.92 (0.953 to 7.392)	1.08 (0.986 to 1.511)	2.00 (1.150 to 2.825)	2.00 (1.216 to 2.891)	
Median (95% CI)	8.69 (2.070 to NC)	2.86 (1.117 to 10.218)	5.65 (3.844 to 21.454)	6.54 (3.811 to 12.156)	
75% quantile (95% CI)	NC (7.392 to NC)	16.85 (3.351 to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.1251		0.7581	
Hazard ratio (95% CI) vs Kd	-	1.88 (0.83 to 4.24)		1.05 (0.76 to 1.45)	
P-value	-	0.1310		0.7593	
Deterioration probability (95% CI)[b]					

A higher score represents a better level of quality of life. Clinical meaningful deterioration change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Role functioning
16.2.6.1.2.17 Efficacy response data - Subgroup analyses by previous treatment with PI and IMiD
16.2.6.1.2.17.6 QLQ-C30 - Time until permanent improvement by 10 pt in role functioning according to previous treatment with PI and IMiD (LOCF) - ITT population

	Yes		No		
	Kd (N=17)	**IKd (N=23)**	**Kd (N=106)**	**IKd (N=156)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	7 (41.2)	2 (8.7)	21 (19.8)	41 (26.3)	0.0132
Number (%) of patients censored	10 (58.8)	21 (91.3)	85 (80.2)	115 (73.7)	
Kaplan-Meier estimates of Role functioning in months					
25% quantile (95% CI)	2.89 (1.018 to 22.144)	23.36 (17.018 to NC)	NC (9.561 to NC)	17.05 (10.973 to NC)	
Median (95% CI)	22.14 (2.891 to NC)	23.36 (23.359 to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (22.144 to NC)	NC (23.359 to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.0039		0.2738	
Hazard ratio (95% CI) vs Kd	-	0.09 (0.01 to 0.71)		1.34 (0.79 to 2.27)	
P-value	-	0.0226		0.2756	
Improvement probability (95% CI)[b]					

A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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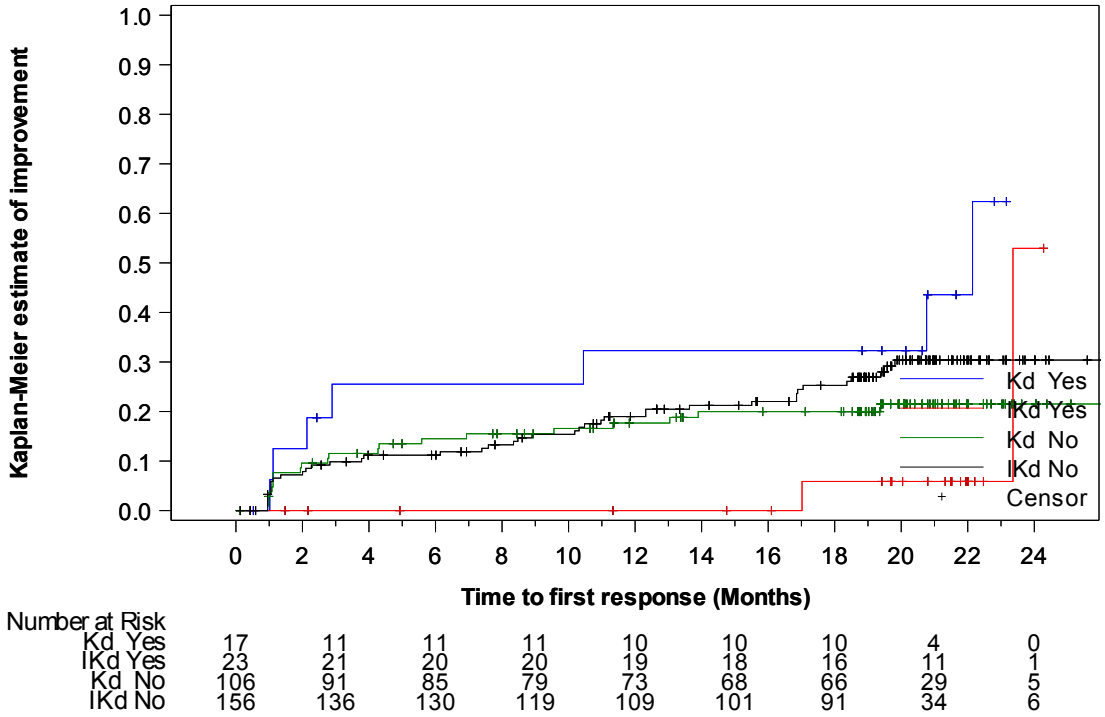
16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Role functioning
16.2.6.1.2.17 Efficacy response data - Subgroup analyses by previous treatment with PI and IMiD
16.2.6.1.2.17.7 QLQ-C30 - Time until permanent improvement by 10 pt in role functioning according to previous treatment with PI and IMiD- Kaplan-Meier curve (LOCF) - ITT population



A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
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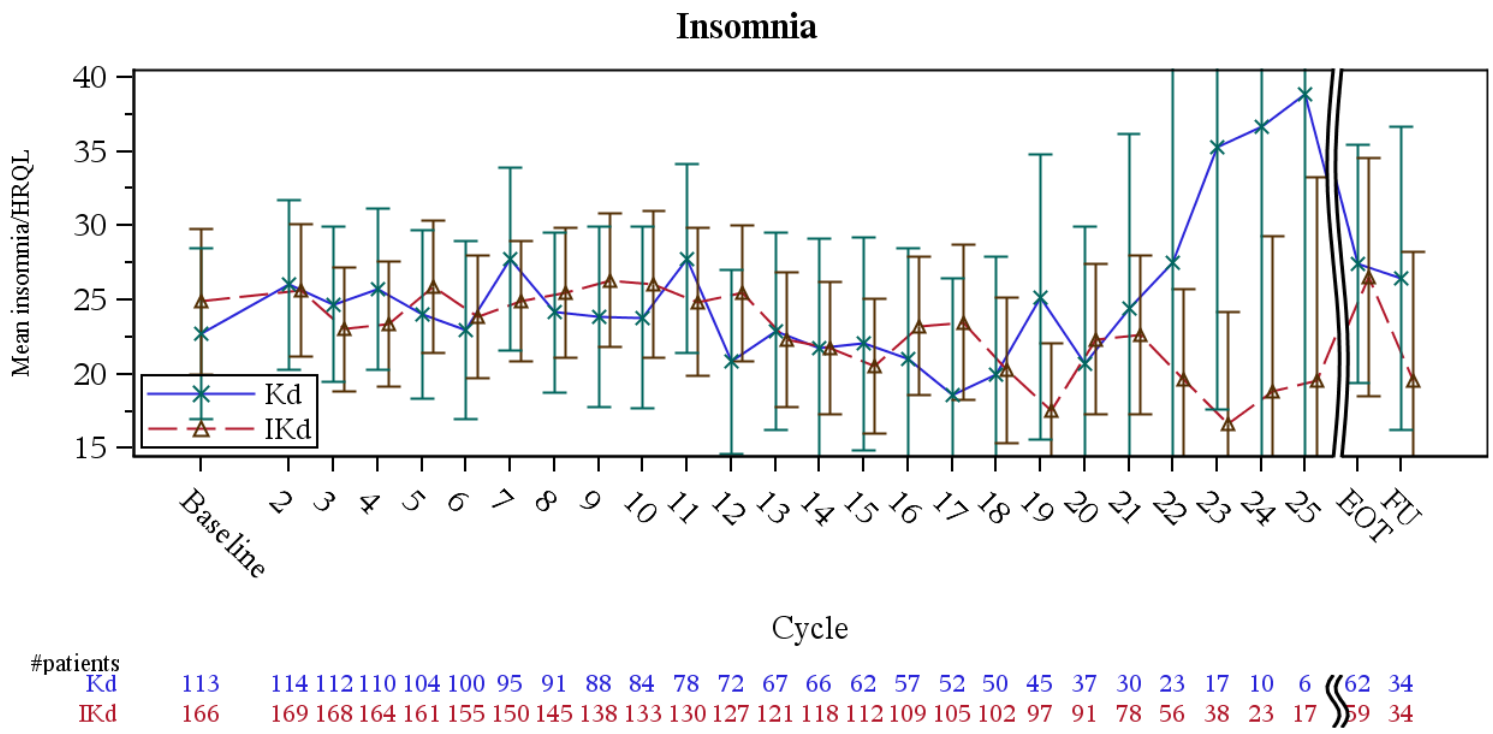
16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Role functioning
16.2.6.1.2.17 Efficacy response data - Subgroup analyses by previous treatment with PI and IMiD
16.2.6.1.2.17.8 QLQ-C30 - Time until permanent deterioration by 10 pt in role functioning according to previous treatment with PI and IMiD (LOCF) - ITT population

	Yes		No		
	Kd (N=17)	**IKd (N=23)**	**Kd (N=106)**	**IKd (N=156)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	4 (23.5)	9 (39.1)	37 (34.9)	50 (32.1)	0.2039
Number (%) of patients censored	13 (76.5)	14 (60.9)	69 (65.1)	106 (67.9)	
Kaplan-Meier estimates of Role functioning in months					
25% quantile (95% CI)	NC (1.314 to NC)	6.44 (1.248 to 19.877)	11.37 (5.782 to 19.154)	14.55 (7.984 to 19.088)	
Median (95% CI)	NC (11.499 to NC)	NC (6.439 to NC)	NC (21.454 to NC)	NC (22.669 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.2687		0.6146	
Hazard ratio (95% CI) vs Kd	-	1.92 (0.59 to 6.26)		0.90 (0.59 to 1.37)	
P-value	-	0.2773		0.6148	
Deterioration probability (95% CI)[b]					

A higher score represents a better level of quality of life. Clinical meaningful deterioration change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
PGM=DEVOPS/SAR650984/EFC15246/CIR_RWE/REPORT/PGM/eff_km_subgp_sr_sig_de_i_t.sas OUT=REPORT/OUTPUT/eff_km_c30_rol_detpl_piimid_de_i_t_x.rtf (07APR2021 14:23)

16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Insomnia
16.2.6.1.2.1 Efficacy response data
16.2.6.1.2.1.1 QLQ-C30 - Mean and 95% CI for insomnia score over time (LOCF) - ITT population



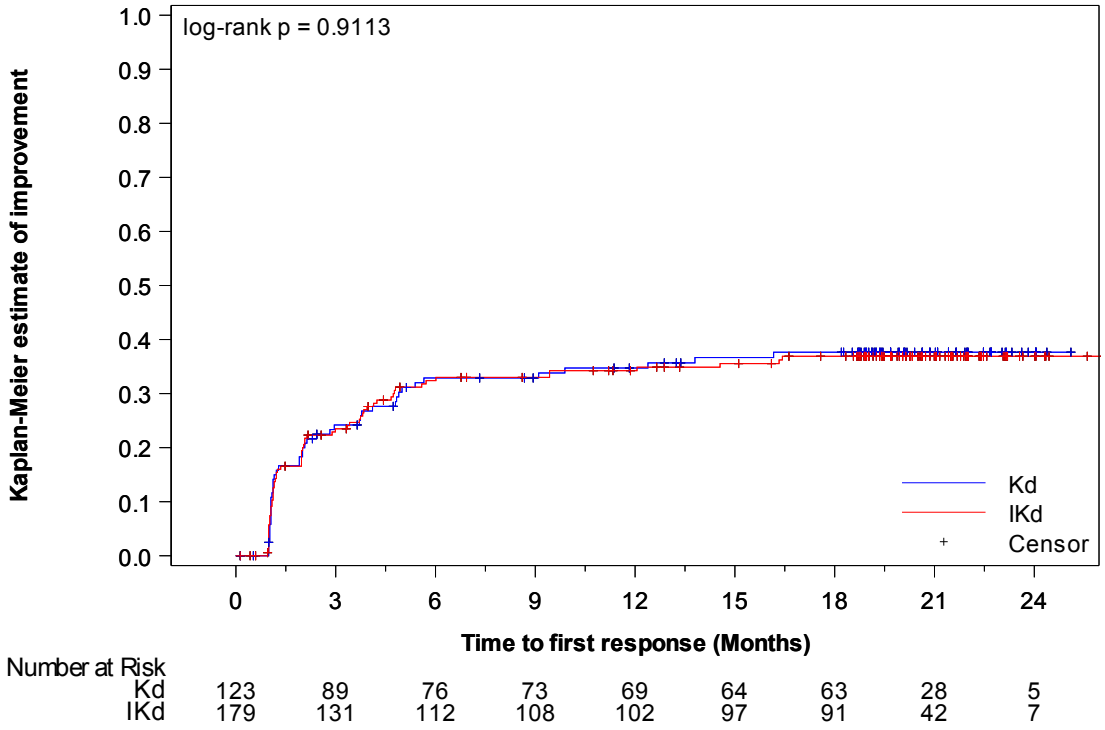
A lower score represents a better level of quality of life. Cycles with less than 20 patients overall are not presented.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
PGM=DEVOPS/SAR650984/EFC15246/CIR_RWE/REPORT/PGM/eff_qlq_line_i_f.sas OUT=REPORT/OUTPUT/eff_qlq_line_c30_ins_de_i_f_x.rtf (12FEB2021 15:16)

16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Insomnia
16.2.6.1.2.1 Efficacy response data
16.2.6.1.2.1.15 QLQ-C30 - Time to first improvement by 15 pt in Insomnia (LOCF) - ITT population

First improvement 15 points Insomnia (%)	**Kd (N=123)**	**IKd (N=179)**
Number (%) of events	44 (35.8)	63 (35.2)
Number (%) of patients censored	79 (64.2)	116 (64.8)
Kaplan-Meier estimates of Insomnia in months		
25% quantile (95% CI)	3.71 (1.906 to 5.651)	3.71 (1.971 to 5.585)
Median (95% CI)	NC (NC to NC)	NC (NC to NC)
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)
Comparison vs. Kd		
Stratified[a] Log-Rank test p-value[b] vs Kd	-	0.9113
Stratified[a] Hazard ratio (95% CI) vs Kd	-	0.98 (0.66 to 1.44)
P-value	-	0.9112
Improvement probability (95% CI)[c]		
3 Months	0.242 (0.170 to 0.321)	0.235 (0.175 to 0.300)
6 Months	0.329 (0.246 to 0.414)	0.324 (0.255 to 0.394)

A lower score represents a better level of quality of life. Clinical meaningful improvement change from baseline less than or equal to -15 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] Stratified on number of prior lines of therapy (1 vs. >1) and Revised International Staging System (R-ISS) stage (I or II vs. III vs. not classified) according to IRT
[b] One-sided significance level is 0.025
[c] Estimated using the Kaplan-Meier method
NA/NC = Not Applicable / Not Calculable
PGM=DEVOPS/SAR650984/EFC15246/CIR_RWE/REPORT/PGM/eff_km_invhr_sr_i_t.sas OUT=REPORT/OUTPUT/eff_km_c30_ins_imp15l_de_i_t_x.rtf (07APR2021 14:23)

16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Insomnia
16.2.6.1.2.1 Efficacy response data
16.2.6.1.2.1.16 QLQ-C30 - Time to first improvement by 15 pt in Insomnia - Kaplan-Meier curve (LOCF) - ITT population



A lower score represents a better level of quality of life. Clinical meaningful improvement change from baseline less than or equal to -15 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
PGM=DEVOPS/SAR650984/EFC15246/CIR_RWE/REPORT/PGM/eff_qlq_km_i_f.sas OUT=REPORT/OUTPUT/eff_km_c30_ins_imp15l_de_i_f_x.rtf (07APR2021 14:24)

16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Insomnia
16.2.6.1.2.1 Efficacy response data
16.2.6.1.2.1.17 QLQ-C30 - Time to first deterioration by 15 pt in Insomnia (LOCF) - ITT population

First deterioration 15 points Insomnia (%)	**Kd (N=123)**	**IKd (N=179)**
Number (%) of events	70 (56.9)	106 (59.2)
Number (%) of patients censored	53 (43.1)	73 (40.8)
Kaplan-Meier estimates of Insomnia in months		
25% quantile (95% CI)	1.94 (1.051 to 3.745)	1.87 (1.117 to 2.825)
Median (95% CI)	8.44 (5.651 to 17.610)	7.43 (4.665 to 12.386)
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)
Comparison vs. Kd		
Stratified[a] Log-Rank test p-value[b] vs Kd	-	0.5026
Stratified[a] Hazard ratio (95% CI) vs Kd	-	1.11 (0.82 to 1.51)
P-value	-	0.5028
Deterioration probability (95% CI)[c]		
3 Months	0.700 (0.610 to 0.774)	0.644 (0.569 to 0.711)
6 Months	0.580 (0.486 to 0.663)	0.539 (0.462 to 0.610)

A lower score represents a better level of quality of life. Clinical meaningful deterioration change from baseline greater than or equal to 15 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] Stratified on number of prior lines of therapy (1 vs. >1) and Revised International Staging System (R-ISS) stage (I or II vs. III vs. not classified) according to IRT
[b] One-sided significance level is 0.025
[c] Estimated using the Kaplan-Meier method
NA/NC = Not Applicable / Not Calculable
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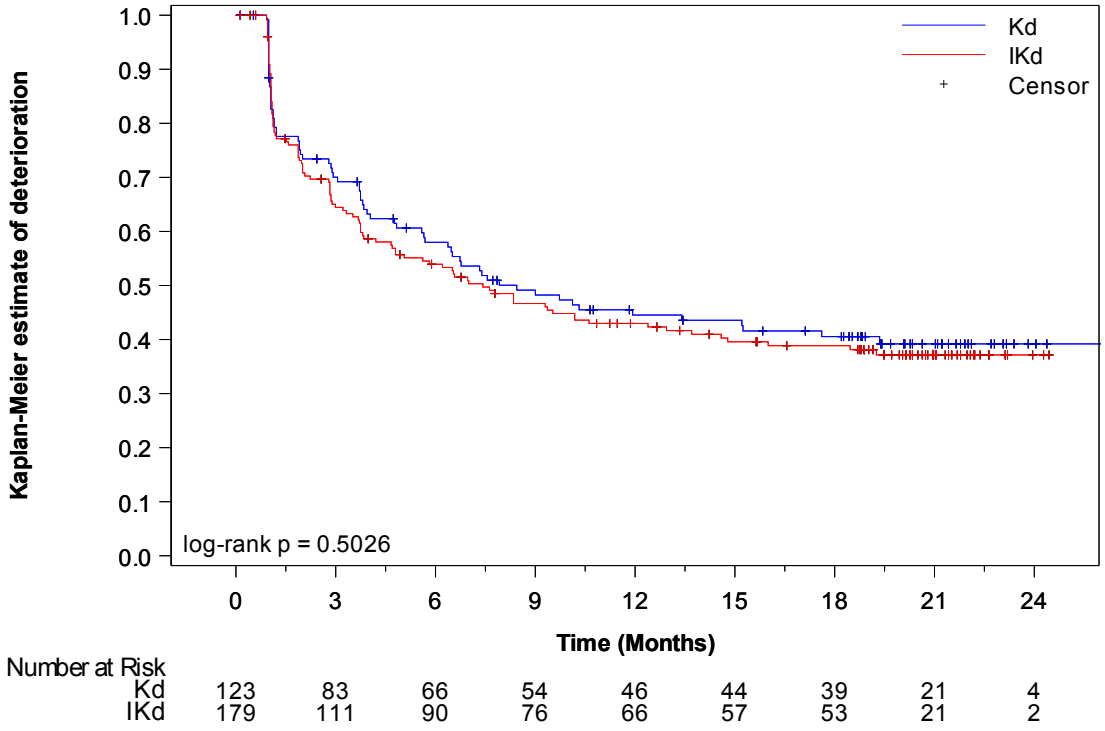
16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Insomnia
16.2.6.1.2.1 Efficacy response data
16.2.6.1.2.1.18 QLQ-C30 - Time to first deterioration by 15 pt in Insomnia - Kaplan-Meier curve (LOCF) - ITT population



A lower score represents a better level of quality of life. Clinical meaningful deterioration change from baseline greater than or equal to 15 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
PGM=DEVOPS/SAR650984/EFC15246/CIR_RWE/REPORT/PGM/eff_qlq_km_i_f.sas OUT=REPORT/OUTPUT/eff_km_c30_ins_det15l_de_i_f_x.rtf (07APR2021 14:24)

16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Insomnia
16.2.6.1.2.1 Efficacy response data
16.2.6.1.2.1.19 QLQ-C30 - Time until permanent improvement by 15 pt in Insomnia (LOCF) - ITT population

First permanent improvement 15 points Insomnia (%)	**Kd (N=123)**	**IKd (N=179)**
Number (%) of events	24 (19.5)	40 (22.3)
Number (%) of patients censored	99 (80.5)	139 (77.7)
Kaplan-Meier estimates of Insomnia in months		
25% quantile (95% CI)	NC (13.799 to NC)	20.70 (17.840 to NC)
Median (95% CI)	NC (NC to NC)	NC (23.721 to NC)
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)
Comparison vs. Kd		
Stratified[a] Log-Rank test p-value[b] vs Kd	-	0.6133
Stratified[a] Hazard ratio (95% CI) vs Kd	-	1.14 (0.69 to 1.89)
P-value	-	0.6135
Improvement probability (95% CI)[c]		
3 Months	0.050 (0.021 to 0.100)	0.080 (0.046 to 0.126)
6 Months	0.076 (0.038 to 0.133)	0.116 (0.073 to 0.168)

A lower score represents a better level of quality of life. Clinical meaningful improvement change from baseline less than or equal to -15 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] Stratified on number of prior lines of therapy (1 vs. >1) and Revised International Staging System (R-ISS) stage (I or II vs. III vs. not classified) according to IRT
[b] One-sided significance level is 0.025
[c] Estimated using the Kaplan-Meier method
NA/NC = Not Applicable / Not Calculable
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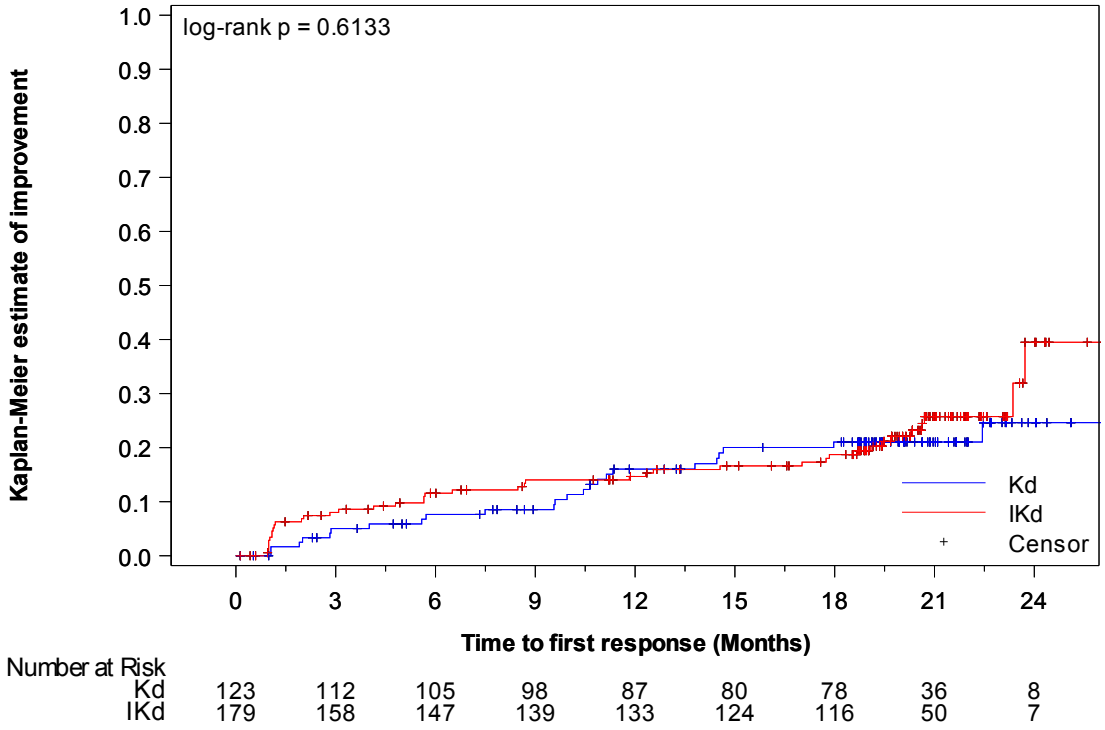
16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Insomnia
16.2.6.1.2.1 Efficacy response data
16.2.6.1.2.1.20 QLQ-C30 - Time until permanent improvement by 15 pt in Insomnia - Kaplan-Meier curve (LOCF) - ITT population



A lower score represents a better level of quality of life. Clinical meaningful improvement change from baseline less than or equal to -15 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
PGM=DEVOPS/SAR650984/EFC15246/CIR_RWE/REPORT/PGM/eff_qlq_km_i_f.sas OUT=REPORT/OUTPUT/eff_km_c30_ins_imp15pl_de_i_f_x.rtf (07APR2021 14:24)

16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Insomnia
16.2.6.1.2.1 Efficacy response data
16.2.6.1.2.1.21 QLQ-C30 - Time until permanent deterioration by 15 pt in Insomnia (LOCF) - ITT population

First permanent deterioration 15 points Insomnia (%)	**Kd (N=123)**	**IKd (N=179)**
Number (%) of events	29 (23.6)	40 (22.3)
Number (%) of patients censored	94 (76.4)	139 (77.7)
Kaplan-Meier estimates of Insomnia in months		
25% quantile (95% CI)	20.60 (17.051 to NC)	21.42 (14.982 to NC)
Median (95% CI)	NC (NC to NC)	NC (NC to NC)
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)
Comparison vs. Kd		
Stratified[a] Log-Rank test p-value[b] vs Kd	-	0.8578
Stratified[a] Hazard ratio (95% CI) vs Kd	-	0.96 (0.59 to 1.55)
P-value	-	0.8573
Deterioration probability (95% CI)[c]		
3 Months	0.917 (0.851 to 0.954)	0.943 (0.896 to 0.969)
6 Months	0.900 (0.830 to 0.942)	0.908 (0.854 to 0.943)

A lower score represents a better level of quality of life. Clinical meaningful deterioration change from baseline greater than or equal to 15 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] Stratified on number of prior lines of therapy (1 vs. >1) and Revised International Staging System (R-ISS) stage (I or II vs. III vs. not classified) according to IRT
[b] One-sided significance level is 0.025
[c] Estimated using the Kaplan-Meier method
NA/NC = Not Applicable / Not Calculable
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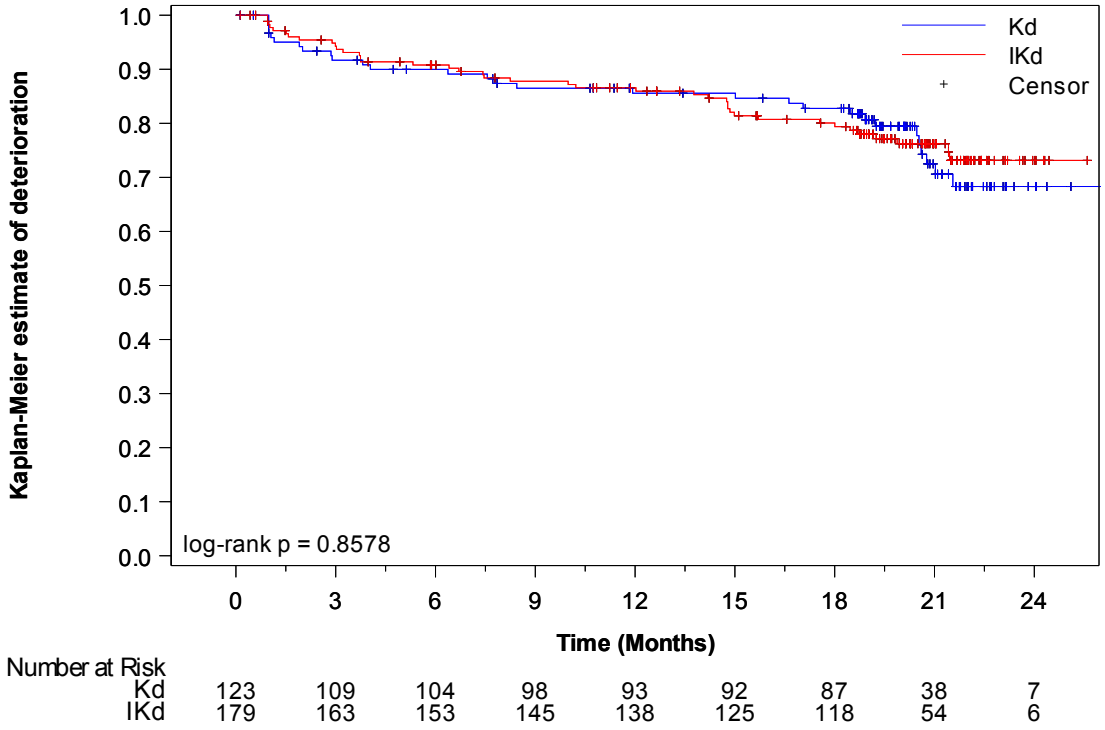
16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Insomnia
16.2.6.1.2.1 Efficacy response data
16.2.6.1.2.1.22 QLQ-C30 - Time until permanent deterioration by 15 pt in Insomnia - Kaplan-Meier curve (LOCF) - ITT population



A lower score represents a better level of quality of life. Clinical meaningful deterioration change from baseline greater than or equal to 15 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
PGM=DEVOPS/SAR650984/EFC15246/CIR_RWE/REPORT/PGM/eff_qlq_km_i_f.sas OUT=REPORT/OUTPUT/eff_km_c30_ins_det15pl_de_i_f_x.rtf (07APR2021 14:24)

16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Insomnia
16.2.6.1.2.2 Efficacy response data - Subgroup analyses by age
16.2.6.1.2.2.3 QLQ-C30 - Time to first improvement by 10 pt in insomnia according to age (LOCF) - ITT population

	<65 years		>=65 years		
	Kd (N=66)	**IKd (N=88)**	**Kd (N=57)**	**IKd (N=91)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	22 (33.3)	29 (33.0)	22 (38.6)	34 (37.4)	0.8908
Number (%) of patients censored	44 (66.7)	59 (67.0)	35 (61.4)	57 (62.6)	
Kaplan-Meier estimates of Insomnia in months					
25% quantile (95% CI)	2.43 (1.051 to NC)	3.81 (1.216 to 16.329)	3.75 (2.004 to 12.386)	3.35 (1.347 to 6.012)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (12.386 to NC)	NC (16.427 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.8969		0.9799	
Hazard ratio (95% CI) vs Kd	-	0.96 (0.55 to 1.68)		1.01 (0.59 to 1.72)	
P-value	-	0.8966		0.9799	
Improvement probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful improvement change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Insomnia
16.2.6.1.2.2 Efficacy response data - Subgroup analyses by age
16.2.6.1.2.2.4 QLQ-C30 - Time to first deterioration by 10 pt in insomnia according to age (LOCF) - ITT population

	<65 years		>=65 years		
	Kd (N=66)	**IKd (N=88)**	**Kd (N=57)**	**IKd (N=91)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	34 (51.5)	51 (58.0)	36 (63.2)	55 (60.4)	0.5785
Number (%) of patients censored	32 (48.5)	37 (42.0)	21 (36.8)	36 (39.6)	
Kaplan-Meier estimates of Insomnia in months					
25% quantile (95% CI)	1.91 (1.051 to 3.844)	1.87 (1.084 to 2.825)	1.94 (1.018 to 3.811)	1.87 (1.051 to 2.990)	
Median (95% CI)	11.93 (4.764 to NC)	7.62 (3.745 to NC)	7.92 (3.811 to 13.405)	7.43 (3.745 to 13.700)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (13.405 to NC)	NC (19.253 to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.4918		0.9479	
Hazard ratio (95% CI) vs Kd	-	1.16 (0.75 to 1.80)		0.99 (0.65 to 1.50)	
P-value	-	0.4922		0.9478	
Deterioration probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful deterioration change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Insomnia
16.2.6.1.2.2 Efficacy response data - Subgroup analyses by age
16.2.6.1.2.2.5 QLQ-C30 - Time until permanent improvement by 10 pt in insomnia according to age (LOCF) - ITT population

	<65 years		>=65 years		
	Kd (N=66)	**IKd (N=88)**	**Kd (N=57)**	**IKd (N=91)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	12 (18.2)	20 (22.7)	12 (21.1)	20 (22.0)	0.7319
Number (%) of patients censored	54 (81.8)	68 (77.3)	45 (78.9)	71 (78.0)	
Kaplan-Meier estimates of Insomnia in months					
25% quantile (95% CI)	22.44 (9.955 to NC)	23.72 (11.828 to NC)	NC (11.335 to NC)	20.70 (14.554 to NC)	
Median (95% CI)	NC (NC to NC)	NC (23.721 to NC)	NC (NC to NC)	NC (23.359 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (23.721 to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.5104		0.9257	
Hazard ratio (95% CI) vs Kd	-	1.27 (0.62 to 2.60)		1.03 (0.51 to 2.12)	
P-value	-	0.5114		0.9260	
Improvement probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful improvement change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
PGM=DEVOPS/SAR650984/EFC15246/CIR_RWE/REPORT/PGM/eff_km_subgp_sr_sig_de_i_t.sas OUT=REPORT/OUTPUT/eff_km_c30_ins_imppl_age_de_i_t_x.rtf (07APR2021 14:33)

16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Insomnia
16.2.6.1.2.2 Efficacy response data - Subgroup analyses by age
16.2.6.1.2.2.6 QLQ-C30 - Time until permanent deterioration by 10 pt in insomnia according to age (LOCF) - ITT population

	<65 years		>=65 years		
	Kd (N=66)	**IKd (N=88)**	**Kd (N=57)**	**IKd (N=91)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	17 (25.8)	20 (22.7)	12 (21.1)	20 (22.0)	0.7284
Number (%) of patients censored	49 (74.2)	68 (77.3)	45 (78.9)	71 (78.0)	
Kaplan-Meier estimates of Insomnia in months					
25% quantile (95% CI)	20.60 (11.926 to NC)	21.42 (14.193 to NC)	NC (7.786 to NC)	21.45 (14.784 to NC)	
Median (95% CI)	NC (21.027 to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.7118		0.8875	
Hazard ratio (95% CI) vs Kd	-	0.89 (0.46 to 1.69)		1.05 (0.51 to 2.15)	
P-value	-	0.7119		0.8882	
Deterioration probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful deterioration change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
PGM=DEVOPS/SAR650984/EFC15246/CIR_RWE/REPORT/PGM/eff_km_subgp_sr_sig_de_i_t.sas OUT=REPORT/OUTPUT/eff_km_c30_ins_detpl_age_de_i_t_x.rtf (07APR2021 14:33)

16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Insomnia
16.2.6.1.2.3 Efficacy response data - Subgroup analyses by gender
16.2.6.1.2.3.3 QLQ-C30 - Time to first improvement by 10 pt in insomnia according to gender (LOCF) - ITT population

	Male		Female		
	Kd (N=68)	**IKd (N=101)**	**Kd (N=55)**	**IKd (N=78)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	17 (25.0)	28 (27.7)	27 (49.1)	35 (44.9)	0.5255
Number (%) of patients censored	51 (75.0)	73 (72.3)	28 (50.9)	43 (55.1)	
Kaplan-Meier estimates of Insomnia in months					
25% quantile (95% CI)	16.16 (2.070 to NC)	5.72 (1.971 to NC)	1.22 (1.051 to 3.745)	2.07 (1.117 to 3.745)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	13.80 (3.745 to NC)	NC (4.764 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.6703		0.6418	
Hazard ratio (95% CI) vs Kd	-	1.14 (0.62 to 2.08)		0.89 (0.54 to 1.47)	
P-value	-	0.6705		0.6420	
Improvement probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful improvement change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Insomnia
16.2.6.1.2.3 Efficacy response data - Subgroup analyses by gender
16.2.6.1.2.3.4 QLQ-C30 - Time to first deterioration by 10 pt in insomnia according to gender (LOCF) - ITT population

	Male		Female		
	Kd (N=68)	**IKd (N=101)**	**Kd (N=55)**	**IKd (N=78)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	40 (58.8)	64 (63.4)	30 (54.5)	42 (53.8)	0.3706
Number (%) of patients censored	28 (41.2)	37 (36.6)	25 (45.5)	36 (46.2)	
Kaplan-Meier estimates of Insomnia in months					
25% quantile (95% CI)	2.00 (1.117 to 4.764)	1.58 (1.084 to 2.234)	1.87 (0.986 to 3.713)	2.07 (1.051 to 3.745)	
Median (95% CI)	7.56 (4.830 to 17.610)	5.62 (2.891 to 9.363)	9.72 (3.713 to NC)	13.70 (5.060 to NC)	
75% quantile (95% CI)	NC (19.351 to NC)	NC (14.587 to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.3172		0.7453	
Hazard ratio (95% CI) vs Kd	-	1.22 (0.82 to 1.82)		0.93 (0.58 to 1.48)	
P-value	-	0.3181		0.7453	
Deterioration probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful deterioration change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Insomnia
16.2.6.1.2.3 Efficacy response data - Subgroup analyses by gender
16.2.6.1.2.3.5 QLQ-C30 - Time until permanent improvement by 10 pt in insomnia according to gender (LOCF) - ITT population

	Male		Female		
	Kd (N=68)	**IKd (N=101)**	**Kd (N=55)**	**IKd (N=78)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	8 (11.8)	19 (18.8)	16 (29.1)	21 (26.9)	0.2330
Number (%) of patients censored	60 (88.2)	82 (81.2)	39 (70.9)	57 (73.1)	
Kaplan-Meier estimates of Insomnia in months					
25% quantile (95% CI)	NC (17.971 to NC)	NC (14.554 to NC)	13.80 (5.585 to NC)	19.48 (8.706 to 23.721)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (22.439 to NC)	23.72 (23.359 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (23.359 to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.2201		0.7974	
Hazard ratio (95% CI) vs Kd	-	1.67 (0.73 to 3.81)		0.92 (0.48 to 1.76)	
P-value	-	0.2253		0.7975	
Improvement probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful improvement change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Insomnia
16.2.6.1.2.3 Efficacy response data - Subgroup analyses by gender
16.2.6.1.2.3.6 QLQ-C30 - Time until permanent deterioration by 10 pt in insomnia according to gender (LOCF) - ITT population

	Male		Female		
	Kd (N=68)	**IKd (N=101)**	**Kd (N=55)**	**IKd (N=78)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	18 (26.5)	24 (23.8)	11 (20.0)	16 (20.5)	0.8666
Number (%) of patients censored	50 (73.5)	77 (76.2)	44 (80.0)	62 (79.5)	
Kaplan-Meier estimates of Insomnia in months					
25% quantile (95% CI)	20.53 (7.556 to NC)	19.25 (12.025 to NC)	21.03 (18.464 to NC)	NC (14.784 to NC)	
Median (95% CI)	NC (21.552 to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.7879		0.9793	
Hazard ratio (95% CI) vs Kd	-	0.92 (0.50 to 1.69)		1.01 (0.47 to 2.18)	
P-value	-	0.7880		0.9793	
Deterioration probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful deterioration change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Insomnia
16.2.6.1.2.4 Efficacy response data - Subgroup analyses by ethnic origin
16.2.6.1.2.4.3 QLQ-C30 - Time to first improvement by 10 pt in insomnia according to ethnic origin (LOCF) - ITT population

	White		Other		
	Kd (N=83)	**IKd (N=131)**	**Kd (N=28)**	**IKd (N=34)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	29 (34.9)	46 (35.1)	14 (50.0)	13 (38.2)	0.4863
Number (%) of patients censored	54 (65.1)	85 (64.9)	14 (50.0)	21 (61.8)	
Kaplan-Meier estimates of Insomnia in months					
25% quantile (95% CI)	3.78 (1.906 to 9.889)	3.81 (1.971 to 9.429)	1.15 (1.051 to 4.107)	2.04 (0.986 to 4.797)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	16.16 (1.281 to NC)	NC (2.990 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.9559		0.4261	
Hazard ratio (95% CI) vs Kd	-	1.01 (0.64 to 1.61)		0.74 (0.35 to 1.57)	
P-value	-	0.9560		0.4279	
Improvement probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful improvement change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Insomnia
16.2.6.1.2.4 Efficacy response data - Subgroup analyses by ethnic origin
16.2.6.1.2.4.4 QLQ-C30 - Time to first deterioration by 10 pt in insomnia according to ethnic origin (LOCF) - ITT population

	White		Other		
	Kd (N=83)	**IKd (N=131)**	**Kd (N=28)**	**IKd (N=34)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	48 (57.8)	80 (61.1)	14 (50.0)	20 (58.8)	0.6520
Number (%) of patients censored	35 (42.2)	51 (38.9)	14 (50.0)	14 (41.2)	
Kaplan-Meier estimates of Insomnia in months					
25% quantile (95% CI)	1.91 (1.051 to 3.745)	1.58 (1.084 to 2.070)	3.84 (1.150 to 7.556)	2.83 (0.986 to 3.811)	
Median (95% CI)	7.92 (4.830 to 19.351)	6.21 (3.515 to 10.612)	11.93 (4.764 to NC)	8.34 (3.680 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (15.211 to NC)	NC (12.386 to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.5037		0.3842	
Hazard ratio (95% CI) vs Kd	-	1.13 (0.79 to 1.62)		1.35 (0.68 to 2.68)	
P-value	-	0.5040		0.3860	
Deterioration probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful deterioration change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Insomnia
16.2.6.1.2.4 Efficacy response data - Subgroup analyses by ethnic origin
16.2.6.1.2.4.5 QLQ-C30 - Time until permanent improvement by 10 pt in insomnia according to ethnic origin (LOCF) - ITT population

	White		Other		
	Kd (N=83)	**IKd (N=131)**	**Kd (N=28)**	**IKd (N=34)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	17 (20.5)	29 (22.1)	6 (21.4)	9 (26.5)	0.6054
Number (%) of patients censored	66 (79.5)	102 (77.9)	22 (78.6)	25 (73.5)	
Kaplan-Meier estimates of Insomnia in months					
25% quantile (95% CI)	22.44 (10.645 to NC)	23.36 (17.741 to NC)	17.97 (5.717 to NC)	8.71 (1.150 to NC)	
Median (95% CI)	NC (NC to NC)	NC (23.359 to NC)	NC (NC to NC)	NC (20.632 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.8235		0.4900	
Hazard ratio (95% CI) vs Kd	-	1.07 (0.59 to 1.95)		1.44 (0.51 to 4.04)	
P-value	-	0.8235		0.4924	
Improvement probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful improvement change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Insomnia
16.2.6.1.2.4 Efficacy response data - Subgroup analyses by ethnic origin
16.2.6.1.2.4.6 QLQ-C30 - Time until permanent deterioration by 10 pt in insomnia according to ethnic origin (LOCF) - ITT population

	White		Other		
	Kd (N=83)	**IKd (N=131)**	**Kd (N=28)**	**IKd (N=34)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	19 (22.9)	31 (23.7)	6 (21.4)	7 (20.6)	0.8586
Number (%) of patients censored	64 (77.1)	100 (76.3)	22 (78.6)	27 (79.4)	
Kaplan-Meier estimates of Insomnia in months					
25% quantile (95% CI)	20.60 (18.464 to NC)	19.88 (14.752 to NC)	21.55 (2.891 to NC)	21.42 (6.407 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (21.552 to NC)	NC (21.421 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.8133		0.9603	
Hazard ratio (95% CI) vs Kd	-	1.07 (0.61 to 1.90)		0.97 (0.33 to 2.90)	
P-value	-	0.8133		0.9602	
Deterioration probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful deterioration change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Insomnia
16.2.6.1.2.5 Efficacy response data - Subgroup analyses by geographical region
16.2.6.1.2.5.3 QLQ-C30 - Time to first improvement by 10 pt in insomnia according to geographical region (LOCF) - ITT population

	Europe		America		Asia		Other countries		
	Kd (N=60)	**IKd (N=85)**	**Kd (N=20)**	**IKd (N=24)**	**Kd (N=21)**	**IKd (N=25)**	**Kd (N=22)**	**IKd (N=45)**	**p-value of treatment-by-subgroup interaction[c]**
Number (%) of events	15 (25.0)	30 (35.3)	9 (45.0)	9 (37.5)	11 (52.4)	9 (36.0)	9 (40.9)	15 (33.3)	0.3373
Number (%) of patients censored	45 (75.0)	55 (64.7)	11 (55.0)	15 (62.5)	10 (47.6)	16 (64.0)	13 (59.1)	30 (66.7)	
Kaplan-Meier estimates of event in months									
25% quantile (95% CI)	9.89 (2.136 to NC)	3.71 (1.216 to 12.057)	1.59 (0.986 to 9.101)	3.84 (0.986 to NC)	1.12 (1.018 to 4.107)	2.04 (0.986 to NC)	2.96 (1.018 to NC)	4.24 (1.117 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (1.281 to NC)	NC (4.140 to NC)	5.39 (1.117 to NC)	NC (2.070 to NC)	NC (2.957 to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (12.386 to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	

A lower score represents a better level of quality of life. Clinical meaningful improvement change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Insomnia
16.2.6.1.2.5 Efficacy response data - Subgroup analyses by geographical region
16.2.6.1.2.5.3 QLQ-C30 - Time to first improvement by 10 pt in insomnia according to geographical region (LOCF) - ITT population

	Europe		America		Asia		Other countries		
	Kd (N=60)	**IKd (N=85)**	**Kd (N=20)**	**IKd (N=24)**	**Kd (N=21)**	**IKd (N=25)**	**Kd (N=22)**	**IKd (N=45)**	**p-value of treatment-by-subgroup interaction[c]**
Comparison vs. Kd									
Log-Rank test p-value[a] vs Kd	-	0.1980		0.7144		0.2670		0.6214	
Hazard ratio (95% CI) vs Kd	-	1.50 (0.81 to 2.78)		0.84 (0.33 to 2.12)		0.61 (0.25 to 1.47)		0.81 (0.36 to 1.86)	
P-value	-	0.2011		0.7147		0.2718		0.6220	
Improvement probability (95% CI)[b]									
3 Months	0.137 (0.064 to 0.238)	0.229 (0.146 to 0.324)	0.350 (0.157 to 0.552)	0.220 (0.080 to 0.403)	0.400 (0.193 to 0.600)	0.333 (0.159 to 0.519)	0.273 (0.111 to 0.464)	0.200 (0.099 to 0.326)	

A lower score represents a better level of quality of life. Clinical meaningful improvement change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Insomnia
16.2.6.1.2.5 Efficacy response data - Subgroup analyses by geographical region
16.2.6.1.2.5.4 QLQ-C30 - Time to first deterioration by 10 pt in insomnia according to geographical region (LOCF) - ITT population

	Europe		America		Asia		Other countries		
	Kd (N=60)	**IKd (N=85)**	**Kd (N=20)**	**IKd (N=24)**	**Kd (N=21)**	**IKd (N=25)**	**Kd (N=22)**	**IKd (N=45)**	**p-value of treatment-by-subgroup interaction[c]**
Number (%) of events	33 (55.0)	47 (55.3)	12 (60.0)	13 (54.2)	10 (47.6)	17 (68.0)	15 (68.2)	29 (64.4)	0.6582
Number (%) of patients censored	27 (45.0)	38 (44.7)	8 (40.0)	11 (45.8)	11 (52.4)	8 (32.0)	7 (31.8)	16 (35.6)	
Kaplan-Meier estimates of event in months									
25% quantile (95% CI)	1.05 (0.986 to 3.713)	2.00 (1.117 to 4.205)	1.56 (0.920 to 8.444)	1.58 (0.986 to 3.844)	3.75 (1.117 to 11.926)	1.97 (0.953 to 3.745)	1.94 (0.986 to 4.830)	1.12 (1.051 to 2.004)	
Median (95% CI)	6.77 (3.713 to NC)	9.30 (5.060 to NC)	13.86 (1.216 to NC)	6.21 (2.858 to NC)	15.21 (3.745 to NC)	6.98 (2.825 to 12.945)	6.01 (1.938 to NC)	3.75 (1.906 to 14.784)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (17.610 to NC)	NC (6.209 to NC)	NC (15.211 to NC)	NC (8.345 to NC)	NC (6.374 to NC)	NC (10.185 to NC)	

A lower score represents a better level of quality of life. Clinical meaningful deterioration change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
PGM=DEVOPS/SAR650984/EFC15246/CIR_RWE/REPORT/PGM/eff_km_subgp_sr_sig_de_i_t.sas OUT=REPORT/OUTPUT/eff_km_c30_ins_detl_greg_de_i_t_x.rtf (07APR2021 14:33)

16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Insomnia
16.2.6.1.2.5 Efficacy response data - Subgroup analyses by geographical region
16.2.6.1.2.5.4 QLQ-C30 - Time to first deterioration by 10 pt in insomnia according to geographical region (LOCF) - ITT population

	Europe		America		Asia		Other countries		
	Kd (N=60)	**IKd (N=85)**	**Kd (N=20)**	**IKd (N=24)**	**Kd (N=21)**	**IKd (N=25)**	**Kd (N=22)**	**IKd (N=45)**	**p-value of treatment-by-subgroup interaction[c]**
Comparison vs. Kd									
Log-Rank test p-value[a] vs Kd	-	0.8243		0.8109		0.1909		0.8479	
Hazard ratio (95% CI) vs Kd	-	0.95 (0.61 to 1.48)		1.10 (0.50 to 2.43)		1.68 (0.77 to 3.66)		1.06 (0.57 to 1.98)	
P-value	-	0.8235		0.8111		0.1958		0.8479	
Deterioration probability (95% CI)[b]									
3 Months	0.658 (0.522 to 0.764)	0.686 (0.574 to 0.774)	0.700 (0.451 to 0.853)	0.691 (0.458 to 0.839)	0.797 (0.545 to 0.919)	0.667 (0.443 to 0.817)	0.727 (0.491 to 0.867)	0.533 (0.379 to 0.666)	

A lower score represents a better level of quality of life. Clinical meaningful deterioration change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
PGM=DEVOPS/SAR650984/EFC15246/CIR_RWE/REPORT/PGM/eff_km_subgp_sr_sig_de_i_t.sas OUT=REPORT/OUTPUT/eff_km_c30_ins_detl_greg_de_i_t_x.rtf (07APR2021 14:33)

16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Insomnia
16.2.6.1.2.5 Efficacy response data - Subgroup analyses by geographical region
16.2.6.1.2.5.5 QLQ-C30 - Time until permanent improvement by 10 pt in insomnia according to geographical region (LOCF) - ITT population

	Europe		America		Asia		Other countries		
	Kd (N=60)	**IKd (N=85)**	**Kd (N=20)**	**IKd (N=24)**	**Kd (N=21)**	**IKd (N=25)**	**Kd (N=22)**	**IKd (N=45)**	**p-value of treatment-by-subgroup interaction[c]**
Number (%) of events	8 (13.3)	19 (22.4)	5 (25.0)	6 (25.0)	4 (19.0)	6 (24.0)	7 (31.8)	9 (20.0)	0.4788
Number (%) of patients censored	52 (86.7)	66 (77.6)	15 (75.0)	18 (75.0)	17 (81.0)	19 (76.0)	15 (68.2)	36 (80.0)	
Kaplan-Meier estimates of event in months									
25% quantile (95% CI)	NC (14.653 to NC)	23.36 (17.741 to 23.721)	14.52 (1.051 to NC)	14.55 (0.986 to NC)	NC (2.825 to NC)	20.63 (0.986 to NC)	14.46 (2.004 to NC)	NC (8.476 to NC)	
Median (95% CI)	NC (NC to NC)	NC (23.359 to NC)	NC (14.522 to NC)	NC (14.554 to NC)	NC (11.138 to NC)	NC (20.632 to NC)	NC (14.456 to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (23.721 to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	

A lower score represents a better level of quality of life. Clinical meaningful improvement change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
PGM=DEVOPS/SAR650984/EFC15246/CIR_RWE/REPORT/PGM/eff_km_subgp_sr_sig_de_i_t.sas OUT=REPORT/OUTPUT/eff_km_c30_ins_imppl_greg_de_i_t_x.rtf (07APR2021 14:33)

16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Insomnia
16.2.6.1.2.5 Efficacy response data - Subgroup analyses by geographical region
16.2.6.1.2.5.5 QLQ-C30 - Time until permanent improvement by 10 pt in insomnia according to geographical region (LOCF) - ITT population

	Europe		America		Asia		Other countries		
	Kd (N=60)	**IKd (N=85)**	**Kd (N=20)**	**IKd (N=24)**	**Kd (N=21)**	**IKd (N=25)**	**Kd (N=22)**	**IKd (N=45)**	**p-value of treatment-by-subgroup interaction[c]**
Comparison vs. Kd									
Log-Rank test p-value[a] vs Kd	-	0.2084		0.8769		0.6539		0.2975	
Hazard ratio (95% CI) vs Kd	-	1.69 (0.74 to 3.87)		1.10 (0.33 to 3.60)		1.33 (0.38 to 4.74)		0.59 (0.22 to 1.60)	
P-value	-	0.2137		0.8773		0.6550		0.3028	
Improvement probability (95% CI)[b]									
3 Months	0.017 (0.001 to 0.081)	0.073 (0.030 to 0.142)	0.150 (0.037 to 0.335)	0.087 (0.015 to 0.242)	0.053 (0.004 to 0.214)	0.125 (0.031 to 0.287)	0.045 (0.003 to 0.189)	0.067 (0.017 to 0.164)	

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The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Insomnia
16.2.6.1.2.5 Efficacy response data - Subgroup analyses by geographical region
16.2.6.1.2.5.6 QLQ-C30 - Time until permanent deterioration by 10 pt in insomnia according to geographical region (LOCF) - ITT population

	Europe		America		Asia		Other countries		
	Kd (N=60)	**IKd (N=85)**	**Kd (N=20)**	**IKd (N=24)**	**Kd (N=21)**	**IKd (N=25)**	**Kd (N=22)**	**IKd (N=45)**	**p-value of treatment-by-subgroup interaction[c]**
Number (%) of events	14 (23.3)	19 (22.4)	4 (20.0)	4 (16.7)	6 (28.6)	7 (28.0)	5 (22.7)	10 (22.2)	0.9899
Number (%) of patients censored	46 (76.7)	66 (77.6)	16 (80.0)	20 (83.3)	15 (71.4)	18 (72.0)	17 (77.3)	35 (77.8)	
Kaplan-Meier estimates of event in months									
25% quantile (95% CI)	20.60 (3.811 to NC)	21.45 (17.544 to NC)	20.62 (1.906 to NC)	NC (0.986 to NC)	11.93 (1.150 to NC)	15.70 (1.018 to NC)	20.53 (4.041 to NC)	NC (5.322 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (20.468 to NC)	NC (NC to NC)	NC (11.926 to NC)	NC (15.704 to NC)	NC (20.534 to NC)	NC (NC to NC)	

A lower score represents a better level of quality of life. Clinical meaningful deterioration change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Insomnia
16.2.6.1.2.5 Efficacy response data - Subgroup analyses by geographical region
16.2.6.1.2.5.6 QLQ-C30 - Time until permanent deterioration by 10 pt in insomnia according to geographical region (LOCF) - ITT population

	Europe		America		Asia		Other countries		
	Kd (N=60)	**IKd (N=85)**	**Kd (N=20)**	**IKd (N=24)**	**Kd (N=21)**	**IKd (N=25)**	**Kd (N=22)**	**IKd (N=45)**	**p-value of treatment-by-subgroup interaction[c]**
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (20.764 to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Kd									
Log-Rank test p-value[a] vs Kd	-	0.7938		0.9441		0.8730		0.8699	
Hazard ratio (95% CI) vs Kd	-	0.91 (0.46 to 1.82)		0.95 (0.24 to 3.81)		0.91 (0.31 to 2.72)		1.09 (0.37 to 3.20)	
P-value	-	0.7938		0.9441		0.8731		0.8699	
Deterioration probability (95% CI)[b]									

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The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Insomnia
16.2.6.1.2.6 Efficacy response data - Subgroup analyses by regulatory region
16.2.6.1.2.6.3 QLQ-C30 - Time to first improvement by 10 pt in insomnia according to regulatory region (LOCF) - ITT population

	Western countries		Other countries		
	Kd (N=55)	**IKd (N=97)**	**Kd (N=68)**	**IKd (N=82)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	16 (29.1)	37 (38.1)	28 (41.2)	26 (31.7)	0.1076
Number (%) of patients censored	39 (70.9)	60 (61.9)	40 (58.8)	56 (68.3)	
Kaplan-Meier estimates of Insomnia in months					
25% quantile (95% CI)	4.83 (2.136 to NC)	3.75 (1.216 to 5.717)	1.28 (1.051 to 5.388)	3.42 (1.971 to NC)	
Median (95% CI)	NC (NC to NC)	NC (16.329 to NC)	NC (5.651 to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.2605		0.2593	
Hazard ratio (95% CI) vs Kd	-	1.40 (0.78 to 2.51)		0.74 (0.43 to 1.26)	
P-value	-	0.2628		0.2611	
Improvement probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful improvement change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Insomnia
16.2.6.1.2.6 Efficacy response data - Subgroup analyses by regulatory region
16.2.6.1.2.6.4 QLQ-C30 - Time to first deterioration by 10 pt in insomnia according to regulatory region (LOCF) - ITT population

	Western countries		Other countries		
	Kd (N=55)	**IKd (N=97)**	**Kd (N=68)**	**IKd (N=82)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	29 (52.7)	48 (49.5)	41 (60.3)	58 (70.7)	0.0732
Number (%) of patients censored	26 (47.3)	49 (50.5)	27 (39.7)	24 (29.3)	
Kaplan-Meier estimates of Insomnia in months					
25% quantile (95% CI)	1.05 (0.986 to 2.858)	1.97 (1.117 to 4.665)	3.06 (1.150 to 4.764)	1.31 (1.051 to 2.793)	
Median (95% CI)	10.32 (2.858 to NC)	18.46 (6.998 to NC)	8.44 (4.830 to 17.610)	3.75 (2.825 to 6.965)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (19.351 to NC)	NC (8.345 to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.4852		0.0566	
Hazard ratio (95% CI) vs Kd	-	0.85 (0.53 to 1.35)		1.47 (0.99 to 2.20)	
P-value	-	0.4857		0.0582	
Deterioration probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful deterioration change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Insomnia
16.2.6.1.2.6 Efficacy response data - Subgroup analyses by regulatory region
16.2.6.1.2.6.5 QLQ-C30 - Time until permanent improvement by 10 pt in insomnia according to regulatory region (LOCF) - ITT population

	Western countries		Other countries		
	Kd (N=55)	**IKd (N=97)**	**Kd (N=68)**	**IKd (N=82)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	11 (20.0)	23 (23.7)	13 (19.1)	17 (20.7)	0.8184
Number (%) of patients censored	44 (80.0)	74 (76.3)	55 (80.9)	65 (79.3)	
Kaplan-Meier estimates of Insomnia in months					
25% quantile (95% CI)	22.44 (11.335 to NC)	20.30 (14.554 to NC)	NC (9.561 to NC)	23.36 (11.828 to NC)	
Median (95% CI)	NC (22.439 to NC)	NC (NC to NC)	NC (NC to NC)	NC (23.359 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.5832		0.7819	
Hazard ratio (95% CI) vs Kd	-	1.22 (0.60 to 2.51)		1.11 (0.54 to 2.28)	
P-value	-	0.5839		0.7820	
Improvement probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful improvement change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Insomnia
16.2.6.1.2.6 Efficacy response data - Subgroup analyses by regulatory region
16.2.6.1.2.6.6 QLQ-C30 - Time until permanent deterioration by 10 pt in insomnia according to regulatory region (LOCF) - ITT population

	Western countries		Other countries		
	Kd (N=55)	**IKd (N=97)**	**Kd (N=68)**	**IKd (N=82)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	13 (23.6)	18 (18.6)	16 (23.5)	22 (26.8)	0.4899
Number (%) of patients censored	42 (76.4)	79 (81.4)	52 (76.5)	60 (73.2)	
Kaplan-Meier estimates of Insomnia in months					
25% quantile (95% CI)	20.60 (4.041 to NC)	NC (18.004 to NC)	20.76 (16.624 to NC)	15.70 (10.218 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (21.552 to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.5281		0.7375	
Hazard ratio (95% CI) vs Kd	-	0.80 (0.39 to 1.62)		1.12 (0.59 to 2.13)	
P-value	-	0.5290		0.7376	
Deterioration probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful deterioration change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Insomnia
16.2.6.1.2.7 Efficacy response data - Subgroup analyses by baseline ECOG PS
16.2.6.1.2.7.3 QLQ-C30 - Time to first improvement by 10 pt in insomnia according to baseline ECOG PS (LOCF) - ITT population

	0 or 1		>1		
	Kd (N=118)	**IKd (N=168)**	**Kd (N=5)**	**IKd (N=11)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	42 (35.6)	59 (35.1)	2 (40.0)	4 (36.4)	0.8389
Number (%) of patients censored	76 (64.4)	109 (64.9)	3 (60.0)	7 (63.6)	
Kaplan-Meier estimates of Insomnia in months					
25% quantile (95% CI)	3.75 (1.281 to 9.101)	3.75 (1.971 to 5.717)	2.07 (1.906 to NC)	1.97 (0.986 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (1.906 to NC)	NC (0.986 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (1.906 to NC)	NC (4.665 to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.8929		0.8293	
Hazard ratio (95% CI) vs Kd	-	0.97 (0.66 to 1.45)		1.21 (0.22 to 6.60)	
P-value	-	0.8927		0.8295	
Improvement probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful improvement change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
PGM=DEVOPS/SAR650984/EFC15246/CIR_RWE/REPORT/PGM/eff_km_subgp_sr_sig_de_i_t.sas OUT=REPORT/OUTPUT/eff_km_c30_ins_impl_ecog_de_i_t_x.rtf (07APR2021 14:33)

16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Insomnia
16.2.6.1.2.7 Efficacy response data - Subgroup analyses by baseline ECOG PS
16.2.6.1.2.7.4 QLQ-C30 - Time to first deterioration by 10 pt in insomnia according to baseline ECOG PS (LOCF) - ITT population

	0 or 1		>1		
	Kd (N=118)	**IKd (N=168)**	**Kd (N=5)**	**IKd (N=11)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	69 (58.5)	102 (60.7)	1 (20.0)	4 (36.4)	0.4714
Number (%) of patients censored	49 (41.5)	66 (39.3)	4 (80.0)	7 (63.6)	
Kaplan-Meier estimates of Insomnia in months					
25% quantile (95% CI)	1.91 (1.051 to 3.713)	1.87 (1.084 to 2.825)	NC (2.858 to NC)	4.80 (0.986 to NC)	
Median (95% CI)	7.56 (5.585 to 15.244)	7.43 (3.844 to 10.612)	NC (2.858 to NC)	NC (0.986 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (2.858 to NC)	NC (6.209 to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.6834		0.4277	
Hazard ratio (95% CI) vs Kd	-	1.07 (0.78 to 1.45)		2.37 (0.26 to 21.22)	
P-value	-	0.6851		0.4417	
Deterioration probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful deterioration change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Insomnia
16.2.6.1.2.7 Efficacy response data - Subgroup analyses by baseline ECOG PS
16.2.6.1.2.7.5 QLQ-C30 - Time until permanent improvement by 10 pt in insomnia according to baseline ECOG PS (LOCF) - ITT population

	0 or 1		>1		
	Kd (N=118)	**IKd (N=168)**	**Kd (N=5)**	**IKd (N=11)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	22 (18.6)	37 (22.0)	2 (40.0)	3 (27.3)	0.5462
Number (%) of patients censored	96 (81.4)	131 (78.0)	3 (60.0)	8 (72.7)	
Kaplan-Meier estimates of Insomnia in months					
25% quantile (95% CI)	NC (13.799 to NC)	20.70 (18.694 to NC)	14.65 (1.906 to NC)	14.55 (0.986 to NC)	
Median (95% CI)	NC (NC to NC)	NC (23.721 to NC)	14.65 (1.906 to NC)	NC (0.986 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (1.906 to NC)	NC (NC to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.5014		0.7080	
Hazard ratio (95% CI) vs Kd	-	1.20 (0.71 to 2.03)		0.71 (0.12 to 4.30)	
P-value	-	0.5020		0.7093	
Improvement probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful improvement change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Insomnia
16.2.6.1.2.7 Efficacy response data - Subgroup analyses by baseline ECOG PS
16.2.6.1.2.7.6 QLQ-C30 - Time until permanent deterioration by 10 pt in insomnia according to baseline ECOG PS (LOCF) - ITT population

	0 or 1		>1		
	Kd (N=118)	**IKd (N=168)**	**Kd (N=5)**	**IKd (N=11)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	28 (23.7)	39 (23.2)	1 (20.0)	1 (9.1)	0.4994
Number (%) of patients censored	90 (76.3)	129 (76.8)	4 (80.0)	10 (90.9)	
Kaplan-Meier estimates of Insomnia in months					
25% quantile (95% CI)	20.60 (17.051 to NC)	21.42 (14.850 to NC)	NC (2.858 to NC)	NC (9.988 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (2.858 to NC)	NC (9.988 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (2.858 to NC)	NC (NC to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.9751		0.5430	
Hazard ratio (95% CI) vs Kd	-	0.99 (0.61 to 1.61)		0.43 (0.03 to 7.04)	
P-value	-	0.9751		0.5543	
Deterioration probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful deterioration change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Insomnia
16.2.6.1.2.8 Efficacy response data - Subgroup analyses by ISS staging at SE
16.2.6.1.2.8.3 QLQ-C30 - Time to first improvement by 10 pt in insomnia according to ISS staging at SE (LOCF) - ITT population

	I		II		III		
	Kd (N=71)	**IKd (N=89)**	**Kd (N=31)**	**IKd (N=63)**	**Kd (N=20)**	**IKd (N=26)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	27 (38.0)	27 (30.3)	11 (35.5)	26 (41.3)	5 (25.0)	9 (34.6)	0.4390
Number (%) of patients censored	44 (62.0)	62 (69.7)	20 (64.5)	37 (58.7)	15 (75.0)	17 (65.4)	
Kaplan-Meier estimates of Insomnia in months							
25% quantile (95% CI)	3.75 (2.004 to 9.101)	4.35 (1.248 to NC)	1.91 (1.051 to NC)	3.35 (1.117 to 5.585)	16.16 (1.018 to NC)	1.97 (0.986 to NC)	
Median (95% CI)	NC (12.386 to NC)	NC (NC to NC)	NC (4.895 to NC)	NC (5.717 to NC)	NC (16.164 to NC)	NC (4.140 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Kd							
Log-Rank test p-value[a] vs Kd	-	0.3454		0.7365		0.4309	
Hazard ratio (95% CI) vs Kd	-	0.77 (0.45 to 1.32)		1.13 (0.56 to 2.29)		1.55 (0.52 to 4.63)	
P-value	-	0.3468		0.7367		0.4345	

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The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Insomnia
16.2.6.1.2.8 Efficacy response data - Subgroup analyses by ISS staging at SE
16.2.6.1.2.8.4 QLQ-C30 - Time to first deterioration by 10 pt in insomnia according to ISS staging at SE (LOCF) - ITT population

	I		II		III		
	Kd (N=71)	**IKd (N=89)**	**Kd (N=31)**	**IKd (N=63)**	**Kd (N=20)**	**IKd (N=26)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	40 (56.3)	56 (62.9)	19 (61.3)	41 (65.1)	10 (50.0)	9 (34.6)	0.5933
Number (%) of patients censored	31 (43.7)	33 (37.1)	12 (38.7)	22 (34.9)	10 (50.0)	17 (65.4)	
Kaplan-Meier estimates of Insomnia in months							
25% quantile (95% CI)	1.91 (1.051 to 4.041)	1.58 (1.051 to 2.825)	1.05 (0.986 to 3.713)	1.12 (1.051 to 2.858)	3.81 (0.986 to 8.444)	3.75 (0.953 to 10.185)	
Median (95% CI)	10.12 (5.585 to NC)	7.00 (3.680 to 13.700)	6.74 (1.938 to NC)	5.06 (2.858 to 12.386)	9.00 (3.811 to NC)	NC (3.745 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (19.253 to NC)	NC (9.725 to NC)	NC (14.587 to NC)	NC (9.002 to NC)	NC (NC to NC)	
Comparison vs. Kd							
Log-Rank test p-value[a] vs Kd	-	0.3982		0.8849		0.4614	
Hazard ratio (95% CI) vs Kd	-	1.19 (0.79 to 1.79)		1.04 (0.60 to 1.79)		0.71 (0.29 to 1.76)	

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The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Insomnia
16.2.6.1.2.8 Efficacy response data - Subgroup analyses by ISS staging at SE
16.2.6.1.2.8.5 QLQ-C30 - Time until permanent improvement by 10 pt in insomnia according to ISS staging at SE (LOCF) - ITT population

	I		II		III		
	Kd (N=71)	**IKd (N=89)**	**Kd (N=31)**	**IKd (N=63)**	**Kd (N=20)**	**IKd (N=26)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	13 (18.3)	17 (19.1)	7 (22.6)	16 (25.4)	3 (15.0)	6 (23.1)	0.7802
Number (%) of patients censored	58 (81.7)	72 (80.9)	24 (77.4)	47 (74.6)	17 (85.0)	20 (76.9)	
Kaplan-Meier estimates of Insomnia in months							
25% quantile (95% CI)	NC (10.645 to NC)	23.72 (19.483 to NC)	14.65 (7.491 to NC)	20.30 (11.828 to NC)	NC (2.858 to NC)	14.55 (0.986 to NC)	
Median (95% CI)	NC (NC to NC)	NC (23.721 to NC)	NC (NC to NC)	NC (23.359 to NC)	NC (17.971 to NC)	NC (14.554 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (23.359 to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Kd							
Log-Rank test p-value[a] vs Kd	-	0.7898		0.9711		0.3725	
Hazard ratio (95% CI) vs Kd	-	1.10 (0.54 to 2.27)		1.02 (0.42 to 2.48)		1.86 (0.46 to 7.47)	
P-value	-	0.7899		0.9712		0.3802	

A lower score represents a better level of quality of life. Clinical meaningful improvement change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Insomnia
16.2.6.1.2.8 Efficacy response data - Subgroup analyses by ISS staging at SE
16.2.6.1.2.8.6 QLQ-C30 - Time until permanent deterioration by 10 pt in insomnia according to ISS staging at SE (LOCF) - ITT population

	I		II		III		
	Kd (N=71)	**IKd (N=89)**	**Kd (N=31)**	**IKd (N=63)**	**Kd (N=20)**	**IKd (N=26)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	16 (22.5)	25 (28.1)	7 (22.6)	11 (17.5)	6 (30.0)	4 (15.4)	0.2800
Number (%) of patients censored	55 (77.5)	64 (71.9)	24 (77.4)	52 (82.5)	14 (70.0)	22 (84.6)	
Kaplan-Meier estimates of Insomnia in months							
25% quantile (95% CI)	20.76 (18.924 to NC)	17.54 (13.766 to NC)	20.53 (1.051 to NC)	NC (19.877 to NC)	8.44 (1.150 to NC)	NC (3.713 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (7.556 to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Kd							
Log-Rank test p-value[a] vs Kd	-	0.3045		0.4467		0.2719	
Hazard ratio (95% CI) vs Kd	-	1.39 (0.74 to 2.60)		0.69 (0.27 to 1.79)		0.50 (0.14 to 1.77)	
P-value	-	0.3066		0.4492		0.2815	

A lower score represents a better level of quality of life. Clinical meaningful deterioration change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Insomnia
16.2.6.1.2.9 Efficacy response data - Subgroup analyses by R-ISS stage at SE
16.2.6.1.2.9.3 QLQ-C30 - Time to first improvement by 10 pt in insomnia according to R-ISS stage at SE (LOCF) - ITT population

	I or II		III		Not classified		
	Kd (N=103)	**IKd (N=155)**	**Kd (N=8)**	**IKd (N=16)**	**Kd (N=12)**	**IKd (N=8)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	39 (37.9)	56 (36.1)	2 (25.0)	6 (37.5)	3 (25.0)	1 (12.5)	0.7051
Number (%) of patients censored	64 (62.1)	99 (63.9)	6 (75.0)	10 (62.5)	9 (75.0)	7 (87.5)	
Kaplan-Meier estimates of Insomnia in months							
25% quantile (95% CI)	2.96 (1.281 to 5.388)	3.71 (1.971 to 5.717)	1.12 (1.051 to NC)	1.08 (0.986 to NC)	NC (0.986 to NC)	NC (2.070 to NC)	
Median (95% CI)	NC (16.164 to NC)	NC (NC to NC)	NC (1.051 to NC)	NC (1.084 to NC)	NC (3.713 to NC)	NC (2.070 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Kd							
Log-Rank test p-value[a] vs Kd	-	0.6724		0.5231		0.8026	
Hazard ratio (95% CI) vs Kd	-	0.92 (0.61 to 1.38)		1.68 (0.34 to 8.31)		0.75 (0.08 to 7.27)	
P-value	-	0.6725		0.5276		0.8033	

A lower score represents a better level of quality of life. Clinical meaningful improvement change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Insomnia
16.2.6.1.2.9 Efficacy response data - Subgroup analyses by R-ISS stage at SE
16.2.6.1.2.9.4 QLQ-C30 - Time to first deterioration by 10 pt in insomnia according to R-ISS stage at SE (LOCF) - ITT population

	I or II		III		Not classified		
	Kd (N=103)	**IKd (N=155)**	**Kd (N=8)**	**IKd (N=16)**	**Kd (N=12)**	**IKd (N=8)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	58 (56.3)	99 (63.9)	4 (50.0)	3 (18.8)	8 (66.7)	4 (50.0)	0.2431
Number (%) of patients censored	45 (43.7)	56 (36.1)	4 (50.0)	13 (81.3)	4 (33.3)	4 (50.0)	
Kaplan-Meier estimates of Insomnia in months							
25% quantile (95% CI)	1.91 (1.051 to 3.745)	1.51 (1.084 to 2.793)	3.81 (0.986 to 7.556)	NC (1.216 to NC)	2.33 (1.051 to 3.844)	2.00 (0.986 to 8.345)	
Median (95% CI)	9.00 (5.684 to 19.351)	6.54 (3.745 to 10.185)	7.56 (0.986 to NC)	NC (9.363 to NC)	4.71 (1.150 to NC)	6.05 (0.986 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (4.764 to NC)	NC (NC to NC)	NC (3.844 to NC)	NC (2.004 to NC)	
Comparison vs. Kd							
Log-Rank test p-value[a] vs Kd	-	0.3109		0.1078		0.9652	
Hazard ratio (95% CI) vs Kd	-	1.18 (0.85 to 1.64)		0.31 (0.07 to 1.40)		1.03 (0.31 to 3.42)	
P-value	-	0.3114		0.1275		0.9650	

A lower score represents a better level of quality of life. Clinical meaningful deterioration change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Insomnia
16.2.6.1.2.9 Efficacy response data - Subgroup analyses by R-ISS stage at SE
16.2.6.1.2.9.5 QLQ-C30 - Time until permanent improvement by 10 pt in insomnia according to R-ISS stage at SE (LOCF) - ITT population

	I or II		III		Not classified		
	Kd (N=103)	**IKd (N=155)**	**Kd (N=8)**	**IKd (N=16)**	**Kd (N=12)**	**IKd (N=8)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	21 (20.4)	34 (21.9)	1 (12.5)	5 (31.3)	2 (16.7)	1 (12.5)	0.5876
Number (%) of patients censored	82 (79.6)	121 (78.1)	7 (87.5)	11 (68.8)	10 (83.3)	7 (87.5)	
Kaplan-Meier estimates of Insomnia in months							
25% quantile (95% CI)	22.44 (11.335 to NC)	23.36 (18.694 to NC)	NC (9.561 to NC)	4.14 (0.986 to NC)	NC (5.585 to NC)	NC (19.088 to NC)	
Median (95% CI)	NC (NC to NC)	NC (23.721 to NC)	NC (9.561 to NC)	NC (1.084 to NC)	NC (13.799 to NC)	NC (19.088 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (9.561 to NC)	NC (NC to NC)	NC (NC to NC)	NC (19.088 to NC)	
Comparison vs. Kd							
Log-Rank test p-value[a] vs Kd	-	0.8861		0.2878		0.9336	
Hazard ratio (95% CI) vs Kd	-	1.04 (0.60 to 1.79)		3.03 (0.35 to 25.96)		1.11 (0.10 to 12.29)	
P-value	-	0.8866		0.3122		0.9336	

A lower score represents a better level of quality of life. Clinical meaningful improvement change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Insomnia
16.2.6.1.2.9 Efficacy response data - Subgroup analyses by R-ISS stage at SE
16.2.6.1.2.9.6 QLQ-C30 - Time until permanent deterioration by 10 pt in insomnia according to R-ISS stage at SE (LOCF) - ITT population

	I or II		III		Not classified		
	Kd (N=103)	**IKd (N=155)**	**Kd (N=8)**	**IKd (N=16)**	**Kd (N=12)**	**IKd (N=8)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	25 (24.3)	38 (24.5)	2 (25.0)	1 (6.3)	2 (16.7)	1 (12.5)	0.5656
Number (%) of patients censored	78 (75.7)	117 (75.5)	6 (75.0)	15 (93.8)	10 (83.3)	7 (87.5)	
Kaplan-Meier estimates of Insomnia in months							
25% quantile (95% CI)	20.53 (15.014 to NC)	19.88 (14.784 to NC)	7.56 (3.811 to NC)	NC (9.988 to NC)	21.55 (18.464 to NC)	NC (3.745 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (3.811 to NC)	NC (NC to NC)	NC (21.552 to NC)	NC (3.745 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (7.556 to NC)	NC (NC to NC)	NC (21.552 to NC)	NC (NC to NC)	
Comparison vs. Kd							
Log-Rank test p-value[a] vs Kd	-	0.8909		0.1702		0.7741	
Hazard ratio (95% CI) vs Kd	-	0.97 (0.58 to 1.60)		0.22 (0.02 to 2.40)		1.42 (0.13 to 16.04)	
P-value	-	0.8905		0.2120		0.7751	

A lower score represents a better level of quality of life. Clinical meaningful deterioration change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Insomnia
16.2.6.1.2.10 Efficacy response data - Subgroup analyses by nb of prior lines
16.2.6.1.2.10.3 QLQ-C30 - Time to first improvement by 10 pt in insomnia according to nb of prior lines (LOCF) - ITT population

	1		>1		
	Kd (N=55)	**IKd (N=79)**	**Kd (N=68)**	**IKd (N=100)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	15 (27.3)	25 (31.6)	29 (42.6)	38 (38.0)	0.4049
Number (%) of patients censored	40 (72.7)	54 (68.4)	39 (57.4)	62 (62.0)	
Kaplan-Meier estimates of Insomnia in months					
25% quantile (95% CI)	4.99 (1.117 to NC)	4.67 (1.216 to NC)	2.07 (1.117 to 5.388)	2.99 (1.248 to 5.585)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (5.651 to NC)	NC (14.554 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.5628		0.5348	
Hazard ratio (95% CI) vs Kd	-	1.21 (0.64 to 2.29)		0.86 (0.53 to 1.39)	
P-value	-	0.5634		0.5352	
Improvement probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful improvement change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Insomnia
16.2.6.1.2.10 Efficacy response data - Subgroup analyses by nb of prior lines
16.2.6.1.2.10.4 QLQ-C30 - Time to first deterioration by 10 pt in insomnia according to nb of prior lines (LOCF) - ITT population

	1		>1		
	Kd (N=55)	**IKd (N=79)**	**Kd (N=68)**	**IKd (N=100)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	31 (56.4)	48 (60.8)	39 (57.4)	58 (58.0)	0.6635
Number (%) of patients censored	24 (43.6)	31 (39.2)	29 (42.6)	42 (42.0)	
Kaplan-Meier estimates of Insomnia in months					
25% quantile (95% CI)	2.00 (1.051 to 3.943)	1.58 (1.051 to 2.825)	1.91 (1.018 to 3.811)	2.00 (1.084 to 3.220)	
Median (95% CI)	7.56 (3.943 to NC)	6.54 (2.891 to 14.587)	8.44 (4.764 to 19.351)	7.79 (3.844 to 16.000)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (19.351 to NC)	NC (NC to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.5392		0.9356	
Hazard ratio (95% CI) vs Kd	-	1.15 (0.73 to 1.81)		1.02 (0.68 to 1.53)	
P-value	-	0.5395		0.9357	
Deterioration probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful deterioration change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Insomnia
16.2.6.1.2.10 Efficacy response data - Subgroup analyses by nb of prior lines
16.2.6.1.2.10.5 QLQ-C30 - Time until permanent improvement by 10 pt in insomnia according to nb of prior lines (LOCF) - ITT population

	1		>1		
	Kd (N=55)	**IKd (N=79)**	**Kd (N=68)**	**IKd (N=100)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	9 (16.4)	15 (19.0)	15 (22.1)	25 (25.0)	0.9712
Number (%) of patients censored	46 (83.6)	64 (81.0)	53 (77.9)	75 (75.0)	
Kaplan-Meier estimates of Insomnia in months					
25% quantile (95% CI)	NC (11.335 to NC)	23.36 (17.840 to NC)	22.44 (10.645 to NC)	19.71 (5.684 to NC)	
Median (95% CI)	NC (NC to NC)	NC (23.359 to NC)	NC (22.439 to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (23.721 to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.6965		0.6764	
Hazard ratio (95% CI) vs Kd	-	1.18 (0.52 to 2.69)		1.15 (0.60 to 2.17)	
P-value	-	0.6968		0.6767	
Improvement probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful improvement change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Insomnia
16.2.6.1.2.10 Efficacy response data - Subgroup analyses by nb of prior lines
16.2.6.1.2.10.6 QLQ-C30 - Time until permanent deterioration by 10 pt in insomnia according to nb of prior lines (LOCF) - ITT population

	1		>1		
	Kd (N=55)	**IKd (N=79)**	**Kd (N=68)**	**IKd (N=100)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	12 (21.8)	20 (25.3)	17 (25.0)	20 (20.0)	0.3549
Number (%) of patients censored	43 (78.2)	59 (74.7)	51 (75.0)	80 (80.0)	
Kaplan-Meier estimates of Insomnia in months					
25% quantile (95% CI)	21.55 (7.556 to NC)	19.88 (14.752 to NC)	20.47 (8.444 to NC)	NC (14.193 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (21.027 to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.5623		0.4393	
Hazard ratio (95% CI) vs Kd	-	1.24 (0.60 to 2.53)		0.78 (0.41 to 1.48)	
P-value	-	0.5631		0.4405	
Deterioration probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful deterioration change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Insomnia
16.2.6.1.2.11 Efficacy response data - Subgroup analyses by cytogenetic abnormality
16.2.6.1.2.11.3 QLQ-C30 - Time to first improvement by 10 pt in insomnia according to cytogenetic abnormality (LOCF) - ITT population

	At least one		None		
	Kd (N=31)	**IKd (N=42)**	**Kd (N=77)**	**IKd (N=114)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	12 (38.7)	19 (45.2)	30 (39.0)	36 (31.6)	0.3426
Number (%) of patients censored	19 (61.3)	23 (54.8)	47 (61.0)	78 (68.4)	
Kaplan-Meier estimates of Insomnia in months					
25% quantile (95% CI)	2.07 (1.051 to 5.651)	2.04 (1.018 to 4.238)	2.83 (1.281 to 9.101)	4.67 (1.971 to 16.427)	
Median (95% CI)	NC (4.830 to NC)	NC (3.713 to NC)	NC (12.386 to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.6240		0.3119	
Hazard ratio (95% CI) vs Kd	-	1.20 (0.58 to 2.47)		0.78 (0.48 to 1.27)	
P-value	-	0.6244		0.3131	
Improvement probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful improvement change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Insomnia
16.2.6.1.2.11 Efficacy response data - Subgroup analyses by cytogenetic abnormality
16.2.6.1.2.11.4 QLQ-C30 - Time to first deterioration by 10 pt in insomnia according to cytogenetic abnormality (LOCF) - ITT population

	At least one		None		
	Kd (N=31)	**IKd (N=42)**	**Kd (N=77)**	**IKd (N=114)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	20 (64.5)	22 (52.4)	41 (53.2)	73 (64.0)	0.1701
Number (%) of patients censored	11 (35.5)	20 (47.6)	36 (46.8)	41 (36.0)	
Kaplan-Meier estimates of Insomnia in months					
25% quantile (95% CI)	3.06 (0.986 to 4.830)	1.87 (1.051 to 3.713)	1.22 (1.051 to 3.713)	1.87 (1.051 to 2.825)	
Median (95% CI)	6.77 (3.811 to 15.211)	12.94 (3.680 to NC)	9.00 (4.041 to NC)	6.57 (3.811 to 9.363)	
75% quantile (95% CI)	NC (9.725 to NC)	NC (NC to NC)	NC (NC to NC)	NC (18.464 to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.3906		0.2247	
Hazard ratio (95% CI) vs Kd	-	0.77 (0.42 to 1.41)		1.27 (0.86 to 1.86)	
P-value	-	0.3919		0.2257	
Deterioration probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful deterioration change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Insomnia
16.2.6.1.2.11 Efficacy response data - Subgroup analyses by cytogenetic abnormality
16.2.6.1.2.11.5 QLQ-C30 - Time until permanent improvement by 10 pt in insomnia according to cytogenetic abnormality (LOCF) - ITT population

	At least one		None		
	Kd (N=31)	**IKd (N=42)**	**Kd (N=77)**	**IKd (N=114)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	6 (19.4)	14 (33.3)	17 (22.1)	19 (16.7)	0.1222
Number (%) of patients censored	25 (80.6)	28 (66.7)	60 (77.9)	95 (83.3)	
Kaplan-Meier estimates of Insomnia in months					
25% quantile (95% CI)	22.44 (9.561 to NC)	17.84 (1.971 to 23.359)	NC (10.645 to NC)	23.72 (19.483 to NC)	
Median (95% CI)	NC (22.439 to NC)	23.36 (20.304 to NC)	NC (NC to NC)	NC (23.721 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (23.359 to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.1840		0.3327	
Hazard ratio (95% CI) vs Kd	-	1.91 (0.72 to 5.05)		0.72 (0.38 to 1.39)	
P-value	-	0.1913		0.3347	
Improvement probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful improvement change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Insomnia
16.2.6.1.2.11 Efficacy response data - Subgroup analyses by cytogenetic abnormality
16.2.6.1.2.11.6 QLQ-C30 - Time until permanent deterioration by 10 pt in insomnia according to cytogenetic abnormality (LOCF) - ITT population

	At least one		None		
	Kd (N=31)	**IKd (N=42)**	**Kd (N=77)**	**IKd (N=114)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	8 (25.8)	8 (19.0)	17 (22.1)	29 (25.4)	0.4233
Number (%) of patients censored	23 (74.2)	34 (81.0)	60 (77.9)	85 (74.6)	
Kaplan-Meier estimates of Insomnia in months					
25% quantile (95% CI)	18.92 (3.811 to NC)	NC (5.322 to NC)	20.53 (8.444 to NC)	19.25 (14.752 to NC)	
Median (95% CI)	NC (21.027 to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.5054		0.6723	
Hazard ratio (95% CI) vs Kd	-	0.72 (0.27 to 1.91)		1.14 (0.63 to 2.07)	
P-value	-	0.5074		0.6725	
Deterioration probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful deterioration change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Insomnia
16.2.6.1.2.12 Efficacy response data - Subgroup analyses by MM type at SE
16.2.6.1.2.12.3 QLQ-C30 - Time to first improvement by 10 pt in insomnia according to MM type at SE (LOCF) - ITT population

	IgG		Non-IgG		
	Kd (N=85)	**IKd (N=126)**	**Kd (N=38)**	**IKd (N=53)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	31 (36.5)	44 (34.9)	13 (34.2)	19 (35.8)	0.9948
Number (%) of patients censored	54 (63.5)	82 (65.1)	25 (65.8)	34 (64.2)	
Kaplan-Meier estimates of Insomnia in months					
25% quantile (95% CI)	3.71 (1.281 to 12.386)	3.71 (1.971 to 6.012)	2.94 (1.051 to NC)	3.81 (1.084 to 14.554)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (5.388 to NC)	NC (14.554 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.9420		0.9744	
Hazard ratio (95% CI) vs Kd	-	0.98 (0.62 to 1.56)		0.99 (0.49 to 2.00)	
P-value	-	0.9419		0.9744	
Improvement probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful improvement change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Insomnia
16.2.6.1.2.12 Efficacy response data - Subgroup analyses by MM type at SE
16.2.6.1.2.12.4 QLQ-C30 - Time to first deterioration by 10 pt in insomnia according to MM type at SE (LOCF) - ITT population

	IgG		Non-IgG		
	Kd (N=85)	**IKd (N=126)**	**Kd (N=38)**	**IKd (N=53)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	50 (58.8)	77 (61.1)	20 (52.6)	29 (54.7)	0.8812
Number (%) of patients censored	35 (41.2)	49 (38.9)	18 (47.4)	24 (45.3)	
Kaplan-Meier estimates of Insomnia in months					
25% quantile (95% CI)	1.91 (1.051 to 3.745)	1.51 (1.051 to 2.234)	3.38 (0.986 to 4.764)	2.83 (1.018 to 3.745)	
Median (95% CI)	7.92 (4.830 to 17.610)	6.54 (3.745 to 10.185)	9.00 (3.811 to NC)	12.39 (3.745 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.6252		0.8430	
Hazard ratio (95% CI) vs Kd	-	1.09 (0.77 to 1.56)		1.06 (0.60 to 1.87)	
P-value	-	0.6253		0.8437	
Deterioration probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful deterioration change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Insomnia
16.2.6.1.2.12 Efficacy response data - Subgroup analyses by MM type at SE
16.2.6.1.2.12.5 QLQ-C30 - Time until permanent improvement by 10 pt in insomnia according to MM type at SE (LOCF) - ITT population

	IgG		Non-IgG		
	Kd (N=85)	**IKd (N=126)**	**Kd (N=38)**	**IKd (N=53)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	18 (21.2)	25 (19.8)	6 (15.8)	15 (28.3)	0.2531
Number (%) of patients censored	67 (78.8)	101 (80.2)	32 (84.2)	38 (71.7)	
Kaplan-Meier estimates of Insomnia in months					
25% quantile (95% CI)	22.44 (11.335 to NC)	23.36 (18.694 to NC)	NC (9.955 to NC)	19.09 (5.651 to 23.721)	
Median (95% CI)	NC (NC to NC)	NC (23.359 to NC)	NC (NC to NC)	23.72 (20.304 to 23.721)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	23.72 (NC to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.8758		0.1726	
Hazard ratio (95% CI) vs Kd	-	0.95 (0.52 to 1.75)		1.93 (0.74 to 5.03)	
P-value	-	0.8752		0.1799	
Improvement probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful improvement change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Insomnia
16.2.6.1.2.12 Efficacy response data - Subgroup analyses by MM type at SE
16.2.6.1.2.12.6 QLQ-C30 - Time until permanent deterioration by 10 pt in insomnia according to MM type at SE (LOCF) - ITT population

	IgG		Non-IgG		
	Kd (N=85)	**IKd (N=126)**	**Kd (N=38)**	**IKd (N=53)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	21 (24.7)	27 (21.4)	8 (21.1)	13 (24.5)	0.7645
Number (%) of patients censored	64 (75.3)	99 (78.6)	30 (78.9)	40 (75.5)	
Kaplan-Meier estimates of Insomnia in months					
25% quantile (95% CI)	20.60 (17.051 to NC)	21.45 (14.784 to NC)	NC (3.811 to NC)	21.42 (6.407 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.7414		0.8303	
Hazard ratio (95% CI) vs Kd	-	0.91 (0.51 to 1.61)		1.10 (0.46 to 2.66)	
P-value	-	0.7415		0.8304	
Deterioration probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful deterioration change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Insomnia
16.2.6.1.2.13 Efficacy response data - Subgroup analyses by previous autologous stem-cell
16.2.6.1.2.13.3 QLQ-C30 - Time to first improvement by 10 pt in insomnia according to previous autologous stem-cell (LOCF) - ITT population

	Yes		No		
	Kd (N=69)	**IKd (N=116)**	**Kd (N=54)**	**IKd (N=63)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	22 (31.9)	41 (35.3)	22 (40.7)	22 (34.9)	0.4065
Number (%) of patients censored	47 (68.1)	75 (64.7)	32 (59.3)	41 (65.1)	
Kaplan-Meier estimates of Insomnia in months					
25% quantile (95% CI)	3.78 (1.150 to NC)	2.99 (1.216 to 6.012)	2.55 (1.051 to 5.388)	3.84 (1.971 to 14.554)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (5.388 to NC)	NC (16.427 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.6250		0.5053	
Hazard ratio (95% CI) vs Kd	-	1.14 (0.68 to 1.91)		0.82 (0.45 to 1.48)	
P-value	-	0.6253		0.5060	
Improvement probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful improvement change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Insomnia
16.2.6.1.2.13 Efficacy response data - Subgroup analyses by previous autologous stem-cell
16.2.6.1.2.13.4 QLQ-C30 - Time to first deterioration by 10 pt in insomnia according to previous autologous stem-cell (LOCF) - ITT population

	Yes		No		
	Kd (N=69)	**IKd (N=116)**	**Kd (N=54)**	**IKd (N=63)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	35 (50.7)	72 (62.1)	35 (64.8)	34 (54.0)	0.0342
Number (%) of patients censored	34 (49.3)	44 (37.9)	19 (35.2)	29 (46.0)	
Kaplan-Meier estimates of Insomnia in months					
25% quantile (95% CI)	2.97 (1.051 to 5.684)	1.12 (1.051 to 2.004)	1.87 (1.018 to 2.924)	3.32 (1.150 to 4.797)	
Median (95% CI)	15.24 (6.505 to NC)	6.21 (2.858 to 10.185)	5.59 (2.924 to 13.405)	9.36 (4.797 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (10.316 to NC)	NC (NC to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.0997		0.1651	
Hazard ratio (95% CI) vs Kd	-	1.40 (0.94 to 2.10)		0.72 (0.45 to 1.15)	
P-value	-	0.1013		0.1671	
Deterioration probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful deterioration change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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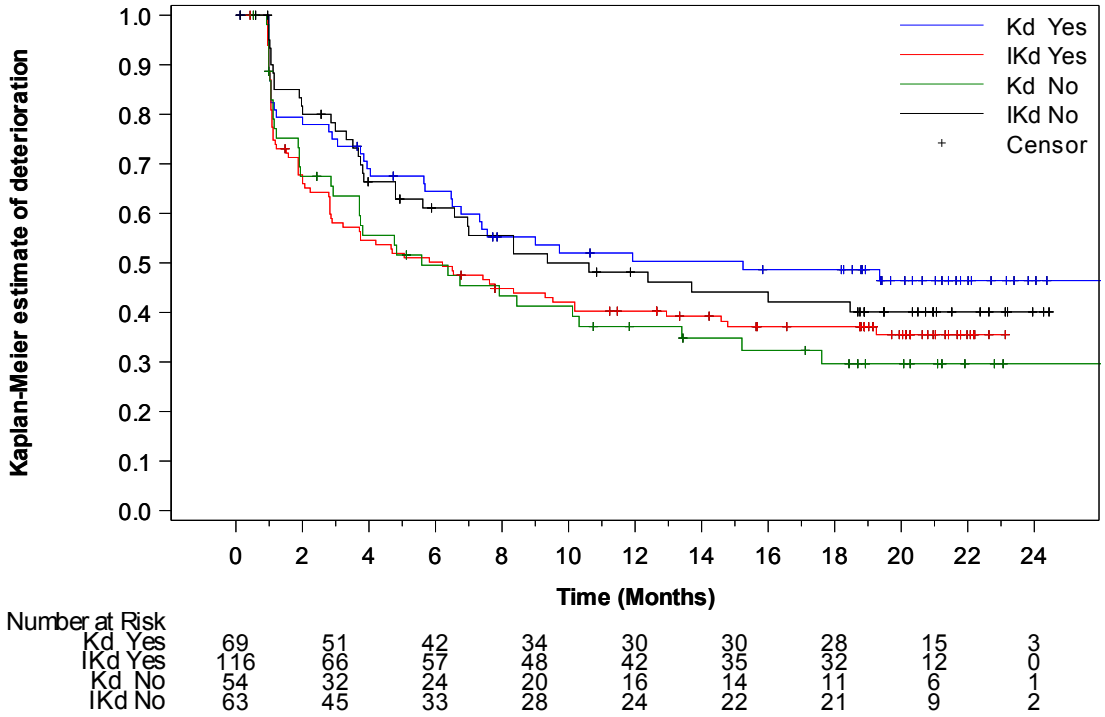
16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Insomnia
16.2.6.1.2.13 Efficacy response data - Subgroup analyses by previous autologous stem-cell
16.2.6.1.2.13.5 QLQ-C30 - Time to first deterioration by 10 pt in insomnia according to previous autologous stem-cell - Kaplan-Meier curve (LOCF) - ITT population



A lower score represents a better level of quality of life. Clinical meaningful deterioration change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
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16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Insomnia
16.2.6.1.2.13 Efficacy response data - Subgroup analyses by previous autologous stem-cell
16.2.6.1.2.13.6 QLQ-C30 - Time until permanent improvement by 10 pt in insomnia according to previous autologous stem-cell (LOCF) - ITT population

	Yes		No		
	Kd (N=69)	**IKd (N=116)**	**Kd (N=54)**	**IKd (N=63)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	10 (14.5)	28 (24.1)	14 (25.9)	12 (19.0)	0.0864
Number (%) of patients censored	59 (85.5)	88 (75.9)	40 (74.1)	51 (81.0)	
Kaplan-Meier estimates of Insomnia in months					
25% quantile (95% CI)	NC (17.971 to NC)	19.71 (12.320 to NC)	14.46 (5.717 to NC)	23.36 (14.554 to NC)	
Median (95% CI)	NC (NC to NC)	NC (23.721 to NC)	NC (NC to NC)	NC (23.359 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (23.359 to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.1151		0.3519	
Hazard ratio (95% CI) vs Kd	-	1.77 (0.86 to 3.65)		0.69 (0.32 to 1.50)	
P-value	-	0.1201		0.3545	
Improvement probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful improvement change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Insomnia
16.2.6.1.2.13 Efficacy response data - Subgroup analyses by previous autologous stem-cell
16.2.6.1.2.13.7 QLQ-C30 - Time until permanent deterioration by 10 pt in insomnia according to previous autologous stem-cell (LOCF) - ITT population

	Yes		No		
	Kd (N=69)	**IKd (N=116)**	**Kd (N=54)**	**IKd (N=63)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	16 (23.2)	26 (22.4)	13 (24.1)	14 (22.2)	0.8763
Number (%) of patients censored	53 (76.8)	90 (77.6)	41 (75.9)	49 (77.8)	
Kaplan-Meier estimates of Insomnia in months					
25% quantile (95% CI)	20.76 (16.624 to NC)	21.42 (14.193 to NC)	19.22 (7.786 to NC)	21.45 (14.752 to NC)	
Median (95% CI)	NC (21.552 to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.9631		0.8113	
Hazard ratio (95% CI) vs Kd	-	0.99 (0.53 to 1.84)		0.91 (0.43 to 1.94)	
P-value	-	0.9630		0.8108	
Deterioration probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful deterioration change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Insomnia
16.2.6.1.2.14 Efficacy response data - Subgroup analyses by baseline eGFR (MDRD)
16.2.6.1.2.14.3 QLQ-C30 - Time to first improvement by 10 pt in insomnia according to baseline eGFR (MDRD) (LOCF) - ITT population

	>=60 mL/min/1.73m2		<60 mL/min/1.73m2		
	Kd (N=93)	**IKd (N=122)**	**Kd (N=18)**	**IKd (N=43)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	36 (38.7)	41 (33.6)	7 (38.9)	18 (41.9)	0.9725
Number (%) of patients censored	57 (61.3)	81 (66.4)	11 (61.1)	25 (58.1)	
Kaplan-Meier estimates of Insomnia in months					
25% quantile (95% CI)	3.33 (1.281 to 4.994)	3.81 (1.971 to 9.429)	1.10 (1.018 to NC)	2.89 (1.051 to 9.429)	
Median (95% CI)	NC (16.164 to NC)	NC (NC to NC)	NC (1.051 to NC)	NC (5.585 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.6164		0.7770	
Hazard ratio (95% CI) vs Kd	-	0.89 (0.57 to 1.40)		0.88 (0.37 to 2.11)	
P-value	-	0.6166		0.7771	
Improvement probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful improvement change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Insomnia
16.2.6.1.2.14 Efficacy response data - Subgroup analyses by baseline eGFR (MDRD)
16.2.6.1.2.14.4 QLQ-C30 - Time to first deterioration by 10 pt in insomnia according to baseline eGFR (MDRD) (LOCF) - ITT population

	>=60 mL/min/1.73m2		<60 mL/min/1.73m2		
	Kd (N=93)	**IKd (N=122)**	**Kd (N=18)**	**IKd (N=43)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	50 (53.8)	76 (62.3)	12 (66.7)	24 (55.8)	0.0523
Number (%) of patients censored	43 (46.2)	46 (37.7)	6 (33.3)	19 (44.2)	
Kaplan-Meier estimates of Insomnia in months					
25% quantile (95% CI)	2.43 (1.117 to 4.764)	1.18 (1.051 to 2.004)	3.75 (0.920 to 4.041)	2.23 (1.018 to 3.844)	
Median (95% CI)	11.93 (6.505 to NC)	6.54 (3.713 to 10.185)	4.04 (1.150 to 15.211)	8.34 (3.318 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (19.253 to NC)	15.21 (4.041 to NC)	NC (NC to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.0864		0.2387	
Hazard ratio (95% CI) vs Kd	-	1.37 (0.96 to 1.95)		0.66 (0.33 to 1.32)	
P-value	-	0.0877		0.2417	
Deterioration probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful deterioration change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Insomnia
16.2.6.1.2.14 Efficacy response data - Subgroup analyses by baseline eGFR (MDRD)
16.2.6.1.2.14.5 QLQ-C30 - Time until permanent improvement by 10 pt in insomnia according to baseline eGFR (MDRD) (LOCF) - ITT population

	>=60 mL/min/1.73m2		<60 mL/min/1.73m2		
	Kd (N=93)	**IKd (N=122)**	**Kd (N=18)**	**IKd (N=43)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	19 (20.4)	26 (21.3)	4 (22.2)	12 (27.9)	0.8144
Number (%) of patients censored	74 (79.6)	96 (78.7)	14 (77.8)	31 (72.1)	
Kaplan-Meier estimates of Insomnia in months					
25% quantile (95% CI)	22.44 (10.875 to NC)	23.72 (17.018 to NC)	13.80 (2.858 to NC)	20.30 (5.651 to NC)	
Median (95% CI)	NC (NC to NC)	NC (23.721 to NC)	NC (11.138 to NC)	23.36 (23.359 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (23.359 to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.6721		0.9405	
Hazard ratio (95% CI) vs Kd	-	1.14 (0.63 to 2.05)		0.96 (0.31 to 2.98)	
P-value	-	0.6723		0.9406	
Improvement probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful improvement change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Insomnia
16.2.6.1.2.14 Efficacy response data - Subgroup analyses by baseline eGFR (MDRD)
16.2.6.1.2.14.6 QLQ-C30 - Time until permanent deterioration by 10 pt in insomnia according to baseline eGFR (MDRD) (LOCF) - ITT population

	>=60 mL/min/1.73m2		<60 mL/min/1.73m2		
	Kd (N=93)	**IKd (N=122)**	**Kd (N=18)**	**IKd (N=43)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	19 (20.4)	34 (27.9)	6 (33.3)	4 (9.3)	0.0040
Number (%) of patients censored	74 (79.6)	88 (72.1)	12 (66.7)	39 (90.7)	
Kaplan-Meier estimates of Insomnia in months					
25% quantile (95% CI)	21.03 (18.924 to NC)	15.70 (10.218 to NC)	16.62 (0.986 to 21.552)	NC (19.877 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	21.55 (16.624 to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (20.468 to NC)	NC (NC to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.1367		0.0062	
Hazard ratio (95% CI) vs Kd	-	1.53 (0.87 to 2.68)		0.20 (0.06 to 0.72)	
P-value	-	0.1396		0.0135	
Deterioration probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful deterioration change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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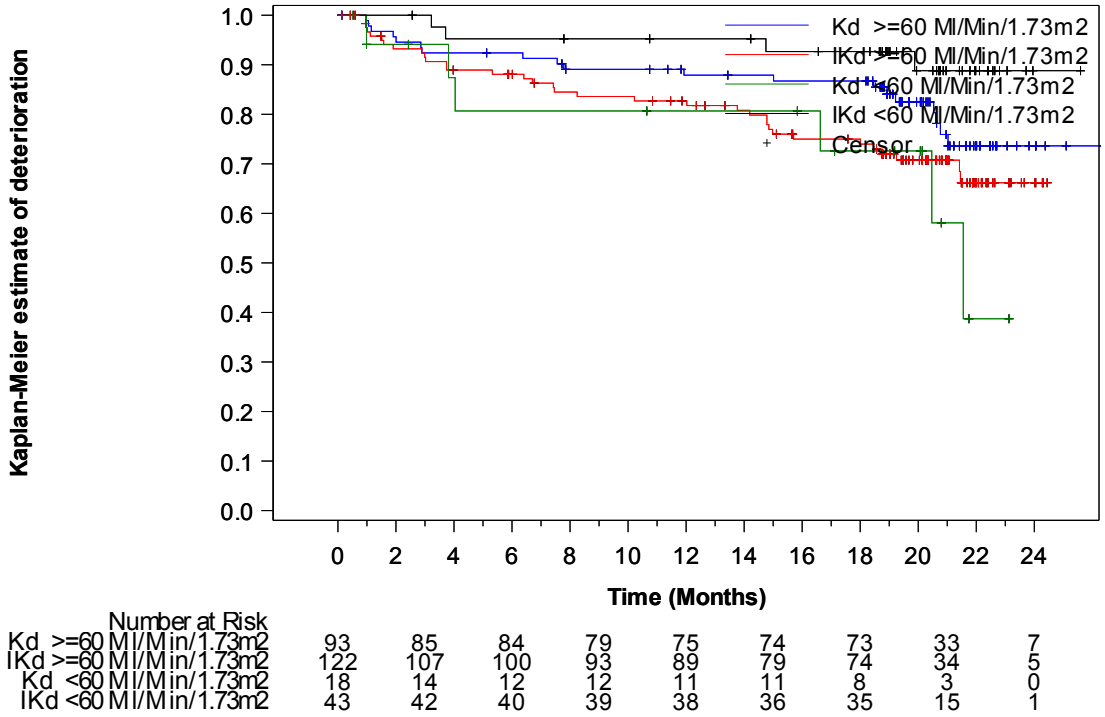
16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Insomnia
16.2.6.1.2.14 Efficacy response data - Subgroup analyses by baseline eGFR (MDRD)
16.2.6.1.2.14.7 QLQ-C30 - Time until permanent deterioration by 10 pt in insomnia according to baseline eGFR (MDRD) - Kaplan-Meier curve (LOCF) - ITT population



Number at Risk

Kd >=60 Ml/Min/1.73m2	93	85	84	79	75	74	73	33	7
IKd >=60 Ml/Min/1.73m2	122	107	100	93	89	79	74	34	5
Kd <60 Ml/Min/1.73m2	18	14	12	12	11	11	8	3	0
IKd <60 Ml/Min/1.73m2	43	42	40	39	38	36	35	15	1

A lower score represents a better level of quality of life. Clinical meaningful deterioration change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
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16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Insomnia
16.2.6.1.2.15 Efficacy response data - Subgroup analyses by previous treatment with PI
16.2.6.1.2.15.3 QLQ-C30 - Time to first improvement by 10 pt in insomnia according to previous treatment with PI (LOCF) - ITT population

	Yes		No		
	Kd (N=47)	**IKd (N=81)**	**Kd (N=76)**	**IKd (N=98)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	20 (42.6)	27 (33.3)	24 (31.6)	36 (36.7)	0.2278
Number (%) of patients censored	27 (57.4)	54 (66.7)	52 (68.4)	62 (63.3)	
Kaplan-Meier estimates of Insomnia in months					
25% quantile (95% CI)	2.14 (1.051 to 4.107)	3.35 (1.248 to 16.427)	4.90 (1.906 to NC)	3.75 (1.216 to 9.429)	
Median (95% CI)	NC (3.778 to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.3308		0.4955	
Hazard ratio (95% CI) vs Kd	-	0.75 (0.42 to 1.34)		1.20 (0.71 to 2.01)	
P-value	-	0.3325		0.4961	
Improvement probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful improvement change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Insomnia
16.2.6.1.2.15 Efficacy response data - Subgroup analyses by previous treatment with PI
16.2.6.1.2.15.4 QLQ-C30 - Time to first deterioration by 10 pt in insomnia according to previous treatment with PI (LOCF) - ITT population

	Yes		No		
	Kd (N=47)	**IKd (N=81)**	**Kd (N=76)**	**IKd (N=98)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	25 (53.2)	42 (51.9)	45 (59.2)	64 (65.3)	0.7870
Number (%) of patients censored	22 (46.8)	39 (48.1)	31 (40.8)	34 (34.7)	
Kaplan-Meier estimates of Insomnia in months					
25% quantile (95% CI)	2.92 (1.051 to 6.735)	2.83 (1.150 to 3.745)	1.22 (1.051 to 3.713)	1.12 (1.051 to 2.004)	
Median (95% CI)	15.21 (6.374 to NC)	12.94 (3.844 to NC)	6.51 (3.811 to 15.244)	6.21 (2.858 to 9.528)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (14.784 to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.8915		0.5340	
Hazard ratio (95% CI) vs Kd	-	1.03 (0.63 to 1.70)		1.13 (0.77 to 1.65)	
P-value	-	0.8920		0.5342	
Deterioration probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful deterioration change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Insomnia
16.2.6.1.2.15 Efficacy response data - Subgroup analyses by previous treatment with PI
16.2.6.1.2.15.5 QLQ-C30 - Time until permanent improvement by 10 pt in insomnia according to previous treatment with PI (LOCF) - ITT population

	Yes		No		
	Kd (N=47)	**IKd (N=81)**	**Kd (N=76)**	**IKd (N=98)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	11 (23.4)	17 (21.0)	13 (17.1)	23 (23.5)	0.6042
Number (%) of patients censored	36 (76.6)	64 (79.0)	63 (82.9)	75 (76.5)	
Kaplan-Meier estimates of Insomnia in months					
25% quantile (95% CI)	14.65 (9.955 to NC)	23.36 (5.684 to NC)	NC (13.799 to NC)	20.30 (17.741 to NC)	
Median (95% CI)	NC (NC to NC)	NC (23.359 to NC)	NC (NC to NC)	NC (23.721 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (23.359 to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.9662		0.4582	
Hazard ratio (95% CI) vs Kd	-	0.98 (0.46 to 2.11)		1.29 (0.65 to 2.55)	
P-value	-	0.9661		0.4595	
Improvement probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful improvement change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Insomnia
16.2.6.1.2.15 Efficacy response data - Subgroup analyses by previous treatment with PI
16.2.6.1.2.15.6 QLQ-C30 - Time until permanent deterioration by 10 pt in insomnia according to previous treatment with PI (LOCF) - ITT population

	Yes		No		
	Kd (N=47)	**IKd (N=81)**	**Kd (N=76)**	**IKd (N=98)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	9 (19.1)	18 (22.2)	20 (26.3)	22 (22.4)	0.4594
Number (%) of patients censored	38 (80.9)	63 (77.8)	56 (73.7)	76 (77.6)	
Kaplan-Meier estimates of Insomnia in months					
25% quantile (95% CI)	20.60 (11.926 to NC)	21.45 (10.218 to NC)	20.47 (8.444 to NC)	21.42 (14.784 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (21.552 to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.6444		0.5675	
Hazard ratio (95% CI) vs Kd	-	1.21 (0.54 to 2.69)		0.84 (0.46 to 1.54)	
P-value	-	0.6449		0.5680	
Deterioration probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful deterioration change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Insomnia
16.2.6.1.2.16 Efficacy response data - Subgroup analyses by previous treatment with IMiD
16.2.6.1.2.16.3 QLQ-C30 - Time to first improvement by 10 pt in insomnia according to previous treatment with IMiD (LOCF) - ITT population

	Yes		No		
	Kd (N=62)	**IKd (N=81)**	**Kd (N=61)**	**IKd (N=98)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	24 (38.7)	25 (30.9)	20 (32.8)	38 (38.8)	0.2041
Number (%) of patients censored	38 (61.3)	56 (69.1)	41 (67.2)	60 (61.2)	
Kaplan-Meier estimates of Insomnia in months					
25% quantile (95% CI)	3.75 (1.117 to 9.101)	4.76 (1.971 to NC)	3.33 (1.150 to NC)	2.07 (1.216 to 4.665)	
Median (95% CI)	NC (12.386 to NC)	NC (NC to NC)	NC (NC to NC)	NC (16.329 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.3109		0.4339	
Hazard ratio (95% CI) vs Kd	-	0.75 (0.43 to 1.31)		1.24 (0.72 to 2.13)	
P-value	-	0.3126		0.4348	
Improvement probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful improvement change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Insomnia
16.2.6.1.2.16 Efficacy response data - Subgroup analyses by previous treatment with IMiD
16.2.6.1.2.16.4 QLQ-C30 - Time to first deterioration by 10 pt in insomnia according to previous treatment with IMiD (LOCF) - ITT population

	Yes		No		
	Kd (N=62)	**IKd (N=81)**	**Kd (N=61)**	**IKd (N=98)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	37 (59.7)	48 (59.3)	33 (54.1)	58 (59.2)	0.3517
Number (%) of patients censored	25 (40.3)	33 (40.7)	28 (45.9)	40 (40.8)	
Kaplan-Meier estimates of Insomnia in months					
25% quantile (95% CI)	1.22 (1.018 to 3.055)	1.51 (1.084 to 2.825)	3.43 (1.117 to 6.505)	2.00 (1.051 to 2.891)	
Median (95% CI)	5.65 (3.055 to 15.211)	7.00 (3.220 to 16.000)	13.40 (6.505 to NC)	7.62 (3.811 to 14.784)	
75% quantile (95% CI)	NC (15.211 to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.7561		0.3106	
Hazard ratio (95% CI) vs Kd	-	0.93 (0.61 to 1.43)		1.25 (0.81 to 1.91)	
P-value	-	0.7549		0.3116	
Deterioration probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful deterioration change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Insomnia
16.2.6.1.2.16 Efficacy response data - Subgroup analyses by previous treatment with IMiD
16.2.6.1.2.16.5 QLQ-C30 - Time until permanent improvement by 10 pt in insomnia according to previous treatment with IMiD (LOCF) - ITT population

	Yes		No		
	Kd (N=62)	**IKd (N=81)**	**Kd (N=61)**	**IKd (N=98)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	15 (24.2)	18 (22.2)	9 (14.8)	22 (22.4)	0.2662
Number (%) of patients censored	47 (75.8)	63 (77.8)	52 (85.2)	76 (77.6)	
Kaplan-Meier estimates of Insomnia in months					
25% quantile (95% CI)	17.97 (10.645 to NC)	20.70 (18.694 to NC)	NC (10.875 to NC)	23.72 (11.828 to NC)	
Median (95% CI)	NC (22.439 to NC)	NC (23.359 to NC)	NC (NC to NC)	NC (23.721 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.7145		0.2286	
Hazard ratio (95% CI) vs Kd	-	0.88 (0.44 to 1.75)		1.60 (0.74 to 3.48)	
P-value	-	0.7147		0.2330	
Improvement probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful improvement change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Insomnia
16.2.6.1.2.16 Efficacy response data - Subgroup analyses by previous treatment with IMiD
16.2.6.1.2.16.6 QLQ-C30 - Time until permanent deterioration by 10 pt in insomnia according to previous treatment with IMiD (LOCF) - ITT population

	Yes		No		
	Kd (N=62)	**IKd (N=81)**	**Kd (N=61)**	**IKd (N=98)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	13 (21.0)	19 (23.5)	16 (26.2)	21 (21.4)	0.4605
Number (%) of patients censored	49 (79.0)	62 (76.5)	45 (73.8)	77 (78.6)	
Kaplan-Meier estimates of Insomnia in months					
25% quantile (95% CI)	20.60 (18.924 to NC)	21.42 (12.025 to NC)	20.76 (7.556 to NC)	NC (14.784 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (21.027 to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.6954		0.5421	
Hazard ratio (95% CI) vs Kd	-	1.15 (0.57 to 2.33)		0.82 (0.43 to 1.57)	
P-value	-	0.6956		0.5428	
Deterioration probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful deterioration change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Insomnia
16.2.6.1.2.17 Efficacy response data - Subgroup analyses by previous treatment with PI and IMiD
16.2.6.1.2.17.3 QLQ-C30 - Time to first improvement by 10 pt in insomnia according to previous treatment with PI and IMiD (LOCF) - ITT population

	Yes		No		
	Kd (N=17)	**IKd (N=23)**	**Kd (N=106)**	**IKd (N=156)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	6 (35.3)	6 (26.1)	38 (35.8)	57 (36.5)	0.4984
Number (%) of patients censored	11 (64.7)	17 (73.9)	68 (64.2)	99 (63.5)	
Kaplan-Meier estimates of Insomnia in months					
25% quantile (95% CI)	2.92 (0.986 to NC)	3.42 (0.986 to NC)	3.71 (1.906 to 9.889)	3.71 (1.971 to 5.585)	
Median (95% CI)	NC (2.070 to NC)	NC (3.417 to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.5185		0.8803	
Hazard ratio (95% CI) vs Kd	-	0.69 (0.22 to 2.14)		1.03 (0.68 to 1.56)	
P-value	-	0.5209		0.8806	
Improvement probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful improvement change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Insomnia
16.2.6.1.2.17 Efficacy response data - Subgroup analyses by previous treatment with PI and IMiD
16.2.6.1.2.17.4 QLQ-C30 - Time to first deterioration by 10 pt in insomnia according to previous treatment with PI and IMiD (LOCF) - ITT population

	Yes		No		
	Kd (N=17)	**IKd (N=23)**	**Kd (N=106)**	**IKd (N=156)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	8 (47.1)	12 (52.2)	62 (58.5)	94 (60.3)	0.9637
Number (%) of patients censored	9 (52.9)	11 (47.8)	44 (41.5)	62 (39.7)	
Kaplan-Meier estimates of Insomnia in months					
25% quantile (95% CI)	2.00 (0.986 to 15.211)	2.86 (0.986 to 6.505)	1.94 (1.051 to 3.745)	1.87 (1.084 to 2.793)	
Median (95% CI)	15.21 (1.216 to NC)	8.34 (3.220 to NC)	7.92 (5.585 to 17.610)	7.00 (3.844 to 12.386)	
75% quantile (95% CI)	NC (15.211 to NC)	NC (9.298 to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.9317		0.6266	
Hazard ratio (95% CI) vs Kd	-	1.04 (0.42 to 2.55)		1.08 (0.79 to 1.49)	
P-value	-	0.9320		0.6267	
Deterioration probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful deterioration change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Insomnia
16.2.6.1.2.17 Efficacy response data - Subgroup analyses by previous treatment with PI and IMiD
16.2.6.1.2.17.5 QLQ-C30 - Time until permanent improvement by 10 pt in insomnia according to previous treatment with PI and IMiD (LOCF) - ITT population

	Yes		No		
	Kd (N=17)	**IKd (N=23)**	**Kd (N=106)**	**IKd (N=156)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	5 (29.4)	4 (17.4)	19 (17.9)	36 (23.1)	0.3204
Number (%) of patients censored	12 (70.6)	19 (82.6)	87 (82.1)	120 (76.9)	
Kaplan-Meier estimates of Insomnia in months					
25% quantile (95% CI)	11.14 (7.491 to NC)	23.36 (0.986 to 23.359)	NC (14.456 to NC)	20.63 (17.018 to NC)	
Median (95% CI)	NC (10.448 to NC)	23.36 (NC to NC)	NC (NC to NC)	NC (23.721 to NC)	
75% quantile (95% CI)	NC (NC to NC)	23.36 (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.5582		0.3518	
Hazard ratio (95% CI) vs Kd	-	0.67 (0.18 to 2.54)		1.30 (0.75 to 2.27)	
P-value	-	0.5606		0.3532	
Improvement probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful improvement change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Insomnia
16.2.6.1.2.17 Efficacy response data - Subgroup analyses by previous treatment with PI and IMiD
16.2.6.1.2.17.6 QLQ-C30 - Time until permanent deterioration by 10 pt in insomnia according to previous treatment with PI and IMiD (LOCF) - ITT population

	Yes		No		
	Kd (N=17)	**IKd (N=23)**	**Kd (N=106)**	**IKd (N=156)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	2 (11.8)	7 (30.4)	27 (25.5)	33 (21.2)	0.1445
Number (%) of patients censored	15 (88.2)	16 (69.6)	79 (74.5)	123 (78.8)	
Kaplan-Meier estimates of Insomnia in months					
25% quantile (95% CI)	NC (20.534 to NC)	19.88 (1.511 to NC)	20.47 (11.926 to NC)	NC (14.982 to NC)	
Median (95% CI)	NC (20.534 to NC)	NC (19.877 to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.1820		0.4652	
Hazard ratio (95% CI) vs Kd	-	2.79 (0.58 to 13.44)		0.83 (0.50 to 1.38)	
P-value	-	0.2012		0.4658	
Deterioration probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful deterioration change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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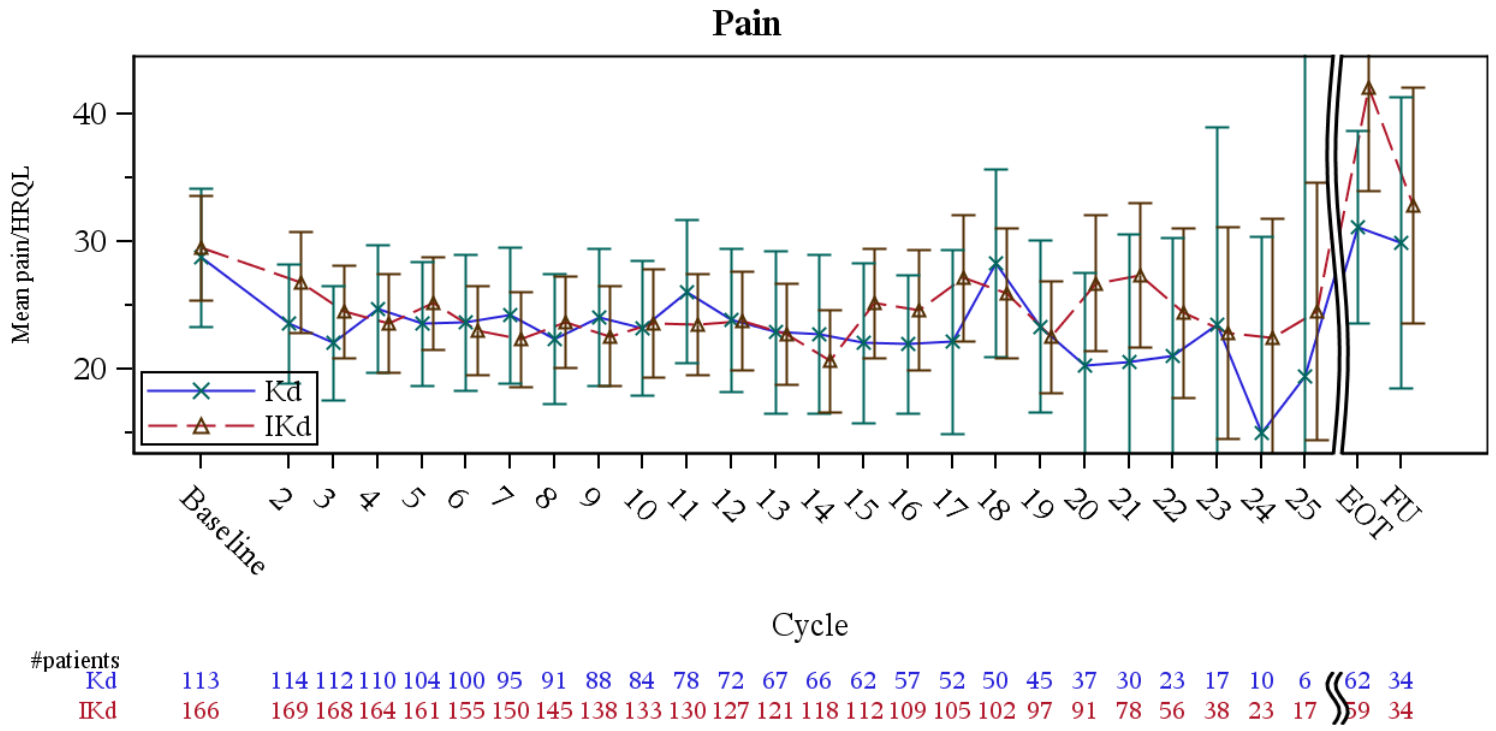
16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Pain
16.2.6.1.2.1 Efficacy response data
16.2.6.1.2.1.1 QLQ-C30 - Mean and 95% CI for pain score over time (LOCF) - ITT population



#patients																									
Kd	113	114	112	110	104	100	95	91	88	84	78	72	67	66	62	57	52	50	45	37	30	23	17	10	6	62	34
IKd	166	169	168	164	161	155	150	145	138	133	130	127	121	118	112	109	105	102	97	91	78	56	38	23	17	59	34

A lower score represents a better level of quality of life. Cycles with less than 20 patients overall are not presented.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
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16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Pain
16.2.6.1.2.1 Efficacy response data
16.2.6.1.2.1.15 QLQ-C30 - Time to first improvement by 15 pt in Pain (LOCF) - ITT population

First improvement 15 points Pain (%)	**Kd (N=123)**	**IKd (N=179)**
Number (%) of events	60 (48.8)	103 (57.5)
Number (%) of patients censored	63 (51.2)	76 (42.5)
Kaplan-Meier estimates of Pain in months		
25% quantile (95% CI)	1.12 (1.018 to 1.906)	1.12 (1.051 to 1.413)
Median (95% CI)	12.94 (2.136 to NC)	3.78 (2.136 to 9.002)
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)
Comparison vs. Kd		
Stratified[a] Log-Rank test p-value[b] vs Kd	-	0.2348
Stratified[a] Hazard ratio (95% CI) vs Kd	-	1.21 (0.88 to 1.67)
P-value	-	0.2355
Improvement probability (95% CI)[c]		
3 Months	0.433 (0.343 to 0.519)	0.476 (0.400 to 0.548)
6 Months	0.477 (0.385 to 0.563)	0.536 (0.459 to 0.607)

A lower score represents a better level of quality of life. Clinical meaningful improvement change from baseline less than or equal to -15 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] Stratified on number of prior lines of therapy (1 vs. >1) and Revised International Staging System (R-ISS) stage (I or II vs. III vs. not classified) according to IRT
[b] One-sided significance level is 0.025
[c] Estimated using the Kaplan-Meier method
NA/NC = Not Applicable / Not Calculable
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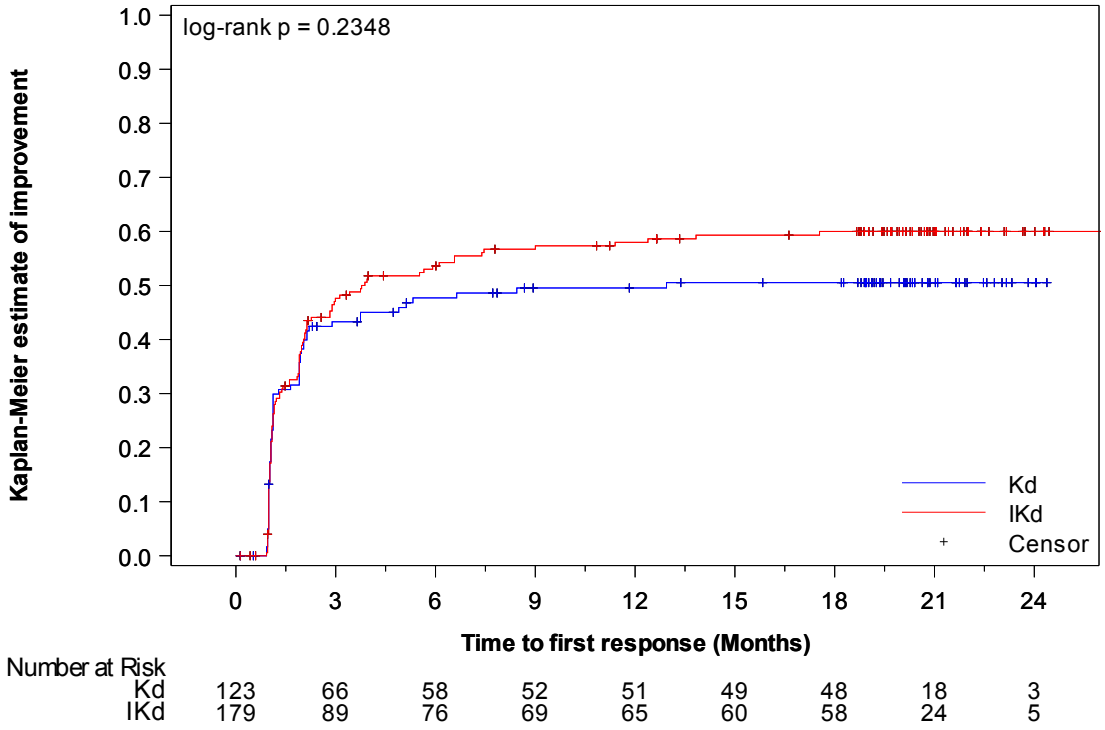
16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Pain
16.2.6.1.2.1 Efficacy response data
16.2.6.1.2.1.16 QLQ-C30 - Time to first improvement by 15 pt in Pain - Kaplan-Meier curve (LOCF) - ITT population



A lower score represents a better level of quality of life. Clinical meaningful improvement change from baseline less than or equal to -15 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
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16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Pain
16.2.6.1.2.1 Efficacy response data
16.2.6.1.2.1.17 QLQ-C30 - Time to first deterioration by 15 pt in Pain (LOCF) - ITT population

First deterioration 15 points Pain (%)	**Kd (N=123)**	**IKd (N=179)**
Number (%) of events	66 (53.7)	106 (59.2)
Number (%) of patients censored	57 (46.3)	73 (40.8)
Kaplan-Meier estimates of Pain in months		
25% quantile (95% CI)	2.79 (1.873 to 3.745)	1.97 (1.150 to 2.760)
Median (95% CI)	16.16 (4.895 to 21.290)	7.62 (3.811 to 12.189)
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)
Comparison vs. Kd		
Stratified[a] Log-Rank test p-value[b] vs Kd	-	0.1449
Stratified[a] Hazard ratio (95% CI) vs Kd	-	1.26 (0.92 to 1.72)
P-value	-	0.1458
Deterioration probability (95% CI)[c]		
3 Months	0.700 (0.609 to 0.773)	0.639 (0.562 to 0.705)
6 Months	0.563 (0.469 to 0.646)	0.528 (0.451 to 0.599)

A lower score represents a better level of quality of life. Clinical meaningful deterioration change from baseline greater than or equal to 15 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] Stratified on number of prior lines of therapy (1 vs. >1) and Revised International Staging System (R-ISS) stage (I or II vs. III vs. not classified) according to IRT
[b] One-sided significance level is 0.025
[c] Estimated using the Kaplan-Meier method
NA/NC = Not Applicable / Not Calculable
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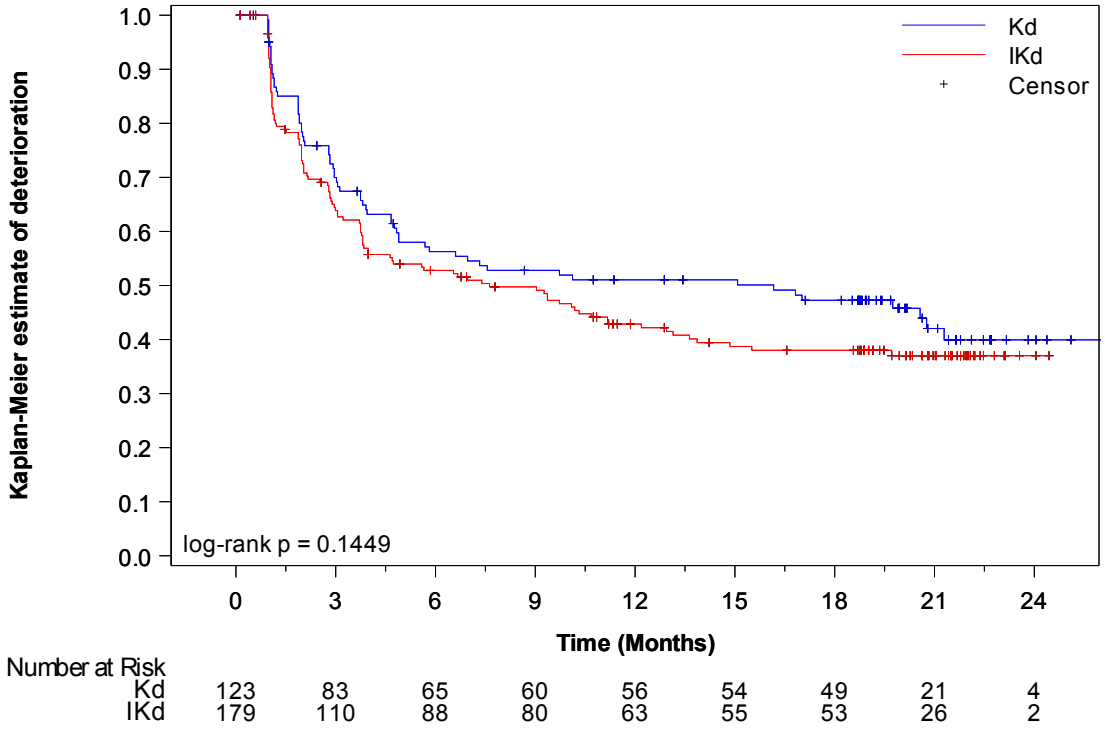
16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Pain
16.2.6.1.2.1 Efficacy response data
16.2.6.1.2.1.18 QLQ-C30 - Time to first deterioration by 15 pt in Pain - Kaplan-Meier curve (LOCF) - ITT population



A lower score represents a better level of quality of life. Clinical meaningful deterioration change from baseline greater than or equal to 15 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
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16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Pain
16.2.6.1.2.1 Efficacy response data
16.2.6.1.2.1.19 QLQ-C30 - Time until permanent improvement by 15 pt in Pain (LOCF) - ITT population

First permanent improvement 15 points Pain (%)	Kd (N=123)	IKd (N=179)
Number (%) of events	34 (27.6)	55 (30.7)
Number (%) of patients censored	89 (72.4)	124 (69.3)
Kaplan-Meier estimates of Pain in months		
25% quantile (95% CI)	18.69 (7.918 to 22.209)	15.64 (10.973 to 20.304)
Median (95% CI)	NC (NC to NC)	24.44 (23.359 to NC)
75% quantile (95% CI)	NC (NC to NC)	NC (24.444 to NC)
Comparison vs. Kd		
Stratified[a] Log-Rank test p-value[b] vs Kd	-	0.5241
Stratified[a] Hazard ratio (95% CI) vs Kd	-	1.15 (0.74 to 1.78)
P-value	-	0.5244
Improvement probability (95% CI)[c]		
3 Months	0.141 (0.086 to 0.210)	0.131 (0.086 to 0.186)
6 Months	0.141 (0.086 to 0.210)	0.161 (0.111 to 0.219)

A lower score represents a better level of quality of life. Clinical meaningful improvement change from baseline less than or equal to -15 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] Stratified on number of prior lines of therapy (1 vs. >1) and Revised International Staging System (R-ISS) stage (I or II vs. III vs. not classified) according to IRT
[b] One-sided significance level is 0.025
[c] Estimated using the Kaplan-Meier method
NA/NC = Not Applicable / Not Calculable
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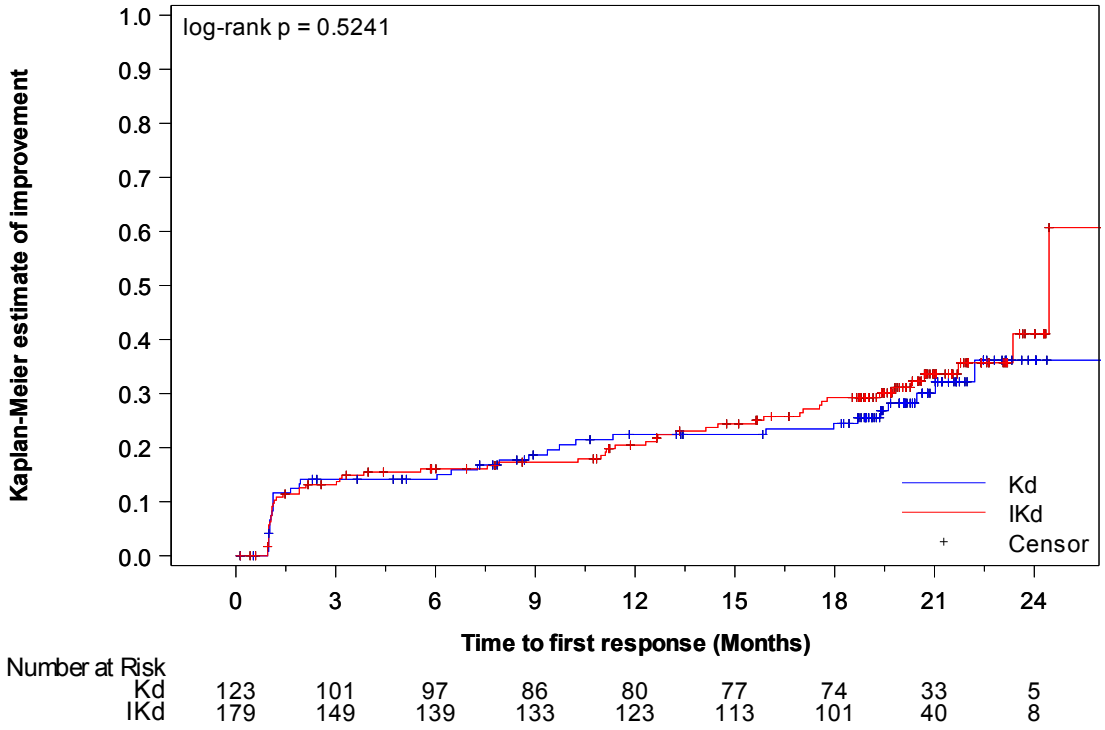
16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Pain
16.2.6.1.2.1 Efficacy response data
16.2.6.1.2.1.20 QLQ-C30 - Time until permanent improvement by 15 pt in Pain - Kaplan-Meier curve (LOCF) - ITT population



A lower score represents a better level of quality of life. Clinical meaningful improvement change from baseline less than or equal to -15 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
PGM=DEVOPS/SAR650984/EFC15246/CIR_RWE/REPORT/PGM/eff_qlq_km_i_f.sas OUT=REPORT/OUTPUT/eff_km_c30_pan_imp15pl_de_i_f_x.rtf (07APR2021 14:23)

16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Pain
16.2.6.1.2.1 Efficacy response data
16.2.6.1.2.1.21 QLQ-C30 - Time until permanent deterioration by 15 pt in Pain (LOCF) - ITT population

First permanent deterioration 15 points Pain (%)	**Kd (N=123)**	**IKd (N=179)**
Number (%) of events	34 (27.6)	56 (31.3)
Number (%) of patients censored	89 (72.4)	123 (68.7)
Kaplan-Meier estimates of Pain in months		
25% quantile (95% CI)	19.15 (13.503 to 23.064)	16.39 (12.945 to 21.520)
Median (95% CI)	NC (23.064 to NC)	23.72 (22.604 to NC)
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)
Comparison vs. Kd		
Stratified[a] Log-Rank test p-value[b] vs Kd	-	0.4649
Stratified[a] Hazard ratio (95% CI) vs Kd	-	1.17 (0.76 to 1.80)
P-value	-	0.4654
Deterioration probability (95% CI)[c]		
3 Months	0.917 (0.850 to 0.954)	0.908 (0.855 to 0.943)
6 Months	0.882 (0.809 to 0.929)	0.879 (0.821 to 0.919)

A lower score represents a better level of quality of life. Clinical meaningful deterioration change from baseline greater than or equal to 15 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] Stratified on number of prior lines of therapy (1 vs. >1) and Revised International Staging System (R-ISS) stage (I or II vs. III vs. not classified) according to IRT
[b] One-sided significance level is 0.025
[c] Estimated using the Kaplan-Meier method
NA/NC = Not Applicable / Not Calculable
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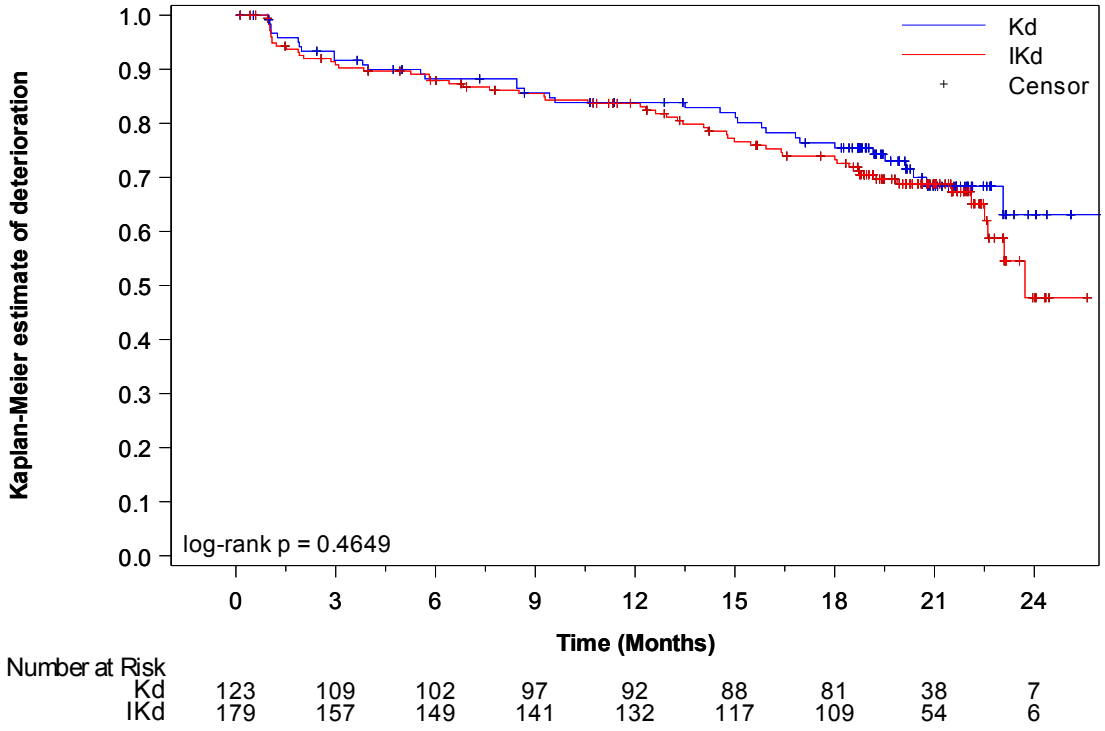
16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Pain
16.2.6.1.2.1 Efficacy response data
16.2.6.1.2.1.22 QLQ-C30 - Time until permanent deterioration by 15 pt in Pain - Kaplan-Meier curve (LOCF) - ITT population



A lower score represents a better level of quality of life. Clinical meaningful deterioration change from baseline greater than or equal to 15 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
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16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Pain
16.2.6.1.2.2 Efficacy response data - Subgroup analyses by age
16.2.6.1.2.2.3 QLQ-C30 - Time to first improvement by 10 pt in pain according to age (LOCF) - ITT population

	<65 years		>=65 years		
	Kd (N=66)	**IKd (N=88)**	**Kd (N=57)**	**IKd (N=91)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	33 (50.0)	50 (56.8)	27 (47.4)	53 (58.2)	0.5815
Number (%) of patients censored	33 (50.0)	38 (43.2)	30 (52.6)	38 (41.8)	
Kaplan-Meier estimates of Pain in months					
25% quantile (95% CI)	1.05 (0.986 to 1.117)	1.08 (0.986 to 1.906)	1.91 (1.084 to 2.136)	1.15 (1.051 to 1.840)	
Median (95% CI)	12.94 (1.281 to NC)	2.99 (1.971 to NC)	NC (2.136 to NC)	3.98 (2.037 to 13.832)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.6570		0.2144	
Hazard ratio (95% CI) vs Kd	-	1.10 (0.71 to 1.71)		1.34 (0.84 to 2.13)	
P-value	-	0.6572		0.2160	
Improvement probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful improvement change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
PGM=DEVOPS/SAR650984/EFC15246/CIR_RWE/REPORT/PGM/eff_km_subgp_sr_sig_de_i_t.sas OUT=REPORT/OUTPUT/eff_km_c30_pan_impl_age_de_i_t_x.rtf (07APR2021 14:30)

16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Pain
16.2.6.1.2.2 Efficacy response data - Subgroup analyses by age
16.2.6.1.2.2.4 QLQ-C30 - Time to first deterioration by 10 pt in pain according to age (LOCF) - ITT population

	<65 years		>=65 years		
	Kd (N=66)	**IKd (N=88)**	**Kd (N=57)**	**IKd (N=91)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	34 (51.5)	49 (55.7)	32 (56.1)	57 (62.6)	0.6012
Number (%) of patients censored	32 (48.5)	39 (44.3)	25 (43.9)	34 (37.4)	
Kaplan-Meier estimates of Pain in months					
25% quantile (95% CI)	1.97 (1.084 to 3.910)	2.00 (1.511 to 3.745)	2.83 (1.906 to 3.745)	1.17 (1.051 to 2.760)	
Median (95% CI)	16.82 (4.665 to NC)	9.03 (3.811 to NC)	15.08 (3.745 to 21.290)	6.97 (2.957 to 11.170)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (20.567 to NC)	NC (13.864 to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.6404		0.2158	
Hazard ratio (95% CI) vs Kd	-	1.11 (0.72 to 1.72)		1.31 (0.85 to 2.03)	
P-value	-	0.6405		0.2172	
Deterioration probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful deterioration change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Pain
16.2.6.1.2.2 Efficacy response data - Subgroup analyses by age
16.2.6.1.2.2.5 QLQ-C30 - Time until permanent improvement by 10 pt in pain according to age (LOCF) - ITT population

	<65 years		>=65 years		
	Kd (N=66)	**IKd (N=88)**	**Kd (N=57)**	**IKd (N=91)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	20 (30.3)	24 (27.3)	14 (24.6)	31 (34.1)	0.2892
Number (%) of patients censored	46 (69.7)	64 (72.7)	43 (75.4)	60 (65.9)	
Kaplan-Meier estimates of Pain in months					
25% quantile (95% CI)	15.93 (1.117 to NC)	14.13 (3.023 to NC)	19.38 (7.918 to NC)	17.05 (7.556 to 20.698)	
Median (95% CI)	NC (21.027 to NC)	NC (NC to NC)	NC (22.209 to NC)	24.44 (21.717 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (24.444 to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.6723		0.2933	
Hazard ratio (95% CI) vs Kd	-	0.88 (0.49 to 1.59)		1.40 (0.74 to 2.64)	
P-value	-	0.6725		0.2956	
Improvement probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful improvement change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Pain
16.2.6.1.2.2 Efficacy response data - Subgroup analyses by age
16.2.6.1.2.2.6 QLQ-C30 - Time until permanent deterioration by 10 pt in pain according to age (LOCF) - ITT population

	<65 years		>=65 years		
	Kd (N=66)	**IKd (N=88)**	**Kd (N=57)**	**IKd (N=91)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	20 (30.3)	27 (30.7)	14 (24.6)	29 (31.9)	0.5008
Number (%) of patients censored	46 (69.7)	61 (69.3)	43 (75.4)	62 (68.1)	
Kaplan-Meier estimates of Pain in months					
25% quantile (95% CI)	16.82 (5.684 to NC)	15.93 (9.298 to 22.505)	20.14 (13.503 to NC)	18.00 (12.616 to 22.111)	
Median (95% CI)	NC (20.764 to NC)	23.72 (22.505 to NC)	NC (23.064 to NC)	23.10 (22.111 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (23.721 to NC)	NC (NC to NC)	NC (23.097 to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.8879		0.2811	
Hazard ratio (95% CI) vs Kd	-	1.04 (0.58 to 1.86)		1.42 (0.75 to 2.69)	
P-value	-	0.8882		0.2836	
Deterioration probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful deterioration change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Pain
16.2.6.1.2.3 Efficacy response data - Subgroup analyses by gender
16.2.6.1.2.3.3 QLQ-C30 - Time to first improvement by 10 pt in pain according to gender (LOCF) - ITT population

	Male		Female		
	Kd (N=68)	**IKd (N=101)**	**Kd (N=55)**	**IKd (N=78)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	27 (39.7)	54 (53.5)	33 (60.0)	49 (62.8)	0.2292
Number (%) of patients censored	41 (60.3)	47 (46.5)	22 (40.0)	29 (37.2)	
Kaplan-Meier estimates of Pain in months					
25% quantile (95% CI)	1.64 (1.051 to 4.895)	1.31 (1.051 to 1.938)	1.05 (0.986 to 1.117)	1.05 (0.986 to 1.216)	
Median (95% CI)	NC (5.322 to NC)	5.52 (2.136 to NC)	2.00 (1.117 to NC)	2.83 (1.906 to 9.002)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.1011		0.9856	
Hazard ratio (95% CI) vs Kd	-	1.47 (0.92 to 2.33)		1.00 (0.64 to 1.55)	
P-value	-	0.1032		0.9856	
Improvement probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful improvement change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Pain
16.2.6.1.2.3 Efficacy response data - Subgroup analyses by gender
16.2.6.1.2.3.4 QLQ-C30 - Time to first deterioration by 10 pt in pain according to gender (LOCF) - ITT population

	Male		Female		
	Kd (N=68)	**IKd (N=101)**	**Kd (N=55)**	**IKd (N=78)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	39 (57.4)	60 (59.4)	27 (49.1)	46 (59.0)	0.5084
Number (%) of patients censored	29 (42.6)	41 (40.6)	28 (50.9)	32 (41.0)	
Kaplan-Meier estimates of Pain in months					
25% quantile (95% CI)	2.79 (1.873 to 3.055)	1.97 (1.084 to 2.793)	2.79 (1.051 to 5.815)	1.97 (1.051 to 3.220)	
Median (95% CI)	6.97 (3.121 to 19.745)	5.65 (3.055 to 10.678)	20.76 (5.815 to NC)	9.72 (3.811 to 14.850)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.6274		0.1898	
Hazard ratio (95% CI) vs Kd	-	1.10 (0.74 to 1.65)		1.37 (0.85 to 2.21)	
P-value	-	0.6276		0.1916	
Deterioration probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful deterioration change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Pain
16.2.6.1.2.3 Efficacy response data - Subgroup analyses by gender
16.2.6.1.2.3.5 QLQ-C30 - Time until permanent improvement by 10 pt in pain according to gender (LOCF) - ITT population

	Male		Female		
	Kd (N=68)	**IKd (N=101)**	**Kd (N=55)**	**IKd (N=78)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	16 (23.5)	27 (26.7)	18 (32.7)	28 (35.9)	0.8133
Number (%) of patients censored	52 (76.5)	74 (73.3)	37 (67.3)	50 (64.1)	
Kaplan-Meier estimates of Pain in months					
25% quantile (95% CI)	19.38 (9.363 to NC)	16.95 (3.844 to NC)	10.22 (1.117 to 22.209)	14.13 (7.556 to 20.304)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (21.027 to NC)	24.44 (23.359 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (24.444 to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.6435		0.9099	
Hazard ratio (95% CI) vs Kd	-	1.16 (0.62 to 2.15)		1.03 (0.57 to 1.87)	
P-value	-	0.6438		0.9102	
Improvement probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful improvement change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Pain
16.2.6.1.2.3 Efficacy response data - Subgroup analyses by gender
16.2.6.1.2.3.6 QLQ-C30 - Time until permanent deterioration by 10 pt in pain according to gender (LOCF) - ITT population

	Male		Female		
	Kd (N=68)	**IKd (N=101)**	**Kd (N=55)**	**IKd (N=78)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	20 (29.4)	33 (32.7)	14 (25.5)	23 (29.5)	0.9598
Number (%) of patients censored	48 (70.6)	68 (67.3)	41 (74.5)	55 (70.5)	
Kaplan-Meier estimates of Pain in months					
25% quantile (95% CI)	15.93 (8.444 to 23.064)	14.78 (6.407 to 21.520)	19.52 (9.593 to NC)	18.76 (12.616 to 23.097)	
Median (95% CI)	NC (23.064 to NC)	NC (22.111 to NC)	NC (NC to NC)	23.72 (22.505 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (23.721 to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.5442		0.6458	
Hazard ratio (95% CI) vs Kd	-	1.19 (0.68 to 2.07)		1.17 (0.60 to 2.27)	
P-value	-	0.5447		0.6462	
Deterioration probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful deterioration change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Pain
16.2.6.1.2.4 Efficacy response data - Subgroup analyses by ethnic origin
16.2.6.1.2.4.3 QLQ-C30 - Time to first improvement by 10 pt in pain according to ethnic origin (LOCF) - ITT population

	White		Other		
	Kd (N=83)	**IKd (N=131)**	**Kd (N=28)**	**IKd (N=34)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	44 (53.0)	78 (59.5)	14 (50.0)	20 (58.8)	0.6879
Number (%) of patients censored	39 (47.0)	53 (40.5)	14 (50.0)	14 (41.2)	
Kaplan-Meier estimates of Pain in months					
25% quantile (95% CI)	1.08 (0.986 to 1.906)	1.12 (1.051 to 1.610)	1.12 (1.018 to 2.037)	1.08 (0.953 to 1.906)	
Median (95% CI)	4.90 (1.906 to NC)	3.88 (2.037 to 9.002)	6.64 (1.117 to NC)	2.99 (1.084 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (5.651 to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.5366		0.4269	
Hazard ratio (95% CI) vs Kd	-	1.12 (0.78 to 1.63)		1.32 (0.67 to 2.61)	
P-value	-	0.5368		0.4284	
Improvement probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful improvement change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Pain
16.2.6.1.2.4 Efficacy response data - Subgroup analyses by ethnic origin
16.2.6.1.2.4.4 QLQ-C30 - Time to first deterioration by 10 pt in pain according to ethnic origin (LOCF) - ITT population

	White		Other		
	Kd (N=83)	**IKd (N=131)**	**Kd (N=28)**	**IKd (N=34)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	45 (54.2)	86 (65.6)	16 (57.1)	16 (47.1)	0.2135
Number (%) of patients censored	38 (45.8)	45 (34.4)	12 (42.9)	18 (52.9)	
Kaplan-Meier estimates of Pain in months					
25% quantile (95% CI)	2.83 (1.873 to 3.745)	1.97 (1.084 to 2.530)	2.83 (1.051 to 6.604)	1.64 (0.986 to 5.585)	
Median (95% CI)	16.16 (4.665 to NC)	4.70 (3.713 to 9.725)	10.12 (2.957 to NC)	15.51 (2.760 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (13.634 to NC)	NC (19.745 to NC)	NC (NC to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.0572		0.7023	
Hazard ratio (95% CI) vs Kd	-	1.42 (0.99 to 2.03)		0.87 (0.44 to 1.75)	
P-value	-	0.0585		0.7025	
Deterioration probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful deterioration change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Pain
16.2.6.1.2.4 Efficacy response data - Subgroup analyses by ethnic origin
16.2.6.1.2.4.5 QLQ-C30 - Time until permanent improvement by 10 pt in pain according to ethnic origin (LOCF) - ITT population

	White		Other		
	Kd (N=83)	**IKd (N=131)**	**Kd (N=28)**	**IKd (N=34)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	25 (30.1)	39 (29.8)	7 (25.0)	13 (38.2)	0.2598
Number (%) of patients censored	58 (69.9)	92 (70.2)	21 (75.0)	21 (61.8)	
Kaplan-Meier estimates of Pain in months					
25% quantile (95% CI)	18.69 (6.045 to 22.209)	17.61 (11.105 to 21.717)	17.97 (1.018 to NC)	12.32 (0.986 to 14.489)	
Median (95% CI)	NC (22.209 to NC)	24.44 (23.359 to NC)	NC (NC to NC)	NC (13.240 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (24.444 to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.8156		0.2625	
Hazard ratio (95% CI) vs Kd	-	0.94 (0.57 to 1.56)		1.68 (0.67 to 4.22)	
P-value	-	0.8144		0.2679	
Improvement probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful improvement change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
PGM=DEVOPS/SAR650984/EFC15246/CIR_RWE/REPORT/PGM/eff_km_subgp_sr_sig_de_i_t.sas OUT=REPORT/OUTPUT/eff_km_c30_pan_imppl_race_de_i_t_x.rtf (07APR2021 14:31)

16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Pain
16.2.6.1.2.4 Efficacy response data - Subgroup analyses by ethnic origin
16.2.6.1.2.4.6 QLQ-C30 - Time until permanent deterioration by 10 pt in pain according to ethnic origin (LOCF) - ITT population

	White		Other		
	Kd (N=83)	**IKd (N=131)**	**Kd (N=28)**	**IKd (N=34)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	22 (26.5)	45 (34.4)	8 (28.6)	9 (26.5)	0.5637
Number (%) of patients censored	61 (73.5)	86 (65.6)	20 (71.4)	25 (73.5)	
Kaplan-Meier estimates of Pain in months					
25% quantile (95% CI)	20.14 (14.554 to NC)	14.75 (9.298 to 19.877)	16.95 (2.957 to NC)	18.73 (6.407 to NC)	
Median (95% CI)	NC (23.064 to NC)	23.72 (22.604 to NC)	NC (19.515 to NC)	NC (18.760 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (23.721 to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.2279		0.9264	
Hazard ratio (95% CI) vs Kd	-	1.37 (0.82 to 2.28)		0.96 (0.37 to 2.48)	
P-value	-	0.2298		0.9263	
Deterioration probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful deterioration change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Pain
16.2.6.1.2.5 Efficacy response data - Subgroup analyses by geographical region
16.2.6.1.2.5.3 QLQ-C30 - Time to first improvement by 10 pt in pain according to geographical region (LOCF) - ITT population

	Europe		America		Asia		Other countries		
	Kd (N=60)	**IKd (N=85)**	**Kd (N=20)**	**IKd (N=24)**	**Kd (N=21)**	**IKd (N=25)**	**Kd (N=22)**	**IKd (N=45)**	**p-value of treatment-by-subgroup interaction[c]**
Number (%) of events	28 (46.7)	43 (50.6)	9 (45.0)	15 (62.5)	11 (52.4)	16 (64.0)	12 (54.5)	29 (64.4)	0.7803
Number (%) of patients censored	32 (53.3)	42 (49.4)	11 (55.0)	9 (37.5)	10 (47.6)	9 (36.0)	10 (45.5)	16 (35.6)	
Kaplan-Meier estimates of event in months									
25% quantile (95% CI)	1.12 (0.986 to 1.906)	1.84 (1.084 to 2.070)	1.59 (0.920 to 2.201)	1.05 (0.953 to 1.610)	1.12 (1.018 to 2.037)	1.05 (0.920 to 1.906)	1.08 (0.953 to 2.136)	1.08 (1.018 to 1.380)	
Median (95% CI)	NC (2.136 to NC)	7.39 (2.136 to NC)	NC (1.281 to NC)	5.52 (1.051 to NC)	4.34 (1.117 to NC)	2.86 (1.084 to NC)	6.78 (1.084 to NC)	2.96 (1.314 to 13.832)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (5.651 to NC)	NC (6.637 to NC)	NC (2.990 to NC)	NC (8.444 to NC)	NC (7.458 to NC)	
Comparison vs. Kd									

A lower score represents a better level of quality of life. Clinical meaningful improvement change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Pain
16.2.6.1.2.5 Efficacy response data - Subgroup analyses by geographical region
16.2.6.1.2.5.3 QLQ-C30 - Time to first improvement by 10 pt in pain according to geographical region (LOCF) - ITT population

	Europe		America		Asia		Other countries		
	Kd (N=60)	**IKd (N=85)**	**Kd (N=20)**	**IKd (N=24)**	**Kd (N=21)**	**IKd (N=25)**	**Kd (N=22)**	**IKd (N=45)**	**p-value of treatment-by-subgroup interaction[c]**
Log-Rank test p-value[a] vs Kd	-	0.8345		0.2195		0.4673		0.5756	
Hazard ratio (95% CI) vs Kd	-	1.05 (0.65 to 1.69)		1.67 (0.73 to 3.83)		1.33 (0.62 to 2.87)		1.21 (0.62 to 2.38)	
P-value	-	0.8353		0.2245		0.4688		0.5762	
Improvement probability (95% CI)[b]									
3 Months	0.395 (0.270 to 0.517)	0.422 (0.315 to 0.526)	0.450 (0.231 to 0.647)	0.484 (0.271 to 0.668)	0.500 (0.271 to 0.692)	0.583 (0.364 to 0.750)	0.455 (0.244 to 0.643)	0.511 (0.358 to 0.645)	
6 Months	0.470 (0.337 to 0.593)	0.498 (0.386 to 0.601)	0.450 (0.231 to 0.647)	0.578 (0.350 to 0.751)	0.500 (0.271 to 0.692)	0.625 (0.403 to 0.784)	0.500 (0.282 to 0.684)	0.534 (0.379 to 0.667)	

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The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Pain
16.2.6.1.2.5 Efficacy response data - Subgroup analyses by geographical region
16.2.6.1.2.5.4 QLQ-C30 - Time to first deterioration by 10 pt in pain according to geographical region (LOCF) - ITT population

	Europe		America		Asia		Other countries		
	Kd (N=60)	**IKd (N=85)**	**Kd (N=20)**	**IKd (N=24)**	**Kd (N=21)**	**IKd (N=25)**	**Kd (N=22)**	**IKd (N=45)**	**p-value of treatment-by-subgroup interaction[c]**
Number (%) of events	28 (46.7)	46 (54.1)	12 (60.0)	13 (54.2)	11 (52.4)	13 (52.0)	15 (68.2)	34 (75.6)	0.9579
Number (%) of patients censored	32 (53.3)	39 (45.9)	8 (40.0)	11 (45.8)	10 (47.6)	12 (48.0)	7 (31.8)	11 (24.4)	
Kaplan-Meier estimates of event in months									
25% quantile (95% CI)	2.79 (1.248 to 3.745)	1.97 (1.183 to 3.745)	1.99 (0.953 to 4.895)	1.97 (0.986 to 3.778)	2.50 (1.051 to 6.604)	1.13 (0.986 to 2.957)	2.96 (1.018 to 4.764)	1.91 (1.051 to 2.793)	
Median (95% CI)	NC (4.665 to NC)	10.32 (3.975 to NC)	8.72 (1.971 to NC)	10.09 (2.037 to NC)	7.56 (2.037 to NC)	12.94 (1.150 to NC)	4.86 (2.957 to 21.290)	3.81 (2.793 to 9.363)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (10.119 to NC)	NC (10.086 to NC)	NC (20.567 to NC)	NC (13.864 to NC)	21.29 (4.895 to NC)	12.19 (9.035 to NC)	

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The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Pain
16.2.6.1.2.5 Efficacy response data - Subgroup analyses by geographical region
16.2.6.1.2.5.4 QLQ-C30 - Time to first deterioration by 10 pt in pain according to geographical region (LOCF) - ITT population

	Europe		America		Asia		Other countries		
	Kd (N=60)	**IKd (N=85)**	**Kd (N=20)**	**IKd (N=24)**	**Kd (N=21)**	**IKd (N=25)**	**Kd (N=22)**	**IKd (N=45)**	**p-value of treatment-by-subgroup interaction[c]**
Comparison vs. Kd									
Log-Rank test p-value[a] vs Kd	-	0.4068		0.9361		0.8221		0.3356	
Hazard ratio (95% CI) vs Kd	-	1.22 (0.76 to 1.95)		1.03 (0.47 to 2.27)		1.10 (0.49 to 2.45)		1.35 (0.73 to 2.48)	
P-value	-	0.4076		0.9361		0.8226		0.3374	
Deterioration probability (95% CI)[b]									
3 Months	0.691 (0.555 to 0.792)	0.698 (0.587 to 0.785)	0.700 (0.451 to 0.853)	0.643 (0.410 to 0.803)	0.696 (0.445 to 0.851)	0.583 (0.364 to 0.750)	0.727 (0.491 to 0.867)	0.556 (0.400 to 0.686)	
6 Months	0.602 (0.464 to 0.715)	0.588 (0.474 to 0.685)	0.550 (0.313 to 0.735)	0.505 (0.286 to 0.688)	0.589 (0.343 to 0.770)	0.542 (0.327 to 0.714)	0.455 (0.244 to 0.643)	0.422 (0.278 to 0.560)	

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The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Pain
16.2.6.1.2.5 Efficacy response data - Subgroup analyses by geographical region
16.2.6.1.2.5.5 QLQ-C30 - Time until permanent improvement by 10 pt in pain according to geographical region (LOCF) - ITT population

	Europe		America		Asia		Other countries		
	Kd (N=60)	**IKd (N=85)**	**Kd (N=20)**	**IKd (N=24)**	**Kd (N=21)**	**IKd (N=25)**	**Kd (N=22)**	**IKd (N=45)**	**p-value of treatment-by-subgroup interaction[c]**
Number (%) of events	15 (25.0)	24 (28.2)	5 (25.0)	11 (45.8)	5 (23.8)	9 (36.0)	9 (40.9)	11 (24.4)	0.1716
Number (%) of patients censored	45 (75.0)	61 (71.8)	15 (75.0)	13 (54.2)	16 (76.2)	16 (64.0)	13 (59.1)	34 (75.6)	
Kaplan-Meier estimates of event in months									
25% quantile (95% CI)	19.61 (1.906 to NC)	19.78 (7.556 to 24.444)	20.47 (0.986 to NC)	1.15 (0.953 to 15.639)	NC (1.018 to NC)	13.24 (0.986 to 17.051)	10.22 (1.084 to 22.209)	21.72 (10.283 to NC)	
Median (95% CI)	NC (NC to NC)	24.44 (23.359 to 24.444)	NC (20.468 to NC)	17.61 (1.906 to NC)	NC (1.117 to NC)	NC (13.240 to NC)	22.21 (10.218 to NC)	NC (21.717 to NC)	

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The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Pain
16.2.6.1.2.5 Efficacy response data - Subgroup analyses by geographical region
16.2.6.1.2.5.5 QLQ-C30 - Time until permanent improvement by 10 pt in pain according to geographical region (LOCF) - ITT population

	Europe		America		Asia		Other countries		
	Kd (N=60)	**IKd (N=85)**	**Kd (N=20)**	**IKd (N=24)**	**Kd (N=21)**	**IKd (N=25)**	**Kd (N=22)**	**IKd (N=45)**	**p-value of treatment-by-subgroup interaction[c]**
75% quantile (95% CI)	NC (NC to NC)	24.44 (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (22.209 to NC)	NC (NC to NC)	
Comparison vs. Kd									
Log-Rank test p-value[a] vs Kd	-	0.8990		0.0984		0.5147		0.1567	
Hazard ratio (95% CI) vs Kd	-	1.04 (0.54 to 2.00)		2.38 (0.82 to 6.86)		1.44 (0.48 to 4.29)		0.53 (0.22 to 1.29)	
P-value	-	0.8994		0.1090		0.5170		0.1634	
Improvement probability (95% CI)[b]									

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The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Pain
16.2.6.1.2.5 Efficacy response data - Subgroup analyses by geographical region
16.2.6.1.2.5.6 QLQ-C30 - Time until permanent deterioration by 10 pt in pain according to geographical region (LOCF) - ITT population

	Europe		America		Asia		Other countries		
	Kd (N=60)	**IKd (N=85)**	**Kd (N=20)**	**IKd (N=24)**	**Kd (N=21)**	**IKd (N=25)**	**Kd (N=22)**	**IKd (N=45)**	**p-value of treatment-by-subgroup interaction[c]**
Number (%) of events	16 (26.7)	22 (25.9)	6 (30.0)	5 (20.8)	7 (33.3)	7 (28.0)	5 (22.7)	22 (48.9)	0.2542
Number (%) of patients censored	44 (73.3)	63 (74.1)	14 (70.0)	19 (79.2)	14 (66.7)	18 (72.0)	17 (77.3)	23 (51.1)	
Kaplan-Meier estimates of event in months									
25% quantile (95% CI)	19.15 (14.554 to NC)	19.25 (13.437 to NC)	14.72 (1.906 to NC)	NC (0.986 to NC)	15.80 (1.051 to NC)	18.76 (1.018 to NC)	20.14 (1.018 to NC)	10.58 (2.858 to 18.070)	
Median (95% CI)	NC (23.064 to NC)	NC (23.721 to NC)	NC (8.674 to NC)	NC (NC to NC)	NC (15.803 to NC)	NC (18.760 to NC)	NC (20.140 to NC)	22.11 (14.752 to 23.097)	

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The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Pain
16.2.6.1.2.5 Efficacy response data - Subgroup analyses by geographical region
16.2.6.1.2.5.6 QLQ-C30 - Time until permanent deterioration by 10 pt in pain according to geographical region (LOCF) - ITT population

	Europe		America		Asia		Other countries		
	Kd (N=60)	**IKd (N=85)**	**Kd (N=20)**	**IKd (N=24)**	**Kd (N=21)**	**IKd (N=25)**	**Kd (N=22)**	**IKd (N=45)**	**p-value of treatment-by-subgroup interaction[c]**
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (22.505 to NC)	NC (NC to NC)	23.10 (22.111 to NC)	
Comparison vs. Kd									
Log-Rank test p-value[a] vs Kd	-	0.8680		0.6352		0.6817		0.0364	
Hazard ratio (95% CI) vs Kd	-	0.95 (0.50 to 1.80)		0.75 (0.23 to 2.46)		0.80 (0.28 to 2.29)		2.72 (1.03 to 7.22)	
P-value	-	0.8674		0.6362		0.6823		0.0444	
Hazard ratio inverted (95% CI) vs IKd		-		1.33 (0.41 to 4.37)		1.24 (0.44 to 3.55)		0.37 (0.14 to 0.98)	
Deterioration probability (95% CI)[b]									

A lower score represents a better level of quality of life. Clinical meaningful deterioration change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Pain
16.2.6.1.2.6 Efficacy response data - Subgroup analyses by regulatory region
16.2.6.1.2.6.3 QLQ-C30 - Time to first improvement by 10 pt in pain according to regulatory region (LOCF) - ITT population

	Western countries		Other countries		
	Kd (N=55)	**IKd (N=97)**	**Kd (N=68)**	**IKd (N=82)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	27 (49.1)	50 (51.5)	33 (48.5)	53 (64.6)	0.1192
Number (%) of patients censored	28 (50.9)	47 (48.5)	35 (51.5)	29 (35.4)	
Kaplan-Meier estimates of Pain in months					
25% quantile (95% CI)	1.08 (0.986 to 1.938)	1.41 (1.117 to 2.037)	1.12 (1.018 to 1.906)	1.05 (0.986 to 1.084)	
Median (95% CI)	12.94 (1.906 to NC)	9.00 (2.891 to NC)	NC (1.938 to NC)	2.14 (1.380 to 3.943)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (7.458 to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.8458		0.0454	
Hazard ratio (95% CI) vs Kd	-	0.95 (0.60 to 1.52)		1.55 (1.01 to 2.40)	
P-value	-	0.8447		0.0472	
Hazard ratio inverted (95% CI) vs IKd		-		0.64 (0.42 to 0.99)	

A lower score represents a better level of quality of life. Clinical meaningful improvement change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Pain
16.2.6.1.2.6 Efficacy response data - Subgroup analyses by regulatory region
16.2.6.1.2.6.4 QLQ-C30 - Time to first deterioration by 10 pt in pain according to regulatory region (LOCF) - ITT population

	Western countries		Other countries		
	Kd (N=55)	**IKd (N=97)**	**Kd (N=68)**	**IKd (N=82)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	23 (41.8)	58 (59.8)	43 (63.2)	48 (58.5)	0.1403
Number (%) of patients censored	32 (58.2)	39 (40.2)	25 (36.8)	34 (41.5)	
Kaplan-Meier estimates of Pain in months					
25% quantile (95% CI)	4.67 (1.873 to 16.164)	2.04 (1.183 to 3.055)	1.97 (1.150 to 2.957)	1.49 (1.051 to 2.136)	
Median (95% CI)	NC (9.725 to NC)	9.36 (3.975 to 13.634)	5.68 (3.023 to 16.821)	4.63 (2.825 to 13.864)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (20.567 to NC)	NC (NC to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.0421		0.9524	
Hazard ratio (95% CI) vs Kd	-	1.64 (1.01 to 2.66)		1.01 (0.67 to 1.53)	
P-value	-	0.0444		0.9525	
Hazard ratio inverted (95% CI) vs IKd		-		0.99 (0.65 to 1.49)	

A lower score represents a better level of quality of life. Clinical meaningful deterioration change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Pain
16.2.6.1.2.6 Efficacy response data - Subgroup analyses by regulatory region
16.2.6.1.2.6.5 QLQ-C30 - Time until permanent improvement by 10 pt in pain according to regulatory region (LOCF) - ITT population

	Western countries		Other countries		
	Kd (N=55)	**IKd (N=97)**	**Kd (N=68)**	**IKd (N=82)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	19 (34.5)	23 (23.7)	15 (22.1)	32 (39.0)	0.0089
Number (%) of patients censored	36 (65.5)	74 (76.3)	53 (77.9)	50 (61.0)	
Kaplan-Meier estimates of Pain in months					
25% quantile (95% CI)	11.33 (1.117 to 19.614)	20.70 (12.320 to NC)	21.03 (6.472 to NC)	11.10 (1.084 to 17.051)	
Median (95% CI)	NC (19.384 to NC)	NC (NC to NC)	NC (NC to NC)	23.36 (17.774 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	24.44 (24.444 to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.1226		0.0319	
Hazard ratio (95% CI) vs Kd	-	0.62 (0.34 to 1.14)		1.94 (1.05 to 3.58)	
P-value	-	0.1260		0.0351	
Hazard ratio inverted (95% CI) vs IKd		-		0.52 (0.28 to 0.95)	

A lower score represents a better level of quality of life. Clinical meaningful improvement change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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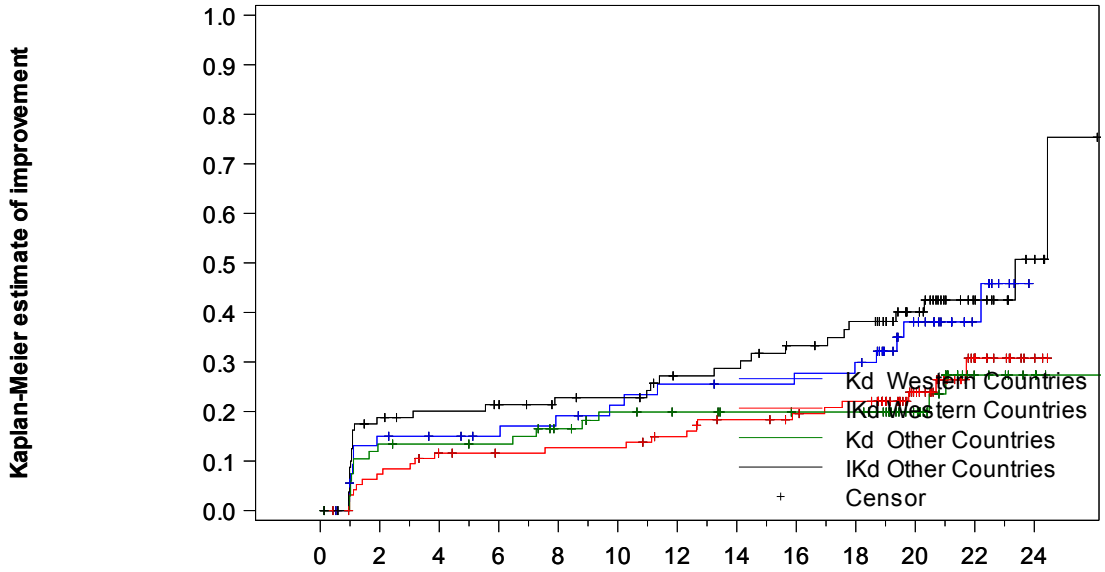
16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Pain
16.2.6.1.2.6 Efficacy response data - Subgroup analyses by regulatory region
16.2.6.1.2.6.6 QLQ-C30 - Time until permanent improvement by 10 pt in pain according to regulatory region- Kaplan-Meier curve (LOCF) - ITT population



Number at Risk									
Kd Western Countries	55	44	41	38	35	34	32	13	0
IKd Western Countries	97	87	80	79	75	69	63	23	3
Kd Other Countries	68	57	56	48	45	43	42	20	5
IKd Other Countries	82	62	59	54	48	44	38	17	5

A lower score represents a better level of quality of life. Clinical meaningful improvement change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
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16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Pain
16.2.6.1.2.6 Efficacy response data - Subgroup analyses by regulatory region
16.2.6.1.2.6.7 QLQ-C30 - Time until permanent deterioration by 10 pt in pain according to regulatory region (LOCF) - ITT population

	Western countries		Other countries		
	Kd (N=55)	**IKd (N=97)**	**Kd (N=68)**	**IKd (N=82)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	11 (20.0)	31 (32.0)	23 (33.8)	25 (30.5)	0.1292
Number (%) of patients censored	44 (80.0)	66 (68.0)	45 (66.2)	57 (69.5)	
Kaplan-Meier estimates of Pain in months					
25% quantile (95% CI)	NC (13.503 to NC)	16.39 (7.622 to 22.604)	15.80 (8.444 to 20.764)	18.43 (12.616 to 22.505)	
Median (95% CI)	NC (NC to NC)	23.10 (22.604 to NC)	NC (20.764 to NC)	23.72 (22.111 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (23.097 to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.1055		0.6820	
Hazard ratio (95% CI) vs Kd	-	1.75 (0.88 to 3.49)		0.89 (0.50 to 1.57)	
P-value	-	0.1101		0.6822	
Deterioration probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful deterioration change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Pain
16.2.6.1.2.7 Efficacy response data - Subgroup analyses by baseline ECOG PS
16.2.6.1.2.7.3 QLQ-C30 - Time to first improvement by 10 pt in pain according to baseline ECOG PS (LOCF) - ITT population

	0 or 1		>1		
	Kd (N=118)	**IKd (N=168)**	**Kd (N=5)**	**IKd (N=11)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	58 (49.2)	95 (56.5)	2 (40.0)	8 (72.7)	0.2407
Number (%) of patients censored	60 (50.8)	73 (43.5)	3 (60.0)	3 (27.3)	
Kaplan-Meier estimates of Pain in months					
25% quantile (95% CI)	1.12 (1.018 to 1.906)	1.12 (1.051 to 1.840)	1.91 (0.986 to NC)	1.02 (0.986 to 1.610)	
Median (95% CI)	12.94 (2.136 to NC)	5.52 (2.136 to 13.832)	NC (0.986 to NC)	1.61 (0.986 to 3.975)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (0.986 to NC)	3.88 (1.216 to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.3977		0.1356	
Hazard ratio (95% CI) vs Kd	-	1.15 (0.83 to 1.60)		3.10 (0.65 to 14.83)	
P-value	-	0.3981		0.1556	
Improvement probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful improvement change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Pain
16.2.6.1.2.7 Efficacy response data - Subgroup analyses by baseline ECOG PS
16.2.6.1.2.7.4 QLQ-C30 - Time to first deterioration by 10 pt in pain according to baseline ECOG PS (LOCF) - ITT population

	0 or 1		>1		
	Kd (N=118)	**IKd (N=168)**	**Kd (N=5)**	**IKd (N=11)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	64 (54.2)	103 (61.3)	2 (40.0)	3 (27.3)	0.5802
Number (%) of patients censored	54 (45.8)	65 (38.7)	3 (60.0)	8 (72.7)	
Kaplan-Meier estimates of Pain in months					
25% quantile (95% CI)	2.79 (1.873 to 3.745)	1.97 (1.117 to 2.760)	2.07 (1.873 to NC)	3.06 (0.986 to NC)	
Median (95% CI)	15.08 (4.895 to 21.290)	7.39 (3.811 to 11.170)	NC (1.873 to NC)	NC (0.986 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (1.873 to NC)	NC (NC to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.1683		0.7367	
Hazard ratio (95% CI) vs Kd	-	1.24 (0.91 to 1.70)		0.74 (0.12 to 4.43)	
P-value	-	0.1691		0.7376	
Deterioration probability (95% CI)[b]					

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The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Pain
16.2.6.1.2.7 Efficacy response data - Subgroup analyses by baseline ECOG PS
16.2.6.1.2.7.5 QLQ-C30 - Time until permanent improvement by 10 pt in pain according to baseline ECOG PS (LOCF) - ITT population

	0 or 1		>1		
	Kd (N=118)	**IKd (N=168)**	**Kd (N=5)**	**IKd (N=11)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	33 (28.0)	49 (29.2)	1 (20.0)	6 (54.5)	0.2061
Number (%) of patients censored	85 (72.0)	119 (70.8)	4 (80.0)	5 (45.5)	
Kaplan-Meier estimates of Pain in months					
25% quantile (95% CI)	18.69 (7.918 to 22.209)	17.54 (11.400 to 21.717)	NC (0.986 to NC)	1.02 (0.986 to 3.121)	
Median (95% CI)	NC (22.209 to NC)	24.44 (23.359 to NC)	NC (0.986 to NC)	3.12 (0.986 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (24.444 to NC)	NC (0.986 to NC)	NC (1.216 to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.9621		0.2064	
Hazard ratio (95% CI) vs Kd	-	1.01 (0.65 to 1.57)		3.59 (0.43 to 29.91)	
P-value	-	0.9621		0.2372	
Improvement probability (95% CI)[b]					

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The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Pain
16.2.6.1.2.7 Efficacy response data - Subgroup analyses by baseline ECOG PS
16.2.6.1.2.7.6 QLQ-C30 - Time until permanent deterioration by 10 pt in pain according to baseline ECOG PS (LOCF) - ITT population

	0 or 1		>1		
	Kd (N=118)	**IKd (N=168)**	**Kd (N=5)**	**IKd (N=11)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	32 (27.1)	55 (32.7)	2 (40.0)	1 (9.1)	0.1134
Number (%) of patients censored	86 (72.9)	113 (67.3)	3 (60.0)	10 (90.9)	
Kaplan-Meier estimates of Pain in months					
25% quantile (95% CI)	19.52 (14.554 to NC)	15.93 (12.320 to 19.877)	13.50 (1.873 to NC)	NC (12.616 to NC)	
Median (95% CI)	NC (23.064 to NC)	23.72 (22.505 to NC)	13.50 (1.873 to NC)	NC (12.616 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (1.873 to NC)	NC (NC to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.2776		0.1689	
Hazard ratio (95% CI) vs Kd	-	1.27 (0.82 to 1.97)		0.21 (0.02 to 2.40)	
P-value	-	0.2788		0.2099	
Deterioration probability (95% CI)[b]					

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The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Pain
16.2.6.1.2.8 Efficacy response data - Subgroup analyses by ISS staging at SE
16.2.6.1.2.8.3 QLQ-C30 - Time to first improvement by 10 pt in pain according to ISS staging at SE (LOCF) - ITT population

	I		II		III		
	Kd (N=71)	**IKd (N=89)**	**Kd (N=31)**	**IKd (N=63)**	**Kd (N=20)**	**IKd (N=26)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	35 (49.3)	51 (57.3)	15 (48.4)	36 (57.1)	10 (50.0)	15 (57.7)	0.9794
Number (%) of patients censored	36 (50.7)	38 (42.7)	16 (51.6)	27 (42.9)	10 (50.0)	11 (42.3)	
Kaplan-Meier estimates of Pain in months							
25% quantile (95% CI)	1.08 (1.018 to 1.643)	1.15 (0.986 to 1.906)	1.91 (0.986 to 2.136)	1.08 (1.018 to 1.938)	0.99 (0.953 to 2.891)	1.05 (0.953 to 1.413)	
Median (95% CI)	12.94 (1.906 to NC)	3.94 (1.971 to NC)	NC (1.906 to NC)	6.57 (2.037 to NC)	5.32 (0.986 to NC)	2.10 (1.084 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (5.322 to NC)	NC (2.136 to NC)	
Comparison vs. Kd							
Log-Rank test p-value[a] vs Kd	-	0.4818		0.5127		0.5503	
Hazard ratio (95% CI) vs Kd	-	1.17 (0.76 to 1.79)		1.22 (0.67 to 2.23)		1.28 (0.57 to 2.85)	
P-value	-	0.4823		0.5134		0.5512	

A lower score represents a better level of quality of life. Clinical meaningful improvement change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Pain
16.2.6.1.2.8 Efficacy response data - Subgroup analyses by ISS staging at SE
16.2.6.1.2.8.4 QLQ-C30 - Time to first deterioration by 10 pt in pain according to ISS staging at SE (LOCF) - ITT population

	I		II		III		
	Kd (N=71)	**IKd (N=89)**	**Kd (N=31)**	**IKd (N=63)**	**Kd (N=20)**	**IKd (N=26)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	35 (49.3)	53 (59.6)	19 (61.3)	46 (73.0)	11 (55.0)	7 (26.9)	0.1275
Number (%) of patients censored	36 (50.7)	36 (40.4)	12 (38.7)	17 (27.0)	9 (45.0)	19 (73.1)	
Kaplan-Meier estimates of Pain in months							
25% quantile (95% CI)	3.75 (2.037 to 4.895)	2.17 (1.183 to 3.713)	1.22 (0.986 to 2.924)	1.08 (1.018 to 1.971)	1.97 (1.084 to 3.121)	3.81 (0.953 to NC)	
Median (95% CI)	20.76 (6.965 to NC)	9.26 (3.844 to 13.864)	4.90 (1.906 to NC)	3.22 (1.971 to 9.035)	5.82 (1.971 to NC)	NC (3.811 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (7.326 to NC)	NC (9.363 to NC)	NC (7.556 to NC)	NC (NC to NC)	
Comparison vs. Kd							
Log-Rank test p-value[a] vs Kd	-	0.1295		0.3819		0.1388	
Hazard ratio (95% CI) vs Kd	-	1.39 (0.91 to 2.13)		1.27 (0.74 to 2.17)		0.49 (0.19 to 1.28)	
P-value	-	0.1312		0.3831		0.1468	

A lower score represents a better level of quality of life. Clinical meaningful deterioration change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Pain
16.2.6.1.2.8 Efficacy response data - Subgroup analyses by ISS staging at SE
16.2.6.1.2.8.5 QLQ-C30 - Time until permanent improvement by 10 pt in pain according to ISS staging at SE (LOCF) - ITT population

	I		II		III		
	Kd (N=71)	**IKd (N=89)**	**Kd (N=31)**	**IKd (N=63)**	**Kd (N=20)**	**IKd (N=26)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	21 (29.6)	26 (29.2)	7 (22.6)	15 (23.8)	6 (30.0)	14 (53.8)	0.2847
Number (%) of patients censored	50 (70.4)	63 (70.8)	24 (77.4)	48 (76.2)	14 (70.0)	12 (46.2)	
Kaplan-Meier estimates of Pain in months							
25% quantile (95% CI)	19.38 (1.643 to 22.209)	17.54 (10.973 to 24.444)	18.69 (6.045 to NC)	20.30 (11.138 to NC)	7.92 (0.953 to NC)	1.08 (0.953 to 10.283)	
Median (95% CI)	NC (22.209 to NC)	24.44 (21.717 to NC)	NC (NC to NC)	NC (23.359 to NC)	NC (7.918 to NC)	11.10 (1.216 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (24.444 to NC)	NC (NC to NC)	NC (23.359 to NC)	NC (NC to NC)	NC (12.320 to NC)	
Comparison vs. Kd							
Log-Rank test p-value[a] vs Kd	-	0.9911		0.9571		0.0803	
Hazard ratio (95% CI) vs Kd	-	1.00 (0.56 to 1.79)		0.98 (0.40 to 2.40)		2.30 (0.88 to 6.02)	
P-value	-	0.9911		0.9569		0.0890	

A lower score represents a better level of quality of life. Clinical meaningful improvement change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Pain
16.2.6.1.2.8 Efficacy response data - Subgroup analyses by ISS staging at SE
16.2.6.1.2.8.6 QLQ-C30 - Time until permanent deterioration by 10 pt in pain according to ISS staging at SE (LOCF) - ITT population

	I		II		III		
	Kd (N=71)	**IKd (N=89)**	**Kd (N=31)**	**IKd (N=63)**	**Kd (N=20)**	**IKd (N=26)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	15 (21.1)	27 (30.3)	9 (29.0)	28 (44.4)	9 (45.0)	1 (3.8)	0.0232
Number (%) of patients censored	56 (78.9)	62 (69.7)	22 (71.0)	35 (55.6)	11 (55.0)	25 (96.2)	
Kaplan-Meier estimates of Pain in months							
25% quantile (95% CI)	23.06 (18.004 to NC)	18.43 (12.945 to 23.097)	16.82 (1.248 to NC)	12.32 (2.858 to 16.427)	8.67 (1.873 to 15.014)	NC (1.051 to NC)	
Median (95% CI)	NC (23.064 to NC)	23.72 (22.505 to NC)	NC (20.370 to NC)	22.60 (18.070 to NC)	15.01 (8.444 to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (23.721 to NC)	NC (NC to NC)	NC (NC to NC)	NC (15.014 to NC)	NC (NC to NC)	
Comparison vs. Kd							
Log-Rank test p-value[a] vs Kd	-	0.1802		0.2406		0.0022	
Hazard ratio (95% CI) vs Kd	-	1.54 (0.82 to 2.89)		1.56 (0.74 to 3.31)		0.08 (0.01 to 0.64)	
P-value	-	0.1836		0.2448		0.0171	

A lower score represents a better level of quality of life. Clinical meaningful deterioration change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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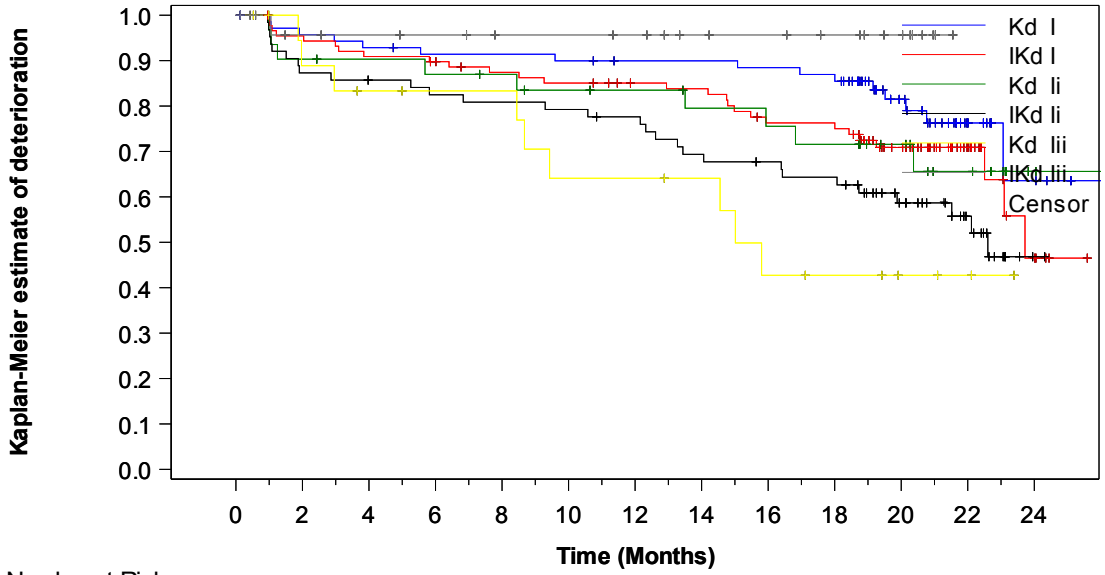
16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Pain
16.2.6.1.2.8 Efficacy response data - Subgroup analyses by ISS staging at SE
16.2.6.1.2.8.7 QLQ-C30 - Time until permanent deterioration by 10 pt in pain according to ISS staging at SE- Kaplan-Meier curve (LOCF) - ITT population



Number at Risk

Kd I	71	66	63	63	60	60	58	26	5
IKd I	89	82	78	73	68	63	60	30	5
Kd Ii	31	27	26	23	22	20	18	9	2
IKd Ii	63	54	51	50	47	41	38	21	1
Kd Iii	20	15	13	11	10	8	5	3	0
IKd Iii	26	20	19	17	16	12	10	2	0

A lower score represents a better level of quality of life. Clinical meaningful deterioration change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
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16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Pain
16.2.6.1.2.9 Efficacy response data - Subgroup analyses by R-ISS stage at SE
16.2.6.1.2.9.3 QLQ-C30 - Time to first improvement by 10 pt in pain according to R-ISS stage at SE (LOCF) - ITT population

	I or II		III		Not classified		
	Kd (N=103)	**IKd (N=155)**	**Kd (N=8)**	**IKd (N=16)**	**Kd (N=12)**	**IKd (N=8)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	49 (47.6)	89 (57.4)	5 (62.5)	9 (56.3)	6 (50.0)	5 (62.5)	0.8120
Number (%) of patients censored	54 (52.4)	66 (42.6)	3 (37.5)	7 (43.8)	6 (50.0)	3 (37.5)	
Kaplan-Meier estimates of Pain in months							
25% quantile (95% CI)	1.12 (1.051 to 1.906)	1.12 (1.051 to 1.840)	1.05 (0.953 to 2.891)	1.02 (0.953 to 1.413)	1.05 (0.953 to 12.945)	2.07 (1.084 to 2.825)	
Median (95% CI)	NC (2.136 to NC)	5.65 (2.267 to 17.544)	2.04 (0.953 to NC)	1.71 (0.986 to NC)	NC (0.986 to NC)	2.48 (1.084 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (1.117 to NC)	NC (1.413 to NC)	NC (12.945 to NC)	3.98 (2.070 to NC)	
Comparison vs. Kd							
Log-Rank test p-value[a] vs Kd	-	0.2813		0.9692		0.3775	
Hazard ratio (95% CI) vs Kd	-	1.21 (0.85 to 1.72)		1.02 (0.34 to 3.06)		1.71 (0.51 to 5.76)	

A lower score represents a better level of quality of life. Clinical meaningful improvement change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Pain
16.2.6.1.2.9 Efficacy response data - Subgroup analyses by R-ISS stage at SE
16.2.6.1.2.9.4 QLQ-C30 - Time to first deterioration by 10 pt in pain according to R-ISS stage at SE (LOCF) - ITT population

	I or II		III		Not classified		
	Kd (N=103)	**IKd (N=155)**	**Kd (N=8)**	**IKd (N=16)**	**Kd (N=12)**	**IKd (N=8)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	53 (51.5)	102 (65.8)	5 (62.5)	3 (18.8)	8 (66.7)	1 (12.5)	0.0109
Number (%) of patients censored	50 (48.5)	53 (34.2)	3 (37.5)	13 (81.3)	4 (33.3)	7 (87.5)	
Kaplan-Meier estimates of Pain in months							
25% quantile (95% CI)	2.83 (1.906 to 3.811)	1.87 (1.084 to 2.136)	1.87 (1.084 to 5.815)	NC (1.051 to NC)	1.87 (0.986 to 5.684)	NC (3.055 to NC)	
Median (95% CI)	19.75 (4.830 to NC)	5.59 (3.745 to 10.086)	5.82 (1.084 to NC)	NC (9.363 to NC)	7.70 (1.150 to NC)	NC (3.055 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (19.713 to NC)	NC (1.971 to NC)	NC (NC to NC)	NC (5.684 to NC)	NC (NC to NC)	
Comparison vs. Kd							
Log-Rank test p-value[a] vs Kd	-	0.0272		0.0356		0.0935	
Hazard ratio (95% CI) vs Kd	-	1.45 (1.04 to 2.02)		0.24 (0.06 to 1.01)		0.20 (0.03 to 1.61)	
P-value	-	0.0281		0.0524		0.1308	

A lower score represents a better level of quality of life. Clinical meaningful deterioration change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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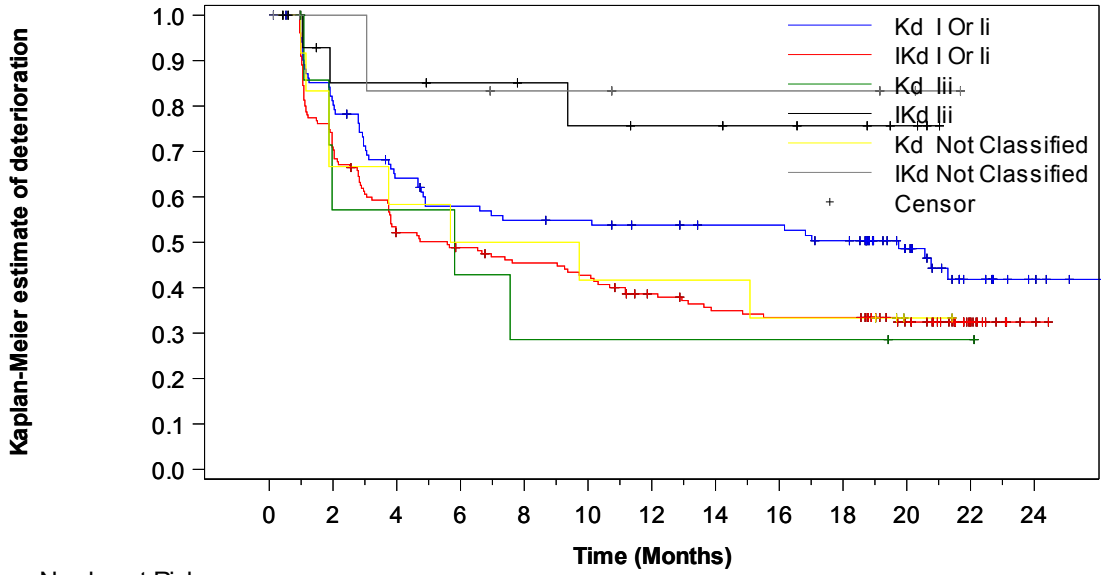
16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Pain
16.2.6.1.2.9 Efficacy response data - Subgroup analyses by R-ISS stage at SE
16.2.6.1.2.9.5 QLQ-C30 - Time to first deterioration by 10 pt in pain according to R-ISS stage at SE- Kaplan-Meier curve (LOCF) - ITT population



Number at Risk									
Kd I Or Ii	103	71	56	52	49	47	43	19	4
IKd I Or Ii	155	93	73	67	53	46	45	24	2
Kd Iii	8	4	3	2	2	2	2	1	0
IKd Iii	16	11	10	9	7	6	5	1	0
Kd Not Classified	12	8	6	6	5	5	4	1	0
IKd Not Classified	8	6	5	4	3	3	3	1	0

A lower score represents a better level of quality of life. Clinical meaningful deterioration change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
PGM=DEVOPS/SAR650984/EFC15246/CIR_RWE/REPORT/PGM/eff_qlq_km_subgp_de_i_f.sas OUT=REPORT/OUTPUT/eff_km_c30_pan_detl_seriss_de_i_f_x.rtf (07APR2021 15:14)

16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Pain
16.2.6.1.2.9 Efficacy response data - Subgroup analyses by R-ISS stage at SE
16.2.6.1.2.9.6 QLQ-C30 - Time until permanent improvement by 10 pt in pain according to R-ISS stage at SE (LOCF) - ITT population

	I or II		III		Not classified		
	Kd (N=103)	**IKd (N=155)**	**Kd (N=8)**	**IKd (N=16)**	**Kd (N=12)**	**IKd (N=8)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	28 (27.2)	45 (29.0)	2 (25.0)	9 (56.3)	4 (33.3)	1 (12.5)	0.2860
Number (%) of patients censored	75 (72.8)	110 (71.0)	6 (75.0)	7 (43.8)	8 (66.7)	7 (87.5)	
Kaplan-Meier estimates of Pain in months							
25% quantile (95% CI)	19.38 (7.261 to 22.209)	17.61 (12.649 to 21.717)	1.12 (0.953 to NC)	1.02 (0.953 to 1.413)	12.37 (0.986 to NC)	NC (1.084 to NC)	
Median (95% CI)	NC (22.209 to NC)	24.44 (23.359 to NC)	NC (0.953 to NC)	1.76 (0.986 to NC)	NC (7.918 to NC)	NC (1.084 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (24.444 to NC)	NC (NC to NC)	NC (1.413 to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Kd							
Log-Rank test p-value[a] vs Kd	-	0.9854		0.1747		0.6314	
Hazard ratio (95% CI) vs Kd	-	1.00 (0.62 to 1.60)		2.77 (0.60 to 12.85)		0.59 (0.07 to 5.29)	
P-value	-	0.9854		0.1933		0.6354	

A lower score represents a better level of quality of life. Clinical meaningful improvement change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Pain
16.2.6.1.2.9 Efficacy response data - Subgroup analyses by R-ISS stage at SE
16.2.6.1.2.9.7 QLQ-C30 - Time until permanent deterioration by 10 pt in pain according to R-ISS stage at SE (LOCF) - ITT population

	I or II		III		Not classified		
	Kd (N=103)	**IKd (N=155)**	**Kd (N=8)**	**IKd (N=16)**	**Kd (N=12)**	**IKd (N=8)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	26 (25.2)	56 (36.1)	4 (50.0)	0 (0.0)	4 (33.3)	0 (0.0)	0.9995
Number (%) of patients censored	77 (74.8)	99 (63.9)	4 (50.0)	16 (100.0)	8 (66.7)	8 (100.0)	
Kaplan-Meier estimates of Pain in months							
25% quantile (95% CI)	20.14 (9.593 to NC)	14.78 (10.579 to 18.760)	9.43 (1.873 to 15.803)	NC (NC to NC)	20.01 (3.975 to 23.064)	NC (NC to NC)	
Median (95% CI)	NC (NC to NC)	23.72 (22.505 to NC)	15.80 (1.873 to NC)	NC (NC to NC)	23.06 (15.080 to 23.064)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (9.429 to NC)	NC (NC to NC)	23.06 (NC to NC)	NC (NC to NC)	
Comparison vs. Kd							
Log-Rank test p-value[a] vs Kd	-	0.1064		0.0033		0.2614	
Hazard ratio (95% CI) vs Kd	-	1.46 (0.92 to 2.33)					

A lower score represents a better level of quality of life. Clinical meaningful deterioration change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Pain
16.2.6.1.2.10 Efficacy response data - Subgroup analyses by nb of prior lines
16.2.6.1.2.10.3 QLQ-C30 - Time to first improvement by 10 pt in pain according to nb of prior lines (LOCF) - ITT population

	1		>1		
	Kd (N=55)	**IKd (N=79)**	**Kd (N=68)**	**IKd (N=100)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	28 (50.9)	40 (50.6)	32 (47.1)	63 (63.0)	0.1379
Number (%) of patients censored	27 (49.1)	39 (49.4)	36 (52.9)	37 (37.0)	
Kaplan-Meier estimates of Pain in months					
25% quantile (95% CI)	1.12 (1.051 to 1.906)	1.84 (1.084 to 2.136)	1.12 (0.986 to 1.938)	1.05 (0.986 to 1.150)	
Median (95% CI)	8.44 (1.906 to NC)	13.83 (2.957 to NC)	NC (1.938 to NC)	2.14 (1.873 to 5.520)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (12.386 to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.7511		0.0663	
Hazard ratio (95% CI) vs Kd	-	0.92 (0.57 to 1.50)		1.49 (0.97 to 2.28)	
P-value	-	0.7512		0.0681	
Improvement probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful improvement change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Pain
16.2.6.1.2.10 Efficacy response data - Subgroup analyses by nb of prior lines
16.2.6.1.2.10.4 QLQ-C30 - Time to first deterioration by 10 pt in pain according to nb of prior lines (LOCF) - ITT population

	1		>1		
	Kd (N=55)	**IKd (N=79)**	**Kd (N=68)**	**IKd (N=100)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	28 (50.9)	49 (62.0)	38 (55.9)	57 (57.0)	0.4708
Number (%) of patients censored	27 (49.1)	30 (38.0)	30 (44.1)	43 (43.0)	
Kaplan-Meier estimates of Pain in months					
25% quantile (95% CI)	2.04 (1.117 to 3.943)	1.15 (1.051 to 2.136)	2.83 (1.873 to 3.910)	2.00 (1.216 to 2.891)	
Median (95% CI)	9.72 (3.943 to NC)	5.59 (3.055 to 12.189)	16.16 (4.665 to 20.764)	9.26 (3.811 to 15.507)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (20.764 to NC)	NC (NC to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.2042		0.6248	
Hazard ratio (95% CI) vs Kd	-	1.35 (0.85 to 2.15)		1.11 (0.73 to 1.67)	
P-value	-	0.2059		0.6249	
Deterioration probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful deterioration change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Pain
16.2.6.1.2.10 Efficacy response data - Subgroup analyses by nb of prior lines
16.2.6.1.2.10.5 QLQ-C30 - Time until permanent improvement by 10 pt in pain according to nb of prior lines (LOCF) - ITT population

	1		>1		
	Kd (N=55)	**IKd (N=79)**	**Kd (N=68)**	**IKd (N=100)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	17 (30.9)	20 (25.3)	17 (25.0)	35 (35.0)	0.1383
Number (%) of patients censored	38 (69.1)	59 (74.7)	51 (75.0)	65 (65.0)	
Kaplan-Meier estimates of Pain in months					
25% quantile (95% CI)	15.93 (1.117 to NC)	20.30 (11.400 to 24.444)	19.38 (7.918 to NC)	12.68 (3.121 to 17.610)	
Median (95% CI)	NC (22.209 to NC)	24.44 (23.359 to NC)	NC (21.027 to NC)	NC (20.698 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (24.444 to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.3650		0.1984	
Hazard ratio (95% CI) vs Kd	-	0.74 (0.38 to 1.42)		1.46 (0.82 to 2.61)	
P-value	-	0.3668		0.2011	
Improvement probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful improvement change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Pain
16.2.6.1.2.10 Efficacy response data - Subgroup analyses by nb of prior lines
16.2.6.1.2.10.6 QLQ-C30 - Time until permanent deterioration by 10 pt in pain according to nb of prior lines (LOCF) - ITT population

	1		>1		
	Kd (N=55)	**IKd (N=79)**	**Kd (N=68)**	**IKd (N=100)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	14 (25.5)	26 (32.9)	20 (29.4)	30 (30.0)	0.5206
Number (%) of patients censored	41 (74.5)	53 (67.1)	48 (70.6)	70 (70.0)	
Kaplan-Meier estimates of Pain in months					
25% quantile (95% CI)	19.52 (8.444 to NC)	16.43 (7.622 to 22.505)	18.00 (8.674 to 20.764)	15.47 (9.298 to 22.604)	
Median (95% CI)	NC (23.064 to NC)	23.72 (22.505 to NC)	NC (20.764 to NC)	NC (22.604 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (23.721 to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.3374		0.9076	
Hazard ratio (95% CI) vs Kd	-	1.37 (0.72 to 2.63)		1.03 (0.59 to 1.82)	
P-value	-	0.3394		0.9079	
Deterioration probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful deterioration change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Pain
16.2.6.1.2.11 Efficacy response data - Subgroup analyses by cytogenetic abnormality
16.2.6.1.2.11.3 QLQ-C30 - Time to first improvement by 10 pt in pain according to cytogenetic abnormality (LOCF) - ITT population

	At least one		None		
	Kd (N=31)	**IKd (N=42)**	**Kd (N=77)**	**IKd (N=114)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	16 (51.6)	25 (59.5)	37 (48.1)	61 (53.5)	0.8764
Number (%) of patients censored	15 (48.4)	17 (40.5)	40 (51.9)	53 (46.5)	
Kaplan-Meier estimates of Pain in months					
25% quantile (95% CI)	1.12 (1.018 to 2.891)	1.12 (0.986 to 1.938)	1.12 (1.018 to 1.938)	1.12 (1.018 to 1.906)	
Median (95% CI)	5.88 (1.906 to NC)	4.85 (1.906 to NC)	NC (1.971 to NC)	6.11 (2.136 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (17.544 to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.5882		0.6046	
Hazard ratio (95% CI) vs Kd	-	1.19 (0.63 to 2.23)		1.11 (0.74 to 1.68)	
P-value	-	0.5886		0.6048	
Improvement probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful improvement change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Pain
16.2.6.1.2.11 Efficacy response data - Subgroup analyses by cytogenetic abnormality
16.2.6.1.2.11.4 QLQ-C30 - Time to first deterioration by 10 pt in pain according to cytogenetic abnormality (LOCF) - ITT population

	At least one		None		
	Kd (N=31)	**IKd (N=42)**	**Kd (N=77)**	**IKd (N=114)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	16 (51.6)	28 (66.7)	42 (54.5)	69 (60.5)	0.6051
Number (%) of patients censored	15 (48.4)	14 (33.3)	35 (45.5)	45 (39.5)	
Kaplan-Meier estimates of Pain in months					
25% quantile (95% CI)	2.07 (1.084 to 3.811)	1.15 (0.986 to 2.793)	2.79 (1.216 to 3.910)	1.97 (1.084 to 2.530)	
Median (95% CI)	16.16 (2.957 to NC)	4.81 (2.760 to 12.945)	10.12 (4.665 to 21.290)	7.39 (3.778 to 11.170)	
75% quantile (95% CI)	NC (NC to NC)	NC (11.170 to NC)	NC (21.290 to NC)	NC (NC to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.2115		0.3152	
Hazard ratio (95% CI) vs Kd	-	1.48 (0.80 to 2.73)		1.22 (0.83 to 1.79)	
P-value	-	0.2144		0.3160	
Deterioration probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful deterioration change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Pain
16.2.6.1.2.11 Efficacy response data - Subgroup analyses by cytogenetic abnormality
16.2.6.1.2.11.5 QLQ-C30 - Time until permanent improvement by 10 pt in pain according to cytogenetic abnormality (LOCF) - ITT population

	At least one		None		
	Kd (N=31)	**IKd (N=42)**	**Kd (N=77)**	**IKd (N=114)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	8 (25.8)	16 (38.1)	22 (28.6)	32 (28.1)	0.3195
Number (%) of patients censored	23 (74.2)	26 (61.9)	55 (71.4)	82 (71.9)	
Kaplan-Meier estimates of Pain in months					
25% quantile (95% CI)	19.38 (1.117 to NC)	10.97 (1.117 to 23.359)	15.93 (6.045 to NC)	17.77 (11.138 to 24.444)	
Median (95% CI)	NC (21.027 to NC)	23.36 (15.869 to NC)	NC (22.209 to NC)	24.44 (24.444 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (23.359 to NC)	NC (NC to NC)	NC (24.444 to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.3318		0.7401	
Hazard ratio (95% CI) vs Kd	-	1.52 (0.65 to 3.56)		0.91 (0.53 to 1.57)	
P-value	-	0.3353		0.7402	
Improvement probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful improvement change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Pain
16.2.6.1.2.11 Efficacy response data - Subgroup analyses by cytogenetic abnormality
16.2.6.1.2.11.6 QLQ-C30 - Time until permanent deterioration by 10 pt in pain according to cytogenetic abnormality (LOCF) - ITT population

	At least one		None		
	Kd (N=31)	**IKd (N=42)**	**Kd (N=77)**	**IKd (N=114)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	7 (22.6)	16 (38.1)	22 (28.6)	35 (30.7)	0.3997
Number (%) of patients censored	24 (77.4)	26 (61.9)	55 (71.4)	79 (69.3)	
Kaplan-Meier estimates of Pain in months					
25% quantile (95% CI)	18.00 (3.811 to NC)	14.78 (3.844 to 22.111)	19.15 (8.444 to NC)	18.07 (12.616 to 22.604)	
Median (95% CI)	NC (NC to NC)	22.51 (16.427 to NC)	NC (NC to NC)	23.72 (22.604 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (22.505 to NC)	NC (NC to NC)	NC (23.721 to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.2082		0.7219	
Hazard ratio (95% CI) vs Kd	-	1.76 (0.72 to 4.28)		1.10 (0.65 to 1.88)	
P-value	-	0.2144		0.7220	
Deterioration probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful deterioration change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Pain
16.2.6.1.2.12 Efficacy response data - Subgroup analyses by MM type at SE
16.2.6.1.2.12.3 QLQ-C30 - Time to first improvement by 10 pt in pain according to MM type at SE (LOCF) - ITT population

	IgG		Non-IgG		
	Kd (N=85)	**IKd (N=126)**	**Kd (N=38)**	**IKd (N=53)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	41 (48.2)	76 (60.3)	19 (50.0)	27 (50.9)	0.2828
Number (%) of patients censored	44 (51.8)	50 (39.7)	19 (50.0)	26 (49.1)	
Kaplan-Meier estimates of Pain in months					
25% quantile (95% CI)	1.08 (1.018 to 1.281)	1.12 (1.051 to 1.314)	1.77 (0.953 to 1.971)	1.91 (0.986 to 2.267)	
Median (95% CI)	NC (2.037 to NC)	2.96 (1.906 to 6.111)	3.75 (1.906 to NC)	17.54 (2.136 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.1214		0.7615	
Hazard ratio (95% CI) vs Kd	-	1.35 (0.92 to 1.97)		0.91 (0.51 to 1.64)	
P-value	-	0.1228		0.7616	
Improvement probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful improvement change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Pain
16.2.6.1.2.12 Efficacy response data - Subgroup analyses by MM type at SE
16.2.6.1.2.12.4 QLQ-C30 - Time to first deterioration by 10 pt in pain according to MM type at SE (LOCF) - ITT population

	IgG		Non-IgG		
	Kd (N=85)	**IKd (N=126)**	**Kd (N=38)**	**IKd (N=53)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	49 (57.6)	74 (58.7)	17 (44.7)	32 (60.4)	0.3135
Number (%) of patients censored	36 (42.4)	52 (41.3)	21 (55.3)	21 (39.6)	
Kaplan-Meier estimates of Pain in months					
25% quantile (95% CI)	2.79 (1.873 to 3.745)	1.97 (1.150 to 2.793)	2.50 (1.051 to 6.965)	1.91 (0.986 to 2.858)	
Median (95% CI)	7.56 (4.665 to 20.764)	9.36 (3.811 to 13.864)	NC (3.745 to NC)	5.59 (2.825 to NC)	
75% quantile (95% CI)	NC (21.290 to NC)	NC (NC to NC)	NC (NC to NC)	NC (13.634 to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.6100		0.1432	
Hazard ratio (95% CI) vs Kd	-	1.10 (0.77 to 1.58)		1.55 (0.86 to 2.79)	
P-value	-	0.6102		0.1464	
Deterioration probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful deterioration change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Pain
16.2.6.1.2.12 Efficacy response data - Subgroup analyses by MM type at SE
16.2.6.1.2.12.5 QLQ-C30 - Time until permanent improvement by 10 pt in pain according to MM type at SE (LOCF) - ITT population

	IgG		Non-IgG		
	Kd (N=85)	**IKd (N=126)**	**Kd (N=38)**	**IKd (N=53)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	25 (29.4)	45 (35.7)	9 (23.7)	10 (18.9)	0.3013
Number (%) of patients censored	60 (70.6)	81 (64.3)	29 (76.3)	43 (81.1)	
Kaplan-Meier estimates of Pain in months					
25% quantile (95% CI)	18.69 (7.261 to 22.209)	14.13 (3.844 to 17.774)	19.38 (1.643 to NC)	NC (7.556 to NC)	
Median (95% CI)	NC (22.209 to NC)	24.44 (21.717 to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (24.444 to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.3693		0.4821	
Hazard ratio (95% CI) vs Kd	-	1.25 (0.77 to 2.04)		0.72 (0.29 to 1.78)	
P-value	-	0.3703		0.4840	
Improvement probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful improvement change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Pain
16.2.6.1.2.12 Efficacy response data - Subgroup analyses by MM type at SE
16.2.6.1.2.12.6 QLQ-C30 - Time until permanent deterioration by 10 pt in pain according to MM type at SE (LOCF) - ITT population

	IgG		Non-IgG		
	Kd (N=85)	**IKd (N=126)**	**Kd (N=38)**	**IKd (N=53)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	25 (29.4)	37 (29.4)	9 (23.7)	19 (35.8)	0.4526
Number (%) of patients censored	60 (70.6)	89 (70.6)	29 (76.3)	34 (64.2)	
Kaplan-Meier estimates of Pain in months					
25% quantile (95% CI)	19.15 (9.429 to 23.064)	18.07 (12.945 to 22.604)	18.00 (8.444 to NC)	14.78 (3.844 to 22.505)	
Median (95% CI)	NC (23.064 to NC)	NC (22.604 to NC)	NC (NC to NC)	23.72 (22.111 to 23.721)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	23.72 (NC to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.8295		0.2502	
Hazard ratio (95% CI) vs Kd	-	1.06 (0.64 to 1.76)		1.59 (0.71 to 3.55)	
P-value	-	0.8303		0.2543	
Deterioration probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful deterioration change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
PGM=DEVOPS/SAR650984/EFC15246/CIR_RWE/REPORT/PGM/eff_km_subgp_sr_sig_de_i_t.sas OUT=REPORT/OUTPUT/eff_km_c30_pan_detpl_semm_de_i_t_x.rtf (07APR2021 14:31)

16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Pain
16.2.6.1.2.13 Efficacy response data - Subgroup analyses by previous autologous stem-cell
16.2.6.1.2.13.3 QLQ-C30 - Time to first improvement by 10 pt in pain according to previous autologous stem-cell (LOCF) - ITT population

	Yes		No		
	Kd (N=69)	**IKd (N=116)**	**Kd (N=54)**	**IKd (N=63)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	34 (49.3)	66 (56.9)	26 (48.1)	37 (58.7)	0.7565
Number (%) of patients censored	35 (50.7)	50 (43.1)	28 (51.9)	26 (41.3)	
Kaplan-Meier estimates of Pain in months					
25% quantile (95% CI)	1.05 (0.986 to 1.281)	1.08 (1.018 to 1.840)	1.91 (1.051 to 2.136)	1.15 (1.051 to 1.906)	
Median (95% CI)	12.94 (1.906 to NC)	3.12 (2.070 to NC)	8.44 (1.971 to NC)	5.65 (1.906 to 11.400)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (11.400 to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.4881		0.3158	
Hazard ratio (95% CI) vs Kd	-	1.16 (0.77 to 1.75)		1.29 (0.78 to 2.13)	
P-value	-	0.4885		0.3172	
Improvement probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful improvement change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Pain
16.2.6.1.2.13 Efficacy response data - Subgroup analyses by previous autologous stem-cell
16.2.6.1.2.13.4 QLQ-C30 - Time to first deterioration by 10 pt in pain according to previous autologous stem-cell (LOCF) - ITT population

	Yes		No		
	Kd (N=69)	**IKd (N=116)**	**Kd (N=54)**	**IKd (N=63)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	37 (53.6)	68 (58.6)	29 (53.7)	38 (60.3)	0.9248
Number (%) of patients censored	32 (46.4)	48 (41.4)	25 (46.3)	25 (39.7)	
Kaplan-Meier estimates of Pain in months					
25% quantile (95% CI)	2.99 (1.873 to 4.764)	1.97 (1.084 to 2.793)	1.97 (1.117 to 2.825)	1.97 (1.117 to 2.891)	
Median (95% CI)	17.02 (5.684 to NC)	9.26 (3.975 to 14.850)	9.72 (2.825 to NC)	4.70 (2.891 to 13.634)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (21.290 to NC)	NC (13.634 to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.3072		0.4774	
Hazard ratio (95% CI) vs Kd	-	1.23 (0.83 to 1.84)		1.19 (0.73 to 1.93)	
P-value	-	0.3081		0.4780	
Deterioration probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful deterioration change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Pain
16.2.6.1.2.13 Efficacy response data - Subgroup analyses by previous autologous stem-cell
16.2.6.1.2.13.5 QLQ-C30 - Time until permanent improvement by 10 pt in pain according to previous autologous stem-cell (LOCF) - ITT population

	Yes		No		
	Kd (N=69)	**IKd (N=116)**	**Kd (N=54)**	**IKd (N=63)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	18 (26.1)	35 (30.2)	16 (29.6)	20 (31.7)	0.7466
Number (%) of patients censored	51 (73.9)	81 (69.8)	38 (70.4)	43 (68.3)	
Kaplan-Meier estimates of Pain in months					
25% quantile (95% CI)	19.38 (6.472 to NC)	16.95 (10.973 to 24.444)	10.22 (1.117 to NC)	12.65 (2.103 to 21.717)	
Median (95% CI)	NC (NC to NC)	24.44 (NC to NC)	NC (22.209 to NC)	23.36 (20.698 to NC)	
75% quantile (95% CI)	NC (NC to NC)	24.44 (NC to NC)	NC (NC to NC)	NC (23.359 to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.5514		0.9584	
Hazard ratio (95% CI) vs Kd	-	1.19 (0.67 to 2.10)		1.02 (0.53 to 1.97)	
P-value	-	0.5519		0.9585	
Improvement probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful improvement change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Pain
16.2.6.1.2.13 Efficacy response data - Subgroup analyses by previous autologous stem-cell
16.2.6.1.2.13.6 QLQ-C30 - Time until permanent deterioration by 10 pt in pain according to previous autologous stem-cell (LOCF) - ITT population

	Yes		No		
	Kd (N=69)	**IKd (N=116)**	**Kd (N=54)**	**IKd (N=63)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	20 (29.0)	35 (30.2)	14 (25.9)	21 (33.3)	0.5437
Number (%) of patients censored	49 (71.0)	81 (69.8)	40 (74.1)	42 (66.7)	
Kaplan-Meier estimates of Pain in months					
25% quantile (95% CI)	16.95 (5.684 to NC)	18.00 (12.156 to 22.111)	19.52 (13.503 to NC)	14.06 (6.834 to 22.604)	
Median (95% CI)	NC (NC to NC)	23.72 (22.505 to NC)	NC (23.064 to NC)	23.10 (22.604 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (23.721 to NC)	NC (NC to NC)	NC (23.097 to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.8205		0.3190	
Hazard ratio (95% CI) vs Kd	-	1.07 (0.62 to 1.85)		1.41 (0.72 to 2.77)	
P-value	-	0.8205		0.3213	
Deterioration probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful deterioration change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Pain
16.2.6.1.2.14 Efficacy response data - Subgroup analyses by baseline eGFR (MDRD)
16.2.6.1.2.14.3 QLQ-C30 - Time to first improvement by 10 pt in pain according to baseline eGFR (MDRD) (LOCF) - ITT population

	>=60 mL/min/1.73m2		<60 mL/min/1.73m2		
	Kd (N=93)	**IKd (N=122)**	**Kd (N=18)**	**IKd (N=43)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	50 (53.8)	72 (59.0)	8 (44.4)	26 (60.5)	0.6566
Number (%) of patients censored	43 (46.2)	50 (41.0)	10 (55.6)	17 (39.5)	
Kaplan-Meier estimates of Pain in months					
25% quantile (95% CI)	1.07 (1.018 to 1.117)	1.08 (0.986 to 1.840)	2.04 (0.920 to 5.322)	1.08 (1.018 to 1.906)	
Median (95% CI)	3.75 (1.906 to NC)	3.12 (2.004 to 9.002)	5.32 (1.938 to NC)	3.88 (1.610 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (5.322 to NC)	NC (17.544 to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.5114		0.4390	
Hazard ratio (95% CI) vs Kd	-	1.13 (0.79 to 1.62)		1.37 (0.62 to 3.02)	
P-value	-	0.5117		0.4410	
Improvement probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful improvement change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Pain
16.2.6.1.2.14 Efficacy response data - Subgroup analyses by baseline eGFR (MDRD)
16.2.6.1.2.14.4 QLQ-C30 - Time to first deterioration by 10 pt in pain according to baseline eGFR (MDRD) (LOCF) - ITT population

	>=60 mL/min/1.73m2		<60 mL/min/1.73m2		
	Kd (N=93)	**IKd (N=122)**	**Kd (N=18)**	**IKd (N=43)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	48 (51.6)	75 (61.5)	13 (72.2)	27 (62.8)	0.0584
Number (%) of patients censored	45 (48.4)	47 (38.5)	5 (27.8)	16 (37.2)	
Kaplan-Meier estimates of Pain in months					
25% quantile (95% CI)	2.87 (1.248 to 3.943)	1.97 (1.150 to 2.793)	2.83 (0.986 to 3.910)	1.08 (0.986 to 2.957)	
Median (95% CI)	19.75 (7.326 to NC)	5.65 (3.745 to 10.678)	3.91 (1.971 to 6.604)	7.39 (2.530 to 19.713)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	6.60 (3.910 to NC)	NC (14.850 to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.0503		0.2261	
Hazard ratio (95% CI) vs Kd	-	1.43 (1.00 to 2.06)		0.66 (0.34 to 1.30)	
P-value	-	0.0516		0.2289	
Deterioration probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful deterioration change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Pain
16.2.6.1.2.14 Efficacy response data - Subgroup analyses by baseline eGFR (MDRD)
16.2.6.1.2.14.5 QLQ-C30 - Time until permanent improvement by 10 pt in pain according to baseline eGFR (MDRD) (LOCF) - ITT population

	>=60 mL/min/1.73m2		<60 mL/min/1.73m2		
	Kd (N=93)	**IKd (N=122)**	**Kd (N=18)**	**IKd (N=43)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	30 (32.3)	34 (27.9)	2 (11.1)	18 (41.9)	0.0743
Number (%) of patients censored	63 (67.7)	88 (72.1)	16 (88.9)	25 (58.1)	
Kaplan-Meier estimates of Pain in months					
25% quantile (95% CI)	10.22 (1.643 to 21.027)	15.87 (11.105 to 21.717)	NC (1.938 to NC)	11.14 (1.084 to 20.698)	
Median (95% CI)	NC (22.209 to NC)	NC (NC to NC)	NC (20.468 to NC)	23.36 (17.610 to 24.444)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	24.44 (23.359 to 24.444)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.6067		0.0881	
Hazard ratio (95% CI) vs Kd	-	0.88 (0.54 to 1.44)		3.32 (0.77 to 14.39)	
P-value	-	0.6070		0.1081	
Improvement probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful improvement change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Pain
16.2.6.1.2.14 Efficacy response data - Subgroup analyses by baseline eGFR (MDRD)
16.2.6.1.2.14.6 QLQ-C30 - Time until permanent deterioration by 10 pt in pain according to baseline eGFR (MDRD) (LOCF) - ITT population

	>=60 mL/min/1.73m2		<60 mL/min/1.73m2		
	Kd (N=93)	**IKd (N=122)**	**Kd (N=18)**	**IKd (N=43)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	25 (26.9)	42 (34.4)	5 (27.8)	12 (27.9)	0.2449
Number (%) of patients censored	68 (73.1)	80 (65.6)	13 (72.2)	31 (72.1)	
Kaplan-Meier estimates of Pain in months					
25% quantile (95% CI)	20.14 (9.593 to NC)	14.98 (9.298 to 19.253)	15.01 (3.975 to NC)	19.88 (8.509 to NC)	
Median (95% CI)	NC (23.064 to NC)	23.10 (22.505 to NC)	NC (14.554 to NC)	NC (22.111 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (23.721 to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.1313		0.5036	
Hazard ratio (95% CI) vs Kd	-	1.46 (0.89 to 2.40)		0.70 (0.24 to 2.00)	
P-value	-	0.1336		0.5056	
Deterioration probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful deterioration change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Pain
16.2.6.1.2.15 Efficacy response data - Subgroup analyses by previous treatment with PI
16.2.6.1.2.15.3 QLQ-C30 - Time to first improvement by 10 pt in pain according to previous treatment with PI (LOCF) - ITT population

	Yes		No		
	Kd (N=47)	**IKd (N=81)**	**Kd (N=76)**	**IKd (N=98)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	24 (51.1)	45 (55.6)	36 (47.4)	58 (59.2)	0.6223
Number (%) of patients censored	23 (48.9)	36 (44.4)	40 (52.6)	40 (40.8)	
Kaplan-Meier estimates of Pain in months					
25% quantile (95% CI)	1.12 (1.018 to 1.971)	1.15 (1.018 to 2.004)	1.12 (1.018 to 1.906)	1.08 (1.018 to 1.840)	
Median (95% CI)	8.44 (1.906 to NC)	5.52 (2.136 to NC)	NC (2.037 to NC)	2.96 (1.906 to 13.832)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.6871		0.2279	
Hazard ratio (95% CI) vs Kd	-	1.11 (0.67 to 1.82)		1.29 (0.85 to 1.96)	
P-value	-	0.6872		0.2292	
Improvement probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful improvement change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Pain
16.2.6.1.2.15 Efficacy response data - Subgroup analyses by previous treatment with PI
16.2.6.1.2.15.4 QLQ-C30 - Time to first deterioration by 10 pt in pain according to previous treatment with PI (LOCF) - ITT population

	Yes		No		
	Kd (N=47)	**IKd (N=81)**	**Kd (N=76)**	**IKd (N=98)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	22 (46.8)	42 (51.9)	44 (57.9)	64 (65.3)	0.9719
Number (%) of patients censored	25 (53.2)	39 (48.1)	32 (42.1)	34 (34.7)	
Kaplan-Meier estimates of Pain in months					
25% quantile (95% CI)	2.07 (1.117 to 4.665)	1.51 (1.051 to 2.793)	2.79 (1.873 to 3.811)	2.04 (1.084 to 2.891)	
Median (95% CI)	NC (3.745 to NC)	11.17 (3.055 to NC)	9.72 (4.665 to 20.764)	6.97 (3.745 to 10.316)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (20.764 to NC)	NC (14.850 to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.4349		0.2827	
Hazard ratio (95% CI) vs Kd	-	1.23 (0.73 to 2.06)		1.23 (0.84 to 1.81)	
P-value	-	0.4357		0.2836	
Deterioration probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful deterioration change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Pain
16.2.6.1.2.15 Efficacy response data - Subgroup analyses by previous treatment with PI
16.2.6.1.2.15.5 QLQ-C30 - Time until permanent improvement by 10 pt in pain according to previous treatment with PI (LOCF) - ITT population

	Yes		No		
	Kd (N=47)	**IKd (N=81)**	**Kd (N=76)**	**IKd (N=98)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	14 (29.8)	29 (35.8)	20 (26.3)	26 (26.5)	0.5386
Number (%) of patients censored	33 (70.2)	52 (64.2)	56 (73.7)	72 (73.5)	
Kaplan-Meier estimates of Pain in months					
25% quantile (95% CI)	15.93 (1.117 to NC)	11.40 (2.103 to 17.774)	20.47 (7.918 to NC)	19.78 (12.682 to NC)	
Median (95% CI)	NC (19.614 to NC)	23.36 (19.351 to NC)	NC (22.209 to NC)	24.44 (24.444 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (23.359 to NC)	NC (NC to NC)	NC (24.444 to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.4979		0.8865	
Hazard ratio (95% CI) vs Kd	-	1.25 (0.66 to 2.36)		0.96 (0.53 to 1.72)	
P-value	-	0.4987		0.8862	
Improvement probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful improvement change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Pain
16.2.6.1.2.15 Efficacy response data - Subgroup analyses by previous treatment with PI
16.2.6.1.2.15.6 QLQ-C30 - Time until permanent deterioration by 10 pt in pain according to previous treatment with PI (LOCF) - ITT population

	Yes		No		
	Kd (N=47)	**IKd (N=81)**	**Kd (N=76)**	**IKd (N=98)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	8 (17.0)	23 (28.4)	26 (34.2)	33 (33.7)	0.1301
Number (%) of patients censored	39 (83.0)	58 (71.6)	50 (65.8)	65 (66.3)	
Kaplan-Meier estimates of Pain in months					
25% quantile (95% CI)	23.06 (13.503 to NC)	18.76 (9.298 to 23.097)	15.93 (8.444 to 20.140)	15.93 (10.579 to 22.111)	
Median (95% CI)	NC (23.064 to NC)	NC (23.097 to NC)	NC (20.370 to NC)	23.72 (22.505 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.1013		0.8352	
Hazard ratio (95% CI) vs Kd	-	1.94 (0.87 to 4.36)		0.95 (0.57 to 1.58)	
P-value	-	0.1075		0.8346	
Deterioration probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful deterioration change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Pain
16.2.6.1.2.16 Efficacy response data - Subgroup analyses by previous treatment with IMiD
16.2.6.1.2.16.3 QLQ-C30 - Time to first improvement by 10 pt in pain according to previous treatment with IMiD (LOCF) - ITT population

	Yes		No		
	Kd (N=62)	**IKd (N=81)**	**Kd (N=61)**	**IKd (N=98)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	28 (45.2)	41 (50.6)	32 (52.5)	62 (63.3)	0.4321
Number (%) of patients censored	34 (54.8)	40 (49.4)	29 (47.5)	36 (36.7)	
Kaplan-Meier estimates of Pain in months					
25% quantile (95% CI)	1.12 (0.986 to 1.906)	1.38 (1.051 to 2.136)	1.12 (1.018 to 1.938)	1.08 (0.986 to 1.150)	
Median (95% CI)	NC (1.938 to NC)	12.39 (2.957 to NC)	5.32 (1.938 to NC)	2.14 (1.906 to 5.914)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (17.544 to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.8552		0.1676	
Hazard ratio (95% CI) vs Kd	-	1.05 (0.65 to 1.69)		1.35 (0.88 to 2.07)	
P-value	-	0.8557		0.1692	
Improvement probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful improvement change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Pain
16.2.6.1.2.16 Efficacy response data - Subgroup analyses by previous treatment with IMiD
16.2.6.1.2.16.4 QLQ-C30 - Time to first deterioration by 10 pt in pain according to previous treatment with IMiD (LOCF) - ITT population

	Yes		No		
	Kd (N=62)	**IKd (N=81)**	**Kd (N=61)**	**IKd (N=98)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	30 (48.4)	52 (64.2)	36 (59.0)	54 (55.1)	0.1044
Number (%) of patients censored	32 (51.6)	29 (35.8)	25 (41.0)	44 (44.9)	
Kaplan-Meier estimates of Pain in months					
25% quantile (95% CI)	2.96 (1.906 to 4.895)	1.87 (1.084 to 2.168)	2.38 (1.084 to 3.745)	2.00 (1.150 to 3.220)	
Median (95% CI)	20.57 (4.895 to NC)	5.65 (2.825 to 11.170)	6.60 (3.745 to 20.764)	7.62 (3.811 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (14.850 to NC)	NC (20.764 to NC)	NC (NC to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.0424		0.8234	
Hazard ratio (95% CI) vs Kd	-	1.59 (1.01 to 2.49)		0.95 (0.62 to 1.45)	
P-value	-	0.0442		0.8225	
Hazard ratio inverted (95% CI) vs IKd		-		1.05 (0.69 to 1.60)	

A lower score represents a better level of quality of life. Clinical meaningful deterioration change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Pain
16.2.6.1.2.16 Efficacy response data - Subgroup analyses by previous treatment with IMiD
16.2.6.1.2.16.5 QLQ-C30 - Time until permanent improvement by 10 pt in pain according to previous treatment with IMiD (LOCF) - ITT population

	Yes		No		
	Kd (N=62)	**IKd (N=81)**	**Kd (N=61)**	**IKd (N=98)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	21 (33.9)	19 (23.5)	13 (21.3)	36 (36.7)	0.0088
Number (%) of patients censored	41 (66.1)	62 (76.5)	48 (78.7)	62 (63.3)	
Kaplan-Meier estimates of Pain in months					
25% quantile (95% CI)	11.33 (1.643 to 20.468)	20.70 (16.953 to NC)	21.03 (6.045 to NC)	10.97 (2.103 to 15.639)	
Median (95% CI)	NC (20.468 to NC)	NC (23.359 to NC)	NC (NC to NC)	24.44 (17.774 to 24.444)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	24.44 (NC to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.0863		0.0492	
Hazard ratio (95% CI) vs Kd	-	0.58 (0.31 to 1.09)		1.88 (0.99 to 3.55)	
P-value	-	0.0901		0.0530	
Improvement probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful improvement change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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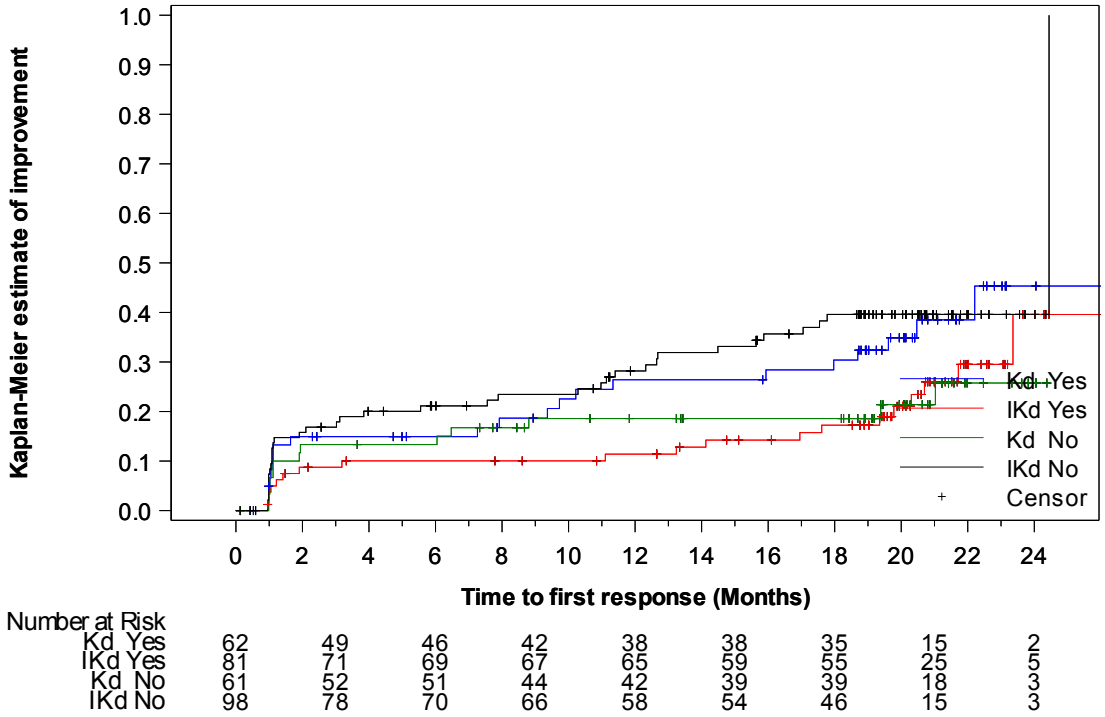
16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Pain
16.2.6.1.2.16 Efficacy response data - Subgroup analyses by previous treatment with IMiD
16.2.6.1.2.16.6 QLQ-C30 - Time until permanent improvement by 10 pt in pain according to previous treatment with IMiD- Kaplan-Meier curve (LOCF) - ITT population



Number at Risk

Kd Yes	62	49	46	42	38	38	35	15	2
IKd Yes	81	71	69	67	65	59	55	25	5
Kd No	61	52	51	44	42	39	39	18	3
IKd No	98	78	70	66	58	54	46	15	3

A lower score represents a better level of quality of life. Clinical meaningful improvement change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
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16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Pain
16.2.6.1.2.16 Efficacy response data - Subgroup analyses by previous treatment with IMiD
16.2.6.1.2.16.7 QLQ-C30 - Time until permanent deterioration by 10 pt in pain according to previous treatment with IMiD (LOCF) - ITT population

	Yes		No		
	Kd (N=62)	**IKd (N=81)**	**Kd (N=61)**	**IKd (N=98)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	15 (24.2)	31 (38.3)	19 (31.1)	25 (25.5)	0.0881
Number (%) of patients censored	47 (75.8)	50 (61.7)	42 (68.9)	73 (74.5)	
Kaplan-Meier estimates of Pain in months					
25% quantile (95% CI)	19.52 (8.444 to NC)	12.62 (5.815 to 18.070)	15.93 (8.444 to 23.064)	19.88 (14.752 to 23.721)	
Median (95% CI)	NC (NC to NC)	23.10 (22.111 to NC)	NC (20.764 to NC)	23.72 (22.505 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (23.721 to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.0833		0.5262	
Hazard ratio (95% CI) vs Kd	-	1.71 (0.92 to 3.18)		0.82 (0.45 to 1.50)	
P-value	-	0.0871		0.5268	
Deterioration probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful deterioration change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Pain
16.2.6.1.2.17 Efficacy response data - Subgroup analyses by previous treatment with PI and IMiD
16.2.6.1.2.17.3 QLQ-C30 - Time to first improvement by 10 pt in pain according to previous treatment with PI and IMiD (LOCF) - ITT population

	Yes		No		
	Kd (N=17)	**IKd (N=23)**	**Kd (N=106)**	**IKd (N=156)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	8 (47.1)	11 (47.8)	52 (49.1)	92 (59.0)	0.3470
Number (%) of patients censored	9 (52.9)	12 (52.2)	54 (50.9)	64 (41.0)	
Kaplan-Meier estimates of Pain in months					
25% quantile (95% CI)	1.03 (0.953 to 12.945)	1.91 (0.986 to 5.520)	1.12 (1.051 to 1.906)	1.08 (1.018 to 1.314)	
Median (95% CI)	12.94 (1.018 to NC)	7.46 (3.417 to NC)	8.44 (2.136 to NC)	2.96 (2.037 to 9.002)	
75% quantile (95% CI)	NC (12.945 to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.6800		0.1542	
Hazard ratio (95% CI) vs Kd	-	0.83 (0.33 to 2.06)		1.28 (0.91 to 1.80)	
P-value	-	0.6805		0.1552	
Improvement probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful improvement change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Pain
16.2.6.1.2.17 Efficacy response data - Subgroup analyses by previous treatment with PI and IMiD
16.2.6.1.2.17.4 QLQ-C30 - Time to first deterioration by 10 pt in pain according to previous treatment with PI and IMiD (LOCF) - ITT population

	Yes		No		
	Kd (N=17)	**IKd (N=23)**	**Kd (N=106)**	**IKd (N=156)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	5 (29.4)	10 (43.5)	61 (57.5)	96 (61.5)	0.5196
Number (%) of patients censored	12 (70.6)	13 (56.5)	45 (42.5)	60 (38.5)	
Kaplan-Meier estimates of Pain in months					
25% quantile (95% CI)	2.83 (1.216 to NC)	1.12 (0.986 to 11.170)	2.79 (1.873 to 3.121)	1.97 (1.150 to 2.825)	
Median (95% CI)	NC (2.825 to NC)	NC (1.511 to NC)	9.72 (4.764 to 20.764)	6.97 (3.811 to 10.678)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.3116		0.3299	
Hazard ratio (95% CI) vs Kd	-	1.73 (0.59 to 5.07)		1.17 (0.85 to 1.62)	
P-value	-	0.3177		0.3304	
Deterioration probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful deterioration change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Pain
16.2.6.1.2.17 Efficacy response data - Subgroup analyses by previous treatment with PI and IMiD
16.2.6.1.2.17.5 QLQ-C30 - Time until permanent improvement by 10 pt in pain according to previous treatment with PI and IMiD (LOCF) - ITT population

	Yes		No		
	Kd (N=17)	**IKd (N=23)**	**Kd (N=106)**	**IKd (N=156)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	7 (41.2)	6 (26.1)	27 (25.5)	49 (31.4)	0.1432
Number (%) of patients censored	10 (58.8)	17 (73.9)	79 (74.5)	107 (68.6)	
Kaplan-Meier estimates of Pain in months					
25% quantile (95% CI)	8.49 (0.953 to 19.614)	20.30 (0.986 to NC)	20.47 (7.918 to NC)	14.13 (7.885 to 19.778)	
Median (95% CI)	NC (1.051 to NC)	23.36 (20.304 to NC)	NC (NC to NC)	24.44 (24.444 to NC)	
75% quantile (95% CI)	NC (19.614 to NC)	NC (23.359 to NC)	NC (NC to NC)	NC (24.444 to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.2029		0.3412	
Hazard ratio (95% CI) vs Kd	-	0.50 (0.17 to 1.49)		1.26 (0.78 to 2.01)	
P-value	-	0.2119		0.3423	

A lower score represents a better level of quality of life. Clinical meaningful improvement change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Pain
16.2.6.1.2.17 Efficacy response data - Subgroup analyses by previous treatment with PI and IMiD
16.2.6.1.2.17.6 QLQ-C30 - Time until permanent deterioration by 10 pt in pain according to previous treatment with PI and IMiD (LOCF) - ITT population

	Yes		No		
	Kd (N=17)	**IKd (N=23)**	**Kd (N=106)**	**IKd (N=156)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	1 (5.9)	7 (30.4)	33 (31.1)	49 (31.4)	0.0971
Number (%) of patients censored	16 (94.1)	16 (69.6)	73 (68.9)	107 (68.6)	
Kaplan-Meier estimates of Pain in months					
25% quantile (95% CI)	NC (13.503 to NC)	13.44 (1.511 to NC)	16.82 (8.674 to 20.764)	16.43 (12.945 to 21.520)	
Median (95% CI)	NC (NC to NC)	23.10 (13.437 to NC)	NC (23.064 to NC)	23.72 (22.505 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (23.097 to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.0427		0.8962	
Hazard ratio (95% CI) vs Kd	-	6.61 (0.81 to 54.07)		1.03 (0.66 to 1.60)	
P-value	-	0.0783		0.8964	
Deterioration probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful deterioration change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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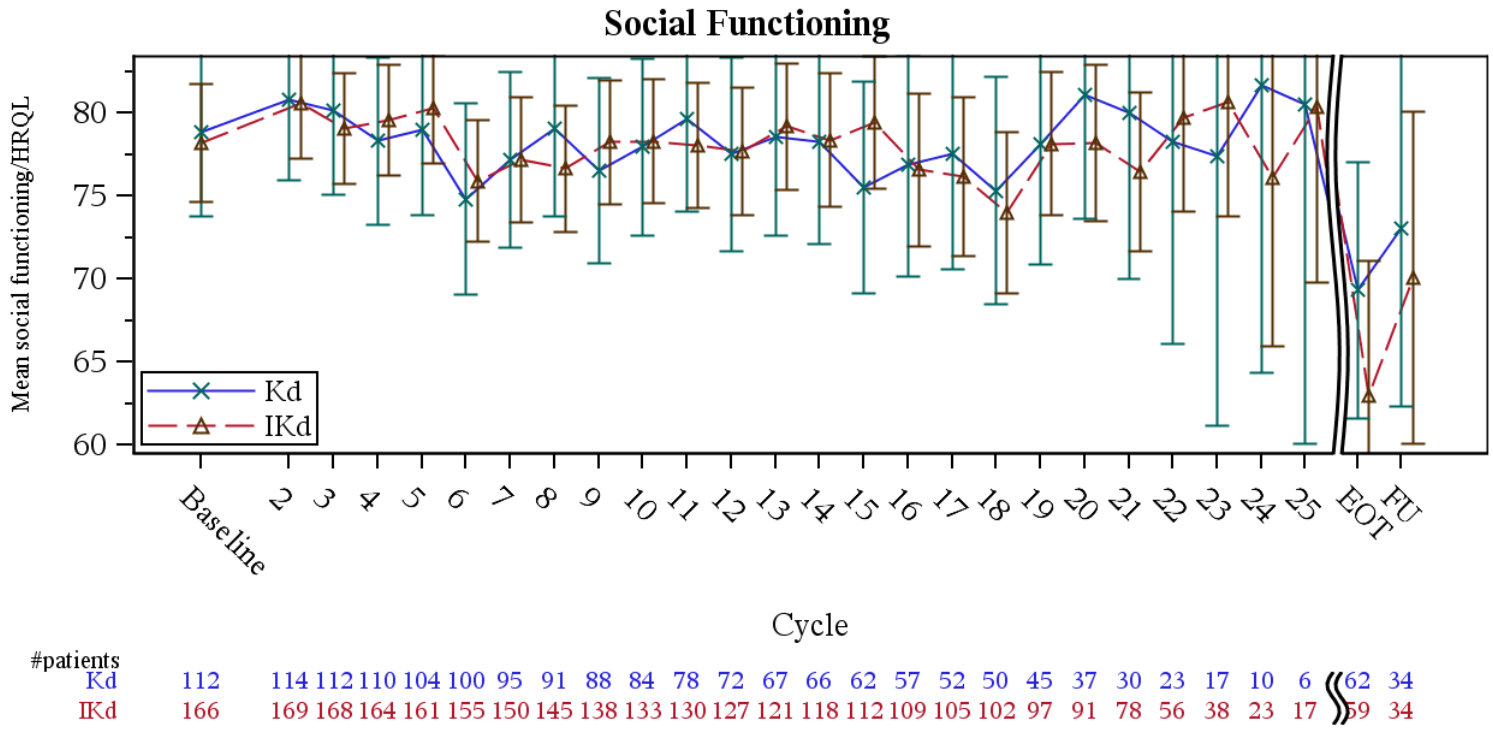
16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Social functioning
16.2.6.1.2.1 Efficacy response data
16.2.6.1.2.1.1 QLQ-C30 - Mean and 95% CI for social functioning score over time (LOCF) - ITT population



#patients																									
Kd	112	114	112	110	104	100	95	91	88	84	78	72	67	66	62	57	52	50	45	37	30	23	17	10	6	62	34
IKd	166	169	168	164	161	155	150	145	138	133	130	127	121	118	112	109	105	102	97	91	78	56	38	23	17	59	34

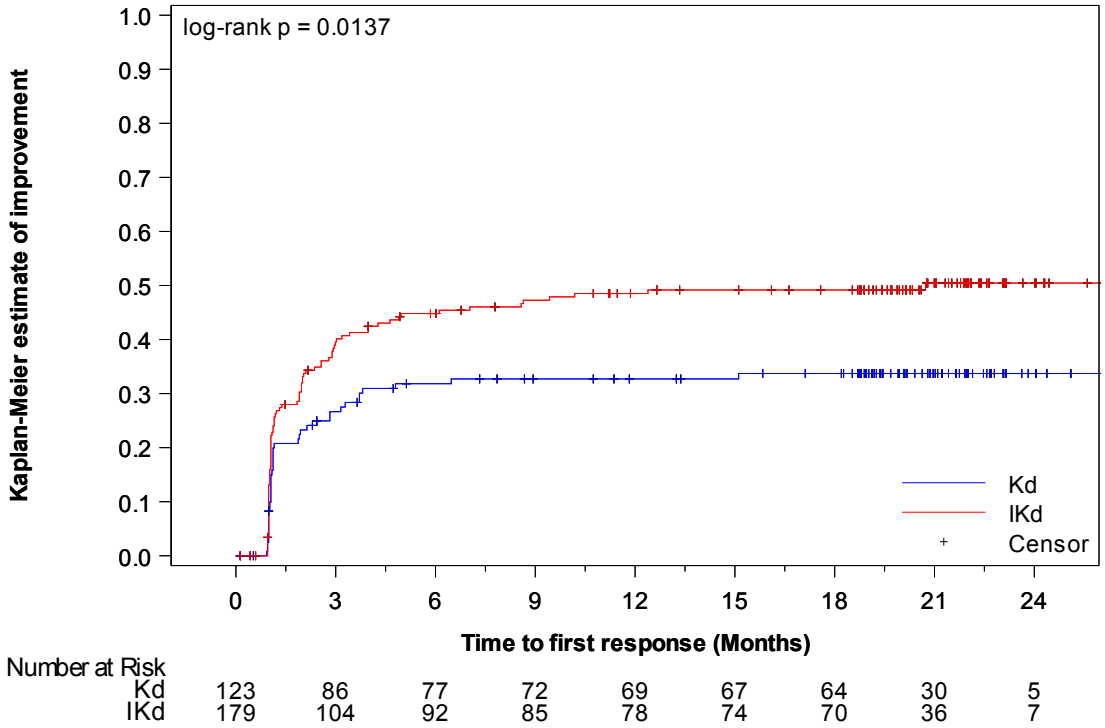
A higher score represents a better level of quality of life. Cycles with less than 20 patients overall are not presented.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
PGM=DEVOPS/SAR650984/EFC15246/CIR_RWE/REPORT/PGM/eff_qlq_line_i_f.sas OUT=REPORT/OUTPUT/eff_qlq_line_c30_soc_de_i_f_x.rtf (12FEB2021 15:16)

16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Social functioning
16.2.6.1.2.1 Efficacy response data
16.2.6.1.2.1.15 QLQ-C30 - Time to first improvement by 15 pt in Social functioning (LOCF) - ITT population

First improvement 15 points Social functioning (%)	**Kd (N=123)**	**IKd (N=179)**
Number (%) of events	40 (32.5)	86 (48.0)
Number (%) of patients censored	83 (67.5)	93 (52.0)
Kaplan-Meier estimates of Social functioning in months		
25% quantile (95% CI)	2.83 (1.117 to 6.472)	1.15 (1.051 to 1.971)
Median (95% CI)	NC (NC to NC)	20.73 (3.975 to NC)
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)
Comparison vs. Kd		
Stratified[a] Log-Rank test p-value[b] vs Kd	-	0.0137
Stratified[a] Hazard ratio (95% CI) vs Kd	-	1.60 (1.10 to 2.33)
P-value	-	0.0146
Stratified[a] Hazard ratio inverted (95% CI) vs IKd	0.63 (0.43 to 0.91)	-
Improvement probability (95% CI)[c]		
3 Months	0.267 (0.191 to 0.348)	0.396 (0.323 to 0.467)

A lower score represents a better level of quality of life. Clinical meaningful improvement change from baseline less than or equal to -15 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] Stratified on number of prior lines of therapy (1 vs. >1) and Revised International Staging System (R-ISS) stage (I or II vs. III vs. not classified) according to IRT
[b] One-sided significance level is 0.025
[c] Estimated using the Kaplan-Meier method
NA/NC = Not Applicable / Not Calculable
PGM=DEVOPS/SAR650984/EFC15246/CIR_RWE/REPORT/PGM/eff_km_invhr_sr_i_t.sas OUT=REPORT/OUTPUT/eff_km_c30_soc_imp15l_de_i_t_x.rtf (07APR2021 14:22)

16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Social functioning
16.2.6.1.2.1 Efficacy response data
16.2.6.1.2.1.16 QLQ-C30 - Time to first improvement by 15 pt in Social functioning - Kaplan-Meier curve (LOCF) - ITT population



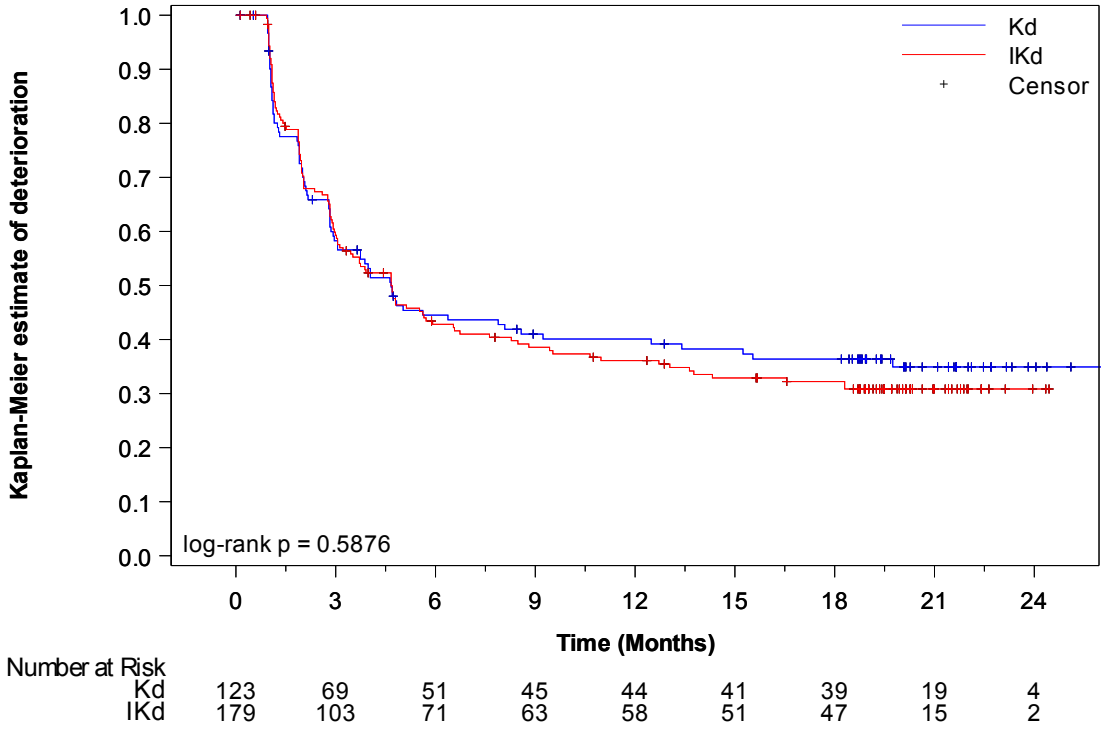
A lower score represents a better level of quality of life. Clinical meaningful improvement change from baseline less than or equal to -15 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
PGM=DEVOPS/SAR650984/EFC15246/CIR_RWE/REPORT/PGM/eff_qlq_km_i_f.sas OUT=REPORT/OUTPUT/eff_km_c30_soc_imp15l_de_i_f_x.rtf (07APR2021 14:24)

16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Social functioning
16.2.6.1.2.1 Efficacy response data
16.2.6.1.2.1.17 QLQ-C30 - Time to first deterioration by 15 pt in Social functioning (LOCF) - ITT population

First deterioration 15 points Social functioning (%)	**Kd (N=123)**	**IKd (N=179)**
Number (%) of events	76 (61.8)	118 (65.9)
Number (%) of patients censored	47 (38.2)	61 (34.1)
Kaplan-Meier estimates of Social functioning in months		
25% quantile (95% CI)	1.91 (1.117 to 2.136)	1.91 (1.314 to 2.037)
Median (95% CI)	4.67 (2.924 to 8.575)	4.67 (3.055 to 6.538)
75% quantile (95% CI)	NC (NC to NC)	NC (18.300 to NC)
Comparison vs. Kd		
Stratified[a] Log-Rank test p-value[b] vs Kd	-	0.5876
Stratified[a] Hazard ratio (95% CI) vs Kd	-	1.08 (0.81 to 1.45)
P-value	-	0.5877
Deterioration probability (95% CI)[c]		
3 Months	0.583 (0.489 to 0.665)	0.593 (0.516 to 0.662)
6 Months	0.445 (0.354 to 0.532)	0.428 (0.354 to 0.501)

A lower score represents a better level of quality of life. Clinical meaningful deterioration change from baseline greater than or equal to 15 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] Stratified on number of prior lines of therapy (1 vs. >1) and Revised International Staging System (R-ISS) stage (I or II vs. III vs. not classified) according to IRT
[b] One-sided significance level is 0.025
[c] Estimated using the Kaplan-Meier method
NA/NC = Not Applicable / Not Calculable
PGM=DEVOPS/SAR650984/EFC15246/CIR_RWE/REPORT/PGM/eff_km_invhr_sr_i_t.sas OUT=REPORT/OUTPUT/eff_km_c30_soc_det15l_de_i_t_x.rtf (07APR2021 14:22)

16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Social functioning
16.2.6.1.2.1 Efficacy response data
16.2.6.1.2.1.18 QLQ-C30 - Time to first deterioration by 15 pt in Social functioning - Kaplan-Meier curve (LOCF) - ITT population



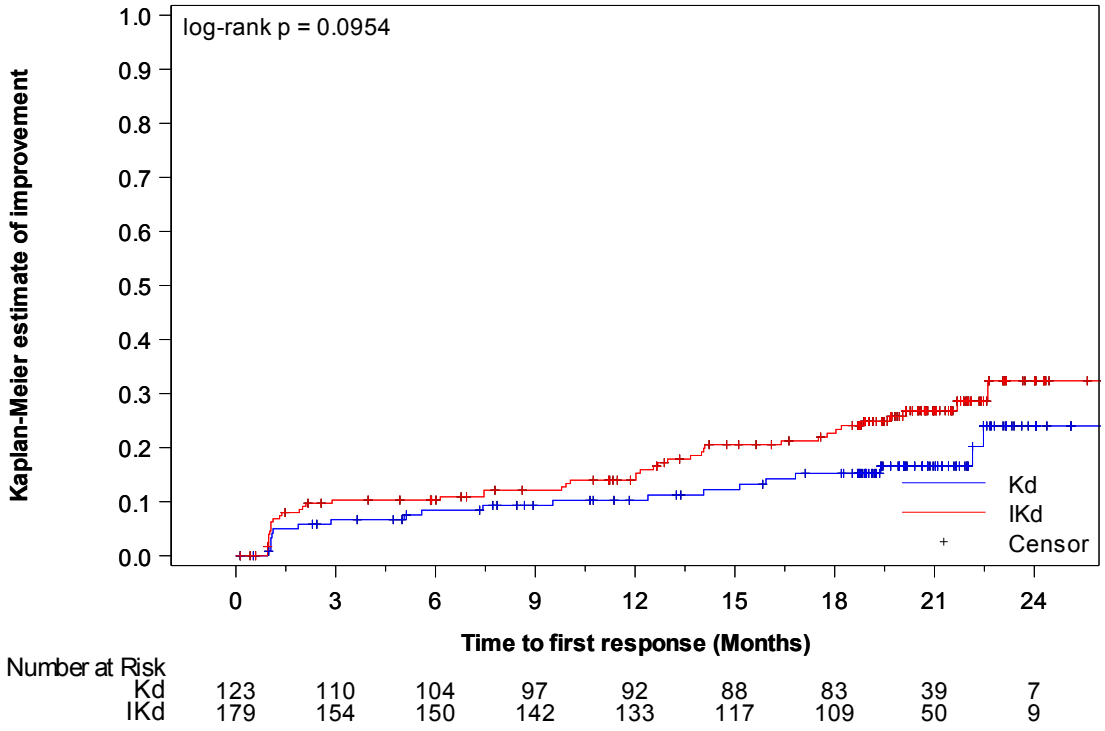
A lower score represents a better level of quality of life. Clinical meaningful deterioration change from baseline greater than or equal to 15 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
PGM=DEVOPS/SAR650984/EFC15246/CIR_RWE/REPORT/PGM/eff_qlq_km_i_f.sas OUT=REPORT/OUTPUT/eff_km_c30_soc_det15l_de_i_f_x.rtf (07APR2021 14:24)

16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Social functioning
16.2.6.1.2.1 Efficacy response data
16.2.6.1.2.1.19 QLQ-C30 - Time until permanent improvement by 15 pt in Social functioning (LOCF) - ITT population

First permanent improvement 15 points Social functioning (%)	**Kd (N=123)**	**IKd (N=179)**
Number (%) of events	20 (16.3)	44 (24.6)
Number (%) of patients censored	103 (83.7)	135 (75.4)
Kaplan-Meier estimates of Social functioning in months		
25% quantile (95% CI)	NC (19.384 to NC)	19.65 (13.667 to NC)
Median (95% CI)	NC (NC to NC)	NC (NC to NC)
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)
Comparison vs. Kd		
Stratified[a] Log-Rank test p-value[b] vs Kd	-	0.0954
Stratified[a] Hazard ratio (95% CI) vs Kd	-	1.56 (0.92 to 2.66)
P-value	-	0.0982
Improvement probability (95% CI)[c]		
3 Months	0.067 (0.031 to 0.121)	0.103 (0.064 to 0.153)
6 Months	0.084 (0.043 to 0.143)	0.103 (0.064 to 0.153)

A lower score represents a better level of quality of life. Clinical meaningful improvement change from baseline less than or equal to -15 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] Stratified on number of prior lines of therapy (1 vs. >1) and Revised International Staging System (R-ISS) stage (I or II vs. III vs. not classified) according to IRT
[b] One-sided significance level is 0.025
[c] Estimated using the Kaplan-Meier method
NA/NC = Not Applicable / Not Calculable
PGM=DEVOPS/SAR650984/EFC15246/CIR_RWE/REPORT/PGM/eff_km_invhr_sr_i_t.sas OUT=REPORT/OUTPUT/eff_km_c30_soc_imp15pl_de_i_t_x.rtf (07APR2021 14:22)

16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Social functioning
16.2.6.1.2.1 Efficacy response data
16.2.6.1.2.1.20 QLQ-C30 - Time until permanent improvement by 15 pt in Social functioning - Kaplan-Meier curve (LOCF) - ITT population



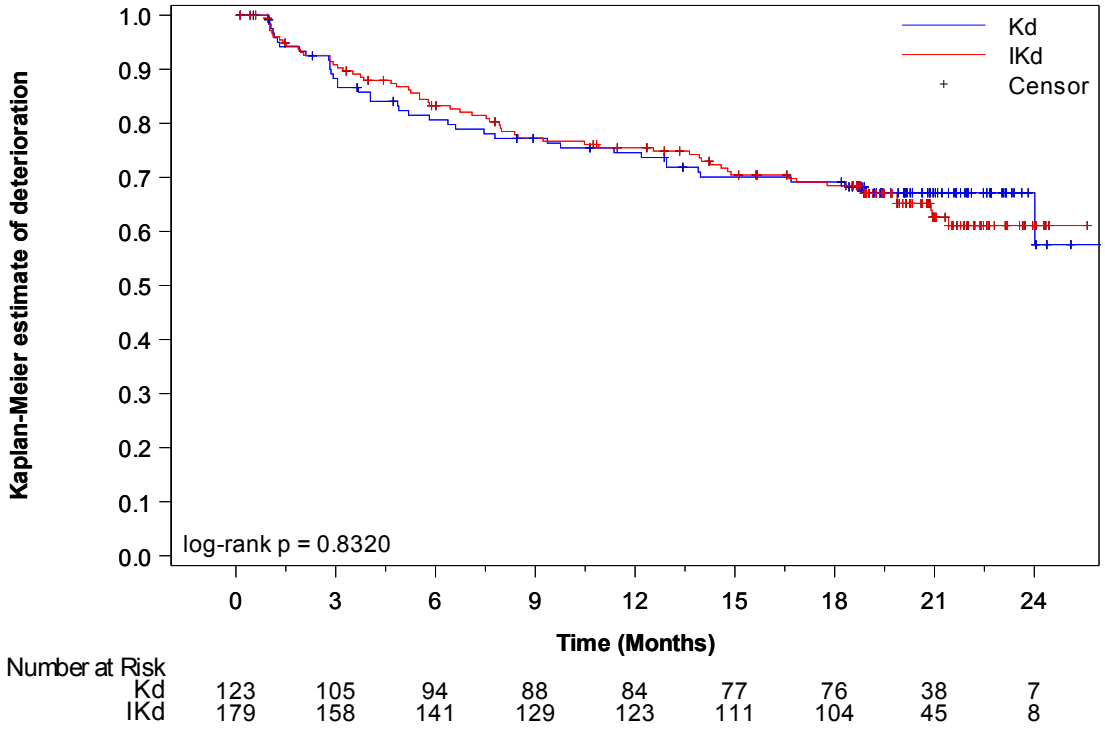
A lower score represents a better level of quality of life. Clinical meaningful improvement change from baseline less than or equal to -15 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
PGM=DEVOPS/SAR650984/EFC15246/CIR_RWE/REPORT/PGM/eff_qlq_km_i_f.sas OUT=REPORT/OUTPUT/eff_km_c30_soc_imp15pl_de_i_f_x.rtf (07APR2021 14:24)

16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Social functioning
16.2.6.1.2.1 Efficacy response data
16.2.6.1.2.1.21 QLQ-C30 - Time until permanent deterioration by 15 pt in Social functioning (LOCF) - ITT population

First permanent deterioration 15 points Social functioning (%)	**Kd (N=123)**	**IKd (N=179)**
Number (%) of events	39 (31.7)	60 (33.5)
Number (%) of patients censored	84 (68.3)	119 (66.5)
Kaplan-Meier estimates of Social functioning in months		
25% quantile (95% CI)	11.37 (4.895 to 18.924)	12.55 (7.097 to 17.774)
Median (95% CI)	NC (24.016 to NC)	NC (NC to NC)
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)
Comparison vs. Kd		
Stratified[a] Log-Rank test p-value[b] vs Kd	-	0.8320
Stratified[a] Hazard ratio (95% CI) vs Kd	-	1.04 (0.70 to 1.57)
P-value	-	0.8328
Deterioration probability (95% CI)[c]		
3 Months	0.883 (0.810 to 0.929)	0.908 (0.855 to 0.943)
6 Months	0.806 (0.723 to 0.867)	0.833 (0.768 to 0.881)

A lower score represents a better level of quality of life. Clinical meaningful deterioration change from baseline greater than or equal to 15 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] Stratified on number of prior lines of therapy (1 vs. >1) and Revised International Staging System (R-ISS) stage (I or II vs. III vs. not classified) according to IRT
[b] One-sided significance level is 0.025
[c] Estimated using the Kaplan-Meier method
NA/NC = Not Applicable / Not Calculable
PGM=DEVOPS/SAR650984/EFC15246/CIR_RWE/REPORT/PGM/eff_km_invhr_sr_i_t.sas OUT=REPORT/OUTPUT/eff_km_c30_soc_det15pl_de_i_t_x.rtf (07APR2021 14:22)

16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Social functioning
16.2.6.1.2.1 Efficacy response data
16.2.6.1.2.1.22 QLQ-C30 - Time until permanent deterioration by 15 pt in Social functioning - Kaplan-Meier curve (LOCF) - ITT population



A lower score represents a better level of quality of life. Clinical meaningful deterioration change from baseline greater than or equal to 15 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
PGM=DEVOPS/SAR650984/EFC15246/CIR_RWE/REPORT/PGM/eff_qlq_km_i_f.sas OUT=REPORT/OUTPUT/eff_km_c30_soc_det15pl_de_i_f_x.rtf (07APR2021 14:24)

16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Social functioning
16.2.6.1.2.2 Efficacy response data - Subgroup analyses by age
16.2.6.1.2.2.3 QLQ-C30 - Time to first improvement by 10 pt in social functioning according to age (LOCF) - ITT population

	<65 years		>=65 years		
	Kd (N=66)	**IKd (N=88)**	**Kd (N=57)**	**IKd (N=91)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	24 (36.4)	40 (45.5)	16 (28.1)	46 (50.5)	0.3558
Number (%) of patients censored	42 (63.6)	48 (54.5)	41 (71.9)	45 (49.5)	
Kaplan-Meier estimates of Social functioning in months					
25% quantile (95% CI)	2.43 (1.051 to 6.472)	1.05 (1.018 to 2.004)	2.83 (1.084 to NC)	1.25 (1.051 to 2.563)	
Median (95% CI)	NC (15.113 to NC)	NC (2.924 to NC)	NC (NC to NC)	9.43 (3.187 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.2195		0.0163	
Hazard ratio (95% CI) vs Kd	-	1.37 (0.83 to 2.28)		1.98 (1.12 to 3.50)	
P-value	-	0.2214		0.0185	
Hazard ratio inverted (95% CI) vs IKd		-		0.50 (0.29 to 0.89)	

A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
PGM=DEVOPS/SAR650984/EFC15246/CIR_RWE/REPORT/PGM/eff_km_subgp_sr_sig_de_i_t.sas OUT=REPORT/OUTPUT/eff_km_c30_soc_impl_age_de_i_t_x.rtf (07APR2021 14:27)

16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Social functioning
16.2.6.1.2.2 Efficacy response data - Subgroup analyses by age
16.2.6.1.2.2.4 QLQ-C30 - Time to first deterioration by 10 pt in social functioning according to age (LOCF) - ITT population

	<65 years		>=65 years		
	Kd (N=66)	**IKd (N=88)**	**Kd (N=57)**	**IKd (N=91)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	36 (54.5)	55 (62.5)	40 (70.2)	63 (69.2)	0.6241
Number (%) of patients censored	30 (45.5)	33 (37.5)	17 (29.8)	28 (30.8)	
Kaplan-Meier estimates of Social functioning in months					
25% quantile (95% CI)	1.91 (1.117 to 2.825)	2.04 (1.183 to 2.924)	1.31 (1.018 to 2.103)	1.89 (1.150 to 1.971)	
Median (95% CI)	7.89 (2.825 to NC)	4.73 (3.121 to 12.715)	4.04 (2.103 to 6.374)	3.52 (2.595 to 5.914)	
75% quantile (95% CI)	NC (NC to NC)	NC (18.300 to NC)	NC (6.374 to NC)	NC (8.805 to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.5699		0.9640	
Hazard ratio (95% CI) vs Kd	-	1.13 (0.74 to 1.72)		0.99 (0.67 to 1.47)	
P-value	-	0.5701		0.9640	
Deterioration probability (95% CI)[b]					

A higher score represents a better level of quality of life. Clinical meaningful deterioration change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
PGM=DEVOPS/SAR650984/EFC15246/CIR_RWE/REPORT/PGM/eff_km_subgp_sr_sig_de_i_t.sas OUT=REPORT/OUTPUT/eff_km_c30_soc_detl_age_de_i_t_x.rtf (07APR2021 14:26)

16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Social functioning
16.2.6.1.2.2 Efficacy response data - Subgroup analyses by age
16.2.6.1.2.2.5 QLQ-C30 - Time until permanent improvement by 10 pt in social functioning according to age (LOCF) - ITT population

	<65 years		>=65 years		
	Kd (N=66)	**IKd (N=88)**	**Kd (N=57)**	**IKd (N=91)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	15 (22.7)	23 (26.1)	5 (8.8)	21 (23.1)	0.1401
Number (%) of patients censored	51 (77.3)	65 (73.9)	52 (91.2)	70 (76.9)	
Kaplan-Meier estimates of Social functioning in months					
25% quantile (95% CI)	22.14 (12.386 to NC)	18.20 (9.922 to NC)	NC (NC to NC)	19.65 (12.682 to NC)	
Median (95% CI)	NC (22.144 to NC)	NC (NC to NC)	NC (NC to NC)	NC (22.604 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.6114		0.0291	
Hazard ratio (95% CI) vs Kd	-	1.18 (0.62 to 2.27)		2.83 (1.07 to 7.50)	
P-value	-	0.6119		0.0369	
Hazard ratio inverted (95% CI) vs IKd		-		0.35 (0.13 to 0.94)	

A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
PGM=DEVOPS/SAR650984/EFC15246/CIR_RWE/REPORT/PGM/eff_km_subgp_sr_sig_de_i_t.sas OUT=REPORT/OUTPUT/eff_km_c30_soc_imppl_age_de_i_t_x.rtf (07APR2021 14:27)

16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Social functioning
16.2.6.1.2.2 Efficacy response data - Subgroup analyses by age
16.2.6.1.2.2.6 QLQ-C30 - Time until permanent deterioration by 10 pt in social functioning according to age (LOCF) - ITT population

	<65 years		>=65 years		
	Kd (N=66)	**IKd (N=88)**	**Kd (N=57)**	**IKd (N=91)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	19 (28.8)	28 (31.8)	20 (35.1)	32 (35.2)	0.7344
Number (%) of patients censored	47 (71.2)	60 (68.2)	37 (64.9)	59 (64.8)	
Kaplan-Meier estimates of Social functioning in months					
25% quantile (95% CI)	11.37 (3.055 to NC)	8.38 (3.844 to NC)	7.79 (4.041 to 18.924)	13.93 (7.524 to 19.877)	
Median (95% CI)	NC (24.016 to NC)	NC (NC to NC)	NC (18.924 to NC)	NC (20.895 to NC)	
75% quantile (95% CI)	NC (24.016 to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.7088		0.9302	
Hazard ratio (95% CI) vs Kd	-	1.12 (0.62 to 2.00)		0.98 (0.56 to 1.71)	
P-value	-	0.7089		0.9300	
Deterioration probability (95% CI)[b]					

A higher score represents a better level of quality of life. Clinical meaningful deterioration change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Social functioning
16.2.6.1.2.3 Efficacy response data - Subgroup analyses by gender
16.2.6.1.2.3.3 QLQ-C30 - Time to first improvement by 10 pt in social functioning according to gender (LOCF) - ITT population

	Male		Female		
	Kd (N=68)	**IKd (N=101)**	**Kd (N=55)**	**IKd (N=78)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	17 (25.0)	43 (42.6)	23 (41.8)	43 (55.1)	0.4023
Number (%) of patients censored	51 (75.0)	58 (57.4)	32 (58.2)	35 (44.9)	
Kaplan-Meier estimates of Social functioning in months					
25% quantile (95% CI)	15.11 (1.906 to NC)	1.84 (1.051 to 2.891)	1.12 (1.018 to 2.825)	1.05 (1.018 to 1.906)	
Median (95% CI)	NC (NC to NC)	NC (4.895 to NC)	NC (2.825 to NC)	4.96 (2.037 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.0201		0.1993	
Hazard ratio (95% CI) vs Kd	-	1.92 (1.10 to 3.37)		1.39 (0.84 to 2.31)	
P-value	-	0.0224		0.2014	
Hazard ratio inverted (95% CI) vs IKd		-		0.72 (0.43 to 1.19)	

A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Social functioning
16.2.6.1.2.3 Efficacy response data - Subgroup analyses by gender
16.2.6.1.2.3.4 QLQ-C30 - Time to first deterioration by 10 pt in social functioning according to gender (LOCF) - ITT population

	Male		Female		
	Kd (N=68)	**IKd (N=101)**	**Kd (N=55)**	**IKd (N=78)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	41 (60.3)	64 (63.4)	35 (63.6)	54 (69.2)	0.9829
Number (%) of patients censored	27 (39.7)	37 (36.6)	20 (36.4)	24 (30.8)	
Kaplan-Meier estimates of Social functioning in months					
25% quantile (95% CI)	1.91 (1.084 to 2.858)	1.94 (1.150 to 2.825)	1.91 (1.018 to 2.136)	1.91 (1.150 to 2.366)	
Median (95% CI)	4.63 (2.924 to 15.540)	4.70 (2.990 to 8.279)	4.68 (2.136 to 13.405)	4.67 (2.825 to 8.476)	
75% quantile (95% CI)	NC (19.745 to NC)	NC (16.559 to NC)	NC (13.405 to NC)	NC (12.715 to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.7561		0.7352	
Hazard ratio (95% CI) vs Kd	-	1.06 (0.72 to 1.57)		1.08 (0.70 to 1.65)	
P-value	-	0.7576		0.7353	
Deterioration probability (95% CI)[b]					

A higher score represents a better level of quality of life. Clinical meaningful deterioration change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Social functioning
16.2.6.1.2.3 Efficacy response data - Subgroup analyses by gender
16.2.6.1.2.3.5 QLQ-C30 - Time until permanent improvement by 10 pt in social functioning according to gender (LOCF) - ITT population

	Male		Female		
	Kd (N=68)	**IKd (N=101)**	**Kd (N=55)**	**IKd (N=78)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	8 (11.8)	26 (25.7)	12 (21.8)	18 (23.1)	0.1267
Number (%) of patients censored	60 (88.2)	75 (74.3)	43 (78.2)	60 (76.9)	
Kaplan-Meier estimates of Social functioning in months					
25% quantile (95% CI)	22.47 (22.144 to NC)	17.51 (9.922 to NC)	NC (5.585 to NC)	20.14 (12.977 to NC)	
Median (95% CI)	NC (22.472 to NC)	NC (22.604 to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.0251		0.9628	
Hazard ratio (95% CI) vs Kd	-	2.40 (1.09 to 5.31)		1.02 (0.49 to 2.11)	
P-value	-	0.0301		0.9629	
Hazard ratio inverted (95% CI) vs IKd		-		0.98 (0.47 to 2.04)	

A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Social functioning
16.2.6.1.2.3 Efficacy response data - Subgroup analyses by gender
16.2.6.1.2.3.6 QLQ-C30 - Time until permanent deterioration by 10 pt in social functioning according to gender (LOCF) - ITT population

	Male		Female		
	Kd (N=68)	**IKd (N=101)**	**Kd (N=55)**	**IKd (N=78)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	22 (32.4)	36 (35.6)	17 (30.9)	24 (30.8)	0.6622
Number (%) of patients censored	46 (67.6)	65 (64.4)	38 (69.1)	54 (69.2)	
Kaplan-Meier estimates of Social functioning in months					
25% quantile (95% CI)	9.36 (3.680 to 24.016)	7.92 (5.191 to 16.624)	12.94 (3.055 to NC)	14.88 (7.984 to 21.421)	
Median (95% CI)	NC (24.016 to NC)	NC (20.928 to NC)	NC (NC to NC)	NC (21.421 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.6545		0.8640	
Hazard ratio (95% CI) vs Kd	-	1.13 (0.66 to 1.92)		0.95 (0.51 to 1.76)	
P-value	-	0.6547		0.8633	
Deterioration probability (95% CI)[b]					

A higher score represents a better level of quality of life. Clinical meaningful deterioration change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Social functioning
16.2.6.1.2.4 Efficacy response data - Subgroup analyses by ethnic origin
16.2.6.1.2.4.3 QLQ-C30 - Time to first improvement by 10 pt in social functioning according to ethnic origin (LOCF) - ITT population

	White		Other		
	Kd (N=83)	**IKd (N=131)**	**Kd (N=28)**	**IKd (N=34)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	23 (27.7)	70 (53.4)	15 (53.6)	12 (35.3)	0.0043
Number (%) of patients censored	60 (72.3)	61 (46.6)	13 (46.4)	22 (64.7)	
Kaplan-Meier estimates of Social functioning in months					
25% quantile (95% CI)	3.29 (1.051 to NC)	1.05 (1.018 to 1.906)	1.12 (1.051 to 1.906)	1.91 (1.018 to NC)	
Median (95% CI)	NC (NC to NC)	6.11 (2.891 to NC)	3.71 (1.117 to NC)	NC (2.004 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (15.113 to NC)	NC (NC to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.0007		0.2067	
Hazard ratio (95% CI) vs Kd	-	2.22 (1.39 to 3.56)		0.62 (0.29 to 1.32)	
P-value	-	0.0009		0.2111	
Hazard ratio inverted (95% CI) vs IKd		-		1.63 (0.76 to 3.48)	

A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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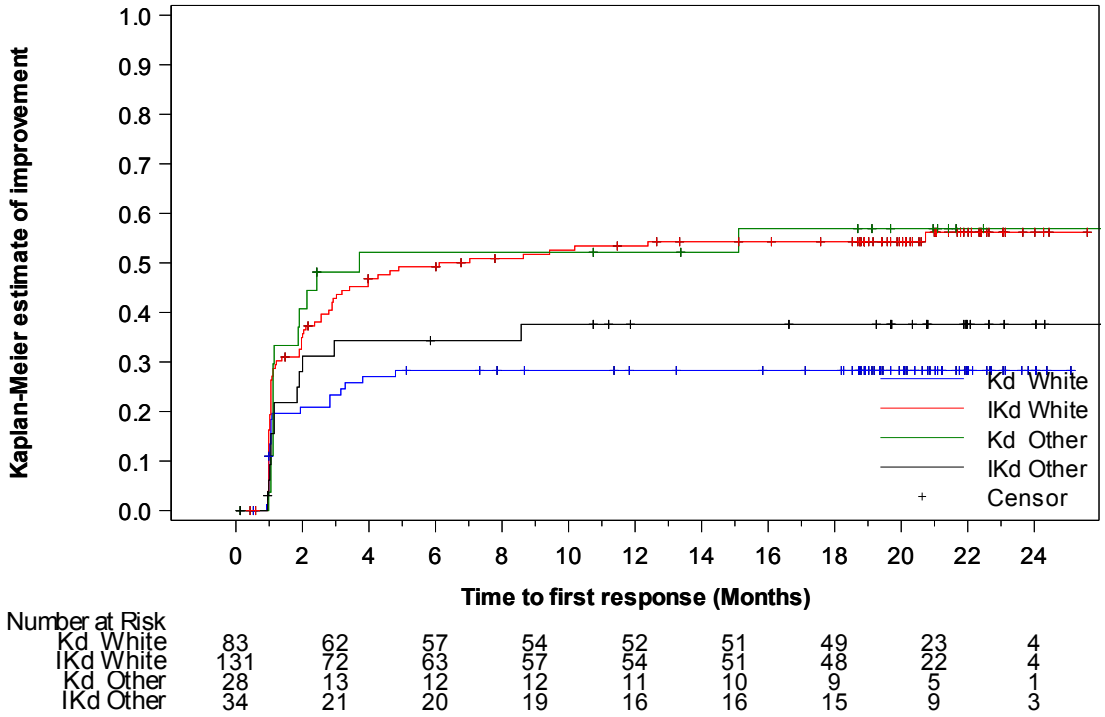
16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Social functioning
16.2.6.1.2.4 Efficacy response data - Subgroup analyses by ethnic origin
16.2.6.1.2.4.4 QLQ-C30 - Time to first improvement by 10 pt in social functioning according to ethnic origin - Kaplan-Meier curve (LOCF) - ITT population



Number at Risk

Kd White	83	62	57	54	52	51	49	23	4
IKd White	131	72	63	57	54	51	48	22	4
Kd Other	28	13	12	12	11	10	9	5	1
IKd Other	34	21	20	19	16	16	15	9	3

A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
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16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Social functioning
16.2.6.1.2.4 Efficacy response data - Subgroup analyses by ethnic origin
16.2.6.1.2.4.5 QLQ-C30 - Time to first deterioration by 10 pt in social functioning according to ethnic origin (LOCF) - ITT population

	White		Other		
	Kd (N=83)	**IKd (N=131)**	**Kd (N=28)**	**IKd (N=34)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	57 (68.7)	84 (64.1)	15 (53.6)	26 (76.5)	0.0575
Number (%) of patients censored	26 (31.3)	47 (35.9)	13 (46.4)	8 (23.5)	
Kaplan-Meier estimates of Social functioning in months					
25% quantile (95% CI)	1.91 (1.051 to 2.136)	1.91 (1.183 to 2.760)	1.15 (1.051 to 2.825)	1.87 (1.018 to 2.037)	
Median (95% CI)	4.04 (2.825 to 6.374)	4.73 (3.220 to 7.622)	5.03 (1.281 to NC)	2.83 (1.906 to 5.125)	
75% quantile (95% CI)	NC (9.232 to NC)	NC (18.300 to NC)	NC (19.745 to NC)	9.48 (3.877 to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.5472		0.0786	
Hazard ratio (95% CI) vs Kd	-	0.90 (0.64 to 1.26)		1.77 (0.93 to 3.36)	
P-value	-	0.5474		0.0825	
Deterioration probability (95% CI)[b]					

A higher score represents a better level of quality of life. Clinical meaningful deterioration change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Social functioning
16.2.6.1.2.4 Efficacy response data - Subgroup analyses by ethnic origin
16.2.6.1.2.4.6 QLQ-C30 - Time until permanent improvement by 10 pt in social functioning according to ethnic origin (LOCF) - ITT population

	White		Other		
	Kd (N=83)	**IKd (N=131)**	**Kd (N=28)**	**IKd (N=34)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	13 (15.7)	34 (26.0)	6 (21.4)	8 (23.5)	0.4344
Number (%) of patients censored	70 (84.3)	97 (74.0)	22 (78.6)	26 (76.5)	
Kaplan-Meier estimates of Social functioning in months					
25% quantile (95% CI)	NC (19.384 to NC)	19.65 (12.682 to NC)	22.47 (1.117 to NC)	18.04 (7.458 to NC)	
Median (95% CI)	NC (NC to NC)	NC (22.604 to NC)	NC (22.472 to NC)	NC (18.037 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.0738		0.8811	
Hazard ratio (95% CI) vs Kd	-	1.78 (0.94 to 3.37)		1.08 (0.38 to 3.13)	
P-value	-	0.0780		0.8816	
Improvement probability (95% CI)[b]					

A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Social functioning
16.2.6.1.2.4 Efficacy response data - Subgroup analyses by ethnic origin
16.2.6.1.2.4.7 QLQ-C30 - Time until permanent deterioration by 10 pt in social functioning according to ethnic origin (LOCF) - ITT population

	White		Other		
	Kd (N=83)	**IKd (N=131)**	**Kd (N=28)**	**IKd (N=34)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	30 (36.1)	43 (32.8)	7 (25.0)	12 (35.3)	0.2586
Number (%) of patients censored	53 (63.9)	88 (67.2)	21 (75.0)	22 (64.7)	
Kaplan-Meier estimates of Social functioning in months					
25% quantile (95% CI)	9.36 (4.041 to 16.690)	14.00 (7.524 to 19.877)	24.02 (1.150 to NC)	9.71 (1.117 to NC)	
Median (95% CI)	NC (NC to NC)	NC (21.421 to NC)	NC (24.016 to NC)	NC (14.587 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (24.016 to NC)	NC (NC to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.6098		0.3253	
Hazard ratio (95% CI) vs Kd	-	0.89 (0.56 to 1.41)		1.59 (0.62 to 4.07)	
P-value	-	0.6100		0.3296	
Deterioration probability (95% CI)[b]					

A higher score represents a better level of quality of life. Clinical meaningful deterioration change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Social functioning
16.2.6.1.2.5 Efficacy response data - Subgroup analyses by geographical region
16.2.6.1.2.5.3 QLQ-C30 - Time to first improvement by 10 pt in social functioning according to geographical region (LOCF) - ITT population

	Europe		America		Asia		Other countries		
	Kd (N=60)	**IKd (N=85)**	**Kd (N=20)**	**IKd (N=24)**	**Kd (N=21)**	**IKd (N=25)**	**Kd (N=22)**	**IKd (N=45)**	**p-value of treatment-by-subgroup interaction[c]**
Number (%) of events	18 (30.0)	41 (48.2)	4 (20.0)	15 (62.5)	12 (57.1)	9 (36.0)	6 (27.3)	21 (46.7)	0.0111
Number (%) of patients censored	42 (70.0)	44 (51.8)	16 (80.0)	9 (37.5)	9 (42.9)	16 (64.0)	16 (72.7)	24 (53.3)	
Kaplan-Meier estimates of event in months									
25% quantile (95% CI)	3.29 (1.051 to NC)	1.22 (1.051 to 2.563)	NC (0.986 to NC)	0.99 (0.953 to 1.051)	1.12 (0.986 to 1.150)	1.95 (0.986 to NC)	4.80 (0.986 to NC)	1.38 (1.018 to 3.417)	
Median (95% CI)	NC (NC to NC)	20.73 (2.924 to NC)	NC (NC to NC)	2.00 (1.051 to NC)	2.28 (1.117 to NC)	NC (2.004 to NC)	NC (4.797 to NC)	NC (3.023 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (2.366 to NC)	NC (2.431 to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Kd									

A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Social functioning
16.2.6.1.2.5 Efficacy response data - Subgroup analyses by geographical region
16.2.6.1.2.5.3 QLQ-C30 - Time to first improvement by 10 pt in social functioning according to geographical region (LOCF) - ITT population

	Europe		America		Asia		Other countries		
	Kd (N=60)	**IKd (N=85)**	**Kd (N=20)**	**IKd (N=24)**	**Kd (N=21)**	**IKd (N=25)**	**Kd (N=22)**	**IKd (N=45)**	**p-value of treatment-by-subgroup interaction[c]**
Log-Rank test p-value[a] vs Kd	-	0.0413		0.0043		0.1296		0.1608	
Hazard ratio (95% CI) vs Kd	-	1.77 (1.02 to 3.08)		4.41 (1.45 to 13.37)		0.52 (0.22 to 1.23)		1.89 (0.76 to 4.70)	
P-value	-	0.0441		0.0088		0.1364		0.1680	
Hazard ratio inverted (95% CI) vs IKd		-		0.23 (0.07 to 0.69)		1.93 (0.81 to 4.61)		0.53 (0.21 to 1.31)	
Improvement probability (95% CI)[b]									
3 Months	0.223 (0.127 to 0.337)	0.399 (0.293 to 0.502)	0.200 (0.062 to 0.393)	0.572 (0.346 to 0.746)	0.550 (0.313 to 0.735)	0.333 (0.159 to 0.519)	0.182 (0.057 to 0.363)	0.333 (0.202 to 0.470)	

A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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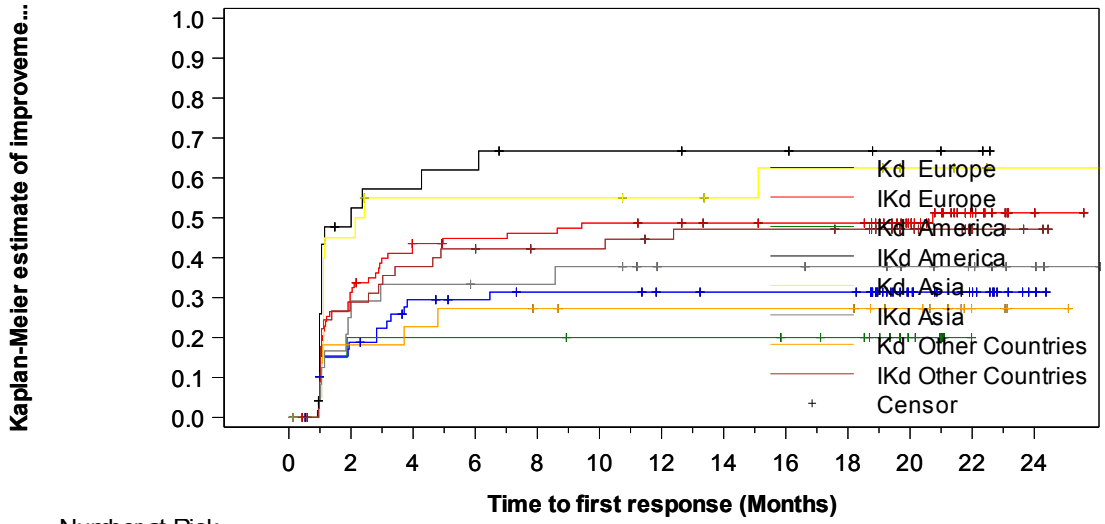
16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Social functioning
16.2.6.1.2.5 Efficacy response data - Subgroup analyses by geographical region
16.2.6.1.2.5.4 QLQ-C30 - Time to first improvement by 10 pt in social functioning according to geographical region - Kaplan-Meier curve (LOCF) - ITT population



Number at Risk									
Kd Europe	60	44	37	35	33	32	32	14	3
IKd Europe	85	49	43	41	39	37	36	18	2
Kd America	20	16	16	15	15	15	13	5	0
IKd America	24	9	8	6	6	5	4	2	0
Kd Asia	21	8	8	8	7	6	5	3	1
IKd Asia	25	16	15	14	11	11	10	7	3
Kd Other Countries	22	18	16	14	14	14	14	8	1
IKd Other Countries	45	30	26	24	22	21	20	9	2

A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
PGM=DEVOPS/SAR650984/EFC15246/CIR_RWE/REPORT/PGM/eff_qlq_km_subgp_de_i_f.sas OUT=REPORT/OUTPUT/eff_km_c30_soc_impl_greg_de_i_f_x.rtf (07APR2021 14:32)

16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Social functioning
16.2.6.1.2.5 Efficacy response data - Subgroup analyses by geographical region
16.2.6.1.2.5.5 QLQ-C30 - Time to first deterioration by 10 pt in social functioning according to geographical region (LOCF) - ITT population

	Europe		America		Asia		Other countries		
	Kd (N=60)	**IKd (N=85)**	**Kd (N=20)**	**IKd (N=24)**	**Kd (N=21)**	**IKd (N=25)**	**Kd (N=22)**	**IKd (N=45)**	**p-value of treatment-by-subgroup interaction[c]**
Number (%) of events	33 (55.0)	51 (60.0)	15 (75.0)	16 (66.7)	11 (52.4)	20 (80.0)	17 (77.3)	31 (68.9)	0.1563
Number (%) of patients censored	27 (45.0)	34 (40.0)	5 (25.0)	8 (33.3)	10 (47.6)	5 (20.0)	5 (22.7)	14 (31.1)	
Kaplan-Meier estimates of event in months									
25% quantile (95% CI)	2.04 (1.018 to 2.924)	1.91 (1.413 to 2.891)	1.05 (0.953 to 1.840)	3.12 (1.051 to 5.520)	1.23 (1.051 to 2.957)	1.89 (0.986 to 2.037)	2.00 (1.084 to 3.877)	1.12 (1.018 to 2.004)	
Median (95% CI)	8.08 (3.745 to NC)	5.13 (3.023 to 14.324)	2.07 (1.051 to 4.698)	10.64 (3.121 to 18.300)	4.50 (1.150 to NC)	2.83 (1.906 to 4.665)	4.44 (2.004 to 12.485)	4.67 (1.971 to 7.622)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (2.168 to NC)	NC (10.645 to NC)	NC (5.027 to NC)	9.12 (2.924 to NC)	19.75 (4.830 to NC)	NC (5.717 to NC)	

A higher score represents a better level of quality of life. Clinical meaningful deterioration change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
PGM=DEVOPS/SAR650984/EFC15246/CIR_RWE/REPORT/PGM/eff_km_subgp_sr_sig_de_i_t.sas OUT=REPORT/OUTPUT/eff_km_c30_soc_detl_greg_de_i_t_x.rtf (07APR2021 14:26)

16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Social functioning
16.2.6.1.2.5 Efficacy response data - Subgroup analyses by geographical region
16.2.6.1.2.5.5 QLQ-C30 - Time to first deterioration by 10 pt in social functioning according to geographical region (LOCF) - ITT population

	Europe		America		Asia		Other countries		
	Kd (N=60)	**IKd (N=85)**	**Kd (N=20)**	**IKd (N=24)**	**Kd (N=21)**	**IKd (N=25)**	**Kd (N=22)**	**IKd (N=45)**	**p-value of treatment-by-subgroup interaction[c]**
Comparison vs. Kd									
Log-Rank test p-value[a] vs Kd	-	0.6961		0.1390		0.1053		0.9019	
Hazard ratio (95% CI) vs Kd	-	1.09 (0.70 to 1.69)		0.59 (0.29 to 1.20)		1.83 (0.87 to 3.82)		1.04 (0.57 to 1.88)	
P-value	-	0.6962		0.1434		0.1105		0.9024	
Deterioration probability (95% CI)[b]									
3 Months	0.638 (0.500 to 0.747)	0.614 (0.501 to 0.709)	0.350 (0.157 to 0.552)	0.776 (0.543 to 0.900)	0.550 (0.313 to 0.735)	0.417 (0.222 to 0.601)	0.682 (0.446 to 0.834)	0.556 (0.400 to 0.686)	
6 Months	0.528 (0.391 to 0.648)	0.480 (0.369 to 0.582)	0.250 (0.091 to 0.449)	0.502 (0.284 to 0.686)	0.450 (0.231 to 0.647)	0.292 (0.130 to 0.476)	0.409 (0.209 to 0.601)	0.370 (0.231 to 0.510)	

A higher score represents a better level of quality of life. Clinical meaningful deterioration change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Social functioning
16.2.6.1.2.5 Efficacy response data - Subgroup analyses by geographical region
16.2.6.1.2.5.6 QLQ-C30 - Time until permanent improvement by 10 pt in social functioning according to geographical region (LOCF) - ITT population

	Europe		America		Asia		Other countries		
	Kd (N=60)	**IKd (N=85)**	**Kd (N=20)**	**IKd (N=24)**	**Kd (N=21)**	**IKd (N=25)**	**Kd (N=22)**	**IKd (N=45)**	**p-value of treatment-by-subgroup interaction[c]**
Number (%) of events	8 (13.3)	18 (21.2)	4 (20.0)	13 (54.2)	4 (19.0)	5 (20.0)	4 (18.2)	8 (17.8)	0.4586
Number (%) of patients censored	52 (86.7)	67 (78.8)	16 (80.0)	11 (45.8)	17 (81.0)	20 (80.0)	18 (81.8)	37 (82.2)	
Kaplan-Meier estimates of event in months									
25% quantile (95% CI)	NC (16.821 to NC)	21.68 (14.094 to NC)	NC (1.051 to NC)	9.92 (0.986 to 13.667)	22.47 (1.051 to NC)	18.04 (1.051 to NC)	22.14 (1.084 to NC)	22.60 (2.891 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	14.06 (9.922 to NC)	NC (22.472 to NC)	NC (18.037 to NC)	NC (22.144 to NC)	NC (22.604 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (14.062 to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	

A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Social functioning
16.2.6.1.2.5 Efficacy response data - Subgroup analyses by geographical region
16.2.6.1.2.5.6 QLQ-C30 - Time until permanent improvement by 10 pt in social functioning according to geographical region (LOCF) - ITT population

	Europe		America		Asia		Other countries		
	Kd (N=60)	**IKd (N=85)**	**Kd (N=20)**	**IKd (N=24)**	**Kd (N=21)**	**IKd (N=25)**	**Kd (N=22)**	**IKd (N=45)**	**p-value of treatment-by-subgroup interaction[c]**
Comparison vs. Kd									
Log-Rank test p-value[a] vs Kd	-	0.2649		0.0217		0.9880		0.8246	
Hazard ratio (95% CI) vs Kd	-	1.60 (0.70 to 3.68)		3.45 (1.12 to 10.64)		1.01 (0.27 to 3.77)		1.15 (0.34 to 3.83)	
P-value	-	0.2694		0.0309		0.9881		0.8247	
Hazard ratio inverted (95% CI) vs IKd		-		0.29 (0.09 to 0.89)		0.99 (0.27 to 3.69)		0.87 (0.26 to 2.92)	
Improvement probability (95% CI)[b]									

A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Social functioning
16.2.6.1.2.5 Efficacy response data - Subgroup analyses by geographical region
16.2.6.1.2.5.7 QLQ-C30 - Time until permanent deterioration by 10 pt in social functioning according to geographical region (LOCF) - ITT population

	Europe		America		Asia		Other countries		
	Kd (N=60)	**IKd (N=85)**	**Kd (N=20)**	**IKd (N=24)**	**Kd (N=21)**	**IKd (N=25)**	**Kd (N=22)**	**IKd (N=45)**	**p-value of treatment-by-subgroup interaction[c]**
Number (%) of events	16 (26.7)	24 (28.2)	7 (35.0)	7 (29.2)	7 (33.3)	9 (36.0)	9 (40.9)	20 (44.4)	0.9381
Number (%) of patients censored	44 (73.3)	61 (71.8)	13 (65.0)	17 (70.8)	14 (66.7)	16 (64.0)	13 (59.1)	25 (55.6)	
Kaplan-Meier estimates of event in months									
25% quantile (95% CI)	18.30 (3.680 to NC)	18.79 (8.378 to NC)	9.36 (1.018 to NC)	16.62 (2.037 to NC)	9.58 (1.117 to NC)	5.65 (1.018 to NC)	6.60 (3.055 to NC)	7.10 (3.745 to 14.587)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (9.363 to NC)	NC (16.624 to NC)	NC (5.191 to NC)	NC (5.782 to NC)	NC (6.604 to NC)	21.42 (7.951 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (20.928 to NC)	NC (24.016 to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	

A higher score represents a better level of quality of life. Clinical meaningful deterioration change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
PGM=DEVOPS/SAR650984/EFC15246/CIR_RWE/REPORT/PGM/eff_km_subgp_sr_sig_de_i_t.sas OUT=REPORT/OUTPUT/eff_km_c30_soc_detpl_greg_de_i_t_x.rtf (07APR2021 14:27)

16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Social functioning
16.2.6.1.2.5 Efficacy response data - Subgroup analyses by geographical region
16.2.6.1.2.5.7 QLQ-C30 - Time until permanent deterioration by 10 pt in social functioning according to geographical region (LOCF) - ITT population

	Europe		America		Asia		Other countries		
	Kd (N=60)	**IKd (N=85)**	**Kd (N=20)**	**IKd (N=24)**	**Kd (N=21)**	**IKd (N=25)**	**Kd (N=22)**	**IKd (N=45)**	**p-value of treatment-by-subgroup interaction[c]**
Comparison vs. Kd									
Log-Rank test p-value[a] vs Kd	-	0.9858		0.7091		0.8370		0.6100	
Hazard ratio (95% CI) vs Kd	-	0.99 (0.53 to 1.87)		0.82 (0.29 to 2.34)		1.11 (0.41 to 3.00)		1.23 (0.56 to 2.70)	
P-value	-	0.9858		0.7095		0.8371		0.6106	
Deterioration probability (95% CI)[b]									
3 Months	0.879 (0.762 to 0.940)	0.928 (0.846 to 0.967)	0.850 (0.604 to 0.949)	0.955 (0.719 to 0.993)	0.800 (0.551 to 0.920)	0.833 (0.615 to 0.934)	1.000 (1.000 to 1.000)	0.889 (0.753 to 0.952)	

A higher score represents a better level of quality of life. Clinical meaningful deterioration change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
PGM=DEVOPS/SAR650984/EFC15246/CIR_RWE/REPORT/PGM/eff_km_subgp_sr_sig_de_i_t.sas OUT=REPORT/OUTPUT/eff_km_c30_soc_detpl_greg_de_i_t_x.rtf (07APR2021 14:27)

16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Social functioning
16.2.6.1.2.6 Efficacy response data - Subgroup analyses by regulatory region
16.2.6.1.2.6.3 QLQ-C30 - Time to first improvement by 10 pt in social functioning according to regulatory region (LOCF) - ITT population

	Western countries		Other countries		
	Kd (N=55)	**IKd (N=97)**	**Kd (N=68)**	**IKd (N=82)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	18 (32.7)	41 (42.3)	22 (32.4)	45 (54.9)	0.3125
Number (%) of patients censored	37 (67.3)	56 (57.7)	46 (67.6)	37 (45.1)	
Kaplan-Meier estimates of Social functioning in months					
25% quantile (95% CI)	3.71 (1.018 to NC)	1.91 (1.051 to 2.891)	1.15 (1.051 to NC)	1.05 (0.986 to 1.906)	
Median (95% CI)	NC (NC to NC)	NC (4.895 to NC)	NC (NC to NC)	6.11 (2.004 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.2837		0.0077	
Hazard ratio (95% CI) vs Kd	-	1.35 (0.78 to 2.35)		1.98 (1.19 to 3.29)	
P-value	-	0.2856		0.0090	
Hazard ratio inverted (95% CI) vs IKd		-		0.51 (0.30 to 0.84)	

A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
PGM=DEVOPS/SAR650984/EFC15246/CIR_RWE/REPORT/PGM/eff_km_subgp_sr_sig_de_i_t.sas OUT=REPORT/OUTPUT/eff_km_c30_soc_impl_rreg_de_i_t_x.rtf (07APR2021 14:27)

16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Social functioning
16.2.6.1.2.6 Efficacy response data - Subgroup analyses by regulatory region
16.2.6.1.2.6.4 QLQ-C30 - Time to first deterioration by 10 pt in social functioning according to regulatory region (LOCF) - ITT population

	Western countries		Other countries		
	Kd (N=55)	**IKd (N=97)**	**Kd (N=68)**	**IKd (N=82)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	29 (52.7)	58 (59.8)	47 (69.1)	60 (73.2)	0.7985
Number (%) of patients censored	26 (47.3)	39 (40.2)	21 (30.9)	22 (26.8)	
Kaplan-Meier estimates of Social functioning in months					
25% quantile (95% CI)	2.07 (1.117 to 3.745)	1.94 (1.216 to 2.825)	1.15 (1.051 to 1.971)	1.91 (1.117 to 2.366)	
Median (95% CI)	7.89 (2.924 to NC)	5.91 (3.055 to 13.766)	3.75 (2.168 to 5.618)	3.71 (2.825 to 4.731)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (8.082 to NC)	16.56 (6.571 to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.5107		0.7455	
Hazard ratio (95% CI) vs Kd	-	1.16 (0.74 to 1.81)		1.07 (0.73 to 1.56)	
P-value	-	0.5111		0.7463	
Deterioration probability (95% CI)[b]					

A higher score represents a better level of quality of life. Clinical meaningful deterioration change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
PGM=DEVOPS/SAR650984/EFC15246/CIR_RWE/REPORT/PGM/eff_km_subgp_sr_sig_de_i_t.sas OUT=REPORT/OUTPUT/eff_km_c30_soc_detl_rreg_de_i_t_x.rtf (07APR2021 14:26)

16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Social functioning
16.2.6.1.2.6 Efficacy response data - Subgroup analyses by regulatory region
16.2.6.1.2.6.5 QLQ-C30 - Time until permanent improvement by 10 pt in social functioning according to regulatory region (LOCF) - ITT population

	Western countries		Other countries		
	Kd (N=55)	**IKd (N=97)**	**Kd (N=68)**	**IKd (N=82)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	11 (20.0)	20 (20.6)	9 (13.2)	24 (29.3)	0.1267
Number (%) of patients censored	44 (80.0)	77 (79.4)	59 (86.8)	58 (70.7)	
Kaplan-Meier estimates of Social functioning in months					
25% quantile (95% CI)	22.14 (14.062 to NC)	22.60 (16.394 to NC)	NC (22.472 to NC)	14.06 (9.791 to NC)	
Median (95% CI)	NC (NC to NC)	NC (22.604 to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.8584		0.0197	
Hazard ratio (95% CI) vs Kd	-	1.07 (0.51 to 2.24)		2.42 (1.12 to 5.20)	
P-value	-	0.8584		0.0239	
Hazard ratio inverted (95% CI) vs IKd		-		0.41 (0.19 to 0.89)	

A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
PGM=DEVOPS/SAR650984/EFC15246/CIR_RWE/REPORT/PGM/eff_km_subgp_sr_sig_de_i_t.sas OUT=REPORT/OUTPUT/eff_km_c30_soc_imppl_rreg_de_i_t_x.rtf (07APR2021 14:27)

16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Social functioning
16.2.6.1.2.6 Efficacy response data - Subgroup analyses by regulatory region
16.2.6.1.2.6.6 QLQ-C30 - Time until permanent deterioration by 10 pt in social functioning according to regulatory region (LOCF) - ITT population

	Western countries		Other countries		
	Kd (N=55)	**IKd (N=97)**	**Kd (N=68)**	**IKd (N=82)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	11 (20.0)	32 (33.0)	28 (41.2)	28 (34.1)	0.0687
Number (%) of patients censored	44 (80.0)	65 (67.0)	40 (58.8)	54 (65.9)	
Kaplan-Meier estimates of Social functioning in months					
25% quantile (95% CI)	NC (7.458 to NC)	13.93 (6.735 to 18.793)	4.90 (2.825 to 12.945)	12.55 (4.665 to 20.895)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (13.897 to NC)	NC (20.928 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.1033		0.3765	
Hazard ratio (95% CI) vs Kd	-	1.75 (0.88 to 3.48)		0.79 (0.47 to 1.33)	
P-value	-	0.1079		0.3776	
Deterioration probability (95% CI)[b]					

A higher score represents a better level of quality of life. Clinical meaningful deterioration change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
PGM=DEVOPS/SAR650984/EFC15246/CIR_RWE/REPORT/PGM/eff_km_subgp_sr_sig_de_i_t.sas OUT=REPORT/OUTPUT/eff_km_c30_soc_detpl_rreg_de_i_t_x.rtf (07APR2021 14:27)

16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Social functioning
16.2.6.1.2.7 Efficacy response data - Subgroup analyses by baseline ECOG PS
16.2.6.1.2.7.3 QLQ-C30 - Time to first improvement by 10 pt in social functioning according to baseline ECOG PS (LOCF) - ITT population

	0 or 1		>1		
	Kd (N=118)	**IKd (N=168)**	**Kd (N=5)**	**IKd (N=11)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	38 (32.2)	80 (47.6)	2 (40.0)	6 (54.5)	0.9834
Number (%) of patients censored	80 (67.8)	88 (52.4)	3 (60.0)	5 (45.5)	
Kaplan-Meier estimates of Social functioning in months					
25% quantile (95% CI)	2.83 (1.117 to 15.113)	1.15 (1.051 to 2.004)	0.99 (0.986 to NC)	1.02 (0.986 to 3.975)	
Median (95% CI)	NC (NC to NC)	NC (4.271 to NC)	NC (0.986 to NC)	3.98 (0.986 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (0.986 to NC)	NC (1.906 to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.0150		0.5223	
Hazard ratio (95% CI) vs Kd	-	1.61 (1.09 to 2.37)		1.68 (0.34 to 8.34)	
P-value	-	0.0159		0.5269	
Hazard ratio inverted (95% CI) vs IKd		-		0.60 (0.12 to 2.96)	

A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
PGM=DEVOPS/SAR650984/EFC15246/CIR_RWE/REPORT/PGM/eff_km_subgp_sr_sig_de_i_t.sas OUT=REPORT/OUTPUT/eff_km_c30_soc_impl_ecog_de_i_t_x.rtf (07APR2021 14:27)

16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Social functioning
16.2.6.1.2.7 Efficacy response data - Subgroup analyses by baseline ECOG PS
16.2.6.1.2.7.4 QLQ-C30 - Time to first deterioration by 10 pt in social functioning according to baseline ECOG PS (LOCF) - ITT population

	0 or 1		>1		
	Kd (N=118)	**IKd (N=168)**	**Kd (N=5)**	**IKd (N=11)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	73 (61.9)	113 (67.3)	3 (60.0)	5 (45.5)	0.7929
Number (%) of patients censored	45 (38.1)	55 (32.7)	2 (40.0)	6 (54.5)	
Kaplan-Meier estimates of Social functioning in months					
25% quantile (95% CI)	1.87 (1.117 to 2.103)	1.91 (1.248 to 2.037)	2.79 (2.070 to NC)	3.06 (1.216 to 4.797)	
Median (95% CI)	4.67 (2.924 to 8.575)	4.67 (3.023 to 6.538)	4.70 (2.070 to NC)	4.80 (1.216 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (16.559 to NC)	NC (2.070 to NC)	NC (3.450 to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.6077		0.8913	
Hazard ratio (95% CI) vs Kd	-	1.08 (0.80 to 1.45)		0.90 (0.22 to 3.81)	
P-value	-	0.6077		0.8914	
Deterioration probability (95% CI)[b]					

A higher score represents a better level of quality of life. Clinical meaningful deterioration change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
PGM=DEVOPS/SAR650984/EFC15246/CIR_RWE/REPORT/PGM/eff_km_subgp_sr_sig_de_i_t.sas OUT=REPORT/OUTPUT/eff_km_c30_soc_detl_ecog_de_i_t_x.rtf (07APR2021 14:26)

16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Social functioning
16.2.6.1.2.7 Efficacy response data - Subgroup analyses by baseline ECOG PS
16.2.6.1.2.7.5 QLQ-C30 - Time until permanent improvement by 10 pt in social functioning according to baseline ECOG PS (LOCF) - ITT population

	0 or 1		>1		
	Kd (N=118)	**IKd (N=168)**	**Kd (N=5)**	**IKd (N=11)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	18 (15.3)	41 (24.4)	2 (40.0)	3 (27.3)	0.4470
Number (%) of patients censored	100 (84.7)	127 (75.6)	3 (60.0)	8 (72.7)	
Kaplan-Meier estimates of Social functioning in months					
25% quantile (95% CI)	NC (22.144 to NC)	19.65 (13.996 to NC)	5.59 (2.858 to NC)	1.91 (0.986 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (2.858 to NC)	NC (0.986 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (2.858 to NC)	NC (NC to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.0668		0.9606	
Hazard ratio (95% CI) vs Kd	-	1.67 (0.96 to 2.91)		0.96 (0.16 to 5.76)	
P-value	-	0.0698		0.9604	
Improvement probability (95% CI)[b]					

A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
PGM=DEVOPS/SAR650984/EFC15246/CIR_RWE/REPORT/PGM/eff_km_subgp_sr_sig_de_i_t.sas OUT=REPORT/OUTPUT/eff_km_c30_soc_imppl_ecog_de_i_t_x.rtf (07APR2021 14:27)

16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Social functioning
16.2.6.1.2.7 Efficacy response data - Subgroup analyses by baseline ECOG PS
16.2.6.1.2.7.6 QLQ-C30 - Time until permanent deterioration by 10 pt in social functioning according to baseline ECOG PS (LOCF) - ITT population

	0 or 1		>1		
	Kd (N=118)	**IKd (N=168)**	**Kd (N=5)**	**IKd (N=11)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	37 (31.4)	56 (33.3)	2 (40.0)	4 (36.4)	0.7583
Number (%) of patients censored	81 (68.6)	112 (66.7)	3 (60.0)	7 (63.6)	
Kaplan-Meier estimates of Social functioning in months					
25% quantile (95% CI)	12.19 (4.895 to 24.016)	12.55 (6.735 to 17.774)	7.79 (2.793 to NC)	20.90 (5.191 to 20.928)	
Median (95% CI)	NC (24.016 to NC)	NC (NC to NC)	NC (2.793 to NC)	20.93 (5.191 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (2.793 to NC)	NC (20.895 to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.7915		0.7998	
Hazard ratio (95% CI) vs Kd	-	1.06 (0.70 to 1.60)		0.80 (0.14 to 4.43)	
P-value	-	0.7926		0.8001	
Deterioration probability (95% CI)[b]					

A higher score represents a better level of quality of life. Clinical meaningful deterioration change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Social functioning
16.2.6.1.2.8 Efficacy response data - Subgroup analyses by ISS staging at SE
16.2.6.1.2.8.3 QLQ-C30 - Time to first improvement by 10 pt in social functioning according to ISS staging at SE (LOCF) - ITT population

	I		II		III		
	Kd (N=71)	**IKd (N=89)**	**Kd (N=31)**	**IKd (N=63)**	**Kd (N=20)**	**IKd (N=26)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	25 (35.2)	36 (40.4)	10 (32.3)	34 (54.0)	5 (25.0)	15 (57.7)	0.1881
Number (%) of patients censored	46 (64.8)	53 (59.6)	21 (67.7)	29 (46.0)	15 (75.0)	11 (42.3)	
Kaplan-Meier estimates of Social functioning in months							
25% quantile (95% CI)	2.83 (1.117 to 15.113)	1.91 (1.051 to 4.271)	1.15 (0.986 to NC)	1.05 (1.018 to 1.971)	3.71 (0.953 to NC)	1.02 (0.953 to 1.906)	
Median (95% CI)	NC (NC to NC)	NC (10.185 to NC)	NC (2.825 to NC)	6.11 (2.004 to NC)	NC (3.713 to NC)	2.56 (1.051 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (2.891 to NC)	
Comparison vs. Kd							
Log-Rank test p-value[a] vs Kd	-	0.5120		0.1013		0.0198	
Hazard ratio (95% CI) vs Kd	-	1.19 (0.71 to 1.98)		1.79 (0.88 to 3.62)		3.15 (1.14 to 8.73)	
P-value	-	0.5125		0.1061		0.0270	

A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Social functioning
16.2.6.1.2.8 Efficacy response data - Subgroup analyses by ISS staging at SE
16.2.6.1.2.8.4 QLQ-C30 - Time to first deterioration by 10 pt in social functioning according to ISS staging at SE (LOCF) - ITT population

	I		II		III		
	Kd (N=71)	**IKd (N=89)**	**Kd (N=31)**	**IKd (N=63)**	**Kd (N=20)**	**IKd (N=26)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	42 (59.2)	62 (69.7)	21 (67.7)	44 (69.8)	12 (60.0)	12 (46.2)	0.2876
Number (%) of patients censored	29 (40.8)	27 (30.3)	10 (32.3)	19 (30.2)	8 (40.0)	14 (53.8)	
Kaplan-Meier estimates of Social functioning in months							
25% quantile (95% CI)	2.00 (1.084 to 2.825)	2.04 (1.150 to 2.858)	1.91 (1.248 to 2.924)	1.87 (1.084 to 1.971)	1.08 (0.953 to 2.793)	1.91 (0.986 to 13.766)	
Median (95% CI)	4.80 (3.055 to NC)	4.67 (3.023 to 5.651)	3.98 (2.070 to 15.540)	4.70 (1.971 to 8.279)	4.04 (1.084 to NC)	16.56 (2.004 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (9.429 to NC)	NC (6.374 to NC)	NC (8.279 to NC)	NC (4.041 to NC)	NC (18.300 to NC)	
Comparison vs. Kd							
Log-Rank test p-value[a] vs Kd	-	0.3369		0.6540		0.2306	
Hazard ratio (95% CI) vs Kd	-	1.21 (0.82 to 1.79)		1.13 (0.67 to 1.89)		0.61 (0.28 to 1.37)	

A higher score represents a better level of quality of life. Clinical meaningful deterioration change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
PGM=DEVOPS/SAR650984/EFC15246/CIR_RWE/REPORT/PGM/eff_km_subgp_sr_sig_de_i_t.sas OUT=REPORT/OUTPUT/eff_km_c30_soc_detl_seiss_de_i_t_x.rtf (07APR2021 14:26)

16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Social functioning
16.2.6.1.2.8 Efficacy response data - Subgroup analyses by ISS staging at SE
16.2.6.1.2.8.5 QLQ-C30 - Time until permanent improvement by 10 pt in social functioning according to ISS staging at SE (LOCF) - ITT population

	I		II		III		
	Kd (N=71)	**IKd (N=89)**	**Kd (N=31)**	**IKd (N=63)**	**Kd (N=20)**	**IKd (N=26)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	11 (15.5)	19 (21.3)	6 (19.4)	17 (27.0)	3 (15.0)	8 (30.8)	0.6824
Number (%) of patients censored	60 (84.5)	70 (78.7)	25 (80.6)	46 (73.0)	17 (85.0)	18 (69.2)	
Kaplan-Meier estimates of Social functioning in months							
25% quantile (95% CI)	NC (19.384 to NC)	NC (12.550 to NC)	22.14 (12.386 to NC)	20.14 (12.682 to NC)	NC (0.953 to NC)	2.10 (0.986 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (22.144 to NC)	NC (22.604 to NC)	NC (NC to NC)	NC (7.458 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Kd							
Log-Rank test p-value[a] vs Kd	-	0.2999		0.4986		0.1873	
Hazard ratio (95% CI) vs Kd	-	1.48 (0.70 to 3.11)		1.38 (0.54 to 3.51)		2.38 (0.63 to 8.99)	
P-value	-	0.3030		0.5005		0.2010	

A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
PGM=DEVOPS/SAR650984/EFC15246/CIR_RWE/REPORT/PGM/eff_km_subgp_sr_sig_de_i_t.sas OUT=REPORT/OUTPUT/eff_km_c30_soc_imppl_seiss_de_i_t_x.rtf (07APR2021 14:27)

16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Social functioning
16.2.6.1.2.8 Efficacy response data - Subgroup analyses by ISS staging at SE
16.2.6.1.2.8.6 QLQ-C30 - Time until permanent deterioration by 10 pt in social functioning according to ISS staging at SE (LOCF) - ITT population

	I		II		III		
	Kd (N=71)	**IKd (N=89)**	**Kd (N=31)**	**IKd (N=63)**	**Kd (N=20)**	**IKd (N=26)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	19 (26.8)	30 (33.7)	10 (32.3)	24 (38.1)	9 (45.0)	6 (23.1)	0.1931
Number (%) of patients censored	52 (73.2)	59 (66.3)	21 (67.7)	39 (61.9)	11 (55.0)	20 (76.9)	
Kaplan-Meier estimates of Social functioning in months							
25% quantile (95% CI)	16.69 (4.895 to NC)	12.55 (5.520 to 21.421)	12.19 (1.906 to NC)	13.63 (5.782 to 19.877)	2.86 (1.051 to 9.363)	10.91 (0.986 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	24.02 (18.300 to NC)	NC (19.877 to NC)	13.96 (2.858 to NC)	NC (10.908 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (24.016 to NC)	NC (NC to NC)	NC (13.963 to NC)	NC (NC to NC)	
Comparison vs. Kd							
Log-Rank test p-value[a] vs Kd	-	0.3764		0.5920		0.1239	
Hazard ratio (95% CI) vs Kd	-	1.30 (0.73 to 2.30)		1.23 (0.58 to 2.58)		0.45 (0.16 to 1.28)	
P-value	-	0.3778		0.5926		0.1337	

A higher score represents a better level of quality of life. Clinical meaningful deterioration change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Social functioning
16.2.6.1.2.9 Efficacy response data - Subgroup analyses by R-ISS stage at SE
16.2.6.1.2.9.3 QLQ-C30 - Time to first improvement by 10 pt in social functioning according to R-ISS stage at SE (LOCF) - ITT population

	I or II		III		Not classified		
	Kd (N=103)	**IKd (N=155)**	**Kd (N=8)**	**IKd (N=16)**	**Kd (N=12)**	**IKd (N=8)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	32 (31.1)	75 (48.4)	3 (37.5)	7 (43.8)	5 (41.7)	4 (50.0)	0.8920
Number (%) of patients censored	71 (68.9)	80 (51.6)	5 (62.5)	9 (56.3)	7 (58.3)	4 (50.0)	
Kaplan-Meier estimates of Social functioning in months							
25% quantile (95% CI)	2.83 (1.117 to NC)	1.15 (1.051 to 1.971)	1.05 (0.953 to NC)	1.91 (0.953 to 4.961)	3.79 (0.953 to NC)	2.92 (1.018 to 3.975)	
Median (95% CI)	NC (NC to NC)	NC (4.271 to NC)	NC (0.953 to NC)	4.96 (1.018 to NC)	NC (0.986 to NC)	3.48 (1.018 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (1.117 to NC)	NC (4.961 to NC)	NC (NC to NC)	NC (2.924 to NC)	
Comparison vs. Kd							
Log-Rank test p-value[a] vs Kd	-	0.0127		0.7876		0.3092	
Hazard ratio (95% CI) vs Kd	-	1.68 (1.11 to 2.55)		1.20 (0.31 to 4.67)		1.99 (0.52 to 7.68)	
P-value	-	0.0138		0.7879		0.3177	
Hazard ratio inverted (95% CI) vs IKd		-		0.83 (0.21 to 3.22)		0.50 (0.13 to 1.94)	

A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Social functioning
16.2.6.1.2.9 Efficacy response data - Subgroup analyses by R-ISS stage at SE
16.2.6.1.2.9.4 QLQ-C30 - Time to first deterioration by 10 pt in social functioning according to R-ISS stage at SE (LOCF) - ITT population

	I or II		III		Not classified		
	Kd (N=103)	**IKd (N=155)**	**Kd (N=8)**	**IKd (N=16)**	**Kd (N=12)**	**IKd (N=8)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	61 (59.2)	109 (70.3)	5 (62.5)	7 (43.8)	10 (83.3)	2 (25.0)	0.0338
Number (%) of patients censored	42 (40.8)	46 (29.7)	3 (37.5)	9 (56.3)	2 (16.7)	6 (75.0)	
Kaplan-Meier estimates of Social functioning in months							
25% quantile (95% CI)	2.00 (1.248 to 2.825)	1.91 (1.183 to 2.037)	1.08 (0.986 to 2.793)	1.91 (1.084 to 18.300)	1.07 (0.953 to 1.873)	3.06 (2.825 to NC)	
Median (95% CI)	5.03 (3.055 to 13.405)	4.67 (2.990 to 5.618)	2.79 (0.986 to NC)	18.30 (1.413 to NC)	2.33 (0.953 to 15.244)	NC (2.825 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (12.715 to NC)	NC (1.117 to NC)	NC (16.559 to NC)	9.95 (1.873 to NC)	NC (3.055 to NC)	
Comparison vs. Kd							
Log-Rank test p-value[a] vs Kd	-	0.1623		0.3155		0.0475	
Hazard ratio (95% CI) vs Kd	-	1.25 (0.91 to 1.71)		0.56 (0.18 to 1.77)		0.24 (0.05 to 1.11)	

A higher score represents a better level of quality of life. Clinical meaningful deterioration change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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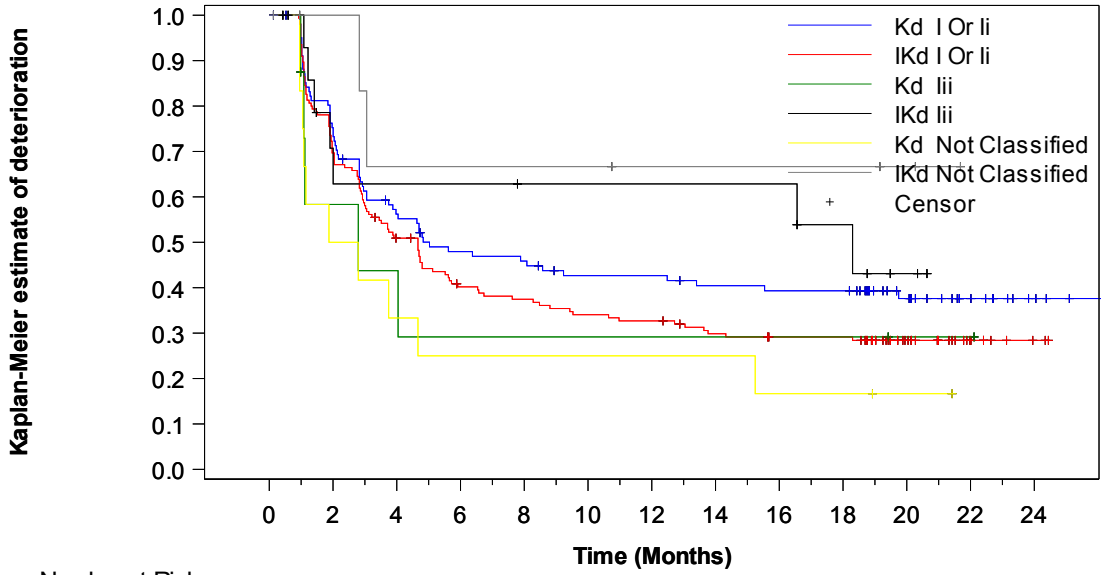
16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Social functioning
16.2.6.1.2.9 Efficacy response data - Subgroup analyses by R-ISS stage at SE
16.2.6.1.2.9.5 QLQ-C30 - Time to first deterioration by 10 pt in social functioning according to R-ISS stage at SE - Kaplan-Meier curve (LOCF) - ITT population



Number at Risk									
Kd I Or Ii	103	61	46	40	39	36	35	17	4
IKd I Or Ii	155	90	59	52	48	41	39	14	2
Kd Iii	8	3	2	2	2	2	2	1	0
IKd Iii	16	8	8	7	7	7	5	0	0
Kd Not Classified	12	5	3	3	3	3	2	1	0
IKd Not Classified	8	5	4	4	3	3	3	1	0

A higher score represents a better level of quality of life. Clinical meaningful deterioration change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
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16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Social functioning
16.2.6.1.2.9 Efficacy response data - Subgroup analyses by R-ISS stage at SE
16.2.6.1.2.9.6 QLQ-C30 - Time until permanent improvement by 10 pt in social functioning according to R-ISS stage at SE (LOCF) - ITT population

	I or II		III		Not classified		
	Kd (N=103)	**IKd (N=155)**	**Kd (N=8)**	**IKd (N=16)**	**Kd (N=12)**	**IKd (N=8)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	15 (14.6)	38 (24.5)	2 (25.0)	5 (31.3)	3 (25.0)	1 (12.5)	0.8442
Number (%) of patients censored	88 (85.4)	117 (75.5)	6 (75.0)	11 (68.8)	9 (75.0)	7 (87.5)	
Kaplan-Meier estimates of Social functioning in months							
25% quantile (95% CI)	NC (22.144 to NC)	20.14 (13.996 to NC)	1.12 (0.953 to NC)	2.10 (0.986 to NC)	22.47 (5.060 to NC)	NC (6.144 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (0.953 to NC)	NC (1.906 to NC)	22.47 (15.934 to NC)	NC (6.144 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (17.511 to NC)	NC (22.472 to NC)	NC (NC to NC)	
Comparison vs. Kd							
Log-Rank test p-value[a] vs Kd	-	0.0831		0.7375		0.8994	
Hazard ratio (95% CI) vs Kd	-	1.69 (0.93 to 3.07)		1.32 (0.26 to 6.85)		1.17 (0.10 to 13.20)	
P-value	-	0.0867		0.7383		0.8995	

A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
PGM=DEVOPS/SAR650984/EFC15246/CIR_RWE/REPORT/PGM/eff_km_subgp_sr_sig_de_i_t.sas OUT=REPORT/OUTPUT/eff_km_c30_soc_imppl_seriss_de_i_t_x.rtf (07APR2021 14:27)

16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Social functioning
16.2.6.1.2.9 Efficacy response data - Subgroup analyses by R-ISS stage at SE
16.2.6.1.2.9.7 QLQ-C30 - Time until permanent deterioration by 10 pt in social functioning according to R-ISS stage at SE (LOCF) - ITT population

	I or II		III		Not classified		
	Kd (N=103)	**IKd (N=155)**	**Kd (N=8)**	**IKd (N=16)**	**Kd (N=12)**	**IKd (N=8)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	30 (29.1)	56 (36.1)	5 (62.5)	3 (18.8)	4 (33.3)	1 (12.5)	0.0816
Number (%) of patients censored	73 (70.9)	99 (63.9)	3 (37.5)	13 (81.3)	8 (66.7)	7 (87.5)	
Kaplan-Meier estimates of Social functioning in months							
25% quantile (95% CI)	9.76 (4.862 to NC)	12.55 (6.439 to 16.854)	2.79 (1.117 to 5.815)	NC (1.413 to NC)	13.42 (11.368 to NC)	NC (2.825 to NC)	
Median (95% CI)	NC (24.016 to NC)	NC (NC to NC)	5.82 (1.117 to NC)	NC (10.908 to NC)	NC (12.945 to NC)	NC (2.825 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (4.041 to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Kd							
Log-Rank test p-value[a] vs Kd	-	0.4048		0.0269		0.6734	
Hazard ratio (95% CI) vs Kd	-	1.21 (0.77 to 1.88)		0.23 (0.05 to 0.95)		0.63 (0.07 to 5.63)	
P-value	-	0.4055		0.0427		0.6762	

A higher score represents a better level of quality of life. Clinical meaningful deterioration change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Social functioning
16.2.6.1.2.10 Efficacy response data - Subgroup analyses by nb of prior lines
16.2.6.1.2.10.3 QLQ-C30 - Time to first improvement by 10 pt in social functioning according to nb of prior lines (LOCF) - ITT population

	1		>1		
	Kd (N=55)	**IKd (N=79)**	**Kd (N=68)**	**IKd (N=100)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	19 (34.5)	37 (46.8)	21 (30.9)	49 (49.0)	0.6326
Number (%) of patients censored	36 (65.5)	42 (53.2)	47 (69.1)	51 (51.0)	
Kaplan-Meier estimates of Social functioning in months					
25% quantile (95% CI)	3.15 (1.051 to NC)	1.22 (1.051 to 2.891)	2.43 (1.018 to NC)	1.15 (1.018 to 1.971)	
Median (95% CI)	NC (15.113 to NC)	NC (3.975 to NC)	NC (NC to NC)	10.18 (2.891 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.1667		0.0297	
Hazard ratio (95% CI) vs Kd	-	1.47 (0.85 to 2.56)		1.75 (1.05 to 2.92)	
P-value	-	0.1694		0.0320	
Hazard ratio inverted (95% CI) vs IKd		-		0.57 (0.34 to 0.95)	

A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Social functioning
16.2.6.1.2.10 Efficacy response data - Subgroup analyses by nb of prior lines
16.2.6.1.2.10.4 QLQ-C30 - Time to first deterioration by 10 pt in social functioning according to nb of prior lines (LOCF) - ITT population

	1		>1		
	Kd (N=55)	**IKd (N=79)**	**Kd (N=68)**	**IKd (N=100)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	32 (58.2)	47 (59.5)	44 (64.7)	71 (71.0)	0.9926
Number (%) of patients censored	23 (41.8)	32 (40.5)	24 (35.3)	29 (29.0)	
Kaplan-Meier estimates of Social functioning in months					
25% quantile (95% CI)	2.10 (1.117 to 3.745)	2.04 (1.413 to 2.924)	1.28 (1.051 to 2.037)	1.87 (1.084 to 1.971)	
Median (95% CI)	6.85 (3.745 to NC)	5.65 (3.220 to 18.300)	3.06 (2.070 to 7.885)	3.71 (2.825 to 5.618)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (9.232 to NC)	NC (8.805 to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.8004		0.7431	
Hazard ratio (95% CI) vs Kd	-	1.06 (0.68 to 1.66)		1.06 (0.73 to 1.55)	
P-value	-	0.8014		0.7448	
Deterioration probability (95% CI)[b]					

A higher score represents a better level of quality of life. Clinical meaningful deterioration change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Social functioning
16.2.6.1.2.10 Efficacy response data - Subgroup analyses by nb of prior lines
16.2.6.1.2.10.5 QLQ-C30 - Time until permanent improvement by 10 pt in social functioning according to nb of prior lines (LOCF) - ITT population

	1		>1		
	Kd (N=55)	**IKd (N=79)**	**Kd (N=68)**	**IKd (N=100)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	13 (23.6)	16 (20.3)	7 (10.3)	28 (28.0)	0.0258
Number (%) of patients censored	42 (76.4)	63 (79.7)	61 (89.7)	72 (72.0)	
Kaplan-Meier estimates of Social functioning in months					
25% quantile (95% CI)	22.14 (1.873 to NC)	NC (12.550 to NC)	NC (19.384 to NC)	17.51 (12.025 to 22.604)	
Median (95% CI)	NC (22.472 to NC)	NC (NC to NC)	NC (NC to NC)	NC (22.604 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.6981		0.0066	
Hazard ratio (95% CI) vs Kd	-	0.87 (0.42 to 1.80)		2.98 (1.30 to 6.83)	
P-value	-	0.6984		0.0097	
Hazard ratio inverted (95% CI) vs IKd		-		0.34 (0.15 to 0.77)	

A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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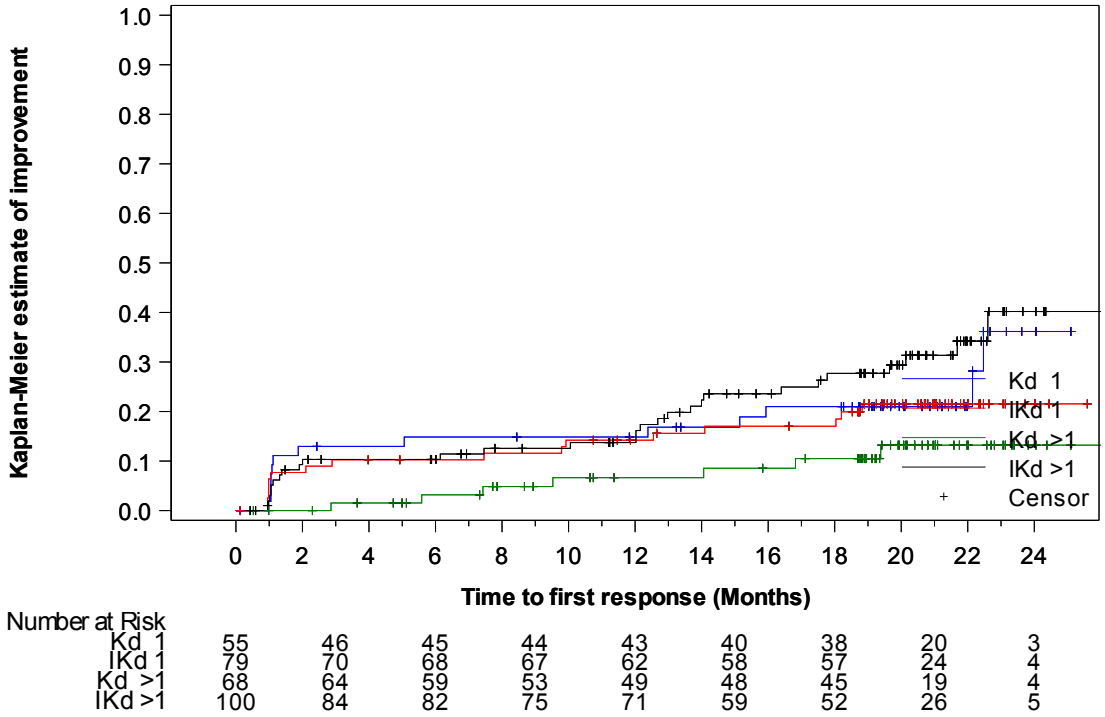
16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Social functioning
16.2.6.1.2.10 Efficacy response data - Subgroup analyses by nb of prior lines
16.2.6.1.2.10.6 QLQ-C30 - Time until permanent improvement by 10 pt in social functioning according to nb of prior lines - Kaplan-Meier curve (LOCF) - ITT population



Number at Risk

Kd 1	55	46	45	44	43	40	38	20	3
IKd 1	79	70	68	67	62	58	57	24	4
Kd >1	68	64	59	53	49	48	45	19	4
IKd >1	100	84	82	75	71	59	52	26	5

A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
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16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Social functioning
16.2.6.1.2.10 Efficacy response data - Subgroup analyses by nb of prior lines
16.2.6.1.2.10.7 QLQ-C30 - Time until permanent deterioration by 10 pt in social functioning according to nb of prior lines (LOCF) - ITT population

	1		>1		
	Kd (N=55)	**IKd (N=79)**	**Kd (N=68)**	**IKd (N=100)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	15 (27.3)	23 (29.1)	24 (35.3)	37 (37.0)	0.9069
Number (%) of patients censored	40 (72.7)	56 (70.9)	44 (64.7)	63 (63.0)	
Kaplan-Meier estimates of Social functioning in months					
25% quantile (95% CI)	18.30 (3.680 to NC)	14.78 (7.918 to NC)	7.79 (3.055 to 13.963)	7.98 (3.844 to 17.774)	
Median (95% CI)	24.02 (24.016 to NC)	NC (NC to NC)	NC (18.924 to NC)	NC (20.895 to NC)	
75% quantile (95% CI)	NC (24.016 to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.8136		0.9286	
Hazard ratio (95% CI) vs Kd	-	1.08 (0.56 to 2.07)		1.02 (0.61 to 1.71)	
P-value	-	0.8136		0.9288	
Deterioration probability (95% CI)[b]					

A higher score represents a better level of quality of life. Clinical meaningful deterioration change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Social functioning
16.2.6.1.2.11 Efficacy response data - Subgroup analyses by cytogenetic abnormality
16.2.6.1.2.11.3 QLQ-C30 - Time to first improvement by 10 pt in social functioning according to cytogenetic abnormality (LOCF) - ITT population

	At least one		None		
	Kd (N=31)	**IKd (N=42)**	**Kd (N=77)**	**IKd (N=114)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	9 (29.0)	18 (42.9)	26 (33.8)	56 (49.1)	0.9499
Number (%) of patients censored	22 (71.0)	24 (57.1)	51 (66.2)	58 (50.9)	
Kaplan-Meier estimates of Social functioning in months					
25% quantile (95% CI)	1.91 (1.051 to NC)	1.84 (0.986 to 2.957)	2.43 (1.051 to 6.472)	1.08 (1.051 to 1.906)	
Median (95% CI)	NC (NC to NC)	NC (2.103 to NC)	NC (NC to NC)	20.73 (3.417 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.3013		0.0480	
Hazard ratio (95% CI) vs Kd	-	1.52 (0.68 to 3.39)		1.59 (1.00 to 2.54)	
P-value	-	0.3049		0.0501	
Improvement probability (95% CI)[b]					

A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Social functioning
16.2.6.1.2.11 Efficacy response data - Subgroup analyses by cytogenetic abnormality
16.2.6.1.2.11.4 QLQ-C30 - Time to first deterioration by 10 pt in social functioning according to cytogenetic abnormality (LOCF) - ITT population

	At least one		None		
	Kd (N=31)	**IKd (N=42)**	**Kd (N=77)**	**IKd (N=114)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	21 (67.7)	27 (64.3)	45 (58.4)	78 (68.4)	0.2760
Number (%) of patients censored	10 (32.3)	15 (35.7)	32 (41.6)	36 (31.6)	
Kaplan-Meier estimates of Social functioning in months					
25% quantile (95% CI)	2.07 (0.986 to 2.825)	1.91 (1.084 to 2.924)	1.91 (1.150 to 2.793)	1.91 (1.183 to 2.366)	
Median (95% CI)	3.89 (2.793 to 12.485)	4.67 (2.760 to 18.300)	5.03 (2.858 to 19.745)	4.67 (2.924 to 5.717)	
75% quantile (95% CI)	NC (4.830 to NC)	NC (9.528 to NC)	NC (NC to NC)	NC (12.715 to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.5829		0.2432	
Hazard ratio (95% CI) vs Kd	-	0.85 (0.48 to 1.51)		1.24 (0.86 to 1.80)	
P-value	-	0.5832		0.2441	
Deterioration probability (95% CI)[b]					

A higher score represents a better level of quality of life. Clinical meaningful deterioration change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Social functioning
16.2.6.1.2.11 Efficacy response data - Subgroup analyses by cytogenetic abnormality
16.2.6.1.2.11.5 QLQ-C30 - Time until permanent improvement by 10 pt in social functioning according to cytogenetic abnormality (LOCF) - ITT population

	At least one		None		
	Kd (N=31)	**IKd (N=42)**	**Kd (N=77)**	**IKd (N=114)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	3 (9.7)	9 (21.4)	15 (19.5)	29 (25.4)	0.4370
Number (%) of patients censored	28 (90.3)	33 (78.6)	62 (80.5)	85 (74.6)	
Kaplan-Meier estimates of Social functioning in months					
25% quantile (95% CI)	NC (7.425 to NC)	NC (1.117 to NC)	22.14 (15.146 to NC)	18.83 (13.996 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.2213		0.3888	
Hazard ratio (95% CI) vs Kd	-	2.21 (0.60 to 8.18)		1.31 (0.70 to 2.45)	
P-value	-	0.2334		0.3903	
Improvement probability (95% CI)[b]					

A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Social functioning
16.2.6.1.2.11 Efficacy response data - Subgroup analyses by cytogenetic abnormality
16.2.6.1.2.11.6 QLQ-C30 - Time until permanent deterioration by 10 pt in social functioning according to cytogenetic abnormality (LOCF) - ITT population

	At least one		None		
	Kd (N=31)	**IKd (N=42)**	**Kd (N=77)**	**IKd (N=114)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	13 (41.9)	17 (40.5)	22 (28.6)	36 (31.6)	0.7271
Number (%) of patients censored	18 (58.1)	25 (59.5)	55 (71.4)	78 (68.4)	
Kaplan-Meier estimates of Social functioning in months					
25% quantile (95% CI)	4.04 (2.103 to 13.963)	6.74 (2.924 to 14.784)	12.94 (4.862 to NC)	14.88 (7.951 to 20.895)	
Median (95% CI)	NC (7.786 to NC)	NC (10.480 to NC)	NC (24.016 to NC)	NC (21.421 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.7689		0.7651	
Hazard ratio (95% CI) vs Kd	-	0.90 (0.44 to 1.85)		1.08 (0.64 to 1.84)	
P-value	-	0.7690		0.7652	
Deterioration probability (95% CI)[b]					

A higher score represents a better level of quality of life. Clinical meaningful deterioration change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Social functioning
16.2.6.1.2.12 Efficacy response data - Subgroup analyses by MM type at SE
16.2.6.1.2.12.3 QLQ-C30 - Time to first improvement by 10 pt in social functioning according to MM type at SE (LOCF) - ITT population

	IgG		Non-IgG		
	Kd (N=85)	**IKd (N=126)**	**Kd (N=38)**	**IKd (N=53)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	27 (31.8)	59 (46.8)	13 (34.2)	27 (50.9)	0.7073
Number (%) of patients censored	58 (68.2)	67 (53.2)	25 (65.8)	26 (49.1)	
Kaplan-Meier estimates of Social functioning in months					
25% quantile (95% CI)	3.71 (1.117 to NC)	1.12 (1.051 to 2.004)	2.04 (0.986 to NC)	1.84 (0.986 to 2.563)	
Median (95% CI)	NC (NC to NC)	NC (3.417 to NC)	NC (3.154 to NC)	20.73 (2.037 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.0220		0.2569	
Hazard ratio (95% CI) vs Kd	-	1.69 (1.07 to 2.67)		1.46 (0.75 to 2.84)	
P-value	-	0.0236		0.2598	
Hazard ratio inverted (95% CI) vs IKd		-		0.68 (0.35 to 1.32)	

A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Social functioning
16.2.6.1.2.12 Efficacy response data - Subgroup analyses by MM type at SE
16.2.6.1.2.12.4 QLQ-C30 - Time to first deterioration by 10 pt in social functioning according to MM type at SE (LOCF) - ITT population

	IgG		Non-IgG		
	Kd (N=85)	**IKd (N=126)**	**Kd (N=38)**	**IKd (N=53)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	53 (62.4)	85 (67.5)	23 (60.5)	33 (62.3)	0.7371
Number (%) of patients censored	32 (37.6)	41 (32.5)	15 (39.5)	20 (37.7)	
Kaplan-Meier estimates of Social functioning in months					
25% quantile (95% CI)	1.31 (1.084 to 2.070)	1.91 (1.183 to 2.037)	2.09 (0.986 to 4.041)	2.04 (1.084 to 3.713)	
Median (95% CI)	3.75 (2.825 to 12.485)	3.75 (2.891 to 5.618)	5.62 (3.055 to NC)	6.74 (3.023 to 18.300)	
75% quantile (95% CI)	NC (19.745 to NC)	NC (12.715 to NC)	NC (9.232 to NC)	NC (13.766 to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.5939		0.9652	
Hazard ratio (95% CI) vs Kd	-	1.10 (0.78 to 1.55)		0.99 (0.58 to 1.68)	
P-value	-	0.5940		0.9651	
Deterioration probability (95% CI)[b]					

A higher score represents a better level of quality of life. Clinical meaningful deterioration change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Social functioning
16.2.6.1.2.12 Efficacy response data - Subgroup analyses by MM type at SE
16.2.6.1.2.12.5 QLQ-C30 - Time until permanent improvement by 10 pt in social functioning according to MM type at SE (LOCF) - ITT population

	IgG		Non-IgG		
	Kd (N=85)	**IKd (N=126)**	**Kd (N=38)**	**IKd (N=53)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	15 (17.6)	31 (24.6)	5 (13.2)	13 (24.5)	0.7205
Number (%) of patients censored	70 (82.4)	95 (75.4)	33 (86.8)	40 (75.5)	
Kaplan-Meier estimates of Social functioning in months					
25% quantile (95% CI)	22.47 (15.934 to NC)	19.65 (12.977 to NC)	NC (5.585 to NC)	16.39 (2.004 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (21.684 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.1896		0.2402	
Hazard ratio (95% CI) vs Kd	-	1.51 (0.81 to 2.79)		1.84 (0.66 to 5.16)	
P-value	-	0.1928		0.2474	
Improvement probability (95% CI)[b]					

A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Social functioning
16.2.6.1.2.12 Efficacy response data - Subgroup analyses by MM type at SE
16.2.6.1.2.12.6 QLQ-C30 - Time until permanent deterioration by 10 pt in social functioning according to MM type at SE (LOCF) - ITT population

	IgG		Non-IgG		
	Kd (N=85)	**IKd (N=126)**	**Kd (N=38)**	**IKd (N=53)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	26 (30.6)	45 (35.7)	13 (34.2)	15 (28.3)	0.4269
Number (%) of patients censored	59 (69.4)	81 (64.3)	25 (65.8)	38 (71.7)	
Kaplan-Meier estimates of Social functioning in months					
25% quantile (95% CI)	11.37 (3.680 to NC)	12.55 (7.524 to 18.793)	9.36 (3.055 to 24.016)	7.92 (3.844 to NC)	
Median (95% CI)	NC (NC to NC)	NC (20.928 to NC)	24.02 (18.924 to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (24.016 to NC)	NC (NC to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.5209		0.6379	
Hazard ratio (95% CI) vs Kd	-	1.17 (0.72 to 1.90)		0.84 (0.40 to 1.77)	
P-value	-	0.5213		0.6383	
Deterioration probability (95% CI)[b]					

A higher score represents a better level of quality of life. Clinical meaningful deterioration change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Social functioning
16.2.6.1.2.13 Efficacy response data - Subgroup analyses by previous autologous stem-cell
16.2.6.1.2.13.3 QLQ-C30 - Time to first improvement by 10 pt in social functioning according to previous autologous stem-cell (LOCF) - ITT population

	Yes		No		
	Kd (N=69)	**IKd (N=116)**	**Kd (N=54)**	**IKd (N=63)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	20 (29.0)	52 (44.8)	20 (37.0)	34 (54.0)	0.7503
Number (%) of patients censored	49 (71.0)	64 (55.2)	34 (63.0)	29 (46.0)	
Kaplan-Meier estimates of Social functioning in months					
25% quantile (95% CI)	3.71 (1.150 to NC)	1.15 (1.018 to 2.366)	1.12 (1.018 to 3.285)	1.13 (1.051 to 2.004)	
Median (95% CI)	NC (NC to NC)	NC (4.961 to NC)	NC (3.285 to NC)	4.12 (2.004 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.0327		0.1186	
Hazard ratio (95% CI) vs Kd	-	1.74 (1.04 to 2.92)		1.55 (0.89 to 2.69)	
P-value	-	0.0350		0.1216	
Hazard ratio inverted (95% CI) vs IKd		-		0.65 (0.37 to 1.12)	

A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Social functioning
16.2.6.1.2.13 Efficacy response data - Subgroup analyses by previous autologous stem-cell
16.2.6.1.2.13.4 QLQ-C30 - Time to first deterioration by 10 pt in social functioning according to previous autologous stem-cell (LOCF) - ITT population

	Yes		No		
	Kd (N=69)	**IKd (N=116)**	**Kd (N=54)**	**IKd (N=63)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	39 (56.5)	79 (68.1)	37 (68.5)	39 (61.9)	0.1660
Number (%) of patients censored	30 (43.5)	37 (31.9)	17 (31.5)	24 (38.1)	
Kaplan-Meier estimates of Social functioning in months					
25% quantile (95% CI)	1.91 (1.051 to 2.825)	1.87 (1.117 to 2.793)	1.91 (1.084 to 2.136)	1.94 (1.248 to 2.760)	
Median (95% CI)	7.89 (2.924 to NC)	4.67 (2.990 to 6.538)	3.88 (2.136 to 4.830)	5.13 (2.760 to 10.973)	
75% quantile (95% CI)	NC (NC to NC)	NC (13.043 to NC)	NC (4.830 to NC)	NC (18.300 to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.2261		0.4318	
Hazard ratio (95% CI) vs Kd	-	1.27 (0.86 to 1.86)		0.83 (0.53 to 1.31)	
P-value	-	0.2272		0.4324	
Deterioration probability (95% CI)[b]					

A higher score represents a better level of quality of life. Clinical meaningful deterioration change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Social functioning
16.2.6.1.2.13 Efficacy response data - Subgroup analyses by previous autologous stem-cell
16.2.6.1.2.13.5 QLQ-C30 - Time until permanent improvement by 10 pt in social functioning according to previous autologous stem-cell (LOCF) - ITT population

	Yes		No		
	Kd (N=69)	**IKd (N=116)**	**Kd (N=54)**	**IKd (N=63)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	9 (13.0)	29 (25.0)	11 (20.4)	15 (23.8)	0.3065
Number (%) of patients censored	60 (87.0)	87 (75.0)	43 (79.6)	48 (76.2)	
Kaplan-Meier estimates of Social functioning in months					
25% quantile (95% CI)	NC (22.144 to NC)	18.83 (12.682 to NC)	NC (7.425 to NC)	20.14 (7.458 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (22.604 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.0472		0.6614	
Hazard ratio (95% CI) vs Kd	-	2.10 (0.99 to 4.44)		1.19 (0.55 to 2.59)	
P-value	-	0.0524		0.6618	
Improvement probability (95% CI)[b]					

A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Social functioning
16.2.6.1.2.13 Efficacy response data - Subgroup analyses by previous autologous stem-cell
16.2.6.1.2.13.6 QLQ-C30 - Time until permanent deterioration by 10 pt in social functioning according to previous autologous stem-cell (LOCF) - ITT population

	Yes		No		
	Kd (N=69)	**IKd (N=116)**	**Kd (N=54)**	**IKd (N=63)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	18 (26.1)	38 (32.8)	21 (38.9)	22 (34.9)	0.4091
Number (%) of patients censored	51 (73.9)	78 (67.2)	33 (61.1)	41 (65.1)	
Kaplan-Meier estimates of Social functioning in months					
25% quantile (95% CI)	11.37 (4.041 to NC)	14.00 (5.782 to 20.928)	9.99 (2.858 to 18.300)	12.55 (5.520 to 19.877)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	24.02 (16.690 to NC)	NC (19.877 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (24.016 to NC)	NC (NC to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.4250		0.7147	
Hazard ratio (95% CI) vs Kd	-	1.26 (0.72 to 2.20)		0.89 (0.49 to 1.63)	
P-value	-	0.4260		0.7139	
Deterioration probability (95% CI)[b]					

A higher score represents a better level of quality of life. Clinical meaningful deterioration change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Social functioning
16.2.6.1.2.14 Efficacy response data - Subgroup analyses by baseline eGFR (MDRD)
16.2.6.1.2.14.3 QLQ-C30 - Time to first improvement by 10 pt in social functioning according to baseline eGFR (MDRD) (LOCF) - ITT population

	>=60 mL/min/1.73m2		<60 mL/min/1.73m2		
	Kd (N=93)	**IKd (N=122)**	**Kd (N=18)**	**IKd (N=43)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	34 (36.6)	57 (46.7)	4 (22.2)	25 (58.1)	0.1803
Number (%) of patients censored	59 (63.4)	65 (53.3)	14 (77.8)	18 (41.9)	
Kaplan-Meier estimates of Social functioning in months					
25% quantile (95% CI)	1.89 (1.051 to 3.285)	1.15 (1.051 to 2.004)	15.11 (0.986 to NC)	1.05 (0.986 to 2.004)	
Median (95% CI)	NC (NC to NC)	20.73 (3.975 to NC)	NC (15.113 to NC)	2.89 (1.971 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.1326		0.0350	
Hazard ratio (95% CI) vs Kd	-	1.38 (0.90 to 2.12)		2.96 (1.03 to 8.50)	
P-value	-	0.1343		0.0445	
Hazard ratio inverted (95% CI) vs IKd		-		0.34 (0.12 to 0.97)	

A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
PGM=DEVOPS/SAR650984/EFC15246/CIR_RWE/REPORT/PGM/eff_km_subgp_sr_sig_de_i_t.sas OUT=REPORT/OUTPUT/eff_km_c30_soc_impl_crcl_de_i_t_x.rtf (07APR2021 14:27)

16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Social functioning
16.2.6.1.2.14 Efficacy response data - Subgroup analyses by baseline eGFR (MDRD)
16.2.6.1.2.14.4 QLQ-C30 - Time to first deterioration by 10 pt in social functioning according to baseline eGFR (MDRD) (LOCF) - ITT population

	>=60 mL/min/1.73m2		<60 mL/min/1.73m2		
	Kd (N=93)	**IKd (N=122)**	**Kd (N=18)**	**IKd (N=43)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	57 (61.3)	83 (68.0)	15 (83.3)	27 (62.8)	0.0083
Number (%) of patients censored	36 (38.7)	39 (32.0)	3 (16.7)	16 (37.2)	
Kaplan-Meier estimates of Social functioning in months					
25% quantile (95% CI)	1.91 (1.084 to 2.793)	1.91 (1.183 to 2.366)	1.31 (0.986 to 1.971)	1.31 (1.051 to 2.793)	
Median (95% CI)	4.75 (3.055 to 15.244)	3.88 (2.924 to 5.520)	2.83 (1.150 to 4.041)	6.57 (2.037 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (9.429 to NC)	4.83 (1.971 to 12.485)	NC (12.715 to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.2197		0.0203	
Hazard ratio (95% CI) vs Kd	-	1.24 (0.88 to 1.73)		0.47 (0.25 to 0.90)	
P-value	-	0.2206		0.0232	
Deterioration probability (95% CI)[b]					

A higher score represents a better level of quality of life. Clinical meaningful deterioration change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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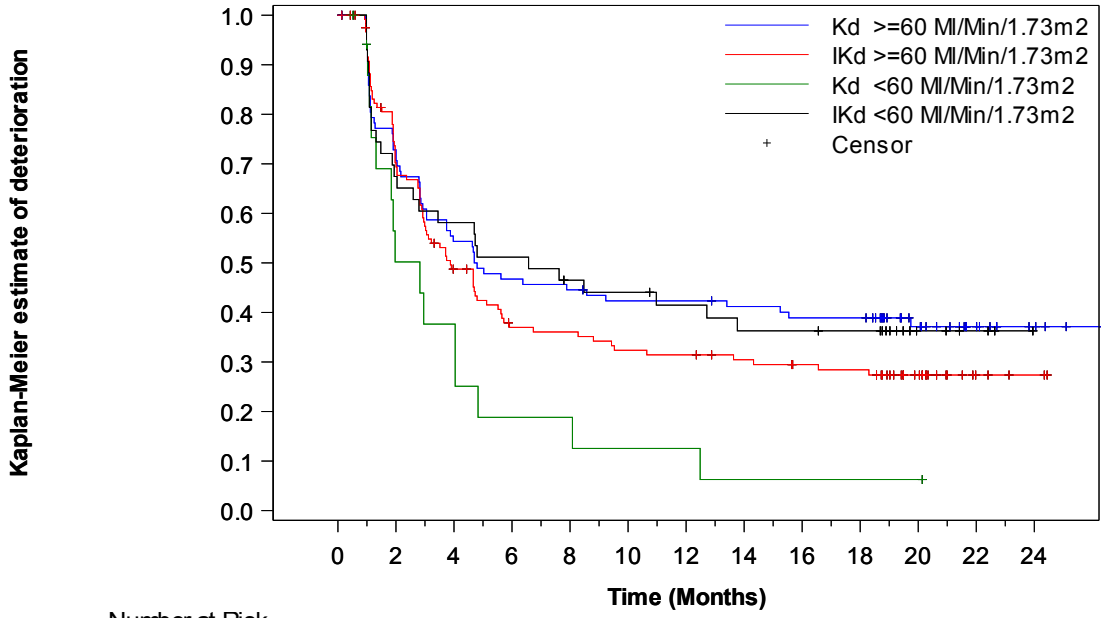
16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Social functioning
16.2.6.1.2.14 Efficacy response data - Subgroup analyses by baseline eGFR (MDRD)
16.2.6.1.2.14.5 QLQ-C30 - Time to first deterioration by 10 pt in social functioning according to baseline eGFR (MDRD) - Kaplan-Meier curve (LOCF) - ITT population



Number at Risk

Kd >=60 Ml/Min/1.73m2	93	56	43	39	38	36	34	17	4
lKd >=60 Ml/Min/1.73m2	122	67	40	37	34	30	27	7	2
Kd <60 Ml/Min/1.73m2	18	6	3	2	2	1	1	0	0
lKd <60 Ml/Min/1.73m2	43	26	22	18	16	14	13	4	0

A higher score represents a better level of quality of life. Clinical meaningful deterioration change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
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16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Social functioning
16.2.6.1.2.14 Efficacy response data - Subgroup analyses by baseline eGFR (MDRD)
16.2.6.1.2.14.6 QLQ-C30 - Time until permanent improvement by 10 pt in social functioning according to baseline eGFR (MDRD) (LOCF) - ITT population

	>=60 mL/min/1.73m2		<60 mL/min/1.73m2		
	Kd (N=93)	**IKd (N=122)**	**Kd (N=18)**	**IKd (N=43)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	18 (19.4)	28 (23.0)	1 (5.6)	14 (32.6)	0.1533
Number (%) of patients censored	75 (80.6)	94 (77.0)	17 (94.4)	29 (67.4)	
Kaplan-Meier estimates of Social functioning in months					
25% quantile (95% CI)	NC (15.146 to NC)	20.14 (12.682 to NC)	22.47 (22.472 to NC)	13.67 (1.051 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (22.472 to NC)	NC (17.774 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (22.472 to NC)	NC (NC to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.4546		0.0532	
Hazard ratio (95% CI) vs Kd	-	1.25 (0.69 to 2.27)		5.84 (0.77 to 44.45)	
P-value	-	0.4555		0.0884	
Improvement probability (95% CI)[b]					

A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Social functioning
16.2.6.1.2.14 Efficacy response data - Subgroup analyses by baseline eGFR (MDRD)
16.2.6.1.2.14.7 QLQ-C30 - Time until permanent deterioration by 10 pt in social functioning according to baseline eGFR (MDRD) (LOCF) - ITT population

	>=60 mL/min/1.73m2		<60 mL/min/1.73m2		
	Kd (N=93)	**IKd (N=122)**	**Kd (N=18)**	**IKd (N=43)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	28 (30.1)	42 (34.4)	9 (50.0)	13 (30.2)	0.0239
Number (%) of patients censored	65 (69.9)	80 (65.6)	9 (50.0)	30 (69.8)	
Kaplan-Meier estimates of Social functioning in months					
25% quantile (95% CI)	13.90 (5.191 to NC)	10.48 (5.782 to 14.883)	3.45 (1.314 to 9.363)	19.88 (1.938 to NC)	
Median (95% CI)	NC (24.016 to NC)	NC (NC to NC)	11.15 (2.858 to NC)	NC (20.895 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (9.363 to NC)	NC (NC to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.3642		0.0583	
Hazard ratio (95% CI) vs Kd	-	1.25 (0.77 to 2.01)		0.45 (0.19 to 1.05)	
P-value	-	0.3652		0.0651	
Deterioration probability (95% CI)[b]					

A higher score represents a better level of quality of life. Clinical meaningful deterioration change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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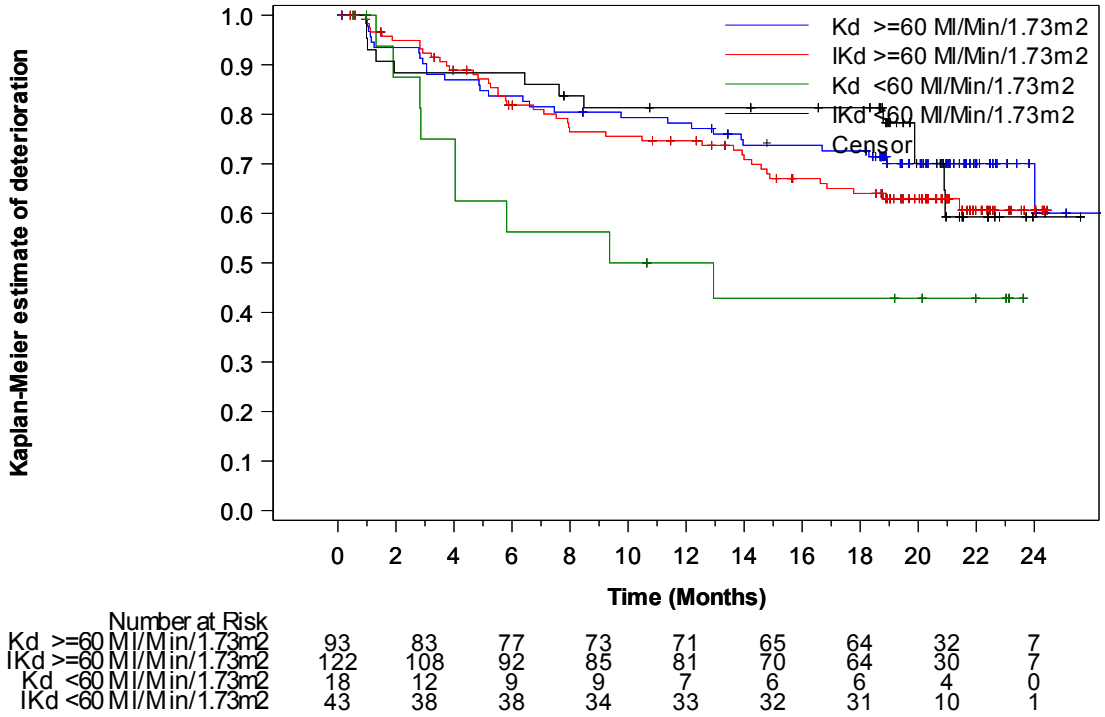
16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Social functioning
16.2.6.1.2.14 Efficacy response data - Subgroup analyses by baseline eGFR (MDRD)
16.2.6.1.2.14.8 QLQ-C30 - Time until permanent deterioration by 10 pt in social functioning according to baseline eGFR (MDRD) - Kaplan-Meier curve (LOCF) - ITT population



A higher score represents a better level of quality of life. Clinical meaningful deterioration change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
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16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Social functioning
16.2.6.1.2.15 Efficacy response data - Subgroup analyses by previous treatment with PI
16.2.6.1.2.15.3 QLQ-C30 - Time to first improvement by 10 pt in social functioning according to previous treatment with PI (LOCF) - ITT population

	Yes		No		
	Kd (N=47)	**IKd (N=81)**	**Kd (N=76)**	**IKd (N=98)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	19 (40.4)	37 (45.7)	21 (27.6)	49 (50.0)	0.0939
Number (%) of patients censored	28 (59.6)	44 (54.3)	55 (72.4)	49 (50.0)	
Kaplan-Meier estimates of Social functioning in months					
25% quantile (95% CI)	1.12 (0.986 to 3.811)	1.97 (1.051 to 2.793)	3.71 (1.117 to NC)	1.08 (1.018 to 1.840)	
Median (95% CI)	NC (2.431 to NC)	NC (3.023 to NC)	NC (NC to NC)	12.39 (2.891 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.6754		0.0035	
Hazard ratio (95% CI) vs Kd	-	1.13 (0.65 to 1.96)		2.11 (1.26 to 3.51)	
P-value	-	0.6756		0.0043	
Hazard ratio inverted (95% CI) vs IKd		-		0.47 (0.28 to 0.79)	

A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Social functioning
16.2.6.1.2.15 Efficacy response data - Subgroup analyses by previous treatment with PI
16.2.6.1.2.15.4 QLQ-C30 - Time to first deterioration by 10 pt in social functioning according to previous treatment with PI (LOCF) - ITT population

	Yes		No		
	Kd (N=47)	**IKd (N=81)**	**Kd (N=76)**	**IKd (N=98)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	29 (61.7)	55 (67.9)	47 (61.8)	63 (64.3)	0.3556
Number (%) of patients censored	18 (38.3)	26 (32.1)	29 (38.2)	35 (35.7)	
Kaplan-Meier estimates of Social functioning in months					
25% quantile (95% CI)	1.91 (1.117 to 2.825)	1.87 (1.117 to 1.971)	1.28 (1.051 to 2.168)	2.04 (1.183 to 3.023)	
Median (95% CI)	4.39 (2.793 to NC)	3.06 (2.595 to 7.622)	4.67 (2.825 to 12.485)	5.13 (3.515 to 10.645)	
75% quantile (95% CI)	NC (15.540 to NC)	NC (8.805 to NC)	NC (19.745 to NC)	NC (16.559 to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.3355		0.8040	
Hazard ratio (95% CI) vs Kd	-	1.25 (0.79 to 1.96)		0.95 (0.65 to 1.39)	
P-value	-	0.3365		0.8033	
Deterioration probability (95% CI)[b]					

A higher score represents a better level of quality of life. Clinical meaningful deterioration change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Social functioning
16.2.6.1.2.15 Efficacy response data - Subgroup analyses by previous treatment with PI
16.2.6.1.2.15.5 QLQ-C30 - Time until permanent improvement by 10 pt in social functioning according to previous treatment with PI (LOCF) - ITT population

	Yes		No		
	Kd (N=47)	**IKd (N=81)**	**Kd (N=76)**	**IKd (N=98)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	7 (14.9)	15 (18.5)	13 (17.1)	29 (29.6)	0.6429
Number (%) of patients censored	40 (85.1)	66 (81.5)	63 (82.9)	69 (70.4)	
Kaplan-Meier estimates of Social functioning in months					
25% quantile (95% CI)	NC (12.386 to NC)	21.68 (12.156 to NC)	22.47 (15.146 to NC)	17.51 (10.053 to 22.604)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.4831		0.0807	
Hazard ratio (95% CI) vs Kd	-	1.38 (0.56 to 3.41)		1.78 (0.92 to 3.42)	
P-value	-	0.4849		0.0850	
Improvement probability (95% CI)[b]					

A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Social functioning
16.2.6.1.2.15 Efficacy response data - Subgroup analyses by previous treatment with PI
16.2.6.1.2.15.6 QLQ-C30 - Time until permanent deterioration by 10 pt in social functioning according to previous treatment with PI (LOCF) - ITT population

	Yes		No		
	Kd (N=47)	**IKd (N=81)**	**Kd (N=76)**	**IKd (N=98)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	15 (31.9)	31 (38.3)	24 (31.6)	29 (29.6)	0.3748
Number (%) of patients censored	32 (68.1)	50 (61.7)	52 (68.4)	69 (70.4)	
Kaplan-Meier estimates of Social functioning in months					
25% quantile (95% CI)	7.79 (2.825 to NC)	8.48 (5.191 to 14.784)	11.37 (4.862 to NC)	16.62 (5.815 to NC)	
Median (95% CI)	NC (24.016 to NC)	NC (19.877 to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.3925		0.6655	
Hazard ratio (95% CI) vs Kd	-	1.31 (0.70 to 2.44)		0.89 (0.52 to 1.52)	
P-value	-	0.3939		0.6657	
Deterioration probability (95% CI)[b]					

A higher score represents a better level of quality of life. Clinical meaningful deterioration change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Social functioning
16.2.6.1.2.16 Efficacy response data - Subgroup analyses by previous treatment with IMiD
16.2.6.1.2.16.3 QLQ-C30 - Time to first improvement by 10 pt in social functioning according to previous treatment with IMiD (LOCF) - ITT population

	Yes		No		
	Kd (N=62)	**IKd (N=81)**	**Kd (N=61)**	**IKd (N=98)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	24 (38.7)	36 (44.4)	16 (26.2)	50 (51.0)	0.0665
Number (%) of patients censored	38 (61.3)	45 (55.6)	45 (73.8)	48 (49.0)	
Kaplan-Meier estimates of Social functioning in months					
25% quantile (95% CI)	1.87 (1.051 to 4.797)	1.38 (1.051 to 2.990)	3.50 (1.117 to NC)	1.12 (1.018 to 1.971)	
Median (95% CI)	NC (4.797 to NC)	NC (4.632 to NC)	NC (NC to NC)	8.57 (2.793 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.6083		0.0025	
Hazard ratio (95% CI) vs Kd	-	1.14 (0.68 to 1.92)		2.33 (1.32 to 4.09)	
P-value	-	0.6086		0.0033	
Hazard ratio inverted (95% CI) vs IKd		-		0.43 (0.24 to 0.76)	

A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Social functioning
16.2.6.1.2.16 Efficacy response data - Subgroup analyses by previous treatment with IMiD
16.2.6.1.2.16.4 QLQ-C30 - Time to first deterioration by 10 pt in social functioning according to previous treatment with IMiD (LOCF) - ITT population

	Yes		No		
	Kd (N=62)	**IKd (N=81)**	**Kd (N=61)**	**IKd (N=98)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	36 (58.1)	52 (64.2)	40 (65.6)	66 (67.3)	0.7411
Number (%) of patients censored	26 (41.9)	29 (35.8)	21 (34.4)	32 (32.7)	
Kaplan-Meier estimates of Social functioning in months					
25% quantile (95% CI)	2.00 (1.117 to 2.793)	1.87 (1.117 to 2.037)	1.56 (1.051 to 2.825)	1.97 (1.347 to 2.825)	
Median (95% CI)	4.04 (2.793 to NC)	4.73 (2.760 to 13.043)	4.67 (2.825 to 8.575)	4.67 (3.023 to 8.279)	
75% quantile (95% CI)	NC (NC to NC)	NC (16.559 to NC)	NC (13.405 to NC)	NC (10.645 to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.5981		0.9203	
Hazard ratio (95% CI) vs Kd	-	1.12 (0.73 to 1.71)		1.02 (0.69 to 1.51)	
P-value	-	0.5983		0.9205	
Deterioration probability (95% CI)[b]					

A higher score represents a better level of quality of life. Clinical meaningful deterioration change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Social functioning
16.2.6.1.2.16 Efficacy response data - Subgroup analyses by previous treatment with IMiD
16.2.6.1.2.16.5 QLQ-C30 - Time until permanent improvement by 10 pt in social functioning according to previous treatment with IMiD (LOCF) - ITT population

	Yes		No		
	Kd (N=62)	**IKd (N=81)**	**Kd (N=61)**	**IKd (N=98)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	16 (25.8)	20 (24.7)	4 (6.6)	24 (24.5)	0.0177
Number (%) of patients censored	46 (74.2)	61 (75.3)	57 (93.4)	74 (75.5)	
Kaplan-Meier estimates of Social functioning in months					
25% quantile (95% CI)	19.38 (5.060 to NC)	20.14 (12.025 to NC)	NC (NC to NC)	19.65 (12.156 to NC)	
Median (95% CI)	NC (22.144 to NC)	NC (22.604 to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.8599		0.0044	
Hazard ratio (95% CI) vs Kd	-	0.94 (0.49 to 1.82)		4.12 (1.43 to 11.86)	
P-value	-	0.8594		0.0088	
Hazard ratio inverted (95% CI) vs IKd		-		0.24 (0.08 to 0.70)	

A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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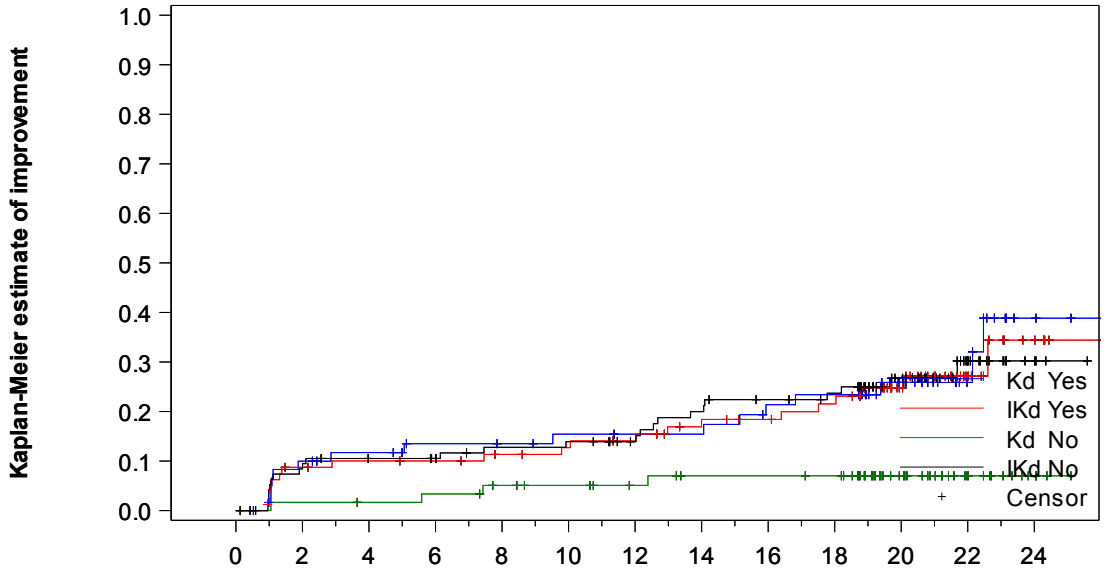
16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Social functioning
16.2.6.1.2.16 Efficacy response data - Subgroup analyses by previous treatment with IMiD
16.2.6.1.2.16.6 QLQ-C30 - Time until permanent improvement by 10 pt in social functioning according to previous treatment with IMiD - Kaplan-Meier curve (LOCF) - ITT population



Number at Risk

Kd Yes	62	51	47	45	43	42	38	18	3
IKd Yes	81	70	69	65	62	54	50	24	5
Kd No	61	59	57	52	49	46	45	21	4
IKd No	98	84	81	77	71	63	59	26	4

A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
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16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Social functioning
16.2.6.1.2.16 Efficacy response data - Subgroup analyses by previous treatment with IMiD
16.2.6.1.2.16.7 QLQ-C30 - Time until permanent deterioration by 10 pt in social functioning according to previous treatment with IMiD (LOCF) - ITT population

	Yes		No		
	Kd (N=62)	**IKd (N=81)**	**Kd (N=61)**	**IKd (N=98)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	20 (32.3)	27 (33.3)	19 (31.1)	33 (33.7)	0.8096
Number (%) of patients censored	42 (67.7)	54 (66.7)	42 (68.9)	65 (66.3)	
Kaplan-Meier estimates of Social functioning in months					
25% quantile (95% CI)	11.37 (4.041 to 24.016)	14.59 (5.782 to 20.895)	9.76 (2.924 to NC)	10.48 (5.191 to 16.854)	
Median (95% CI)	24.02 (24.016 to NC)	NC (21.421 to NC)	NC (NC to NC)	NC (20.928 to NC)	
75% quantile (95% CI)	NC (24.016 to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.9995		0.7536	
Hazard ratio (95% CI) vs Kd	-	1.00 (0.56 to 1.78)		1.09 (0.62 to 1.92)	
P-value	-	1.0000		0.7537	
Deterioration probability (95% CI)[b]					

A higher score represents a better level of quality of life. Clinical meaningful deterioration change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
PGM=DEVOPS/SAR650984/EFC15246/CIR_RWE/REPORT/PGM/eff_km_subgp_sr_sig_de_i_t.sas OUT=REPORT/OUTPUT/eff_km_c30_soc_detpl_imid_de_i_t_x.rtf (07APR2021 14:27)

16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Social functioning
16.2.6.1.2.17 Efficacy response data - Subgroup analyses by previous treatment with PI and IMiD
16.2.6.1.2.17.3 QLQ-C30 - Time to first improvement by 10 pt in social functioning according to previous treatment with PI and IMiD (LOCF) - ITT population

	Yes		No		
	Kd (N=17)	**IKd (N=23)**	**Kd (N=106)**	**IKd (N=156)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	9 (52.9)	8 (34.8)	31 (29.2)	78 (50.0)	0.0098
Number (%) of patients censored	8 (47.1)	15 (65.2)	75 (70.8)	78 (50.0)	
Kaplan-Meier estimates of Social functioning in months					
25% quantile (95% CI)	1.03 (0.953 to 3.811)	3.42 (0.986 to NC)	3.29 (1.117 to NC)	1.12 (1.051 to 1.906)	
Median (95% CI)	3.81 (1.018 to NC)	NC (3.417 to NC)	NC (NC to NC)	9.43 (2.990 to NC)	
75% quantile (95% CI)	NC (3.811 to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.1664		0.0011	
Hazard ratio (95% CI) vs Kd	-	0.52 (0.20 to 1.34)		1.97 (1.30 to 2.99)	
P-value	-	0.1741		0.0014	
Hazard ratio inverted (95% CI) vs IKd		-		0.51 (0.33 to 0.77)	

A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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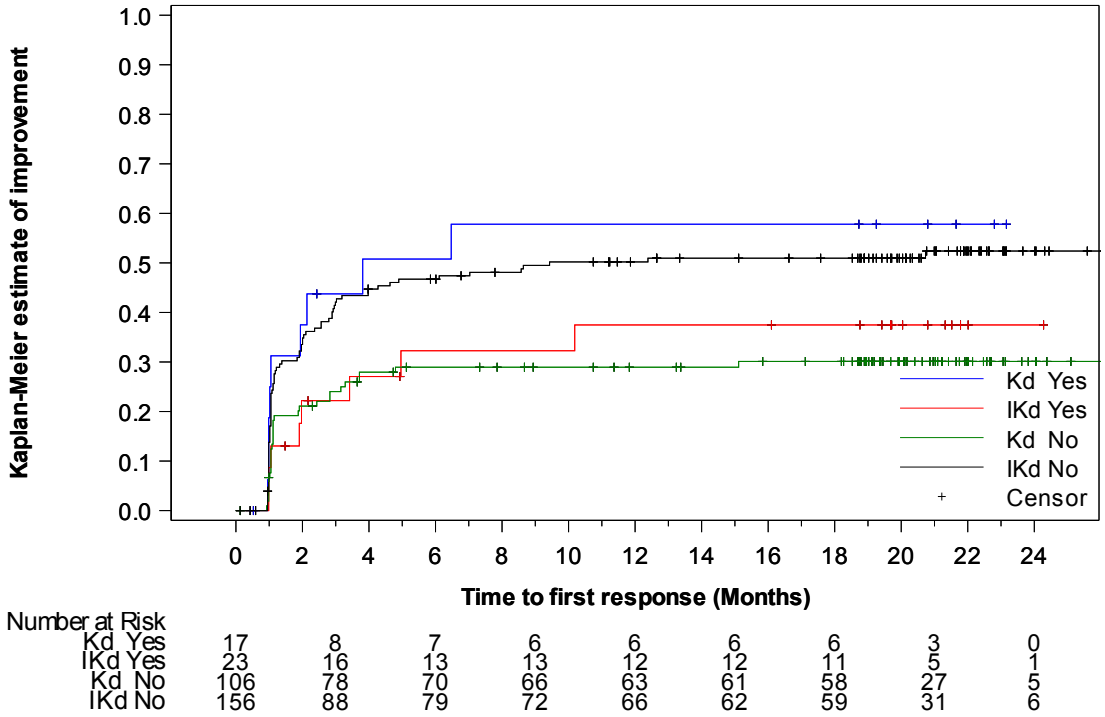
16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Social functioning
16.2.6.1.2.17 Efficacy response data - Subgroup analyses by previous treatment with PI and IMiD
16.2.6.1.2.17.4 QLQ-C30 - Time to first improvement by 10 pt in social functioning according to previous treatment with PI and IMiD - Kaplan-Meier curve (LOCF) - ITT population



A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
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16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Social functioning
16.2.6.1.2.17 Efficacy response data - Subgroup analyses by previous treatment with PI and IMiD
16.2.6.1.2.17.5 QLQ-C30 - Time to first deterioration by 10 pt in social functioning according to previous treatment with PI and IMiD (LOCF) - ITT population

	Yes		No		
	Kd (N=17)	**IKd (N=23)**	**Kd (N=106)**	**IKd (N=156)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	7 (41.2)	15 (65.2)	69 (65.1)	103 (66.0)	0.0810
Number (%) of patients censored	10 (58.8)	8 (34.8)	37 (34.9)	53 (34.0)	
Kaplan-Meier estimates of Social functioning in months					
25% quantile (95% CI)	2.43 (1.314 to NC)	1.22 (0.986 to 1.873)	1.84 (1.084 to 2.103)	1.97 (1.478 to 2.793)	
Median (95% CI)	NC (2.070 to NC)	2.60 (1.248 to NC)	4.63 (2.858 to 7.885)	4.73 (3.450 to 7.622)	
75% quantile (95% CI)	NC (NC to NC)	NC (2.858 to NC)	NC (15.540 to NC)	NC (16.559 to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.0879		0.8240	
Hazard ratio (95% CI) vs Kd	-	2.15 (0.87 to 5.29)		0.97 (0.71 to 1.31)	
P-value	-	0.0957		0.8234	
Deterioration probability (95% CI)[b]					

A higher score represents a better level of quality of life. Clinical meaningful deterioration change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Social functioning
16.2.6.1.2.17 Efficacy response data - Subgroup analyses by previous treatment with PI and IMiD
16.2.6.1.2.17.6 QLQ-C30 - Time until permanent improvement by 10 pt in social functioning according to previous treatment with PI and IMiD (LOCF) - ITT population

	Yes		No		
	Kd (N=17)	**IKd (N=23)**	**Kd (N=106)**	**IKd (N=156)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	5 (29.4)	2 (8.7)	15 (14.2)	42 (26.9)	0.0256
Number (%) of patients censored	12 (70.6)	21 (91.3)	91 (85.8)	114 (73.1)	
Kaplan-Meier estimates of Social functioning in months					
25% quantile (95% CI)	15.93 (0.953 to NC)	NC (9.791 to NC)	NC (22.472 to NC)	18.04 (12.682 to 22.604)	
Median (95% CI)	NC (15.934 to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (22.144 to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.1341		0.0161	
Hazard ratio (95% CI) vs Kd	-	0.30 (0.06 to 1.58)		2.03 (1.13 to 3.66)	
P-value	-	0.1564		0.0185	
Hazard ratio inverted (95% CI) vs IKd		-		0.49 (0.27 to 0.89)	

A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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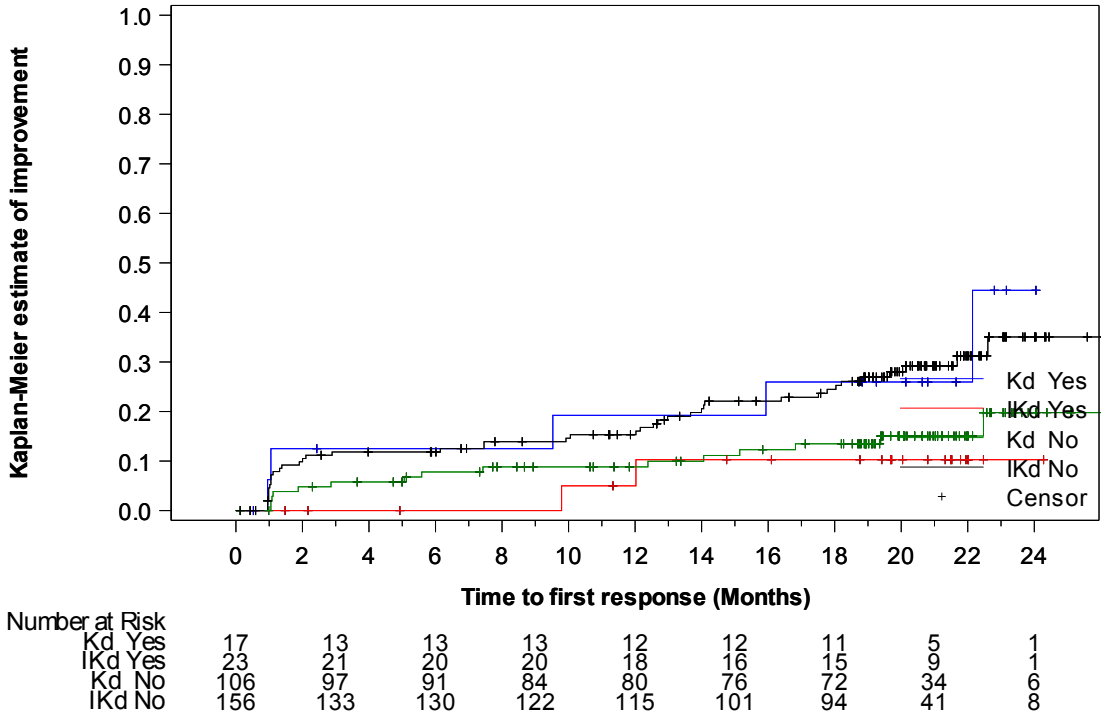
16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Social functioning
16.2.6.1.2.17 Efficacy response data - Subgroup analyses by previous treatment with PI and IMiD
16.2.6.1.2.17.7 QLQ-C30 - Time until permanent improvement by 10 pt in social functioning according to previous treatment with PI and IMiD - Kaplan-Meier curve (LOCF) - ITT population



A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
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16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Social functioning
16.2.6.1.2.17 Efficacy response data - Subgroup analyses by previous treatment with PI and IMiD
16.2.6.1.2.17.8 QLQ-C30 - Time until permanent deterioration by 10 pt in social functioning according to previous treatment with PI and IMiD (LOCF) - ITT population

	Yes		No		
	Kd (N=17)	**IKd (N=23)**	**Kd (N=106)**	**IKd (N=156)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	4 (23.5)	9 (39.1)	35 (33.0)	51 (32.7)	0.3894
Number (%) of patients censored	13 (76.5)	14 (60.9)	71 (67.0)	105 (67.3)	
Kaplan-Meier estimates of Social functioning in months					
25% quantile (95% CI)	24.02 (1.314 to NC)	10.91 (1.413 to 21.421)	9.76 (4.041 to 18.300)	13.63 (6.735 to 17.774)	
Median (95% CI)	24.02 (24.016 to NC)	NC (10.908 to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (24.016 to NC)	NC (21.421 to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.3285		0.9071	
Hazard ratio (95% CI) vs Kd	-	1.79 (0.55 to 5.90)		0.97 (0.63 to 1.50)	
P-value	-	0.3351		0.9068	
Deterioration probability (95% CI)[b]					

A higher score represents a better level of quality of life. Clinical meaningful deterioration change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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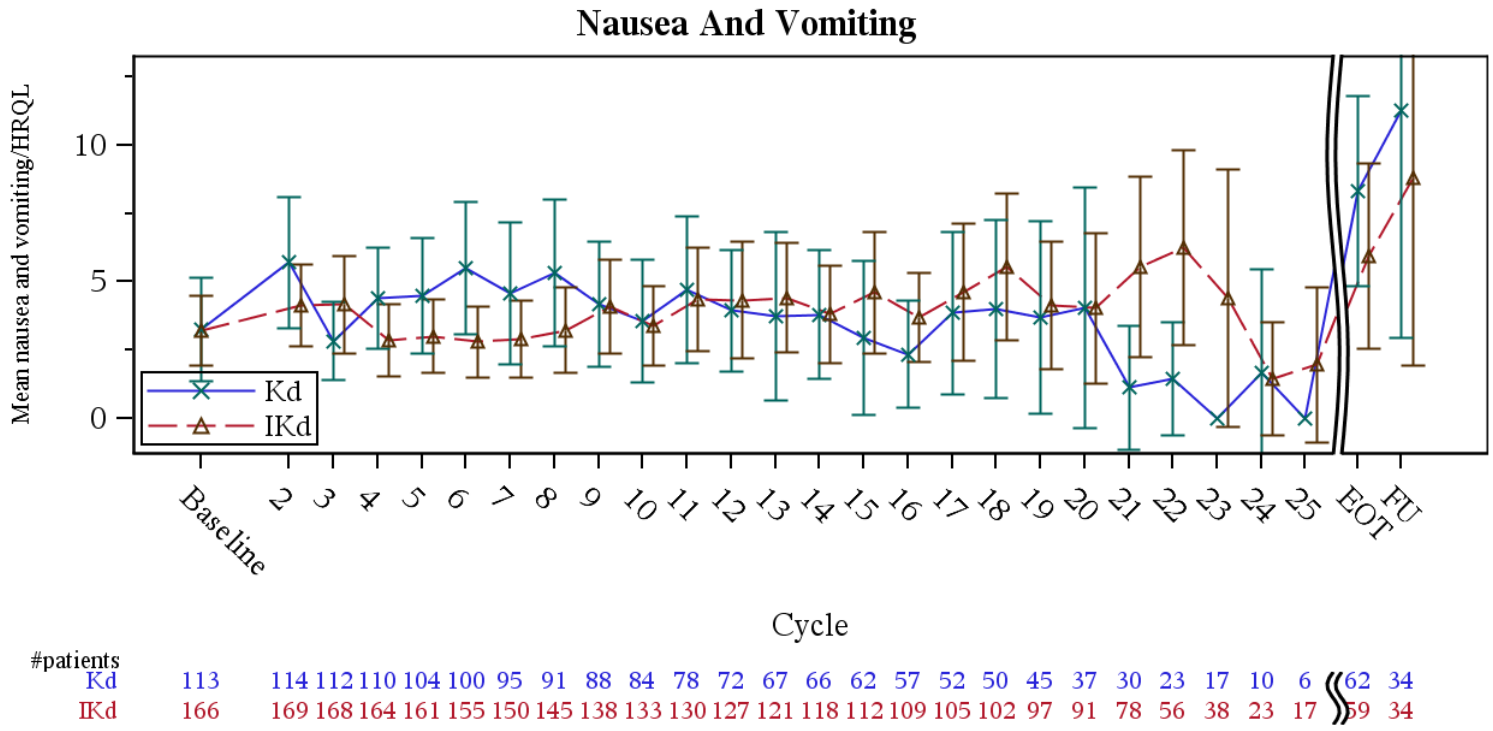
16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Nausea and vomiting
16.2.6.1.2.1 Efficacy response data
16.2.6.1.2.1.1 QLQ-C30 - Mean and 95% CI for nausea and vomiting score over time (LOCF) - ITT population



A lower score represents a better level of quality of life. Cycles with less than 20 patients overall are not presented.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
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16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Nausea and vomiting
16.2.6.1.2.1 Efficacy response data
16.2.6.1.2.1.15 QLQ-C30 - Time to first improvement by 15 pt in Nausea and vomiting (LOCF) - ITT population

First improvement 15 points Nausea and vomiting (%)	**Kd (N=123)**	**IKd (N=179)**
Number (%) of events	12 (9.8)	26 (14.5)
Number (%) of patients censored	111 (90.2)	153 (85.5)
Kaplan-Meier estimates of Nausea and vomiting in months		
25% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)
Median (95% CI)	NC (NC to NC)	NC (NC to NC)
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)
Comparison vs. Kd		
Stratified[a] Log-Rank test p-value[b] vs Kd	-	0.2134
Stratified[a] Hazard ratio (95% CI) vs Kd	-	1.54 (0.78 to 3.06)
P-value	-	0.2170
Improvement probability (95% CI)[c]		
3 Months	0.100 (0.055 to 0.162)	0.120 (0.077 to 0.173)
6 Months	0.100 (0.055 to 0.162)	0.149 (0.101 to 0.207)

A lower score represents a better level of quality of life. Clinical meaningful improvement change from baseline less than or equal to -15 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] Stratified on number of prior lines of therapy (1 vs. >1) and Revised International Staging System (R-ISS) stage (I or II vs. III vs. not classified) according to IRT
[b] One-sided significance level is 0.025
[c] Estimated using the Kaplan-Meier method
NA/NC = Not Applicable / Not Calculable
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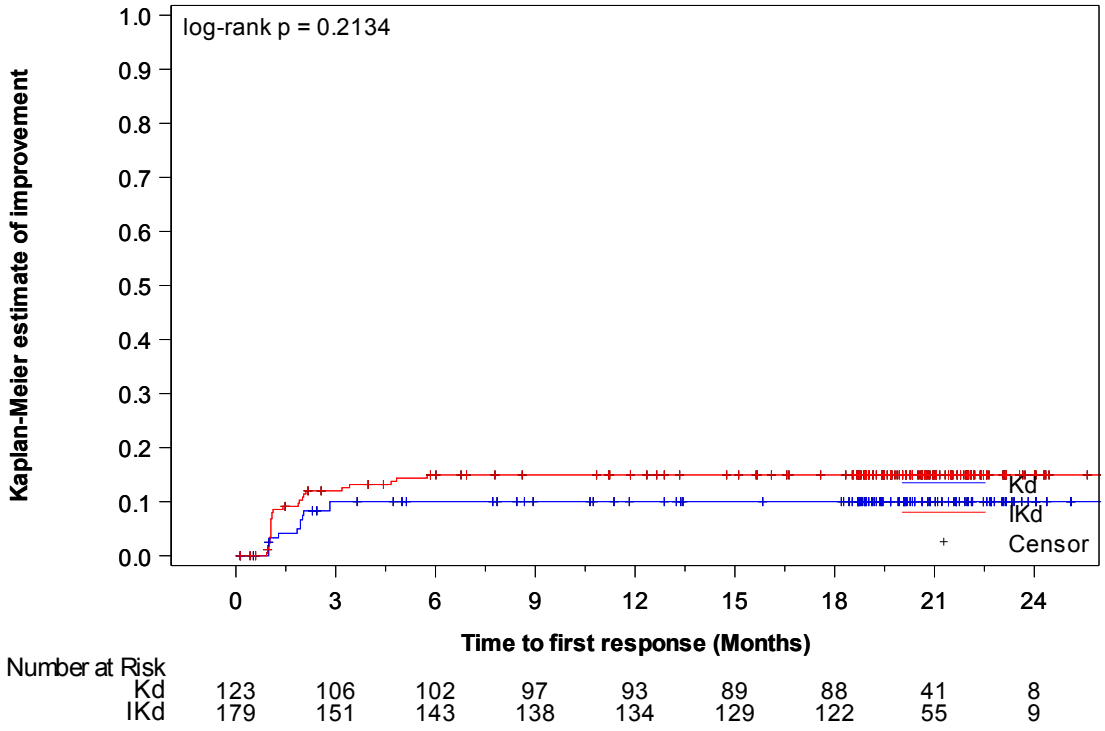
16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Nausea and vomiting
16.2.6.1.2.1 Efficacy response data
16.2.6.1.2.1.16 QLQ-C30 - Time to first improvement by 15 pt in Nausea and vomiting - Kaplan-Meier curve (LOCF) - ITT population



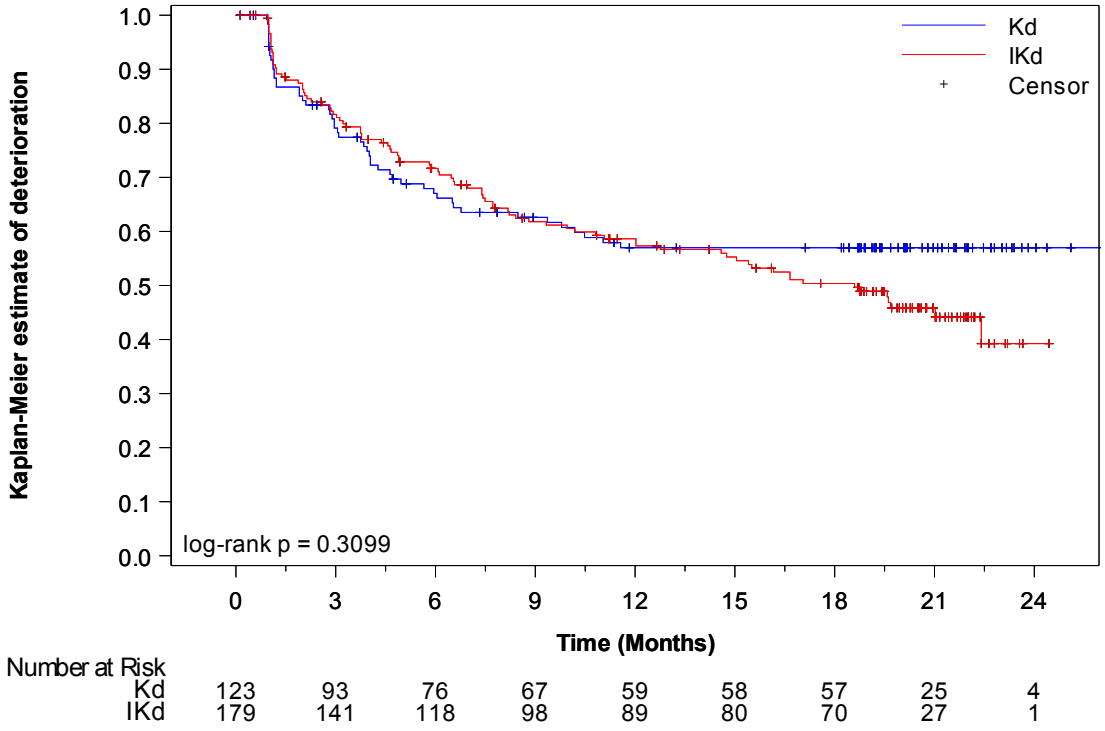
A lower score represents a better level of quality of life. Clinical meaningful improvement change from baseline less than or equal to -15 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
PGM=DEVOPS/SAR650984/EFC15246/CIR_RWE/REPORT/PGM/eff_qlq_km_i_f.sas OUT=REPORT/OUTPUT/eff_km_c30_nau_imp15l_de_i_f_x.rtf (07APR2021 14:24)

16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Nausea and vomiting
16.2.6.1.2.1 Efficacy response data
16.2.6.1.2.1.17 QLQ-C30 - Time to first deterioration by 15 pt in Nausea and vomiting (LOCF) - ITT population

First deterioration 15 points Nausea and vomiting (%)	**Kd (N=123)**	**IKd (N=179)**
Number (%) of events	50 (40.7)	89 (49.7)
Number (%) of patients censored	73 (59.3)	90 (50.3)
Kaplan-Meier estimates of Nausea and vomiting in months		
25% quantile (95% CI)	3.94 (2.793 to 5.947)	4.67 (3.023 to 6.965)
Median (95% CI)	NC (10.480 to NC)	18.60 (12.025 to NC)
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)
Comparison vs. Kd		
Stratified[a] Log-Rank test p-value[b] vs Kd	-	0.3099
Stratified[a] Hazard ratio (95% CI) vs Kd	-	1.20 (0.85 to 1.70)
P-value	-	0.3106
Deterioration probability (95% CI)[c]		
3 Months	0.791 (0.707 to 0.854)	0.817 (0.751 to 0.867)
6 Months	0.670 (0.578 to 0.747)	0.717 (0.643 to 0.778)

A lower score represents a better level of quality of life. Clinical meaningful deterioration change from baseline greater than or equal to 15 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] Stratified on number of prior lines of therapy (1 vs. >1) and Revised International Staging System (R-ISS) stage (I or II vs. III vs. not classified) according to IRT
[b] One-sided significance level is 0.025
[c] Estimated using the Kaplan-Meier method
NA/NC = Not Applicable / Not Calculable
PGM=DEVOPS/SAR650984/EFC15246/CIR_RWE/REPORT/PGM/eff_km_invhr_sr_i_t.sas OUT=REPORT/OUTPUT/eff_km_c30_nau_det15l_de_i_t_x.rtf (07APR2021 14:22)

16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Nausea and vomiting
16.2.6.1.2.1 Efficacy response data
16.2.6.1.2.1.18 QLQ-C30 - Time to first deterioration by 15 pt in Nausea and vomiting - Kaplan-Meier curve (LOCF) - ITT population



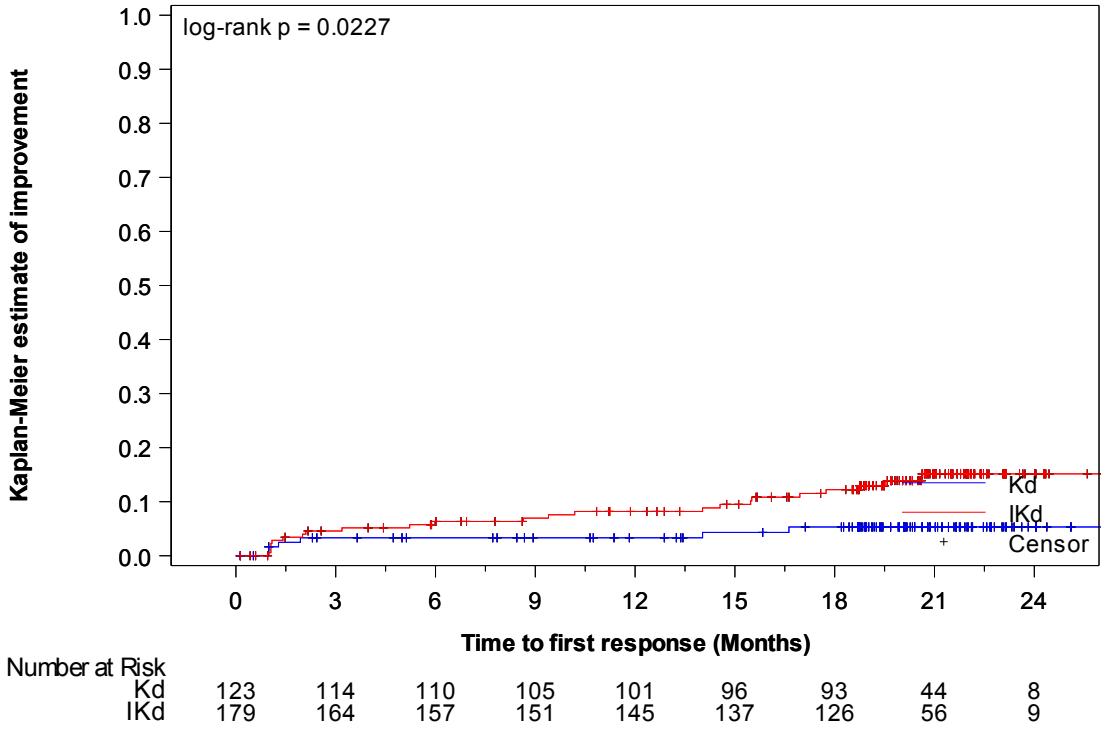
A lower score represents a better level of quality of life. Clinical meaningful deterioration change from baseline greater than or equal to 15 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
PGM=DEVOPS/SAR650984/EFC15246/CIR_RWE/REPORT/PGM/eff_qlq_km_i_f.sas OUT=REPORT/OUTPUT/eff_km_c30_nau_det15l_de_i_f_x.rtf (07APR2021 14:24)

16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Nausea and vomiting
16.2.6.1.2.1 Efficacy response data
16.2.6.1.2.1.19 QLQ-C30 - Time until permanent improvement by 15 pt in Nausea and vomiting (LOCF) - ITT population

First permanent improvement 15 points Nausea and vomiting (%)	Kd (N=123)	IKd (N=179)
Number (%) of events	6 (4.9)	23 (12.8)
Number (%) of patients censored	117 (95.1)	156 (87.2)
Kaplan-Meier estimates of Nausea and vomiting in months		
25% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)
Median (95% CI)	NC (NC to NC)	NC (NC to NC)
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)
Comparison vs. Kd		
Stratified[a] Log-Rank test p-value[b] vs Kd	-	0.0227
Stratified[a] Hazard ratio (95% CI) vs Kd	-	2.73 (1.11 to 6.71)
P-value	-	0.0288
Stratified[a] Hazard ratio inverted (95% CI) vs IKd	0.37 (0.15 to 0.90)	-
Improvement probability (95% CI)[c]		
3 Months	0.033 (0.011 to 0.077)	0.046 (0.021 to 0.084)

A lower score represents a better level of quality of life. Clinical meaningful improvement change from baseline less than or equal to -15 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] Stratified on number of prior lines of therapy (1 vs. >1) and Revised International Staging System (R-ISS) stage (I or II vs. III vs. not classified) according to IRT
[b] One-sided significance level is 0.025
[c] Estimated using the Kaplan-Meier method
NA/NC = Not Applicable / Not Calculable
PGM=DEVOPS/SAR650984/EFC15246/CIR_RWE/REPORT/PGM/eff_km_invhr_sr_i_t.sas OUT=REPORT/OUTPUT/eff_km_c30_nau_imp15pl_de_i_t_x.rtf (07APR2021 14:23)

16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Nausea and vomiting
16.2.6.1.2.1 Efficacy response data
16.2.6.1.2.1.20 QLQ-C30 - Time until permanent improvement by 15 pt in Nausea and vomiting - Kaplan-Meier curve (LOCF) - ITT population



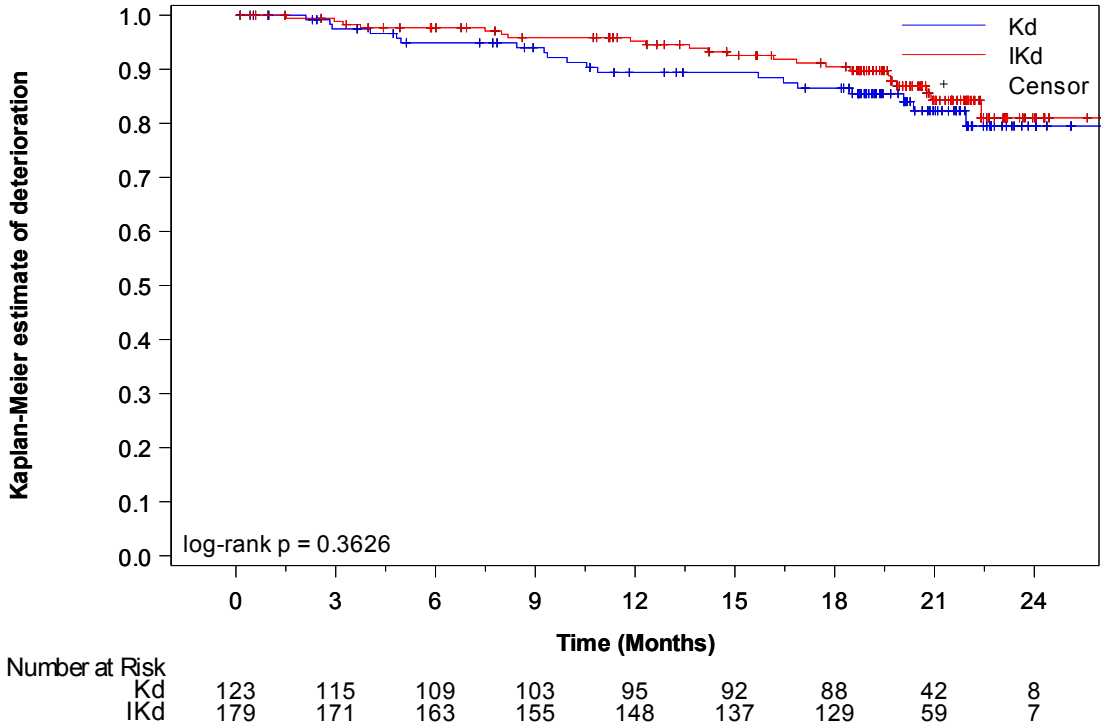
A lower score represents a better level of quality of life. Clinical meaningful improvement change from baseline less than or equal to -15 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
PGM=DEVOPS/SAR650984/EFC15246/CIR_RWE/REPORT/PGM/eff_qlq_km_i_f.sas OUT=REPORT/OUTPUT/eff_km_c30_nau_imp15pl_de_i_f_x.rtf (07APR2021 14:24)

16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Nausea and vomiting
16.2.6.1.2.1 Efficacy response data
16.2.6.1.2.1.21 QLQ-C30 - Time until permanent deterioration by 15 pt in Nausea and vomiting (LOCF) - ITT population

First permanent deterioration 15 points Nausea and vomiting (%)	Kd (N=123)	IKd (N=179)
Number (%) of events	19 (15.4)	22 (12.3)
Number (%) of patients censored	104 (84.6)	157 (87.7)
Kaplan-Meier estimates of Nausea and vomiting in months		
25% quantile (95% CI)	NC (20.370 to NC)	NC (22.407 to NC)
Median (95% CI)	NC (NC to NC)	NC (NC to NC)
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)
Comparison vs. Kd		
Stratified[a] Log-Rank test p-value[b] vs Kd	-	0.3626
Stratified[a] Hazard ratio (95% CI) vs Kd	-	0.75 (0.41 to 1.39)
P-value	-	0.3642
Deterioration probability (95% CI)[c]		
3 Months	0.975 (0.924 to 0.992)	0.988 (0.955 to 0.997)
6 Months	0.949 (0.890 to 0.977)	0.977 (0.940 to 0.991)

A lower score represents a better level of quality of life. Clinical meaningful deterioration change from baseline greater than or equal to 15 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] Stratified on number of prior lines of therapy (1 vs. >1) and Revised International Staging System (R-ISS) stage (I or II vs. III vs. not classified) according to IRT
[b] One-sided significance level is 0.025
[c] Estimated using the Kaplan-Meier method
NA/NC = Not Applicable / Not Calculable
PGM=DEVOPS/SAR650984/EFC15246/CIR_RWE/REPORT/PGM/eff_km_invhr_sr_i_t.sas OUT=REPORT/OUTPUT/eff_km_c30_nau_det15pl_de_i_t_x.rtf (07APR2021 14:23)

16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Nausea and vomiting
16.2.6.1.2.1 Efficacy response data
16.2.6.1.2.1.22 QLQ-C30 - Time until permanent deterioration by 15 pt in Nausea and vomiting - Kaplan-Meier curve (LOCF) - ITT population



A lower score represents a better level of quality of life. Clinical meaningful deterioration change from baseline greater than or equal to 15 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
PGM=DEVOPS/SAR650984/EFC15246/CIR_RWE/REPORT/PGM/eff_qlq_km_i_f.sas OUT=REPORT/OUTPUT/eff_km_c30_nau_det15pl_de_i_f_x.rtf (07APR2021 14:24)

16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Nausea and vomiting
16.2.6.1.2.2 Efficacy response data - Subgroup analyses by age
16.2.6.1.2.2.3 QLQ-C30 - Time to first improvement by 10 pt in nausea and vomiting according to age (LOCF) - ITT population

	<65 years		>=65 years		
	Kd (N=66)	**IKd (N=88)**	**Kd (N=57)**	**IKd (N=91)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	9 (13.6)	10 (11.4)	3 (5.3)	16 (17.6)	0.0623
Number (%) of patients censored	57 (86.4)	78 (88.6)	54 (94.7)	75 (82.4)	
Kaplan-Meier estimates of Nausea and vomiting in months					
25% quantile (95% CI)	NC (2.825 to NC)	NC (NC to NC)	NC (NC to NC)	NC (3.187 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.6864		0.0334	
Hazard ratio (95% CI) vs Kd	-	0.83 (0.34 to 2.04)		3.51 (1.02 to 12.03)	
P-value	-	0.6868		0.0462	
Hazard ratio inverted (95% CI) vs IKd		-		0.29 (0.08 to 0.98)	

A lower score represents a better level of quality of life. Clinical meaningful improvement change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
PGM=DEVOPS/SAR650984/EFC15246/CIR_RWE/REPORT/PGM/eff_km_subgp_sr_sig_de_i_t.sas OUT=REPORT/OUTPUT/eff_km_c30_nau_impl_age_de_i_t_x.rtf (07APR2021 14:29)

16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Nausea and vomiting
16.2.6.1.2.2 Efficacy response data - Subgroup analyses by age
16.2.6.1.2.2.4 QLQ-C30 - Time to first deterioration by 10 pt in nausea and vomiting according to age (LOCF) - ITT population

	<65 years		>=65 years		
	Kd (N=66)	**IKd (N=88)**	**Kd (N=57)**	**IKd (N=91)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	29 (43.9)	42 (47.7)	21 (36.8)	47 (51.6)	0.3108
Number (%) of patients censored	37 (56.1)	46 (52.3)	36 (63.2)	44 (48.4)	
Kaplan-Meier estimates of Nausea and vomiting in months					
25% quantile (95% CI)	3.09 (1.906 to 6.538)	3.78 (2.136 to 8.181)	4.63 (2.103 to 9.791)	4.67 (2.267 to 7.425)	
Median (95% CI)	NC (6.768 to NC)	19.61 (12.025 to NC)	NC (9.791 to NC)	16.16 (8.805 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (22.407 to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.8992		0.1440	
Hazard ratio (95% CI) vs Kd	-	1.03 (0.64 to 1.66)		1.46 (0.88 to 2.45)	
P-value	-	0.8994		0.1465	
Deterioration probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful deterioration change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
PGM=DEVOPS/SAR650984/EFC15246/CIR_RWE/REPORT/PGM/eff_km_subgp_sr_sig_de_i_t.sas OUT=REPORT/OUTPUT/eff_km_c30_nau_detl_age_de_i_t_x.rtf (07APR2021 14:29)

16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Nausea and vomiting
16.2.6.1.2.2 Efficacy response data - Subgroup analyses by age
16.2.6.1.2.2.5 QLQ-C30 - Time until permanent improvement by 10 pt in nausea and vomiting according to age (LOCF) - ITT population

	<65 years		>=65 years		
	Kd (N=66)	**IKd (N=88)**	**Kd (N=57)**	**IKd (N=91)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	5 (7.6)	8 (9.1)	1 (1.8)	15 (16.5)	0.0750
Number (%) of patients censored	61 (92.4)	80 (90.9)	56 (98.2)	76 (83.5)	
Kaplan-Meier estimates of Nausea and vomiting in months					
25% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (18.760 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.7634		0.0063	
Hazard ratio (95% CI) vs Kd	-	1.19 (0.39 to 3.63)		9.87 (1.30 to 74.73)	
P-value	-	0.7637		0.0266	
Hazard ratio inverted (95% CI) vs IKd		-		0.10 (0.01 to 0.77)	

A lower score represents a better level of quality of life. Clinical meaningful improvement change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Nausea and vomiting
16.2.6.1.2.2 Efficacy response data - Subgroup analyses by age
16.2.6.1.2.2.6 QLQ-C30 - Time until permanent deterioration by 10 pt in nausea and vomiting according to age (LOCF) - ITT population

	<65 years		>=65 years		
	Kd (N=66)	**IKd (N=88)**	**Kd (N=57)**	**IKd (N=91)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	11 (16.7)	13 (14.8)	8 (14.0)	9 (9.9)	0.7033
Number (%) of patients censored	55 (83.3)	75 (85.2)	49 (86.0)	82 (90.1)	
Kaplan-Meier estimates of Nausea and vomiting in months					
25% quantile (95% CI)	NC (16.887 to NC)	NC (19.680 to NC)	NC (18.530 to NC)	NC (NC to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.7649		0.4310	
Hazard ratio (95% CI) vs Kd	-	0.88 (0.40 to 1.98)		0.68 (0.26 to 1.77)	
P-value	-	0.7650		0.4337	
Deterioration probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful deterioration change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Nausea and vomiting
16.2.6.1.2.3 Efficacy response data - Subgroup analyses by gender
16.2.6.1.2.3.3 QLQ-C30 - Time to first improvement by 10 pt in nausea and vomiting according to gender (LOCF) - ITT population

	Male		Female		
	Kd (N=68)	**IKd (N=101)**	**Kd (N=55)**	**IKd (N=78)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	5 (7.4)	17 (16.8)	7 (12.7)	9 (11.5)	0.1559
Number (%) of patients censored	63 (92.6)	84 (83.2)	48 (87.3)	69 (88.5)	
Kaplan-Meier estimates of Nausea and vomiting in months					
25% quantile (95% CI)	NC (NC to NC)	NC (3.417 to NC)	NC (2.004 to NC)	NC (NC to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.0698		0.8091	
Hazard ratio (95% CI) vs Kd	-	2.44 (0.90 to 6.62)		0.89 (0.33 to 2.38)	
P-value	-	0.0794		0.8092	
Improvement probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful improvement change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
PGM=DEVOPS/SAR650984/EFC15246/CIR_RWE/REPORT/PGM/eff_km_subgp_sr_sig_de_i_t.sas OUT=REPORT/OUTPUT/eff_km_c30_nau_impl_sex_de_i_t_x.rtf (07APR2021 14:29)

16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Nausea and vomiting
16.2.6.1.2.3 Efficacy response data - Subgroup analyses by gender
16.2.6.1.2.3.4 QLQ-C30 - Time to first deterioration by 10 pt in nausea and vomiting according to gender (LOCF) - ITT population

	Male		Female		
	Kd (N=68)	**IKd (N=101)**	**Kd (N=55)**	**IKd (N=78)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	21 (30.9)	40 (39.6)	29 (52.7)	49 (62.8)	0.8642
Number (%) of patients censored	47 (69.1)	61 (60.4)	26 (47.3)	29 (37.2)	
Kaplan-Meier estimates of Nausea and vomiting in months					
25% quantile (95% CI)	5.95 (3.088 to NC)	7.39 (3.778 to 15.507)	2.79 (1.051 to 4.271)	2.92 (1.216 to 4.895)	
Median (95% CI)	NC (NC to NC)	22.41 (17.051 to NC)	8.48 (4.271 to NC)	8.80 (6.111 to 15.047)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (19.614 to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.3501		0.5062	
Hazard ratio (95% CI) vs Kd	-	1.29 (0.76 to 2.18)		1.17 (0.74 to 1.85)	
P-value	-	0.3514		0.5066	
Deterioration probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful deterioration change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
PGM=DEVOPS/SAR650984/EFC15246/CIR_RWE/REPORT/PGM/eff_km_subgp_sr_sig_de_i_t.sas OUT=REPORT/OUTPUT/eff_km_c30_nau_detl_sex_de_i_t_x.rtf (07APR2021 14:29)

16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Nausea and vomiting
16.2.6.1.2.3 Efficacy response data - Subgroup analyses by gender
16.2.6.1.2.3.5 QLQ-C30 - Time until permanent improvement by 10 pt in nausea and vomiting according to gender (LOCF) - ITT population

	Male		Female		
	Kd (N=68)	**IKd (N=101)**	**Kd (N=55)**	**IKd (N=78)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	2 (2.9)	14 (13.9)	4 (7.3)	9 (11.5)	0.2247
Number (%) of patients censored	66 (97.1)	87 (86.1)	51 (92.7)	69 (88.5)	
Kaplan-Meier estimates of Nausea and vomiting in months					
25% quantile (95% CI)	NC (NC to NC)	NC (19.515 to NC)	NC (NC to NC)	NC (NC to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.0197		0.4734	
Hazard ratio (95% CI) vs Kd	-	4.91 (1.11 to 21.59)		1.53 (0.47 to 4.98)	
P-value	-	0.0354		0.4769	
Hazard ratio inverted (95% CI) vs IKd		-		0.65 (0.20 to 2.12)	

A lower score represents a better level of quality of life. Clinical meaningful improvement change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
PGM=DEVOPS/SAR650984/EFC15246/CIR_RWE/REPORT/PGM/eff_km_subgp_sr_sig_de_i_t.sas OUT=REPORT/OUTPUT/eff_km_c30_nau_imppl_sex_de_i_t_x.rtf (07APR2021 14:30)

16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Nausea and vomiting
16.2.6.1.2.3 Efficacy response data - Subgroup analyses by gender
16.2.6.1.2.3.6 QLQ-C30 - Time until permanent deterioration by 10 pt in nausea and vomiting according to gender (LOCF) - ITT population

	Male		Female		
	Kd (N=68)	**IKd (N=101)**	**Kd (N=55)**	**IKd (N=78)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	6 (8.8)	11 (10.9)	13 (23.6)	11 (14.1)	0.2108
Number (%) of patients censored	62 (91.2)	90 (89.1)	42 (76.4)	67 (85.9)	
Kaplan-Meier estimates of Nausea and vomiting in months					
25% quantile (95% CI)	NC (NC to NC)	NC (20.895 to NC)	21.95 (10.546 to NC)	NC (19.614 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.6207		0.1523	
Hazard ratio (95% CI) vs Kd	-	1.28 (0.47 to 3.48)		0.56 (0.25 to 1.25)	
P-value	-	0.6216		0.1580	
Deterioration probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful deterioration change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
PGM=DEVOPS/SAR650984/EFC15246/CIR_RWE/REPORT/PGM/eff_km_subgp_sr_sig_de_i_t.sas OUT=REPORT/OUTPUT/eff_km_c30_nau_detpl_sex_de_i_t_x.rtf (07APR2021 14:29)

16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Nausea and vomiting
16.2.6.1.2.4 Efficacy response data - Subgroup analyses by ethnic origin
16.2.6.1.2.4.3 QLQ-C30 - Time to first improvement by 10 pt in nausea and vomiting according to ethnic origin (LOCF) - ITT population

	White		Other		
	Kd (N=83)	**IKd (N=131)**	**Kd (N=28)**	**IKd (N=34)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	10 (12.0)	15 (11.5)	2 (7.1)	7 (20.6)	0.1903
Number (%) of patients censored	73 (88.0)	116 (88.5)	26 (92.9)	27 (79.4)	
Kaplan-Meier estimates of Nausea and vomiting in months					
25% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (2.037 to NC)	NC (1.084 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.9141		0.1350	
Hazard ratio (95% CI) vs Kd	-	0.96 (0.43 to 2.13)		3.12 (0.65 to 15.00)	
P-value	-	0.9137		0.1564	
Improvement probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful improvement change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
PGM=DEVOPS/SAR650984/EFC15246/CIR_RWE/REPORT/PGM/eff_km_subgp_sr_sig_de_i_t.sas OUT=REPORT/OUTPUT/eff_km_c30_nau_impl_race_de_i_t_x.rtf (07APR2021 14:29)

16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Nausea and vomiting
16.2.6.1.2.4 Efficacy response data - Subgroup analyses by ethnic origin
16.2.6.1.2.4.4 QLQ-C30 - Time to first deterioration by 10 pt in nausea and vomiting according to ethnic origin (LOCF) - ITT population

	White		Other		
	Kd (N=83)	**IKd (N=131)**	**Kd (N=28)**	**IKd (N=34)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	34 (41.0)	62 (47.3)	13 (46.4)	21 (61.8)	0.7989
Number (%) of patients censored	49 (59.0)	69 (52.7)	15 (53.6)	13 (38.2)	
Kaplan-Meier estimates of Nausea and vomiting in months					
25% quantile (95% CI)	4.70 (3.088 to 8.476)	4.57 (2.595 to 6.472)	2.00 (1.018 to 2.957)	8.41 (2.825 to 15.409)	
Median (95% CI)	NC (10.185 to NC)	19.61 (9.955 to NC)	NC (2.825 to NC)	16.16 (9.331 to 19.680)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	21.03 (17.051 to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.3725		0.6035	
Hazard ratio (95% CI) vs Kd	-	1.21 (0.80 to 1.84)		1.20 (0.60 to 2.42)	
P-value	-	0.3733		0.6039	
Deterioration probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful deterioration change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Nausea and vomiting
16.2.6.1.2.4 Efficacy response data - Subgroup analyses by ethnic origin
16.2.6.1.2.4.5 QLQ-C30 - Time until permanent improvement by 10 pt in nausea and vomiting according to ethnic origin (LOCF) - ITT population

	White		Other		
	Kd (N=83)	**IKd (N=131)**	**Kd (N=28)**	**IKd (N=34)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	5 (6.0)	14 (10.7)	1 (3.6)	6 (17.6)	0.3569
Number (%) of patients censored	78 (94.0)	117 (89.3)	27 (96.4)	28 (82.4)	
Kaplan-Meier estimates of Nausea and vomiting in months					
25% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (2.004 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.2561		0.0788	
Hazard ratio (95% CI) vs Kd	-	1.79 (0.65 to 4.98)		5.42 (0.65 to 45.06)	
P-value	-	0.2629		0.1176	
Improvement probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful improvement change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Nausea and vomiting
16.2.6.1.2.4 Efficacy response data - Subgroup analyses by ethnic origin
16.2.6.1.2.4.6 QLQ-C30 - Time until permanent deterioration by 10 pt in nausea and vomiting according to ethnic origin (LOCF) - ITT population

	White		Other		
	Kd (N=83)	**IKd (N=131)**	**Kd (N=28)**	**IKd (N=34)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	14 (16.9)	16 (12.2)	4 (14.3)	6 (17.6)	0.4489
Number (%) of patients censored	69 (83.1)	115 (87.8)	24 (85.7)	28 (82.4)	
Kaplan-Meier estimates of Nausea and vomiting in months					
25% quantile (95% CI)	NC (20.074 to NC)	NC (20.895 to NC)	NC (2.891 to NC)	NC (14.784 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.3626		0.7558	
Hazard ratio (95% CI) vs Kd	-	0.72 (0.35 to 1.47)		1.22 (0.34 to 4.34)	
P-value	-	0.3648		0.7562	
Deterioration probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful deterioration change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Nausea and vomiting
16.2.6.1.2.5 Efficacy response data - Subgroup analyses by geographical region
16.2.6.1.2.5.3 QLQ-C30 - Time to first improvement by 10 pt in nausea and vomiting according to geographical region (LOCF) - ITT population

	Europe		**America**		**Asia**		**Other countries**		
	Kd (N=60)	**IKd (N=85)**	**Kd (N=20)**	**IKd (N=24)**	**Kd (N=21)**	**IKd (N=25)**	**Kd (N=22)**	**IKd (N=45)**	**p-value of treatment-by-subgroup interaction[c]**
Number (%) of events	4 (6.7)	7 (8.2)	5 (25.0)	5 (20.8)	1 (4.8)	6 (24.0)	2 (9.1)	8 (17.8)	0.4982
Number (%) of patients censored	56 (93.3)	78 (91.8)	15 (75.0)	19 (79.2)	20 (95.2)	19 (76.0)	20 (90.9)	37 (82.2)	
Kaplan-Meier estimates of event in months									
25% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (0.986 to NC)	NC (0.953 to NC)	NC (2.037 to NC)	NC (0.986 to NC)	NC (0.986 to NC)	NC (1.117 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (1.938 to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Kd									

A lower score represents a better level of quality of life. Clinical meaningful improvement change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
PGM=DEVOPS/SAR650984/EFC15246/CIR_RWE/REPORT/PGM/eff_km_subgp_sr_sig_de_i_t.sas OUT=REPORT/OUTPUT/eff_km_c30_nau_impl_greg_de_i_t_x.rtf (07APR2021 14:29)

16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Nausea and vomiting
16.2.6.1.2.5 Efficacy response data - Subgroup analyses by geographical region
16.2.6.1.2.5.3 QLQ-C30 - Time to first improvement by 10 pt in nausea and vomiting according to geographical region (LOCF) - ITT population

	Europe		America		Asia		Other countries		
	Kd (N=60)	**IKd (N=85)**	**Kd (N=20)**	**IKd (N=24)**	**Kd (N=21)**	**IKd (N=25)**	**Kd (N=22)**	**IKd (N=45)**	**p-value of treatment-by-subgroup interaction[c]**
Log-Rank test p-value[a] vs Kd	-	0.7134		0.8107		0.0808		0.3675	
Hazard ratio (95% CI) vs Kd	-	1.26 (0.37 to 4.30)		0.86 (0.25 to 2.97)		5.37 (0.65 to 44.59)		2.01 (0.43 to 9.47)	
P-value	-	0.7140		0.8108		0.1197		0.3771	
Improvement probability (95% CI)[b]									
3 Months	0.069 (0.022 to 0.154)	0.072 (0.030 to 0.141)	0.250 (0.091 to 0.449)	0.175 (0.054 to 0.351)	0.050 (0.003 to 0.205)	0.125 (0.031 to 0.287)	0.091 (0.016 to 0.251)	0.178 (0.083 to 0.301)	
6 Months	0.069 (0.022 to 0.154)	0.085 (0.037 to 0.157)	0.250 (0.091 to 0.449)	0.220 (0.080 to 0.405)	0.050 (0.003 to 0.205)	0.250 (0.102 to 0.431)	0.091 (0.016 to 0.251)	0.178 (0.083 to 0.301)	

A lower score represents a better level of quality of life. Clinical meaningful improvement change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Nausea and vomiting
16.2.6.1.2.5 Efficacy response data - Subgroup analyses by geographical region
16.2.6.1.2.5.4 QLQ-C30 - Time to first deterioration by 10 pt in nausea and vomiting according to geographical region (LOCF) - ITT population

	Europe		America		Asia		Other countries		
	Kd (N=60)	**IKd (N=85)**	**Kd (N=20)**	**IKd (N=24)**	**Kd (N=21)**	**IKd (N=25)**	**Kd (N=22)**	**IKd (N=45)**	**p-value of treatment-by-subgroup interaction[c]**
Number (%) of events	20 (33.3)	40 (47.1)	11 (55.0)	13 (54.2)	11 (52.4)	15 (60.0)	8 (36.4)	21 (46.7)	0.5833
Number (%) of patients censored	40 (66.7)	45 (52.9)	9 (45.0)	11 (45.8)	10 (47.6)	10 (40.0)	14 (63.6)	24 (53.3)	
Kaplan-Meier estimates of event in months									
25% quantile (95% CI)	6.77 (2.825 to 11.565)	3.22 (2.004 to 6.078)	3.52 (0.920 to 5.651)	3.78 (1.051 to 7.721)	1.61 (1.018 to 2.957)	9.33 (1.117 to 16.657)	4.01 (0.986 to NC)	8.18 (1.380 to 14.752)	
Median (95% CI)	NC (11.565 to NC)	22.41 (6.571 to NC)	9.36 (3.088 to NC)	7.72 (3.778 to NC)	4.04 (1.216 to NC)	17.05 (15.047 to 21.027)	NC (4.008 to NC)	19.61 (12.025 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (22.407 to NC)	NC (10.480 to NC)	NC (8.214 to NC)	NC (5.947 to NC)	21.03 (18.760 to NC)	NC (NC to NC)	NC (NC to NC)	

A lower score represents a better level of quality of life. Clinical meaningful deterioration change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Nausea and vomiting
16.2.6.1.2.5 Efficacy response data - Subgroup analyses by geographical region
16.2.6.1.2.5.4 QLQ-C30 - Time to first deterioration by 10 pt in nausea and vomiting according to geographical region (LOCF) - ITT population

	Europe		America		Asia		Other countries		
	Kd (N=60)	**IKd (N=85)**	**Kd (N=20)**	**IKd (N=24)**	**Kd (N=21)**	**IKd (N=25)**	**Kd (N=22)**	**IKd (N=45)**	**p-value of treatment-by-subgroup interaction[c]**
Comparison vs. Kd									
Log-Rank test p-value[a] vs Kd	-	0.0951		0.8965		0.8392		0.6156	
Hazard ratio (95% CI) vs Kd	-	1.58 (0.92 to 2.70)		1.05 (0.47 to 2.36)		0.92 (0.42 to 2.02)		1.23 (0.55 to 2.78)	
P-value	-	0.0979		0.8967		0.8393		0.6163	
Deterioration probability (95% CI)[b]									
3 Months	0.862 (0.743 to 0.929)	0.770 (0.664 to 0.847)	0.800 (0.551 to 0.920)	0.824 (0.596 to 0.930)	0.538 (0.299 to 0.728)	0.917 (0.706 to 0.978)	0.818 (0.585 to 0.928)	0.844 (0.701 to 0.923)	

A lower score represents a better level of quality of life. Clinical meaningful deterioration change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Nausea and vomiting
16.2.6.1.2.5 Efficacy response data - Subgroup analyses by geographical region
16.2.6.1.2.5.5 QLQ-C30 - Time until permanent improvement by 10 pt in nausea and vomiting according to geographical region (LOCF) - ITT population

	Europe		America		Asia		Other countries		
	Kd (N=60)	**IKd (N=85)**	**Kd (N=20)**	**IKd (N=24)**	**Kd (N=21)**	**IKd (N=25)**	**Kd (N=22)**	**IKd (N=45)**	**p-value of treatment-by-subgroup interaction[c]**
Number (%) of events	2 (3.3)	7 (8.2)	3 (15.0)	4 (16.7)	0 (0.0)	5 (20.0)	1 (4.5)	7 (15.6)	0.8504
Number (%) of patients censored	58 (96.7)	78 (91.8)	17 (85.0)	20 (83.3)	21 (100.0)	20 (80.0)	21 (95.5)	38 (84.4)	
Kaplan-Meier estimates of event in months									
25% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (0.986 to NC)	NC (1.051 to NC)	NC (NC to NC)	20.63 (0.986 to NC)	NC (16.624 to NC)	NC (16.953 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (20.632 to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	

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The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Nausea and vomiting
16.2.6.1.2.5 Efficacy response data - Subgroup analyses by geographical region
16.2.6.1.2.5.5 QLQ-C30 - Time until permanent improvement by 10 pt in nausea and vomiting according to geographical region (LOCF) - ITT population

	Europe		America		Asia		Other countries		
	Kd (N=60)	**IKd (N=85)**	**Kd (N=20)**	**IKd (N=24)**	**Kd (N=21)**	**IKd (N=25)**	**Kd (N=22)**	**IKd (N=45)**	**p-value of treatment-by-subgroup interaction[c]**
Comparison vs. Kd									
Log-Rank test p-value[a] vs Kd	-	0.2581		0.7938		0.0338		0.1828	
Hazard ratio (95% CI) vs Kd	-	2.41 (0.50 to 11.59)		1.22 (0.27 to 5.46)				3.76 (0.46 to 30.58)	
P-value	-	0.2734		0.7942		0.9964		0.2152	
Improvement probability (95% CI)[b]									
3 Months	0.034 (0.006 to 0.105)	0.024 (0.005 to 0.076)	0.100 (0.017 to 0.272)	0.043 (0.003 to 0.182)		0.125 (0.031 to 0.287)		0.044 (0.008 to 0.133)	

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The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Nausea and vomiting
16.2.6.1.2.5 Efficacy response data - Subgroup analyses by geographical region
16.2.6.1.2.5.6 QLQ-C30 - Time until permanent deterioration by 10 pt in nausea and vomiting according to geographical region (LOCF) - ITT population

	Europe		America		Asia		Other countries		
	Kd (N=60)	**IKd (N=85)**	**Kd (N=20)**	**IKd (N=24)**	**Kd (N=21)**	**IKd (N=25)**	**Kd (N=22)**	**IKd (N=45)**	**p-value of treatment-by-subgroup interaction[c]**
Number (%) of events	7 (11.7)	9 (10.6)	5 (25.0)	4 (16.7)	3 (14.3)	5 (20.0)	4 (18.2)	4 (8.9)	0.7999
Number (%) of patients censored	53 (88.3)	76 (89.4)	15 (75.0)	20 (83.3)	18 (85.7)	20 (80.0)	18 (81.8)	41 (91.1)	
Kaplan-Meier estimates of event in months									
25% quantile (95% CI)	NC (20.370 to NC)	NC (22.407 to NC)	18.53 (9.265 to NC)	20.83 (11.860 to NC)	NC (2.825 to NC)	19.68 (7.984 to NC)	NC (4.961 to NC)	NC (19.614 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (18.530 to NC)	NC (20.764 to NC)	NC (NC to NC)	NC (19.680 to NC)	NC (20.074 to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (20.895 to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	

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CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Nausea and vomiting
16.2.6.1.2.5 Efficacy response data - Subgroup analyses by geographical region
16.2.6.1.2.5.6 QLQ-C30 - Time until permanent deterioration by 10 pt in nausea and vomiting according to geographical region (LOCF) - ITT population

	Europe		America		Asia		Other countries		
	Kd (N=60)	**IKd (N=85)**	**Kd (N=20)**	**IKd (N=24)**	**Kd (N=21)**	**IKd (N=25)**	**Kd (N=22)**	**IKd (N=45)**	**p-value of treatment-by-subgroup interaction[c]**
Comparison vs. Kd									
Log-Rank test p-value[a] vs Kd	-	0.8428		0.5934		0.7123		0.3157	
Hazard ratio (95% CI) vs Kd	-	0.90 (0.34 to 2.43)		0.70 (0.19 to 2.61)		1.31 (0.31 to 5.49)		0.50 (0.12 to 2.00)	
P-value	-	0.8429		0.5954		0.7131		0.3254	
Deterioration probability (95% CI)[b]									
3 Months	0.983 (0.884 to 0.998)	0.988 (0.918 to 0.998)	1.000 (1.000 to 1.000)	1.000 (1.000 to 1.000)	0.895 (0.641 to 0.973)	1.000 (1.000 to 1.000)	1.000 (1.000 to 1.000)	0.978 (0.853 to 0.997)	

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CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Nausea and vomiting
16.2.6.1.2.6 Efficacy response data - Subgroup analyses by regulatory region
16.2.6.1.2.6.3 QLQ-C30 - Time to first improvement by 10 pt in nausea and vomiting according to regulatory region (LOCF) - ITT population

	Western countries		Other countries		
	Kd (N=55)	**IKd (N=97)**	**Kd (N=68)**	**IKd (N=82)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	4 (7.3)	14 (14.4)	8 (11.8)	12 (14.6)	0.5059
Number (%) of patients censored	51 (92.7)	83 (85.6)	60 (88.2)	70 (85.4)	
Kaplan-Meier estimates of Nausea and vomiting in months					
25% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (5.749 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.1894		0.5976	
Hazard ratio (95% CI) vs Kd	-	2.07 (0.68 to 6.29)		1.27 (0.52 to 3.11)	
P-value	-	0.1992		0.5985	
Improvement probability (95% CI)[b]					

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CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Nausea and vomiting
16.2.6.1.2.6 Efficacy response data - Subgroup analyses by regulatory region
16.2.6.1.2.6.4 QLQ-C30 - Time to first deterioration by 10 pt in nausea and vomiting according to regulatory region (LOCF) - ITT population

	Western countries		Other countries		
	Kd (N=55)	**IKd (N=97)**	**Kd (N=68)**	**IKd (N=82)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	18 (32.7)	38 (39.2)	32 (47.1)	51 (62.2)	0.7234
Number (%) of patients censored	37 (67.3)	59 (60.8)	36 (52.9)	31 (37.8)	
Kaplan-Meier estimates of Nausea and vomiting in months					
25% quantile (95% CI)	4.96 (1.216 to NC)	4.90 (2.825 to 8.411)	3.94 (1.906 to 5.651)	3.78 (2.004 to 6.571)	
Median (95% CI)	NC (NC to NC)	NC (15.507 to NC)	NC (5.947 to NC)	12.02 (7.721 to 18.760)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	22.41 (19.614 to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.6012		0.1817	
Hazard ratio (95% CI) vs Kd	-	1.16 (0.66 to 2.03)		1.35 (0.87 to 2.10)	
P-value	-	0.6016		0.1834	
Deterioration probability (95% CI)[b]					

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CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Nausea and vomiting
16.2.6.1.2.6 Efficacy response data - Subgroup analyses by regulatory region
16.2.6.1.2.6.5 QLQ-C30 - Time until permanent improvement by 10 pt in nausea and vomiting according to regulatory region (LOCF) - ITT population

	Western countries		Other countries		
	Kd (N=55)	**IKd (N=97)**	**Kd (N=68)**	**IKd (N=82)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	1 (1.8)	12 (12.4)	5 (7.4)	11 (13.4)	0.2570
Number (%) of patients censored	54 (98.2)	85 (87.6)	63 (92.6)	71 (86.6)	
Kaplan-Meier estimates of Nausea and vomiting in months					
25% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (20.632 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.0295		0.2461	
Hazard ratio (95% CI) vs Kd	-	6.99 (0.91 to 53.78)		1.85 (0.64 to 5.33)	
P-value	-	0.0617		0.2537	
Improvement probability (95% CI)[b]					

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CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Nausea and vomiting
16.2.6.1.2.6 Efficacy response data - Subgroup analyses by regulatory region
16.2.6.1.2.6.6 QLQ-C30 - Time until permanent deterioration by 10 pt in nausea and vomiting according to regulatory region (LOCF) - ITT population

	Western countries		Other countries		
	Kd (N=55)	**IKd (N=97)**	**Kd (N=68)**	**IKd (N=82)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	8 (14.5)	7 (7.2)	11 (16.2)	15 (18.3)	0.2244
Number (%) of patients censored	47 (85.5)	90 (92.8)	57 (83.8)	67 (81.7)	
Kaplan-Meier estimates of Nausea and vomiting in months					
25% quantile (95% CI)	NC (15.704 to NC)	NC (NC to NC)	NC (18.530 to NC)	22.41 (19.614 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.1483		0.8273	
Hazard ratio (95% CI) vs Kd	-	0.48 (0.17 to 1.33)		1.09 (0.50 to 2.38)	
P-value	-	0.1574		0.8274	
Deterioration probability (95% CI)[b]					

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CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Nausea and vomiting
16.2.6.1.2.7 Efficacy response data - Subgroup analyses by baseline ECOG PS
16.2.6.1.2.7.3 QLQ-C30 - Time to first improvement by 10 pt in nausea and vomiting according to baseline ECOG PS (LOCF) - ITT population

	0 or 1		>1		
	Kd (N=118)	**IKd (N=168)**	**Kd (N=5)**	**IKd (N=11)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	12 (10.2)	24 (14.3)	0 (0.0)	2 (18.2)	0.9871
Number (%) of patients censored	106 (89.8)	144 (85.7)	5 (100.0)	9 (81.8)	
Kaplan-Meier estimates of Nausea and vomiting in months					
25% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (1.906 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (1.906 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.3164		0.2774	
Hazard ratio (95% CI) vs Kd	-	1.42 (0.71 to 2.84)			
P-value	-	0.3190		0.9979	
Improvement probability (95% CI)[b]					

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The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Nausea and vomiting
16.2.6.1.2.7 Efficacy response data - Subgroup analyses by baseline ECOG PS
16.2.6.1.2.7.4 QLQ-C30 - Time to first deterioration by 10 pt in nausea and vomiting according to baseline ECOG PS (LOCF) - ITT population

	0 or 1		>1		
	Kd (N=118)	**IKd (N=168)**	**Kd (N=5)**	**IKd (N=11)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	48 (40.7)	84 (50.0)	2 (40.0)	5 (45.5)	0.8759
Number (%) of patients censored	70 (59.3)	84 (50.0)	3 (60.0)	6 (54.5)	
Kaplan-Meier estimates of Nausea and vomiting in months					
25% quantile (95% CI)	3.94 (2.793 to 6.045)	4.90 (3.023 to 7.392)	4.70 (0.986 to NC)	3.12 (0.986 to 8.181)	
Median (95% CI)	NC (10.480 to NC)	18.60 (12.025 to NC)	NC (0.986 to NC)	8.18 (0.986 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (0.986 to NC)	NC (4.370 to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.2995		0.6690	
Hazard ratio (95% CI) vs Kd	-	1.21 (0.85 to 1.72)		1.43 (0.28 to 7.42)	
P-value	-	0.3002		0.6707	
Deterioration probability (95% CI)[b]					

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CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Nausea and vomiting
16.2.6.1.2.7 Efficacy response data - Subgroup analyses by baseline ECOG PS
16.2.6.1.2.7.5 QLQ-C30 - Time until permanent improvement by 10 pt in nausea and vomiting according to baseline ECOG PS (LOCF) - ITT population

	0 or 1		>1		
	Kd (N=118)	**IKd (N=168)**	**Kd (N=5)**	**IKd (N=11)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	6 (5.1)	21 (12.5)	0 (0.0)	2 (18.2)	0.9906
Number (%) of patients censored	112 (94.9)	147 (87.5)	5 (100.0)	9 (81.8)	
Kaplan-Meier estimates of Nausea and vomiting in months					
25% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (2.103 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (2.103 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.0405		0.3721	
Hazard ratio (95% CI) vs Kd	-	2.50 (1.01 to 6.19)			
P-value	-	0.0479		0.9981	
Hazard ratio inverted (95% CI) vs IKd		-		0.9981	

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The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
PGM=DEVOPS/SAR650984/EFC15246/CIR_RWE/REPORT/PGM/eff_km_subgp_sr_sig_de_i_t.sas OUT=REPORT/OUTPUT/eff_km_c30_nau_imppl_ecog_de_i_t_x.rtf (07APR2021 14:29)

16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Nausea and vomiting
16.2.6.1.2.7 Efficacy response data - Subgroup analyses by baseline ECOG PS
16.2.6.1.2.7.6 QLQ-C30 - Time until permanent deterioration by 10 pt in nausea and vomiting according to baseline ECOG PS (LOCF) - ITT population

	0 or 1		>1		
	Kd (N=118)	**IKd (N=168)**	**Kd (N=5)**	**IKd (N=11)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	19 (16.1)	21 (12.5)	0 (0.0)	1 (9.1)	0.9882
Number (%) of patients censored	99 (83.9)	147 (87.5)	5 (100.0)	10 (90.9)	
Kaplan-Meier estimates of Nausea and vomiting in months					
25% quantile (95% CI)	NC (20.074 to NC)	NC (22.407 to NC)	NC (NC to NC)	NC (8.181 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (8.181 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.3914		0.5050	
Hazard ratio (95% CI) vs Kd	-	0.76 (0.41 to 1.42)			
P-value	-	0.3929		0.9986	
Deterioration probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful deterioration change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
PGM=DEVOPS/SAR650984/EFC15246/CIR_RWE/REPORT/PGM/eff_km_subgp_sr_sig_de_i_t.sas OUT=REPORT/OUTPUT/eff_km_c30_nau_detpl_ecog_de_i_t_x.rtf (07APR2021 14:29)

16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Nausea and vomiting
16.2.6.1.2.8 Efficacy response data - Subgroup analyses by ISS staging at SE
16.2.6.1.2.8.3 QLQ-C30 - Time to first improvement by 10 pt in nausea and vomiting according to ISS staging at SE (LOCF) - ITT population

	I		II		III		
	Kd (N=71)	**IKd (N=89)**	**Kd (N=31)**	**IKd (N=63)**	**Kd (N=20)**	**IKd (N=26)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	7 (9.9)	12 (13.5)	3 (9.7)	9 (14.3)	2 (10.0)	5 (19.2)	0.8900
Number (%) of patients censored	64 (90.1)	77 (86.5)	28 (90.3)	54 (85.7)	18 (90.0)	21 (80.8)	
Kaplan-Meier estimates of Nausea and vomiting in months							
25% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (2.825 to NC)	NC (1.873 to NC)	NC (1.938 to NC)	NC (0.953 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Kd							
Log-Rank test p-value[a] vs Kd	-	0.5106		0.5315		0.3280	
Hazard ratio (95% CI) vs Kd	-	1.37 (0.54 to 3.47)		1.51 (0.41 to 5.59)		2.22 (0.43 to 11.45)	
P-value	-	0.5123		0.5347		0.3408	

A lower score represents a better level of quality of life. Clinical meaningful improvement change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Nausea and vomiting
16.2.6.1.2.8 Efficacy response data - Subgroup analyses by ISS staging at SE
16.2.6.1.2.8.4 QLQ-C30 - Time to first deterioration by 10 pt in nausea and vomiting according to ISS staging at SE (LOCF) - ITT population

	I		II		III		
	Kd (N=71)	**IKd (N=89)**	**Kd (N=31)**	**IKd (N=63)**	**Kd (N=20)**	**IKd (N=26)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	31 (43.7)	48 (53.9)	10 (32.3)	33 (52.4)	8 (40.0)	7 (26.9)	0.3283
Number (%) of patients censored	40 (56.3)	41 (46.1)	21 (67.7)	30 (47.6)	12 (60.0)	19 (73.1)	
Kaplan-Meier estimates of Nausea and vomiting in months							
25% quantile (95% CI)	3.94 (2.103 to 6.505)	3.78 (2.037 to 7.392)	4.70 (1.216 to NC)	5.82 (1.511 to 7.392)	4.04 (0.986 to 11.565)	8.41 (0.986 to NC)	
Median (95% CI)	NC (6.768 to NC)	16.16 (9.331 to NC)	NC (10.185 to NC)	16.66 (7.491 to NC)	NC (4.041 to NC)	NC (8.411 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (22.407 to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (19.680 to NC)	
Comparison vs. Kd							
Log-Rank test p-value[a] vs Kd	-	0.3246		0.1728		0.3794	
Hazard ratio (95% CI) vs Kd	-	1.25 (0.80 to 1.97)		1.63 (0.80 to 3.30)		0.64 (0.23 to 1.76)	
P-value	-	0.3256		0.1770		0.3834	

A lower score represents a better level of quality of life. Clinical meaningful deterioration change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Nausea and vomiting
16.2.6.1.2.8 Efficacy response data - Subgroup analyses by ISS staging at SE
16.2.6.1.2.8.5 QLQ-C30 - Time until permanent improvement by 10 pt in nausea and vomiting according to ISS staging at SE (LOCF) - ITT population

	I		II		III		
	Kd (N=71)	**IKd (N=89)**	**Kd (N=31)**	**IKd (N=63)**	**Kd (N=20)**	**IKd (N=26)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	4 (5.6)	10 (11.2)	2 (6.5)	8 (12.7)	0 (0.0)	5 (19.2)	0.9916
Number (%) of patients censored	67 (94.4)	79 (88.8)	29 (93.5)	55 (87.3)	20 (100.0)	21 (80.8)	
Kaplan-Meier estimates of Nausea and vomiting in months							
25% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (19.515 to NC)	NC (NC to NC)	14.55 (1.413 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (14.554 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Kd							
Log-Rank test p-value[a] vs Kd	-	0.2095		0.4382		0.0367	
Hazard ratio (95% CI) vs Kd	-	2.07 (0.65 to 6.60)		1.83 (0.39 to 8.62)			
P-value	-	0.2195		0.4451		0.9964	

A lower score represents a better level of quality of life. Clinical meaningful improvement change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Nausea and vomiting
16.2.6.1.2.8 Efficacy response data - Subgroup analyses by ISS staging at SE
16.2.6.1.2.8.6 QLQ-C30 - Time until permanent deterioration by 10 pt in nausea and vomiting according to ISS staging at SE (LOCF) - ITT population

	I		II		III		
	Kd (N=71)	**IKd (N=89)**	**Kd (N=31)**	**IKd (N=63)**	**Kd (N=20)**	**IKd (N=26)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	12 (16.9)	13 (14.6)	4 (12.9)	7 (11.1)	3 (15.0)	2 (7.7)	0.9126
Number (%) of patients censored	59 (83.1)	76 (85.4)	27 (87.1)	56 (88.9)	17 (85.0)	24 (92.3)	
Kaplan-Meier estimates of Nausea and vomiting in months							
25% quantile (95% CI)	NC (16.460 to NC)	22.41 (20.764 to NC)	NC (16.887 to NC)	NC (19.877 to NC)	NC (4.041 to NC)	NC (8.181 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (20.370 to NC)	NC (NC to NC)	NC (NC to NC)	NC (19.680 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Kd							
Log-Rank test p-value[a] vs Kd	-	0.7793		0.6617		0.4809	
Hazard ratio (95% CI) vs Kd	-	0.89 (0.41 to 1.96)		0.76 (0.22 to 2.60)		0.53 (0.09 to 3.18)	
P-value	-	0.7794		0.6627		0.4882	

A lower score represents a better level of quality of life. Clinical meaningful deterioration change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Nausea and vomiting
16.2.6.1.2.9 Efficacy response data - Subgroup analyses by R-ISS stage at SE
16.2.6.1.2.9.3 QLQ-C30 - Time to first improvement by 10 pt in nausea and vomiting according to R-ISS stage at SE (LOCF) - ITT population

	I or II		III		Not classified		
	Kd (N=103)	**IKd (N=155)**	**Kd (N=8)**	**IKd (N=16)**	**Kd (N=12)**	**IKd (N=8)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	10 (9.7)	19 (12.3)	1 (12.5)	5 (31.3)	1 (8.3)	2 (25.0)	0.5230
Number (%) of patients censored	93 (90.3)	136 (87.7)	7 (87.5)	11 (68.8)	11 (91.7)	6 (75.0)	
Kaplan-Meier estimates of Nausea and vomiting in months							
25% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (2.037 to NC)	2.00 (0.953 to NC)	NC (0.986 to NC)	4.67 (1.084 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (2.037 to NC)	NC (1.906 to NC)	NC (NC to NC)	NC (1.084 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (4.665 to NC)	
Comparison vs. Kd							
Log-Rank test p-value[a] vs Kd	-	0.5592		0.2574		0.2197	
Hazard ratio (95% CI) vs Kd	-	1.26 (0.58 to 2.70)		3.23 (0.38 to 27.74)		4.01 (0.36 to 44.34)	
P-value	-	0.5600		0.2845		0.2567	

A lower score represents a better level of quality of life. Clinical meaningful improvement change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Nausea and vomiting
16.2.6.1.2.9 Efficacy response data - Subgroup analyses by R-ISS stage at SE
16.2.6.1.2.9.4 QLQ-C30 - Time to first deterioration by 10 pt in nausea and vomiting according to R-ISS stage at SE (LOCF) - ITT population

	I or II		III		Not classified		
	Kd (N=103)	**IKd (N=155)**	**Kd (N=8)**	**IKd (N=16)**	**Kd (N=12)**	**IKd (N=8)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	40 (38.8)	84 (54.2)	5 (62.5)	3 (18.8)	5 (41.7)	2 (25.0)	0.0487
Number (%) of patients censored	63 (61.2)	71 (45.8)	3 (37.5)	13 (81.3)	7 (58.3)	6 (75.0)	
Kaplan-Meier estimates of Nausea and vomiting in months							
25% quantile (95% CI)	4.27 (2.103 to 6.538)	4.57 (2.858 to 6.472)	2.96 (2.004 to 4.041)	NC (0.986 to NC)	3.27 (0.986 to NC)	9.33 (2.070 to NC)	
Median (95% CI)	NC (10.185 to NC)	16.66 (10.809 to 21.027)	4.04 (2.004 to NC)	NC (8.181 to NC)	NC (1.150 to NC)	NC (2.070 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	11.56 (4.041 to NC)	NC (NC to NC)	NC (NC to NC)	NC (9.331 to NC)	
Comparison vs. Kd							
Log-Rank test p-value[a] vs Kd	-	0.0907		0.0491		0.7743	
Hazard ratio (95% CI) vs Kd	-	1.38 (0.95 to 2.02)		0.26 (0.06 to 1.10)		0.79 (0.15 to 4.07)	
P-value	-	0.0921		0.0665		0.7749	

A lower score represents a better level of quality of life. Clinical meaningful deterioration change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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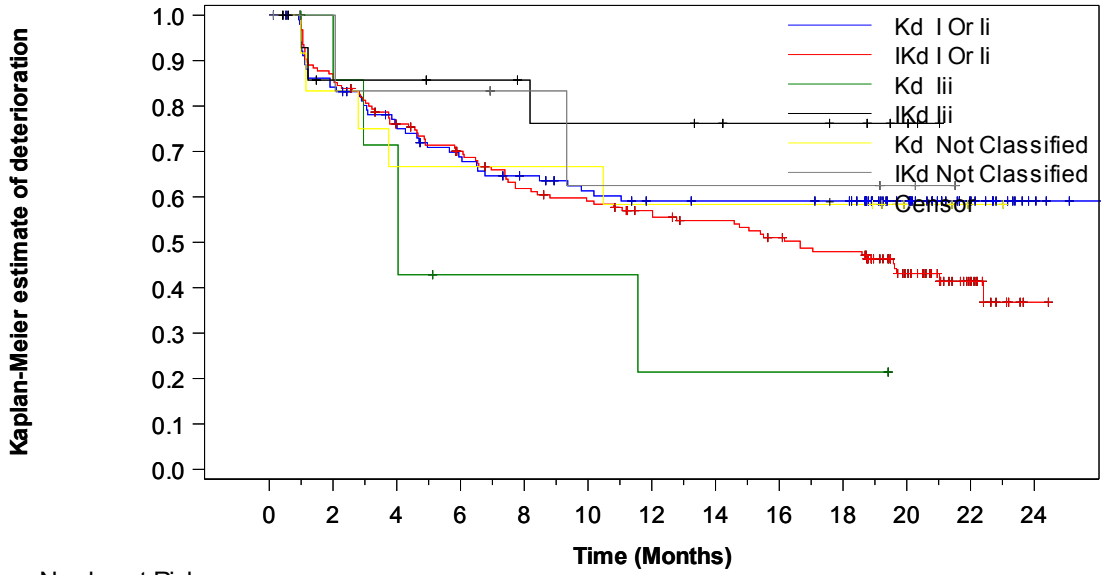
16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Nausea and vomiting
16.2.6.1.2.9 Efficacy response data - Subgroup analyses by R-ISS stage at SE
16.2.6.1.2.9.5 QLQ-C30 - Time to first deterioration by 10 pt in nausea and vomiting according to R-ISS stage at SE - Kaplan-Meier curve (LOCF) - ITT population



Number at Risk									
Kd I Or Ii	103	79	66	57	51	50	49	22	4
IKd I Or Ii	155	125	103	86	78	71	62	25	1
Kd Iii	8	5	2	2	1	1	1	0	0
IKd Iii	16	11	10	8	8	6	5	1	0
Kd Not Classified	12	9	8	8	7	7	7	3	0
IKd Not Classified	8	5	5	4	3	3	3	1	0

A lower score represents a better level of quality of life. Clinical meaningful deterioration change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
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16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Nausea and vomiting
16.2.6.1.2.9 Efficacy response data - Subgroup analyses by R-ISS stage at SE
16.2.6.1.2.9.6 QLQ-C30 - Time until permanent improvement by 10 pt in nausea and vomiting according to R-ISS stage at SE (LOCF) - ITT population

	I or II		III		Not classified		
	Kd (N=103)	**IKd (N=155)**	**Kd (N=8)**	**IKd (N=16)**	**Kd (N=12)**	**IKd (N=8)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	5 (4.9)	16 (10.3)	0 (0.0)	5 (31.3)	1 (8.3)	2 (25.0)	0.7646
Number (%) of patients censored	98 (95.1)	139 (89.7)	8 (100.0)	11 (68.8)	11 (91.7)	6 (75.0)	
Kaplan-Meier estimates of Nausea and vomiting in months							
25% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	5.98 (1.413 to NC)	NC (16.624 to NC)	10.18 (5.224 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (2.103 to NC)	NC (NC to NC)	NC (5.224 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (10.185 to NC)	
Comparison vs. Kd							
Log-Rank test p-value[a] vs Kd	-	0.1546		0.0872		0.1070	
Hazard ratio (95% CI) vs Kd	-	2.04 (0.75 to 5.58)				5.85 (0.52 to 65.85)	
P-value	-	0.1634		0.9966		0.1529	

A lower score represents a better level of quality of life. Clinical meaningful improvement change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
PGM=DEVOPS/SAR650984/EFC15246/CIR_RWE/REPORT/PGM/eff_km_subgp_sr_sig_de_i_t.sas OUT=REPORT/OUTPUT/eff_km_c30_nau_imppl_seriss_de_i_t_x.rtf (07APR2021 14:30)

16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Nausea and vomiting
16.2.6.1.2.9 Efficacy response data - Subgroup analyses by R-ISS stage at SE
16.2.6.1.2.9.7 QLQ-C30 - Time until permanent deterioration by 10 pt in nausea and vomiting according to R-ISS stage at SE (LOCF) - ITT population

	I or II		III		Not classified		
	Kd (N=103)	**IKd (N=155)**	**Kd (N=8)**	**IKd (N=16)**	**Kd (N=12)**	**IKd (N=8)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	17 (16.5)	21 (13.5)	1 (12.5)	1 (6.3)	1 (8.3)	0 (0.0)	0.9898
Number (%) of patients censored	86 (83.5)	134 (86.5)	7 (87.5)	15 (93.8)	11 (91.7)	8 (100.0)	
Kaplan-Meier estimates of Nausea and vomiting in months							
25% quantile (95% CI)	NC (20.074 to NC)	NC (22.407 to NC)	NC (4.041 to NC)	NC (8.181 to NC)	NC (9.265 to NC)	NC (NC to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (4.041 to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Kd							
Log-Rank test p-value[a] vs Kd	-	0.4030		0.6118		0.5186	
Hazard ratio (95% CI) vs Kd	-	0.76 (0.40 to 1.44)		0.49 (0.03 to 7.93)			
P-value	-	0.4045		0.6191		0.9986	

A lower score represents a better level of quality of life. Clinical meaningful deterioration change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
PGM=DEVOPS/SAR650984/EFC15246/CIR_RWE/REPORT/PGM/eff_km_subgp_sr_sig_de_i_t.sas OUT=REPORT/OUTPUT/eff_km_c30_nau_detpl_seriss_de_i_t_x.rtf (07APR2021 14:29)

16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Nausea and vomiting
16.2.6.1.2.10 Efficacy response data - Subgroup analyses by nb of prior lines
16.2.6.1.2.10.3 QLQ-C30 - Time to first improvement by 10 pt in nausea and vomiting according to nb of prior lines (LOCF) - ITT population

	1		>1		
	Kd (N=55)	**IKd (N=79)**	**Kd (N=68)**	**IKd (N=100)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	3 (5.5)	13 (16.5)	9 (13.2)	13 (13.0)	0.1315
Number (%) of patients censored	52 (94.5)	66 (83.5)	59 (86.8)	87 (87.0)	
Kaplan-Meier estimates of Nausea and vomiting in months					
25% quantile (95% CI)	NC (NC to NC)	NC (4.665 to NC)	NC (NC to NC)	NC (NC to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.0569		0.9816	
Hazard ratio (95% CI) vs Kd	-	3.17 (0.90 to 11.13)		0.99 (0.42 to 2.32)	
P-value	-	0.0715		0.9816	
Improvement probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful improvement change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Nausea and vomiting
16.2.6.1.2.10 Efficacy response data - Subgroup analyses by nb of prior lines
16.2.6.1.2.10.4 QLQ-C30 - Time to first deterioration by 10 pt in nausea and vomiting according to nb of prior lines (LOCF) - ITT population

	1		>1		
	Kd (N=55)	**IKd (N=79)**	**Kd (N=68)**	**IKd (N=100)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	21 (38.2)	41 (51.9)	29 (42.6)	48 (48.0)	0.3219
Number (%) of patients censored	34 (61.8)	38 (48.1)	39 (57.4)	52 (52.0)	
Kaplan-Meier estimates of Nausea and vomiting in months					
25% quantile (95% CI)	3.94 (1.906 to 10.480)	3.75 (2.037 to 6.111)	4.01 (1.216 to 6.505)	5.82 (3.121 to 8.805)	
Median (95% CI)	NC (9.791 to NC)	12.78 (7.491 to NC)	NC (6.538 to NC)	19.58 (14.752 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (22.407 to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.1733		0.8540	
Hazard ratio (95% CI) vs Kd	-	1.44 (0.85 to 2.44)		1.04 (0.66 to 1.66)	
P-value	-	0.1757		0.8547	
Deterioration probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful deterioration change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
PGM=DEVOPS/SAR650984/EFC15246/CIR_RWE/REPORT/PGM/eff_km_subgp_sr_sig_de_i_t.sas OUT=REPORT/OUTPUT/eff_km_c30_nau_detl_plne_de_i_t_x.rtf (07APR2021 14:29)

16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Nausea and vomiting
16.2.6.1.2.10 Efficacy response data - Subgroup analyses by nb of prior lines
16.2.6.1.2.10.5 QLQ-C30 - Time until permanent improvement by 10 pt in nausea and vomiting according to nb of prior lines (LOCF) - ITT population

	1		>1		
	Kd (N=55)	**IKd (N=79)**	**Kd (N=68)**	**IKd (N=100)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	1 (1.8)	12 (15.2)	5 (7.4)	11 (11.0)	0.1318
Number (%) of patients censored	54 (98.2)	67 (84.8)	63 (92.6)	89 (89.0)	
Kaplan-Meier estimates of Nausea and vomiting in months					
25% quantile (95% CI)	NC (NC to NC)	NC (18.760 to NC)	NC (NC to NC)	NC (NC to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.0118		0.4566	
Hazard ratio (95% CI) vs Kd	-	8.75 (1.14 to 67.34)		1.49 (0.52 to 4.29)	
P-value	-	0.0371		0.4597	
Hazard ratio inverted (95% CI) vs IKd		-		0.67 (0.23 to 1.93)	

A lower score represents a better level of quality of life. Clinical meaningful improvement change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
PGM=DEVOPS/SAR650984/EFC15246/CIR_RWE/REPORT/PGM/eff_km_subgp_sr_sig_de_i_t.sas OUT=REPORT/OUTPUT/eff_km_c30_nau_imppl_plne_de_i_t_x.rtf (07APR2021 14:30)

16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Nausea and vomiting
16.2.6.1.2.10 Efficacy response data - Subgroup analyses by nb of prior lines
16.2.6.1.2.10.6 QLQ-C30 - Time until permanent deterioration by 10 pt in nausea and vomiting according to nb of prior lines (LOCF) - ITT population

	1		>1		
	Kd (N=55)	**IKd (N=79)**	**Kd (N=68)**	**IKd (N=100)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	8 (14.5)	12 (15.2)	11 (16.2)	10 (10.0)	0.3419
Number (%) of patients censored	47 (85.5)	67 (84.8)	57 (83.8)	90 (90.0)	
Kaplan-Meier estimates of Nausea and vomiting in months					
25% quantile (95% CI)	NC (16.460 to NC)	NC (19.877 to NC)	21.95 (18.530 to NC)	NC (22.407 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.9228		0.2090	
Hazard ratio (95% CI) vs Kd	-	1.05 (0.43 to 2.56)		0.58 (0.25 to 1.37)	
P-value	-	0.9231		0.2146	
Deterioration probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful deterioration change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Nausea and vomiting
16.2.6.1.2.11 Efficacy response data - Subgroup analyses by cytogenetic abnormality
16.2.6.1.2.11.3 QLQ-C30 - Time to first improvement by 10 pt in nausea and vomiting according to cytogenetic abnormality (LOCF) - ITT population

	At least one		None		
	Kd (N=31)	**IKd (N=42)**	**Kd (N=77)**	**IKd (N=114)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	1 (3.2)	9 (21.4)	10 (13.0)	13 (11.4)	0.0678
Number (%) of patients censored	30 (96.8)	33 (78.6)	67 (87.0)	101 (88.6)	
Kaplan-Meier estimates of Nausea and vomiting in months					
25% quantile (95% CI)	NC (NC to NC)	NC (1.117 to NC)	NC (NC to NC)	NC (NC to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.0334		0.7629	
Hazard ratio (95% CI) vs Kd	-	6.88 (0.87 to 54.35)		0.88 (0.39 to 2.01)	
P-value	-	0.0673		0.7631	
Improvement probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful improvement change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Nausea and vomiting
16.2.6.1.2.11 Efficacy response data - Subgroup analyses by cytogenetic abnormality
16.2.6.1.2.11.4 QLQ-C30 - Time to first deterioration by 10 pt in nausea and vomiting according to cytogenetic abnormality (LOCF) - ITT population

	At least one		None		
	Kd (N=31)	**IKd (N=42)**	**Kd (N=77)**	**IKd (N=114)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	16 (51.6)	18 (42.9)	31 (40.3)	65 (57.0)	0.0571
Number (%) of patients censored	15 (48.4)	24 (57.1)	46 (59.7)	49 (43.0)	
Kaplan-Meier estimates of Nausea and vomiting in months					
25% quantile (95% CI)	2.89 (1.117 to 5.651)	7.72 (2.136 to 15.409)	3.94 (1.216 to 6.538)	3.32 (2.004 to 5.815)	
Median (95% CI)	6.77 (4.041 to NC)	NC (12.025 to NC)	NC (9.791 to NC)	14.75 (7.721 to 19.680)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (22.407 to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.2195		0.0738	
Hazard ratio (95% CI) vs Kd	-	0.66 (0.33 to 1.29)		1.48 (0.96 to 2.26)	
P-value	-	0.2228		0.0756	
Deterioration probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful deterioration change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Nausea and vomiting
16.2.6.1.2.11 Efficacy response data - Subgroup analyses by cytogenetic abnormality
16.2.6.1.2.11.5 QLQ-C30 - Time until permanent improvement by 10 pt in nausea and vomiting according to cytogenetic abnormality (LOCF) - ITT population

	At least one		None		
	Kd (N=31)	**IKd (N=42)**	**Kd (N=77)**	**IKd (N=114)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	0 (0.0)	8 (19.0)	5 (6.5)	12 (10.5)	0.9895
Number (%) of patients censored	31 (100.0)	34 (81.0)	72 (93.5)	102 (89.5)	
Kaplan-Meier estimates of Nausea and vomiting in months					
25% quantile (95% CI)	NC (NC to NC)	20.63 (15.474 to NC)	NC (NC to NC)	NC (NC to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.0134		0.3804	
Hazard ratio (95% CI) vs Kd	-			1.59 (0.56 to 4.51)	
P-value	-	0.9931		0.3847	
Improvement probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful improvement change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Nausea and vomiting
16.2.6.1.2.11 Efficacy response data - Subgroup analyses by cytogenetic abnormality
16.2.6.1.2.11.6 QLQ-C30 - Time until permanent deterioration by 10 pt in nausea and vomiting according to cytogenetic abnormality (LOCF) - ITT population

	At least one		None		
	Kd (N=31)	**IKd (N=42)**	**Kd (N=77)**	**IKd (N=114)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	9 (29.0)	3 (7.1)	9 (11.7)	19 (16.7)	0.0183
Number (%) of patients censored	22 (71.0)	39 (92.9)	68 (88.3)	95 (83.3)	
Kaplan-Meier estimates of Nausea and vomiting in months					
25% quantile (95% CI)	18.53 (2.891 to NC)	NC (NC to NC)	NC (20.370 to NC)	22.41 (19.877 to NC)	
Median (95% CI)	NC (20.074 to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.0166		0.3955	
Hazard ratio (95% CI) vs Kd	-	0.23 (0.06 to 0.85)		1.41 (0.64 to 3.11)	
P-value	-	0.0281		0.3979	
Deterioration probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful deterioration change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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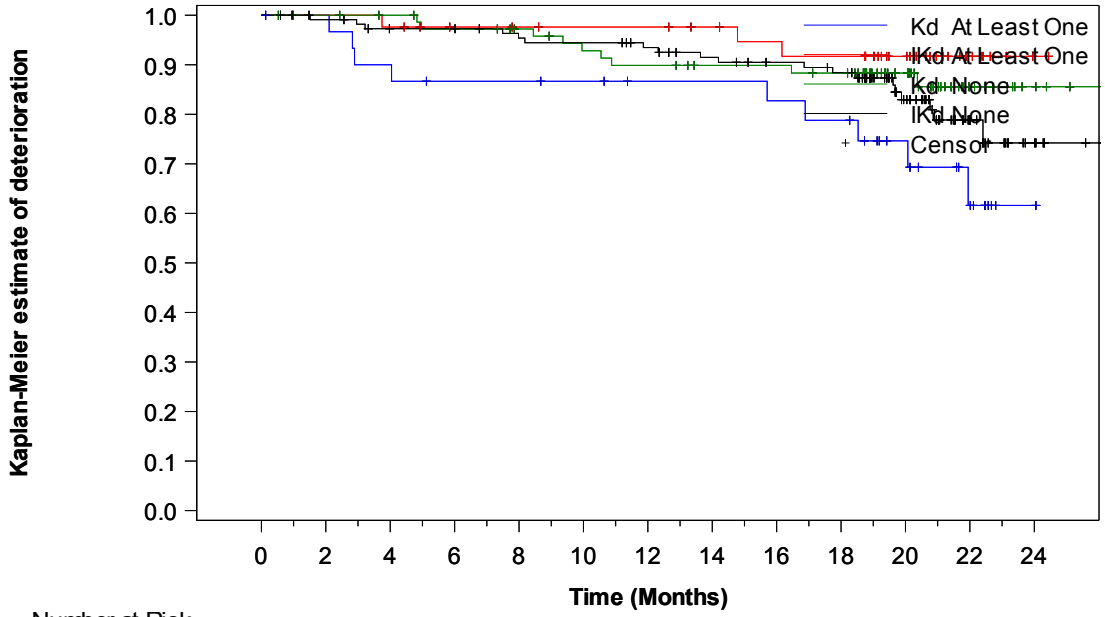
16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Nausea and vomiting
16.2.6.1.2.11 Efficacy response data - Subgroup analyses by cytogenetic abnormality
16.2.6.1.2.11.7 QLQ-C30 - Time until permanent deterioration by 10 pt in nausea and vomiting according to cytogenetic abnormality - Kaplan-Meier curve (LOCF) - ITT population



Number at Risk									
Kd At Least One	31	27	25	24	22	22	20	11	1
IKd At Least One	42	42	38	36	36	32	31	14	1
Kd None	77	74	70	65	61	58	56	26	6
IKd None	114	108	105	100	96	89	84	36	6

A lower score represents a better level of quality of life. Clinical meaningful deterioration change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
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16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Nausea and vomiting
16.2.6.1.2.12 Efficacy response data - Subgroup analyses by MM type at SE
16.2.6.1.2.12.3 QLQ-C30 - Time to first improvement by 10 pt in nausea and vomiting according to MM type at SE (LOCF) - ITT population

	IgG		Non-IgG		
	Kd (N=85)	**IKd (N=126)**	**Kd (N=38)**	**IKd (N=53)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	11 (12.9)	21 (16.7)	1 (2.6)	5 (9.4)	0.4023
Number (%) of patients censored	74 (87.1)	105 (83.3)	37 (97.4)	48 (90.6)	
Kaplan-Meier estimates of Nausea and vomiting in months					
25% quantile (95% CI)	NC (NC to NC)	NC (5.749 to NC)	NC (NC to NC)	NC (NC to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.4259		0.2288	
Hazard ratio (95% CI) vs Kd	-	1.34 (0.65 to 2.79)		3.45 (0.40 to 29.51)	
P-value	-	0.4276		0.2585	
Improvement probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful improvement change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
PGM=DEVOPS/SAR650984/EFC15246/CIR_RWE/REPORT/PGM/eff_km_subgp_sr_sig_de_i_t.sas OUT=REPORT/OUTPUT/eff_km_c30_nau_impl_semm_de_i_t_x.rtf (07APR2021 14:29)

16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Nausea and vomiting
16.2.6.1.2.12 Efficacy response data - Subgroup analyses by MM type at SE
16.2.6.1.2.12.4 QLQ-C30 - Time to first deterioration by 10 pt in nausea and vomiting according to MM type at SE (LOCF) - ITT population

	IgG		Non-IgG		
	Kd (N=85)	**IKd (N=126)**	**Kd (N=38)**	**IKd (N=53)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	37 (43.5)	69 (54.8)	13 (34.2)	20 (37.7)	0.6689
Number (%) of patients censored	48 (56.5)	57 (45.2)	25 (65.8)	33 (62.3)	
Kaplan-Meier estimates of Nausea and vomiting in months					
25% quantile (95% CI)	3.06 (1.906 to 4.632)	4.37 (2.595 to 6.538)	6.51 (1.216 to NC)	6.47 (2.070 to 15.507)	
Median (95% CI)	NC (6.768 to NC)	15.41 (8.214 to 21.027)	NC (9.363 to NC)	NC (15.507 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (22.407 to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.2448		0.8867	
Hazard ratio (95% CI) vs Kd	-	1.27 (0.85 to 1.89)		1.05 (0.52 to 2.11)	
P-value	-	0.2459		0.8872	
Deterioration probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful deterioration change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
PGM=DEVOPS/SAR650984/EFC15246/CIR_RWE/REPORT/PGM/eff_km_subgp_sr_sig_de_i_t.sas OUT=REPORT/OUTPUT/eff_km_c30_nau_detl_semm_de_i_t_x.rtf (07APR2021 14:29)

16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Nausea and vomiting
16.2.6.1.2.12 Efficacy response data - Subgroup analyses by MM type at SE
16.2.6.1.2.12.5 QLQ-C30 - Time until permanent improvement by 10 pt in nausea and vomiting according to MM type at SE (LOCF) - ITT population

	IgG		Non-IgG		
	Kd (N=85)	**IKd (N=126)**	**Kd (N=38)**	**IKd (N=53)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	5 (5.9)	19 (15.1)	1 (2.6)	4 (7.5)	0.9688
Number (%) of patients censored	80 (94.1)	107 (84.9)	37 (97.4)	49 (92.5)	
Kaplan-Meier estimates of Nausea and vomiting in months					
25% quantile (95% CI)	NC (NC to NC)	NC (20.632 to NC)	NC (NC to NC)	NC (NC to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.0433		0.3372	
Hazard ratio (95% CI) vs Kd	-	2.66 (0.99 to 7.11)		2.79 (0.31 to 25.00)	
P-value	-	0.0520		0.3582	
Improvement probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful improvement change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Nausea and vomiting
16.2.6.1.2.12 Efficacy response data - Subgroup analyses by MM type at SE
16.2.6.1.2.12.6 QLQ-C30 - Time until permanent deterioration by 10 pt in nausea and vomiting according to MM type at SE (LOCF) - ITT population

	IgG		Non-IgG		
	Kd (N=85)	**IKd (N=126)**	**Kd (N=38)**	**IKd (N=53)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	13 (15.3)	17 (13.5)	6 (15.8)	5 (9.4)	0.4372
Number (%) of patients censored	72 (84.7)	109 (86.5)	32 (84.2)	48 (90.6)	
Kaplan-Meier estimates of Nausea and vomiting in months					
25% quantile (95% CI)	NC (20.074 to NC)	NC (20.895 to NC)	NC (9.363 to NC)	NC (19.614 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.8141		0.2852	
Hazard ratio (95% CI) vs Kd	-	0.92 (0.45 to 1.89)		0.53 (0.16 to 1.73)	
P-value	-	0.8141		0.2933	
Deterioration probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful deterioration change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Nausea and vomiting
16.2.6.1.2.13 Efficacy response data - Subgroup analyses by previous autologous stem-cell
16.2.6.1.2.13.3 QLQ-C30 - Time to first improvement by 10 pt in nausea and vomiting according to previous autologous stem-cell (LOCF) - ITT population

	Yes		No		
	Kd (N=69)	**IKd (N=116)**	**Kd (N=54)**	**IKd (N=63)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	8 (11.6)	14 (12.1)	4 (7.4)	12 (19.0)	0.1812
Number (%) of patients censored	61 (88.4)	102 (87.9)	50 (92.6)	51 (81.0)	
Kaplan-Meier estimates of Nausea and vomiting in months					
25% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (1.413 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.9190		0.0677	
Hazard ratio (95% CI) vs Kd	-	1.05 (0.44 to 2.49)		2.75 (0.89 to 8.53)	
P-value	-	0.9194		0.0799	
Improvement probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful improvement change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Nausea and vomiting
16.2.6.1.2.13 Efficacy response data - Subgroup analyses by previous autologous stem-cell
16.2.6.1.2.13.4 QLQ-C30 - Time to first deterioration by 10 pt in nausea and vomiting according to previous autologous stem-cell (LOCF) - ITT population

	Yes		No		
	Kd (N=69)	**IKd (N=116)**	**Kd (N=54)**	**IKd (N=63)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	31 (44.9)	60 (51.7)	19 (35.2)	29 (46.0)	0.8402
Number (%) of patients censored	38 (55.1)	56 (48.3)	35 (64.8)	34 (54.0)	
Kaplan-Meier estimates of Nausea and vomiting in months					
25% quantile (95% CI)	3.84 (1.906 to 6.538)	3.75 (2.267 to 5.815)	4.01 (1.216 to 9.791)	7.39 (2.595 to 12.780)	
Median (95% CI)	NC (6.768 to NC)	15.51 (8.214 to NC)	NC (9.791 to NC)	21.03 (12.780 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (22.407 to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.5411		0.4329	
Hazard ratio (95% CI) vs Kd	-	1.14 (0.74 to 1.77)		1.26 (0.71 to 2.25)	
P-value	-	0.5414		0.4339	
Deterioration probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful deterioration change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Nausea and vomiting
16.2.6.1.2.13 Efficacy response data - Subgroup analyses by previous autologous stem-cell
16.2.6.1.2.13.5 QLQ-C30 - Time until permanent improvement by 10 pt in nausea and vomiting according to previous autologous stem-cell (LOCF) - ITT population

	Yes		No		
	Kd (N=69)	**IKd (N=116)**	**Kd (N=54)**	**IKd (N=63)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	3 (4.3)	12 (10.3)	3 (5.6)	11 (17.5)	0.7443
Number (%) of patients censored	66 (95.7)	104 (89.7)	51 (94.4)	52 (82.5)	
Kaplan-Meier estimates of Nausea and vomiting in months					
25% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (15.507 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.1636		0.0572	
Hazard ratio (95% CI) vs Kd	-	2.39 (0.67 to 8.47)		3.22 (0.90 to 11.56)	
P-value	-	0.1770		0.0723	
Improvement probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful improvement change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Nausea and vomiting
16.2.6.1.2.13 Efficacy response data - Subgroup analyses by previous autologous stem-cell
16.2.6.1.2.13.6 QLQ-C30 - Time until permanent deterioration by 10 pt in nausea and vomiting according to previous autologous stem-cell (LOCF) - ITT population

	Yes		No		
	Kd (N=69)	**IKd (N=116)**	**Kd (N=54)**	**IKd (N=63)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	12 (17.4)	13 (11.2)	7 (13.0)	9 (14.3)	0.4266
Number (%) of patients censored	57 (82.6)	103 (88.8)	47 (87.0)	54 (85.7)	
Kaplan-Meier estimates of Nausea and vomiting in months					
25% quantile (95% CI)	NC (18.530 to NC)	NC (NC to NC)	NC (16.460 to NC)	22.41 (19.877 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (22.407 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.2571		0.8729	
Hazard ratio (95% CI) vs Kd	-	0.64 (0.29 to 1.40)		1.08 (0.40 to 2.91)	
P-value	-	0.2611		0.8735	
Deterioration probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful deterioration change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Nausea and vomiting
16.2.6.1.2.14 Efficacy response data - Subgroup analyses by baseline eGFR (MDRD)
16.2.6.1.2.14.3 QLQ-C30 - Time to first improvement by 10 pt in nausea and vomiting according to baseline eGFR (MDRD) (LOCF) - ITT population

	>=60 mL/min/1.73m2		<60 mL/min/1.73m2		
	Kd (N=93)	**IKd (N=122)**	**Kd (N=18)**	**IKd (N=43)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	9 (9.7)	17 (13.9)	3 (16.7)	5 (11.6)	0.2464
Number (%) of patients censored	84 (90.3)	105 (86.1)	15 (83.3)	38 (88.4)	
Kaplan-Meier estimates of Nausea and vomiting in months					
25% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (0.986 to NC)	NC (4.665 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.2937		0.4537	
Hazard ratio (95% CI) vs Kd	-	1.54 (0.68 to 3.45)		0.58 (0.14 to 2.44)	
P-value	-	0.2974		0.4592	
Improvement probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful improvement change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Nausea and vomiting
16.2.6.1.2.14 Efficacy response data - Subgroup analyses by baseline eGFR (MDRD)
16.2.6.1.2.14.4 QLQ-C30 - Time to first deterioration by 10 pt in nausea and vomiting according to baseline eGFR (MDRD) (LOCF) - ITT population

	>=60 mL/min/1.73m2		<60 mL/min/1.73m2		
	Kd (N=93)	**IKd (N=122)**	**Kd (N=18)**	**IKd (N=43)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	39 (41.9)	60 (49.2)	8 (44.4)	23 (53.5)	0.6674
Number (%) of patients censored	54 (58.1)	62 (50.8)	10 (55.6)	20 (46.5)	
Kaplan-Meier estimates of Nausea and vomiting in months					
25% quantile (95% CI)	3.89 (1.906 to 5.947)	4.67 (2.004 to 7.721)	4.04 (0.920 to 9.363)	6.08 (3.318 to 7.491)	
Median (95% CI)	NC (9.791 to NC)	18.76 (14.587 to NC)	11.56 (4.041 to NC)	10.81 (7.392 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (22.407 to NC)	NC (11.565 to NC)	NC (NC to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.3421		0.9008	
Hazard ratio (95% CI) vs Kd	-	1.22 (0.81 to 1.82)		0.95 (0.42 to 2.13)	
P-value	-	0.3429		0.9008	
Deterioration probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful deterioration change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Nausea and vomiting
16.2.6.1.2.14 Efficacy response data - Subgroup analyses by baseline eGFR (MDRD)
16.2.6.1.2.14.5 QLQ-C30 - Time until permanent improvement by 10 pt in nausea and vomiting according to baseline eGFR (MDRD) (LOCF) - ITT population

	>=60 mL/min/1.73m2		<60 mL/min/1.73m2		
	Kd (N=93)	**IKd (N=122)**	**Kd (N=18)**	**IKd (N=43)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	4 (4.3)	15 (12.3)	2 (11.1)	5 (11.6)	0.1837
Number (%) of patients censored	89 (95.7)	107 (87.7)	16 (88.9)	38 (88.4)	
Kaplan-Meier estimates of Nausea and vomiting in months					
25% quantile (95% CI)	NC (NC to NC)	NC (20.632 to NC)	NC (0.986 to NC)	NC (18.760 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.0325		0.8193	
Hazard ratio (95% CI) vs Kd	-	3.13 (1.04 to 9.43)		0.83 (0.16 to 4.27)	
P-value	-	0.0427		0.8195	
Hazard ratio inverted (95% CI) vs IKd		-		1.21 (0.23 to 6.25)	

A lower score represents a better level of quality of life. Clinical meaningful improvement change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Nausea and vomiting
16.2.6.1.2.14 Efficacy response data - Subgroup analyses by baseline eGFR (MDRD)
16.2.6.1.2.14.6 QLQ-C30 - Time until permanent deterioration by 10 pt in nausea and vomiting according to baseline eGFR (MDRD) (LOCF) - ITT population

	>=60 mL/min/1.73m2		<60 mL/min/1.73m2		
	Kd (N=93)	**IKd (N=122)**	**Kd (N=18)**	**IKd (N=43)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	14 (15.1)	16 (13.1)	4 (22.2)	6 (14.0)	0.3293
Number (%) of patients censored	79 (84.9)	106 (86.9)	14 (77.8)	37 (86.0)	
Kaplan-Meier estimates of Nausea and vomiting in months					
25% quantile (95% CI)	NC (20.370 to NC)	NC (20.895 to NC)	20.07 (4.041 to NC)	NC (19.877 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (9.363 to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.8648		0.2509	
Hazard ratio (95% CI) vs Kd	-	0.94 (0.46 to 1.93)		0.48 (0.14 to 1.72)	
P-value	-	0.8644		0.2613	
Deterioration probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful deterioration change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
PGM=DEVOPS/SAR650984/EFC15246/CIR_RWE/REPORT/PGM/eff_km_subgp_sr_sig_de_i_t.sas OUT=REPORT/OUTPUT/eff_km_c30_nau_detpl_crcl_de_i_t_x.rtf (07APR2021 14:29)

16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Nausea and vomiting
16.2.6.1.2.15 Efficacy response data - Subgroup analyses by previous treatment with PI
16.2.6.1.2.15.3 QLQ-C30 - Time to first improvement by 10 pt in nausea and vomiting according to previous treatment with PI (LOCF) - ITT population

	Yes		No		
	Kd (N=47)	**IKd (N=81)**	**Kd (N=76)**	**IKd (N=98)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	5 (10.6)	13 (16.0)	7 (9.2)	13 (13.3)	0.9850
Number (%) of patients censored	42 (89.4)	68 (84.0)	69 (90.8)	85 (86.7)	
Kaplan-Meier estimates of Nausea and vomiting in months					
25% quantile (95% CI)	NC (NC to NC)	NC (4.830 to NC)	NC (NC to NC)	NC (NC to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.4165		0.3874	
Hazard ratio (95% CI) vs Kd	-	1.53 (0.54 to 4.29)		1.50 (0.60 to 3.75)	
P-value	-	0.4201		0.3907	
Improvement probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful improvement change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
PGM=DEVOPS/SAR650984/EFC15246/CIR_RWE/REPORT/PGM/eff_km_subgp_sr_sig_de_i_t.sas OUT=REPORT/OUTPUT/eff_km_c30_nau_impl_pi_de_i_t_x.rtf (07APR2021 14:29)

16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Nausea and vomiting
16.2.6.1.2.15 Efficacy response data - Subgroup analyses by previous treatment with PI
16.2.6.1.2.15.4 QLQ-C30 - Time to first deterioration by 10 pt in nausea and vomiting according to previous treatment with PI (LOCF) - ITT population

	Yes		No		
	Kd (N=47)	**IKd (N=81)**	**Kd (N=76)**	**IKd (N=98)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	13 (27.7)	35 (43.2)	37 (48.7)	54 (55.1)	0.2247
Number (%) of patients censored	34 (72.3)	46 (56.8)	39 (51.3)	44 (44.9)	
Kaplan-Meier estimates of Nausea and vomiting in months					
25% quantile (95% CI)	6.54 (1.216 to NC)	6.11 (1.511 to 9.331)	3.09 (1.906 to 4.632)	3.78 (2.267 to 6.472)	
Median (95% CI)	NC (NC to NC)	NC (14.752 to NC)	11.04 (4.961 to NC)	15.05 (7.721 to 21.027)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (22.407 to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.1056		0.8030	
Hazard ratio (95% CI) vs Kd	-	1.68 (0.89 to 3.18)		1.05 (0.69 to 1.60)	
P-value	-	0.1098		0.8039	
Deterioration probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful deterioration change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Nausea and vomiting
16.2.6.1.2.15 Efficacy response data - Subgroup analyses by previous treatment with PI
16.2.6.1.2.15.5 QLQ-C30 - Time until permanent improvement by 10 pt in nausea and vomiting according to previous treatment with PI (LOCF) - ITT population

	Yes		No		
	Kd (N=47)	**IKd (N=81)**	**Kd (N=76)**	**IKd (N=98)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	3 (6.4)	11 (13.6)	3 (3.9)	12 (12.2)	0.6940
Number (%) of patients censored	44 (93.6)	70 (86.4)	73 (96.1)	86 (87.8)	
Kaplan-Meier estimates of Nausea and vomiting in months					
25% quantile (95% CI)	NC (NC to NC)	NC (20.632 to NC)	NC (NC to NC)	NC (NC to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.2131		0.0620	
Hazard ratio (95% CI) vs Kd	-	2.20 (0.61 to 7.90)		3.13 (0.88 to 11.10)	
P-value	-	0.2250		0.0769	
Improvement probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful improvement change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Nausea and vomiting
16.2.6.1.2.15 Efficacy response data - Subgroup analyses by previous treatment with PI
16.2.6.1.2.15.6 QLQ-C30 - Time until permanent deterioration by 10 pt in nausea and vomiting according to previous treatment with PI (LOCF) - ITT population

	Yes		No		
	Kd (N=47)	**IKd (N=81)**	**Kd (N=76)**	**IKd (N=98)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	4 (8.5)	7 (8.6)	15 (19.7)	15 (15.3)	0.6046
Number (%) of patients censored	43 (91.5)	74 (91.4)	61 (80.3)	83 (84.7)	
Kaplan-Meier estimates of Nausea and vomiting in months					
25% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	21.95 (15.704 to NC)	NC (20.764 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.9625		0.3863	
Hazard ratio (95% CI) vs Kd	-	1.03 (0.30 to 3.52)		0.73 (0.36 to 1.49)	
P-value	-	0.9627		0.3882	
Deterioration probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful deterioration change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Nausea and vomiting
16.2.6.1.2.16 Efficacy response data - Subgroup analyses by previous treatment with IMiD
16.2.6.1.2.16.3 QLQ-C30 - Time to first improvement by 10 pt in nausea and vomiting according to previous treatment with IMiD (LOCF) - ITT population

	Yes		No		
	Kd (N=62)	**IKd (N=81)**	**Kd (N=61)**	**IKd (N=98)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	5 (8.1)	13 (16.0)	7 (11.5)	13 (13.3)	0.4248
Number (%) of patients censored	57 (91.9)	68 (84.0)	54 (88.5)	85 (86.7)	
Kaplan-Meier estimates of Nausea and vomiting in months					
25% quantile (95% CI)	NC (NC to NC)	NC (3.417 to NC)	NC (NC to NC)	NC (NC to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.1637		0.7217	
Hazard ratio (95% CI) vs Kd	-	2.05 (0.73 to 5.75)		1.18 (0.47 to 2.96)	
P-value	-	0.1728		0.7220	
Improvement probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful improvement change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Nausea and vomiting
16.2.6.1.2.16 Efficacy response data - Subgroup analyses by previous treatment with IMiD
16.2.6.1.2.16.4 QLQ-C30 - Time to first deterioration by 10 pt in nausea and vomiting according to previous treatment with IMiD (LOCF) - ITT population

	Yes		No		
	Kd (N=62)	**IKd (N=81)**	**Kd (N=61)**	**IKd (N=98)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	24 (38.7)	42 (51.9)	26 (42.6)	47 (48.0)	0.5521
Number (%) of patients censored	38 (61.3)	39 (48.1)	35 (57.4)	51 (52.0)	
Kaplan-Meier estimates of Nausea and vomiting in months					
25% quantile (95% CI)	4.04 (1.216 to 6.538)	2.86 (1.511 to 7.392)	3.75 (1.906 to 6.768)	6.08 (3.778 to 8.214)	
Median (95% CI)	NC (8.476 to NC)	16.66 (7.721 to NC)	NC (6.768 to NC)	18.60 (9.955 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (22.407 to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.2387		0.6949	
Hazard ratio (95% CI) vs Kd	-	1.35 (0.82 to 2.23)		1.10 (0.68 to 1.78)	
P-value	-	0.2405		0.6950	
Deterioration probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful deterioration change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Nausea and vomiting
16.2.6.1.2.16 Efficacy response data - Subgroup analyses by previous treatment with IMiD
16.2.6.1.2.16.5 QLQ-C30 - Time until permanent improvement by 10 pt in nausea and vomiting according to previous treatment with IMiD (LOCF) - ITT population

	Yes		No		
	Kd (N=62)	**IKd (N=81)**	**Kd (N=61)**	**IKd (N=98)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	4 (6.5)	12 (14.8)	2 (3.3)	11 (11.2)	0.6517
Number (%) of patients censored	58 (93.5)	69 (85.2)	59 (96.7)	87 (88.8)	
Kaplan-Meier estimates of Nausea and vomiting in months					
25% quantile (95% CI)	NC (NC to NC)	NC (17.741 to NC)	NC (NC to NC)	NC (NC to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.1396		0.0768	
Hazard ratio (95% CI) vs Kd	-	2.29 (0.74 to 7.10)		3.57 (0.79 to 16.11)	
P-value	-	0.1511		0.0978	
Improvement probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful improvement change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Nausea and vomiting
16.2.6.1.2.16 Efficacy response data - Subgroup analyses by previous treatment with IMiD
16.2.6.1.2.16.6 QLQ-C30 - Time until permanent deterioration by 10 pt in nausea and vomiting according to previous treatment with IMiD (LOCF) - ITT population

	Yes		No		
	Kd (N=62)	**IKd (N=81)**	**Kd (N=61)**	**IKd (N=98)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	9 (14.5)	10 (12.3)	10 (16.4)	12 (12.2)	0.8472
Number (%) of patients censored	53 (85.5)	71 (87.7)	51 (83.6)	86 (87.8)	
Kaplan-Meier estimates of Nausea and vomiting in months					
25% quantile (95% CI)	NC (16.460 to NC)	NC (20.764 to NC)	NC (18.530 to NC)	NC (22.407 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.6797		0.5027	
Hazard ratio (95% CI) vs Kd	-	0.83 (0.34 to 2.04)		0.75 (0.32 to 1.74)	
P-value	-	0.6802		0.5042	
Deterioration probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful deterioration change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Nausea and vomiting
16.2.6.1.2.17 Efficacy response data - Subgroup analyses by previous treatment with PI and IMiD
16.2.6.1.2.17.3 QLQ-C30 - Time to first improvement by 10 pt in nausea and vomiting according to previous treatment with PI and IMiD (LOCF) - ITT population

	Yes		No		
	Kd (N=17)	**IKd (N=23)**	**Kd (N=106)**	**IKd (N=156)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	1 (5.9)	3 (13.0)	11 (10.4)	23 (14.7)	0.7367
Number (%) of patients censored	16 (94.1)	20 (87.0)	95 (89.6)	133 (85.3)	
Kaplan-Meier estimates of Nausea and vomiting in months					
25% quantile (95% CI)	NC (1.938 to NC)	NC (1.051 to NC)	NC (NC to NC)	NC (NC to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.4762		0.2945	
Hazard ratio (95% CI) vs Kd	-	2.23 (0.23 to 21.43)		1.47 (0.71 to 3.01)	
P-value	-	0.4879		0.2975	
Improvement probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful improvement change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Nausea and vomiting
16.2.6.1.2.17 Efficacy response data - Subgroup analyses by previous treatment with PI and IMiD
16.2.6.1.2.17.4 QLQ-C30 - Time to first deterioration by 10 pt in nausea and vomiting according to previous treatment with PI and IMiD (LOCF) - ITT population

	Yes		No		
	Kd (N=17)	**IKd (N=23)**	**Kd (N=106)**	**IKd (N=156)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	4 (23.5)	12 (52.2)	46 (43.4)	77 (49.4)	0.1401
Number (%) of patients censored	13 (76.5)	11 (47.8)	60 (56.6)	79 (50.6)	
Kaplan-Meier estimates of Nausea and vomiting in months					
25% quantile (95% CI)	6.54 (0.986 to NC)	2.60 (0.986 to 7.425)	3.84 (2.103 to 5.651)	4.90 (3.318 to 7.392)	
Median (95% CI)	NC (6.538 to NC)	14.75 (2.825 to NC)	NC (9.363 to NC)	18.60 (12.025 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (19.614 to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.1119		0.6303	
Hazard ratio (95% CI) vs Kd	-	2.44 (0.78 to 7.56)		1.09 (0.76 to 1.58)	
P-value	-	0.1238		0.6304	
Deterioration probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful deterioration change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Nausea and vomiting
16.2.6.1.2.17 Efficacy response data - Subgroup analyses by previous treatment with PI and IMiD
16.2.6.1.2.17.5 QLQ-C30 - Time until permanent improvement by 10 pt in nausea and vomiting according to previous treatment with PI and IMiD (LOCF) - ITT population

	Yes		No		
	Kd (N=17)	**IKd (N=23)**	**Kd (N=106)**	**IKd (N=156)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	1 (5.9)	3 (13.0)	5 (4.7)	20 (12.8)	0.8580
Number (%) of patients censored	16 (94.1)	20 (87.0)	101 (95.3)	136 (87.2)	
Kaplan-Meier estimates of Nausea and vomiting in months					
25% quantile (95% CI)	NC (1.938 to NC)	NC (1.413 to NC)	NC (NC to NC)	NC (NC to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.4832		0.0330	
Hazard ratio (95% CI) vs Kd	-	2.20 (0.23 to 21.17)		2.78 (1.04 to 7.40)	
P-value	-	0.4944		0.0411	
Hazard ratio inverted (95% CI) vs IKd		-		0.36 (0.14 to 0.96)	

A lower score represents a better level of quality of life. Clinical meaningful improvement change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
PGM=DEVOPS/SAR650984/EFC15246/CIR_RWE/REPORT/PGM/eff_km_subgp_sr_sig_de_i_t.sas OUT=REPORT/OUTPUT/eff_km_c30_nau_imppl_piimid_de_i_t_x.rtf (07APR2021 14:29)

16.2.6.1 Health-related quality-of-life endpoints - QLQ-C30
16.2.6.1.2 Nausea and vomiting
16.2.6.1.2.17 Efficacy response data - Subgroup analyses by previous treatment with PI and IMiD
16.2.6.1.2.17.6 QLQ-C30 - Time until permanent deterioration by 10 pt in nausea and vomiting according to previous treatment with PI and IMiD (LOCF) - ITT population

	Yes		No		
	Kd (N=17)	**IKd (N=23)**	**Kd (N=106)**	**IKd (N=156)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	1 (5.9)	3 (13.0)	18 (17.0)	19 (12.2)	0.3016
Number (%) of patients censored	16 (94.1)	20 (87.0)	88 (83.0)	137 (87.8)	
Kaplan-Meier estimates of Nausea and vomiting in months					
25% quantile (95% CI)	NC (9.955 to NC)	NC (1.511 to NC)	NC (20.074 to NC)	NC (22.407 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.4546		0.2653	
Hazard ratio (95% CI) vs Kd	-	2.31 (0.24 to 22.25)		0.69 (0.36 to 1.32)	
P-value	-	0.4677		0.2679	
Deterioration probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful deterioration change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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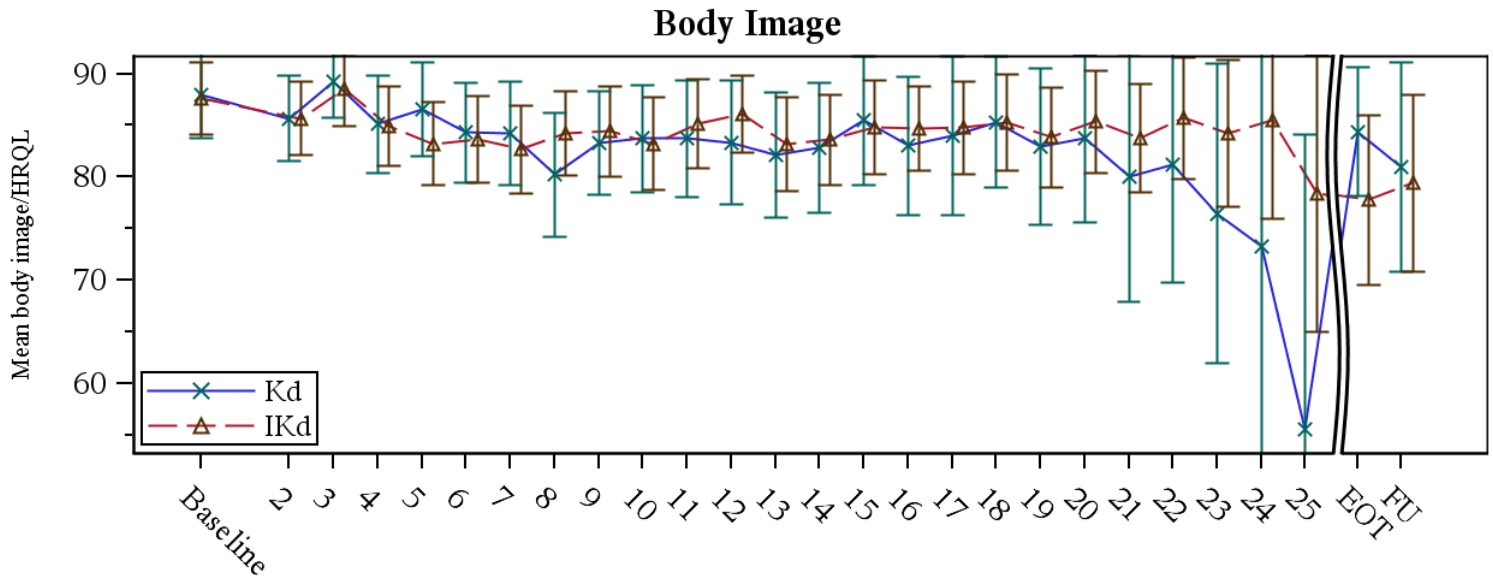
16.2.6.1 Health-related quality-of-life endpoints - QLQ-MY20
16.2.6.1.2 Body image
16.2.6.1.2.1 Efficacy response data
16.2.6.1.2.1.1 QLQ-MY20 - Mean and 95% CI for body image score over time - ITT population



#patients																										
Kd	114	114	112	110	104	100	95	91	88	84	78	72	67	66	62	57	52	50	45	37	30	23	17	10	6	62	35
IKd	167	170	168	164	161	155	150	146	139	133	130	127	121	118	112	109	105	102	97	91	78	56	38	23	17	60	34

A higher score represents a better level of quality of life. Cycles with less than 20 patients overall are not presented.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
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16.2.6.1 Health-related quality-of-life endpoints - QLQ-MY20
16.2.6.1.2 Body image
16.2.6.1.2.1 Efficacy response data
16.2.6.1.2.1.15 QLQ-MY20 - Time to first improvement by 15 pt in Body image (LOCF) - ITT population

First improvement 15 points Body image (%)	**Kd (N=123)**	**IKd (N=179)**
Number (%) of events	28 (22.8)	40 (22.3)
Number (%) of patients censored	95 (77.2)	139 (77.7)
Kaplan-Meier estimates of body image in months		
25% quantile (95% CI)	NC (2.234 to NC)	NC (2.595 to NC)
Median (95% CI)	NC (NC to NC)	NC (NC to NC)
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)
Comparison vs. Kd		
Stratified[a] Log-Rank test p-value[b] vs Kd	-	0.9627
Stratified[a] Hazard ratio (95% CI) vs Kd	-	0.99 (0.61 to 1.61)
P-value	-	0.9626
Improvement probability (95% CI)[c]		
3 Months	0.183 (0.120 to 0.257)	0.195 (0.140 to 0.257)
6 Months	0.217 (0.148 to 0.295)	0.207 (0.150 to 0.270)

A lower score represents a better level of quality of life. Clinical meaningful improvement change from baseline less than or equal to -15 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] Stratified on number of prior lines of therapy (1 vs. >1) and Revised International Staging System (R-ISS) stage (I or II vs. III vs. not classified) according to IRT
[b] One-sided significance level is 0.025
[c] Estimated using the Kaplan-Meier method
NA/NC = Not Applicable / Not Calculable
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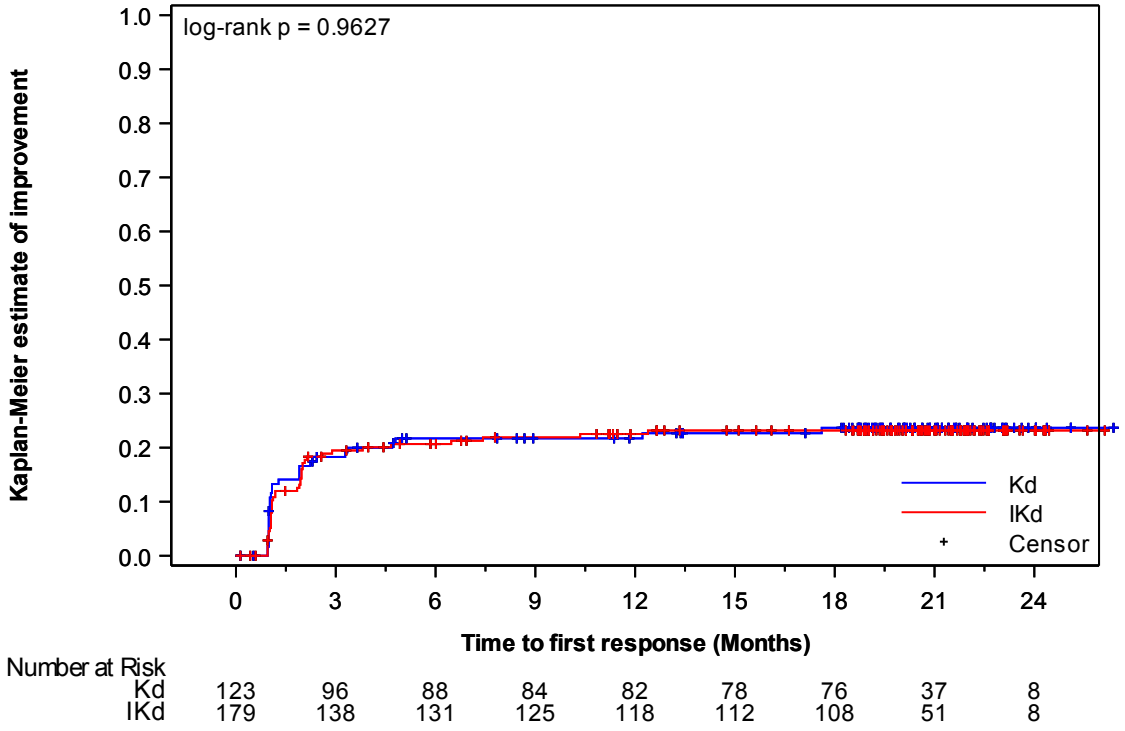
16.2.6.1 Health-related quality-of-life endpoints - QLQ-MY20
16.2.6.1.2 Body image
16.2.6.1.2.1 Efficacy response data
16.2.6.1.2.1.16 QLQ-MY20 - Time to first improvement by 15 pt in Body image - Kaplan-Meier curve (LOCF) - ITT population



A lower score represents a better level of quality of life. Clinical meaningful improvement change from baseline less than or equal to -15 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
PGM=DEVOPS/SAR650984/EFC15246/CIR_RWE/REPORT/PGM/eff_qlq_km_i_f.sas OUT=REPORT/OUTPUT/eff_km_my20_bdy_imp15l_de_i_f_x.rtf (07APR2021 14:25)

16.2.6.1 Health-related quality-of-life endpoints - QLQ-MY20
16.2.6.1.2 Body image
16.2.6.1.2.1 Efficacy response data
16.2.6.1.2.1.17 QLQ-MY20 - Time to first deterioration by 15 pt in Body image (LOCF) - ITT population

First deterioration 15 points Body image (%)	**Kd (N=123)**	**IKd (N=179)**
Number (%) of events	59 (48.0)	102 (57.0)
Number (%) of patients censored	64 (52.0)	77 (43.0)
Kaplan-Meier estimates of body image in months		
25% quantile (95% CI)	2.86 (1.314 to 5.322)	2.83 (1.971 to 3.417)
Median (95% CI)	20.57 (7.261 to NC)	8.97 (6.505 to 15.671)
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)
Comparison vs. Kd		
Stratified[a] Log-Rank test p-value[b] vs Kd	-	0.2246
Stratified[a] Hazard ratio (95% CI) vs Kd	-	1.22 (0.88 to 1.70)
P-value	-	0.2254
Deterioration probability (95% CI)[c]		
3 Months	0.725 (0.636 to 0.796)	0.719 (0.646 to 0.780)
6 Months	0.647 (0.554 to 0.726)	0.592 (0.515 to 0.661)

A lower score represents a better level of quality of life. Clinical meaningful deterioration change from baseline greater than or equal to 15 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] Stratified on number of prior lines of therapy (1 vs. >1) and Revised International Staging System (R-ISS) stage (I or II vs. III vs. not classified) according to IRT
[b] One-sided significance level is 0.025
[c] Estimated using the Kaplan-Meier method
NA/NC = Not Applicable / Not Calculable
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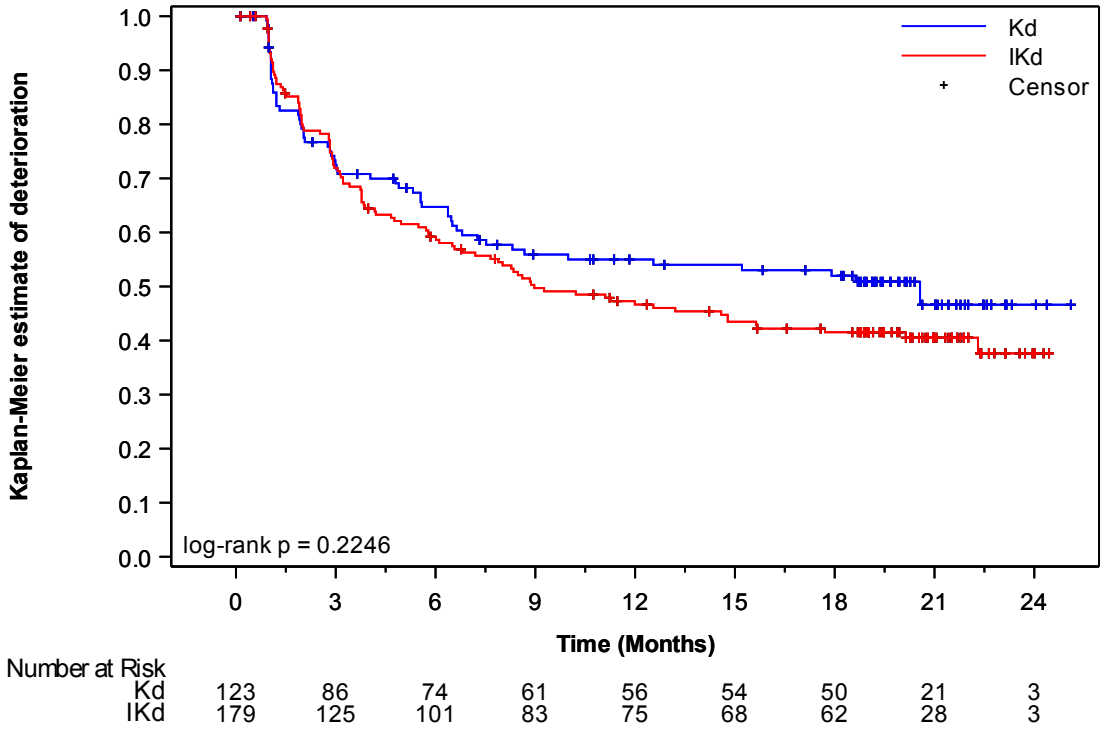
16.2.6.1 Health-related quality-of-life endpoints - QLQ-MY20
16.2.6.1.2 Body image
16.2.6.1.2.1 Efficacy response data
16.2.6.1.2.1.18 QLQ-MY20 - Time to first deterioration by 15 pt in Body image - Kaplan-Meier curve (LOCF) - ITT population



A lower score represents a better level of quality of life. Clinical meaningful deterioration change from baseline greater than or equal to 15 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
PGM=DEVOPS/SAR650984/EFC15246/CIR_RWE/REPORT/PGM/eff_qlq_km_i_f.sas OUT=REPORT/OUTPUT/eff_km_my20_bdy_det15l_de_i_f_x.rtf (07APR2021 14:25)

16.2.6.1 Health-related quality-of-life endpoints - QLQ-MY20
16.2.6.1.2 Body image
16.2.6.1.2.1 Efficacy response data
16.2.6.1.2.1.19 QLQ-MY20 - Time until permanent improvement by 15 pt in Body image (LOCF) - ITT population

First permanent improvement 15 points Body image (%)	**Kd (N=123)**	**IKd (N=179)**
Number (%) of events	12 (9.8)	22 (12.3)
Number (%) of patients censored	111 (90.2)	157 (87.7)
Kaplan-Meier estimates of body image in months		
25% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)
Median (95% CI)	NC (NC to NC)	NC (NC to NC)
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)
Comparison vs. Kd		
Stratified[a] Log-Rank test p-value[b] vs Kd	-	0.5201
Stratified[a] Hazard ratio (95% CI) vs Kd	-	1.26 (0.62 to 2.55)
P-value	-	0.5210
Improvement probability (95% CI)[c]		
3 Months	0.066 (0.031 to 0.120)	0.051 (0.025 to 0.091)
6 Months	0.066 (0.031 to 0.120)	0.075 (0.042 to 0.121)

A lower score represents a better level of quality of life. Clinical meaningful improvement change from baseline less than or equal to -15 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] Stratified on number of prior lines of therapy (1 vs. >1) and Revised International Staging System (R-ISS) stage (I or II vs. III vs. not classified) according to IRT
[b] One-sided significance level is 0.025
[c] Estimated using the Kaplan-Meier method
NA/NC = Not Applicable / Not Calculable
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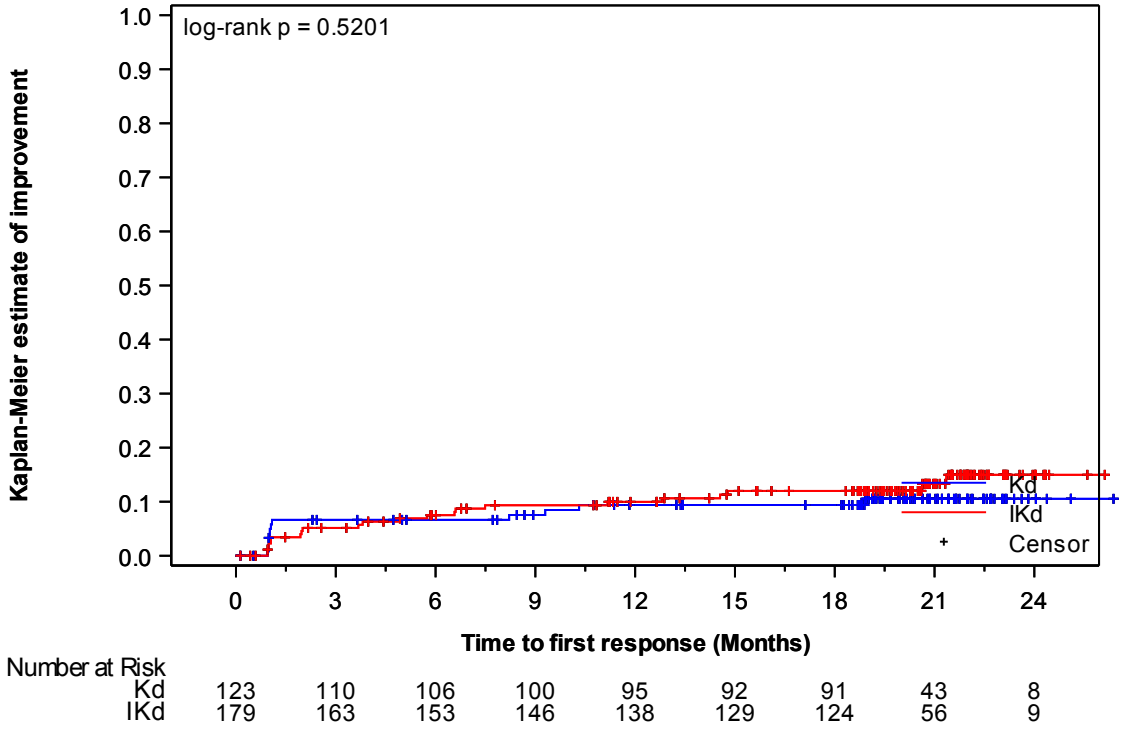
16.2.6.1 Health-related quality-of-life endpoints - QLQ-MY20
16.2.6.1.2 Body image
16.2.6.1.2.1 Efficacy response data
16.2.6.1.2.1.20 QLQ-MY20 - Time until permanent improvement by 15 pt in Body image - Kaplan-Meier curve (LOCF) - ITT population



A lower score represents a better level of quality of life. Clinical meaningful improvement change from baseline less than or equal to -15 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.

16.2.6.1 Health-related quality-of-life endpoints - QLQ-MY20
16.2.6.1.2 Body image
16.2.6.1.2.1 Efficacy response data
16.2.6.1.2.1.21 QLQ-MY20 - Time until permanent deterioration by 15 pt in Body image (LOCF) - ITT population

First permanent deterioration 15 points Body image (%)	**Kd (N=123)**	**IKd (N=179)**
Number (%) of events	30 (24.4)	42 (23.5)
Number (%) of patients censored	93 (75.6)	137 (76.5)
Kaplan-Meier estimates of body image in months		
25% quantile (95% CI)	20.57 (11.302 to NC)	20.90 (14.949 to NC)
Median (95% CI)	NC (NC to NC)	24.44 (24.444 to NC)
75% quantile (95% CI)	NC (NC to NC)	NC (24.444 to NC)
Comparison vs. Kd		
Stratified[a] Log-Rank test p-value[b] vs Kd	-	0.6532
Stratified[a] Hazard ratio (95% CI) vs Kd	-	0.90 (0.56 to 1.44)
P-value	-	0.6534
Deterioration probability (95% CI)[c]		
3 Months	0.925 (0.861 to 0.960)	0.931 (0.882 to 0.960)
6 Months	0.899 (0.829 to 0.942)	0.914 (0.861 to 0.947)

A lower score represents a better level of quality of life. Clinical meaningful deterioration change from baseline greater than or equal to 15 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] Stratified on number of prior lines of therapy (1 vs. >1) and Revised International Staging System (R-ISS) stage (I or II vs. III vs. not classified) according to IRT
[b] One-sided significance level is 0.025
[c] Estimated using the Kaplan-Meier method
NA/NC = Not Applicable / Not Calculable
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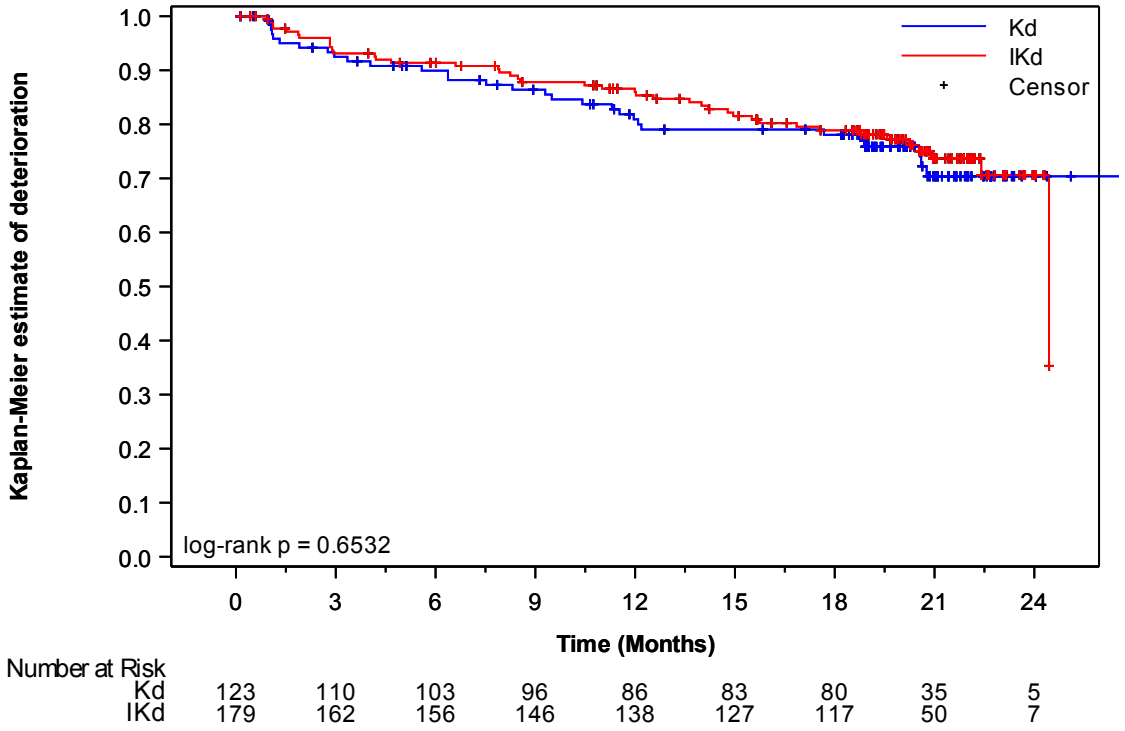
16.2.6.1 Health-related quality-of-life endpoints - QLQ-MY20
16.2.6.1.2 Body image
16.2.6.1.2.1 Efficacy response data
16.2.6.1.2.1.22 QLQ-MY20 - Time until permanent deterioration by 15 pt in Body image - Kaplan-Meier curve (LOCF) - ITT population



A lower score represents a better level of quality of life. Clinical meaningful deterioration change from baseline greater than or equal to 15 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.

16.2.6.1 Health-related quality-of-life endpoints - QLQ-MY20
16.2.6.1.2 Body image
16.2.6.1.2.2 Efficacy response data - Subgroup analyses by age
16.2.6.1.2.2.3 QLQ-MY20 - Time to first improvement by 10 pt in body image according to age (LOCF) - ITT population

	<65 years		>=65 years		
	Kd (N=66)	**IKd (N=88)**	**Kd (N=57)**	**IKd (N=91)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	16 (24.2)	20 (22.7)	12 (21.1)	20 (22.0)	0.8565
Number (%) of patients censored	50 (75.8)	68 (77.3)	45 (78.9)	71 (78.0)	
Kaplan-Meier estimates of body image in months					
25% quantile (95% CI)	NC (1.281 to NC)	NC (1.971 to NC)	NC (1.906 to NC)	NC (2.070 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.8432		0.9488	
Hazard ratio (95% CI) vs Kd	-	0.94 (0.48 to 1.81)		1.02 (0.50 to 2.09)	
P-value	-	0.8426		0.9489	
Improvement probability (95% CI)[b]					

A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.1 Health-related quality-of-life endpoints - QLQ-MY20
16.2.6.1.2 Body image
16.2.6.1.2.2 Efficacy response data - Subgroup analyses by age
16.2.6.1.2.2.4 QLQ-MY20 - Time to first deterioration by 10 pt in body image according to age (LOCF) - ITT population

	<65 years		>=65 years		
	Kd (N=66)	**IKd (N=88)**	**Kd (N=57)**	**IKd (N=91)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	30 (45.5)	48 (54.5)	29 (50.9)	54 (59.3)	0.7575
Number (%) of patients censored	36 (54.5)	40 (45.5)	28 (49.1)	37 (40.7)	
Kaplan-Meier estimates of body image in months					
25% quantile (95% CI)	2.04 (1.084 to 5.585)	2.83 (1.906 to 4.665)	4.04 (1.906 to 6.374)	2.89 (1.478 to 3.417)	
Median (95% CI)	NC (6.374 to NC)	13.21 (6.505 to NC)	17.91 (6.374 to NC)	8.34 (4.205 to 14.784)	
75% quantile (95% CI)	NC (NC to NC)	NC (22.308 to NC)	NC (20.567 to NC)	NC (NC to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.5433		0.2677	
Hazard ratio (95% CI) vs Kd	-	1.15 (0.73 to 1.82)		1.29 (0.82 to 2.03)	
P-value	-	0.5437		0.2690	
Deterioration probability (95% CI)[b]					

A higher score represents a better level of quality of life. Clinical meaningful deterioration change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
PGM=DEVOPS/SAR650984/EFC15246/CIR_RWE/REPORT/PGM/eff_km_subgp_sr_sig_de_i_t.sas OUT=REPORT/OUTPUT/eff_km_my20_bdy_detl_age_de_i_t_x.rtf (07APR2021 14:39)

16.2.6.1 Health-related quality-of-life endpoints - QLQ-MY20
16.2.6.1.2 Body image
16.2.6.1.2.2 Efficacy response data - Subgroup analyses by age
16.2.6.1.2.2.5 QLQ-MY20 - Time until permanent improvement by 10 pt in body image according to age (LOCF) - ITT population

	<65 years		>=65 years		
	Kd (N=66)	**IKd (N=88)**	**Kd (N=57)**	**IKd (N=91)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	7 (10.6)	11 (12.5)	5 (8.8)	11 (12.1)	0.8273
Number (%) of patients censored	59 (89.4)	77 (87.5)	52 (91.2)	80 (87.9)	
Kaplan-Meier estimates of body image in months					
25% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (21.355 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.7475		0.5502	
Hazard ratio (95% CI) vs Kd	-	1.17 (0.45 to 3.01)		1.38 (0.48 to 3.97)	
P-value	-	0.7477		0.5519	
Improvement probability (95% CI)[b]					

A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.1 Health-related quality-of-life endpoints - QLQ-MY20
16.2.6.1.2 Body image
16.2.6.1.2.2 Efficacy response data - Subgroup analyses by age
16.2.6.1.2.2.6 QLQ-MY20 - Time until permanent deterioration by 10 pt in body image according to age (LOCF) - ITT population

	<65 years		>=65 years		
	Kd (N=66)	**IKd (N=88)**	**Kd (N=57)**	**IKd (N=91)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	16 (24.2)	20 (22.7)	14 (24.6)	22 (24.2)	0.8509
Number (%) of patients censored	50 (75.8)	68 (77.3)	43 (75.4)	69 (75.8)	
Kaplan-Meier estimates of body image in months					
25% quantile (95% CI)	20.60 (6.374 to NC)	22.41 (12.550 to NC)	18.92 (11.302 to NC)	20.53 (13.996 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	24.44 (24.444 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (24.444 to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.7375		0.9109	
Hazard ratio (95% CI) vs Kd	-	0.89 (0.46 to 1.73)		0.96 (0.49 to 1.88)	
P-value	-	0.7377		0.9105	
Deterioration probability (95% CI)[b]					

A higher score represents a better level of quality of life. Clinical meaningful deterioration change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
PGM=DEVOPS/SAR650984/EFC15246/CIR_RWE/REPORT/PGM/eff_km_subgp_sr_sig_de_i_t.sas OUT=REPORT/OUTPUT/eff_km_my20_bdy_detpl_age_de_i_t_x.rtf (07APR2021 14:40)

16.2.6.1 Health-related quality-of-life endpoints - QLQ-MY20
16.2.6.1.2 Body image
16.2.6.1.2.3 Efficacy response data - Subgroup analyses by gender
16.2.6.1.2.3.3 QLQ-MY20 - Time to first improvement by 10 pt in body image according to gender (LOCF) - ITT population

	Male		Female		
	Kd (N=68)	**IKd (N=101)**	**Kd (N=55)**	**IKd (N=78)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	10 (14.7)	21 (20.8)	18 (32.7)	19 (24.4)	0.1498
Number (%) of patients censored	58 (85.3)	80 (79.2)	37 (67.3)	59 (75.6)	
Kaplan-Meier estimates of body image in months					
25% quantile (95% CI)	NC (2.234 to NC)	NC (1.971 to NC)	3.35 (0.986 to NC)	NC (1.971 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.3446		0.2953	
Hazard ratio (95% CI) vs Kd	-	1.43 (0.68 to 3.05)		0.71 (0.37 to 1.35)	
P-value	-	0.3473		0.2977	
Improvement probability (95% CI)[b]					

A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.1 Health-related quality-of-life endpoints - QLQ-MY20
16.2.6.1.2 Body image
16.2.6.1.2.3 Efficacy response data - Subgroup analyses by gender
16.2.6.1.2.3.4 QLQ-MY20 - Time to first deterioration by 10 pt in body image according to gender (LOCF) - ITT population

	Male		Female		
	Kd (N=68)	**IKd (N=101)**	**Kd (N=55)**	**IKd (N=78)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	33 (48.5)	60 (59.4)	26 (47.3)	42 (53.8)	0.8920
Number (%) of patients censored	35 (51.5)	41 (40.6)	29 (52.7)	36 (46.2)	
Kaplan-Meier estimates of body image in months					
25% quantile (95% CI)	2.04 (1.117 to 3.055)	2.79 (1.873 to 3.220)	5.55 (1.216 to 7.524)	2.96 (1.906 to 6.012)	
Median (95% CI)	15.21 (4.041 to NC)	8.02 (4.172 to 14.784)	20.57 (7.524 to NC)	14.78 (7.655 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (22.308 to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.3565		0.5342	
Hazard ratio (95% CI) vs Kd	-	1.22 (0.80 to 1.87)		1.17 (0.72 to 1.90)	
P-value	-	0.3573		0.5346	
Deterioration probability (95% CI)[b]					

A higher score represents a better level of quality of life. Clinical meaningful deterioration change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.1 Health-related quality-of-life endpoints - QLQ-MY20
16.2.6.1.2 Body image
16.2.6.1.2.3 Efficacy response data - Subgroup analyses by gender
16.2.6.1.2.3.5 QLQ-MY20 - Time until permanent improvement by 10 pt in body image according to gender (LOCF) - ITT population

	Male		Female		
	Kd (N=68)	**IKd (N=101)**	**Kd (N=55)**	**IKd (N=78)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	6 (8.8)	12 (11.9)	6 (10.9)	10 (12.8)	0.8754
Number (%) of patients censored	62 (91.2)	89 (88.1)	49 (89.1)	68 (87.2)	
Kaplan-Meier estimates of body image in months					
25% quantile (95% CI)	NC (NC to NC)	NC (21.355 to NC)	NC (NC to NC)	NC (20.632 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.5706		0.7357	
Hazard ratio (95% CI) vs Kd	-	1.33 (0.50 to 3.54)		1.19 (0.43 to 3.28)	
P-value	-	0.5719		0.7360	
Improvement probability (95% CI)[b]					

A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.1 Health-related quality-of-life endpoints - QLQ-MY20
16.2.6.1.2 Body image
16.2.6.1.2.3 Efficacy response data - Subgroup analyses by gender
16.2.6.1.2.3.6 QLQ-MY20 - Time until permanent deterioration by 10 pt in body image according to gender (LOCF) - ITT population

	Male		Female		
	Kd (N=68)	**IKd (N=101)**	**Kd (N=55)**	**IKd (N=78)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	15 (22.1)	24 (23.8)	15 (27.3)	18 (23.1)	0.5931
Number (%) of patients censored	53 (77.9)	77 (76.2)	40 (72.7)	60 (76.9)	
Kaplan-Meier estimates of body image in months					
25% quantile (95% CI)	20.60 (6.374 to NC)	20.24 (12.550 to NC)	18.92 (8.312 to NC)	20.90 (14.784 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (20.764 to NC)	24.44 (24.444 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (24.444 to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.8893		0.5344	
Hazard ratio (95% CI) vs Kd	-	1.05 (0.55 to 2.00)		0.80 (0.41 to 1.60)	
P-value	-	0.8898		0.5352	
Deterioration probability (95% CI)[b]					

A higher score represents a better level of quality of life. Clinical meaningful deterioration change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
PGM=DEVOPS/SAR650984/EFC15246/CIR_RWE/REPORT/PGM/eff_km_subgp_sr_sig_de_i_t.sas OUT=REPORT/OUTPUT/eff_km_my20_bdy_detpl_sex_de_i_t_x.rtf (07APR2021 14:40)

16.2.6.1 Health-related quality-of-life endpoints - QLQ-MY20
16.2.6.1.2 Body image
16.2.6.1.2.4 Efficacy response data - Subgroup analyses by ethnic origin
16.2.6.1.2.4.3 QLQ-MY20 - Time to first improvement by 10 pt in body image according to ethnic origin (LOCF) - ITT population

	White		Other		
	Kd (N=83)	**IKd (N=131)**	**Kd (N=28)**	**IKd (N=34)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	17 (20.5)	32 (24.4)	10 (35.7)	8 (23.5)	0.2453
Number (%) of patients censored	66 (79.5)	99 (75.6)	18 (64.3)	26 (76.5)	
Kaplan-Meier estimates of body image in months					
25% quantile (95% CI)	NC (2.234 to NC)	12.39 (2.004 to NC)	1.91 (0.986 to NC)	NC (1.084 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (2.431 to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.5305		0.3294	
Hazard ratio (95% CI) vs Kd	-	1.21 (0.67 to 2.17)		0.63 (0.25 to 1.60)	
P-value	-	0.5311		0.3336	
Improvement probability (95% CI)[b]					

A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.1 Health-related quality-of-life endpoints - QLQ-MY20
16.2.6.1.2 Body image
16.2.6.1.2.4 Efficacy response data - Subgroup analyses by ethnic origin
16.2.6.1.2.4.4 QLQ-MY20 - Time to first deterioration by 10 pt in body image according to ethnic origin (LOCF) - ITT population

	White		Other		
	Kd (N=83)	**IKd (N=131)**	**Kd (N=28)**	**IKd (N=34)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	38 (45.8)	77 (58.8)	19 (67.9)	20 (58.8)	0.1418
Number (%) of patients censored	45 (54.2)	54 (41.2)	9 (32.1)	14 (41.2)	
Kaplan-Meier estimates of body image in months					
25% quantile (95% CI)	3.02 (1.216 to 6.374)	2.83 (1.906 to 3.417)	1.22 (1.051 to 2.957)	2.89 (1.117 to 4.205)	
Median (95% CI)	NC (7.261 to NC)	8.48 (5.815 to 15.671)	5.55 (1.314 to 18.628)	8.61 (3.121 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (8.674 to NC)	NC (13.207 to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.1152		0.4894	
Hazard ratio (95% CI) vs Kd	-	1.37 (0.93 to 2.01)		0.80 (0.43 to 1.50)	
P-value	-	0.1167		0.4903	
Deterioration probability (95% CI)[b]					

A higher score represents a better level of quality of life. Clinical meaningful deterioration change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.1 Health-related quality-of-life endpoints - QLQ-MY20
16.2.6.1.2 Body image
16.2.6.1.2.4 Efficacy response data - Subgroup analyses by ethnic origin
16.2.6.1.2.4.5 QLQ-MY20 - Time until permanent improvement by 10 pt in body image according to ethnic origin (LOCF) - ITT population

	White		Other		
	Kd (N=83)	**IKd (N=131)**	**Kd (N=28)**	**IKd (N=34)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	8 (9.6)	17 (13.0)	3 (10.7)	5 (14.7)	0.9577
Number (%) of patients censored	75 (90.4)	114 (87.0)	25 (89.3)	29 (85.3)	
Kaplan-Meier estimates of body image in months					
25% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (8.214 to NC)	NC (3.811 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.4711		0.6475	
Hazard ratio (95% CI) vs Kd	-	1.36 (0.59 to 3.15)		1.39 (0.33 to 5.84)	
P-value	-	0.4729		0.6490	

A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.1 Health-related quality-of-life endpoints - QLQ-MY20
16.2.6.1.2 Body image
16.2.6.1.2.4 Efficacy response data - Subgroup analyses by ethnic origin
16.2.6.1.2.4.6 QLQ-MY20 - Time until permanent deterioration by 10 pt in body image according to ethnic origin (LOCF) - ITT population

	White		Other		
	Kd (N=83)	**IKd (N=131)**	**Kd (N=28)**	**IKd (N=34)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	18 (21.7)	32 (24.4)	11 (39.3)	9 (26.5)	0.3028
Number (%) of patients censored	65 (78.3)	99 (75.6)	17 (60.7)	25 (73.5)	
Kaplan-Meier estimates of body image in months					
25% quantile (95% CI)	20.60 (11.302 to NC)	20.90 (14.193 to NC)	3.35 (1.051 to 18.825)	16.85 (6.604 to NC)	
Median (95% CI)	NC (NC to NC)	24.44 (24.444 to NC)	NC (10.415 to NC)	NC (20.238 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (24.444 to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.7386		0.2709	
Hazard ratio (95% CI) vs Kd	-	1.10 (0.62 to 1.97)		0.61 (0.25 to 1.48)	
P-value	-	0.7387		0.2756	
Deterioration probability (95% CI)[b]					

A higher score represents a better level of quality of life. Clinical meaningful deterioration change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.1 Health-related quality-of-life endpoints - QLQ-MY20
16.2.6.1.2 Body image
16.2.6.1.2.5 Efficacy response data - Subgroup analyses by geographical region
16.2.6.1.2.5.3 QLQ-MY20 - Time to first improvement by 10 pt in body image according to geographical region (LOCF) - ITT population

	Europe		America		Asia		Other countries		
	Kd (N=60)	**IKd (N=85)**	**Kd (N=20)**	**IKd (N=24)**	**Kd (N=21)**	**IKd (N=25)**	**Kd (N=22)**	**IKd (N=45)**	**p-value of treatment-by-subgroup interaction[c]**
Number (%) of events	13 (21.7)	15 (17.6)	6 (30.0)	6 (25.0)	8 (38.1)	6 (24.0)	1 (4.5)	13 (28.9)	0.1763
Number (%) of patients censored	47 (78.3)	70 (82.4)	14 (70.0)	18 (75.0)	13 (61.9)	19 (76.0)	21 (95.5)	32 (71.1)	
Kaplan-Meier estimates of event in months									
25% quantile (95% CI)	NC (1.018 to NC)	NC (2.595 to NC)	10.48 (0.953 to NC)	7.43 (0.953 to NC)	2.17 (0.986 to NC)	NC (1.051 to NC)	NC (1.084 to NC)	3.81 (1.084 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (3.351 to NC)	NC (7.425 to NC)	NC (1.906 to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	

A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
PGM=DEVOPS/SAR650984/EFC15246/CIR_RWE/REPORT/PGM/eff_km_subgp_sr_sig_de_i_t.sas OUT=REPORT/OUTPUT/eff_km_my20_bdy_impl_greg_de_i_t_x.rtf (07APR2021 14:39)

16.2.6.1 Health-related quality-of-life endpoints - QLQ-MY20
16.2.6.1.2 Body image
16.2.6.1.2.5 Efficacy response data - Subgroup analyses by geographical region
16.2.6.1.2.5.3 QLQ-MY20 - Time to first improvement by 10 pt in body image according to geographical region (LOCF) - ITT population

	Europe		America		Asia		Other countries		
	Kd (N=60)	**IKd (N=85)**	**Kd (N=20)**	**IKd (N=24)**	**Kd (N=21)**	**IKd (N=25)**	**Kd (N=22)**	**IKd (N=45)**	**p-value of treatment-by-subgroup interaction[c]**
Comparison vs. Kd									
Log-Rank test p-value[a] vs Kd	-	0.4847		0.8059		0.3127		0.0259	
Hazard ratio (95% CI) vs Kd	-	0.77 (0.37 to 1.61)		0.87 (0.28 to 2.69)		0.58 (0.20 to 1.68)		7.21 (0.94 to 55.14)	
P-value	-	0.4859		0.8061		0.3185		0.0570	
Improvement probability (95% CI)[b]									
3 Months	0.188 (0.100 to 0.296)	0.157 (0.089 to 0.243)	0.200 (0.062 to 0.393)	0.220 (0.080 to 0.405)	0.300 (0.123 to 0.501)	0.208 (0.076 to 0.385)	0.045 (0.003 to 0.189)	0.244 (0.132 to 0.376)	

A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
PGM=DEVOPS/SAR650984/EFC15246/CIR_RWE/REPORT/PGM/eff_km_subgp_sr_sig_de_i_t.sas OUT=REPORT/OUTPUT/eff_km_my20_bdy_impl_greg_de_i_t_x.rtf (07APR2021 14:39)

16.2.6.1 Health-related quality-of-life endpoints - QLQ-MY20
16.2.6.1.2 Body image
16.2.6.1.2.5 Efficacy response data - Subgroup analyses by geographical region
16.2.6.1.2.5.4 QLQ-MY20 - Time to first deterioration by 10 pt in body image according to geographical region (LOCF) - ITT population

	Europe		America		Asia		Other countries		
	Kd (N=60)	**IKd (N=85)**	**Kd (N=20)**	**IKd (N=24)**	**Kd (N=21)**	**IKd (N=25)**	**Kd (N=22)**	**IKd (N=45)**	**p-value of treatment-by-subgroup interaction[c]**
Number (%) of events	21 (35.0)	43 (50.6)	12 (60.0)	14 (58.3)	15 (71.4)	16 (64.0)	11 (50.0)	29 (64.4)	0.3278
Number (%) of patients censored	39 (65.0)	42 (49.4)	8 (40.0)	10 (41.7)	6 (28.6)	9 (36.0)	11 (50.0)	16 (35.6)	
Kaplan-Meier estimates of event in months									
25% quantile (95% CI)	6.47 (2.760 to 17.906)	2.53 (1.347 to 3.778)	1.58 (0.920 to 5.552)	2.92 (1.051 to 5.487)	1.17 (1.051 to 2.037)	2.83 (0.986 to 3.778)	3.02 (0.953 to 7.524)	3.42 (1.906 to 5.815)	
Median (95% CI)	NC (17.906 to NC)	17.71 (5.717 to NC)	6.42 (1.216 to NC)	8.87 (2.924 to NC)	2.97 (1.117 to 15.211)	8.28 (2.825 to 14.784)	9.99 (3.023 to NC)	8.48 (4.665 to 15.671)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (7.261 to NC)	NC (8.969 to NC)	20.57 (2.990 to NC)	NC (11.105 to NC)	NC (NC to NC)	NC (15.639 to NC)	

A higher score represents a better level of quality of life. Clinical meaningful deterioration change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
PGM=DEVOPS/SAR650984/EFC15246/CIR_RWE/REPORT/PGM/eff_km_subgp_sr_sig_de_i_t.sas OUT=REPORT/OUTPUT/eff_km_my20_bdy_detl_greg_de_i_t_x.rtf (07APR2021 14:39)

16.2.6.1 Health-related quality-of-life endpoints - QLQ-MY20
16.2.6.1.2 Body image
16.2.6.1.2.5 Efficacy response data - Subgroup analyses by geographical region
16.2.6.1.2.5.4 QLQ-MY20 - Time to first deterioration by 10 pt in body image according to geographical region (LOCF) - ITT population

	Europe		America		Asia		Other countries		
	Kd (N=60)	**IKd (N=85)**	**Kd (N=20)**	**IKd (N=24)**	**Kd (N=21)**	**IKd (N=25)**	**Kd (N=22)**	**IKd (N=45)**	**p-value of treatment-by-subgroup interaction[c]**
Comparison vs. Kd									
Log-Rank test p-value[a] vs Kd	-	0.0684		0.9456		0.4127		0.4899	
Hazard ratio (95% CI) vs Kd	-	1.62 (0.96 to 2.73)		0.97 (0.45 to 2.11)		0.75 (0.37 to 1.51)		1.28 (0.64 to 2.56)	
P-value	-	0.0711		0.9455		0.4143		0.4910	
Deterioration probability (95% CI)[b]									
3 Months	0.827 (0.703 to 0.903)	0.699 (0.588 to 0.785)	0.650 (0.403 to 0.815)	0.732 (0.498 to 0.870)	0.450 (0.231 to 0.647)	0.667 (0.443 to 0.817)	0.773 (0.537 to 0.898)	0.778 (0.626 to 0.874)	

A higher score represents a better level of quality of life. Clinical meaningful deterioration change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
PGM=DEVOPS/SAR650984/EFC15246/CIR_RWE/REPORT/PGM/eff_km_subgp_sr_sig_de_i_t.sas OUT=REPORT/OUTPUT/eff_km_my20_bdy_detl_greg_de_i_t_x.rtf (07APR2021 14:39)

16.2.6.1 Health-related quality-of-life endpoints - QLQ-MY20
16.2.6.1.2 Body image
16.2.6.1.2.5 Efficacy response data - Subgroup analyses by geographical region
16.2.6.1.2.5.5 QLQ-MY20 - Time until permanent improvement by 10 pt in body image according to geographical region (LOCF) - ITT population

	Europe		America		Asia		Other countries		
	Kd (N=60)	**IKd (N=85)**	**Kd (N=20)**	**IKd (N=24)**	**Kd (N=21)**	**IKd (N=25)**	**Kd (N=22)**	**IKd (N=45)**	**p-value of treatment-by-subgroup interaction[c]**
Number (%) of events	6 (10.0)	8 (9.4)	3 (15.0)	6 (25.0)	2 (9.5)	3 (12.0)	1 (4.5)	5 (11.1)	0.7635
Number (%) of patients censored	54 (90.0)	77 (90.6)	17 (85.0)	18 (75.0)	19 (90.5)	22 (88.0)	21 (95.5)	40 (88.9)	
Kaplan-Meier estimates of event in months									
25% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (1.051 to NC)	14.78 (0.953 to NC)	NC (1.018 to NC)	NC (3.680 to NC)	NC (1.084 to NC)	NC (21.355 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (14.784 to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	

A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.1 Health-related quality-of-life endpoints - QLQ-MY20
16.2.6.1.2 Body image
16.2.6.1.2.5 Efficacy response data - Subgroup analyses by geographical region
16.2.6.1.2.5.5 QLQ-MY20 - Time until permanent improvement by 10 pt in body image according to geographical region (LOCF) - ITT population

	Europe		America		Asia		Other countries		
	Kd (N=60)	**IKd (N=85)**	**Kd (N=20)**	**IKd (N=24)**	**Kd (N=21)**	**IKd (N=25)**	**Kd (N=22)**	**IKd (N=45)**	**p-value of treatment-by-subgroup interaction[c]**
Comparison vs. Kd									
Log-Rank test p-value[a] vs Kd	-	0.8622		0.2976		0.8354		0.3502	
Hazard ratio (95% CI) vs Kd	-	0.91 (0.32 to 2.62)		2.06 (0.51 to 8.28)		1.21 (0.20 to 7.24)		2.68 (0.31 to 22.97)	
P-value	-	0.8623		0.3079		0.8357		0.3693	
Improvement probability (95% CI)[b]									
3 Months	0.085 (0.031 to 0.173)	0.060 (0.022 to 0.125)	0.050 (0.003 to 0.205)	0.085 (0.015 to 0.238)	0.050 (0.003 to 0.205)		0.045 (0.003 to 0.189)	0.044 (0.008 to 0.133)	

A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.1 Health-related quality-of-life endpoints - QLQ-MY20
16.2.6.1.2 Body image
16.2.6.1.2.5 Efficacy response data - Subgroup analyses by geographical region
16.2.6.1.2.5.6 QLQ-MY20 - Time until permanent deterioration by 10 pt in body image according to geographical region (LOCF) - ITT population

	Europe		America		Asia		Other countries		
	Kd (N=60)	**IKd (N=85)**	**Kd (N=20)**	**IKd (N=24)**	**Kd (N=21)**	**IKd (N=25)**	**Kd (N=22)**	**IKd (N=45)**	**p-value of treatment-by-subgroup interaction[c]**
Number (%) of events	11 (18.3)	20 (23.5)	3 (15.0)	2 (8.3)	10 (47.6)	7 (28.0)	6 (27.3)	13 (28.9)	0.4668
Number (%) of patients censored	49 (81.7)	65 (76.5)	17 (85.0)	22 (91.7)	11 (52.4)	18 (72.0)	16 (72.7)	32 (71.1)	
Kaplan-Meier estimates of event in months									
25% quantile (95% CI)	20.76 (12.189 to NC)	22.41 (14.193 to 24.444)	NC (5.585 to NC)	NC (1.117 to NC)	2.14 (1.051 to 17.676)	14.78 (1.117 to NC)	11.96 (4.041 to NC)	18.79 (8.246 to NC)	
Median (95% CI)	NC (NC to NC)	24.44 (NC to NC)	NC (NC to NC)	NC (NC to NC)	18.83 (1.314 to NC)	NC (14.784 to NC)	NC (11.959 to NC)	NC (20.534 to NC)	

A higher score represents a better level of quality of life. Clinical meaningful deterioration change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.1 Health-related quality-of-life endpoints - QLQ-MY20
16.2.6.1.2 Body image
16.2.6.1.2.5 Efficacy response data - Subgroup analyses by geographical region
16.2.6.1.2.5.6 QLQ-MY20 - Time until permanent deterioration by 10 pt in body image according to geographical region (LOCF) - ITT population

	Europe		**America**		**Asia**		**Other countries**		
	Kd (N=60)	**IKd (N=85)**	**Kd (N=20)**	**IKd (N=24)**	**Kd (N=21)**	**IKd (N=25)**	**Kd (N=22)**	**IKd (N=45)**	**p-value of treatment-by-subgroup interaction[c]**
75% quantile (95% CI)	NC (NC to NC)	24.44 (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (18.825 to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Kd									
Log-Rank test p-value[a] vs Kd	-	0.6718		0.5801		0.1450		0.9036	
Hazard ratio (95% CI) vs Kd	-	1.17 (0.56 to 2.47)		0.61 (0.10 to 3.63)		0.49 (0.19 to 1.30)		1.06 (0.40 to 2.79)	
P-value	-	0.6722		0.5840		0.1534		0.9036	
Deterioration probability (95% CI)[b]									

A higher score represents a better level of quality of life. Clinical meaningful deterioration change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.1 Health-related quality-of-life endpoints - QLQ-MY20
16.2.6.1.2 Body image
16.2.6.1.2.6 Efficacy response data - Subgroup analyses by regulatory region
16.2.6.1.2.6.3 QLQ-MY20 - Time to first improvement by 10 pt in body image according to regulatory region (LOCF) - ITT population

	Western countries		Other countries		
	Kd (N=55)	**IKd (N=97)**	**Kd (N=68)**	**IKd (N=82)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	11 (20.0)	20 (20.6)	17 (25.0)	20 (24.4)	0.9232
Number (%) of patients censored	44 (80.0)	77 (79.4)	51 (75.0)	62 (75.6)	
Kaplan-Meier estimates of body image in months					
25% quantile (95% CI)	NC (0.986 to NC)	NC (2.891 to NC)	17.61 (1.906 to NC)	6.47 (1.938 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.9434		0.9691	
Hazard ratio (95% CI) vs Kd	-	0.97 (0.47 to 2.03)		1.01 (0.53 to 1.93)	
P-value	-	0.9431		0.9692	
Improvement probability (95% CI)[b]					

A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.1 Health-related quality-of-life endpoints - QLQ-MY20
16.2.6.1.2 Body image
16.2.6.1.2.6 Efficacy response data - Subgroup analyses by regulatory region
16.2.6.1.2.6.4 QLQ-MY20 - Time to first deterioration by 10 pt in body image according to regulatory region (LOCF) - ITT population

	Western countries		Other countries		
	Kd (N=55)	**IKd (N=97)**	**Kd (N=68)**	**IKd (N=82)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	22 (40.0)	49 (50.5)	37 (54.4)	53 (64.6)	0.9113
Number (%) of patients censored	33 (60.0)	48 (49.5)	31 (45.6)	29 (35.4)	
Kaplan-Meier estimates of body image in months					
25% quantile (95% CI)	6.37 (1.117 to 7.524)	2.92 (1.938 to 3.844)	2.04 (1.117 to 3.055)	2.79 (1.511 to 3.417)	
Median (95% CI)	NC (7.524 to NC)	12.55 (7.655 to NC)	12.55 (4.797 to NC)	7.20 (4.205 to 14.587)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (15.639 to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.3292		0.3063	
Hazard ratio (95% CI) vs Kd	-	1.28 (0.78 to 2.12)		1.24 (0.82 to 1.89)	
P-value	-	0.3305		0.3073	
Deterioration probability (95% CI)[b]					

A higher score represents a better level of quality of life. Clinical meaningful deterioration change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
PGM=DEVOPS/SAR650984/EFC15246/CIR_RWE/REPORT/PGM/eff_km_subgp_sr_sig_de_i_t.sas OUT=REPORT/OUTPUT/eff_km_my20_bdy_detl_rreg_de_i_t_x.rtf (07APR2021 14:39)

16.2.6.1 Health-related quality-of-life endpoints - QLQ-MY20
16.2.6.1.2 Body image
16.2.6.1.2.6 Efficacy response data - Subgroup analyses by regulatory region
16.2.6.1.2.6.5 QLQ-MY20 - Time until permanent improvement by 10 pt in body image according to regulatory region (LOCF) - ITT population

	Western countries		Other countries		
	Kd (N=55)	**IKd (N=97)**	**Kd (N=68)**	**IKd (N=82)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	6 (10.9)	10 (10.3)	6 (8.8)	12 (14.6)	0.3656
Number (%) of patients censored	49 (89.1)	87 (89.7)	62 (91.2)	70 (85.4)	
Kaplan-Meier estimates of body image in months					
25% quantile (95% CI)	NC (NC to NC)	NC (21.355 to NC)	NC (NC to NC)	NC (20.632 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.8433		0.2643	
Hazard ratio (95% CI) vs Kd	-	0.90 (0.33 to 2.49)		1.74 (0.65 to 4.62)	
P-value	-	0.8434		0.2704	

A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
PGM=DEVOPS/SAR650984/EFC15246/CIR_RWE/REPORT/PGM/eff_km_subgp_sr_sig_de_i_t.sas OUT=REPORT/OUTPUT/eff_km_my20_bdy_imppl_rreg_de_i_t_x.rtf (07APR2021 14:40)

16.2.6.1 Health-related quality-of-life endpoints - QLQ-MY20
16.2.6.1.2 Body image
16.2.6.1.2.6 Efficacy response data - Subgroup analyses by regulatory region
16.2.6.1.2.6.6 QLQ-MY20 - Time until permanent deterioration by 10 pt in body image according to regulatory region (LOCF) - ITT population

	Western countries		Other countries		
	Kd (N=55)	**IKd (N=97)**	**Kd (N=68)**	**IKd (N=82)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	15 (27.3)	17 (17.5)	15 (22.1)	25 (30.5)	0.0975
Number (%) of patients censored	40 (72.7)	80 (82.5)	53 (77.9)	57 (69.5)	
Kaplan-Meier estimates of body image in months					
25% quantile (95% CI)	20.57 (7.524 to NC)	NC (18.793 to NC)	NC (9.495 to NC)	16.85 (7.918 to 24.444)	
Median (95% CI)	NC (20.764 to NC)	NC (NC to NC)	NC (NC to NC)	24.44 (22.407 to 24.444)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	24.44 (NC to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.1577		0.3217	
Hazard ratio (95% CI) vs Kd	-	0.61 (0.30 to 1.22)		1.38 (0.73 to 2.62)	
P-value	-	0.1619		0.3238	
Deterioration probability (95% CI)[b]					

A higher score represents a better level of quality of life. Clinical meaningful deterioration change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
PGM=DEVOPS/SAR650984/EFC15246/CIR_RWE/REPORT/PGM/eff_km_subgp_sr_sig_de_i_t.sas OUT=REPORT/OUTPUT/eff_km_my20_bdy_detpl_rreg_de_i_t_x.rtf (07APR2021 14:40)

16.2.6.1 Health-related quality-of-life endpoints - QLQ-MY20
16.2.6.1.2 Body image
16.2.6.1.2.7 Efficacy response data - Subgroup analyses by baseline ECOG PS
16.2.6.1.2.7.3 QLQ-MY20 - Time to first improvement by 10 pt in body image according to baseline ECOG PS (LOCF) - ITT population

	0 or 1		>1		
	Kd (N=118)	**IKd (N=168)**	**Kd (N=5)**	**IKd (N=11)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	27 (22.9)	38 (22.6)	1 (20.0)	2 (18.2)	0.9885
Number (%) of patients censored	91 (77.1)	130 (77.4)	4 (80.0)	9 (81.8)	
Kaplan-Meier estimates of body image in months					
25% quantile (95% CI)	NC (2.234 to NC)	NC (2.136 to NC)	NC (0.986 to NC)	NC (1.938 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (0.986 to NC)	NC (1.938 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (0.986 to NC)	NC (NC to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.9074		0.9378	
Hazard ratio (95% CI) vs Kd	-	0.97 (0.59 to 1.59)		0.91 (0.08 to 10.09)	
P-value	-	0.9072		0.9379	
Improvement probability (95% CI)[b]					

A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
PGM=DEVOPS/SAR650984/EFC15246/CIR_RWE/REPORT/PGM/eff_km_subgp_sr_sig_de_i_t.sas OUT=REPORT/OUTPUT/eff_km_my20_bdy_impl_ecog_de_i_t_x.rtf (07APR2021 14:39)

16.2.6.1 Health-related quality-of-life endpoints - QLQ-MY20
16.2.6.1.2 Body image
16.2.6.1.2.7 Efficacy response data - Subgroup analyses by baseline ECOG PS
16.2.6.1.2.7.4 QLQ-MY20 - Time to first deterioration by 10 pt in body image according to baseline ECOG PS (LOCF) - ITT population

	0 or 1		>1		
	Kd (N=118)	**IKd (N=168)**	**Kd (N=5)**	**IKd (N=11)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	57 (48.3)	96 (57.1)	2 (40.0)	6 (54.5)	0.6745
Number (%) of patients censored	61 (51.7)	72 (42.9)	3 (60.0)	5 (45.5)	
Kaplan-Meier estimates of body image in months					
25% quantile (95% CI)	2.83 (1.216 to 5.322)	2.83 (1.938 to 3.745)	5.59 (2.070 to NC)	3.12 (1.216 to 6.505)	
Median (95% CI)	20.57 (6.801 to NC)	9.26 (6.571 to 17.708)	NC (2.070 to NC)	6.51 (1.216 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (2.070 to NC)	NC (3.877 to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.2896		0.5371	
Hazard ratio (95% CI) vs Kd	-	1.19 (0.86 to 1.66)		1.65 (0.33 to 8.19)	
P-value	-	0.2903		0.5413	
Deterioration probability (95% CI)[b]					

A higher score represents a better level of quality of life. Clinical meaningful deterioration change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.1 Health-related quality-of-life endpoints - QLQ-MY20
16.2.6.1.2 Body image
16.2.6.1.2.7 Efficacy response data - Subgroup analyses by baseline ECOG PS
16.2.6.1.2.7.5 QLQ-MY20 - Time until permanent improvement by 10 pt in body image according to baseline ECOG PS (LOCF) - ITT population

	0 or 1		>1		
	Kd (N=118)	**IKd (N=168)**	**Kd (N=5)**	**IKd (N=11)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	11 (9.3)	20 (11.9)	1 (20.0)	2 (18.2)	0.8420
Number (%) of patients censored	107 (90.7)	148 (88.1)	4 (80.0)	9 (81.8)	
Kaplan-Meier estimates of body image in months					
25% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (9.298 to NC)	NC (1.938 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (9.298 to NC)	NC (1.938 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (9.298 to NC)	NC (NC to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.5166		0.9120	
Hazard ratio (95% CI) vs Kd	-	1.27 (0.61 to 2.66)		0.87 (0.08 to 9.83)	
P-value	-	0.5177		0.9121	

A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.1 Health-related quality-of-life endpoints - QLQ-MY20
16.2.6.1.2 Body image
16.2.6.1.2.7 Efficacy response data - Subgroup analyses by baseline ECOG PS
16.2.6.1.2.7.6 QLQ-MY20 - Time until permanent deterioration by 10 pt in body image according to baseline ECOG PS (LOCF) - ITT population

	0 or 1		>1		
	Kd (N=118)	**IKd (N=168)**	**Kd (N=5)**	**IKd (N=11)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	29 (24.6)	40 (23.8)	1 (20.0)	2 (18.2)	0.9631
Number (%) of patients censored	89 (75.4)	128 (76.2)	4 (80.0)	9 (81.8)	
Kaplan-Meier estimates of body image in months					
25% quantile (95% CI)	20.57 (11.302 to NC)	20.53 (14.784 to NC)	NC (5.585 to NC)	20.90 (7.885 to NC)	
Median (95% CI)	NC (NC to NC)	24.44 (24.444 to NC)	NC (5.585 to NC)	NC (7.885 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (24.444 to NC)	NC (5.585 to NC)	NC (20.895 to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.7829		0.8404	
Hazard ratio (95% CI) vs Kd	-	0.93 (0.58 to 1.51)		0.78 (0.07 to 8.65)	
P-value	-	0.7817		0.8408	
Deterioration probability (95% CI)[b]					

A higher score represents a better level of quality of life. Clinical meaningful deterioration change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.1 Health-related quality-of-life endpoints - QLQ-MY20
16.2.6.1.2 Body image
16.2.6.1.2.8 Efficacy response data - Subgroup analyses by ISS staging at SE
16.2.6.1.2.8.3 QLQ-MY20 - Time to first improvement by 10 pt in body image according to ISS staging at SE (LOCF) - ITT population

	I		II		III		
	Kd (N=71)	**IKd (N=89)**	**Kd (N=31)**	**IKd (N=63)**	**Kd (N=20)**	**IKd (N=26)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	19 (26.8)	18 (20.2)	5 (16.1)	13 (20.6)	4 (20.0)	9 (34.6)	0.2654
Number (%) of patients censored	52 (73.2)	71 (79.8)	26 (83.9)	50 (79.4)	16 (80.0)	17 (65.4)	
Kaplan-Meier estimates of body image in months							
25% quantile (95% CI)	4.70 (1.084 to NC)	NC (2.070 to NC)	NC (1.281 to NC)	NC (1.971 to NC)	NC (0.986 to NC)	1.08 (0.953 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (12.222 to NC)	NC (1.938 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Kd							
Log-Rank test p-value[a] vs Kd	-	0.3391		0.6606		0.2383	
Hazard ratio (95% CI) vs Kd	-	0.73 (0.38 to 1.39)		1.26 (0.45 to 3.53)		2.01 (0.62 to 6.54)	
P-value	-	0.3410		0.6614		0.2478	

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The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.1 Health-related quality-of-life endpoints - QLQ-MY20
16.2.6.1.2 Body image
16.2.6.1.2.8 Efficacy response data - Subgroup analyses by ISS staging at SE
16.2.6.1.2.8.4 QLQ-MY20 - Time to first deterioration by 10 pt in body image according to ISS staging at SE (LOCF) - ITT population

	I		II		III		
	Kd (N=71)	**IKd (N=89)**	**Kd (N=31)**	**IKd (N=63)**	**Kd (N=20)**	**IKd (N=26)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	31 (43.7)	50 (56.2)	19 (61.3)	41 (65.1)	8 (40.0)	11 (42.3)	0.6764
Number (%) of patients censored	40 (56.3)	39 (43.8)	12 (38.7)	22 (34.9)	12 (60.0)	15 (57.7)	
Kaplan-Meier estimates of body image in months							
25% quantile (95% CI)	3.06 (1.938 to 6.637)	3.06 (1.938 to 5.487)	1.22 (0.986 to 5.585)	1.97 (1.117 to 3.417)	2.96 (0.953 to 8.674)	2.83 (0.953 to 11.992)	
Median (95% CI)	NC (7.261 to NC)	13.21 (7.655 to NC)	8.31 (1.873 to NC)	5.78 (3.778 to 10.218)	NC (2.957 to NC)	12.55 (3.154 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (22.308 to NC)	NC (12.550 to NC)	NC (14.587 to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Kd							
Log-Rank test p-value[a] vs Kd	-	0.1796		0.9656		0.9037	
Hazard ratio (95% CI) vs Kd	-	1.36 (0.87 to 2.13)		1.01 (0.59 to 1.75)		1.06 (0.42 to 2.63)	

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The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.1 Health-related quality-of-life endpoints - QLQ-MY20
16.2.6.1.2 Body image
16.2.6.1.2.8 Efficacy response data - Subgroup analyses by ISS staging at SE
16.2.6.1.2.8.5 QLQ-MY20 - Time until permanent improvement by 10 pt in body image according to ISS staging at SE (LOCF) - ITT population

	I		II		III		
	Kd (N=71)	**IKd (N=89)**	**Kd (N=31)**	**IKd (N=63)**	**Kd (N=20)**	**IKd (N=26)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	7 (9.9)	9 (10.1)	3 (9.7)	6 (9.5)	2 (10.0)	7 (26.9)	0.4137
Number (%) of patients censored	64 (90.1)	80 (89.9)	28 (90.3)	57 (90.5)	18 (90.0)	19 (73.1)	
Kaplan-Meier estimates of body image in months							
25% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (10.316 to NC)	NC (21.355 to NC)	NC (1.051 to NC)	11.17 (0.953 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (11.170 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Kd							
Log-Rank test p-value[a] vs Kd	-	0.9679		0.9160		0.1228	
Hazard ratio (95% CI) vs Kd	-	1.02 (0.38 to 2.74)		0.93 (0.23 to 3.71)		3.23 (0.67 to 15.62)	
P-value	-	0.9680		0.9161		0.1445	

A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.1 Health-related quality-of-life endpoints - QLQ-MY20
16.2.6.1.2 Body image
16.2.6.1.2.8 Efficacy response data - Subgroup analyses by ISS staging at SE
16.2.6.1.2.8.6 QLQ-MY20 - Time until permanent deterioration by 10 pt in body image according to ISS staging at SE (LOCF) - ITT population

	I		II		III		
	Kd (N=71)	**IKd (N=89)**	**Kd (N=31)**	**IKd (N=63)**	**Kd (N=20)**	**IKd (N=26)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	15 (21.1)	20 (22.5)	11 (35.5)	16 (25.4)	3 (15.0)	6 (23.1)	0.2968
Number (%) of patients censored	56 (78.9)	69 (77.5)	20 (64.5)	47 (74.6)	17 (85.0)	20 (76.9)	
Kaplan-Meier estimates of body image in months							
25% quantile (95% CI)	20.76 (17.676 to NC)	22.41 (14.949 to NC)	8.31 (1.314 to NC)	20.24 (8.542 to NC)	NC (1.117 to NC)	18.79 (0.986 to NC)	
Median (95% CI)	NC (NC to NC)	24.44 (22.407 to NC)	NC (11.302 to NC)	NC (NC to NC)	NC (NC to NC)	NC (18.793 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (24.444 to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Kd							
Log-Rank test p-value[a] vs Kd	-	0.7309		0.1648		0.4760	
Hazard ratio (95% CI) vs Kd	-	1.12 (0.58 to 2.20)		0.58 (0.27 to 1.26)		1.65 (0.41 to 6.59)	
P-value	-	0.7311		0.1697		0.4806	

A higher score represents a better level of quality of life. Clinical meaningful deterioration change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.1 Health-related quality-of-life endpoints - QLQ-MY20
16.2.6.1.2 Body image
16.2.6.1.2.9 Efficacy response data - Subgroup analyses by R-ISS stage at SE
16.2.6.1.2.9.3 QLQ-MY20 - Time to first improvement by 10 pt in body image according to R-ISS stage at SE (LOCF) - ITT population

	I or II		III		Not classified		
	Kd (N=103)	**IKd (N=155)**	**Kd (N=8)**	**IKd (N=16)**	**Kd (N=12)**	**IKd (N=8)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	25 (24.3)	33 (21.3)	2 (25.0)	5 (31.3)	1 (8.3)	2 (25.0)	0.3831
Number (%) of patients censored	78 (75.7)	122 (78.7)	6 (75.0)	11 (68.8)	11 (91.7)	6 (75.0)	
Kaplan-Meier estimates of body image in months							
25% quantile (95% CI)	17.61 (1.906 to NC)	NC (2.595 to NC)	12.22 (1.084 to NC)	1.94 (0.953 to NC)	NC (0.953 to NC)	4.67 (2.004 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (1.084 to NC)	NC (1.084 to NC)	NC (NC to NC)	NC (2.004 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (12.222 to NC)	NC (NC to NC)	NC (NC to NC)	NC (4.665 to NC)	
Comparison vs. Kd							
Log-Rank test p-value[a] vs Kd	-	0.4964		0.6561		0.2399	
Hazard ratio (95% CI) vs Kd	-	0.84 (0.50 to 1.40)		1.45 (0.28 to 7.50)		3.82 (0.35 to 42.22)	
P-value	-	0.4969		0.6579		0.2747	

A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.1 Health-related quality-of-life endpoints - QLQ-MY20
16.2.6.1.2 Body image
16.2.6.1.2.9 Efficacy response data - Subgroup analyses by R-ISS stage at SE
16.2.6.1.2.9.4 QLQ-MY20 - Time to first deterioration by 10 pt in body image according to R-ISS stage at SE (LOCF) - ITT population

	I or II		III		Not classified		
	Kd (N=103)	**IKd (N=155)**	**Kd (N=8)**	**IKd (N=16)**	**Kd (N=12)**	**IKd (N=8)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	48 (46.6)	94 (60.6)	4 (50.0)	6 (37.5)	7 (58.3)	2 (25.0)	0.3201
Number (%) of patients censored	55 (53.4)	61 (39.4)	4 (50.0)	10 (62.5)	5 (41.7)	6 (75.0)	
Kaplan-Meier estimates of body image in months							
25% quantile (95% CI)	2.86 (1.314 to 5.585)	2.83 (1.938 to 3.417)	1.12 (1.051 to 8.674)	3.75 (0.953 to NC)	2.91 (1.051 to 6.472)	3.06 (2.825 to NC)	
Median (95% CI)	20.57 (7.261 to NC)	8.84 (5.815 to 14.784)	8.67 (1.051 to NC)	NC (1.413 to NC)	8.23 (1.084 to NC)	NC (2.825 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (4.895 to NC)	NC (12.550 to NC)	NC (6.472 to NC)	NC (3.055 to NC)	
Comparison vs. Kd							
Log-Rank test p-value[a] vs Kd	-	0.1114		0.5189		0.3766	
Hazard ratio (95% CI) vs Kd	-	1.33 (0.94 to 1.88)		0.66 (0.18 to 2.35)		0.50 (0.10 to 2.40)	
P-value	-	0.1126		0.5217		0.3861	

A higher score represents a better level of quality of life. Clinical meaningful deterioration change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.6.1 Health-related quality-of-life endpoints - QLQ-MY20
16.2.6.1.2 Body image
16.2.6.1.2.9 Efficacy response data - Subgroup analyses by R-ISS stage at SE
16.2.6.1.2.9.5 QLQ-MY20 - Time until permanent improvement by 10 pt in body image according to R-ISS stage at SE (LOCF) - ITT population

	I or II		III		Not classified		
	Kd (N=103)	**IKd (N=155)**	**Kd (N=8)**	**IKd (N=16)**	**Kd (N=12)**	**IKd (N=8)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	11 (10.7)	17 (11.0)	0 (0.0)	4 (25.0)	1 (8.3)	1 (12.5)	0.8596
Number (%) of patients censored	92 (89.3)	138 (89.0)	8 (100.0)	12 (75.0)	11 (91.7)	7 (87.5)	
Kaplan-Meier estimates of body image in months							
25% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	14.55 (0.953 to NC)	NC (0.953 to NC)	NC (2.004 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (6.604 to NC)	NC (NC to NC)	NC (2.004 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (14.554 to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Kd							
Log-Rank test p-value[a] vs Kd	-	0.9730		0.1057		0.6815	
Hazard ratio (95% CI) vs Kd	-	0.99 (0.46 to 2.11)				1.77 (0.11 to 28.35)	
P-value	-	0.9730		0.9969		0.6856	

A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
PGM=DEVOPS/SAR650984/EFC15246/CIR_RWE/REPORT/PGM/eff_km_subgp_sr_sig_de_i_t.sas OUT=REPORT/OUTPUT/eff_km_my20_bdy_imppl_seriss_de_i_t_x.rtf (07APR2021 14:40)

16.2.6.1 Health-related quality-of-life endpoints - QLQ-MY20
16.2.6.1.2 Body image
16.2.6.1.2.9 Efficacy response data - Subgroup analyses by R-ISS stage at SE
16.2.6.1.2.9.6 QLQ-MY20 - Time until permanent deterioration by 10 pt in body image according to R-ISS stage at SE (LOCF) - ITT population

	I or II		III		Not classified		
	Kd (N=103)	**IKd (N=155)**	**Kd (N=8)**	**IKd (N=16)**	**Kd (N=12)**	**IKd (N=8)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	26 (25.2)	40 (25.8)	1 (12.5)	1 (6.3)	3 (25.0)	1 (12.5)	0.8783
Number (%) of patients censored	77 (74.8)	115 (74.2)	7 (87.5)	15 (93.8)	9 (75.0)	7 (87.5)	
Kaplan-Meier estimates of body image in months							
25% quantile (95% CI)	18.92 (9.495 to NC)	20.53 (14.784 to NC)	NC (1.117 to NC)	NC (7.885 to NC)	20.76 (1.084 to NC)	NC (2.825 to NC)	
Median (95% CI)	NC (NC to NC)	24.44 (24.444 to NC)	NC (1.117 to NC)	NC (NC to NC)	NC (11.959 to NC)	NC (2.825 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (24.444 to NC)	NC (NC to NC)	NC (NC to NC)	NC (20.764 to NC)	NC (NC to NC)	
Comparison vs. Kd							
Log-Rank test p-value[a] vs Kd	-	0.8573		0.5360		0.7958	
Hazard ratio (95% CI) vs Kd	-	0.96 (0.58 to 1.57)		0.43 (0.03 to 6.88)		0.74 (0.08 to 7.17)	
P-value	-	0.8566		0.5481		0.7966	

A higher score represents a better level of quality of life. Clinical meaningful deterioration change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.1 Health-related quality-of-life endpoints - QLQ-MY20
16.2.6.1.2 Body image
16.2.6.1.2.10 Efficacy response data - Subgroup analyses by nb of prior lines
16.2.6.1.2.10.3 QLQ-MY20 - Time to first improvement by 10 pt in body image according to nb of prior lines (LOCF) - ITT population

	1		>1		
	Kd (N=55)	**IKd (N=79)**	**Kd (N=68)**	**IKd (N=100)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	9 (16.4)	19 (24.1)	19 (27.9)	21 (21.0)	0.1517
Number (%) of patients censored	46 (83.6)	60 (75.9)	49 (72.1)	79 (79.0)	
Kaplan-Meier estimates of body image in months					
25% quantile (95% CI)	NC (3.285 to NC)	NC (2.070 to NC)	4.70 (1.051 to NC)	NC (1.938 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.3030		0.3000	
Hazard ratio (95% CI) vs Kd	-	1.51 (0.68 to 3.34)		0.72 (0.39 to 1.34)	
P-value	-	0.3065		0.3021	
Improvement probability (95% CI)[b]					

A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.1 Health-related quality-of-life endpoints - QLQ-MY20
16.2.6.1.2 Body image
16.2.6.1.2.10 Efficacy response data - Subgroup analyses by nb of prior lines
16.2.6.1.2.10.4 QLQ-MY20 - Time to first deterioration by 10 pt in body image according to nb of prior lines (LOCF) - ITT population

	1		>1		
	Kd (N=55)	**IKd (N=79)**	**Kd (N=68)**	**IKd (N=100)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	30 (54.5)	39 (49.4)	29 (42.6)	63 (63.0)	0.0350
Number (%) of patients censored	25 (45.5)	40 (50.6)	39 (57.4)	37 (37.0)	
Kaplan-Meier estimates of body image in months					
25% quantile (95% CI)	1.31 (1.051 to 5.322)	3.06 (1.478 to 5.487)	3.06 (1.938 to 6.505)	2.83 (1.906 to 3.220)	
Median (95% CI)	8.10 (5.322 to NC)	22.31 (7.195 to NC)	NC (8.312 to NC)	7.66 (4.172 to 11.105)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (15.671 to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.4577		0.0220	
Hazard ratio (95% CI) vs Kd	-	0.83 (0.52 to 1.34)		1.66 (1.07 to 2.58)	
P-value	-	0.4583		0.0235	
Hazard ratio inverted (95% CI) vs IKd		-		0.60 (0.39 to 0.93)	

A higher score represents a better level of quality of life. Clinical meaningful deterioration change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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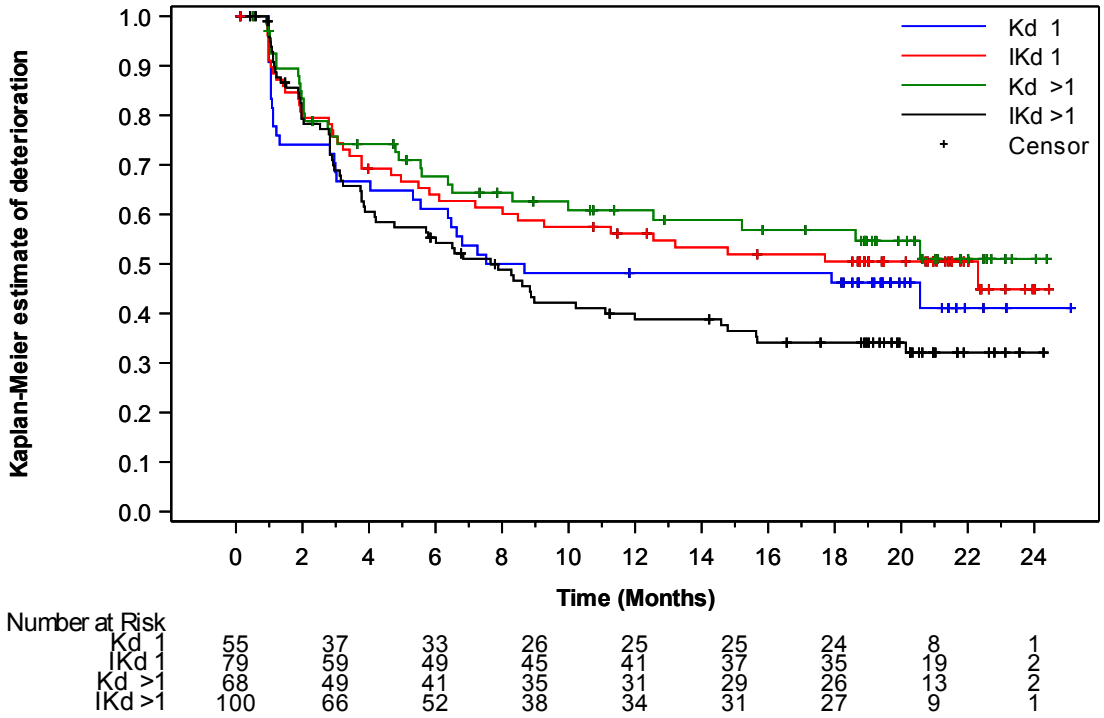
16.2.6.1 Health-related quality-of-life endpoints - QLQ-MY20
16.2.6.1.2 Body image
16.2.6.1.2.10 Efficacy response data - Subgroup analyses by nb of prior lines
16.2.6.1.2.10.5 QLQ-MY20 - Time to first deterioration by 10 pt in body image according to nb of prior lines - Kaplan-Meier curve (LOCF) - ITT population



Number at Risk

Kd 1	55	37	33	26	25	25	24	8	1
IKd 1	79	59	49	45	41	37	35	19	2
Kd >1	68	49	41	35	31	29	26	13	2
IKd >1	100	66	52	38	34	31	27	9	1

A higher score represents a better level of quality of life. Clinical meaningful deterioration change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
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16.2.6.1 Health-related quality-of-life endpoints - QLQ-MY20
16.2.6.1.2 Body image
16.2.6.1.2.10 Efficacy response data - Subgroup analyses by nb of prior lines
16.2.6.1.2.10.6 QLQ-MY20 - Time until permanent improvement by 10 pt in body image according to nb of prior lines (LOCF) - ITT population

	1		>1		
	Kd (N=55)	**IKd (N=79)**	**Kd (N=68)**	**IKd (N=100)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	3 (5.5)	11 (13.9)	9 (13.2)	11 (11.0)	0.1316
Number (%) of patients censored	52 (94.5)	68 (86.1)	59 (86.8)	89 (89.0)	
Kaplan-Meier estimates of body image in months					
25% quantile (95% CI)	NC (NC to NC)	NC (20.632 to NC)	NC (18.924 to NC)	NC (NC to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.1196		0.6346	
Hazard ratio (95% CI) vs Kd	-	2.65 (0.74 to 9.51)		0.81 (0.33 to 1.95)	
P-value	-	0.1345		0.6352	

A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.1 Health-related quality-of-life endpoints - QLQ-MY20
16.2.6.1.2 Body image
16.2.6.1.2.10 Efficacy response data - Subgroup analyses by nb of prior lines
16.2.6.1.2.10.7 QLQ-MY20 - Time until permanent deterioration by 10 pt in body image according to nb of prior lines (LOCF) - ITT population

	1		>1		
	Kd (N=55)	**IKd (N=79)**	**Kd (N=68)**	**IKd (N=100)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	18 (32.7)	17 (21.5)	12 (17.6)	25 (25.0)	0.0720
Number (%) of patients censored	37 (67.3)	62 (78.5)	56 (82.4)	75 (75.0)	
Kaplan-Meier estimates of body image in months					
25% quantile (95% CI)	12.19 (2.957 to 20.764)	24.44 (15.507 to NC)	NC (11.959 to NC)	20.24 (11.992 to NC)	
Median (95% CI)	NC (20.600 to NC)	24.44 (24.444 to NC)	NC (NC to NC)	NC (22.407 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (24.444 to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.1345		0.3238	
Hazard ratio (95% CI) vs Kd	-	0.61 (0.31 to 1.18)		1.41 (0.71 to 2.81)	
P-value	-	0.1386		0.3262	
Deterioration probability (95% CI)[b]					

A higher score represents a better level of quality of life. Clinical meaningful deterioration change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.1 Health-related quality-of-life endpoints - QLQ-MY20
16.2.6.1.2 Body image
16.2.6.1.2.11 Efficacy response data - Subgroup analyses by cytogenetic abnormality
16.2.6.1.2.11.3 QLQ-MY20 - Time to first improvement by 10 pt in body image according to cytogenetic abnormality (LOCF) - ITT population

	At least one		None		
	Kd (N=31)	**IKd (N=42)**	**Kd (N=77)**	**IKd (N=114)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	9 (29.0)	12 (28.6)	18 (23.4)	22 (19.3)	0.6823
Number (%) of patients censored	22 (71.0)	30 (71.4)	59 (76.6)	92 (80.7)	
Kaplan-Meier estimates of body image in months					
25% quantile (95% CI)	12.22 (1.084 to NC)	2.89 (1.084 to NC)	NC (1.084 to NC)	NC (2.595 to NC)	
Median (95% CI)	NC (17.610 to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.9740		0.4668	
Hazard ratio (95% CI) vs Kd	-	0.99 (0.42 to 2.34)		0.79 (0.43 to 1.48)	
P-value	-	0.9739		0.4677	
Improvement probability (95% CI)[b]					

A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.1 Health-related quality-of-life endpoints - QLQ-MY20
16.2.6.1.2 Body image
16.2.6.1.2.11 Efficacy response data - Subgroup analyses by cytogenetic abnormality
16.2.6.1.2.11.4 QLQ-MY20 - Time to first deterioration by 10 pt in body image according to cytogenetic abnormality (LOCF) - ITT population

	At least one		None		
	Kd (N=31)	**IKd (N=42)**	**Kd (N=77)**	**IKd (N=114)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	11 (35.5)	25 (59.5)	40 (51.9)	66 (57.9)	0.1987
Number (%) of patients censored	20 (64.5)	17 (40.5)	37 (48.1)	48 (42.1)	
Kaplan-Meier estimates of body image in months					
25% quantile (95% CI)	6.51 (1.051 to NC)	3.42 (0.986 to 5.717)	1.97 (1.117 to 4.797)	2.79 (1.906 to 3.778)	
Median (95% CI)	NC (8.674 to NC)	11.27 (4.961 to NC)	12.55 (5.552 to NC)	8.87 (6.012 to 20.140)	
75% quantile (95% CI)	NC (NC to NC)	NC (15.671 to NC)	NC (NC to NC)	NC (22.308 to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.0732		0.6541	
Hazard ratio (95% CI) vs Kd	-	1.89 (0.93 to 3.85)		1.09 (0.74 to 1.62)	
P-value	-	0.0782		0.6542	
Deterioration probability (95% CI)[b]					

A higher score represents a better level of quality of life. Clinical meaningful deterioration change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.1 Health-related quality-of-life endpoints - QLQ-MY20
16.2.6.1.2 Body image
16.2.6.1.2.11 Efficacy response data - Subgroup analyses by cytogenetic abnormality
16.2.6.1.2.11.5 QLQ-MY20 - Time until permanent improvement by 10 pt in body image according to cytogenetic abnormality (LOCF) - ITT population

	At least one		None		
	Kd (N=31)	**IKd (N=42)**	**Kd (N=77)**	**IKd (N=114)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	1 (3.2)	5 (11.9)	10 (13.0)	14 (12.3)	0.2349
Number (%) of patients censored	30 (96.8)	37 (88.1)	67 (87.0)	100 (87.7)	
Kaplan-Meier estimates of body image in months					
25% quantile (95% CI)	NC (NC to NC)	NC (20.632 to NC)	NC (NC to NC)	NC (NC to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.1793		0.8502	
Hazard ratio (95% CI) vs Kd	-	3.92 (0.46 to 33.58)		0.92 (0.41 to 2.08)	
P-value	-	0.2132		0.8502	

A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
PGM=DEVOPS/SAR650984/EFC15246/CIR_RWE/REPORT/PGM/eff_km_subgp_sr_sig_de_i_t.sas OUT=REPORT/OUTPUT/eff_km_my20_bdy_imppl_cyto_de_i_t_x.rtf (07APR2021 14:40)

16.2.6.1 Health-related quality-of-life endpoints - QLQ-MY20
16.2.6.1.2 Body image
16.2.6.1.2.11 Efficacy response data - Subgroup analyses by cytogenetic abnormality
16.2.6.1.2.11.6 QLQ-MY20 - Time until permanent deterioration by 10 pt in body image according to cytogenetic abnormality (LOCF) - ITT population

	At least one		None		
	Kd (N=31)	**IKd (N=42)**	**Kd (N=77)**	**IKd (N=114)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	3 (9.7)	9 (21.4)	23 (29.9)	29 (25.4)	0.1456
Number (%) of patients censored	28 (90.3)	33 (78.6)	54 (70.1)	85 (74.6)	
Kaplan-Meier estimates of body image in months					
25% quantile (95% CI)	NC (18.924 to NC)	NC (7.885 to NC)	12.19 (7.524 to NC)	20.53 (14.193 to 24.444)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	24.44 (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	24.44 (NC to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.1995		0.4167	
Hazard ratio (95% CI) vs Kd	-	2.30 (0.62 to 8.49)		0.80 (0.46 to 1.38)	
P-value	-	0.2125		0.4177	
Deterioration probability (95% CI)[b]					

A higher score represents a better level of quality of life. Clinical meaningful deterioration change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
PGM=DEVOPS/SAR650984/EFC15246/CIR_RWE/REPORT/PGM/eff_km_subgp_sr_sig_de_i_t.sas OUT=REPORT/OUTPUT/eff_km_my20_bdy_detpl_cyto_de_i_t_x.rtf (07APR2021 14:40)

16.2.6.1 Health-related quality-of-life endpoints - QLQ-MY20
16.2.6.1.2 Body image
16.2.6.1.2.12 Efficacy response data - Subgroup analyses by MM type at SE
16.2.6.1.2.12.3 QLQ-MY20 - Time to first improvement by 10 pt in body image according to MM type at SE (LOCF) - ITT population

	IgG		Non-IgG		
	Kd (N=85)	**IKd (N=126)**	**Kd (N=38)**	**IKd (N=53)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	17 (20.0)	29 (23.0)	11 (28.9)	11 (20.8)	0.2476
Number (%) of patients censored	68 (80.0)	97 (77.0)	27 (71.1)	42 (79.2)	
Kaplan-Meier estimates of body image in months					
25% quantile (95% CI)	NC (2.431 to NC)	NC (2.136 to NC)	2.76 (1.018 to NC)	NC (1.183 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.5758		0.3134	
Hazard ratio (95% CI) vs Kd	-	1.19 (0.65 to 2.16)		0.65 (0.28 to 1.51)	
P-value	-	0.5763		0.3170	

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The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
PGM=DEVOPS/SAR650984/EFC15246/CIR_RWE/REPORT/PGM/eff_km_subgp_sr_sig_de_i_t.sas OUT=REPORT/OUTPUT/eff_km_my20_bdy_impl_semm_de_i_t_x.rtf (07APR2021 14:39)

16.2.6.1 Health-related quality-of-life endpoints - QLQ-MY20
16.2.6.1.2 Body image
16.2.6.1.2.12 Efficacy response data - Subgroup analyses by MM type at SE
16.2.6.1.2.12.4 QLQ-MY20 - Time to first deterioration by 10 pt in body image according to MM type at SE (LOCF) - ITT population

	IgG		Non-IgG		
	Kd (N=85)	**IKd (N=126)**	**Kd (N=38)**	**IKd (N=53)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	42 (49.4)	70 (55.6)	17 (44.7)	32 (60.4)	0.6088
Number (%) of patients censored	43 (50.6)	56 (44.4)	21 (55.3)	21 (39.6)	
Kaplan-Meier estimates of body image in months					
25% quantile (95% CI)	2.83 (1.117 to 5.552)	2.89 (1.938 to 3.778)	2.86 (1.051 to 6.505)	2.83 (1.018 to 3.778)	
Median (95% CI)	18.63 (6.637 to NC)	11.10 (6.834 to 22.308)	20.57 (5.585 to NC)	8.28 (3.778 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (22.308 to NC)	NC (20.567 to NC)	NC (15.639 to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.4764		0.2686	
Hazard ratio (95% CI) vs Kd	-	1.15 (0.78 to 1.68)		1.39 (0.77 to 2.51)	
P-value	-	0.4767		0.2708	
Deterioration probability (95% CI)[b]					

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The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.1 Health-related quality-of-life endpoints - QLQ-MY20
16.2.6.1.2 Body image
16.2.6.1.2.12 Efficacy response data - Subgroup analyses by MM type at SE
16.2.6.1.2.12.5 QLQ-MY20 - Time until permanent improvement by 10 pt in body image according to MM type at SE (LOCF) - ITT population

	IgG		Non-IgG		
	Kd (N=85)	**IKd (N=126)**	**Kd (N=38)**	**IKd (N=53)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	8 (9.4)	15 (11.9)	4 (10.5)	7 (13.2)	0.8798
Number (%) of patients censored	77 (90.6)	111 (88.1)	34 (89.5)	46 (86.8)	
Kaplan-Meier estimates of body image in months					
25% quantile (95% CI)	NC (NC to NC)	NC (21.355 to NC)	NC (1.051 to NC)	NC (12.813 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.5268		0.8080	
Hazard ratio (95% CI) vs Kd	-	1.32 (0.56 to 3.11)		1.16 (0.34 to 3.98)	
P-value	-	0.5281		0.8082	

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CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
PGM=DEVOPS/SAR650984/EFC15246/CIR_RWE/REPORT/PGM/eff_km_subgp_sr_sig_de_i_t.sas OUT=REPORT/OUTPUT/eff_km_my20_bdy_imppl_semm_de_i_t_x.rtf (07APR2021 14:40)

16.2.6.1 Health-related quality-of-life endpoints - QLQ-MY20
16.2.6.1.2 Body image
16.2.6.1.2.12 Efficacy response data - Subgroup analyses by MM type at SE
16.2.6.1.2.12.6 QLQ-MY20 - Time until permanent deterioration by 10 pt in body image according to MM type at SE (LOCF) - ITT population

	IgG		Non-IgG		
	Kd (N=85)	**IKd (N=126)**	**Kd (N=38)**	**IKd (N=53)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	19 (22.4)	29 (23.0)	11 (28.9)	13 (24.5)	0.4230
Number (%) of patients censored	66 (77.6)	97 (77.0)	27 (71.1)	40 (75.5)	
Kaplan-Meier estimates of body image in months					
25% quantile (95% CI)	20.76 (11.959 to NC)	20.90 (14.784 to NC)	10.41 (4.041 to NC)	20.24 (7.885 to NC)	
Median (95% CI)	NC (NC to NC)	24.44 (24.444 to NC)	NC (18.924 to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (24.444 to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.8439		0.4255	
Hazard ratio (95% CI) vs Kd	-	1.06 (0.59 to 1.89)		0.72 (0.32 to 1.61)	
P-value	-	0.8447		0.4275	

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CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.1 Health-related quality-of-life endpoints - QLQ-MY20
16.2.6.1.2 Body image
16.2.6.1.2.13 Efficacy response data - Subgroup analyses by previous autologous stem-cell
16.2.6.1.2.13.3 QLQ-MY20 - Time to first improvement by 10 pt in body image according to previous autologous stem-cell (LOCF) - ITT population

	Yes		No		
	Kd (N=69)	**IKd (N=116)**	**Kd (N=54)**	**IKd (N=63)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	17 (24.6)	20 (17.2)	11 (20.4)	20 (31.7)	0.0792
Number (%) of patients censored	52 (75.4)	96 (82.8)	43 (79.6)	43 (68.3)	
Kaplan-Meier estimates of body image in months					
25% quantile (95% CI)	17.61 (1.051 to NC)	NC (12.386 to NC)	NC (1.906 to NC)	2.33 (1.840 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.2343		0.1975	
Hazard ratio (95% CI) vs Kd	-	0.68 (0.35 to 1.29)		1.61 (0.77 to 3.37)	
P-value	-	0.2372		0.2018	
Improvement probability (95% CI)[b]					

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CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.1 Health-related quality-of-life endpoints - QLQ-MY20
16.2.6.1.2 Body image
16.2.6.1.2.13 Efficacy response data - Subgroup analyses by previous autologous stem-cell
16.2.6.1.2.13.4 QLQ-MY20 - Time to first deterioration by 10 pt in body image according to previous autologous stem-cell (LOCF) - ITT population

	Yes		No		
	Kd (N=69)	**IKd (N=116)**	**Kd (N=54)**	**IKd (N=63)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	29 (42.0)	69 (59.5)	30 (55.6)	33 (52.4)	0.0722
Number (%) of patients censored	40 (58.0)	47 (40.5)	24 (44.4)	30 (47.6)	
Kaplan-Meier estimates of body image in months					
25% quantile (95% CI)	3.02 (1.938 to 6.472)	2.83 (1.906 to 3.220)	1.91 (1.051 to 4.797)	3.42 (1.478 to 6.571)	
Median (95% CI)	NC (6.801 to NC)	7.89 (5.487 to 15.671)	9.99 (4.797 to NC)	12.55 (6.571 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (22.308 to NC)	NC (20.567 to NC)	NC (NC to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.0435		0.5445	
Hazard ratio (95% CI) vs Kd	-	1.56 (1.01 to 2.41)		0.86 (0.52 to 1.41)	
P-value	-	0.0453		0.5449	
Hazard ratio inverted (95% CI) vs IKd		-		1.17 (0.71 to 1.91)	

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The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.6.1 Health-related quality-of-life endpoints - QLQ-MY20
16.2.6.1.2 Body image
16.2.6.1.2.13 Efficacy response data - Subgroup analyses by previous autologous stem-cell
16.2.6.1.2.13.5 QLQ-MY20 - Time until permanent improvement by 10 pt in body image according to previous autologous stem-cell (LOCF) - ITT population

	Yes		No		
	Kd (N=69)	**IKd (N=116)**	**Kd (N=54)**	**IKd (N=63)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	8 (11.6)	9 (7.8)	4 (7.4)	13 (20.6)	0.0489
Number (%) of patients censored	61 (88.4)	107 (92.2)	50 (92.6)	50 (79.4)	
Kaplan-Meier estimates of body image in months					
25% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	21.36 (6.604 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.3844		0.0545	
Hazard ratio (95% CI) vs Kd	-	0.66 (0.25 to 1.70)		2.86 (0.93 to 8.77)	
P-value	-	0.3878		0.0662	

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CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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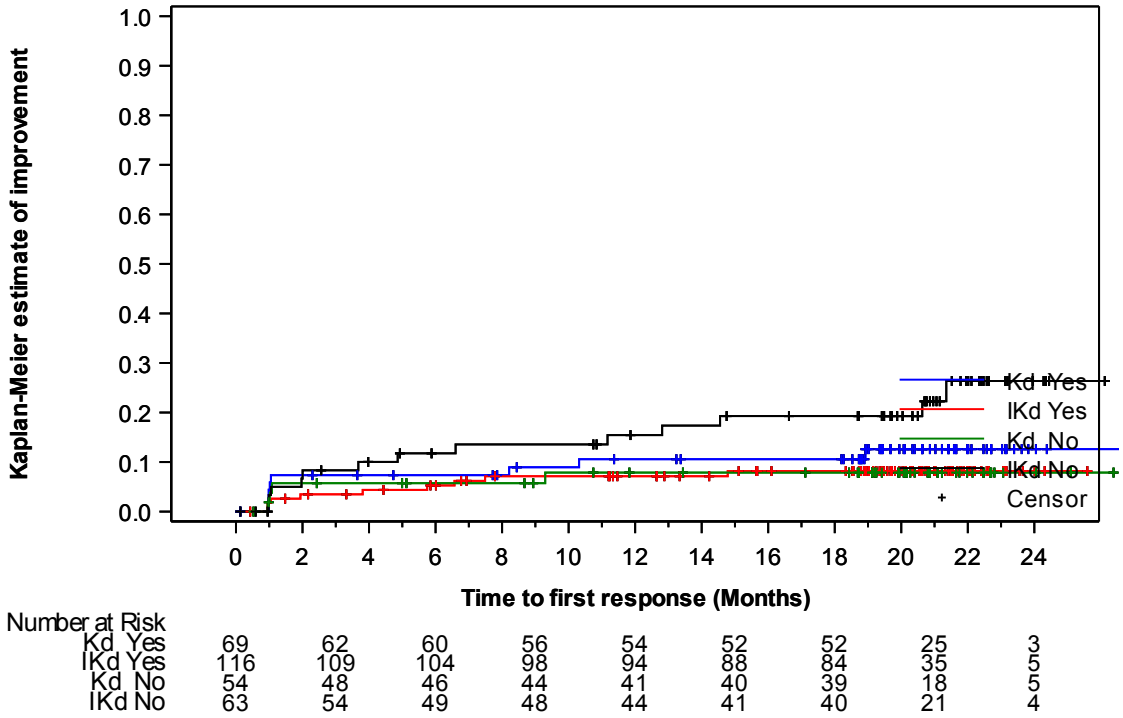
16.2.6.1 Health-related quality-of-life endpoints - QLQ-MY20
16.2.6.1.2 Body image
16.2.6.1.2.13 Efficacy response data - Subgroup analyses by previous autologous stem-cell
16.2.6.1.2.13.6 QLQ-MY20 - Time until permanent improvement by 10 pt in body image according to previous autologous stem-cell - Kaplan-Meier curve (LOCF) - ITT population



A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
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16.2.6.1 Health-related quality-of-life endpoints - QLQ-MY20
16.2.6.1.2 Body image
16.2.6.1.2.13 Efficacy response data - Subgroup analyses by previous autologous stem-cell
16.2.6.1.2.13.7 QLQ-MY20 - Time until permanent deterioration by 10 pt in body image according to previous autologous stem-cell (LOCF) - ITT population

	Yes		No		
	Kd (N=69)	**IKd (N=116)**	**Kd (N=54)**	**IKd (N=63)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	16 (23.2)	26 (22.4)	14 (25.9)	16 (25.4)	0.9901
Number (%) of patients censored	53 (76.8)	90 (77.6)	40 (74.1)	47 (74.6)	
Kaplan-Meier estimates of body image in months					
25% quantile (95% CI)	20.76 (7.524 to NC)	24.44 (14.193 to 24.444)	18.83 (10.415 to NC)	19.58 (10.480 to NC)	
Median (95% CI)	NC (NC to NC)	24.44 (NC to NC)	NC (20.567 to NC)	NC (22.407 to NC)	
75% quantile (95% CI)	NC (NC to NC)	24.44 (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.8560		0.8628	
Hazard ratio (95% CI) vs Kd	-	0.94 (0.51 to 1.76)		0.94 (0.46 to 1.92)	
P-value	-	0.8550		0.8624	
Deterioration probability (95% CI)[b]					

A higher score represents a better level of quality of life. Clinical meaningful deterioration change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.1 Health-related quality-of-life endpoints - QLQ-MY20
16.2.6.1.2 Body image
16.2.6.1.2.14 Efficacy response data - Subgroup analyses by baseline eGFR (MDRD)
16.2.6.1.2.14.3 QLQ-MY20 - Time to first improvement by 10 pt in body image according to baseline eGFR (MDRD) (LOCF) - ITT population

	>=60 mL/min/1.73m2		<60 mL/min/1.73m2		
	Kd (N=93)	**IKd (N=122)**	**Kd (N=18)**	**IKd (N=43)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	23 (24.7)	26 (21.3)	4 (22.2)	14 (32.6)	0.5455
Number (%) of patients censored	70 (75.3)	96 (78.7)	14 (77.8)	29 (67.4)	
Kaplan-Meier estimates of body image in months					
25% quantile (95% CI)	17.61 (1.906 to NC)	NC (2.004 to NC)	4.80 (0.986 to NC)	3.81 (1.084 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (4.797 to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.6647		0.6811	
Hazard ratio (95% CI) vs Kd	-	0.88 (0.50 to 1.55)		1.26 (0.42 to 3.83)	
P-value	-	0.6649		0.6818	
Improvement probability (95% CI)[b]					

A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.1 Health-related quality-of-life endpoints - QLQ-MY20
16.2.6.1.2 Body image
16.2.6.1.2.14 Efficacy response data - Subgroup analyses by baseline eGFR (MDRD)
16.2.6.1.2.14.4 QLQ-MY20 - Time to first deterioration by 10 pt in body image according to baseline eGFR (MDRD) (LOCF) - ITT population

	>=60 mL/min/1.73m2		<60 mL/min/1.73m2		
	Kd (N=93)	**IKd (N=122)**	**Kd (N=18)**	**IKd (N=43)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	47 (50.5)	74 (60.7)	10 (55.6)	23 (53.5)	0.2903
Number (%) of patients censored	46 (49.5)	48 (39.3)	8 (44.4)	20 (46.5)	
Kaplan-Meier estimates of body image in months					
25% quantile (95% CI)	2.40 (1.216 to 4.797)	2.83 (1.938 to 3.778)	4.04 (0.920 to 9.988)	2.83 (0.986 to 3.877)	
Median (95% CI)	20.57 (6.505 to NC)	8.28 (5.782 to 13.207)	9.99 (1.314 to NC)	14.78 (3.220 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (22.308 to NC)	NC (9.988 to NC)	NC (NC to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.1895		0.6436	
Hazard ratio (95% CI) vs Kd	-	1.28 (0.89 to 1.84)		0.84 (0.40 to 1.77)	
P-value	-	0.1906		0.6440	
Deterioration probability (95% CI)[b]					

A higher score represents a better level of quality of life. Clinical meaningful deterioration change from baseline less than or equal to -10 pt.
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CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.1 Health-related quality-of-life endpoints - QLQ-MY20
16.2.6.1.2 Body image
16.2.6.1.2.14 Efficacy response data - Subgroup analyses by baseline eGFR (MDRD)
16.2.6.1.2.14.5 QLQ-MY20 - Time until permanent improvement by 10 pt in body image according to baseline eGFR (MDRD) (LOCF) - ITT population

	>=60 mL/min/1.73m2		<60 mL/min/1.73m2		
	Kd (N=93)	**IKd (N=122)**	**Kd (N=18)**	**IKd (N=43)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	8 (8.6)	14 (11.5)	3 (16.7)	8 (18.6)	0.5952
Number (%) of patients censored	85 (91.4)	108 (88.5)	15 (83.3)	35 (81.4)	
Kaplan-Meier estimates of body image in months					
25% quantile (95% CI)	NC (NC to NC)	NC (21.355 to NC)	NC (0.986 to NC)	NC (7.491 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.4177		0.8843	
Hazard ratio (95% CI) vs Kd	-	1.43 (0.60 to 3.41)		0.91 (0.24 to 3.42)	
P-value	-	0.4202		0.8843	
Improvement probability (95% CI)[b]					

A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.1 Health-related quality-of-life endpoints - QLQ-MY20
16.2.6.1.2 Body image
16.2.6.1.2.14 Efficacy response data - Subgroup analyses by baseline eGFR (MDRD)
16.2.6.1.2.14.6 QLQ-MY20 - Time until permanent deterioration by 10 pt in body image according to baseline eGFR (MDRD) (LOCF) - ITT population

	>=60 mL/min/1.73m2		<60 mL/min/1.73m2		
	Kd (N=93)	**IKd (N=122)**	**Kd (N=18)**	**IKd (N=43)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	25 (26.9)	31 (25.4)	4 (22.2)	10 (23.3)	0.5805
Number (%) of patients censored	68 (73.1)	91 (74.6)	14 (77.8)	33 (76.7)	
Kaplan-Meier estimates of body image in months					
25% quantile (95% CI)	18.92 (9.495 to NC)	15.74 (12.025 to NC)	11.96 (1.084 to NC)	20.90 (17.577 to 24.444)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (11.959 to NC)	24.44 (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	24.44 (NC to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.9653		0.4410	
Hazard ratio (95% CI) vs Kd	-	0.99 (0.58 to 1.67)		0.63 (0.19 to 2.06)	
P-value	-	0.9653		0.4449	
Deterioration probability (95% CI)[b]					

A higher score represents a better level of quality of life. Clinical meaningful deterioration change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
PGM=DEVOPS/SAR650984/EFC15246/CIR_RWE/REPORT/PGM/eff_km_subgp_sr_sig_de_i_t.sas OUT=REPORT/OUTPUT/eff_km_my20_bdy_detpl_crcl_de_i_t_x.rtf (07APR2021 14:40)

16.2.6.1 Health-related quality-of-life endpoints - QLQ-MY20
16.2.6.1.2 Body image
16.2.6.1.2.15 Efficacy response data - Subgroup analyses by previous treatment with PI
16.2.6.1.2.15.3 QLQ-MY20 - Time to first improvement by 10 pt in body image according to previous treatment with PI (LOCF) - ITT population

	Yes		No		
	Kd (N=47)	**IKd (N=81)**	**Kd (N=76)**	**IKd (N=98)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	9 (19.1)	20 (24.7)	19 (25.0)	20 (20.4)	0.2212
Number (%) of patients censored	38 (80.9)	61 (75.3)	57 (75.0)	78 (79.6)	
Kaplan-Meier estimates of body image in months					
25% quantile (95% CI)	NC (3.285 to NC)	7.43 (1.938 to NC)	12.22 (1.018 to NC)	NC (2.136 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.3820		0.3841	
Hazard ratio (95% CI) vs Kd	-	1.42 (0.65 to 3.12)		0.76 (0.40 to 1.42)	
P-value	-	0.3845		0.3857	
Improvement probability (95% CI)[b]					

A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.1 Health-related quality-of-life endpoints - QLQ-MY20
16.2.6.1.2 Body image
16.2.6.1.2.15 Efficacy response data - Subgroup analyses by previous treatment with PI
16.2.6.1.2.15.4 QLQ-MY20 - Time to first deterioration by 10 pt in body image according to previous treatment with PI (LOCF) - ITT population

	Yes		No		
	Kd (N=47)	**IKd (N=81)**	**Kd (N=76)**	**IKd (N=98)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	27 (57.4)	42 (51.9)	32 (42.1)	60 (61.2)	0.0833
Number (%) of patients censored	20 (42.6)	39 (48.1)	44 (57.9)	38 (38.8)	
Kaplan-Meier estimates of body image in months					
25% quantile (95% CI)	2.04 (1.216 to 5.552)	2.83 (1.873 to 4.172)	3.06 (1.084 to 6.637)	2.89 (1.873 to 3.778)	
Median (95% CI)	8.31 (2.858 to NC)	11.99 (4.961 to NC)	NC (7.524 to NC)	8.34 (5.487 to 15.639)	
75% quantile (95% CI)	NC (20.567 to NC)	NC (NC to NC)	NC (NC to NC)	NC (22.308 to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.5996		0.0464	
Hazard ratio (95% CI) vs Kd	-	0.88 (0.54 to 1.43)		1.54 (1.00 to 2.37)	
P-value	-	0.5998		0.0481	
Hazard ratio inverted (95% CI) vs IKd		-		0.65 (0.42 to 1.00)	

A higher score represents a better level of quality of life. Clinical meaningful deterioration change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.1 Health-related quality-of-life endpoints - QLQ-MY20
16.2.6.1.2 Body image
16.2.6.1.2.15 Efficacy response data - Subgroup analyses by previous treatment with PI
16.2.6.1.2.15.5 QLQ-MY20 - Time until permanent improvement by 10 pt in body image according to previous treatment with PI (LOCF) - ITT population

	Yes		No		
	Kd (N=47)	**IKd (N=81)**	**Kd (N=76)**	**IKd (N=98)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	2 (4.3)	12 (14.8)	10 (13.2)	10 (10.2)	0.0630
Number (%) of patients censored	45 (95.7)	69 (85.2)	66 (86.8)	88 (89.8)	
Kaplan-Meier estimates of body image in months					
25% quantile (95% CI)	NC (NC to NC)	NC (14.554 to NC)	NC (18.924 to NC)	NC (NC to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.0602		0.4892	
Hazard ratio (95% CI) vs Kd	-	3.80 (0.85 to 16.97)		0.73 (0.31 to 1.77)	
P-value	-	0.0807		0.4909	
Improvement probability (95% CI)[b]					

A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.1 Health-related quality-of-life endpoints - QLQ-MY20
16.2.6.1.2 Body image
16.2.6.1.2.15 Efficacy response data - Subgroup analyses by previous treatment with PI
16.2.6.1.2.15.6 QLQ-MY20 - Time until permanent deterioration by 10 pt in body image according to previous treatment with PI (LOCF) - ITT population

	Yes		No		
	Kd (N=47)	**IKd (N=81)**	**Kd (N=76)**	**IKd (N=98)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	15 (31.9)	21 (25.9)	15 (19.7)	21 (21.4)	0.6685
Number (%) of patients censored	32 (68.1)	60 (74.1)	61 (80.3)	77 (78.6)	
Kaplan-Meier estimates of body image in months					
25% quantile (95% CI)	18.83 (6.374 to 20.764)	19.58 (8.246 to NC)	NC (11.532 to NC)	22.41 (15.507 to NC)	
Median (95% CI)	NC (20.567 to NC)	NC (NC to NC)	NC (NC to NC)	24.44 (24.444 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (24.444 to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.5421		0.9801	
Hazard ratio (95% CI) vs Kd	-	0.81 (0.42 to 1.58)		1.01 (0.52 to 1.96)	
P-value	-	0.5428		0.9801	
Deterioration probability (95% CI)[b]					

A higher score represents a better level of quality of life. Clinical meaningful deterioration change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.1 Health-related quality-of-life endpoints - QLQ-MY20
16.2.6.1.2 Body image
16.2.6.1.2.16 Efficacy response data - Subgroup analyses by previous treatment with IMiD
16.2.6.1.2.16.3 QLQ-MY20 - Time to first improvement by 10 pt in body image according to previous treatment with IMiD (LOCF) - ITT population

	Yes		No		
	Kd (N=62)	**IKd (N=81)**	**Kd (N=61)**	**IKd (N=98)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	13 (21.0)	12 (14.8)	15 (24.6)	28 (28.6)	0.2563
Number (%) of patients censored	49 (79.0)	69 (85.2)	46 (75.4)	70 (71.4)	
Kaplan-Meier estimates of body image in months					
25% quantile (95% CI)	NC (1.906 to NC)	NC (12.386 to NC)	17.61 (1.084 to NC)	2.89 (1.906 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.3090		0.5856	
Hazard ratio (95% CI) vs Kd	-	0.67 (0.30 to 1.46)		1.19 (0.64 to 2.23)	
P-value	-	0.3123		0.5861	
Improvement probability (95% CI)[b]					

A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.1 Health-related quality-of-life endpoints - QLQ-MY20
16.2.6.1.2 Body image
16.2.6.1.2.16 Efficacy response data - Subgroup analyses by previous treatment with IMiD
16.2.6.1.2.16.4 QLQ-MY20 - Time to first deterioration by 10 pt in body image according to previous treatment with IMiD (LOCF) - ITT population

	Yes		No		
	Kd (N=62)	**IKd (N=81)**	**Kd (N=61)**	**IKd (N=98)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	33 (53.2)	49 (60.5)	26 (42.6)	53 (54.1)	0.5524
Number (%) of patients censored	29 (46.8)	32 (39.5)	35 (57.4)	45 (45.9)	
Kaplan-Meier estimates of body image in months					
25% quantile (95% CI)	2.07 (1.051 to 6.472)	2.53 (1.413 to 3.154)	2.99 (1.938 to 6.374)	3.12 (1.971 to 4.205)	
Median (95% CI)	12.55 (6.472 to NC)	8.61 (3.844 to 20.140)	NC (6.374 to NC)	11.27 (6.111 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (22.308 to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.6613		0.2030	
Hazard ratio (95% CI) vs Kd	-	1.10 (0.71 to 1.72)		1.36 (0.85 to 2.17)	
P-value	-	0.6614		0.2048	
Deterioration probability (95% CI)[b]					

A higher score represents a better level of quality of life. Clinical meaningful deterioration change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.1 Health-related quality-of-life endpoints - QLQ-MY20
16.2.6.1.2 Body image
16.2.6.1.2.16 Efficacy response data - Subgroup analyses by previous treatment with IMiD
16.2.6.1.2.16.5 QLQ-MY20 - Time until permanent improvement by 10 pt in body image according to previous treatment with IMiD (LOCF) - ITT population

	Yes		No		
	Kd (N=62)	**IKd (N=81)**	**Kd (N=61)**	**IKd (N=98)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	6 (9.7)	3 (3.7)	6 (9.8)	19 (19.4)	0.0422
Number (%) of patients censored	56 (90.3)	78 (96.3)	55 (90.2)	79 (80.6)	
Kaplan-Meier estimates of body image in months					
25% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (12.813 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.1405		0.1121	
Hazard ratio (95% CI) vs Kd	-	0.37 (0.09 to 1.47)		2.07 (0.83 to 5.19)	
P-value	-	0.1573		0.1201	

A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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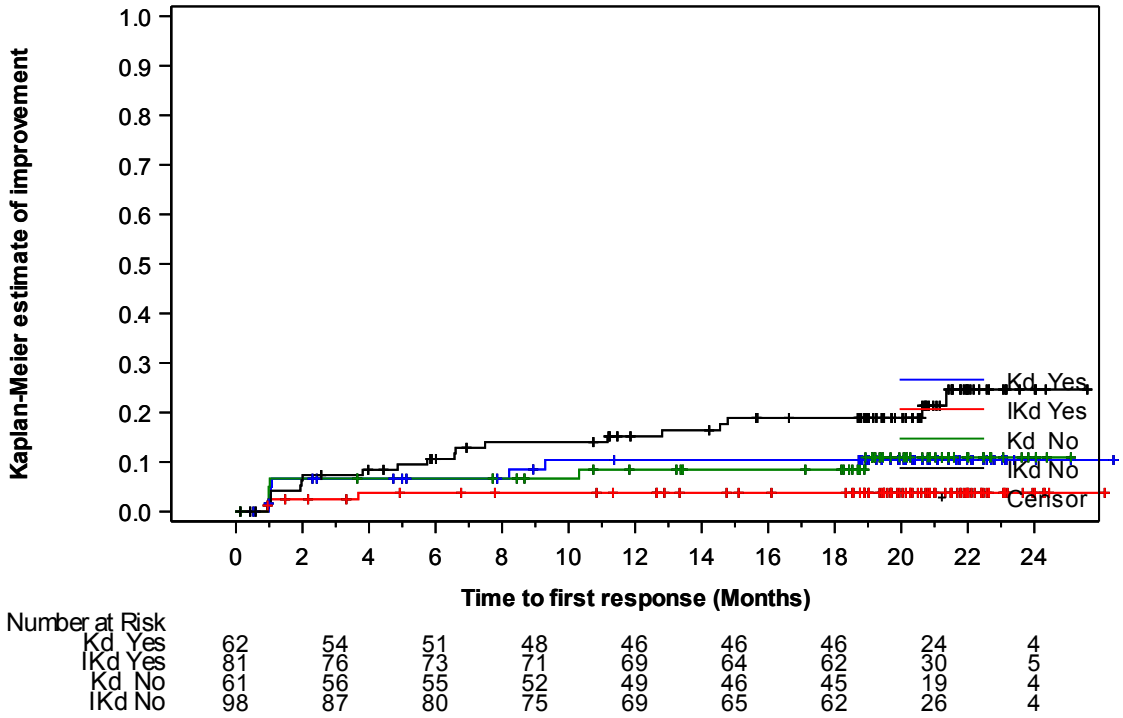
16.2.6.1 Health-related quality-of-life endpoints - QLQ-MY20
16.2.6.1.2 Body image
16.2.6.1.2.16 Efficacy response data - Subgroup analyses by previous treatment with IMiD
16.2.6.1.2.16.6 QLQ-MY20 - Time until permanent improvement by 10 pt in body image according to previous treatment with IMiD - Kaplan-Meier curve (LOCF) - ITT population



A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
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16.2.6.1 Health-related quality-of-life endpoints - QLQ-MY20
16.2.6.1.2 Body image
16.2.6.1.2.16 Efficacy response data - Subgroup analyses by previous treatment with IMiD
16.2.6.1.2.16.7 QLQ-MY20 - Time until permanent deterioration by 10 pt in body image according to previous treatment with IMiD (LOCF) - ITT population

	Yes		No		
	Kd (N=62)	**IKd (N=81)**	**Kd (N=61)**	**IKd (N=98)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	15 (24.2)	15 (18.5)	15 (24.6)	27 (27.6)	0.4707
Number (%) of patients censored	47 (75.8)	66 (81.5)	46 (75.4)	71 (72.4)	
Kaplan-Meier estimates of body image in months					
25% quantile (95% CI)	20.60 (11.302 to NC)	NC (12.025 to NC)	20.57 (6.374 to NC)	19.58 (13.996 to 24.444)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	24.44 (22.407 to 24.444)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	24.44 (NC to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.3913		0.8882	
Hazard ratio (95% CI) vs Kd	-	0.73 (0.36 to 1.50)		1.05 (0.55 to 1.98)	
P-value	-	0.3932		0.8888	
Deterioration probability (95% CI)[b]					

A higher score represents a better level of quality of life. Clinical meaningful deterioration change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
PGM=DEVOPS/SAR650984/EFC15246/CIR_RWE/REPORT/PGM/eff_km_subgp_sr_sig_de_i_t.sas OUT=REPORT/OUTPUT/eff_km_my20_bdy_detpl_imid_de_i_t_x.rtf (07APR2021 14:40)

16.2.6.1 Health-related quality-of-life endpoints - QLQ-MY20
16.2.6.1.2 Body image
16.2.6.1.2.17 Efficacy response data - Subgroup analyses by previous treatment with PI and IMiD
16.2.6.1.2.17.3 QLQ-MY20 - Time to first improvement by 10 pt in body image according to previous treatment with PI and IMiD (LOCF) - ITT population

	Yes		No		
	Kd (N=17)	**IKd (N=23)**	**Kd (N=106)**	**IKd (N=156)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	2 (11.8)	2 (8.7)	26 (24.5)	38 (24.4)	0.7513
Number (%) of patients censored	15 (88.2)	21 (91.3)	80 (75.5)	118 (75.6)	
Kaplan-Meier estimates of body image in months					
25% quantile (95% CI)	NC (1.906 to NC)	NC (1.971 to NC)	17.61 (1.906 to NC)	12.39 (2.004 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.7320		0.9517	
Hazard ratio (95% CI) vs Kd	-	0.71 (0.10 to 5.05)		0.98 (0.60 to 1.62)	
P-value	-	0.7332		0.9516	

A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.1 Health-related quality-of-life endpoints - QLQ-MY20
16.2.6.1.2 Body image
16.2.6.1.2.17 Efficacy response data - Subgroup analyses by previous treatment with PI and IMiD
16.2.6.1.2.17.4 QLQ-MY20 - Time to first deterioration by 10 pt in body image according to previous treatment with PI and IMiD (LOCF) - ITT population

	Yes		No		
	Kd (N=17)	**IKd (N=23)**	**Kd (N=106)**	**IKd (N=156)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	11 (64.7)	11 (47.8)	48 (45.3)	91 (58.3)	0.1470
Number (%) of patients censored	6 (35.3)	12 (52.2)	58 (54.7)	65 (41.7)	
Kaplan-Meier estimates of body image in months					
25% quantile (95% CI)	1.69 (0.986 to 6.801)	1.91 (0.986 to 3.877)	2.99 (1.873 to 5.552)	2.92 (1.971 to 3.778)	
Median (95% CI)	7.56 (1.314 to NC)	NC (1.971 to NC)	20.57 (7.261 to NC)	8.87 (6.505 to 15.639)	
75% quantile (95% CI)	NC (6.801 to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.3799		0.1015	
Hazard ratio (95% CI) vs Kd	-	0.69 (0.30 to 1.59)		1.34 (0.94 to 1.90)	
P-value	-	0.3827		0.1027	

A higher score represents a better level of quality of life. Clinical meaningful deterioration change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.1 Health-related quality-of-life endpoints - QLQ-MY20
16.2.6.1.2 Body image
16.2.6.1.2.17 Efficacy response data - Subgroup analyses by previous treatment with PI and IMiD
16.2.6.1.2.17.5 QLQ-MY20 - Time until permanent improvement by 10 pt in body image according to previous treatment with PI and IMiD (LOCF) - ITT population

	Yes		No		
	Kd (N=17)	**IKd (N=23)**	**Kd (N=106)**	**IKd (N=156)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	0 (0.0)	0 (0.0)	12 (11.3)	22 (14.1)	0.9999
Number (%) of patients censored	17 (100.0)	23 (100.0)	94 (88.7)	134 (85.9)	
Kaplan-Meier estimates of body image in months					
25% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (21.355 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-			0.5304	
Hazard ratio (95% CI) vs Kd	-			1.25 (0.62 to 2.53)	
P-value	-			0.5313	

A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.1 Health-related quality-of-life endpoints - QLQ-MY20
16.2.6.1.2 Body image
16.2.6.1.2.17 Efficacy response data - Subgroup analyses by previous treatment with PI and IMiD
16.2.6.1.2.17.6 QLQ-MY20 - Time until permanent deterioration by 10 pt in body image according to previous treatment with PI and IMiD (LOCF) - ITT population

	Yes		No		
	Kd (N=17)	**IKd (N=23)**	**Kd (N=106)**	**IKd (N=156)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	7 (41.2)	5 (21.7)	23 (21.7)	37 (23.7)	0.2650
Number (%) of patients censored	10 (58.8)	18 (78.3)	83 (78.3)	119 (76.3)	
Kaplan-Meier estimates of body image in months					
25% quantile (95% CI)	9.86 (1.051 to 20.764)	20.90 (1.511 to NC)	20.57 (11.959 to NC)	20.53 (14.949 to NC)	
Median (95% CI)	NC (9.298 to NC)	NC (20.895 to NC)	NC (NC to NC)	24.44 (24.444 to NC)	
75% quantile (95% CI)	NC (20.764 to NC)	NC (NC to NC)	NC (NC to NC)	NC (24.444 to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.2300		0.8387	
Hazard ratio (95% CI) vs Kd	-	0.50 (0.16 to 1.58)		1.06 (0.63 to 1.78)	
P-value	-	0.2392		0.8396	

A higher score represents a better level of quality of life. Clinical meaningful deterioration change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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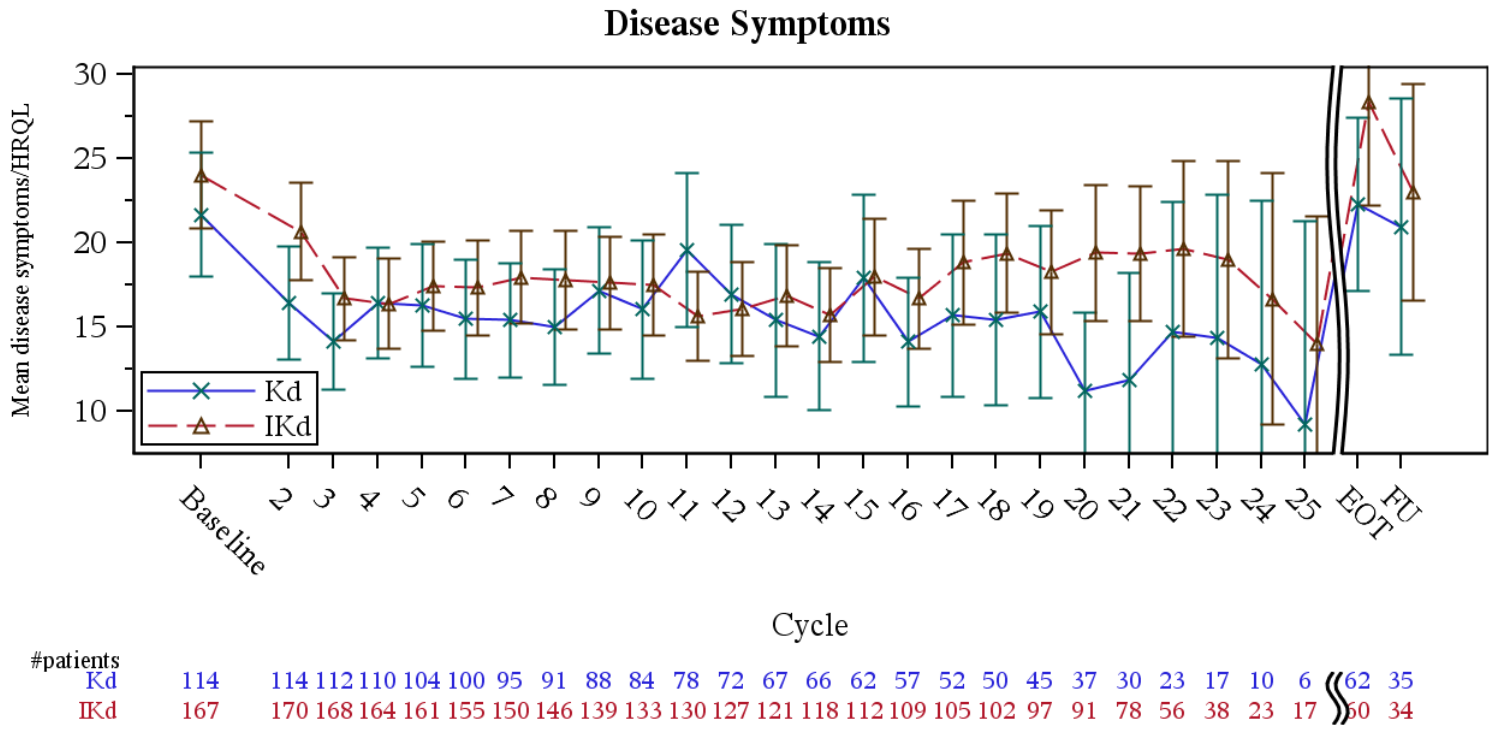
16.2.6.1 Health-related quality-of-life endpoints - QLQ-MY20
16.2.6.1.2 Disease symptoms
16.2.6.1.2.1 Efficacy response data
16.2.6.1.2.1.1 QLQ-MY20 - Mean and 95% CI for disease symptoms score over time (LOCF) - ITT population



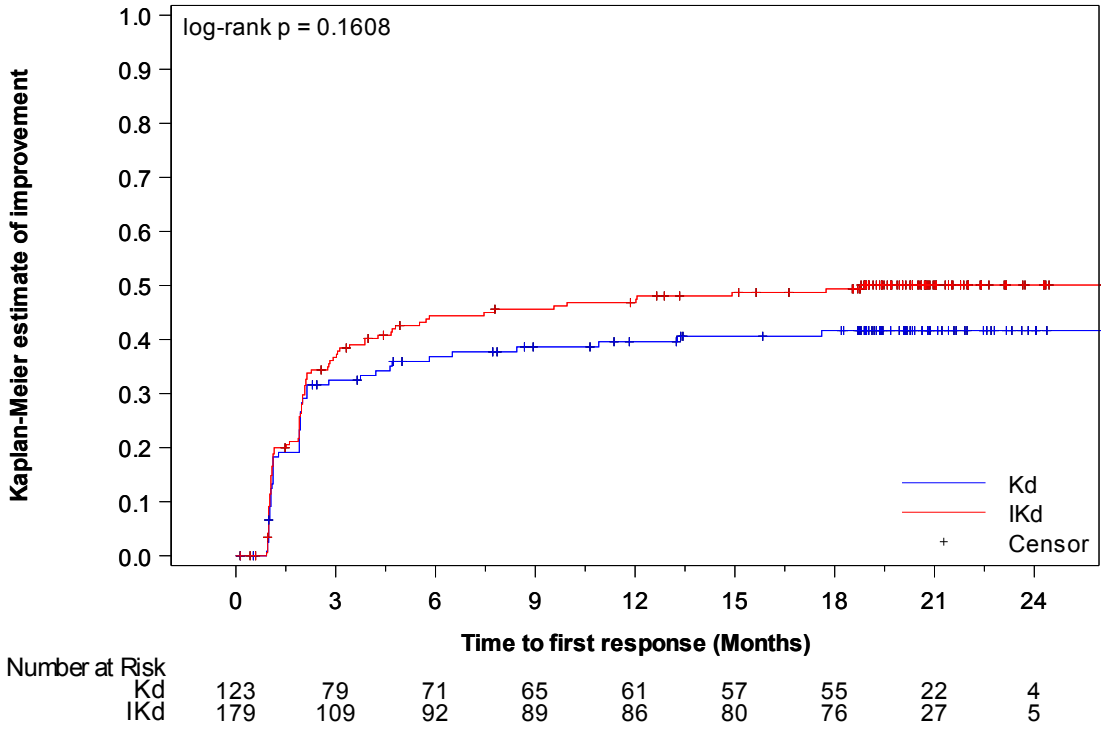
A lower score represents a better level of quality of life. Cycles with less than 20 patients overall are not presented.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
PGM=DEVOPS/SAR650984/EFC15246/CIR_RWE/REPORT/PGM/eff_qlq_line_i_f.sas OUT=REPORT/OUTPUT/eff_qlq_line_my20_dis_de_i_f_x.rtf (12FEB2021 15:16)

16.2.6.1 Health-related quality-of-life endpoints - QLQ-MY20
16.2.6.1.2 Disease symptoms
16.2.6.1.2.1 Efficacy response data
16.2.6.1.2.1.15 QLQ-MY20 - Time to first improvement by 15 pt in disease symptoms (LOCF) - ITT population

First improvement 15 points Disease symptoms (%)	**Kd (N=123)**	**IKd (N=179)**
Number (%) of events	49 (39.8)	86 (48.0)
Number (%) of patients censored	74 (60.2)	93 (52.0)
Kaplan-Meier estimates of disease symptoms in months		
25% quantile (95% CI)	1.94 (1.117 to 3.745)	1.91 (1.117 to 2.070)
Median (95% CI)	NC (13.273 to NC)	18.79 (4.797 to NC)
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)
Comparison vs. Kd		
Stratified[a] Log-Rank test p-value[b] vs Kd	-	0.1608
Stratified[a] Hazard ratio (95% CI) vs Kd	-	1.29 (0.90 to 1.84)
P-value	-	0.1619
Improvement probability (95% CI)[c]		
3 Months	0.325 (0.243 to 0.409)	0.367 (0.296 to 0.438)
6 Months	0.368 (0.283 to 0.454)	0.444 (0.369 to 0.516)

A lower score represents a better level of quality of life. Clinical meaningful improvement change from baseline less than or equal to -15 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] Stratified on number of prior lines of therapy (1 vs. >1) and Revised International Staging System (R-ISS) stage (I or II vs. III vs. not classified) according to IRT
[b] One-sided significance level is 0.025
[c] Estimated using the Kaplan-Meier method
NA/NC = Not Applicable / Not Calculable
PGM=DEVOPS/SAR650984/EFC15246/CIR_RWE/REPORT/PGM/eff_km_invhr_sr_i_t.sas OUT=REPORT/OUTPUT/eff_km_my20_dis_imp15l_de_i_t_x.rtf (07APR2021 14:23)

16.2.6.1 Health-related quality-of-life endpoints - QLQ-MY20
16.2.6.1.2 Disease symptoms
16.2.6.1.2.1 Efficacy response data
16.2.6.1.2.1.16 QLQ-MY20 - Time to first improvement by 15 pt in disease symptoms - Kaplan-Meier curve (LOCF) - ITT population



A lower score represents a better level of quality of life. Clinical meaningful improvement change from baseline less than or equal to -15 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
PGM=DEVOPS/SAR650984/EFC15246/CIR_RWE/REPORT/PGM/eff_qlq_km_i_f.sas OUT=REPORT/OUTPUT/eff_km_my20_dis_imp15l_de_i_f_x.rtf (07APR2021 14:25)

16.2.6.1 Health-related quality-of-life endpoints - QLQ-MY20
16.2.6.1.2 Disease symptoms
16.2.6.1.2.1 Efficacy response data
16.2.6.1.2.1.17 QLQ-MY20 - Time to first deterioration by 15 pt in disease symptoms (LOCF) - ITT population

First deterioration 15 points Disease symptoms (%)	**Kd (N=123)**	**IKd (N=179)**
Number (%) of events	45 (36.6)	77 (43.0)
Number (%) of patients censored	78 (63.4)	102 (57.0)
Kaplan-Meier estimates of disease symptoms in months		
25% quantile (95% CI)	6.51 (4.665 to 14.653)	5.55 (3.088 to 6.637)
Median (95% CI)	NC (21.552 to NC)	NC (14.160 to NC)
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)
Comparison vs. Kd		
Stratified[a] Log-Rank test p-value[b] vs Kd	-	0.1652
Stratified[a] Hazard ratio (95% CI) vs Kd	-	1.30 (0.90 to 1.89)
P-value	-	0.1664
Deterioration probability (95% CI)[c]		
3 Months	0.883 (0.810 to 0.929)	0.822 (0.757 to 0.872)
6 Months	0.762 (0.674 to 0.829)	0.717 (0.644 to 0.778)

A lower score represents a better level of quality of life. Clinical meaningful deterioration change from baseline greater than or equal to 15 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] Stratified on number of prior lines of therapy (1 vs. >1) and Revised International Staging System (R-ISS) stage (I or II vs. III vs. not classified) according to IRT
[b] One-sided significance level is 0.025
[c] Estimated using the Kaplan-Meier method
NA/NC = Not Applicable / Not Calculable
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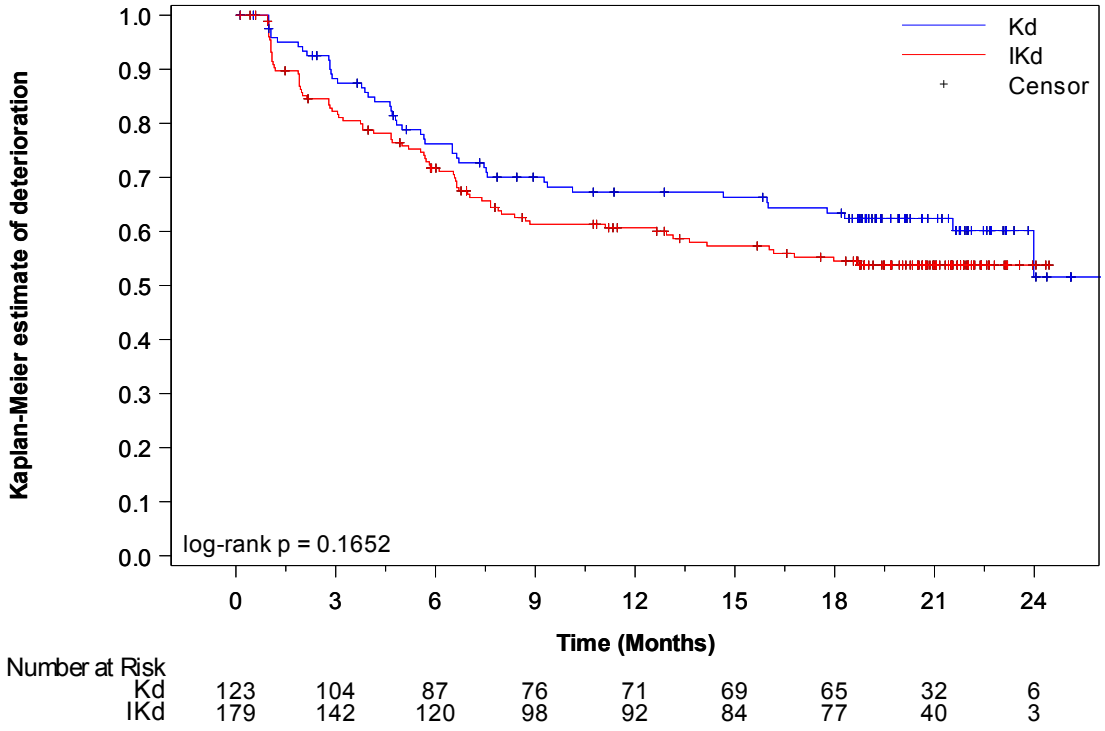
16.2.6.1 Health-related quality-of-life endpoints - QLQ-MY20
16.2.6.1.2 Disease symptoms
16.2.6.1.2.1 Efficacy response data
16.2.6.1.2.1.18 QLQ-MY20 - Time to first deterioration by 15 pt in disease symptoms - Kaplan-Meier curve (LOCF) - ITT population



A lower score represents a better level of quality of life. Clinical meaningful deterioration change from baseline greater than or equal to 15 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
PGM=DEVOPS/SAR650984/EFC15246/CIR_RWE/REPORT/PGM/eff_qlq_km_i_f.sas OUT=REPORT/OUTPUT/eff_km_my20_dis_det15l_de_i_f_x.rtf (07APR2021 14:25)

16.2.6.1 Health-related quality-of-life endpoints - QLQ-MY20
16.2.6.1.2 Disease symptoms
16.2.6.1.2.1 Efficacy response data
16.2.6.1.2.1.19 QLQ-MY20 - Time until permanent improvement by 15 pt in disease symptoms (LOCF) - ITT population

First permanent improvement 15 points Disease symptoms (%)	**Kd (N=123)**	**IKd (N=179)**
Number (%) of events	26 (21.1)	47 (26.3)
Number (%) of patients censored	97 (78.9)	132 (73.7)
Kaplan-Meier estimates of disease symptoms in months		
25% quantile (95% CI)	22.21 (12.517 to NC)	18.79 (14.127 to 23.359)
Median (95% CI)	NC (NC to NC)	NC (23.228 to NC)
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)
Comparison vs. Kd		
Stratified[a] Log-Rank test p-value[b] vs Kd	-	0.3741
Stratified[a] Hazard ratio (95% CI) vs Kd	-	1.24 (0.77 to 2.02)
P-value	-	0.3750
Improvement probability (95% CI)[c]		
3 Months	0.075 (0.037 to 0.131)	0.092 (0.055 to 0.140)
6 Months	0.084 (0.043 to 0.142)	0.110 (0.069 to 0.161)

A lower score represents a better level of quality of life. Clinical meaningful improvement change from baseline less than or equal to -15 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] Stratified on number of prior lines of therapy (1 vs. >1) and Revised International Staging System (R-ISS) stage (I or II vs. III vs. not classified) according to IRT
[b] One-sided significance level is 0.025
[c] Estimated using the Kaplan-Meier method
NA/NC = Not Applicable / Not Calculable
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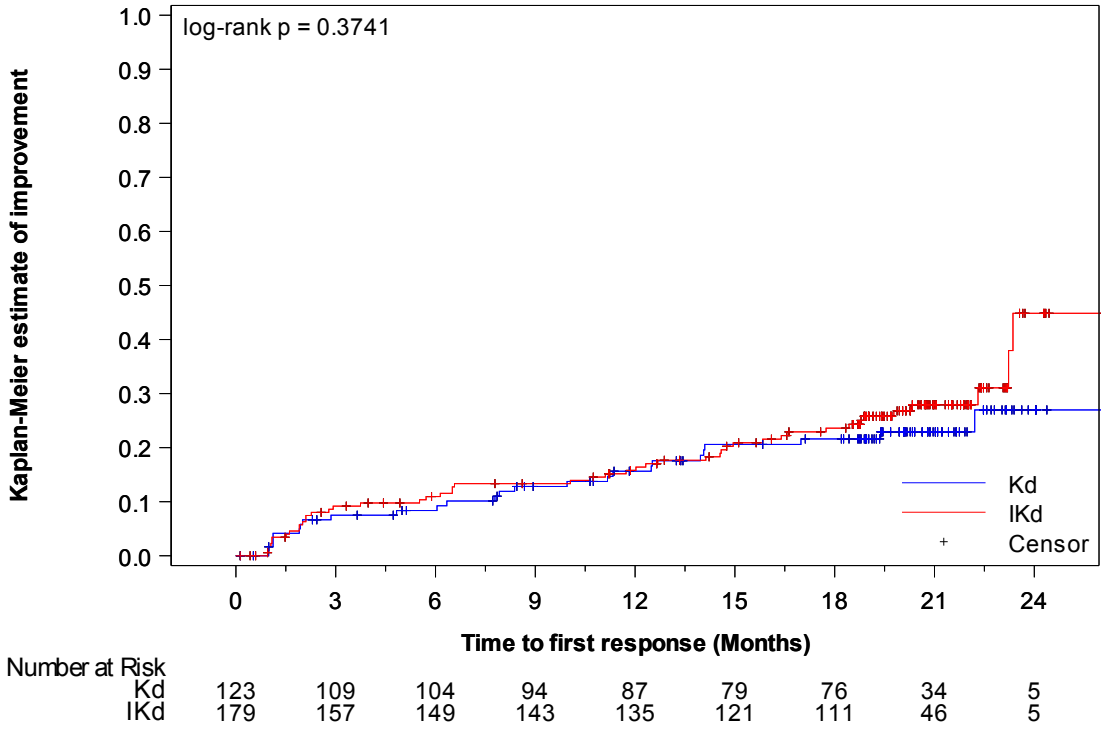
16.2.6.1 Health-related quality-of-life endpoints - QLQ-MY20
16.2.6.1.2 Disease symptoms
16.2.6.1.2.1 Efficacy response data
16.2.6.1.2.1.20 QLQ-MY20 - Time until permanent improvement by 15 pt in disease symptoms - Kaplan-Meier curve (LOCF) - ITT population



A lower score represents a better level of quality of life. Clinical meaningful improvement change from baseline less than or equal to -15 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.

16.2.6.1 Health-related quality-of-life endpoints - QLQ-MY20
16.2.6.1.2 Disease symptoms
16.2.6.1.2.1 Efficacy response data
16.2.6.1.2.1.21 QLQ-MY20 - Time until permanent deterioration by 15 pt in disease symptoms (LOCF) - ITT population

First permanent deterioration 15 points Disease symptoms (%)	**Kd (N=123)**	**IKd (N=179)**
Number (%) of events	21 (17.1)	30 (16.8)
Number (%) of patients censored	102 (82.9)	149 (83.2)
Kaplan-Meier estimates of disease symptoms in months		
25% quantile (95% CI)	23.98 (19.220 to NC)	NC (19.877 to NC)
Median (95% CI)	NC (23.984 to NC)	NC (NC to NC)
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)
Comparison vs. Kd		
Stratified[a] Log-Rank test p-value[b] vs Kd	-	0.9272
Stratified[a] Hazard ratio (95% CI) vs Kd	-	0.97 (0.56 to 1.70)
P-value	-	0.9270
Deterioration probability (95% CI)[c]		
3 Months	0.983 (0.934 to 0.996)	0.971 (0.933 to 0.988)
6 Months	0.940 (0.878 to 0.971)	0.942 (0.895 to 0.969)

A lower score represents a better level of quality of life. Clinical meaningful deterioration change from baseline greater than or equal to 15 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] Stratified on number of prior lines of therapy (1 vs. >1) and Revised International Staging System (R-ISS) stage (I or II vs. III vs. not classified) according to IRT
[b] One-sided significance level is 0.025
[c] Estimated using the Kaplan-Meier method
NA/NC = Not Applicable / Not Calculable
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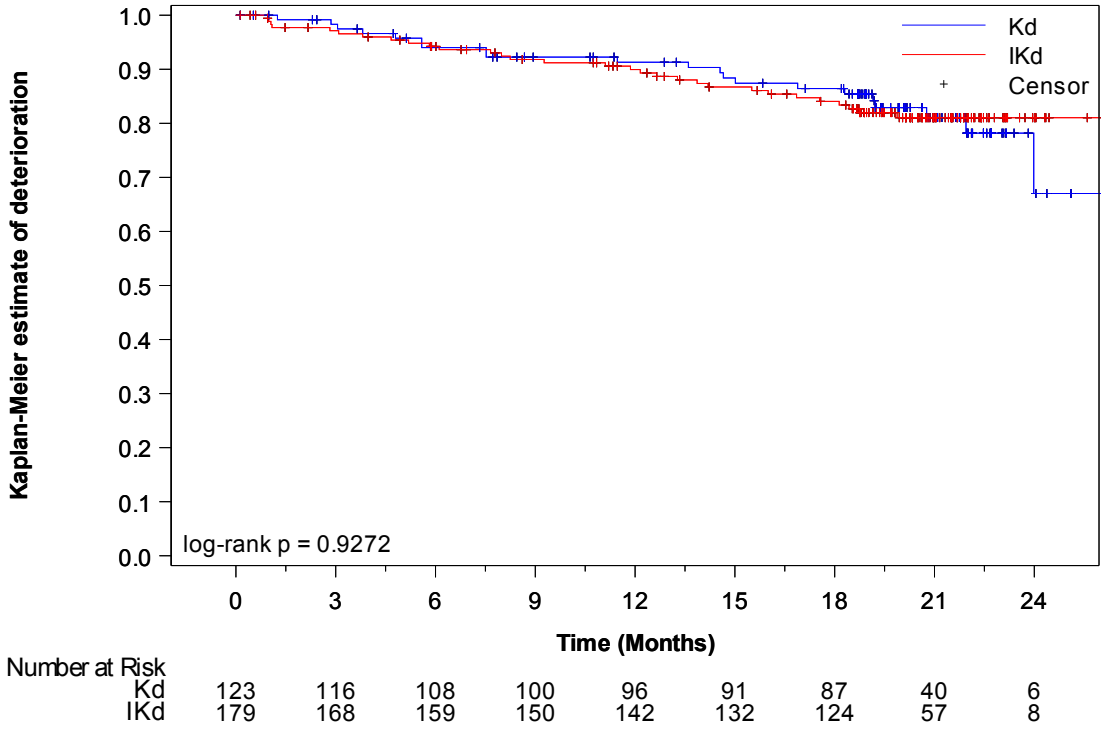
16.2.6.1 Health-related quality-of-life endpoints - QLQ-MY20
16.2.6.1.2 Disease symptoms
16.2.6.1.2.1 Efficacy response data
16.2.6.1.2.1.22 QLQ-MY20 - Time until permanent deterioration by 15 pt in disease symptoms - Kaplan-Meier curve (LOCF) - ITT population



A lower score represents a better level of quality of life. Clinical meaningful deterioration change from baseline greater than or equal to 15 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
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16.2.6.1 Health-related quality-of-life endpoints - QLQ-MY20
16.2.6.1.2 Disease symptoms
16.2.6.1.2.2 Efficacy response data - Subgroup analyses by age
16.2.6.1.2.2.3 QLQ-MY20 - Time to first improvement by 10 pt in disease symptoms according to age (LOCF) - ITT population

	<65 years		>=65 years		
	Kd (N=66)	**IKd (N=88)**	**Kd (N=57)**	**IKd (N=91)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	32 (48.5)	49 (55.7)	32 (56.1)	62 (68.1)	0.8381
Number (%) of patients censored	34 (51.5)	39 (44.3)	25 (43.9)	29 (31.9)	
Kaplan-Meier estimates of disease symptoms in months					
25% quantile (95% CI)	1.12 (1.051 to 1.906)	1.12 (1.018 to 1.906)	1.15 (1.051 to 2.103)	1.35 (1.051 to 1.938)	
Median (95% CI)	18.69 (1.971 to NC)	5.72 (1.971 to NC)	4.63 (2.103 to NC)	2.96 (2.070 to 5.060)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (8.805 to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.4365		0.2238	
Hazard ratio (95% CI) vs Kd	-	1.19 (0.76 to 1.86)		1.30 (0.85 to 2.00)	
P-value	-	0.4371		0.2252	
Improvement probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful improvement change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
PGM=DEVOPS/SAR650984/EFC15246/CIR_RWE/REPORT/PGM/eff_km_subgp_sr_sig_de_i_t.sas OUT=REPORT/OUTPUT/eff_km_my20_dis_impl_age_de_i_t_x.rtf (07APR2021 14:42)

16.2.6.1 Health-related quality-of-life endpoints - QLQ-MY20
16.2.6.1.2 Disease symptoms
16.2.6.1.2.2 Efficacy response data - Subgroup analyses by age
16.2.6.1.2.2.4 QLQ-MY20 - Time to first deterioration by 10 pt in disease symptoms according to age (LOCF) - ITT population

	<65 years		>=65 years		
	Kd (N=66)	**IKd (N=88)**	**Kd (N=57)**	**IKd (N=91)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	28 (42.4)	50 (56.8)	30 (52.6)	47 (51.6)	0.3062
Number (%) of patients censored	38 (57.6)	38 (43.2)	27 (47.4)	44 (48.4)	
Kaplan-Meier estimates of disease symptoms in months					
25% quantile (95% CI)	3.71 (1.906 to 8.312)	2.83 (1.183 to 4.665)	2.96 (1.248 to 4.994)	2.81 (1.150 to 4.632)	
Median (95% CI)	NC (9.265 to NC)	11.10 (5.684 to 19.647)	16.00 (4.994 to NC)	12.94 (6.571 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.1148		0.9058	
Hazard ratio (95% CI) vs Kd	-	1.45 (0.91 to 2.30)		1.03 (0.65 to 1.63)	
P-value	-	0.1169		0.9061	
Deterioration probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful deterioration change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
PGM=DEVOPS/SAR650984/EFC15246/CIR_RWE/REPORT/PGM/eff_km_subgp_sr_sig_de_i_t.sas OUT=REPORT/OUTPUT/eff_km_my20_dis_detl_age_de_i_t_x.rtf (07APR2021 14:42)

16.2.6.1 Health-related quality-of-life endpoints - QLQ-MY20
16.2.6.1.2 Disease symptoms
16.2.6.1.2.2 Efficacy response data - Subgroup analyses by age
16.2.6.1.2.2.5 QLQ-MY20 - Time until permanent improvement by 10 pt in disease symptoms according to age (LOCF) - ITT population

	<65 years		>=65 years		
	Kd (N=66)	**IKd (N=88)**	**Kd (N=57)**	**IKd (N=91)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	16 (24.2)	26 (29.5)	17 (29.8)	32 (35.2)	0.9636
Number (%) of patients censored	50 (75.8)	62 (70.5)	40 (70.2)	59 (64.8)	
Kaplan-Meier estimates of disease symptoms in months					
25% quantile (95% CI)	19.38 (1.906 to NC)	18.79 (5.717 to 21.684)	15.70 (4.698 to NC)	13.70 (6.604 to 19.581)	
Median (95% CI)	NC (NC to NC)	NC (21.684 to NC)	NC (22.209 to NC)	23.23 (19.778 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.6544		0.5545	
Hazard ratio (95% CI) vs Kd	-	1.15 (0.62 to 2.15)		1.19 (0.66 to 2.15)	
P-value	-	0.6547		0.5550	
Improvement probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful improvement change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
PGM=DEVOPS/SAR650984/EFC15246/CIR_RWE/REPORT/PGM/eff_km_subgp_sr_sig_de_i_t.sas OUT=REPORT/OUTPUT/eff_km_my20_dis_imppl_age_de_i_t_x.rtf (07APR2021 14:42)

16.2.6.1 Health-related quality-of-life endpoints - QLQ-MY20
16.2.6.1.2 Disease symptoms
16.2.6.1.2.2 Efficacy response data - Subgroup analyses by age
16.2.6.1.2.2.6 QLQ-MY20 - Time until permanent deterioration by 10 pt in disease symptoms according to age (LOCF) - ITT population

	<65 years		>=65 years		
	Kd (N=66)	**IKd (N=88)**	**Kd (N=57)**	**IKd (N=91)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	15 (22.7)	21 (23.9)	14 (24.6)	18 (19.8)	0.6464
Number (%) of patients censored	51 (77.3)	67 (76.1)	43 (75.4)	73 (80.2)	
Kaplan-Meier estimates of disease symptoms in months					
25% quantile (95% CI)	20.76 (7.524 to NC)	18.76 (11.335 to NC)	19.22 (13.602 to NC)	NC (14.456 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (23.064 to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.9647		0.5661	
Hazard ratio (95% CI) vs Kd	-	1.02 (0.52 to 1.97)		0.82 (0.41 to 1.64)	
P-value	-	0.9647		0.5667	
Deterioration probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful deterioration change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.1 Health-related quality-of-life endpoints - QLQ-MY20
16.2.6.1.2 Disease symptoms
16.2.6.1.2.3 Efficacy response data - Subgroup analyses by gender
16.2.6.1.2.3.3 QLQ-MY20 - Time to first improvement by 10 pt in disease symptoms according to gender (LOCF) - ITT population

	Male		Female		
	Kd (N=68)	**IKd (N=101)**	**Kd (N=55)**	**IKd (N=78)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	28 (41.2)	56 (55.4)	36 (65.5)	55 (70.5)	0.2369
Number (%) of patients censored	40 (58.8)	45 (44.6)	19 (34.5)	23 (29.5)	
Kaplan-Meier estimates of disease symptoms in months					
25% quantile (95% CI)	1.91 (1.084 to 8.444)	1.51 (1.084 to 1.938)	1.05 (0.986 to 1.906)	1.12 (1.018 to 1.906)	
Median (95% CI)	NC (8.509 to NC)	5.72 (2.136 to NC)	2.14 (1.906 to 4.797)	2.50 (1.971 to 4.665)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (4.797 to NC)	NC (6.505 to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.0752		0.8410	
Hazard ratio (95% CI) vs Kd	-	1.51 (0.96 to 2.37)		1.04 (0.69 to 1.59)	
P-value	-	0.0773		0.8417	
Improvement probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful improvement change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.1 Health-related quality-of-life endpoints - QLQ-MY20
16.2.6.1.2 Disease symptoms
16.2.6.1.2.3 Efficacy response data - Subgroup analyses by gender
16.2.6.1.2.3.4 QLQ-MY20 - Time to first deterioration by 10 pt in disease symptoms according to gender (LOCF) - ITT population

	Male		Female		
	Kd (N=68)	**IKd (N=101)**	**Kd (N=55)**	**IKd (N=78)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	35 (51.5)	53 (52.5)	23 (41.8)	44 (56.4)	0.3028
Number (%) of patients censored	33 (48.5)	48 (47.5)	32 (58.2)	34 (43.6)	
Kaplan-Meier estimates of disease symptoms in months					
25% quantile (95% CI)	2.96 (1.971 to 4.994)	2.86 (1.084 to 4.665)	3.06 (1.117 to 9.265)	2.83 (1.873 to 4.665)	
Median (95% CI)	15.97 (5.585 to NC)	12.65 (6.571 to NC)	NC (9.265 to NC)	12.94 (5.717 to NC)	
75% quantile (95% CI)	NC (21.552 to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.8280		0.1274	
Hazard ratio (95% CI) vs Kd	-	1.05 (0.68 to 1.61)		1.48 (0.89 to 2.45)	
P-value	-	0.8288		0.1299	
Deterioration probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful deterioration change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.1 Health-related quality-of-life endpoints - QLQ-MY20
16.2.6.1.2 Disease symptoms
16.2.6.1.2.3 Efficacy response data - Subgroup analyses by gender
16.2.6.1.2.3.5 QLQ-MY20 - Time until permanent improvement by 10 pt in disease symptoms according to gender (LOCF) - ITT population

	Male		Female		
	Kd (N=68)	**IKd (N=101)**	**Kd (N=55)**	**IKd (N=78)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	13 (19.1)	30 (29.7)	20 (36.4)	28 (35.9)	0.2190
Number (%) of patients censored	55 (80.9)	71 (70.3)	35 (63.6)	50 (64.1)	
Kaplan-Meier estimates of disease symptoms in months					
25% quantile (95% CI)	NC (10.283 to NC)	18.79 (8.345 to 20.468)	10.68 (1.117 to 17.610)	14.95 (5.717 to 20.304)	
Median (95% CI)	NC (NC to NC)	NC (21.454 to NC)	NC (17.610 to NC)	23.23 (21.684 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (23.228 to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.1813		0.7686	
Hazard ratio (95% CI) vs Kd	-	1.55 (0.81 to 2.98)		0.92 (0.52 to 1.63)	
P-value	-	0.1850		0.7686	
Improvement probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful improvement change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.1 Health-related quality-of-life endpoints - QLQ-MY20
16.2.6.1.2 Disease symptoms
16.2.6.1.2.3 Efficacy response data - Subgroup analyses by gender
16.2.6.1.2.3.6 QLQ-MY20 - Time until permanent deterioration by 10 pt in disease symptoms according to gender (LOCF) - ITT population

	Male		Female		
	Kd (N=68)	**IKd (N=101)**	**Kd (N=55)**	**IKd (N=78)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	19 (27.9)	27 (26.7)	10 (18.2)	12 (15.4)	0.7416
Number (%) of patients censored	49 (72.1)	74 (73.3)	45 (81.8)	66 (84.6)	
Kaplan-Meier estimates of disease symptoms in months					
25% quantile (95% CI)	19.22 (5.717 to 23.064)	17.48 (11.335 to NC)	NC (15.014 to NC)	NC (18.431 to NC)	
Median (95% CI)	NC (23.064 to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.8966		0.6231	
Hazard ratio (95% CI) vs Kd	-	0.96 (0.53 to 1.73)		0.81 (0.35 to 1.88)	
P-value	-	0.8962		0.6238	
Deterioration probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful deterioration change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.1 Health-related quality-of-life endpoints - QLQ-MY20
16.2.6.1.2 Disease symptoms
16.2.6.1.2.4 Efficacy response data - Subgroup analyses by ethnic origin
16.2.6.1.2.4.3 QLQ-MY20 - Time to first improvement by 10 pt in disease symptoms according to ethnic origin (LOCF) - ITT population

	White		Other		
	Kd (N=83)	**IKd (N=131)**	**Kd (N=28)**	**IKd (N=34)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	46 (55.4)	87 (66.4)	15 (53.6)	18 (52.9)	0.5214
Number (%) of patients censored	37 (44.6)	44 (33.6)	13 (46.4)	16 (47.1)	
Kaplan-Meier estimates of disease symptoms in months					
25% quantile (95% CI)	1.12 (1.051 to 1.906)	1.12 (1.051 to 1.906)	1.12 (1.018 to 2.103)	1.15 (0.986 to 2.103)	
Median (95% CI)	4.63 (1.938 to NC)	2.89 (1.971 to 4.862)	8.44 (1.150 to NC)	7.46 (1.906 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (15.836 to NC)	NC (9.626 to NC)	NC (NC to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.1741		0.9917	
Hazard ratio (95% CI) vs Kd	-	1.28 (0.90 to 1.83)		1.00 (0.51 to 1.99)	
P-value	-	0.1752		0.9917	
Improvement probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful improvement change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.1 Health-related quality-of-life endpoints - QLQ-MY20
16.2.6.1.2 Disease symptoms
16.2.6.1.2.4 Efficacy response data - Subgroup analyses by ethnic origin
16.2.6.1.2.4.4 QLQ-MY20 - Time to first deterioration by 10 pt in disease symptoms according to ethnic origin (LOCF) - ITT population

	White		Other		
	Kd (N=83)	**IKd (N=131)**	**Kd (N=28)**	**IKd (N=34)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	38 (45.8)	75 (57.3)	16 (57.1)	20 (58.8)	0.6557
Number (%) of patients censored	45 (54.2)	56 (42.7)	12 (42.9)	14 (41.2)	
Kaplan-Meier estimates of disease symptoms in months					
25% quantile (95% CI)	3.02 (1.906 to 4.994)	2.83 (1.216 to 4.140)	2.96 (1.051 to 5.651)	2.14 (0.986 to 4.665)	
Median (95% CI)	NC (8.444 to NC)	7.43 (5.749 to 16.164)	12.45 (2.957 to NC)	7.98 (2.760 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (17.906 to NC)	NC (17.906 to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.1096		0.6532	
Hazard ratio (95% CI) vs Kd	-	1.37 (0.93 to 2.03)		1.16 (0.60 to 2.24)	
P-value	-	0.1111		0.6535	
Deterioration probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful deterioration change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.1 Health-related quality-of-life endpoints - QLQ-MY20
16.2.6.1.2 Disease symptoms
16.2.6.1.2.4 Efficacy response data - Subgroup analyses by ethnic origin
16.2.6.1.2.4.5 QLQ-MY20 - Time until permanent improvement by 10 pt in disease symptoms according to ethnic origin (LOCF) - ITT population

	White		Other		
	Kd (N=83)	**IKd (N=131)**	**Kd (N=28)**	**IKd (N=34)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	26 (31.3)	46 (35.1)	6 (21.4)	9 (26.5)	0.8186
Number (%) of patients censored	57 (68.7)	85 (64.9)	22 (78.6)	25 (73.5)	
Kaplan-Meier estimates of disease symptoms in months					
25% quantile (95% CI)	12.94 (4.698 to 22.209)	14.55 (6.604 to 19.614)	NC (1.051 to NC)	15.84 (2.004 to NC)	
Median (95% CI)	NC (22.209 to NC)	23.23 (21.454 to NC)	NC (NC to NC)	NC (18.891 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.7268		0.7330	
Hazard ratio (95% CI) vs Kd	-	1.09 (0.67 to 1.76)		1.20 (0.43 to 3.36)	
P-value	-	0.7269		0.7333	
Improvement probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful improvement change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.1 Health-related quality-of-life endpoints - QLQ-MY20
16.2.6.1.2 Disease symptoms
16.2.6.1.2.4 Efficacy response data - Subgroup analyses by ethnic origin
16.2.6.1.2.4.6 QLQ-MY20 - Time until permanent deterioration by 10 pt in disease symptoms according to ethnic origin (LOCF) - ITT population

	White		Other		
	Kd (N=83)	**IKd (N=131)**	**Kd (N=28)**	**IKd (N=34)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	18 (21.7)	28 (21.4)	8 (28.6)	9 (26.5)	0.9831
Number (%) of patients censored	65 (78.3)	103 (78.6)	20 (71.4)	25 (73.5)	
Kaplan-Meier estimates of disease symptoms in months					
25% quantile (95% CI)	23.06 (15.014 to NC)	NC (17.478 to NC)	17.91 (4.797 to NC)	13.86 (5.848 to NC)	
Median (95% CI)	NC (23.064 to NC)	NC (NC to NC)	NC (17.906 to NC)	NC (19.647 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.9570		0.9717	
Hazard ratio (95% CI) vs Kd	-	0.98 (0.54 to 1.78)		0.98 (0.38 to 2.55)	
P-value	-	0.9569		0.9716	
Deterioration probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful deterioration change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
PGM=DEVOPS/SAR650984/EFC15246/CIR_RWE/REPORT/PGM/eff_km_subgp_sr_sig_de_i_t.sas OUT=REPORT/OUTPUT/eff_km_my20_dis_detpl_race_de_i_t_x.rtf (07APR2021 14:42)

16.2.6.1 Health-related quality-of-life endpoints - QLQ-MY20
16.2.6.1.2 Disease symptoms
16.2.6.1.2.5 Efficacy response data - Subgroup analyses by geographical region
16.2.6.1.2.5.3 QLQ-MY20 - Time to first improvement by 10 pt in disease symptoms according to geographical region (LOCF) - ITT population

	Europe		America		Asia		Other countries		
	Kd (N=60)	**IKd (N=85)**	**Kd (N=20)**	**IKd (N=24)**	**Kd (N=21)**	**IKd (N=25)**	**Kd (N=22)**	**IKd (N=45)**	**p-value of treatment-by-subgroup interaction[c]**
Number (%) of events	26 (43.3)	50 (58.8)	13 (65.0)	17 (70.8)	11 (52.4)	14 (56.0)	14 (63.6)	30 (66.7)	0.8323
Number (%) of patients censored	34 (56.7)	35 (41.2)	7 (35.0)	7 (29.2)	10 (47.6)	11 (44.0)	8 (36.4)	15 (33.3)	
Kaplan-Meier estimates of event in months									
25% quantile (95% CI)	1.91 (1.018 to 2.825)	1.22 (1.051 to 1.971)	1.59 (0.920 to 1.971)	1.08 (0.986 to 1.906)	1.12 (1.018 to 4.797)	1.10 (0.920 to 2.070)	1.08 (0.953 to 1.938)	1.61 (1.018 to 1.971)	
Median (95% CI)	NC (2.858 to NC)	5.06 (2.070 to 17.150)	2.92 (1.281 to NC)	2.10 (1.117 to 7.458)	8.44 (1.117 to NC)	3.43 (1.117 to NC)	4.39 (1.084 to NC)	2.83 (1.938 to 9.593)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (3.745 to NC)	15.84 (2.891 to NC)	NC (9.626 to NC)	NC (17.544 to NC)	NC (6.637 to NC)	NC (6.604 to NC)	
Comparison vs. Kd									

A lower score represents a better level of quality of life. Clinical meaningful improvement change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.1 Health-related quality-of-life endpoints - QLQ-MY20
16.2.6.1.2 Disease symptoms
16.2.6.1.2.5 Efficacy response data - Subgroup analyses by geographical region
16.2.6.1.2.5.3 QLQ-MY20 - Time to first improvement by 10 pt in disease symptoms according to geographical region (LOCF) - ITT population

	Europe		America		Asia		Other countries		
	Kd (N=60)	**IKd (N=85)**	**Kd (N=20)**	**IKd (N=24)**	**Kd (N=21)**	**IKd (N=25)**	**Kd (N=22)**	**IKd (N=45)**	**p-value of treatment-by-subgroup interaction[c]**
Log-Rank test p-value[a] vs Kd	-	0.1182		0.4959		0.8320		0.9197	
Hazard ratio (95% CI) vs Kd	-	1.46 (0.91 to 2.34)		1.28 (0.62 to 2.65)		1.09 (0.49 to 2.40)		1.03 (0.55 to 1.95)	
P-value	-	0.1204		0.4970		0.8327		0.9202	
Improvement probability (95% CI)[b]									
3 Months	0.380 (0.256 to 0.502)	0.434 (0.326 to 0.537)	0.500 (0.271 to 0.692)	0.627 (0.394 to 0.792)	0.400 (0.193 to 0.600)	0.458 (0.256 to 0.640)	0.500 (0.282 to 0.684)	0.556 (0.400 to 0.686)	
6 Months	0.418 (0.289 to 0.541)	0.523 (0.410 to 0.625)	0.650 (0.403 to 0.815)	0.674 (0.438 to 0.828)	0.455 (0.233 to 0.653)	0.542 (0.327 to 0.714)	0.500 (0.282 to 0.684)	0.601 (0.443 to 0.727)	

A lower score represents a better level of quality of life. Clinical meaningful improvement change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.1 Health-related quality-of-life endpoints - QLQ-MY20
16.2.6.1.2 Disease symptoms
16.2.6.1.2.5 Efficacy response data - Subgroup analyses by geographical region
16.2.6.1.2.5.4 QLQ-MY20 - Time to first deterioration by 10 pt in disease symptoms according to geographical region (LOCF) - ITT population

	Europe		America		Asia		Other countries		
	Kd (N=60)	**IKd (N=85)**	**Kd (N=20)**	**IKd (N=24)**	**Kd (N=21)**	**IKd (N=25)**	**Kd (N=22)**	**IKd (N=45)**	**p-value of treatment-by-subgroup interaction[c]**
Number (%) of events	25 (41.7)	44 (51.8)	11 (55.0)	7 (29.2)	10 (47.6)	17 (68.0)	12 (54.5)	29 (64.4)	0.1957
Number (%) of patients censored	35 (58.3)	41 (48.2)	9 (45.0)	17 (70.8)	11 (52.4)	8 (32.0)	10 (45.5)	16 (35.6)	
Kaplan-Meier estimates of event in months									
25% quantile (95% CI)	2.92 (1.248 to 5.585)	3.06 (1.873 to 5.717)	2.45 (0.953 to 9.363)	5.36 (0.986 to NC)	2.96 (1.051 to 17.906)	1.53 (0.953 to 2.858)	4.99 (1.084 to 15.967)	1.91 (1.051 to 4.172)	
Median (95% CI)	NC (5.585 to NC)	12.65 (5.815 to NC)	13.06 (1.971 to NC)	NC (5.355 to NC)	21.55 (2.957 to NC)	5.80 (1.906 to 17.906)	17.77 (4.994 to NC)	7.39 (2.891 to 19.647)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (16.000 to NC)	NC (NC to NC)	NC (21.552 to NC)	17.97 (7.984 to NC)	NC (20.074 to NC)	NC (16.033 to NC)	

A lower score represents a better level of quality of life. Clinical meaningful deterioration change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.1 Health-related quality-of-life endpoints - QLQ-MY20
16.2.6.1.2 Disease symptoms
16.2.6.1.2.5 Efficacy response data - Subgroup analyses by geographical region
16.2.6.1.2.5.4 QLQ-MY20 - Time to first deterioration by 10 pt in disease symptoms according to geographical region (LOCF) - ITT population

	Europe		America		Asia		Other countries		
	Kd (N=60)	**IKd (N=85)**	**Kd (N=20)**	**IKd (N=24)**	**Kd (N=21)**	**IKd (N=25)**	**Kd (N=22)**	**IKd (N=45)**	**p-value of treatment-by-subgroup interaction[c]**
Comparison vs. Kd									
Log-Rank test p-value[a] vs Kd	-	0.4124		0.1406		0.1291		0.2512	
Hazard ratio (95% CI) vs Kd	-	1.23 (0.75 to 2.01)		0.50 (0.19 to 1.28)		1.82 (0.83 to 3.99)		1.48 (0.75 to 2.90)	
P-value	-	0.4132		0.1487		0.1347		0.2543	
Deterioration probability (95% CI)[b]									
3 Months	0.741 (0.608 to 0.835)	0.759 (0.651 to 0.837)	0.700 (0.451 to 0.853)	0.913 (0.695 to 0.978)	0.650 (0.403 to 0.815)	0.583 (0.364 to 0.750)	0.909 (0.683 to 0.976)	0.644 (0.487 to 0.765)	

A lower score represents a better level of quality of life. Clinical meaningful deterioration change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.1 Health-related quality-of-life endpoints - QLQ-MY20
16.2.6.1.2 Disease symptoms
16.2.6.1.2.5 Efficacy response data - Subgroup analyses by geographical region
16.2.6.1.2.5.5 QLQ-MY20 - Time until permanent improvement by 10 pt in disease symptoms according to geographical region (LOCF) - ITT population

	Europe		America		Asia		Other countries		
	Kd (N=60)	**IKd (N=85)**	**Kd (N=20)**	**IKd (N=24)**	**Kd (N=21)**	**IKd (N=25)**	**Kd (N=22)**	**IKd (N=45)**	**p-value of treatment-by-subgroup interaction[c]**
Number (%) of events	15 (25.0)	27 (31.8)	5 (25.0)	11 (45.8)	5 (23.8)	5 (20.0)	8 (36.4)	15 (33.3)	0.4202
Number (%) of patients censored	45 (75.0)	58 (68.2)	15 (75.0)	13 (54.2)	16 (76.2)	20 (80.0)	14 (63.6)	30 (66.7)	
Kaplan-Meier estimates of event in months									
25% quantile (95% CI)	16.99 (9.955 to NC)	19.61 (7.885 to 21.454)	17.61 (0.920 to NC)	2.10 (0.986 to 12.320)	10.28 (1.018 to NC)	NC (1.018 to NC)	10.68 (1.051 to NC)	14.95 (6.571 to NC)	
Median (95% CI)	NC (NC to NC)	23.23 (21.454 to NC)	NC (17.610 to NC)	15.84 (2.103 to NC)	NC (10.283 to NC)	NC (NC to NC)	NC (10.678 to NC)	NC (18.793 to NC)	

A lower score represents a better level of quality of life. Clinical meaningful improvement change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.1 Health-related quality-of-life endpoints - QLQ-MY20
16.2.6.1.2 Disease symptoms
16.2.6.1.2.5 Efficacy response data - Subgroup analyses by geographical region
16.2.6.1.2.5.5 QLQ-MY20 - Time until permanent improvement by 10 pt in disease symptoms according to geographical region (LOCF) - ITT population

	Europe		**America**		**Asia**		**Other countries**		
	Kd (N=60)	**IKd (N=85)**	**Kd (N=20)**	**IKd (N=24)**	**Kd (N=21)**	**IKd (N=25)**	**Kd (N=22)**	**IKd (N=45)**	**p-value of treatment-by-subgroup interaction[c]**
75% quantile (95% CI)	NC (NC to NC)	NC (23.228 to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (22.209 to NC)	NC (NC to NC)	
Comparison vs. Kd									
Log-Rank test p-value[a] vs Kd	-	0.4856		0.1172		0.6777		0.6639	
Hazard ratio (95% CI) vs Kd	-	1.25 (0.67 to 2.36)		2.28 (0.79 to 6.58)		0.77 (0.22 to 2.66)		0.83 (0.35 to 1.95)	
P-value	-	0.4865		0.1276		0.6786		0.6643	
Improvement probability (95% CI)[b]									

A lower score represents a better level of quality of life. Clinical meaningful improvement change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.1 Health-related quality-of-life endpoints - QLQ-MY20
16.2.6.1.2 Disease symptoms
16.2.6.1.2.5 Efficacy response data - Subgroup analyses by geographical region
16.2.6.1.2.5.6 QLQ-MY20 - Time until permanent deterioration by 10 pt in disease symptoms according to geographical region (LOCF) - ITT population

	Europe		America		Asia		Other countries		
	Kd (N=60)	**IKd (N=85)**	**Kd (N=20)**	**IKd (N=24)**	**Kd (N=21)**	**IKd (N=25)**	**Kd (N=22)**	**IKd (N=45)**	**p-value of treatment-by-subgroup interaction[c]**
Number (%) of events	12 (20.0)	16 (18.8)	6 (30.0)	2 (8.3)	7 (33.3)	7 (28.0)	4 (18.2)	14 (31.1)	0.2767
Number (%) of patients censored	48 (80.0)	69 (81.2)	14 (70.0)	22 (91.7)	14 (66.7)	18 (72.0)	18 (81.8)	31 (68.9)	
Kaplan-Meier estimates of event in months									
25% quantile (95% CI)	23.06 (14.653 to NC)	NC (16.986 to NC)	17.18 (1.971 to NC)	NC (11.860 to NC)	17.68 (1.314 to NC)	11.33 (4.961 to NC)	NC (3.055 to NC)	17.54 (5.257 to NC)	
Median (95% CI)	NC (23.064 to NC)	NC (NC to NC)	NC (13.602 to NC)	NC (NC to NC)	NC (17.676 to NC)	NC (11.335 to NC)	NC (19.614 to NC)	NC (20.797 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	

A lower score represents a better level of quality of life. Clinical meaningful deterioration change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.1 Health-related quality-of-life endpoints - QLQ-MY20
16.2.6.1.2 Disease symptoms
16.2.6.1.2.5 Efficacy response data - Subgroup analyses by geographical region
16.2.6.1.2.5.6 QLQ-MY20 - Time until permanent deterioration by 10 pt in disease symptoms according to geographical region (LOCF) - ITT population

	Europe		America		Asia		Other countries		
	Kd (N=60)	**IKd (N=85)**	**Kd (N=20)**	**IKd (N=24)**	**Kd (N=21)**	**IKd (N=25)**	**Kd (N=22)**	**IKd (N=45)**	**p-value of treatment-by-subgroup interaction[c]**
Comparison vs. Kd									
Log-Rank test p-value[a] vs Kd	-	0.7441		0.1055		0.7191		0.2429	
Hazard ratio (95% CI) vs Kd	-	0.88 (0.42 to 1.87)		0.29 (0.06 to 1.43)		0.83 (0.29 to 2.35)		1.92 (0.63 to 5.83)	
P-value	-	0.7442		0.1286		0.7195		0.2512	
Deterioration probability (95% CI)[b]									
3 Months	0.966 (0.869 to 0.991)	0.964 (0.892 to 0.988)	0.900 (0.656 to 0.974)	1.000 (1.000 to 1.000)	0.950 (0.695 to 0.993)	1.000 (1.000 to 1.000)	1.000 (1.000 to 1.000)	0.933 (0.807 to 0.978)	

A lower score represents a better level of quality of life. Clinical meaningful deterioration change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.1 Health-related quality-of-life endpoints - QLQ-MY20
16.2.6.1.2 Disease symptoms
16.2.6.1.2.6 Efficacy response data - Subgroup analyses by regulatory region
16.2.6.1.2.6.3 QLQ-MY20 - Time to first improvement by 10 pt in disease symptoms according to regulatory region (LOCF) - ITT population

	Western countries		Other countries		
	Kd (N=55)	**IKd (N=97)**	**Kd (N=68)**	**IKd (N=82)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	26 (47.3)	52 (53.6)	38 (55.9)	59 (72.0)	0.2387
Number (%) of patients censored	29 (52.7)	45 (46.4)	30 (44.1)	23 (28.0)	
Kaplan-Meier estimates of disease symptoms in months					
25% quantile (95% CI)	1.12 (1.018 to 2.825)	1.91 (1.117 to 2.070)	1.12 (1.051 to 1.906)	1.05 (0.986 to 1.511)	
Median (95% CI)	18.69 (2.136 to NC)	9.59 (3.023 to NC)	4.80 (1.938 to NC)	2.07 (1.906 to 2.924)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	17.54 (3.121 to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.7175		0.0298	
Hazard ratio (95% CI) vs Kd	-	1.09 (0.68 to 1.75)		1.57 (1.04 to 2.36)	
P-value	-	0.7176		0.0312	
Hazard ratio inverted (95% CI) vs IKd		-		0.64 (0.42 to 0.96)	

A lower score represents a better level of quality of life. Clinical meaningful improvement change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.1 Health-related quality-of-life endpoints - QLQ-MY20
16.2.6.1.2 Disease symptoms
16.2.6.1.2.6 Efficacy response data - Subgroup analyses by regulatory region
16.2.6.1.2.6.4 QLQ-MY20 - Time to first deterioration by 10 pt in disease symptoms according to regulatory region (LOCF) - ITT population

	Western countries		Other countries		
	Kd (N=55)	**IKd (N=97)**	**Kd (N=68)**	**IKd (N=82)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	21 (38.2)	53 (54.6)	37 (54.4)	44 (53.7)	0.3584
Number (%) of patients censored	34 (61.8)	44 (45.4)	31 (45.6)	38 (46.3)	
Kaplan-Meier estimates of disease symptoms in months					
25% quantile (95% CI)	3.71 (1.084 to 5.651)	2.79 (1.183 to 4.140)	2.96 (1.906 to 5.585)	2.83 (1.216 to 4.665)	
Median (95% CI)	NC (5.651 to NC)	9.36 (5.749 to NC)	17.48 (5.618 to NC)	12.94 (5.684 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.1493		0.7089	
Hazard ratio (95% CI) vs Kd	-	1.45 (0.87 to 2.40)		1.09 (0.70 to 1.68)	
P-value	-	0.1517		0.7096	
Deterioration probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful deterioration change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
PGM=DEVOPS/SAR650984/EFC15246/CIR_RWE/REPORT/PGM/eff_km_subgp_sr_sig_de_i_t.sas OUT=REPORT/OUTPUT/eff_km_my20_dis_detl_rreg_de_i_t_x.rtf (07APR2021 14:42)

16.2.6.1 Health-related quality-of-life endpoints - QLQ-MY20
16.2.6.1.2 Disease symptoms
16.2.6.1.2.6 Efficacy response data - Subgroup analyses by regulatory region
16.2.6.1.2.6.5 QLQ-MY20 - Time until permanent improvement by 10 pt in disease symptoms according to regulatory region (LOCF) - ITT population

	Western countries		Other countries		
	Kd (N=55)	**IKd (N=97)**	**Kd (N=68)**	**IKd (N=82)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	17 (30.9)	27 (27.8)	16 (23.5)	31 (37.8)	0.1135
Number (%) of patients censored	38 (69.1)	70 (72.2)	52 (76.5)	51 (62.2)	
Kaplan-Meier estimates of disease symptoms in months					
25% quantile (95% CI)	11.33 (1.117 to NC)	19.58 (11.006 to NC)	17.61 (10.283 to NC)	10.64 (2.267 to 18.760)	
Median (95% CI)	NC (22.209 to NC)	NC (NC to NC)	NC (NC to NC)	23.23 (19.614 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (23.228 to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.5619		0.0996	
Hazard ratio (95% CI) vs Kd	-	0.84 (0.45 to 1.53)		1.65 (0.90 to 3.02)	
P-value	-	0.5624		0.1032	
Improvement probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful improvement change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.1 Health-related quality-of-life endpoints - QLQ-MY20
16.2.6.1.2 Disease symptoms
16.2.6.1.2.6 Efficacy response data - Subgroup analyses by regulatory region
16.2.6.1.2.6.6 QLQ-MY20 - Time until permanent deterioration by 10 pt in disease symptoms according to regulatory region (LOCF) - ITT population

	Western countries		Other countries		
	Kd (N=55)	**IKd (N=97)**	**Kd (N=68)**	**IKd (N=82)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	8 (14.5)	23 (23.7)	21 (30.9)	16 (19.5)	0.0507
Number (%) of patients censored	47 (85.5)	74 (76.3)	47 (69.1)	66 (80.5)	
Kaplan-Meier estimates of disease symptoms in months					
25% quantile (95% CI)	NC (13.602 to NC)	19.65 (12.156 to NC)	17.91 (8.444 to 23.064)	NC (14.193 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (21.027 to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.2164		0.1104	
Hazard ratio (95% CI) vs Kd	-	1.65 (0.74 to 3.69)		0.59 (0.31 to 1.14)	
P-value	-	0.2215		0.1145	
Deterioration probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful deterioration change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.1 Health-related quality-of-life endpoints - QLQ-MY20
16.2.6.1.2 Disease symptoms
16.2.6.1.2.7 Efficacy response data - Subgroup analyses by baseline ECOG PS
16.2.6.1.2.7.3 QLQ-MY20 - Time to first improvement by 10 pt in disease symptoms according to baseline ECOG PS (LOCF) - ITT population

	0 or 1		>1		
	Kd (N=118)	**IKd (N=168)**	**Kd (N=5)**	**IKd (N=11)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	61 (51.7)	103 (61.3)	3 (60.0)	8 (72.7)	0.4742
Number (%) of patients censored	57 (48.3)	65 (38.7)	2 (40.0)	3 (27.3)	
Kaplan-Meier estimates of disease symptoms in months					
25% quantile (95% CI)	1.12 (1.051 to 1.906)	1.15 (1.051 to 1.906)	1.05 (0.986 to NC)	1.02 (0.986 to 1.610)	
Median (95% CI)	8.51 (2.825 to NC)	3.42 (2.136 to 8.805)	2.86 (0.986 to NC)	1.61 (0.986 to 3.877)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (0.986 to NC)	3.12 (1.216 to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.2084		0.3950	
Hazard ratio (95% CI) vs Kd	-	1.23 (0.89 to 1.68)		1.77 (0.47 to 6.72)	
P-value	-	0.2092		0.4012	
Improvement probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful improvement change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
PGM=DEVOPS/SAR650984/EFC15246/CIR_RWE/REPORT/PGM/eff_km_subgp_sr_sig_de_i_t.sas OUT=REPORT/OUTPUT/eff_km_my20_dis_impl_ecog_de_i_t_x.rtf (07APR2021 14:42)

16.2.6.1 Health-related quality-of-life endpoints - QLQ-MY20
16.2.6.1.2 Disease symptoms
16.2.6.1.2.7 Efficacy response data - Subgroup analyses by baseline ECOG PS
16.2.6.1.2.7.4 QLQ-MY20 - Time to first deterioration by 10 pt in disease symptoms according to baseline ECOG PS (LOCF) - ITT population

	0 or 1		>1		
	Kd (N=118)	**IKd (N=168)**	**Kd (N=5)**	**IKd (N=11)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	55 (46.6)	95 (56.5)	3 (60.0)	2 (18.2)	0.0779
Number (%) of patients censored	63 (53.4)	73 (43.5)	2 (40.0)	9 (81.8)	
Kaplan-Meier estimates of disease symptoms in months					
25% quantile (95% CI)	2.96 (1.971 to 4.895)	2.79 (1.314 to 3.811)	3.78 (1.938 to 6.637)	NC (2.990 to NC)	
Median (95% CI)	21.55 (9.363 to NC)	9.36 (6.571 to 17.906)	6.64 (1.938 to NC)	NC (2.990 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (1.938 to NC)	NC (NC to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.1115		0.1388	
Hazard ratio (95% CI) vs Kd	-	1.31 (0.94 to 1.82)		0.28 (0.05 to 1.69)	
P-value	-	0.1125		0.1651	
Deterioration probability (95% CI)[b]					

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The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.1 Health-related quality-of-life endpoints - QLQ-MY20
16.2.6.1.2 Disease symptoms
16.2.6.1.2.7 Efficacy response data - Subgroup analyses by baseline ECOG PS
16.2.6.1.2.7.5 QLQ-MY20 - Time until permanent improvement by 10 pt in disease symptoms according to baseline ECOG PS (LOCF) - ITT population

	0 or 1		>1		
	Kd (N=118)	**IKd (N=168)**	**Kd (N=5)**	**IKd (N=11)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	32 (27.1)	53 (31.5)	1 (20.0)	5 (45.5)	0.3594
Number (%) of patients censored	86 (72.9)	115 (68.5)	4 (80.0)	6 (54.5)	
Kaplan-Meier estimates of disease symptoms in months					
25% quantile (95% CI)	15.70 (10.283 to NC)	15.84 (10.645 to 19.680)	NC (4.698 to NC)	1.22 (0.986 to 21.454)	
Median (95% CI)	NC (NC to NC)	NC (23.228 to NC)	NC (4.698 to NC)	21.45 (0.986 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (4.698 to NC)	NC (1.610 to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.6225		0.2704	
Hazard ratio (95% CI) vs Kd	-	1.12 (0.72 to 1.73)		3.18 (0.36 to 27.84)	
P-value	-	0.6227		0.2955	
Improvement probability (95% CI)[b]					

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CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.1 Health-related quality-of-life endpoints - QLQ-MY20
16.2.6.1.2 Disease symptoms
16.2.6.1.2.7 Efficacy response data - Subgroup analyses by baseline ECOG PS
16.2.6.1.2.7.6 QLQ-MY20 - Time until permanent deterioration by 10 pt in disease symptoms according to baseline ECOG PS (LOCF) - ITT population

	0 or 1		>1		
	Kd (N=118)	**IKd (N=168)**	**Kd (N=5)**	**IKd (N=11)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	27 (22.9)	37 (22.0)	2 (40.0)	2 (18.2)	0.3984
Number (%) of patients censored	91 (77.1)	131 (78.0)	3 (60.0)	9 (81.8)	
Kaplan-Meier estimates of disease symptoms in months					
25% quantile (95% CI)	21.03 (16.887 to NC)	20.80 (16.986 to NC)	10.12 (5.585 to NC)	NC (4.961 to NC)	
Median (95% CI)	NC (23.064 to NC)	NC (NC to NC)	14.65 (5.585 to NC)	NC (4.961 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (5.585 to NC)	NC (NC to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.8338		0.3528	
Hazard ratio (95% CI) vs Kd	-	0.95 (0.58 to 1.56)		0.40 (0.06 to 2.92)	
P-value	-	0.8331		0.3686	
Deterioration probability (95% CI)[b]					

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CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.1 Health-related quality-of-life endpoints - QLQ-MY20
16.2.6.1.2 Disease symptoms
16.2.6.1.2.8 Efficacy response data - Subgroup analyses by ISS staging at SE
16.2.6.1.2.8.3 QLQ-MY20 - Time to first improvement by 10 pt in disease symptoms according to ISS staging at SE (LOCF) - ITT population

	I		II		III		
	Kd (N=71)	**IKd (N=89)**	**Kd (N=31)**	**IKd (N=63)**	**Kd (N=20)**	**IKd (N=26)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	38 (53.5)	52 (58.4)	15 (48.4)	44 (69.8)	10 (50.0)	14 (53.8)	0.5256
Number (%) of patients censored	33 (46.5)	37 (41.6)	16 (51.6)	19 (30.2)	10 (50.0)	12 (46.2)	
Kaplan-Meier estimates of disease symptoms in months							
25% quantile (95% CI)	1.12 (1.051 to 1.938)	1.87 (1.018 to 2.004)	1.28 (0.986 to 5.651)	1.08 (1.051 to 1.906)	1.05 (0.953 to 2.858)	1.08 (0.953 to 2.891)	
Median (95% CI)	8.44 (2.103 to NC)	3.78 (2.136 to NC)	18.69 (2.136 to NC)	2.79 (1.938 to 5.717)	3.84 (1.051 to NC)	6.11 (1.084 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (6.604 to NC)	NC (3.844 to NC)	NC (6.111 to NC)	
Comparison vs. Kd							
Log-Rank test p-value[a] vs Kd	-	0.6190		0.0844		0.8407	
Hazard ratio (95% CI) vs Kd	-	1.11 (0.73 to 1.69)		1.67 (0.93 to 3.00)		1.09 (0.48 to 2.45)	
P-value	-	0.6191		0.0880		0.8408	

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The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.6.1 Health-related quality-of-life endpoints - QLQ-MY20
16.2.6.1.2 Disease symptoms
16.2.6.1.2.8 Efficacy response data - Subgroup analyses by ISS staging at SE
16.2.6.1.2.8.4 QLQ-MY20 - Time to first deterioration by 10 pt in disease symptoms according to ISS staging at SE (LOCF) - ITT population

	I		II		III		
	Kd (N=71)	**IKd (N=89)**	**Kd (N=31)**	**IKd (N=63)**	**Kd (N=20)**	**IKd (N=26)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	28 (39.4)	49 (55.1)	19 (61.3)	38 (60.3)	11 (55.0)	10 (38.5)	0.0798
Number (%) of patients censored	43 (60.6)	40 (44.9)	12 (38.7)	25 (39.7)	9 (45.0)	16 (61.5)	
Kaplan-Meier estimates of disease symptoms in months							
25% quantile (95% CI)	5.59 (2.957 to 17.478)	2.83 (1.906 to 4.665)	1.97 (0.986 to 3.778)	1.12 (1.018 to 4.140)	1.97 (1.018 to 2.957)	3.81 (0.953 to 16.033)	
Median (95% CI)	NC (17.774 to NC)	12.65 (5.749 to NC)	8.31 (2.924 to NC)	7.03 (4.172 to 19.647)	3.04 (1.971 to NC)	NC (3.811 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (9.363 to NC)	NC (NC to NC)	NC (3.055 to NC)	NC (NC to NC)	
Comparison vs. Kd							
Log-Rank test p-value[a] vs Kd	-	0.0401		0.9266		0.1769	
Hazard ratio (95% CI) vs Kd	-	1.62 (1.02 to 2.58)		0.97 (0.56 to 1.69)		0.56 (0.23 to 1.32)	

A lower score represents a better level of quality of life. Clinical meaningful deterioration change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.6.1 Health-related quality-of-life endpoints - QLQ-MY20
16.2.6.1.2 Disease symptoms
16.2.6.1.2.8 Efficacy response data - Subgroup analyses by ISS staging at SE
16.2.6.1.2.8.5 QLQ-MY20 - Time until permanent improvement by 10 pt in disease symptoms according to ISS staging at SE (LOCF) - ITT population

	I		II		III		
	Kd (N=71)	**IKd (N=89)**	**Kd (N=31)**	**IKd (N=63)**	**Kd (N=20)**	**IKd (N=26)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	20 (28.2)	27 (30.3)	8 (25.8)	20 (31.7)	4 (20.0)	10 (38.5)	0.4945
Number (%) of patients censored	51 (71.8)	62 (69.7)	23 (74.2)	43 (68.3)	16 (80.0)	16 (61.5)	
Kaplan-Meier estimates of disease symptoms in months							
25% quantile (95% CI)	16.99 (1.906 to NC)	18.89 (11.006 to 21.684)	15.38 (1.117 to NC)	14.55 (5.914 to NC)	NC (0.953 to NC)	3.75 (0.986 to 18.793)	
Median (95% CI)	NC (22.209 to NC)	23.23 (21.684 to NC)	NC (NC to NC)	NC (NC to NC)	NC (10.283 to NC)	19.68 (3.745 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (23.228 to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (19.680 to NC)	
Comparison vs. Kd							
Log-Rank test p-value[a] vs Kd	-	0.8686		0.7324		0.1826	
Hazard ratio (95% CI) vs Kd	-	1.05 (0.59 to 1.87)		1.15 (0.51 to 2.62)		2.16 (0.68 to 6.90)	
P-value	-	0.8690		0.7326		0.1934	

A lower score represents a better level of quality of life. Clinical meaningful improvement change from baseline less than or equal to -10 pt.
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CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
PGM=DEVOPS/SAR650984/EFC15246/CIR_RWE/REPORT/PGM/eff_km_subgp_sr_sig_de_i_t.sas OUT=REPORT/OUTPUT/eff_km_my20_dis_imppl_seiss_de_i_t_x.rtf (07APR2021 14:43)

16.2.6.1 Health-related quality-of-life endpoints - QLQ-MY20
16.2.6.1.2 Disease symptoms
16.2.6.1.2.8 Efficacy response data - Subgroup analyses by ISS staging at SE
16.2.6.1.2.8.6 QLQ-MY20 - Time until permanent deterioration by 10 pt in disease symptoms according to ISS staging at SE (LOCF) - ITT population

	I		II		III		
	Kd (N=71)	**IKd (N=89)**	**Kd (N=31)**	**IKd (N=63)**	**Kd (N=20)**	**IKd (N=26)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	12 (16.9)	20 (22.5)	10 (32.3)	17 (27.0)	7 (35.0)	2 (7.7)	0.0735
Number (%) of patients censored	59 (83.1)	69 (77.5)	21 (67.7)	46 (73.0)	13 (65.0)	24 (92.3)	
Kaplan-Meier estimates of disease symptoms in months							
25% quantile (95% CI)	23.06 (19.220 to NC)	20.80 (13.864 to NC)	16.89 (1.971 to NC)	19.65 (11.860 to NC)	8.44 (1.971 to NC)	NC (0.986 to NC)	
Median (95% CI)	NC (23.064 to NC)	NC (NC to NC)	NC (17.380 to NC)	NC (NC to NC)	NC (5.717 to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Kd							
Log-Rank test p-value[a] vs Kd	-	0.3605		0.5058		0.0293	
Hazard ratio (95% CI) vs Kd	-	1.39 (0.68 to 2.85)		0.77 (0.35 to 1.68)		0.21 (0.04 to 0.99)	
P-value	-	0.3627		0.5070		0.0489	

A lower score represents a better level of quality of life. Clinical meaningful deterioration change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
PGM=DEVOPS/SAR650984/EFC15246/CIR_RWE/REPORT/PGM/eff_km_subgp_sr_sig_de_i_t.sas OUT=REPORT/OUTPUT/eff_km_my20_dis_detpl_seiss_de_i_t_x.rtf (07APR2021 14:42)

16.2.6.1 Health-related quality-of-life endpoints - QLQ-MY20
16.2.6.1.2 Disease symptoms
16.2.6.1.2.9 Efficacy response data - Subgroup analyses by R-ISS stage at SE
16.2.6.1.2.9.3 QLQ-MY20 - Time to first improvement by 10 pt in disease symptoms according to R-ISS stage at SE (LOCF) - ITT population

	I or II		III		Not classified		
	Kd (N=103)	**IKd (N=155)**	**Kd (N=8)**	**IKd (N=16)**	**Kd (N=12)**	**IKd (N=8)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	52 (50.5)	97 (62.6)	4 (50.0)	9 (56.3)	8 (66.7)	5 (62.5)	0.8521
Number (%) of patients censored	51 (49.5)	58 (37.4)	4 (50.0)	7 (43.8)	4 (33.3)	3 (37.5)	
Kaplan-Meier estimates of disease symptoms in months							
25% quantile (95% CI)	1.12 (1.051 to 1.938)	1.51 (1.051 to 1.938)	1.05 (0.986 to 1.117)	1.02 (0.953 to 1.216)	1.53 (0.953 to 4.632)	1.08 (1.018 to 1.906)	
Median (95% CI)	9.63 (2.825 to NC)	3.42 (2.267 to 8.805)	1.12 (0.986 to NC)	1.66 (0.986 to NC)	6.54 (0.986 to NC)	1.53 (1.018 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (1.084 to NC)	NC (1.216 to NC)	NC (4.632 to NC)	3.75 (1.084 to NC)	
Comparison vs. Kd							
Log-Rank test p-value[a] vs Kd	-	0.1776		0.7671		0.2818	
Hazard ratio (95% CI) vs Kd	-	1.26 (0.90 to 1.77)		1.19 (0.37 to 3.89)		1.86 (0.59 to 5.83)	
P-value	-	0.1785		0.7674		0.2887	

A lower score represents a better level of quality of life. Clinical meaningful improvement change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.1 Health-related quality-of-life endpoints - QLQ-MY20
16.2.6.1.2 Disease symptoms
16.2.6.1.2.9 Efficacy response data - Subgroup analyses by R-ISS stage at SE
16.2.6.1.2.9.4 QLQ-MY20 - Time to first deterioration by 10 pt in disease symptoms according to R-ISS stage at SE (LOCF) - ITT population

	I or II		III		Not classified		
	Kd (N=103)	**IKd (N=155)**	**Kd (N=8)**	**IKd (N=16)**	**Kd (N=12)**	**IKd (N=8)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	49 (47.6)	93 (60.0)	4 (50.0)	3 (18.8)	5 (41.7)	1 (12.5)	0.0531
Number (%) of patients censored	54 (52.4)	62 (40.0)	4 (50.0)	13 (81.3)	7 (58.3)	7 (87.5)	
Kaplan-Meier estimates of disease symptoms in months							
25% quantile (95% CI)	2.96 (1.938 to 4.994)	2.10 (1.183 to 3.745)	1.12 (1.051 to 3.055)	9.36 (3.745 to NC)	5.24 (1.906 to NC)	NC (2.825 to NC)	
Median (95% CI)	20.07 (9.265 to NC)	7.43 (5.717 to 16.033)	3.06 (1.051 to NC)	NC (6.637 to NC)	21.55 (3.713 to NC)	NC (2.825 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (2.760 to NC)	NC (NC to NC)	NC (21.552 to NC)	NC (NC to NC)	
Comparison vs. Kd							
Log-Rank test p-value[a] vs Kd	-	0.0810		0.0367		0.4109	
Hazard ratio (95% CI) vs Kd	-	1.36 (0.96 to 1.92)		0.23 (0.05 to 1.03)		0.42 (0.05 to 3.58)	
P-value	-	0.0822		0.0547		0.4255	

A lower score represents a better level of quality of life. Clinical meaningful deterioration change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.1 Health-related quality-of-life endpoints - QLQ-MY20
16.2.6.1.2 Disease symptoms
16.2.6.1.2.9 Efficacy response data - Subgroup analyses by R-ISS stage at SE
16.2.6.1.2.9.5 QLQ-MY20 - Time until permanent improvement by 10 pt in disease symptoms according to R-ISS stage at SE (LOCF) - ITT population

	I or II		III		Not classified		
	Kd (N=103)	**IKd (N=155)**	**Kd (N=8)**	**IKd (N=16)**	**Kd (N=12)**	**IKd (N=8)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	27 (26.2)	48 (31.0)	2 (25.0)	6 (37.5)	4 (33.3)	4 (50.0)	0.3145
Number (%) of patients censored	76 (73.8)	107 (69.0)	6 (75.0)	10 (62.5)	8 (66.7)	4 (50.0)	
Kaplan-Meier estimates of disease symptoms in months							
25% quantile (95% CI)	16.99 (6.045 to NC)	18.43 (11.006 to 20.468)	10.28 (1.117 to NC)	2.10 (0.986 to 19.680)	14.01 (0.953 to NC)	1.15 (1.084 to 21.454)	
Median (95% CI)	NC (NC to NC)	NC (23.228 to NC)	NC (1.117 to NC)	19.68 (1.216 to NC)	NC (10.678 to NC)	12.60 (1.084 to 21.454)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (10.283 to NC)	NC (19.680 to NC)	NC (NC to NC)	21.45 (1.150 to 21.454)	
Comparison vs. Kd							
Log-Rank test p-value[a] vs Kd	-	0.7279		0.4760		0.1253	

A lower score represents a better level of quality of life. Clinical meaningful improvement change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.1 Health-related quality-of-life endpoints - QLQ-MY20
16.2.6.1.2 Disease symptoms
16.2.6.1.2.9 Efficacy response data - Subgroup analyses by R-ISS stage at SE
16.2.6.1.2.9.6 QLQ-MY20 - Time until permanent deterioration by 10 pt in disease symptoms according to R-ISS stage at SE (LOCF) - ITT population

	I or II		III		Not classified		
	Kd (N=103)	**IKd (N=155)**	**Kd (N=8)**	**IKd (N=16)**	**Kd (N=12)**	**IKd (N=8)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	25 (24.3)	38 (24.5)	3 (37.5)	1 (6.3)	1 (8.3)	0 (0.0)	0.2953
Number (%) of patients censored	78 (75.7)	117 (75.5)	5 (62.5)	15 (93.8)	11 (91.7)	8 (100.0)	
Kaplan-Meier estimates of disease symptoms in months							
25% quantile (95% CI)	19.61 (13.602 to NC)	19.88 (14.193 to NC)	4.80 (3.811 to NC)	NC (6.637 to NC)	23.06 (NC to NC)	NC (NC to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (3.811 to NC)	NC (NC to NC)	23.06 (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (15.014 to NC)	NC (NC to NC)	23.06 (NC to NC)	NC (NC to NC)	
Comparison vs. Kd							
Log-Rank test p-value[a] vs Kd	-	0.8460		0.0580			
Hazard ratio (95% CI) vs Kd	-	0.95 (0.57 to 1.58)		0.15 (0.02 to 1.44)			
P-value	-	0.8451		0.1005			

A lower score represents a better level of quality of life. Clinical meaningful deterioration change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.1 Health-related quality-of-life endpoints - QLQ-MY20
16.2.6.1.2 Disease symptoms
16.2.6.1.2.10 Efficacy response data - Subgroup analyses by nb of prior lines
16.2.6.1.2.10.3 QLQ-MY20 - Time to first improvement by 10 pt in disease symptoms according to nb of prior lines (LOCF) - ITT population

	1		>1		
	Kd (N=55)	**IKd (N=79)**	**Kd (N=68)**	**IKd (N=100)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	25 (45.5)	48 (60.8)	39 (57.4)	63 (63.0)	0.3576
Number (%) of patients censored	30 (54.5)	31 (39.2)	29 (42.6)	37 (37.0)	
Kaplan-Meier estimates of disease symptoms in months					
25% quantile (95% CI)	1.91 (1.051 to 5.651)	1.87 (1.051 to 2.070)	1.08 (0.986 to 1.906)	1.08 (1.051 to 1.906)	
Median (95% CI)	NC (5.651 to NC)	4.86 (2.891 to 17.150)	3.75 (1.906 to NC)	2.50 (1.971 to 5.520)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (12.057 to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.0881		0.6235	
Hazard ratio (95% CI) vs Kd	-	1.52 (0.94 to 2.47)		1.11 (0.74 to 1.65)	
P-value	-	0.0904		0.6236	
Improvement probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful improvement change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.1 Health-related quality-of-life endpoints - QLQ-MY20
16.2.6.1.2 Disease symptoms
16.2.6.1.2.10 Efficacy response data - Subgroup analyses by nb of prior lines
16.2.6.1.2.10.4 QLQ-MY20 - Time to first deterioration by 10 pt in disease symptoms according to nb of prior lines (LOCF) - ITT population

	1		>1		
	Kd (N=55)	**IKd (N=79)**	**Kd (N=68)**	**IKd (N=100)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	28 (50.9)	44 (55.7)	30 (44.1)	53 (53.0)	0.7180
Number (%) of patients censored	27 (49.1)	35 (44.3)	38 (55.9)	47 (47.0)	
Kaplan-Meier estimates of disease symptoms in months					
25% quantile (95% CI)	2.92 (1.117 to 4.830)	2.14 (1.084 to 4.632)	3.78 (1.971 to 9.265)	2.83 (1.314 to 5.355)	
Median (95% CI)	17.77 (4.830 to NC)	7.98 (4.665 to NC)	NC (9.363 to NC)	13.63 (5.848 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.5818		0.2511	
Hazard ratio (95% CI) vs Kd	-	1.14 (0.71 to 1.84)		1.30 (0.83 to 2.03)	
P-value	-	0.5821		0.2524	
Deterioration probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful deterioration change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.1 Health-related quality-of-life endpoints - QLQ-MY20
16.2.6.1.2 Disease symptoms
16.2.6.1.2.10 Efficacy response data - Subgroup analyses by nb of prior lines
16.2.6.1.2.10.5 QLQ-MY20 - Time until permanent improvement by 10 pt in disease symptoms according to nb of prior lines (LOCF) - ITT population

	1		>1		
	Kd (N=55)	**IKd (N=79)**	**Kd (N=68)**	**IKd (N=100)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	12 (21.8)	27 (34.2)	21 (30.9)	31 (31.0)	0.2509
Number (%) of patients censored	43 (78.2)	52 (65.8)	47 (69.1)	69 (69.0)	
Kaplan-Meier estimates of disease symptoms in months					
25% quantile (95% CI)	22.21 (1.117 to NC)	18.76 (9.561 to 20.468)	12.94 (6.045 to 19.384)	12.68 (2.924 to 20.304)	
Median (95% CI)	NC (22.209 to NC)	23.23 (20.468 to NC)	NC (19.384 to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (23.228 to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.1441		0.8584	
Hazard ratio (95% CI) vs Kd	-	1.65 (0.84 to 3.27)		0.95 (0.55 to 1.65)	
P-value	-	0.1484		0.8576	
Improvement probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful improvement change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
PGM=DEVOPS/SAR650984/EFC15246/CIR_RWE/REPORT/PGM/eff_km_subgp_sr_sig_de_i_t.sas OUT=REPORT/OUTPUT/eff_km_my20_dis_imppl_plne_de_i_t_x.rtf (07APR2021 14:43)

16.2.6.1 Health-related quality-of-life endpoints - QLQ-MY20
16.2.6.1.2 Disease symptoms
16.2.6.1.2.10 Efficacy response data - Subgroup analyses by nb of prior lines
16.2.6.1.2.10.6 QLQ-MY20 - Time until permanent deterioration by 10 pt in disease symptoms according to nb of prior lines (LOCF) - ITT population

	1		>1		
	Kd (N=55)	**IKd (N=79)**	**Kd (N=68)**	**IKd (N=100)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	16 (29.1)	15 (19.0)	13 (19.1)	24 (24.0)	0.1949
Number (%) of patients censored	39 (70.9)	64 (81.0)	55 (80.9)	76 (76.0)	
Kaplan-Meier estimates of disease symptoms in months					
25% quantile (95% CI)	19.61 (5.717 to NC)	NC (13.864 to NC)	NC (14.653 to NC)	18.43 (13.273 to NC)	
Median (95% CI)	NC (23.064 to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (23.064 to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.2173		0.5512	
Hazard ratio (95% CI) vs Kd	-	0.64 (0.32 to 1.30)		1.23 (0.62 to 2.41)	
P-value	-	0.2210		0.5519	
Deterioration probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful deterioration change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.1 Health-related quality-of-life endpoints - QLQ-MY20
16.2.6.1.2 Disease symptoms
16.2.6.1.2.11 Efficacy response data - Subgroup analyses by cytogenetic abnormality
16.2.6.1.2.11.3 QLQ-MY20 - Time to first improvement by 10 pt in disease symptoms according to cytogenetic abnormality (LOCF) - ITT population

	At least one		None		
	Kd (N=31)	**IKd (N=42)**	**Kd (N=77)**	**IKd (N=114)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	15 (48.4)	28 (66.7)	41 (53.2)	64 (56.1)	0.3521
Number (%) of patients censored	16 (51.6)	14 (33.3)	36 (46.8)	50 (43.9)	
Kaplan-Meier estimates of disease symptoms in months					
25% quantile (95% CI)	1.12 (1.018 to 1.906)	1.05 (0.953 to 2.004)	1.12 (1.051 to 1.938)	1.48 (1.051 to 1.906)	
Median (95% CI)	9.63 (1.150 to NC)	2.92 (1.938 to 6.505)	8.51 (2.136 to NC)	7.46 (2.267 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (6.111 to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.2132		0.7958	
Hazard ratio (95% CI) vs Kd	-	1.49 (0.79 to 2.79)		1.05 (0.71 to 1.56)	
P-value	-	0.2162		0.7969	
Improvement probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful improvement change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
PGM=DEVOPS/SAR650984/EFC15246/CIR_RWE/REPORT/PGM/eff_km_subgp_sr_sig_de_i_t.sas OUT=REPORT/OUTPUT/eff_km_my20_dis_impl_cyto_de_i_t_x.rtf (07APR2021 14:42)

16.2.6.1 Health-related quality-of-life endpoints - QLQ-MY20
16.2.6.1.2 Disease symptoms
16.2.6.1.2.11 Efficacy response data - Subgroup analyses by cytogenetic abnormality
16.2.6.1.2.11.4 QLQ-MY20 - Time to first deterioration by 10 pt in disease symptoms according to cytogenetic abnormality (LOCF) - ITT population

	At least one		None		
	Kd (N=31)	**IKd (N=42)**	**Kd (N=77)**	**IKd (N=114)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	16 (51.6)	25 (59.5)	37 (48.1)	62 (54.4)	0.9326
Number (%) of patients censored	15 (48.4)	17 (40.5)	40 (51.9)	52 (45.6)	
Kaplan-Meier estimates of disease symptoms in months					
25% quantile (95% CI)	3.06 (1.051 to 4.994)	2.76 (1.084 to 4.961)	2.92 (1.314 to 3.778)	1.97 (1.117 to 4.632)	
Median (95% CI)	16.00 (4.665 to NC)	6.64 (4.665 to NC)	17.91 (8.444 to NC)	12.65 (6.571 to NC)	
75% quantile (95% CI)	NC (20.074 to NC)	NC (17.906 to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.6592		0.3771	
Hazard ratio (95% CI) vs Kd	-	1.15 (0.61 to 2.16)		1.20 (0.80 to 1.81)	
P-value	-	0.6595		0.3777	
Deterioration probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful deterioration change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.1 Health-related quality-of-life endpoints - QLQ-MY20
16.2.6.1.2 Disease symptoms
16.2.6.1.2.11 Efficacy response data - Subgroup analyses by cytogenetic abnormality
16.2.6.1.2.11.5 QLQ-MY20 - Time until permanent improvement by 10 pt in disease symptoms according to cytogenetic abnormality (LOCF) - ITT population

	At least one		None		
	Kd (N=31)	**IKd (N=42)**	**Kd (N=77)**	**IKd (N=114)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	7 (22.6)	11 (26.2)	21 (27.3)	38 (33.3)	0.9797
Number (%) of patients censored	24 (77.4)	31 (73.8)	56 (72.7)	76 (66.7)	
Kaplan-Meier estimates of disease symptoms in months					
25% quantile (95% CI)	17.61 (10.283 to NC)	18.76 (2.793 to NC)	15.38 (1.938 to NC)	17.74 (7.885 to 20.304)	
Median (95% CI)	NC (17.610 to NC)	NC (19.680 to NC)	NC (22.209 to NC)	NC (21.684 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.7935		0.6137	
Hazard ratio (95% CI) vs Kd	-	1.13 (0.44 to 2.93)		1.15 (0.67 to 1.96)	
P-value	-	0.7936		0.6140	
Improvement probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful improvement change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.1 Health-related quality-of-life endpoints - QLQ-MY20
16.2.6.1.2 Disease symptoms
16.2.6.1.2.11 Efficacy response data - Subgroup analyses by cytogenetic abnormality
16.2.6.1.2.11.6 QLQ-MY20 - Time until permanent deterioration by 10 pt in disease symptoms according to cytogenetic abnormality (LOCF) - ITT population

	At least one		None		
	Kd (N=31)	**IKd (N=42)**	**Kd (N=77)**	**IKd (N=114)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	5 (16.1)	10 (23.8)	22 (28.6)	25 (21.9)	0.2828
Number (%) of patients censored	26 (83.9)	32 (76.2)	55 (71.4)	89 (78.1)	
Kaplan-Meier estimates of disease symptoms in months					
25% quantile (95% CI)	NC (11.466 to NC)	18.76 (5.815 to NC)	17.91 (8.444 to NC)	20.80 (16.000 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.5139		0.2799	
Hazard ratio (95% CI) vs Kd	-	1.43 (0.49 to 4.18)		0.73 (0.41 to 1.29)	
P-value	-	0.5161		0.2819	
Deterioration probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful deterioration change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.1 Health-related quality-of-life endpoints - QLQ-MY20
16.2.6.1.2 Disease symptoms
16.2.6.1.2.12 Efficacy response data - Subgroup analyses by MM type at SE
16.2.6.1.2.12.3 QLQ-MY20 - Time to first improvement by 10 pt in disease symptoms according to MM type at SE (LOCF) - ITT population

	IgG		Non-IgG		
	Kd (N=85)	**IKd (N=126)**	**Kd (N=38)**	**IKd (N=53)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	46 (54.1)	78 (61.9)	18 (47.4)	33 (62.3)	0.9951
Number (%) of patients censored	39 (45.9)	48 (38.1)	20 (52.6)	20 (37.7)	
Kaplan-Meier estimates of disease symptoms in months					
25% quantile (95% CI)	1.15 (1.051 to 1.938)	1.12 (1.051 to 1.873)	1.10 (0.986 to 1.971)	1.91 (0.986 to 2.004)	
Median (95% CI)	8.44 (2.825 to NC)	3.02 (2.070 to 6.505)	8.51 (1.906 to NC)	3.42 (1.971 to 17.544)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (15.901 to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.2127		0.4279	
Hazard ratio (95% CI) vs Kd	-	1.26 (0.88 to 1.81)		1.26 (0.71 to 2.24)	
P-value	-	0.2137		0.4289	
Improvement probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful improvement change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.1 Health-related quality-of-life endpoints - QLQ-MY20
16.2.6.1.2 Disease symptoms
16.2.6.1.2.12 Efficacy response data - Subgroup analyses by MM type at SE
16.2.6.1.2.12.4 QLQ-MY20 - Time to first deterioration by 10 pt in disease symptoms according to MM type at SE (LOCF) - ITT population

	IgG		Non-IgG		
	Kd (N=85)	**IKd (N=126)**	**Kd (N=38)**	**IKd (N=53)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	44 (51.8)	66 (52.4)	14 (36.8)	31 (58.5)	0.1681
Number (%) of patients censored	41 (48.2)	60 (47.6)	24 (63.2)	22 (41.5)	
Kaplan-Meier estimates of disease symptoms in months					
25% quantile (95% CI)	2.96 (1.873 to 4.665)	2.89 (1.873 to 4.961)	3.78 (1.216 to 17.478)	2.76 (0.986 to 4.172)	
Median (95% CI)	17.91 (5.651 to NC)	13.63 (6.669 to NC)	NC (8.312 to NC)	7.43 (3.811 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.7570		0.0822	
Hazard ratio (95% CI) vs Kd	-	1.06 (0.72 to 1.56)		1.74 (0.92 to 3.27)	
P-value	-	0.7583		0.0862	
Deterioration probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful deterioration change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.1 Health-related quality-of-life endpoints - QLQ-MY20
16.2.6.1.2 Disease symptoms
16.2.6.1.2.12 Efficacy response data - Subgroup analyses by MM type at SE
16.2.6.1.2.12.5 QLQ-MY20 - Time until permanent improvement by 10 pt in disease symptoms according to MM type at SE (LOCF) - ITT population

	IgG		Non-IgG		
	Kd (N=85)	**IKd (N=126)**	**Kd (N=38)**	**IKd (N=53)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	23 (27.1)	41 (32.5)	10 (26.3)	17 (32.1)	0.8680
Number (%) of patients censored	62 (72.9)	85 (67.5)	28 (73.7)	36 (67.9)	
Kaplan-Meier estimates of disease symptoms in months					
25% quantile (95% CI)	16.99 (10.678 to NC)	15.47 (8.674 to 20.468)	10.28 (1.051 to NC)	13.70 (2.793 to 20.304)	
Median (95% CI)	NC (NC to NC)	NC (21.684 to NC)	NC (NC to NC)	NC (19.680 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.4650		0.7826	
Hazard ratio (95% CI) vs Kd	-	1.21 (0.73 to 2.02)		1.12 (0.51 to 2.44)	
P-value	-	0.4657		0.7827	

A lower score represents a better level of quality of life. Clinical meaningful improvement change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.1 Health-related quality-of-life endpoints - QLQ-MY20
16.2.6.1.2 Disease symptoms
16.2.6.1.2.12 Efficacy response data - Subgroup analyses by MM type at SE
16.2.6.1.2.12.6 QLQ-MY20 - Time until permanent deterioration by 10 pt in disease symptoms according to MM type at SE (LOCF) - ITT population

	IgG		Non-IgG		
	Kd (N=85)	**IKd (N=126)**	**Kd (N=38)**	**IKd (N=53)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	22 (25.9)	26 (20.6)	7 (18.4)	13 (24.5)	0.3681
Number (%) of patients censored	63 (74.1)	100 (79.4)	31 (81.6)	40 (75.5)	
Kaplan-Meier estimates of disease symptoms in months					
25% quantile (95% CI)	19.61 (13.602 to NC)	NC (16.986 to NC)	21.03 (5.585 to NC)	18.76 (5.618 to NC)	
Median (95% CI)	NC (23.064 to NC)	NC (NC to NC)	NC (21.027 to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.4127		0.6016	
Hazard ratio (95% CI) vs Kd	-	0.79 (0.45 to 1.39)		1.28 (0.51 to 3.20)	
P-value	-	0.4137		0.6025	

A lower score represents a better level of quality of life. Clinical meaningful deterioration change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.1 Health-related quality-of-life endpoints - QLQ-MY20
16.2.6.1.2 Disease symptoms
16.2.6.1.2.13 Efficacy response data - Subgroup analyses by previous autologous stem-cell
16.2.6.1.2.13.3 QLQ-MY20 - Time to first improvement by 10 pt in disease symptoms according to previous autologous stem-cell (LOCF) - ITT population

	Yes		No		
	Kd (N=69)	**IKd (N=116)**	**Kd (N=54)**	**IKd (N=63)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	31 (44.9)	66 (56.9)	33 (61.1)	45 (71.4)	0.8256
Number (%) of patients censored	38 (55.1)	50 (43.1)	21 (38.9)	18 (28.6)	
Kaplan-Meier estimates of disease symptoms in months					
25% quantile (95% CI)	1.12 (1.018 to 3.745)	1.87 (1.117 to 2.004)	1.12 (1.051 to 1.938)	1.05 (0.986 to 1.478)	
Median (95% CI)	NC (4.632 to NC)	5.72 (2.891 to NC)	2.83 (1.938 to 10.908)	2.07 (1.478 to 3.417)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (6.637 to NC)	8.80 (3.417 to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.2315		0.1620	
Hazard ratio (95% CI) vs Kd	-	1.30 (0.85 to 1.99)		1.38 (0.88 to 2.16)	
P-value	-	0.2328		0.1638	
Improvement probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful improvement change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.1 Health-related quality-of-life endpoints - QLQ-MY20
16.2.6.1.2 Disease symptoms
16.2.6.1.2.13 Efficacy response data - Subgroup analyses by previous autologous stem-cell
16.2.6.1.2.13.4 QLQ-MY20 - Time to first deterioration by 10 pt in disease symptoms according to previous autologous stem-cell (LOCF) - ITT population

	Yes		No		
	Kd (N=69)	**IKd (N=116)**	**Kd (N=54)**	**IKd (N=63)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	34 (49.3)	72 (62.1)	24 (44.4)	25 (39.7)	0.1268
Number (%) of patients censored	35 (50.7)	44 (37.9)	30 (55.6)	38 (60.3)	
Kaplan-Meier estimates of disease symptoms in months					
25% quantile (95% CI)	3.02 (1.971 to 5.618)	1.91 (1.084 to 3.745)	2.96 (1.216 to 5.585)	4.17 (2.760 to 11.105)	
Median (95% CI)	20.07 (5.651 to NC)	6.64 (5.355 to 13.634)	NC (5.585 to NC)	NC (11.105 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.0756		0.5572	
Hazard ratio (95% CI) vs Kd	-	1.45 (0.96 to 2.17)		0.85 (0.48 to 1.48)	
P-value	-	0.0773		0.5577	
Deterioration probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful deterioration change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.1 Health-related quality-of-life endpoints - QLQ-MY20
16.2.6.1.2 Disease symptoms
16.2.6.1.2.13 Efficacy response data - Subgroup analyses by previous autologous stem-cell
16.2.6.1.2.13.5 QLQ-MY20 - Time until permanent improvement by 10 pt in disease symptoms according to previous autologous stem-cell (LOCF) - ITT population

	Yes		No		
	Kd (N=69)	**IKd (N=116)**	**Kd (N=54)**	**IKd (N=63)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	15 (21.7)	38 (32.8)	18 (33.3)	20 (31.7)	0.2430
Number (%) of patients censored	54 (78.3)	78 (67.2)	36 (66.7)	43 (68.3)	
Kaplan-Meier estimates of disease symptoms in months					
25% quantile (95% CI)	NC (10.678 to NC)	18.43 (7.885 to 20.304)	10.68 (1.117 to 22.209)	11.20 (5.914 to 19.680)	
Median (95% CI)	NC (NC to NC)	23.23 (21.454 to NC)	NC (16.986 to NC)	NC (19.680 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (23.228 to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.1591		0.8258	
Hazard ratio (95% CI) vs Kd	-	1.53 (0.84 to 2.79)		0.93 (0.49 to 1.76)	
P-value	-	0.1623		0.8254	
Improvement probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful improvement change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.1 Health-related quality-of-life endpoints - QLQ-MY20
16.2.6.1.2 Disease symptoms
16.2.6.1.2.13 Efficacy response data - Subgroup analyses by previous autologous stem-cell
16.2.6.1.2.13.6 QLQ-MY20 - Time until permanent deterioration by 10 pt in disease symptoms according to previous autologous stem-cell (LOCF) - ITT population

	Yes		No		
	Kd (N=69)	**IKd (N=116)**	**Kd (N=54)**	**IKd (N=63)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	16 (23.2)	25 (21.6)	13 (24.1)	14 (22.2)	0.9285
Number (%) of patients censored	53 (76.8)	91 (78.4)	41 (75.9)	49 (77.8)	
Kaplan-Meier estimates of disease symptoms in months					
25% quantile (95% CI)	20.76 (11.466 to NC)	NC (13.273 to NC)	21.03 (14.653 to NC)	20.80 (13.864 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (23.064 to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.7372		0.8901	
Hazard ratio (95% CI) vs Kd	-	0.90 (0.48 to 1.68)		0.95 (0.45 to 2.02)	
P-value	-	0.7373		0.8900	
Deterioration probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful deterioration change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
PGM=DEVOPS/SAR650984/EFC15246/CIR_RWE/REPORT/PGM/eff_km_subgp_sr_sig_de_i_t.sas OUT=REPORT/OUTPUT/eff_km_my20_dis_detpl_auto_de_i_t_x.rtf (07APR2021 14:42)

16.2.6.1 Health-related quality-of-life endpoints - QLQ-MY20
16.2.6.1.2 Disease symptoms
16.2.6.1.2.14 Efficacy response data - Subgroup analyses by baseline eGFR (MDRD)
16.2.6.1.2.14.3 QLQ-MY20 - Time to first improvement by 10 pt in disease symptoms according to baseline eGFR (MDRD) (LOCF) - ITT population

	>=60 mL/min/1.73m2		<60 mL/min/1.73m2		
	Kd (N=93)	**IKd (N=122)**	**Kd (N=18)**	**IKd (N=43)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	51 (54.8)	72 (59.0)	10 (55.6)	33 (76.7)	0.8347
Number (%) of patients censored	42 (45.2)	50 (41.0)	8 (44.4)	10 (23.3)	
Kaplan-Meier estimates of disease symptoms in months					
25% quantile (95% CI)	1.12 (1.051 to 1.906)	1.15 (1.051 to 1.906)	1.05 (0.920 to 1.150)	1.05 (0.986 to 1.971)	
Median (95% CI)	6.14 (2.136 to NC)	3.02 (2.037 to 11.302)	1.94 (0.986 to NC)	2.89 (1.610 to 6.505)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (1.938 to NC)	12.06 (3.877 to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.3740		0.7826	
Hazard ratio (95% CI) vs Kd	-	1.18 (0.82 to 1.68)		1.10 (0.54 to 2.24)	
P-value	-	0.3745		0.7827	
Improvement probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful improvement change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.1 Health-related quality-of-life endpoints - QLQ-MY20
16.2.6.1.2 Disease symptoms
16.2.6.1.2.14 Efficacy response data - Subgroup analyses by baseline eGFR (MDRD)
16.2.6.1.2.14.4 QLQ-MY20 - Time to first deterioration by 10 pt in disease symptoms according to baseline eGFR (MDRD) (LOCF) - ITT population

	>=60 mL/min/1.73m2		<60 mL/min/1.73m2		
	Kd (N=93)	**IKd (N=122)**	**Kd (N=18)**	**IKd (N=43)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	44 (47.3)	75 (61.5)	10 (55.6)	20 (46.5)	0.0417
Number (%) of patients censored	49 (52.7)	47 (38.5)	8 (44.4)	23 (53.5)	
Kaplan-Meier estimates of disease symptoms in months					
25% quantile (95% CI)	3.01 (1.906 to 5.585)	2.10 (1.150 to 3.745)	2.89 (1.018 to 4.830)	3.22 (1.018 to 7.031)	
Median (95% CI)	NC (9.265 to NC)	6.67 (4.665 to 12.945)	12.45 (2.825 to NC)	NC (6.637 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (19.647 to NC)	NC (4.830 to NC)	NC (NC to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.0154		0.3192	
Hazard ratio (95% CI) vs Kd	-	1.58 (1.09 to 2.29)		0.68 (0.32 to 1.46)	
P-value	-	0.0163		0.3219	
Hazard ratio inverted (95% CI) vs IKd		-		1.47 (0.69 to 3.15)	

A lower score represents a better level of quality of life. Clinical meaningful deterioration change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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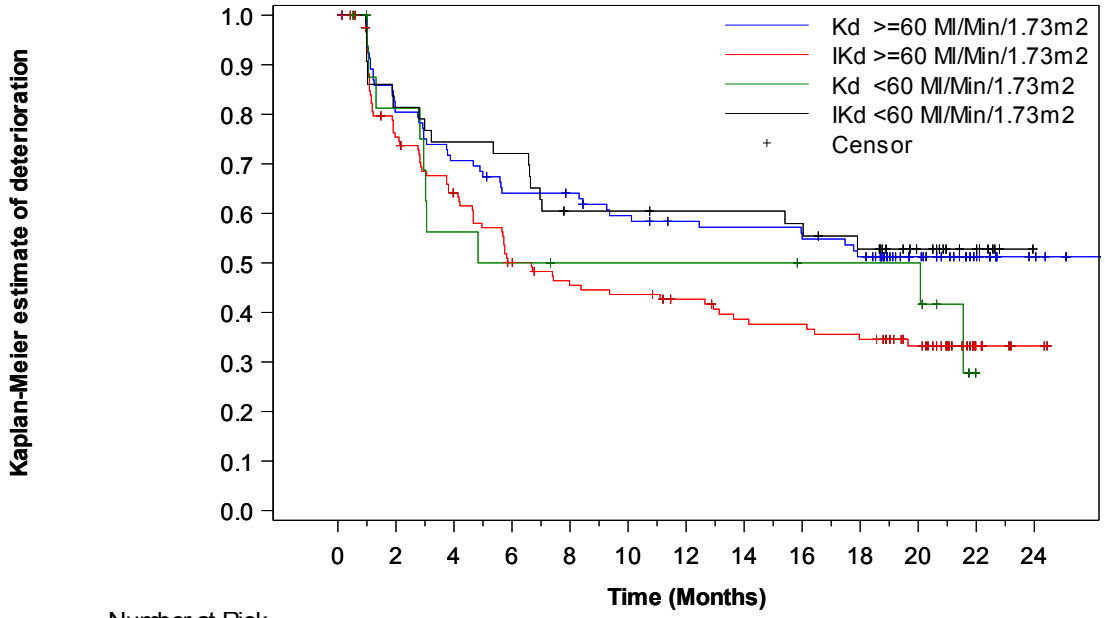
16.2.6.1 Health-related quality-of-life endpoints - QLQ-MY20
16.2.6.1.2 Disease symptoms
16.2.6.1.2.14 Efficacy response data - Subgroup analyses by baseline eGFR (MDRD)
16.2.6.1.2.14.5 QLQ-MY20 - Time to first deterioration by 10 pt in disease symptoms according to baseline eGFR (MDRD) - Kaplan-Meier curve (LOCF) - ITT population



Number at Risk

Kd >=60 Ml/Min/1.73m2	93	69	58	54	49	48	43	21	5
lKd >=60 Ml/Min/1.73m2	122	79	56	48	43	37	34	17	2
Kd <60 Ml/Min/1.73m2	18	11	8	7	7	7	6	3	0
lKd <60 Ml/Min/1.73m2	43	33	31	25	24	24	20	8	0

A lower score represents a better level of quality of life. Clinical meaningful deterioration change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
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16.2.6.1 Health-related quality-of-life endpoints - QLQ-MY20
16.2.6.1.2 Disease symptoms
16.2.6.1.2.14 Efficacy response data - Subgroup analyses by baseline eGFR (MDRD)
16.2.6.1.2.14.6 QLQ-MY20 - Time until permanent improvement by 10 pt in disease symptoms according to baseline eGFR (MDRD) (LOCF) - ITT population

	>=60 mL/min/1.73m2		<60 mL/min/1.73m2		
	Kd (N=93)	**IKd (N=122)**	**Kd (N=18)**	**IKd (N=43)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	28 (30.1)	40 (32.8)	4 (22.2)	15 (34.9)	0.7818
Number (%) of patients censored	65 (69.9)	82 (67.2)	14 (77.8)	28 (65.1)	
Kaplan-Meier estimates of disease symptoms in months					
25% quantile (95% CI)	15.38 (6.045 to NC)	14.95 (9.561 to 19.614)	12.94 (0.920 to NC)	6.60 (1.084 to 23.228)	
Median (95% CI)	NC (22.209 to NC)	NC (21.454 to NC)	NC (12.945 to NC)	23.23 (20.304 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (23.228 to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.7211		0.6277	
Hazard ratio (95% CI) vs Kd	-	1.09 (0.67 to 1.77)		1.31 (0.44 to 3.96)	
P-value	-	0.7212		0.6289	
Improvement probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful improvement change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.1 Health-related quality-of-life endpoints - QLQ-MY20
16.2.6.1.2 Disease symptoms
16.2.6.1.2.14 Efficacy response data - Subgroup analyses by baseline eGFR (MDRD)
16.2.6.1.2.14.7 QLQ-MY20 - Time until permanent deterioration by 10 pt in disease symptoms according to baseline eGFR (MDRD) (LOCF) - ITT population

	>=60 mL/min/1.73m2		<60 mL/min/1.73m2		
	Kd (N=93)	**IKd (N=122)**	**Kd (N=18)**	**IKd (N=43)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	22 (23.7)	31 (25.4)	4 (22.2)	6 (14.0)	0.2018
Number (%) of patients censored	71 (76.3)	91 (74.6)	14 (77.8)	37 (86.0)	
Kaplan-Meier estimates of disease symptoms in months					
25% quantile (95% CI)	21.03 (17.380 to NC)	18.76 (12.649 to NC)	15.01 (1.314 to NC)	NC (14.456 to NC)	
Median (95% CI)	NC (23.064 to NC)	NC (NC to NC)	NC (15.014 to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.5836		0.2761	
Hazard ratio (95% CI) vs Kd	-	1.16 (0.67 to 2.01)		0.50 (0.14 to 1.78)	
P-value	-	0.5840		0.2856	
Deterioration probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful deterioration change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.1 Health-related quality-of-life endpoints - QLQ-MY20
16.2.6.1.2 Disease symptoms
16.2.6.1.2.15 Efficacy response data - Subgroup analyses by previous treatment with PI
16.2.6.1.2.15.3 QLQ-MY20 - Time to first improvement by 10 pt in disease symptoms according to previous treatment with PI (LOCF) - ITT population

	Yes		No		
	Kd (N=47)	**IKd (N=81)**	**Kd (N=76)**	**IKd (N=98)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	25 (53.2)	53 (65.4)	39 (51.3)	58 (59.2)	0.4185
Number (%) of patients censored	22 (46.8)	28 (34.6)	37 (48.7)	40 (40.8)	
Kaplan-Meier estimates of disease symptoms in months					
25% quantile (95% CI)	1.91 (1.051 to 2.136)	1.12 (1.018 to 1.906)	1.08 (1.051 to 1.906)	1.15 (1.051 to 1.938)	
Median (95% CI)	9.63 (2.103 to NC)	2.92 (2.037 to 4.862)	8.44 (1.938 to NC)	5.06 (2.004 to 17.150)	
75% quantile (95% CI)	NC (NC to NC)	NC (5.717 to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.1054		0.5735	
Hazard ratio (95% CI) vs Kd	-	1.48 (0.92 to 2.38)		1.12 (0.75 to 1.69)	
P-value	-	0.1076		0.5737	
Improvement probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful improvement change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.1 Health-related quality-of-life endpoints - QLQ-MY20
16.2.6.1.2 Disease symptoms
16.2.6.1.2.15 Efficacy response data - Subgroup analyses by previous treatment with PI
16.2.6.1.2.15.4 QLQ-MY20 - Time to first deterioration by 10 pt in disease symptoms according to previous treatment with PI (LOCF) - ITT population

	Yes		No		
	Kd (N=47)	**IKd (N=81)**	**Kd (N=76)**	**IKd (N=98)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	22 (46.8)	40 (49.4)	36 (47.4)	57 (58.2)	0.6281
Number (%) of patients censored	25 (53.2)	41 (50.6)	40 (52.6)	41 (41.8)	
Kaplan-Meier estimates of disease symptoms in months					
25% quantile (95% CI)	3.71 (1.314 to 5.618)	3.81 (1.906 to 5.749)	2.96 (1.117 to 5.651)	1.91 (1.084 to 3.745)	
Median (95% CI)	NC (4.994 to NC)	12.94 (6.637 to NC)	20.07 (9.265 to NC)	8.38 (5.355 to 16.427)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.6967		0.1848	
Hazard ratio (95% CI) vs Kd	-	1.11 (0.66 to 1.87)		1.33 (0.87 to 2.01)	
P-value	-	0.6969		0.1862	
Deterioration probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful deterioration change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.1 Health-related quality-of-life endpoints - QLQ-MY20
16.2.6.1.2 Disease symptoms
16.2.6.1.2.15 Efficacy response data - Subgroup analyses by previous treatment with PI
16.2.6.1.2.15.5 QLQ-MY20 - Time until permanent improvement by 10 pt in disease symptoms according to previous treatment with PI (LOCF) - ITT population

	Yes		No		
	Kd (N=47)	**IKd (N=81)**	**Kd (N=76)**	**IKd (N=98)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	12 (25.5)	26 (32.1)	21 (27.6)	32 (32.7)	0.6982
Number (%) of patients censored	35 (74.5)	55 (67.9)	55 (72.4)	66 (67.3)	
Kaplan-Meier estimates of disease symptoms in months					
25% quantile (95% CI)	16.99 (1.117 to NC)	12.32 (5.717 to 19.680)	15.38 (1.938 to NC)	18.79 (8.674 to 20.468)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (22.209 to NC)	NC (21.454 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.4637		0.7251	
Hazard ratio (95% CI) vs Kd	-	1.29 (0.65 to 2.56)		1.10 (0.64 to 1.91)	
P-value	-	0.4650		0.7252	
Improvement probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful improvement change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.1 Health-related quality-of-life endpoints - QLQ-MY20
16.2.6.1.2 Disease symptoms
16.2.6.1.2.15 Efficacy response data - Subgroup analyses by previous treatment with PI
16.2.6.1.2.15.6 QLQ-MY20 - Time until permanent deterioration by 10 pt in disease symptoms according to previous treatment with PI (LOCF) - ITT population

	Yes		No		
	Kd (N=47)	**IKd (N=81)**	**Kd (N=76)**	**IKd (N=98)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	9 (19.1)	17 (21.0)	20 (26.3)	22 (22.4)	0.4482
Number (%) of patients censored	38 (80.9)	64 (79.0)	56 (73.7)	76 (77.6)	
Kaplan-Meier estimates of disease symptoms in months					
25% quantile (95% CI)	23.06 (14.653 to NC)	NC (13.864 to NC)	19.22 (9.232 to NC)	20.80 (13.273 to NC)	
Median (95% CI)	NC (23.064 to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.6534		0.4690	
Hazard ratio (95% CI) vs Kd	-	1.20 (0.53 to 2.71)		0.80 (0.44 to 1.47)	
P-value	-	0.6539		0.4699	
Deterioration probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful deterioration change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.1 Health-related quality-of-life endpoints - QLQ-MY20
16.2.6.1.2 Disease symptoms
16.2.6.1.2.16 Efficacy response data - Subgroup analyses by previous treatment with IMiD
16.2.6.1.2.16.3 QLQ-MY20 - Time to first improvement by 10 pt in disease symptoms according to previous treatment with IMiD (LOCF) - ITT population

	Yes		No		
	Kd (N=62)	**IKd (N=81)**	**Kd (N=61)**	**IKd (N=98)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	33 (53.2)	43 (53.1)	31 (50.8)	68 (69.4)	0.0776
Number (%) of patients censored	29 (46.8)	38 (46.9)	30 (49.2)	30 (30.6)	
Kaplan-Meier estimates of disease symptoms in months					
25% quantile (95% CI)	1.08 (1.051 to 1.906)	1.51 (1.051 to 1.971)	1.91 (1.051 to 2.136)	1.08 (1.018 to 1.906)	
Median (95% CI)	8.44 (1.906 to NC)	11.47 (2.103 to NC)	8.51 (2.136 to NC)	2.89 (1.971 to 3.778)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (6.505 to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.7605		0.0204	
Hazard ratio (95% CI) vs Kd	-	0.93 (0.59 to 1.47)		1.65 (1.08 to 2.52)	
P-value	-	0.7593		0.0217	
Hazard ratio inverted (95% CI) vs IKd		-		0.61 (0.40 to 0.93)	

A lower score represents a better level of quality of life. Clinical meaningful improvement change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.1 Health-related quality-of-life endpoints - QLQ-MY20
16.2.6.1.2 Disease symptoms
16.2.6.1.2.16 Efficacy response data - Subgroup analyses by previous treatment with IMiD
16.2.6.1.2.16.4 QLQ-MY20 - Time to first deterioration by 10 pt in disease symptoms according to previous treatment with IMiD (LOCF) - ITT population

	Yes		No		
	Kd (N=62)	**IKd (N=81)**	**Kd (N=61)**	**IKd (N=98)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	25 (40.3)	46 (56.8)	33 (54.1)	51 (52.0)	0.0860
Number (%) of patients censored	37 (59.7)	35 (43.2)	28 (45.9)	47 (48.0)	
Kaplan-Meier estimates of disease symptoms in months					
25% quantile (95% CI)	3.71 (1.938 to 12.452)	1.97 (1.084 to 3.745)	2.94 (1.248 to 4.665)	3.75 (1.906 to 4.961)	
Median (95% CI)	NC (15.967 to NC)	11.10 (5.355 to NC)	10.12 (4.665 to NC)	13.14 (6.702 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.0446		0.7494	
Hazard ratio (95% CI) vs Kd	-	1.64 (1.01 to 2.67)		0.93 (0.60 to 1.44)	
P-value	-	0.0468		0.7495	
Hazard ratio inverted (95% CI) vs IKd		-		1.07 (0.69 to 1.66)	

A lower score represents a better level of quality of life. Clinical meaningful deterioration change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.1 Health-related quality-of-life endpoints - QLQ-MY20
16.2.6.1.2 Disease symptoms
16.2.6.1.2.16 Efficacy response data - Subgroup analyses by previous treatment with IMiD
16.2.6.1.2.16.5 QLQ-MY20 - Time until permanent improvement by 10 pt in disease symptoms according to previous treatment with IMiD (LOCF) - ITT population

	Yes		No		
	Kd (N=62)	**IKd (N=81)**	**Kd (N=61)**	**IKd (N=98)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	20 (32.3)	21 (25.9)	13 (21.3)	37 (37.8)	0.0260
Number (%) of patients censored	42 (67.7)	60 (74.1)	48 (78.7)	61 (62.2)	
Kaplan-Meier estimates of disease symptoms in months					
25% quantile (95% CI)	11.33 (1.117 to 22.209)	19.58 (8.674 to NC)	NC (10.678 to NC)	12.32 (5.914 to 18.891)	
Median (95% CI)	NC (22.209 to NC)	NC (NC to NC)	NC (NC to NC)	23.23 (20.304 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (23.228 to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.2843		0.0383	
Hazard ratio (95% CI) vs Kd	-	0.72 (0.39 to 1.32)		1.93 (1.02 to 3.63)	
P-value	-	0.2866		0.0418	
Hazard ratio inverted (95% CI) vs IKd		-		0.52 (0.28 to 0.98)	

A lower score represents a better level of quality of life. Clinical meaningful improvement change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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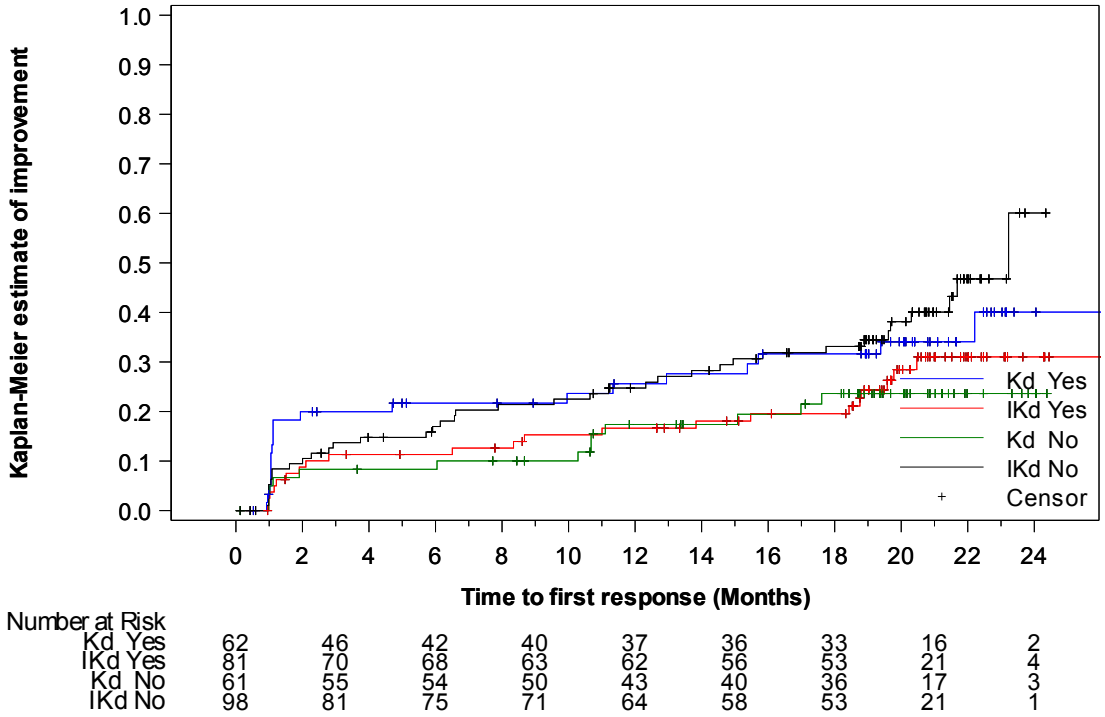
16.2.6.1 Health-related quality-of-life endpoints - QLQ-MY20
16.2.6.1.2 Disease symptoms
16.2.6.1.2.16 Efficacy response data - Subgroup analyses by previous treatment with IMiD
16.2.6.1.2.16.6 QLQ-MY20 - Time until permanent improvement by 10 pt in disease symptoms according to previous treatment with IMiD - Kaplan-Meier curve (LOCF) - ITT population



A lower score represents a better level of quality of life. Clinical meaningful improvement change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
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16.2.6.1 Health-related quality-of-life endpoints - QLQ-MY20
16.2.6.1.2 Disease symptoms
16.2.6.1.2.16 Efficacy response data - Subgroup analyses by previous treatment with IMiD
16.2.6.1.2.16.7 QLQ-MY20 - Time until permanent deterioration by 10 pt in disease symptoms according to previous treatment with IMiD (LOCF) - ITT population

	Yes		No		
	Kd (N=62)	**IKd (N=81)**	**Kd (N=61)**	**IKd (N=98)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	11 (17.7)	22 (27.2)	18 (29.5)	17 (17.3)	0.0281
Number (%) of patients censored	51 (82.3)	59 (72.8)	43 (70.5)	81 (82.7)	
Kaplan-Meier estimates of disease symptoms in months					
25% quantile (95% CI)	NC (17.676 to NC)	18.43 (12.156 to NC)	17.38 (5.717 to 23.064)	NC (17.478 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (20.764 to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.1695		0.0704	
Hazard ratio (95% CI) vs Kd	-	1.65 (0.80 to 3.41)		0.55 (0.28 to 1.06)	
P-value	-	0.1740		0.0747	
Deterioration probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful deterioration change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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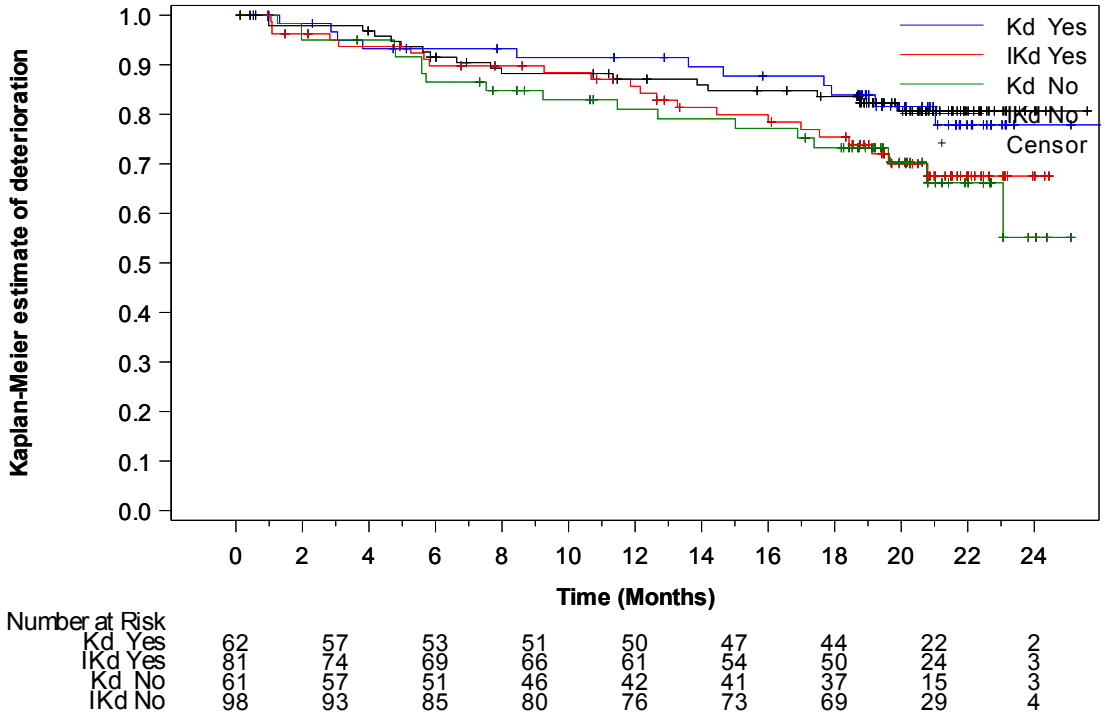
16.2.6.1 Health-related quality-of-life endpoints - QLQ-MY20
16.2.6.1.2 Disease symptoms
16.2.6.1.2.16 Efficacy response data - Subgroup analyses by previous treatment with IMiD
16.2.6.1.2.16.8 QLQ-MY20 - Time until permanent deterioration by 10 pt in disease symptoms according to previous treatment with IMiD - Kaplan-Meier curve (LOCF) - ITT population



A lower score represents a better level of quality of life. Clinical meaningful deterioration change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
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16.2.6.1 Health-related quality-of-life endpoints - QLQ-MY20
16.2.6.1.2 Disease symptoms
16.2.6.1.2.17 Efficacy response data - Subgroup analyses by previous treatment with PI and IMiD
16.2.6.1.2.17.3 QLQ-MY20 - Time to first improvement by 10 pt in disease symptoms according to previous treatment with PI and IMiD (LOCF) - ITT population

	Yes		No		
	Kd (N=17)	**IKd (N=23)**	**Kd (N=106)**	**IKd (N=156)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	8 (47.1)	12 (52.2)	56 (52.8)	99 (63.5)	0.7020
Number (%) of patients censored	9 (52.9)	11 (47.8)	50 (47.2)	57 (36.5)	
Kaplan-Meier estimates of disease symptoms in months					
25% quantile (95% CI)	1.08 (1.018 to 18.694)	1.51 (0.986 to 3.877)	1.12 (1.051 to 1.906)	1.12 (1.051 to 1.906)	
Median (95% CI)	18.69 (1.051 to NC)	5.52 (1.906 to NC)	6.64 (2.793 to NC)	2.96 (2.070 to 6.505)	
75% quantile (95% CI)	NC (18.694 to NC)	NC (5.520 to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.8919		0.1309	
Hazard ratio (95% CI) vs Kd	-	1.06 (0.43 to 2.61)		1.29 (0.93 to 1.79)	
P-value	-	0.8925		0.1319	

A lower score represents a better level of quality of life. Clinical meaningful improvement change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.1 Health-related quality-of-life endpoints - QLQ-MY20
16.2.6.1.2 Disease symptoms
16.2.6.1.2.17 Efficacy response data - Subgroup analyses by previous treatment with PI and IMiD
16.2.6.1.2.17.4 QLQ-MY20 - Time to first deterioration by 10 pt in disease symptoms according to previous treatment with PI and IMiD (LOCF) - ITT population

	Yes		No		
	Kd (N=17)	**IKd (N=23)**	**Kd (N=106)**	**IKd (N=156)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	7 (41.2)	10 (43.5)	51 (48.1)	87 (55.8)	0.8926
Number (%) of patients censored	10 (58.8)	13 (56.5)	55 (51.9)	69 (44.2)	
Kaplan-Meier estimates of disease symptoms in months					
25% quantile (95% CI)	3.27 (1.216 to NC)	2.99 (0.986 to 11.105)	2.96 (1.938 to 4.994)	2.83 (1.873 to 4.172)	
Median (95% CI)	NC (2.825 to NC)	NC (2.990 to NC)	20.07 (9.265 to NC)	12.65 (6.604 to 17.971)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.7994		0.2303	
Hazard ratio (95% CI) vs Kd	-	1.13 (0.43 to 2.98)		1.24 (0.87 to 1.75)	
P-value	-	0.7995		0.2312	
Deterioration probability (95% CI)[b]					

A lower score represents a better level of quality of life. Clinical meaningful deterioration change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.1 Health-related quality-of-life endpoints - QLQ-MY20
16.2.6.1.2 Disease symptoms
16.2.6.1.2.17 Efficacy response data - Subgroup analyses by previous treatment with PI and IMiD
16.2.6.1.2.17.5 QLQ-MY20 - Time until permanent improvement by 10 pt in disease symptoms according to previous treatment with PI and IMiD (LOCF) - ITT population

	Yes		No		
	Kd (N=17)	**IKd (N=23)**	**Kd (N=106)**	**IKd (N=156)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	5 (29.4)	5 (21.7)	28 (26.4)	53 (34.0)	0.2914
Number (%) of patients censored	12 (70.6)	18 (78.3)	78 (73.6)	103 (66.0)	
Kaplan-Meier estimates of disease symptoms in months					
25% quantile (95% CI)	5.54 (1.018 to NC)	NC (1.216 to NC)	16.99 (10.678 to NC)	13.83 (7.885 to 19.614)	
Median (95% CI)	NC (1.117 to NC)	NC (NC to NC)	NC (NC to NC)	NC (21.684 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.4331		0.2838	
Hazard ratio (95% CI) vs Kd	-	0.61 (0.18 to 2.12)		1.28 (0.81 to 2.03)	
P-value	-	0.4377		0.2851	

A lower score represents a better level of quality of life. Clinical meaningful improvement change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.1 Health-related quality-of-life endpoints - QLQ-MY20
16.2.6.1.2 Disease symptoms
16.2.6.1.2.17 Efficacy response data - Subgroup analyses by previous treatment with PI and IMiD
16.2.6.1.2.17.6 QLQ-MY20 - Time until permanent deterioration by 10 pt in disease symptoms according to previous treatment with PI and IMiD (LOCF) - ITT population

	Yes		No		
	Kd (N=17)	**IKd (N=23)**	**Kd (N=106)**	**IKd (N=156)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	3 (17.6)	5 (21.7)	26 (24.5)	34 (21.8)	0.5370
Number (%) of patients censored	14 (82.4)	18 (78.3)	80 (75.5)	122 (78.2)	
Kaplan-Meier estimates of disease symptoms in months					
25% quantile (95% CI)	21.03 (1.314 to NC)	18.43 (5.257 to NC)	19.61 (13.602 to NC)	20.80 (16.000 to NC)	
Median (95% CI)	NC (21.027 to NC)	NC (18.431 to NC)	NC (23.064 to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.6612		0.5502	
Hazard ratio (95% CI) vs Kd	-	1.38 (0.33 to 5.78)		0.86 (0.51 to 1.43)	
P-value	-	0.6625		0.5506	

A lower score represents a better level of quality of life. Clinical meaningful deterioration change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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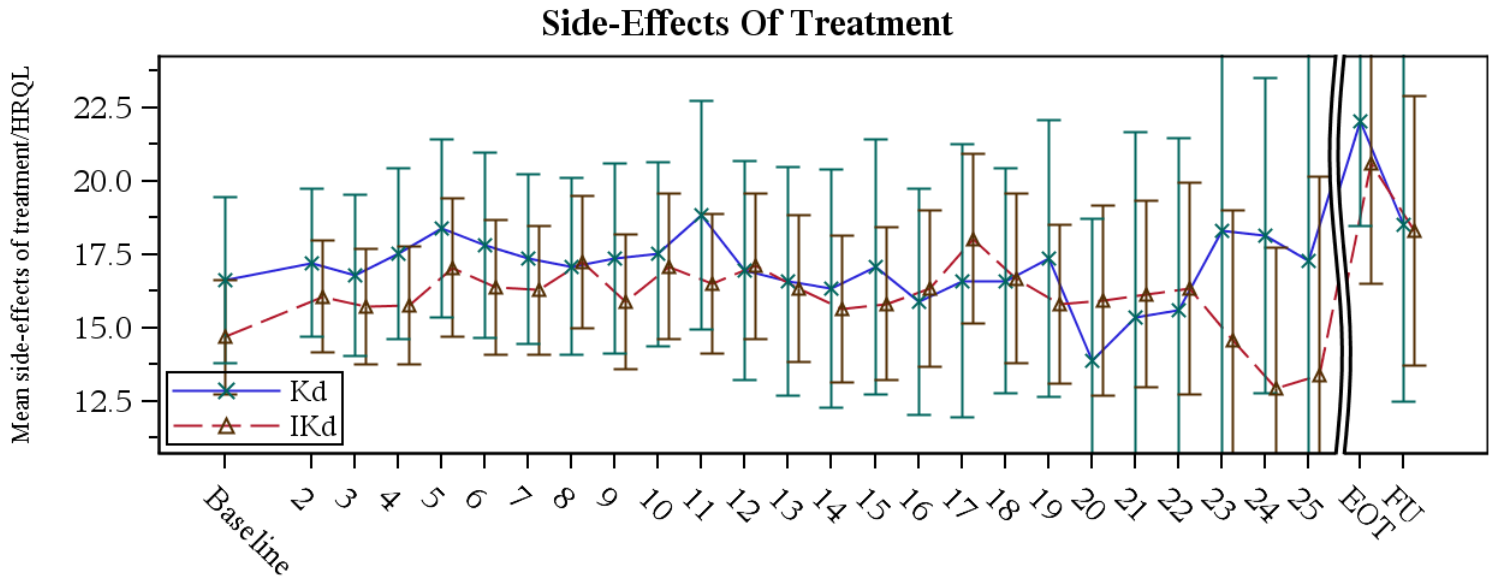
16.2.6.1 Health-related quality-of-life endpoints - QLQ-MY20
16.2.6.1.2 Side-effects of treatment
16.2.6.1.2.1 Efficacy response data
16.2.6.1.2.1.1 QLQ-MY20 - Mean and 95% CI for side-effects of treatment score over time - ITT population



#patients																										
Kd	114	114	112	110	104	100	95	91	88	84	78	72	67	66	62	57	52	50	45	37	30	23	17	10	6	62	35
IKd	167	170	168	164	161	155	150	146	139	133	130	127	121	118	112	109	105	102	97	91	78	56	38	23	17	60	34

A lower score represents a better level of quality of life. Cycles with less than 20 patients overall are not presented.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
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16.2.6.1 Health-related quality-of-life endpoints - QLQ-MY20
16.2.6.1.2 Side-effects of treatment
16.2.6.1.2.1 Efficacy response data
16.2.6.1.2.1.15 QLQ-MY20 - Time to first improvement by 15 pt in side-effects of treatment (LOCF) - ITT population

First improvement 15 points Side effects of treatment (%)	**Kd (N=123)**	**IKd (N=179)**
Number (%) of events	24 (19.5)	29 (16.2)
Number (%) of patients censored	99 (80.5)	150 (83.8)
Kaplan-Meier estimates of side-effects of treatment in months		
25% quantile (95% CI)	NC (7.491 to NC)	NC (NC to NC)
Median (95% CI)	NC (NC to NC)	NC (NC to NC)
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)
Comparison vs. Kd		
Stratified[a] Log-Rank test p-value[b] vs Kd	-	0.5278
Stratified[a] Hazard ratio (95% CI) vs Kd	-	0.84 (0.49 to 1.45)
P-value	-	0.5283
Improvement probability (95% CI)[c]		
3 Months	0.083 (0.042 to 0.141)	0.098 (0.059 to 0.147)
6 Months	0.160 (0.101 to 0.231)	0.127 (0.082 to 0.181)

A lower score represents a better level of quality of life. Clinical meaningful improvement change from baseline less than or equal to -15 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] Stratified on number of prior lines of therapy (1 vs. >1) and Revised International Staging System (R-ISS) stage (I or II vs. III vs. not classified) according to IRT
[b] One-sided significance level is 0.025
[c] Estimated using the Kaplan-Meier method
NA/NC = Not Applicable / Not Calculable
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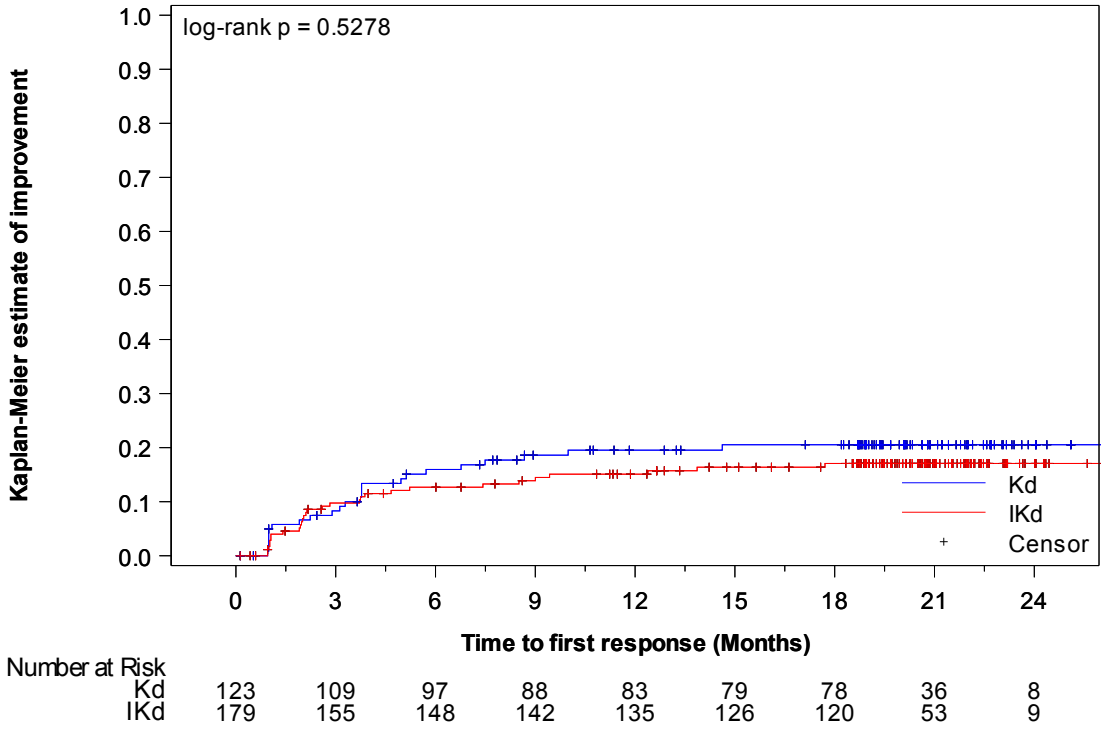
16.2.6.1 Health-related quality-of-life endpoints - QLQ-MY20
16.2.6.1.2 Side-effects of treatment
16.2.6.1.2.1 Efficacy response data
16.2.6.1.2.1.16 QLQ-MY20 - Time to first improvement by 15 pt in side-effects of treatment - Kaplan-Meier curve (LOCF) - ITT population



A lower score represents a better level of quality of life. Clinical meaningful improvement change from baseline less than or equal to -15 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
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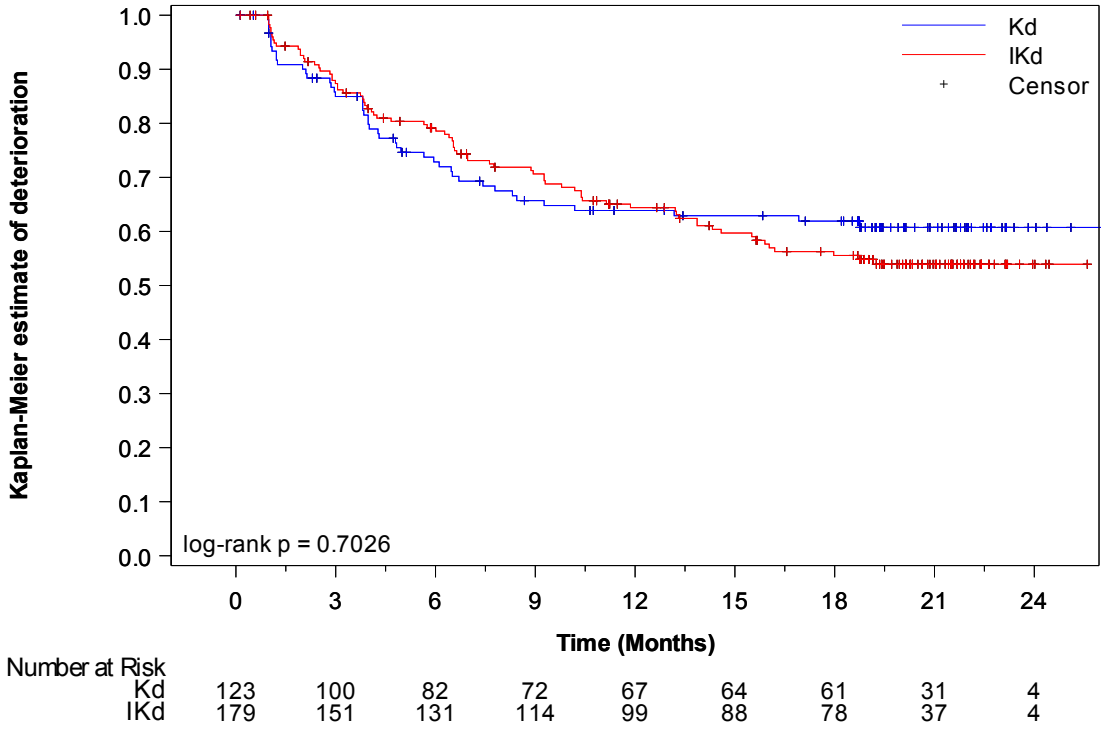
16.2.6.1 Health-related quality-of-life endpoints - QLQ-MY20
16.2.6.1.2 Side-effects of treatment
16.2.6.1.2.1 Efficacy response data
16.2.6.1.2.1.17 QLQ-MY20 - Time to first deterioration by 15 pt in side-effects of treatment (LOCF) - ITT population

First deterioration 15 points Side effects of treatment (%)	**Kd (N=123)**	**IKd (N=179)**
Number (%) of events	45 (36.6)	75 (41.9)
Number (%) of patients censored	78 (63.4)	104 (58.1)
Kaplan-Meier estimates of side-effects of treatment in months		
25% quantile (95% CI)	4.96 (3.811 to 8.312)	6.57 (4.140 to 9.791)
Median (95% CI)	NC (NC to NC)	NC (15.901 to NC)
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)
Comparison vs. Kd		
Stratified[a] Log-Rank test p-value[b] vs Kd	-	0.7026
Stratified[a] Hazard ratio (95% CI) vs Kd	-	1.07 (0.74 to 1.56)
P-value	-	0.7026
Deterioration probability (95% CI)[c]		
3 Months	0.850 (0.772 to 0.902)	0.874 (0.814 to 0.915)
6 Months	0.729 (0.638 to 0.800)	0.792 (0.723 to 0.845)

A lower score represents a better level of quality of life. Clinical meaningful deterioration change from baseline greater than or equal to 15 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] Stratified on number of prior lines of therapy (1 vs. >1) and Revised International Staging System (R-ISS) stage (I or II vs. III vs. not classified) according to IRT
[b] One-sided significance level is 0.025
[c] Estimated using the Kaplan-Meier method
NA/NC = Not Applicable / Not Calculable
PGM=DEVOPS/SAR650984/EFC15246/CIR_RWE/REPORT/PGM/eff_km_invhr_sr_i_t.sas OUT=REPORT/OUTPUT/eff_km_my20_eff_det15l_de_i_t_x.rtf (07APR2021 14:23)

16.2.6.1 Health-related quality-of-life endpoints - QLQ-MY20
16.2.6.1.2 Side-effects of treatment
16.2.6.1.2.1 Efficacy response data
16.2.6.1.2.1.18 QLQ-MY20 - Time to first deterioration by 15 pt in side-effects of treatment - Kaplan-Meier curve (LOCF) - ITT population



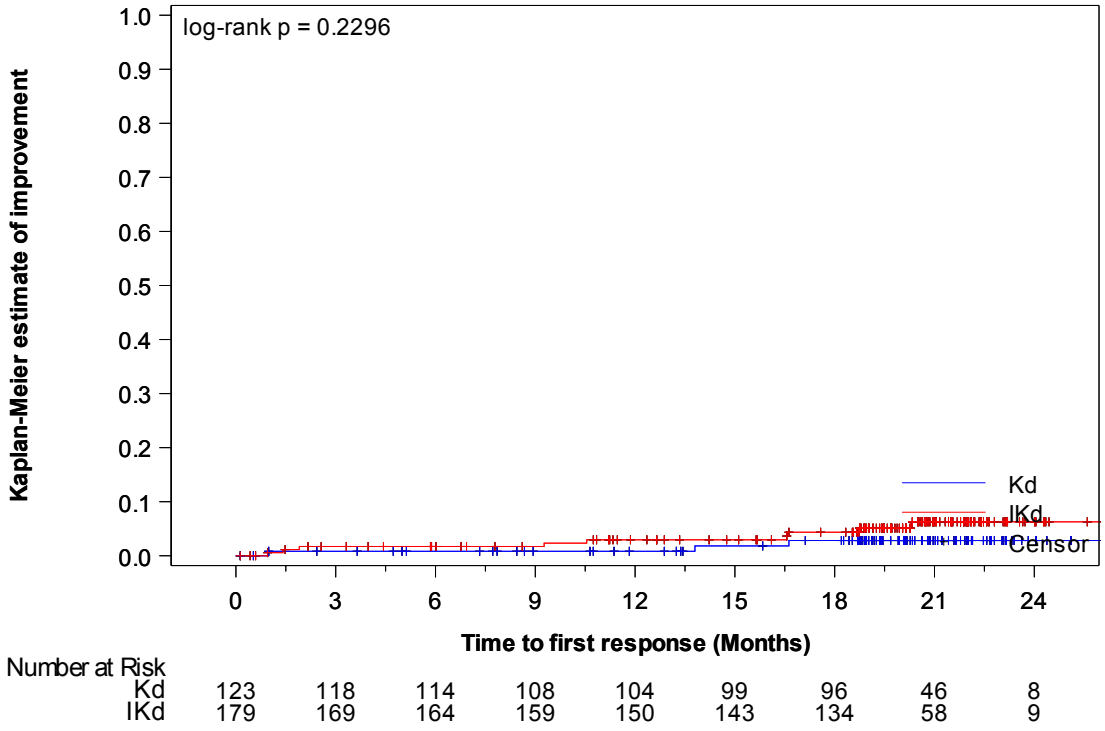
A lower score represents a better level of quality of life. Clinical meaningful deterioration change from baseline greater than or equal to 15 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
PGM=DEVOPS/SAR650984/EFC15246/CIR_RWE/REPORT/PGM/eff_qlq_km_i_f.sas OUT=REPORT/OUTPUT/eff_km_my20_eff_det15l_de_i_f_x.rtf (07APR2021 14:25)

16.2.6.1 Health-related quality-of-life endpoints - QLQ-MY20
16.2.6.1.2 Side-effects of treatment
16.2.6.1.2.1 Efficacy response data
16.2.6.1.2.1.19 QLQ-MY20 - Time until permanent improvement by 15 pt in side-effects of treatment (LOCF) - ITT population

First permanent improvement 15 points Side effects of treatment (%)	**Kd (N=123)**	**IKd (N=179)**
Number (%) of events	3 (2.4)	9 (5.0)
Number (%) of patients censored	120 (97.6)	170 (95.0)
Kaplan-Meier estimates of side-effects of treatment in months		
25% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)
Median (95% CI)	NC (NC to NC)	NC (NC to NC)
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)
Comparison vs. Kd		
Stratified[a] Log-Rank test p-value[b] vs Kd	-	0.2296
Stratified[a] Hazard ratio (95% CI) vs Kd	-	2.19 (0.59 to 8.12)
P-value	-	0.2413
Improvement probability (95% CI)[c]		
3 Months	0.008 (0.001 to 0.041)	0.017 (0.005 to 0.046)
6 Months	0.008 (0.001 to 0.041)	0.017 (0.005 to 0.046)

A lower score represents a better level of quality of life. Clinical meaningful improvement change from baseline less than or equal to -15 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] Stratified on number of prior lines of therapy (1 vs. >1) and Revised International Staging System (R-ISS) stage (I or II vs. III vs. not classified) according to IRT
[b] One-sided significance level is 0.025
[c] Estimated using the Kaplan-Meier method
NA/NC = Not Applicable / Not Calculable
PGM=DEVOPS/SAR650984/EFC15246/CIR_RWE/REPORT/PGM/eff_km_invhr_sr_i_t.sas OUT=REPORT/OUTPUT/eff_km_my20_eff_imp15pl_de_i_t_x.rtf (07APR2021 14:23)

16.2.6.1 Health-related quality-of-life endpoints - QLQ-MY20
16.2.6.1.2 Side-effects of treatment
16.2.6.1.2.1 Efficacy response data
16.2.6.1.2.1.20 QLQ-MY20 - Time until permanent improvement by 15 pt in side-effects of treatment - Kaplan-Meier curve (LOCF) - ITT population



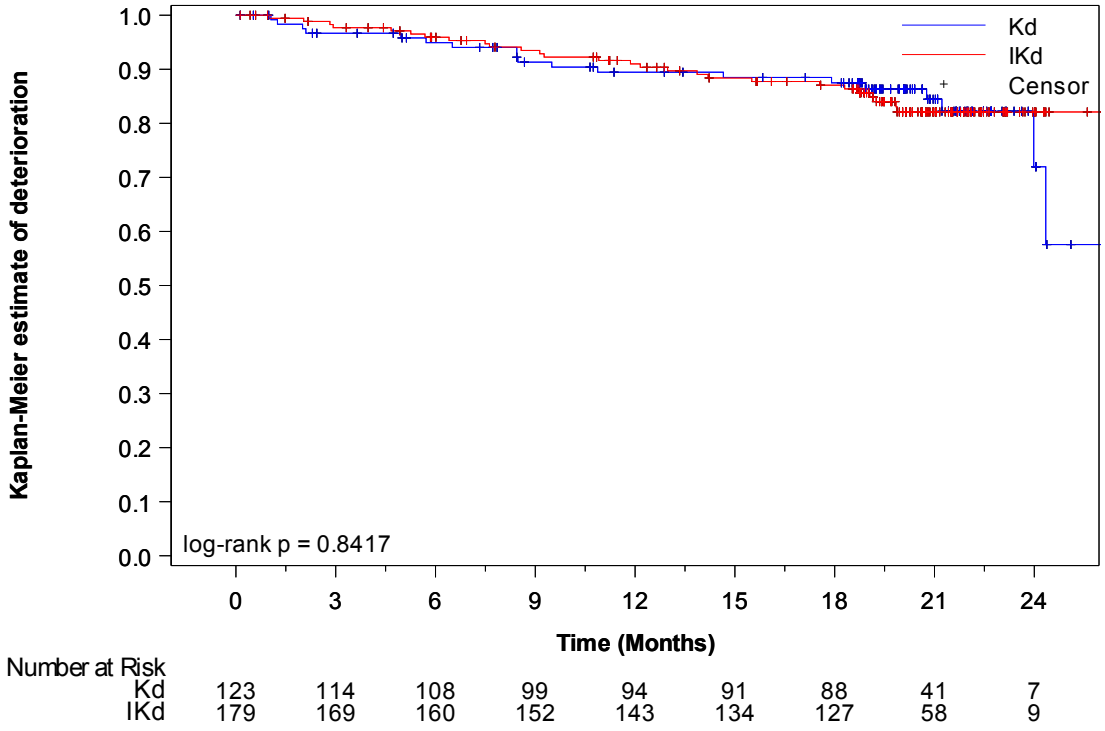
A lower score represents a better level of quality of life. Clinical meaningful improvement change from baseline less than or equal to -15 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
PGM=DEVOPS/SAR650984/EFC15246/CIR_RWE/REPORT/PGM/eff_qlq_km_i_f.sas OUT=REPORT/OUTPUT/eff_km_my20_eff_imp15pl_de_i_f_x.rtf (07APR2021 14:25)

16.2.6.1 Health-related quality-of-life endpoints - QLQ-MY20
16.2.6.1.2 Side-effects of treatment
16.2.6.1.2.1 Efficacy response data
16.2.6.1.2.1.21 QLQ-MY20 - Time until permanent deterioration by 15 pt in side-effects of treatment (LOCF) - ITT population

First permanent deterioration 15 points Side effects of treatment (%)	**Kd (N=123)**	**IKd (N=179)**
Number (%) of events	19 (15.4)	27 (15.1)
Number (%) of patients censored	104 (84.6)	152 (84.9)
Kaplan-Meier estimates of side-effects of treatment in months		
25% quantile (95% CI)	23.98 (21.224 to NC)	NC (19.877 to NC)
Median (95% CI)	NC (23.984 to NC)	NC (NC to NC)
75% quantile (95% CI)	NC (24.345 to NC)	NC (NC to NC)
Comparison vs. Kd		
Stratified[a] Log-Rank test p-value[b] vs Kd	-	0.8417
Stratified[a] Hazard ratio (95% CI) vs Kd	-	0.94 (0.52 to 1.70)
P-value	-	0.8408
Deterioration probability (95% CI)[c]		
3 Months	0.967 (0.914 to 0.987)	0.977 (0.940 to 0.991)
6 Months	0.949 (0.890 to 0.977)	0.959 (0.916 to 0.980)

A lower score represents a better level of quality of life. Clinical meaningful deterioration change from baseline greater than or equal to 15 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] Stratified on number of prior lines of therapy (1 vs. >1) and Revised International Staging System (R-ISS) stage (I or II vs. III vs. not classified) according to IRT
[b] One-sided significance level is 0.025
[c] Estimated using the Kaplan-Meier method
NA/NC = Not Applicable / Not Calculable
PGM=DEVOPS/SAR650984/EFC15246/CIR_RWE/REPORT/PGM/eff_km_invhr_sr_i_t.sas OUT=REPORT/OUTPUT/eff_km_my20_eff_det15pl_de_i_t_x.rtf (07APR2021 14:23)

16.2.6.1 Health-related quality-of-life endpoints - QLQ-MY20
16.2.6.1.2 Side-effects of treatment
16.2.6.1.2.1 Efficacy response data
16.2.6.1.2.1.22 QLQ-MY20 - Time until permanent deterioration by 15 pt in side-effects of treatment - Kaplan-Meier curve (LOCF) - ITT population



A lower score represents a better level of quality of life. Clinical meaningful deterioration change from baseline greater than or equal to 15 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
PGM=DEVOPS/SAR650984/EFC15246/CIR_RWE/REPORT/PGM/eff_qlq_km_i_f.sas OUT=REPORT/OUTPUT/eff_km_my20_eff_det15pl_de_i_f_x.rtf (07APR2021 14:25)

16.2.6.1 Health-related quality-of-life endpoints - QLQ-MY20
16.2.6.1.2 Side-effects of treatment
16.2.6.1.2.2 Efficacy response data - Subgroup analyses by age
16.2.6.1.2.2.3 QLQ-MY20 - Time to first improvement by 10 pt in side-effects of treatment according to age (LOCF) - ITT population

	<65 years		>=65 years		
	Kd (N=66)	**IKd (N=88)**	**Kd (N=57)**	**IKd (N=91)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	21 (31.8)	28 (31.8)	20 (35.1)	35 (38.5)	0.7636
Number (%) of patients censored	45 (68.2)	60 (68.2)	37 (64.9)	56 (61.5)	
Kaplan-Meier estimates of side-effects of treatment in months					
25% quantile (95% CI)	2.96 (1.281 to NC)	3.71 (2.103 to NC)	4.63 (1.051 to 14.850)	3.19 (1.971 to 9.002)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (14.850 to NC)	NC (17.478 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.9139		0.7499	
Hazard ratio (95% CI) vs Kd	-	0.97 (0.55 to 1.71)		1.09 (0.63 to 1.89)	
P-value	-	0.9137		0.7500	

A lower score represents a better level of quality of life. Clinical meaningful improvement change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
PGM=DEVOPS/SAR650984/EFC15246/CIR_RWE/REPORT/PGM/eff_km_subgp_sr_sig_de_i_t.sas OUT=REPORT/OUTPUT/eff_km_my20_eff_impl_age_de_i_t_x.rtf (07APR2021 14:43)

16.2.6.1 Health-related quality-of-life endpoints - QLQ-MY20
16.2.6.1.2 Side-effects of treatment
16.2.6.1.2.2 Efficacy response data - Subgroup analyses by age
16.2.6.1.2.2.4 QLQ-MY20 - Time to first deterioration by 10 pt in side-effects of treatment according to age (LOCF) - ITT population

	<65 years		>=65 years		
	Kd (N=66)	**IKd (N=88)**	**Kd (N=57)**	**IKd (N=91)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	34 (51.5)	50 (56.8)	29 (50.9)	58 (63.7)	0.2866
Number (%) of patients censored	32 (48.5)	38 (43.2)	28 (49.1)	33 (36.3)	
Kaplan-Meier estimates of side-effects of treatment in months					
25% quantile (95% CI)	1.97 (1.117 to 3.055)	2.10 (1.873 to 4.665)	2.04 (1.216 to 4.830)	1.87 (1.150 to 3.055)	
Median (95% CI)	10.18 (3.811 to NC)	10.41 (5.782 to NC)	13.54 (4.830 to NC)	5.65 (3.778 to 8.739)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (13.864 to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.8464		0.0957	
Hazard ratio (95% CI) vs Kd	-	1.04 (0.68 to 1.61)		1.46 (0.93 to 2.28)	
P-value	-	0.8470		0.0977	

A lower score represents a better level of quality of life. Clinical meaningful deterioration change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
PGM=DEVOPS/SAR650984/EFC15246/CIR_RWE/REPORT/PGM/eff_km_subgp_sr_sig_de_i_t.sas OUT=REPORT/OUTPUT/eff_km_my20_eff_detl_age_de_i_t_x.rtf (07APR2021 14:43)

16.2.6.1 Health-related quality-of-life endpoints - QLQ-MY20
16.2.6.1.2 Side-effects of treatment
16.2.6.1.2.2 Efficacy response data - Subgroup analyses by age
16.2.6.1.2.2.5 QLQ-MY20 - Time until permanent improvement by 10 pt in side-effects of treatment according to age (LOCF) - ITT population

	<65 years		>=65 years		
	Kd (N=66)	**IKd (N=88)**	**Kd (N=57)**	**IKd (N=91)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	5 (7.6)	11 (12.5)	6 (10.5)	12 (13.2)	0.6981
Number (%) of patients censored	61 (92.4)	77 (87.5)	51 (89.5)	79 (86.8)	
Kaplan-Meier estimates of side-effects of treatment in months					
25% quantile (95% CI)	NC (NC to NC)	NC (20.304 to NC)	NC (19.450 to NC)	NC (20.534 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.3275		0.6472	
Hazard ratio (95% CI) vs Kd	-	1.69 (0.59 to 4.85)		1.26 (0.47 to 3.35)	
P-value	-	0.3331		0.6480	

A lower score represents a better level of quality of life. Clinical meaningful improvement change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.1 Health-related quality-of-life endpoints - QLQ-MY20
16.2.6.1.2 Side-effects of treatment
16.2.6.1.2.2 Efficacy response data - Subgroup analyses by age
16.2.6.1.2.2.6 QLQ-MY20 - Time until permanent deterioration by 10 pt in side-effects of treatment according to age (LOCF) - ITT population

	<65 years		>=65 years		
	Kd (N=66)	**IKd (N=88)**	**Kd (N=57)**	**IKd (N=91)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	16 (24.2)	21 (23.9)	18 (31.6)	26 (28.6)	0.7322
Number (%) of patients censored	50 (75.8)	67 (76.1)	39 (68.4)	65 (71.4)	
Kaplan-Meier estimates of side-effects of treatment in months					
25% quantile (95% CI)	20.76 (9.495 to NC)	20.24 (11.860 to NC)	15.15 (7.786 to NC)	18.79 (11.926 to 21.717)	
Median (95% CI)	24.02 (24.016 to NC)	NC (NC to NC)	NC (20.304 to NC)	NC (21.717 to NC)	
75% quantile (95% CI)	NC (24.016 to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.9645		0.6436	
Hazard ratio (95% CI) vs Kd	-	1.01 (0.53 to 1.95)		0.87 (0.48 to 1.58)	
P-value	-	0.9645		0.6439	

A lower score represents a better level of quality of life. Clinical meaningful deterioration change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
PGM=DEVOPS/SAR650984/EFC15246/CIR_RWE/REPORT/PGM/eff_km_subgp_sr_sig_de_i_t.sas OUT=REPORT/OUTPUT/eff_km_my20_eff_detpl_age_de_i_t_x.rtf (07APR2021 14:44)

16.2.6.1 Health-related quality-of-life endpoints - QLQ-MY20
16.2.6.1.2 Side-effects of treatment
16.2.6.1.2.3 Efficacy response data - Subgroup analyses by gender
16.2.6.1.2.3.3 QLQ-MY20 - Time to first improvement by 10 pt in side-effects of treatment according to gender (LOCF) - ITT population

	Male		Female		
	Kd (N=68)	**IKd (N=101)**	**Kd (N=55)**	**IKd (N=78)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	19 (27.9)	29 (28.7)	22 (40.0)	34 (43.6)	0.7883
Number (%) of patients censored	49 (72.1)	72 (71.3)	33 (60.0)	44 (56.4)	
Kaplan-Meier estimates of side-effects of treatment in months					
25% quantile (95% CI)	6.51 (1.281 to NC)	5.72 (2.924 to NC)	3.12 (1.018 to 10.940)	2.83 (1.051 to 8.641)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (10.940 to NC)	NC (12.057 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.9850		0.7305	
Hazard ratio (95% CI) vs Kd	-	0.99 (0.56 to 1.77)		1.10 (0.64 to 1.88)	
P-value	-	0.9850		0.7306	

A lower score represents a better level of quality of life. Clinical meaningful improvement change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.1 Health-related quality-of-life endpoints - QLQ-MY20
16.2.6.1.2 Side-effects of treatment
16.2.6.1.2.3 Efficacy response data - Subgroup analyses by gender
16.2.6.1.2.3.4 QLQ-MY20 - Time to first deterioration by 10 pt in side-effects of treatment according to gender (LOCF) - ITT population

	Male		Female		
	Kd (N=68)	**IKd (N=101)**	**Kd (N=55)**	**IKd (N=78)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	34 (50.0)	53 (52.5)	29 (52.7)	55 (70.5)	0.4902
Number (%) of patients censored	34 (50.0)	48 (47.5)	26 (47.3)	23 (29.5)	
Kaplan-Meier estimates of side-effects of treatment in months					
25% quantile (95% CI)	2.89 (1.216 to 4.994)	2.10 (1.577 to 3.811)	1.87 (1.051 to 2.891)	1.94 (1.117 to 3.220)	
Median (95% CI)	13.54 (5.618 to NC)	8.38 (5.552 to NC)	7.43 (2.891 to NC)	6.70 (4.205 to 10.185)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (12.320 to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.6456		0.1640	
Hazard ratio (95% CI) vs Kd	-	1.11 (0.72 to 1.70)		1.38 (0.88 to 2.16)	
P-value	-	0.6457		0.1658	

A lower score represents a better level of quality of life. Clinical meaningful deterioration change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
PGM=DEVOPS/SAR650984/EFC15246/CIR_RWE/REPORT/PGM/eff_km_subgp_sr_sig_de_i_t.sas OUT=REPORT/OUTPUT/eff_km_my20_eff_detl_sex_de_i_t_x.rtf (07APR2021 14:43)

16.2.6.1 Health-related quality-of-life endpoints - QLQ-MY20
16.2.6.1.2 Side-effects of treatment
16.2.6.1.2.3 Efficacy response data - Subgroup analyses by gender
16.2.6.1.2.3.5 QLQ-MY20 - Time until permanent improvement by 10 pt in side-effects of treatment according to gender (LOCF) - ITT population

	Male		Female		
	Kd (N=68)	**IKd (N=101)**	**Kd (N=55)**	**IKd (N=78)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	3 (4.4)	10 (9.9)	8 (14.5)	13 (16.7)	0.3437
Number (%) of patients censored	65 (95.6)	91 (90.1)	47 (85.5)	65 (83.3)	
Kaplan-Meier estimates of side-effects of treatment in months					
25% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (15.047 to NC)	NC (18.760 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.1960		0.8615	
Hazard ratio (95% CI) vs Kd	-	2.29 (0.63 to 8.31)		1.08 (0.45 to 2.61)	
P-value	-	0.2088		0.8615	

A lower score represents a better level of quality of life. Clinical meaningful improvement change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
PGM=DEVOPS/SAR650984/EFC15246/CIR_RWE/REPORT/PGM/eff_km_subgp_sr_sig_de_i_t.sas OUT=REPORT/OUTPUT/eff_km_my20_eff_imppl_sex_de_i_t_x.rtf (07APR2021 14:44)

16.2.6.1 Health-related quality-of-life endpoints - QLQ-MY20
16.2.6.1.2 Side-effects of treatment
16.2.6.1.2.3 Efficacy response data - Subgroup analyses by gender
16.2.6.1.2.3.6 QLQ-MY20 - Time until permanent deterioration by 10 pt in side-effects of treatment according to gender (LOCF) - ITT population

	Male		Female		
	Kd (N=68)	**IKd (N=101)**	**Kd (N=55)**	**IKd (N=78)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	19 (27.9)	24 (23.8)	15 (27.3)	23 (29.5)	0.6191
Number (%) of patients censored	49 (72.1)	77 (76.2)	40 (72.7)	55 (70.5)	
Kaplan-Meier estimates of side-effects of treatment in months					
25% quantile (95% CI)	20.30 (8.444 to 24.016)	19.25 (14.193 to NC)	18.92 (8.312 to NC)	17.77 (9.955 to NC)	
Median (95% CI)	24.02 (21.224 to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (24.016 to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.6063		0.8382	
Hazard ratio (95% CI) vs Kd	-	0.85 (0.47 to 1.56)		1.07 (0.56 to 2.05)	
P-value	-	0.6067		0.8393	

A lower score represents a better level of quality of life. Clinical meaningful deterioration change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
PGM=DEVOPS/SAR650984/EFC15246/CIR_RWE/REPORT/PGM/eff_km_subgp_sr_sig_de_i_t.sas OUT=REPORT/OUTPUT/eff_km_my20_eff_detpl_sex_de_i_t_x.rtf (07APR2021 14:44)

16.2.6.1 Health-related quality-of-life endpoints - QLQ-MY20
16.2.6.1.2 Side-effects of treatment
16.2.6.1.2.4 Efficacy response data - Subgroup analyses by ethnic origin
16.2.6.1.2.4.3 QLQ-MY20 - Time to first improvement by 10 pt in side-effects of treatment according to ethnic origin (LOCF) - ITT population

	White		Other		
	Kd (N=83)	**IKd (N=131)**	**Kd (N=28)**	**IKd (N=34)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	30 (36.1)	46 (35.1)	9 (32.1)	12 (35.3)	0.6142
Number (%) of patients censored	53 (63.9)	85 (64.9)	19 (67.9)	22 (64.7)	
Kaplan-Meier estimates of side-effects of treatment in months					
25% quantile (95% CI)	2.79 (1.051 to 6.768)	3.75 (2.825 to 11.499)	11.01 (1.084 to NC)	2.07 (1.018 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (11.532 to NC)	NC (2.957 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.7953		0.6982	
Hazard ratio (95% CI) vs Kd	-	0.94 (0.59 to 1.49)		1.19 (0.50 to 2.82)	
P-value	-	0.7939		0.6986	

A lower score represents a better level of quality of life. Clinical meaningful improvement change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
PGM=DEVOPS/SAR650984/EFC15246/CIR_RWE/REPORT/PGM/eff_km_subgp_sr_sig_de_i_t.sas OUT=REPORT/OUTPUT/eff_km_my20_eff_impl_race_de_i_t_x.rtf (07APR2021 14:43)

16.2.6.1 Health-related quality-of-life endpoints - QLQ-MY20
16.2.6.1.2 Side-effects of treatment
16.2.6.1.2.4 Efficacy response data - Subgroup analyses by ethnic origin
16.2.6.1.2.4.4 QLQ-MY20 - Time to first deterioration by 10 pt in side-effects of treatment according to ethnic origin (LOCF) - ITT population

	White		Other		
	Kd (N=83)	**IKd (N=131)**	**Kd (N=28)**	**IKd (N=34)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	44 (53.0)	83 (63.4)	13 (46.4)	21 (61.8)	0.9717
Number (%) of patients censored	39 (47.0)	48 (36.6)	15 (53.6)	13 (38.2)	
Kaplan-Meier estimates of side-effects of treatment in months					
25% quantile (95% CI)	2.00 (1.216 to 3.975)	1.91 (1.150 to 2.825)	1.97 (1.051 to 10.119)	4.68 (1.150 to 5.585)	
Median (95% CI)	12.55 (4.830 to NC)	6.70 (4.205 to 9.528)	16.16 (2.037 to NC)	7.66 (4.797 to 17.971)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (13.207 to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.1406		0.3798	
Hazard ratio (95% CI) vs Kd	-	1.32 (0.91 to 1.90)		1.36 (0.68 to 2.74)	
P-value	-	0.1418		0.3816	

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The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
PGM=DEVOPS/SAR650984/EFC15246/CIR_RWE/REPORT/PGM/eff_km_subgp_sr_sig_de_i_t.sas OUT=REPORT/OUTPUT/eff_km_my20_eff_detl_race_de_i_t_x.rtf (07APR2021 14:43)

16.2.6.1 Health-related quality-of-life endpoints - QLQ-MY20
16.2.6.1.2 Side-effects of treatment
16.2.6.1.2.4 Efficacy response data - Subgroup analyses by ethnic origin
16.2.6.1.2.4.5 QLQ-MY20 - Time until permanent improvement by 10 pt in side-effects of treatment according to ethnic origin (LOCF) - ITT population

	White		Other		
	Kd (N=83)	**IKd (N=131)**	**Kd (N=28)**	**IKd (N=34)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	9 (10.8)	14 (10.7)	0 (0.0)	6 (17.6)	0.9884
Number (%) of patients censored	74 (89.2)	117 (89.3)	28 (100.0)	28 (82.4)	
Kaplan-Meier estimates of side-effects of treatment in months					
25% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (10.185 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.9412		0.0202	
Hazard ratio (95% CI) vs Kd	-	0.97 (0.42 to 2.24)			
P-value	-	0.9410		0.9961	

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The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.1 Health-related quality-of-life endpoints - QLQ-MY20
16.2.6.1.2 Side-effects of treatment
16.2.6.1.2.4 Efficacy response data - Subgroup analyses by ethnic origin
16.2.6.1.2.4.6 QLQ-MY20 - Time until permanent deterioration by 10 pt in side-effects of treatment according to ethnic origin (LOCF) - ITT population

	White		Other		
	Kd (N=83)	**IKd (N=131)**	**Kd (N=28)**	**IKd (N=34)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	22 (26.5)	37 (28.2)	8 (28.6)	7 (20.6)	0.4499
Number (%) of patients censored	61 (73.5)	94 (71.8)	20 (71.4)	27 (79.4)	
Kaplan-Meier estimates of side-effects of treatment in months					
25% quantile (95% CI)	20.37 (9.988 to NC)	18.79 (11.926 to 21.717)	16.99 (3.811 to NC)	NC (6.407 to NC)	
Median (95% CI)	NC (21.224 to NC)	NC (NC to NC)	24.02 (16.986 to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (24.016 to NC)	NC (NC to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.7049		0.5150	
Hazard ratio (95% CI) vs Kd	-	1.11 (0.65 to 1.88)		0.71 (0.26 to 1.97)	
P-value	-	0.7050		0.5169	

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The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.1 Health-related quality-of-life endpoints - QLQ-MY20
16.2.6.1.2 Side-effects of treatment
16.2.6.1.2.5 Efficacy response data - Subgroup analyses by geographical region
16.2.6.1.2.5.3 QLQ-MY20 - Time to first improvement by 10 pt in side-effects of treatment according to geographical region (LOCF) - ITT population

	Europe		America		Asia		Other countries		
	Kd (N=60)	**IKd (N=85)**	**Kd (N=20)**	**IKd (N=24)**	**Kd (N=21)**	**IKd (N=25)**	**Kd (N=22)**	**IKd (N=45)**	**p-value of treatment-by-subgroup interaction[c]**
Number (%) of events	16 (26.7)	30 (35.3)	12 (60.0)	9 (37.5)	5 (23.8)	9 (36.0)	8 (36.4)	15 (33.3)	0.3453
Number (%) of patients censored	44 (73.3)	55 (64.7)	8 (40.0)	15 (62.5)	16 (76.2)	16 (64.0)	14 (63.6)	30 (66.7)	
Kaplan-Meier estimates of event in months									
25% quantile (95% CI)	4.63 (1.906 to NC)	5.22 (2.825 to 16.329)	1.02 (0.986 to 1.971)	2.10 (0.986 to NC)	18.79 (0.986 to NC)	2.48 (0.986 to NC)	6.28 (0.986 to NC)	3.88 (1.051 to NC)	
Median (95% CI)	NC (NC to NC)	NC (20.041 to NC)	10.94 (1.018 to NC)	NC (2.103 to NC)	NC (18.793 to NC)	NC (2.957 to NC)	NC (6.275 to NC)	NC (NC to NC)	

A lower score represents a better level of quality of life. Clinical meaningful improvement change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.1 Health-related quality-of-life endpoints - QLQ-MY20
16.2.6.1.2 Side-effects of treatment
16.2.6.1.2.5 Efficacy response data - Subgroup analyses by geographical region
16.2.6.1.2.5.3 QLQ-MY20 - Time to first improvement by 10 pt in side-effects of treatment according to geographical region (LOCF) - ITT population

	Europe		America		Asia		Other countries		
	Kd (N=60)	**IKd (N=85)**	**Kd (N=20)**	**IKd (N=24)**	**Kd (N=21)**	**IKd (N=25)**	**Kd (N=22)**	**IKd (N=45)**	**p-value of treatment-by-subgroup interaction[c]**
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (11.006 to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Kd									
Log-Rank test p-value[a] vs Kd	-	0.3866		0.1650		0.4070		0.9017	
Hazard ratio (95% CI) vs Kd	-	1.31 (0.71 to 2.40)		0.55 (0.23 to 1.30)		1.58 (0.53 to 4.72)		0.95 (0.40 to 2.23)	
P-value	-	0.3880		0.1714		0.4111		0.9017	
Improvement probability (95% CI)[b]									

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The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.1 Health-related quality-of-life endpoints - QLQ-MY20
16.2.6.1.2 Side-effects of treatment
16.2.6.1.2.5 Efficacy response data - Subgroup analyses by geographical region
16.2.6.1.2.5.4 QLQ-MY20 - Time to first deterioration by 10 pt in side-effects of treatment according to geographical region (LOCF) - ITT population

	Europe		America		Asia		Other countries		
	Kd (N=60)	**IKd (N=85)**	**Kd (N=20)**	**IKd (N=24)**	**Kd (N=21)**	**IKd (N=25)**	**Kd (N=22)**	**IKd (N=45)**	**p-value of treatment-by-subgroup interaction[c]**
Number (%) of events	27 (45.0)	49 (57.6)	14 (70.0)	15 (62.5)	9 (42.9)	15 (60.0)	13 (59.1)	29 (64.4)	0.9434
Number (%) of patients censored	33 (55.0)	36 (42.4)	6 (30.0)	9 (37.5)	12 (57.1)	10 (40.0)	9 (40.9)	16 (35.6)	
Kaplan-Meier estimates of event in months									
25% quantile (95% CI)	1.94 (1.051 to 6.472)	2.79 (1.183 to 4.205)	2.89 (0.953 to 4.665)	2.37 (1.051 to 3.811)	1.59 (1.051 to 11.499)	4.75 (1.018 to 6.407)	2.00 (0.986 to 5.618)	1.12 (1.051 to 2.825)	
Median (95% CI)	NC (6.472 to NC)	9.20 (5.552 to NC)	5.78 (2.891 to 16.789)	6.80 (2.366 to 18.760)	NC (1.216 to NC)	10.18 (4.797 to NC)	13.54 (2.004 to NC)	5.62 (1.938 to 15.507)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (6.801 to NC)	NC (6.801 to NC)	NC (NC to NC)	NC (13.207 to NC)	NC (15.934 to NC)	NC (7.425 to NC)	

A lower score represents a better level of quality of life. Clinical meaningful deterioration change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.1 Health-related quality-of-life endpoints - QLQ-MY20
16.2.6.1.2 Side-effects of treatment
16.2.6.1.2.5 Efficacy response data - Subgroup analyses by geographical region
16.2.6.1.2.5.4 QLQ-MY20 - Time to first deterioration by 10 pt in side-effects of treatment according to geographical region (LOCF) - ITT population

	Europe		America		Asia		Other countries		
	Kd (N=60)	**IKd (N=85)**	**Kd (N=20)**	**IKd (N=24)**	**Kd (N=21)**	**IKd (N=25)**	**Kd (N=22)**	**IKd (N=45)**	**p-value of treatment-by-subgroup interaction[c]**
Comparison vs. Kd									
Log-Rank test p-value[a] vs Kd	-	0.3211		0.9084		0.5491		0.4421	
Hazard ratio (95% CI) vs Kd	-	1.27 (0.79 to 2.03)		1.04 (0.50 to 2.17)		1.29 (0.56 to 2.95)		1.29 (0.67 to 2.49)	
P-value	-	0.3223		0.9085		0.5502		0.4434	
Deterioration probability (95% CI)[b]									
3 Months	0.690 (0.554 to 0.792)	0.723 (0.613 to 0.806)	0.700 (0.451 to 0.853)	0.639 (0.406 to 0.801)	0.650 (0.403 to 0.815)	0.833 (0.615 to 0.934)	0.727 (0.491 to 0.867)	0.556 (0.400 to 0.686)	

A lower score represents a better level of quality of life. Clinical meaningful deterioration change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.1 Health-related quality-of-life endpoints - QLQ-MY20
16.2.6.1.2 Side-effects of treatment
16.2.6.1.2.5 Efficacy response data - Subgroup analyses by geographical region
16.2.6.1.2.5.5 QLQ-MY20 - Time until permanent improvement by 10 pt in side-effects of treatment according to geographical region (LOCF) - ITT population

	Europe		America		Asia		Other countries		
	Kd (N=60)	**IKd (N=85)**	**Kd (N=20)**	**IKd (N=24)**	**Kd (N=21)**	**IKd (N=25)**	**Kd (N=22)**	**IKd (N=45)**	**p-value of treatment-by-subgroup interaction[c]**
Number (%) of events	5 (8.3)	12 (14.1)	3 (15.0)	3 (12.5)	0 (0.0)	4 (16.0)	3 (13.6)	4 (8.9)	0.7900
Number (%) of patients censored	55 (91.7)	73 (85.9)	17 (85.0)	21 (87.5)	21 (100.0)	21 (84.0)	19 (86.4)	41 (91.1)	
Kaplan-Meier estimates of event in months									
25% quantile (95% CI)	NC (NC to NC)	NC (20.304 to NC)	NC (0.986 to NC)	NC (5.585 to NC)	NC (NC to NC)	NC (0.986 to NC)	NC (13.799 to NC)	NC (20.534 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (19.450 to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	

A lower score represents a better level of quality of life. Clinical meaningful improvement change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
PGM=DEVOPS/SAR650984/EFC15246/CIR_RWE/REPORT/PGM/eff_km_subgp_sr_sig_de_i_t.sas OUT=REPORT/OUTPUT/eff_km_my20_eff_imppl_greg_de_i_t_x.rtf (07APR2021 14:44)

16.2.6.1 Health-related quality-of-life endpoints - QLQ-MY20
16.2.6.1.2 Side-effects of treatment
16.2.6.1.2.5 Efficacy response data - Subgroup analyses by geographical region
16.2.6.1.2.5.5 QLQ-MY20 - Time until permanent improvement by 10 pt in side-effects of treatment according to geographical region (LOCF) - ITT population

	Europe		America		Asia		Other countries		
	Kd (N=60)	**IKd (N=85)**	**Kd (N=20)**	**IKd (N=24)**	**Kd (N=21)**	**IKd (N=25)**	**Kd (N=22)**	**IKd (N=45)**	**p-value of treatment-by-subgroup interaction[c]**
Comparison vs. Kd									
Log-Rank test p-value[a] vs Kd	-	0.3390		0.9948		0.0641		0.6098	
Hazard ratio (95% CI) vs Kd	-	1.65 (0.58 to 4.70)		1.01 (0.20 to 5.00)				0.68 (0.15 to 3.03)	
P-value	-	0.3443		0.9948		0.9968		0.6120	
Improvement probability (95% CI)[b]									
3 Months	0.069 (0.022 to 0.152)	0.036 (0.010 to 0.093)	0.050 (0.003 to 0.205)			0.083 (0.014 to 0.233)		0.044 (0.008 to 0.133)	

A lower score represents a better level of quality of life. Clinical meaningful improvement change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
PGM=DEVOPS/SAR650984/EFC15246/CIR_RWE/REPORT/PGM/eff_km_subgp_sr_sig_de_i_t.sas OUT=REPORT/OUTPUT/eff_km_my20_eff_imppl_greg_de_i_t_x.rtf (07APR2021 14:44)

16.2.6.1 Health-related quality-of-life endpoints - QLQ-MY20
16.2.6.1.2 Side-effects of treatment
16.2.6.1.2.5 Efficacy response data - Subgroup analyses by geographical region
16.2.6.1.2.5.6 QLQ-MY20 - Time until permanent deterioration by 10 pt in side-effects of treatment according to geographical region (LOCF) - ITT population

	Europe		America		Asia		Other countries		
	Kd (N=60)	**IKd (N=85)**	**Kd (N=20)**	**IKd (N=24)**	**Kd (N=21)**	**IKd (N=25)**	**Kd (N=22)**	**IKd (N=45)**	**p-value of treatment-by-subgroup interaction[c]**
Number (%) of events	17 (28.3)	22 (25.9)	5 (25.0)	6 (25.0)	7 (33.3)	6 (24.0)	5 (22.7)	13 (28.9)	0.6837
Number (%) of patients censored	43 (71.7)	63 (74.1)	15 (75.0)	18 (75.0)	14 (66.7)	19 (76.0)	17 (77.3)	32 (71.1)	
Kaplan-Meier estimates of event in months									
25% quantile (95% CI)	19.15 (12.189 to 21.224)	19.88 (13.996 to NC)	20.76 (6.801 to NC)	12.32 (1.577 to NC)	11.50 (2.957 to 24.016)	15.70 (1.018 to NC)	NC (2.004 to NC)	18.79 (5.815 to NC)	
Median (95% CI)	NC (20.600 to NC)	NC (NC to NC)	NC (20.764 to NC)	NC (12.320 to NC)	24.02 (11.499 to NC)	NC (15.704 to NC)	NC (NC to NC)	NC (20.238 to NC)	

A lower score represents a better level of quality of life. Clinical meaningful deterioration change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.1 Health-related quality-of-life endpoints - QLQ-MY20
16.2.6.1.2 Side-effects of treatment
16.2.6.1.2.5 Efficacy response data - Subgroup analyses by geographical region
16.2.6.1.2.5.6 QLQ-MY20 - Time until permanent deterioration by 10 pt in side-effects of treatment according to geographical region (LOCF) - ITT population

	Europe		America		Asia		Other countries		
	Kd (N=60)	**IKd (N=85)**	**Kd (N=20)**	**IKd (N=24)**	**Kd (N=21)**	**IKd (N=25)**	**Kd (N=22)**	**IKd (N=45)**	**p-value of treatment-by-subgroup interaction[c]**
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (24.016 to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Kd									
Log-Rank test p-value[a] vs Kd	-	0.5834		0.6476		0.4595		0.5581	
Hazard ratio (95% CI) vs Kd	-	0.84 (0.44 to 1.58)		1.32 (0.40 to 4.33)		0.66 (0.22 to 1.98)		1.36 (0.48 to 3.82)	
P-value	-	0.5839		0.6486		0.4626		0.5597	
Deterioration probability (95% CI)[b]									

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The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.1 Health-related quality-of-life endpoints - QLQ-MY20
16.2.6.1.2 Side-effects of treatment
16.2.6.1.2.6 Efficacy response data - Subgroup analyses by regulatory region
16.2.6.1.2.6.3 QLQ-MY20 - Time to first improvement by 10 pt in side-effects of treatment according to regulatory region (LOCF) - ITT population

	Western countries		Other countries		
	Kd (N=55)	**IKd (N=97)**	**Kd (N=68)**	**IKd (N=82)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	16 (29.1)	32 (33.0)	25 (36.8)	31 (37.8)	0.9632
Number (%) of patients censored	39 (70.9)	65 (67.0)	43 (63.2)	51 (62.2)	
Kaplan-Meier estimates of side-effects of treatment in months					
25% quantile (95% CI)	6.51 (1.906 to NC)	5.72 (2.924 to 20.041)	2.96 (1.051 to 11.006)	2.14 (1.051 to 8.641)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (18.793 to NC)	NC (16.427 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.7920		0.8106	
Hazard ratio (95% CI) vs Kd	-	1.08 (0.59 to 1.98)		1.07 (0.63 to 1.81)	
P-value	-	0.7921		0.8111	

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The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.1 Health-related quality-of-life endpoints - QLQ-MY20
16.2.6.1.2 Side-effects of treatment
16.2.6.1.2.6 Efficacy response data - Subgroup analyses by regulatory region
16.2.6.1.2.6.4 QLQ-MY20 - Time to first deterioration by 10 pt in side-effects of treatment according to regulatory region (LOCF) - ITT population

	Western countries		Other countries		
	Kd (N=55)	**IKd (N=97)**	**Kd (N=68)**	**IKd (N=82)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	25 (45.5)	53 (54.6)	38 (55.9)	55 (67.1)	0.6840
Number (%) of patients censored	30 (54.5)	44 (45.4)	30 (44.1)	27 (32.9)	
Kaplan-Meier estimates of side-effects of treatment in months					
25% quantile (95% CI)	1.91 (0.986 to 6.472)	1.91 (1.183 to 3.220)	2.83 (1.248 to 4.304)	2.53 (1.150 to 3.844)	
Median (95% CI)	NC (4.041 to NC)	10.41 (5.552 to NC)	11.50 (4.665 to NC)	6.01 (4.665 to 9.528)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (12.320 to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.5264		0.1659	
Hazard ratio (95% CI) vs Kd	-	1.17 (0.72 to 1.88)		1.34 (0.88 to 2.03)	
P-value	-	0.5268		0.1674	

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CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.1 Health-related quality-of-life endpoints - QLQ-MY20
16.2.6.1.2 Side-effects of treatment
16.2.6.1.2.6 Efficacy response data - Subgroup analyses by regulatory region
16.2.6.1.2.6.5 QLQ-MY20 - Time until permanent improvement by 10 pt in side-effects of treatment according to regulatory region (LOCF) - ITT population

	Western countries		Other countries		
	Kd (N=55)	**IKd (N=97)**	**Kd (N=68)**	**IKd (N=82)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	5 (9.1)	11 (11.3)	6 (8.8)	12 (14.6)	0.6659
Number (%) of patients censored	50 (90.9)	86 (88.7)	62 (91.2)	70 (85.4)	
Kaplan-Meier estimates of side-effects of treatment in months					
25% quantile (95% CI)	NC (NC to NC)	NC (20.731 to NC)	NC (NC to NC)	NC (18.760 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.6964		0.2883	
Hazard ratio (95% CI) vs Kd	-	1.23 (0.43 to 3.55)		1.69 (0.63 to 4.51)	
P-value	-	0.6970		0.2939	

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The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.1 Health-related quality-of-life endpoints - QLQ-MY20
16.2.6.1.2 Side-effects of treatment
16.2.6.1.2.6 Efficacy response data - Subgroup analyses by regulatory region
16.2.6.1.2.6.6 QLQ-MY20 - Time until permanent deterioration by 10 pt in side-effects of treatment according to regulatory region (LOCF) - ITT population

	Western countries		Other countries		
	Kd (N=55)	**IKd (N=97)**	**Kd (N=68)**	**IKd (N=82)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	18 (32.7)	26 (26.8)	16 (23.5)	21 (25.6)	0.4611
Number (%) of patients censored	37 (67.3)	71 (73.2)	52 (76.5)	61 (74.4)	
Kaplan-Meier estimates of side-effects of treatment in months					
25% quantile (95% CI)	15.15 (7.524 to 20.600)	19.25 (10.908 to NC)	20.76 (11.499 to NC)	18.14 (12.320 to NC)	
Median (95% CI)	NC (20.370 to NC)	NC (NC to NC)	NC (24.016 to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (24.016 to NC)	NC (NC to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.4632		0.7461	
Hazard ratio (95% CI) vs Kd	-	0.80 (0.44 to 1.46)		1.11 (0.58 to 2.13)	
P-value	-	0.4641		0.7462	

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The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.1 Health-related quality-of-life endpoints - QLQ-MY20
16.2.6.1.2 Side-effects of treatment
16.2.6.1.2.7 Efficacy response data - Subgroup analyses by baseline ECOG PS
16.2.6.1.2.7.3 QLQ-MY20 - Time to first improvement by 10 pt in side-effects of treatment according to baseline ECOG PS (LOCF) - ITT population

	0 or 1		>1		
	Kd (N=118)	**IKd (N=168)**	**Kd (N=5)**	**IKd (N=11)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	39 (33.1)	57 (33.9)	2 (40.0)	6 (54.5)	0.5028
Number (%) of patients censored	79 (66.9)	111 (66.1)	3 (60.0)	5 (45.5)	
Kaplan-Meier estimates of side-effects of treatment in months					
25% quantile (95% CI)	4.21 (1.906 to 14.850)	3.84 (2.825 to 11.499)	1.05 (0.986 to NC)	1.91 (0.986 to 3.877)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (0.986 to NC)	3.88 (0.986 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (0.986 to NC)	NC (1.938 to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.9851		0.5574	
Hazard ratio (95% CI) vs Kd	-	1.00 (0.66 to 1.50)		1.61 (0.32 to 7.99)	
P-value	-	0.9851		0.5611	

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The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.1 Health-related quality-of-life endpoints - QLQ-MY20
16.2.6.1.2 Side-effects of treatment
16.2.6.1.2.7 Efficacy response data - Subgroup analyses by baseline ECOG PS
16.2.6.1.2.7.4 QLQ-MY20 - Time to first deterioration by 10 pt in side-effects of treatment according to baseline ECOG PS (LOCF) - ITT population

	0 or 1		>1		
	Kd (N=118)	**IKd (N=168)**	**Kd (N=5)**	**IKd (N=11)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	60 (50.8)	103 (61.3)	3 (60.0)	5 (45.5)	0.5578
Number (%) of patients censored	58 (49.2)	65 (38.7)	2 (40.0)	6 (54.5)	
Kaplan-Meier estimates of side-effects of treatment in months					
25% quantile (95% CI)	1.97 (1.216 to 3.811)	2.04 (1.478 to 3.055)	6.80 (0.986 to 7.786)	2.99 (1.216 to 10.415)	
Median (95% CI)	13.54 (4.994 to NC)	6.97 (5.552 to 12.320)	7.79 (0.986 to NC)	10.41 (1.216 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (0.986 to NC)	NC (3.055 to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.1635		0.7537	
Hazard ratio (95% CI) vs Kd	-	1.25 (0.91 to 1.72)		0.79 (0.19 to 3.38)	
P-value	-	0.1644		0.7541	

A lower score represents a better level of quality of life. Clinical meaningful deterioration change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.1 Health-related quality-of-life endpoints - QLQ-MY20
16.2.6.1.2 Side-effects of treatment
16.2.6.1.2.7 Efficacy response data - Subgroup analyses by baseline ECOG PS
16.2.6.1.2.7.5 QLQ-MY20 - Time until permanent improvement by 10 pt in side-effects of treatment according to baseline ECOG PS (LOCF) - ITT population

	0 or 1		>1		
	Kd (N=118)	**IKd (N=168)**	**Kd (N=5)**	**IKd (N=11)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	11 (9.3)	21 (12.5)	0 (0.0)	2 (18.2)	0.9890
Number (%) of patients censored	107 (90.7)	147 (87.5)	5 (100.0)	9 (81.8)	
Kaplan-Meier estimates of side-effects of treatment in months					
25% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (1.906 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (1.906 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.4325		0.3043	
Hazard ratio (95% CI) vs Kd	-	1.34 (0.65 to 2.78)			
P-value	-	0.4341		0.9979	

A lower score represents a better level of quality of life. Clinical meaningful improvement change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.1 Health-related quality-of-life endpoints - QLQ-MY20
16.2.6.1.2 Side-effects of treatment
16.2.6.1.2.7 Efficacy response data - Subgroup analyses by baseline ECOG PS
16.2.6.1.2.7.6 QLQ-MY20 - Time until permanent deterioration by 10 pt in side-effects of treatment according to baseline ECOG PS (LOCF) - ITT population

	0 or 1		>1		
	Kd (N=118)	**IKd (N=168)**	**Kd (N=5)**	**IKd (N=11)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	32 (27.1)	45 (26.8)	2 (40.0)	2 (18.2)	0.2572
Number (%) of patients censored	86 (72.9)	123 (73.2)	3 (60.0)	9 (81.8)	
Kaplan-Meier estimates of side-effects of treatment in months					
25% quantile (95% CI)	20.30 (12.189 to 24.016)	18.79 (13.864 to NC)	7.29 (6.801 to NC)	NC (10.908 to NC)	
Median (95% CI)	NC (24.016 to NC)	NC (NC to NC)	NC (6.801 to NC)	NC (10.908 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (6.801 to NC)	NC (NC to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.9767		0.1618	
Hazard ratio (95% CI) vs Kd	-	0.99 (0.63 to 1.56)		0.26 (0.04 to 1.95)	
P-value	-	0.9767		0.1905	

A lower score represents a better level of quality of life. Clinical meaningful deterioration change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
PGM=DEVOPS/SAR650984/EFC15246/CIR_RWE/REPORT/PGM/eff_km_subgp_sr_sig_de_i_t.sas OUT=REPORT/OUTPUT/eff_km_my20_eff_detpl_ecog_de_i_t_x.rtf (07APR2021 14:44)

16.2.6.1 Health-related quality-of-life endpoints - QLQ-MY20
16.2.6.1.2 Side-effects of treatment
16.2.6.1.2.8 Efficacy response data - Subgroup analyses by ISS staging at SE
16.2.6.1.2.8.3 QLQ-MY20 - Time to first improvement by 10 pt in side-effects of treatment according to ISS staging at SE (LOCF) - ITT population

	I		II		III		
	Kd (N=71)	**IKd (N=89)**	**Kd (N=31)**	**IKd (N=63)**	**Kd (N=20)**	**IKd (N=26)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	25 (35.2)	27 (30.3)	8 (25.8)	25 (39.7)	7 (35.0)	10 (38.5)	0.4575
Number (%) of patients censored	46 (64.8)	62 (69.7)	23 (74.2)	38 (60.3)	13 (65.0)	16 (61.5)	
Kaplan-Meier estimates of side-effects of treatment in months							
25% quantile (95% CI)	4.96 (1.938 to 14.850)	7.43 (2.136 to NC)	4.21 (0.986 to NC)	3.75 (1.051 to 11.499)	1.08 (0.953 to NC)	2.10 (0.986 to 3.844)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (12.057 to NC)	NC (1.084 to NC)	NC (2.103 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Kd							
Log-Rank test p-value[a] vs Kd	-	0.5149		0.2797		0.8741	
Hazard ratio (95% CI) vs Kd	-	0.83 (0.48 to 1.44)		1.55 (0.70 to 3.43)		1.08 (0.41 to 2.85)	
P-value	-	0.5155		0.2838		0.8741	

A lower score represents a better level of quality of life. Clinical meaningful improvement change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
PGM=DEVOPS/SAR650984/EFC15246/CIR_RWE/REPORT/PGM/eff_km_subgp_sr_sig_de_i_t.sas OUT=REPORT/OUTPUT/eff_km_my20_eff_impl_seiss_de_i_t_x.rtf (07APR2021 14:44)

16.2.6.1 Health-related quality-of-life endpoints - QLQ-MY20
16.2.6.1.2 Side-effects of treatment
16.2.6.1.2.8 Efficacy response data - Subgroup analyses by ISS staging at SE
16.2.6.1.2.8.4 QLQ-MY20 - Time to first deterioration by 10 pt in side-effects of treatment according to ISS staging at SE (LOCF) - ITT population

	I		II		III		
	Kd (N=71)	**IKd (N=89)**	**Kd (N=31)**	**IKd (N=63)**	**Kd (N=20)**	**IKd (N=26)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	35 (49.3)	58 (65.2)	20 (64.5)	42 (66.7)	7 (35.0)	8 (30.8)	0.4049
Number (%) of patients censored	36 (50.7)	31 (34.8)	11 (35.5)	21 (33.3)	13 (65.0)	18 (69.2)	
Kaplan-Meier estimates of side-effects of treatment in months							
25% quantile (95% CI)	2.20 (1.906 to 4.238)	2.02 (1.150 to 3.055)	1.22 (0.986 to 4.304)	1.91 (1.051 to 2.990)	4.76 (0.986 to NC)	5.55 (0.986 to NC)	
Median (95% CI)	16.79 (4.830 to NC)	6.74 (4.665 to 11.400)	7.79 (1.873 to 15.540)	5.78 (3.220 to 13.996)	NC (4.764 to NC)	NC (5.552 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (17.971 to NC)	NC (10.185 to NC)	NC (13.996 to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Kd							
Log-Rank test p-value[a] vs Kd	-	0.0845		0.8823		0.8127	
Hazard ratio (95% CI) vs Kd	-	1.44 (0.95 to 2.20)		0.96 (0.56 to 1.64)		0.88 (0.32 to 2.44)	
P-value	-	0.0863		0.8814		0.8128	

A lower score represents a better level of quality of life. Clinical meaningful deterioration change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.1 Health-related quality-of-life endpoints - QLQ-MY20
16.2.6.1.2 Side-effects of treatment
16.2.6.1.2.8 Efficacy response data - Subgroup analyses by ISS staging at SE
16.2.6.1.2.8.5 QLQ-MY20 - Time until permanent improvement by 10 pt in side-effects of treatment according to ISS staging at SE (LOCF) - ITT population

	I		II		III		
	Kd (N=71)	**IKd (N=89)**	**Kd (N=31)**	**IKd (N=63)**	**Kd (N=20)**	**IKd (N=26)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	6 (8.5)	12 (13.5)	2 (6.5)	7 (11.1)	2 (10.0)	4 (15.4)	0.9922
Number (%) of patients censored	65 (91.5)	77 (86.5)	29 (93.5)	56 (88.9)	18 (90.0)	22 (84.6)	
Kaplan-Meier estimates of side-effects of treatment in months							
25% quantile (95% CI)	NC (NC to NC)	NC (20.534 to NC)	NC (15.047 to NC)	NC (20.731 to NC)	NC (2.891 to NC)	NC (1.413 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Kd							
Log-Rank test p-value[a] vs Kd	-	0.3224		0.5638		0.5138	
Hazard ratio (95% CI) vs Kd	-	1.63 (0.61 to 4.35)		1.58 (0.33 to 7.63)		1.75 (0.32 to 9.56)	
P-value	-	0.3273		0.5672		0.5193	

A lower score represents a better level of quality of life. Clinical meaningful improvement change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
PGM=DEVOPS/SAR650984/EFC15246/CIR_RWE/REPORT/PGM/eff_km_subgp_sr_sig_de_i_t.sas OUT=REPORT/OUTPUT/eff_km_my20_eff_imppl_seiss_de_i_t_x.rtf (07APR2021 14:44)

16.2.6.1 Health-related quality-of-life endpoints - QLQ-MY20
16.2.6.1.2 Side-effects of treatment
16.2.6.1.2.8 Efficacy response data - Subgroup analyses by ISS staging at SE
16.2.6.1.2.8.6 QLQ-MY20 - Time until permanent deterioration by 10 pt in side-effects of treatment according to ISS staging at SE (LOCF) - ITT population

	I		II		III		
	Kd (N=71)	**IKd (N=89)**	**Kd (N=31)**	**IKd (N=63)**	**Kd (N=20)**	**IKd (N=26)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	17 (23.9)	23 (25.8)	14 (45.2)	21 (33.3)	3 (15.0)	3 (11.5)	0.4363
Number (%) of patients censored	54 (76.1)	66 (74.2)	17 (54.8)	42 (66.7)	17 (85.0)	23 (88.5)	
Kaplan-Meier estimates of side-effects of treatment in months							
25% quantile (95% CI)	20.60 (15.146 to NC)	19.25 (9.955 to NC)	9.99 (1.248 to 18.300)	18.14 (6.538 to 20.238)	NC (2.957 to NC)	NC (0.986 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	24.02 (11.499 to 24.016)	NC (20.238 to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	24.02 (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Kd							
Log-Rank test p-value[a] vs Kd	-	0.6665		0.1882		0.7568	
Hazard ratio (95% CI) vs Kd	-	1.15 (0.61 to 2.15)		0.64 (0.32 to 1.25)		0.78 (0.16 to 3.86)	

A lower score represents a better level of quality of life. Clinical meaningful deterioration change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.1 Health-related quality-of-life endpoints - QLQ-MY20
16.2.6.1.2 Side-effects of treatment
16.2.6.1.2.9 Efficacy response data - Subgroup analyses by R-ISS stage at SE
16.2.6.1.2.9.3 QLQ-MY20 - Time to first improvement by 10 pt in side-effects of treatment according to R-ISS stage at SE (LOCF) - ITT population

	I or II		III		Not classified		
	Kd (N=103)	**IKd (N=155)**	**Kd (N=8)**	**IKd (N=16)**	**Kd (N=12)**	**IKd (N=8)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	30 (29.1)	52 (33.5)	4 (50.0)	7 (43.8)	7 (58.3)	4 (50.0)	0.9608
Number (%) of patients censored	73 (70.9)	103 (66.5)	4 (50.0)	9 (56.3)	5 (41.7)	4 (50.0)	
Kaplan-Meier estimates of side-effects of treatment in months							
25% quantile (95% CI)	6.51 (1.938 to NC)	3.88 (2.825 to 15.573)	1.05 (1.051 to 3.121)	1.94 (0.986 to 2.957)	2.35 (0.953 to 6.768)	2.83 (1.018 to 16.329)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	3.12 (1.051 to NC)	2.96 (1.906 to NC)	12.78 (0.986 to NC)	10.78 (1.018 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (1.084 to NC)	NC (2.957 to NC)	NC (6.768 to NC)	NC (2.825 to NC)	
Comparison vs. Kd							
Log-Rank test p-value[a] vs Kd	-	0.6290		0.7622		0.8742	
Hazard ratio (95% CI) vs Kd	-	1.12 (0.71 to 1.75)		0.83 (0.24 to 2.84)		1.10 (0.32 to 3.79)	
P-value	-	0.6292		0.7625		0.8742	

A lower score represents a better level of quality of life. Clinical meaningful improvement change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.1 Health-related quality-of-life endpoints - QLQ-MY20
16.2.6.1.2 Side-effects of treatment
16.2.6.1.2.9 Efficacy response data - Subgroup analyses by R-ISS stage at SE
16.2.6.1.2.9.4 QLQ-MY20 - Time to first deterioration by 10 pt in side-effects of treatment according to R-ISS stage at SE (LOCF) - ITT population

	I or II		III		Not classified		
	Kd (N=103)	**IKd (N=155)**	**Kd (N=8)**	**IKd (N=16)**	**Kd (N=12)**	**IKd (N=8)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	55 (53.4)	103 (66.5)	2 (25.0)	3 (18.8)	6 (50.0)	2 (25.0)	0.5525
Number (%) of patients censored	48 (46.6)	52 (33.5)	6 (75.0)	13 (81.3)	6 (50.0)	6 (75.0)	
Kaplan-Meier estimates of side-effects of treatment in months							
25% quantile (95% CI)	1.97 (1.216 to 3.811)	1.94 (1.183 to 2.891)	3.98 (1.117 to NC)	NC (1.216 to NC)	2.86 (1.084 to 6.472)	3.06 (1.018 to NC)	
Median (95% CI)	12.55 (4.994 to NC)	6.64 (4.797 to 9.199)	NC (1.117 to NC)	NC (10.415 to NC)	NC (1.150 to NC)	NC (1.018 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (17.971 to NC)	NC (NC to NC)	NC (NC to NC)	NC (6.472 to NC)	NC (3.055 to NC)	
Comparison vs. Kd							
Log-Rank test p-value[a] vs Kd	-	0.1144		0.6774		0.5943	
Hazard ratio (95% CI) vs Kd	-	1.30 (0.94 to 1.81)		0.68 (0.11 to 4.12)		0.65 (0.13 to 3.22)	
P-value	-	0.1155		0.6791		0.5973	

A lower score represents a better level of quality of life. Clinical meaningful deterioration change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.1 Health-related quality-of-life endpoints - QLQ-MY20
16.2.6.1.2 Side-effects of treatment
16.2.6.1.2.9 Efficacy response data - Subgroup analyses by R-ISS stage at SE
16.2.6.1.2.9.5 QLQ-MY20 - Time until permanent improvement by 10 pt in side-effects of treatment according to R-ISS stage at SE (LOCF) - ITT population

	I or II		III		Not classified		
	Kd (N=103)	**IKd (N=155)**	**Kd (N=8)**	**IKd (N=16)**	**Kd (N=12)**	**IKd (N=8)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	7 (6.8)	17 (11.0)	1 (12.5)	4 (25.0)	3 (25.0)	2 (25.0)	0.8705
Number (%) of patients censored	96 (93.2)	138 (89.0)	7 (87.5)	12 (75.0)	9 (75.0)	6 (75.0)	
Kaplan-Meier estimates of side-effects of treatment in months							
25% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (2.891 to NC)	15.41 (1.413 to NC)	NC (7.392 to NC)	10.18 (5.224 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (2.891 to NC)	NC (5.585 to NC)	NC (13.799 to NC)	NC (5.224 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (10.185 to NC)	
Comparison vs. Kd							
Log-Rank test p-value[a] vs Kd	-	0.3379		0.4249		0.4698	
Hazard ratio (95% CI) vs Kd	-	1.53 (0.64 to 3.70)		2.38 (0.26 to 21.50)		1.92 (0.32 to 11.60)	
P-value	-	0.3417		0.4390		0.4774	

A lower score represents a better level of quality of life. Clinical meaningful improvement change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.1 Health-related quality-of-life endpoints - QLQ-MY20
16.2.6.1.2 Side-effects of treatment
16.2.6.1.2.9 Efficacy response data - Subgroup analyses by R-ISS stage at SE
16.2.6.1.2.9.6 QLQ-MY20 - Time until permanent deterioration by 10 pt in side-effects of treatment according to R-ISS stage at SE (LOCF) - ITT population

	I or II		III		Not classified		
	Kd (N=103)	**IKd (N=155)**	**Kd (N=8)**	**IKd (N=16)**	**Kd (N=12)**	**IKd (N=8)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	32 (31.1)	45 (29.0)	1 (12.5)	2 (12.5)	1 (8.3)	0 (0.0)	0.9964
Number (%) of patients censored	71 (68.9)	110 (71.0)	7 (87.5)	14 (87.5)	11 (91.7)	8 (100.0)	
Kaplan-Meier estimates of side-effects of treatment in months							
25% quantile (95% CI)	16.99 (9.331 to 20.764)	18.76 (12.320 to 21.717)	NC (3.877 to NC)	NC (10.908 to NC)	NC (20.304 to NC)	NC (NC to NC)	
Median (95% CI)	NC (24.016 to NC)	NC (NC to NC)	NC (3.877 to NC)	NC (14.620 to NC)	NC (20.304 to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Kd							
Log-Rank test p-value[a] vs Kd	-	0.5949		0.9504		0.5930	
Hazard ratio (95% CI) vs Kd	-	0.88 (0.56 to 1.39)		0.93 (0.08 to 10.29)			
P-value	-	0.5951		0.9504		0.9988	

A lower score represents a better level of quality of life. Clinical meaningful deterioration change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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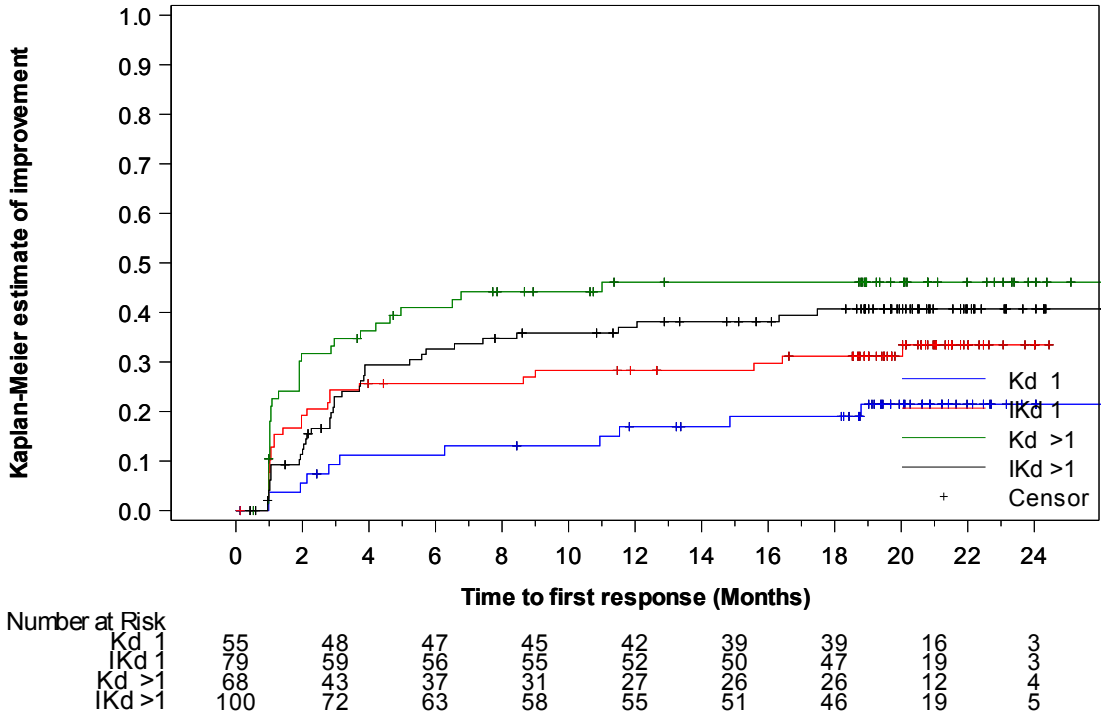
16.2.6.1 Health-related quality-of-life endpoints - QLQ-MY20
16.2.6.1.2 Side-effects of treatment
16.2.6.1.2.10 Efficacy response data - Subgroup analyses by nb of prior lines
16.2.6.1.2.10.3 QLQ-MY20 - Time to first improvement by 10 pt in side-effects of treatment according to nb of prior lines (LOCF) - ITT population

	1		>1		
	Kd (N=55)	**IKd (N=79)**	**Kd (N=68)**	**IKd (N=100)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	11 (20.0)	25 (31.6)	30 (44.1)	38 (38.0)	0.0480
Number (%) of patients censored	44 (80.0)	54 (68.4)	38 (55.9)	62 (62.0)	
Kaplan-Meier estimates of side-effects of treatment in months					
25% quantile (95% CI)	NC (6.275 to NC)	3.71 (1.150 to NC)	1.91 (1.018 to 3.745)	3.71 (2.267 to 6.571)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (4.205 to NC)	NC (16.329 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.1181		0.2501	
Hazard ratio (95% CI) vs Kd	-	1.75 (0.86 to 3.55)		0.76 (0.47 to 1.22)	
P-value	-	0.1230		0.2516	

A lower score represents a better level of quality of life. Clinical meaningful improvement change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
PGM=DEVOPS/SAR650984/EFC15246/CIR_RWE/REPORT/PGM/eff_km_subgp_sr_sig_de_i_t.sas OUT=REPORT/OUTPUT/eff_km_my20_eff_impl_plne_de_i_t_x.rtf (07APR2021 14:43)

16.2.6.1 Health-related quality-of-life endpoints - QLQ-MY20
16.2.6.1.2 Side-effects of treatment
16.2.6.1.2.10 Efficacy response data - Subgroup analyses by nb of prior lines
16.2.6.1.2.10.4 QLQ-MY20 - Time to first improvement by 10 pt in side-effects of treatment according to nb of prior lines - Kaplan-Meier curve (LOCF) - ITT population



A lower score represents a better level of quality of life. Clinical meaningful improvement change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
PGM=DEVOPS/SAR650984/EFC15246/CIR_RWE/REPORT/PGM/eff_qlq_km_subgp_de_i_f.sas OUT=REPORT/OUTPUT/eff_km_my20_eff_impl_plne_de_i_f_x.rtf (07APR2021 15:12)

16.2.6.1 Health-related quality-of-life endpoints - QLQ-MY20
16.2.6.1.2 Side-effects of treatment
16.2.6.1.2.10 Efficacy response data - Subgroup analyses by nb of prior lines
16.2.6.1.2.10.5 QLQ-MY20 - Time to first deterioration by 10 pt in side-effects of treatment according to nb of prior lines (LOCF) - ITT population

	1		>1		
	Kd (N=55)	**IKd (N=79)**	**Kd (N=68)**	**IKd (N=100)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	31 (56.4)	51 (64.6)	32 (47.1)	57 (57.0)	0.8583
Number (%) of patients censored	24 (43.6)	28 (35.4)	36 (52.9)	43 (43.0)	
Kaplan-Meier estimates of side-effects of treatment in months					
25% quantile (95% CI)	1.97 (1.084 to 2.891)	1.91 (1.117 to 3.055)	3.06 (1.216 to 6.801)	2.79 (1.183 to 3.844)	
Median (95% CI)	6.47 (2.891 to NC)	6.70 (3.811 to 10.185)	16.16 (7.425 to NC)	9.53 (5.585 to 17.971)	
75% quantile (95% CI)	NC (NC to NC)	NC (13.207 to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.4784		0.2895	
Hazard ratio (95% CI) vs Kd	-	1.18 (0.75 to 1.84)		1.26 (0.82 to 1.95)	
P-value	-	0.4789		0.2906	

A lower score represents a better level of quality of life. Clinical meaningful deterioration change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
PGM=DEVOPS/SAR650984/EFC15246/CIR_RWE/REPORT/PGM/eff_km_subgp_sr_sig_de_i_t.sas OUT=REPORT/OUTPUT/eff_km_my20_eff_detl_plne_de_i_t_x.rtf (07APR2021 14:43)

16.2.6.1 Health-related quality-of-life endpoints - QLQ-MY20
16.2.6.1.2 Side-effects of treatment
16.2.6.1.2.10 Efficacy response data - Subgroup analyses by nb of prior lines
16.2.6.1.2.10.6 QLQ-MY20 - Time until permanent improvement by 10 pt in side-effects of treatment according to nb of prior lines (LOCF) - ITT population

	1		>1		
	Kd (N=55)	**IKd (N=79)**	**Kd (N=68)**	**IKd (N=100)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	3 (5.5)	10 (12.7)	8 (11.8)	13 (13.0)	0.3167
Number (%) of patients censored	52 (94.5)	69 (87.3)	60 (88.2)	87 (87.0)	
Kaplan-Meier estimates of side-effects of treatment in months					
25% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (19.450 to NC)	NC (20.534 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.1706		0.8672	
Hazard ratio (95% CI) vs Kd	-	2.40 (0.66 to 8.71)		1.08 (0.45 to 2.60)	
P-value	-	0.1843		0.8673	

A lower score represents a better level of quality of life. Clinical meaningful improvement change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
PGM=DEVOPS/SAR650984/EFC15246/CIR_RWE/REPORT/PGM/eff_km_subgp_sr_sig_de_i_t.sas OUT=REPORT/OUTPUT/eff_km_my20_eff_imppl_plne_de_i_t_x.rtf (07APR2021 14:44)

16.2.6.1 Health-related quality-of-life endpoints - QLQ-MY20
16.2.6.1.2 Side-effects of treatment
16.2.6.1.2.10 Efficacy response data - Subgroup analyses by nb of prior lines
16.2.6.1.2.10.7 QLQ-MY20 - Time until permanent deterioration by 10 pt in side-effects of treatment according to nb of prior lines (LOCF) - ITT population

	1		>1		
	Kd (N=55)	**IKd (N=79)**	**Kd (N=68)**	**IKd (N=100)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	17 (30.9)	27 (34.2)	17 (25.0)	20 (20.0)	0.3723
Number (%) of patients censored	38 (69.1)	52 (65.8)	51 (75.0)	80 (80.0)	
Kaplan-Meier estimates of side-effects of treatment in months					
25% quantile (95% CI)	18.30 (3.877 to 24.016)	14.62 (6.735 to 19.877)	19.15 (9.988 to NC)	21.72 (14.193 to NC)	
Median (95% CI)	24.02 (24.016 to NC)	NC (20.238 to NC)	NC (21.224 to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (24.016 to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.6844		0.4014	
Hazard ratio (95% CI) vs Kd	-	1.13 (0.62 to 2.08)		0.76 (0.40 to 1.45)	
P-value	-	0.6846		0.4029	

A lower score represents a better level of quality of life. Clinical meaningful deterioration change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
PGM=DEVOPS/SAR650984/EFC15246/CIR_RWE/REPORT/PGM/eff_km_subgp_sr_sig_de_i_t.sas OUT=REPORT/OUTPUT/eff_km_my20_eff_detpl_plne_de_i_t_x.rtf (07APR2021 14:44)

16.2.6.1 Health-related quality-of-life endpoints - QLQ-MY20
16.2.6.1.2 Side-effects of treatment
16.2.6.1.2.11 Efficacy response data - Subgroup analyses by cytogenetic abnormality
16.2.6.1.2.11.3 QLQ-MY20 - Time to first improvement by 10 pt in side-effects of treatment according to cytogenetic abnormality (LOCF) - ITT population

	At least one		None		
	Kd (N=31)	**IKd (N=42)**	**Kd (N=77)**	**IKd (N=114)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	14 (45.2)	17 (40.5)	20 (26.0)	37 (32.5)	0.4049
Number (%) of patients censored	17 (54.8)	25 (59.5)	57 (74.0)	77 (67.5)	
Kaplan-Meier estimates of side-effects of treatment in months					
25% quantile (95% CI)	2.86 (1.051 to 4.205)	1.97 (1.018 to 7.425)	11.53 (1.906 to NC)	3.88 (2.825 to 16.427)	
Median (95% CI)	NC (3.121 to NC)	NC (5.585 to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.6855		0.4193	
Hazard ratio (95% CI) vs Kd	-	0.86 (0.43 to 1.75)		1.25 (0.73 to 2.16)	
P-value	-	0.6858		0.4203	

A lower score represents a better level of quality of life. Clinical meaningful improvement change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
PGM=DEVOPS/SAR650984/EFC15246/CIR_RWE/REPORT/PGM/eff_km_subgp_sr_sig_de_i_t.sas OUT=REPORT/OUTPUT/eff_km_my20_eff_impl_cyto_de_i_t_x.rtf (07APR2021 14:43)

16.2.6.1 Health-related quality-of-life endpoints - QLQ-MY20
16.2.6.1.2 Side-effects of treatment
16.2.6.1.2.11 Efficacy response data - Subgroup analyses by cytogenetic abnormality
16.2.6.1.2.11.4 QLQ-MY20 - Time to first deterioration by 10 pt in side-effects of treatment according to cytogenetic abnormality (LOCF) - ITT population

	At least one		None		
	Kd (N=31)	**IKd (N=42)**	**Kd (N=77)**	**IKd (N=114)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	11 (35.5)	21 (50.0)	45 (58.4)	78 (68.4)	0.7249
Number (%) of patients censored	20 (64.5)	21 (50.0)	32 (41.6)	36 (31.6)	
Kaplan-Meier estimates of side-effects of treatment in months					
25% quantile (95% CI)	4.83 (1.873 to NC)	2.92 (1.084 to 7.655)	1.87 (1.084 to 2.201)	1.87 (1.150 to 2.858)	
Median (95% CI)	NC (5.618 to NC)	15.51 (6.735 to NC)	10.12 (4.041 to 16.789)	5.65 (3.844 to 7.622)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (12.320 to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.3346		0.2592	
Hazard ratio (95% CI) vs Kd	-	1.43 (0.69 to 2.97)		1.24 (0.86 to 1.78)	
P-value	-	0.3372		0.2601	

A lower score represents a better level of quality of life. Clinical meaningful deterioration change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.1 Health-related quality-of-life endpoints - QLQ-MY20
16.2.6.1.2 Side-effects of treatment
16.2.6.1.2.11 Efficacy response data - Subgroup analyses by cytogenetic abnormality
16.2.6.1.2.11.5 QLQ-MY20 - Time until permanent improvement by 10 pt in side-effects of treatment according to cytogenetic abnormality (LOCF) - ITT population

	At least one		None		
	Kd (N=31)	**IKd (N=42)**	**Kd (N=77)**	**IKd (N=114)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	3 (9.7)	5 (11.9)	5 (6.5)	14 (12.3)	0.6525
Number (%) of patients censored	28 (90.3)	37 (88.1)	72 (93.5)	100 (87.7)	
Kaplan-Meier estimates of side-effects of treatment in months					
25% quantile (95% CI)	NC (19.450 to NC)	NC (18.760 to NC)	NC (NC to NC)	NC (20.731 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.7729		0.2299	
Hazard ratio (95% CI) vs Kd	-	1.23 (0.29 to 5.17)		1.85 (0.67 to 5.14)	
P-value	-	0.7733		0.2373	

A lower score represents a better level of quality of life. Clinical meaningful improvement change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.1 Health-related quality-of-life endpoints - QLQ-MY20
16.2.6.1.2 Side-effects of treatment
16.2.6.1.2.11 Efficacy response data - Subgroup analyses by cytogenetic abnormality
16.2.6.1.2.11.6 QLQ-MY20 - Time until permanent deterioration by 10 pt in side-effects of treatment according to cytogenetic abnormality (LOCF) - ITT population

	At least one		None		
	Kd (N=31)	**IKd (N=42)**	**Kd (N=77)**	**IKd (N=114)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	6 (19.4)	12 (28.6)	24 (31.2)	34 (29.8)	0.4733
Number (%) of patients censored	25 (80.6)	30 (71.4)	53 (68.8)	80 (70.2)	
Kaplan-Meier estimates of side-effects of treatment in months					
25% quantile (95% CI)	NC (7.786 to NC)	15.70 (6.407 to NC)	16.99 (8.444 to 21.224)	17.77 (10.908 to 21.717)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	24.02 (21.224 to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (24.016 to NC)	NC (NC to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.5039		0.8263	
Hazard ratio (95% CI) vs Kd	-	1.39 (0.52 to 3.72)		0.94 (0.56 to 1.59)	
P-value	-	0.5059		0.8253	

A lower score represents a better level of quality of life. Clinical meaningful deterioration change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.1 Health-related quality-of-life endpoints - QLQ-MY20
16.2.6.1.2 Side-effects of treatment
16.2.6.1.2.12 Efficacy response data - Subgroup analyses by MM type at SE
16.2.6.1.2.12.3 QLQ-MY20 - Time to first improvement by 10 pt in side-effects of treatment according to MM type at SE (LOCF) - ITT population

	IgG		Non-IgG		
	Kd (N=85)	**IKd (N=126)**	**Kd (N=38)**	**IKd (N=53)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	27 (31.8)	47 (37.3)	14 (36.8)	16 (30.2)	0.1756
Number (%) of patients censored	58 (68.2)	79 (62.7)	24 (63.2)	37 (69.8)	
Kaplan-Meier estimates of side-effects of treatment in months					
25% quantile (95% CI)	6.51 (1.906 to NC)	2.92 (1.971 to 6.571)	1.94 (0.986 to 4.961)	8.64 (2.825 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (2.793 to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.3730		0.3041	
Hazard ratio (95% CI) vs Kd	-	1.24 (0.77 to 1.99)		0.69 (0.34 to 1.41)	
P-value	-	0.3740		0.3069	

A lower score represents a better level of quality of life. Clinical meaningful improvement change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.1 Health-related quality-of-life endpoints - QLQ-MY20
16.2.6.1.2 Side-effects of treatment
16.2.6.1.2.12 Efficacy response data - Subgroup analyses by MM type at SE
16.2.6.1.2.12.4 QLQ-MY20 - Time to first deterioration by 10 pt in side-effects of treatment according to MM type at SE (LOCF) - ITT population

	IgG		Non-IgG		
	Kd (N=85)	**IKd (N=126)**	**Kd (N=38)**	**IKd (N=53)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	46 (54.1)	77 (61.1)	17 (44.7)	31 (58.5)	0.8585
Number (%) of patients censored	39 (45.9)	49 (38.9)	21 (55.3)	22 (41.5)	
Kaplan-Meier estimates of side-effects of treatment in months					
25% quantile (95% CI)	1.94 (1.084 to 2.891)	1.91 (1.150 to 2.793)	3.06 (1.873 to 8.312)	3.84 (1.873 to 5.618)	
Median (95% CI)	12.55 (4.304 to NC)	6.97 (4.205 to 12.320)	15.54 (5.618 to NC)	7.66 (5.585 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (15.507 to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.3227		0.4030	
Hazard ratio (95% CI) vs Kd	-	1.20 (0.83 to 1.73)		1.29 (0.71 to 2.33)	
P-value	-	0.3233		0.4043	

A lower score represents a better level of quality of life. Clinical meaningful deterioration change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.1 Health-related quality-of-life endpoints - QLQ-MY20
16.2.6.1.2 Side-effects of treatment
16.2.6.1.2.12 Efficacy response data - Subgroup analyses by MM type at SE
16.2.6.1.2.12.5 QLQ-MY20 - Time until permanent improvement by 10 pt in side-effects of treatment according to MM type at SE (LOCF) - ITT population

	IgG		Non-IgG		
	Kd (N=85)	**IKd (N=126)**	**Kd (N=38)**	**IKd (N=53)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	8 (9.4)	17 (13.5)	3 (7.9)	6 (11.3)	0.9693
Number (%) of patients censored	77 (90.6)	109 (86.5)	35 (92.1)	47 (88.7)	
Kaplan-Meier estimates of side-effects of treatment in months					
25% quantile (95% CI)	NC (NC to NC)	NC (20.731 to NC)	NC (NC to NC)	NC (20.304 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.3819		0.6249	
Hazard ratio (95% CI) vs Kd	-	1.45 (0.63 to 3.36)		1.41 (0.35 to 5.64)	
P-value	-	0.3847		0.6266	

A lower score represents a better level of quality of life. Clinical meaningful improvement change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
PGM=DEVOPS/SAR650984/EFC15246/CIR_RWE/REPORT/PGM/eff_km_subgp_sr_sig_de_i_t.sas OUT=REPORT/OUTPUT/eff_km_my20_eff_imppl_semm_de_i_t_x.rtf (07APR2021 14:44)

16.2.6.1 Health-related quality-of-life endpoints - QLQ-MY20
16.2.6.1.2 Side-effects of treatment
16.2.6.1.2.12 Efficacy response data - Subgroup analyses by MM type at SE
16.2.6.1.2.12.6 QLQ-MY20 - Time until permanent deterioration by 10 pt in side-effects of treatment according to MM type at SE (LOCF) - ITT population

	IgG		Non-IgG		
	Kd (N=85)	**IKd (N=126)**	**Kd (N=38)**	**IKd (N=53)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	23 (27.1)	34 (27.0)	11 (28.9)	13 (24.5)	0.5144
Number (%) of patients censored	62 (72.9)	92 (73.0)	27 (71.1)	40 (75.5)	
Kaplan-Meier estimates of side-effects of treatment in months					
25% quantile (95% CI)	20.37 (9.495 to NC)	19.25 (11.926 to NC)	15.67 (6.801 to 24.016)	18.76 (6.735 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	24.02 (18.924 to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (24.016 to NC)	NC (NC to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.8667		0.5923	
Hazard ratio (95% CI) vs Kd	-	1.05 (0.62 to 1.78)		0.80 (0.36 to 1.80)	
P-value	-	0.8672		0.5930	

A lower score represents a better level of quality of life. Clinical meaningful deterioration change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
PGM=DEVOPS/SAR650984/EFC15246/CIR_RWE/REPORT/PGM/eff_km_subgp_sr_sig_de_i_t.sas OUT=REPORT/OUTPUT/eff_km_my20_eff_detpl_semm_de_i_t_x.rtf (07APR2021 14:44)

16.2.6.1 Health-related quality-of-life endpoints - QLQ-MY20
16.2.6.1.2 Side-effects of treatment
16.2.6.1.2.13 Efficacy response data - Subgroup analyses by previous autologous stem-cell
16.2.6.1.2.13.3 QLQ-MY20 - Time to first improvement by 10 pt in side-effects of treatment according to previous autologous stem-cell (LOCF) - ITT population

	Yes		No		
	Kd (N=69)	**IKd (N=116)**	**Kd (N=54)**	**IKd (N=63)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	21 (30.4)	38 (32.8)	20 (37.0)	25 (39.7)	0.9474
Number (%) of patients censored	48 (69.6)	78 (67.2)	34 (63.0)	38 (60.3)	
Kaplan-Meier estimates of side-effects of treatment in months					
25% quantile (95% CI)	4.21 (1.906 to NC)	3.19 (2.136 to 17.478)	3.75 (1.018 to 11.006)	3.88 (1.413 to 11.499)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (11.006 to NC)	NC (11.499 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.7758		0.8576	
Hazard ratio (95% CI) vs Kd	-	1.08 (0.63 to 1.84)		1.06 (0.59 to 1.90)	
P-value	-	0.7759		0.8580	

A lower score represents a better level of quality of life. Clinical meaningful improvement change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.1 Health-related quality-of-life endpoints - QLQ-MY20
16.2.6.1.2 Side-effects of treatment
16.2.6.1.2.13 Efficacy response data - Subgroup analyses by previous autologous stem-cell
16.2.6.1.2.13.4 QLQ-MY20 - Time to first deterioration by 10 pt in side-effects of treatment according to previous autologous stem-cell (LOCF) - ITT population

	Yes		No		
	Kd (N=69)	**IKd (N=116)**	**Kd (N=54)**	**IKd (N=63)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	32 (46.4)	75 (64.7)	31 (57.4)	33 (52.4)	0.0820
Number (%) of patients censored	37 (53.6)	41 (35.3)	23 (42.6)	30 (47.6)	
Kaplan-Meier estimates of side-effects of treatment in months					
25% quantile (95% CI)	2.43 (1.084 to 4.665)	2.00 (1.511 to 2.858)	2.00 (1.216 to 2.891)	3.02 (1.117 to 5.125)	
Median (95% CI)	NC (5.618 to NC)	6.64 (4.665 to 10.415)	10.12 (2.891 to NC)	11.40 (5.125 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (15.507 to NC)	NC (16.789 to NC)	NC (NC to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.0405		0.5912	
Hazard ratio (95% CI) vs Kd	-	1.54 (1.02 to 2.33)		0.87 (0.54 to 1.43)	
P-value	-	0.0421		0.5915	
Hazard ratio inverted (95% CI) vs IKd		-		1.14 (0.70 to 1.87)	

A lower score represents a better level of quality of life. Clinical meaningful deterioration change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.1 Health-related quality-of-life endpoints - QLQ-MY20
16.2.6.1.2 Side-effects of treatment
16.2.6.1.2.13 Efficacy response data - Subgroup analyses by previous autologous stem-cell
16.2.6.1.2.13.5 QLQ-MY20 - Time until permanent improvement by 10 pt in side-effects of treatment according to previous autologous stem-cell (LOCF) - ITT population

	Yes		No		
	Kd (N=69)	**IKd (N=116)**	**Kd (N=54)**	**IKd (N=63)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	4 (5.8)	15 (12.9)	7 (13.0)	8 (12.7)	0.2578
Number (%) of patients censored	65 (94.2)	101 (87.1)	47 (87.0)	55 (87.3)	
Kaplan-Meier estimates of side-effects of treatment in months					
25% quantile (95% CI)	NC (NC to NC)	NC (20.534 to NC)	NC (15.047 to NC)	NC (20.731 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.1283		0.9538	
Hazard ratio (95% CI) vs Kd	-	2.30 (0.76 to 6.93)		0.97 (0.35 to 2.68)	
P-value	-	0.1394		0.9537	

A lower score represents a better level of quality of life. Clinical meaningful improvement change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.1 Health-related quality-of-life endpoints - QLQ-MY20
16.2.6.1.2 Side-effects of treatment
16.2.6.1.2.13 Efficacy response data - Subgroup analyses by previous autologous stem-cell
16.2.6.1.2.13.6 QLQ-MY20 - Time until permanent deterioration by 10 pt in side-effects of treatment according to previous autologous stem-cell (LOCF) - ITT population

	Yes		No		
	Kd (N=69)	**IKd (N=116)**	**Kd (N=54)**	**IKd (N=63)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	15 (21.7)	29 (25.0)	19 (35.2)	18 (28.6)	0.3328
Number (%) of patients censored	54 (78.3)	87 (75.0)	35 (64.8)	45 (71.4)	
Kaplan-Meier estimates of side-effects of treatment in months					
25% quantile (95% CI)	20.76 (13.602 to NC)	19.25 (11.926 to NC)	15.15 (8.312 to 20.304)	18.14 (7.984 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	24.02 (18.924 to NC)	NC (21.717 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (24.016 to NC)	NC (NC to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.5699		0.4166	
Hazard ratio (95% CI) vs Kd	-	1.20 (0.64 to 2.23)		0.77 (0.40 to 1.46)	
P-value	-	0.5705		0.4180	

A lower score represents a better level of quality of life. Clinical meaningful deterioration change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.1 Health-related quality-of-life endpoints - QLQ-MY20
16.2.6.1.2 Side-effects of treatment
16.2.6.1.2.14 Efficacy response data - Subgroup analyses by baseline eGFR (MDRD)
16.2.6.1.2.14.3 QLQ-MY20 - Time to first improvement by 10 pt in side-effects of treatment according to baseline eGFR (MDRD) (LOCF) - ITT population

	>=60 mL/min/1.73m2		<60 mL/min/1.73m2		
	Kd (N=93)	**IKd (N=122)**	**Kd (N=18)**	**IKd (N=43)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	31 (33.3)	41 (33.6)	8 (44.4)	17 (39.5)	0.4517
Number (%) of patients censored	62 (66.7)	81 (66.4)	10 (55.6)	26 (60.5)	
Kaplan-Meier estimates of side-effects of treatment in months					
25% quantile (95% CI)	4.19 (1.906 to 14.850)	3.75 (2.136 to 11.499)	1.97 (0.986 to 18.793)	2.96 (1.051 to 16.427)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	18.79 (1.906 to NC)	NC (12.057 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (18.793 to NC)	NC (NC to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.8705		0.4422	
Hazard ratio (95% CI) vs Kd	-	1.04 (0.65 to 1.66)		0.72 (0.31 to 1.67)	
P-value	-	0.8708		0.4441	

A lower score represents a better level of quality of life. Clinical meaningful improvement change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.1 Health-related quality-of-life endpoints - QLQ-MY20
16.2.6.1.2 Side-effects of treatment
16.2.6.1.2.14 Efficacy response data - Subgroup analyses by baseline eGFR (MDRD)
16.2.6.1.2.14.4 QLQ-MY20 - Time to first deterioration by 10 pt in side-effects of treatment according to baseline eGFR (MDRD) (LOCF) - ITT population

	>=60 mL/min/1.73m2		<60 mL/min/1.73m2		
	Kd (N=93)	**IKd (N=122)**	**Kd (N=18)**	**IKd (N=43)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	48 (51.6)	79 (64.8)	9 (50.0)	25 (58.1)	0.4643
Number (%) of patients censored	45 (48.4)	43 (35.2)	9 (50.0)	18 (41.9)	
Kaplan-Meier estimates of side-effects of treatment in months					
25% quantile (95% CI)	1.95 (1.216 to 2.891)	1.91 (1.150 to 2.924)	4.04 (1.084 to 11.762)	2.86 (1.051 to 5.552)	
Median (95% CI)	15.54 (4.665 to NC)	6.64 (4.665 to 10.415)	11.76 (4.041 to NC)	7.62 (3.844 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (15.507 to NC)	NC (11.762 to NC)	NC (NC to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.0510		0.8892	
Hazard ratio (95% CI) vs Kd	-	1.43 (1.00 to 2.05)		1.06 (0.49 to 2.27)	
P-value	-	0.0522		0.8892	

A lower score represents a better level of quality of life. Clinical meaningful deterioration change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.1 Health-related quality-of-life endpoints - QLQ-MY20
16.2.6.1.2 Side-effects of treatment
16.2.6.1.2.14 Efficacy response data - Subgroup analyses by baseline eGFR (MDRD)
16.2.6.1.2.14.5 QLQ-MY20 - Time until permanent improvement by 10 pt in side-effects of treatment according to baseline eGFR (MDRD) (LOCF) - ITT population

	>=60 mL/min/1.73m2		<60 mL/min/1.73m2		
	Kd (N=93)	**IKd (N=122)**	**Kd (N=18)**	**IKd (N=43)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	7 (7.5)	14 (11.5)	2 (11.1)	6 (14.0)	0.5798
Number (%) of patients censored	86 (92.5)	108 (88.5)	16 (88.9)	37 (86.0)	
Kaplan-Meier estimates of side-effects of treatment in months					
25% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (2.891 to NC)	NC (20.304 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.2796		0.9570	
Hazard ratio (95% CI) vs Kd	-	1.64 (0.66 to 4.07)		0.96 (0.19 to 4.75)	
P-value	-	0.2846		0.9570	

A lower score represents a better level of quality of life. Clinical meaningful improvement change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.1 Health-related quality-of-life endpoints - QLQ-MY20
16.2.6.1.2 Side-effects of treatment
16.2.6.1.2.14 Efficacy response data - Subgroup analyses by baseline eGFR (MDRD)
16.2.6.1.2.14.6 QLQ-MY20 - Time until permanent deterioration by 10 pt in side-effects of treatment according to baseline eGFR (MDRD) (LOCF) - ITT population

	>=60 mL/min/1.73m2		<60 mL/min/1.73m2		
	Kd (N=93)	**IKd (N=122)**	**Kd (N=18)**	**IKd (N=43)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	28 (30.1)	32 (26.2)	2 (11.1)	12 (27.9)	0.3227
Number (%) of patients censored	65 (69.9)	90 (73.8)	16 (88.9)	31 (72.1)	
Kaplan-Meier estimates of side-effects of treatment in months					
25% quantile (95% CI)	20.30 (9.988 to 21.224)	18.79 (13.864 to NC)	NC (4.041 to NC)	19.88 (6.538 to NC)	
Median (95% CI)	NC (24.016 to NC)	NC (NC to NC)	NC (NC to NC)	NC (19.877 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.7906		0.3424	
Hazard ratio (95% CI) vs Kd	-	0.93 (0.56 to 1.55)		2.04 (0.45 to 9.11)	
P-value	-	0.7901		0.3524	

A lower score represents a better level of quality of life. Clinical meaningful deterioration change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.1 Health-related quality-of-life endpoints - QLQ-MY20
16.2.6.1.2 Side-effects of treatment
16.2.6.1.2.15 Efficacy response data - Subgroup analyses by previous treatment with PI
16.2.6.1.2.15.3 QLQ-MY20 - Time to first improvement by 10 pt in side-effects of treatment according to previous treatment with PI (LOCF) - ITT population

	Yes		No		
	Kd (N=47)	**IKd (N=81)**	**Kd (N=76)**	**IKd (N=98)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	11 (23.4)	34 (42.0)	30 (39.5)	29 (29.6)	0.0126
Number (%) of patients censored	36 (76.6)	47 (58.0)	46 (60.5)	69 (70.4)	
Kaplan-Meier estimates of side-effects of treatment in months					
25% quantile (95% CI)	NC (1.906 to NC)	2.83 (1.413 to 5.224)	2.86 (1.051 to 6.768)	5.72 (2.825 to NC)	
Median (95% CI)	NC (NC to NC)	NC (9.002 to NC)	NC (11.532 to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.0441		0.1354	
Hazard ratio (95% CI) vs Kd	-	1.98 (1.00 to 3.92)		0.68 (0.41 to 1.13)	
P-value	-	0.0483		0.1378	
Hazard ratio inverted (95% CI) vs IKd		-		1.47 (0.88 to 2.45)	

A lower score represents a better level of quality of life. Clinical meaningful improvement change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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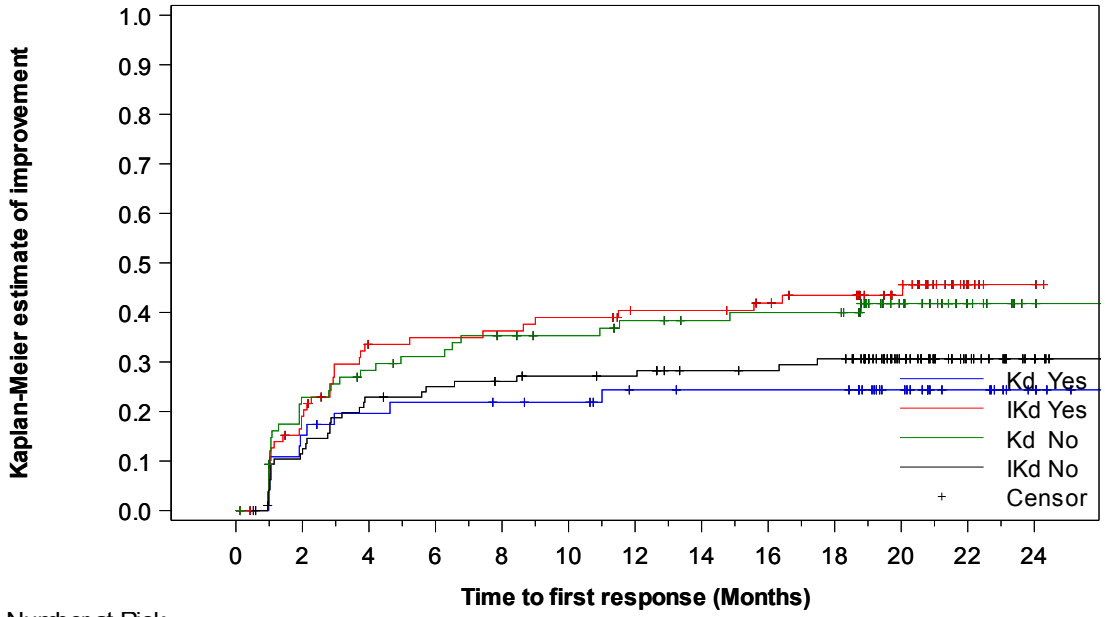
16.2.6.1 Health-related quality-of-life endpoints - QLQ-MY20
16.2.6.1.2 Side-effects of treatment
16.2.6.1.2.15 Efficacy response data - Subgroup analyses by previous treatment with PI
16.2.6.1.2.15.4 QLQ-MY20 - Time to first improvement by 10 pt in side-effects of treatment according to previous treatment with PI - Kaplan-Meier curve (LOCF) - ITT population



Number at Risk

Kd Yes	47	36	35	33	29	28	28	12	5
IKd Yes	81	53	48	46	41	40	35	14	2
Kd No	76	55	49	43	40	37	37	16	2
IKd No	98	78	71	67	66	61	58	24	6

A lower score represents a better level of quality of life. Clinical meaningful improvement change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
PGM=DEVOPS/SAR650984/EFC15246/CIR_RWE/REPORT/PGM/eff_qlq_km_subgp_de_i_f.sas OUT=REPORT/OUTPUT/eff_km_my20_eff_impl_pi_de_i_f_x.rtf (07APR2021 15:02)

16.2.6.1 Health-related quality-of-life endpoints - QLQ-MY20
16.2.6.1.2 Side-effects of treatment
16.2.6.1.2.15 Efficacy response data - Subgroup analyses by previous treatment with PI
16.2.6.1.2.15.5 QLQ-MY20 - Time to first deterioration by 10 pt in side-effects of treatment according to previous treatment with PI (LOCF) - ITT population

	Yes		No		
	Kd (N=47)	**IKd (N=81)**	**Kd (N=76)**	**IKd (N=98)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	27 (57.4)	47 (58.0)	36 (47.4)	61 (62.2)	0.3500
Number (%) of patients censored	20 (42.6)	34 (42.0)	40 (52.6)	37 (37.8)	
Kaplan-Meier estimates of side-effects of treatment in months					
25% quantile (95% CI)	1.97 (1.216 to 4.830)	2.10 (1.150 to 3.713)	2.20 (1.117 to 4.304)	2.04 (1.183 to 3.220)	
Median (95% CI)	10.12 (2.891 to NC)	7.43 (4.665 to 17.971)	16.79 (4.764 to NC)	6.97 (4.698 to 12.682)	
75% quantile (95% CI)	NC (15.540 to NC)	NC (NC to NC)	NC (NC to NC)	NC (18.760 to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.9080		0.1162	
Hazard ratio (95% CI) vs Kd	-	1.03 (0.64 to 1.65)		1.39 (0.92 to 2.10)	
P-value	-	0.9083		0.1179	

A lower score represents a better level of quality of life. Clinical meaningful deterioration change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
PGM=DEVOPS/SAR650984/EFC15246/CIR_RWE/REPORT/PGM/eff_km_subgp_sr_sig_de_i_t.sas OUT=REPORT/OUTPUT/eff_km_my20_eff_detl_pi_de_i_t_x.rtf (07APR2021 14:43)

16.2.6.1 Health-related quality-of-life endpoints - QLQ-MY20
16.2.6.1.2 Side-effects of treatment
16.2.6.1.2.15 Efficacy response data - Subgroup analyses by previous treatment with PI
16.2.6.1.2.15.6 QLQ-MY20 - Time until permanent improvement by 10 pt in side-effects of treatment according to previous treatment with PI (LOCF) - ITT population

	Yes		No		
	Kd (N=47)	**IKd (N=81)**	**Kd (N=76)**	**IKd (N=98)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	4 (8.5)	14 (17.3)	7 (9.2)	9 (9.2)	0.2967
Number (%) of patients censored	43 (91.5)	67 (82.7)	69 (90.8)	89 (90.8)	
Kaplan-Meier estimates of side-effects of treatment in months					
25% quantile (95% CI)	NC (19.450 to NC)	NC (18.136 to NC)	NC (NC to NC)	NC (NC to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.1688		0.9524	
Hazard ratio (95% CI) vs Kd	-	2.14 (0.70 to 6.51)		0.97 (0.36 to 2.61)	
P-value	-	0.1791		0.9523	

A lower score represents a better level of quality of life. Clinical meaningful improvement change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
PGM=DEVOPS/SAR650984/EFC15246/CIR_RWE/REPORT/PGM/eff_km_subgp_sr_sig_de_i_t.sas OUT=REPORT/OUTPUT/eff_km_my20_eff_imppl_pi_de_i_t_x.rtf (07APR2021 14:44)

16.2.6.1 Health-related quality-of-life endpoints - QLQ-MY20
16.2.6.1.2 Side-effects of treatment
16.2.6.1.2.15 Efficacy response data - Subgroup analyses by previous treatment with PI
16.2.6.1.2.15.7 QLQ-MY20 - Time until permanent deterioration by 10 pt in side-effects of treatment according to previous treatment with PI (LOCF) - ITT population

	Yes		No		
	Kd (N=47)	**IKd (N=81)**	**Kd (N=76)**	**IKd (N=98)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	14 (29.8)	19 (23.5)	20 (26.3)	28 (28.6)	0.4784
Number (%) of patients censored	33 (70.2)	62 (76.5)	56 (73.7)	70 (71.4)	
Kaplan-Meier estimates of side-effects of treatment in months					
25% quantile (95% CI)	18.30 (9.331 to 24.016)	19.88 (13.864 to NC)	19.15 (8.444 to NC)	17.77 (11.860 to NC)	
Median (95% CI)	24.02 (20.304 to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (24.016 to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.5080		0.7650	
Hazard ratio (95% CI) vs Kd	-	0.79 (0.40 to 1.58)		1.09 (0.61 to 1.94)	
P-value	-	0.5089		0.7651	

A lower score represents a better level of quality of life. Clinical meaningful deterioration change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.1 Health-related quality-of-life endpoints - QLQ-MY20
16.2.6.1.2 Side-effects of treatment
16.2.6.1.2.16 Efficacy response data - Subgroup analyses by previous treatment with IMiD
16.2.6.1.2.16.3 QLQ-MY20 - Time to first improvement by 10 pt in side-effects of treatment according to previous treatment with IMiD (LOCF) - ITT population

	Yes		No		
	Kd (N=62)	**IKd (N=81)**	**Kd (N=61)**	**IKd (N=98)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	23 (37.1)	23 (28.4)	18 (29.5)	40 (40.8)	0.0775
Number (%) of patients censored	39 (62.9)	58 (71.6)	43 (70.5)	58 (59.2)	
Kaplan-Meier estimates of side-effects of treatment in months					
25% quantile (95% CI)	4.21 (1.051 to 14.850)	5.72 (2.825 to NC)	3.79 (1.906 to NC)	2.86 (1.938 to 7.425)	
Median (95% CI)	NC (14.850 to NC)	NC (NC to NC)	NC (NC to NC)	NC (15.573 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.2323		0.1908	
Hazard ratio (95% CI) vs Kd	-	0.70 (0.40 to 1.26)		1.45 (0.83 to 2.52)	
P-value	-	0.2347		0.1934	

A lower score represents a better level of quality of life. Clinical meaningful improvement change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.1 Health-related quality-of-life endpoints - QLQ-MY20
16.2.6.1.2 Side-effects of treatment
16.2.6.1.2.16 Efficacy response data - Subgroup analyses by previous treatment with IMiD
16.2.6.1.2.16.4 QLQ-MY20 - Time to first deterioration by 10 pt in side-effects of treatment according to previous treatment with IMiD (LOCF) - ITT population

	Yes		No		
	Kd (N=62)	**IKd (N=81)**	**Kd (N=61)**	**IKd (N=98)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	31 (50.0)	51 (63.0)	32 (52.5)	57 (58.2)	0.7507
Number (%) of patients censored	31 (50.0)	30 (37.0)	29 (47.5)	41 (41.8)	
Kaplan-Meier estimates of side-effects of treatment in months					
25% quantile (95% CI)	1.97 (1.150 to 4.041)	1.91 (1.183 to 2.924)	2.83 (1.150 to 4.830)	2.83 (1.150 to 3.844)	
Median (95% CI)	12.55 (4.041 to NC)	6.64 (3.778 to 13.207)	13.54 (4.830 to NC)	8.38 (5.125 to 15.507)	
75% quantile (95% CI)	NC (NC to NC)	NC (16.197 to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.2524		0.4595	
Hazard ratio (95% CI) vs Kd	-	1.30 (0.83 to 2.03)		1.18 (0.76 to 1.82)	
P-value	-	0.2538		0.4600	

A lower score represents a better level of quality of life. Clinical meaningful deterioration change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.1 Health-related quality-of-life endpoints - QLQ-MY20
16.2.6.1.2 Side-effects of treatment
16.2.6.1.2.16 Efficacy response data - Subgroup analyses by previous treatment with IMiD
16.2.6.1.2.16.5 QLQ-MY20 - Time until permanent improvement by 10 pt in side-effects of treatment according to previous treatment with IMiD (LOCF) - ITT population

	Yes		No		
	Kd (N=62)	**IKd (N=81)**	**Kd (N=61)**	**IKd (N=98)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	9 (14.5)	10 (12.3)	2 (3.3)	13 (13.3)	0.0578
Number (%) of patients censored	53 (85.5)	71 (87.7)	59 (96.7)	85 (86.7)	
Kaplan-Meier estimates of side-effects of treatment in months					
25% quantile (95% CI)	NC (15.047 to NC)	NC (20.534 to NC)	NC (NC to NC)	NC (20.304 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.6321		0.0359	
Hazard ratio (95% CI) vs Kd	-	0.80 (0.33 to 1.98)		4.30 (0.97 to 19.07)	
P-value	-	0.6328		0.0546	

A lower score represents a better level of quality of life. Clinical meaningful improvement change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.1 Health-related quality-of-life endpoints - QLQ-MY20
16.2.6.1.2 Side-effects of treatment
16.2.6.1.2.16 Efficacy response data - Subgroup analyses by previous treatment with IMiD
16.2.6.1.2.16.6 QLQ-MY20 - Time until permanent deterioration by 10 pt in side-effects of treatment according to previous treatment with IMiD (LOCF) - ITT population

	Yes		No		
	Kd (N=62)	**IKd (N=81)**	**Kd (N=61)**	**IKd (N=98)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	17 (27.4)	22 (27.2)	17 (27.9)	25 (25.5)	0.8181
Number (%) of patients censored	45 (72.6)	59 (72.8)	44 (72.1)	73 (74.5)	
Kaplan-Meier estimates of side-effects of treatment in months					
25% quantile (95% CI)	18.92 (9.331 to NC)	18.79 (9.265 to NC)	19.15 (6.801 to NC)	18.76 (13.996 to NC)	
Median (95% CI)	24.02 (24.016 to NC)	NC (NC to NC)	NC (20.370 to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (24.016 to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.9818		0.7575	
Hazard ratio (95% CI) vs Kd	-	0.99 (0.53 to 1.87)		0.91 (0.49 to 1.68)	
P-value	-	0.9817		0.7576	

A lower score represents a better level of quality of life. Clinical meaningful deterioration change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.1 Health-related quality-of-life endpoints - QLQ-MY20
16.2.6.1.2 Side-effects of treatment
16.2.6.1.2.17 Efficacy response data - Subgroup analyses by previous treatment with PI and IMiD
16.2.6.1.2.17.3 QLQ-MY20 - Time to first improvement by 10 pt in side-effects of treatment according to previous treatment with PI and IMiD (LOCF) - ITT population

	Yes		No		
	Kd (N=17)	**IKd (N=23)**	**Kd (N=106)**	**IKd (N=156)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	3 (17.6)	6 (26.1)	38 (35.8)	57 (36.5)	0.5970
Number (%) of patients censored	14 (82.4)	17 (73.9)	68 (64.2)	99 (63.5)	
Kaplan-Meier estimates of side-effects of treatment in months					
25% quantile (95% CI)	NC (0.986 to NC)	3.88 (0.986 to NC)	3.75 (1.906 to 11.006)	3.71 (2.267 to 8.641)	
Median (95% CI)	NC (NC to NC)	NC (3.877 to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.6411		0.9897	
Hazard ratio (95% CI) vs Kd	-	1.39 (0.35 to 5.55)		1.00 (0.67 to 1.51)	
P-value	-	0.6426		0.9897	

A lower score represents a better level of quality of life. Clinical meaningful improvement change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.1 Health-related quality-of-life endpoints - QLQ-MY20
16.2.6.1.2 Side-effects of treatment
16.2.6.1.2.17 Efficacy response data - Subgroup analyses by previous treatment with PI and IMiD
16.2.6.1.2.17.4 QLQ-MY20 - Time to first deterioration by 10 pt in side-effects of treatment according to previous treatment with PI and IMiD (LOCF) - ITT population

	Yes		No		
	Kd (N=17)	**IKd (N=23)**	**Kd (N=106)**	**IKd (N=156)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	10 (58.8)	15 (65.2)	53 (50.0)	93 (59.6)	0.8282
Number (%) of patients censored	7 (41.2)	8 (34.8)	53 (50.0)	63 (40.4)	
Kaplan-Meier estimates of side-effects of treatment in months					
25% quantile (95% CI)	1.97 (0.986 to 8.312)	2.10 (0.986 to 5.552)	2.04 (1.216 to 3.975)	2.07 (1.183 to 3.055)	
Median (95% CI)	8.31 (1.971 to NC)	5.59 (2.103 to 16.197)	15.93 (4.994 to NC)	7.66 (5.552 to 13.207)	
75% quantile (95% CI)	NC (8.312 to NC)	NC (5.618 to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.6382		0.1981	
Hazard ratio (95% CI) vs Kd	-	1.21 (0.54 to 2.71)		1.25 (0.89 to 1.75)	
P-value	-	0.6387		0.1990	

A lower score represents a better level of quality of life. Clinical meaningful deterioration change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
PGM=DEVOPS/SAR650984/EFC15246/CIR_RWE/REPORT/PGM/eff_km_subgp_sr_sig_de_i_t.sas OUT=REPORT/OUTPUT/eff_km_my20_eff_detl_piimid_de_i_t_x.rtf (07APR2021 14:43)

16.2.6.1 Health-related quality-of-life endpoints - QLQ-MY20
16.2.6.1.2 Side-effects of treatment
16.2.6.1.2.17 Efficacy response data - Subgroup analyses by previous treatment with PI and IMiD
16.2.6.1.2.17.5 QLQ-MY20 - Time until permanent improvement by 10 pt in side-effects of treatment according to previous treatment with PI and IMiD (LOCF) - ITT population

	Yes		No		
	Kd (N=17)	**IKd (N=23)**	**Kd (N=106)**	**IKd (N=156)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	2 (11.8)	4 (17.4)	9 (8.5)	19 (12.2)	0.9657
Number (%) of patients censored	15 (88.2)	19 (82.6)	97 (91.5)	137 (87.8)	
Kaplan-Meier estimates of side-effects of treatment in months					
25% quantile (95% CI)	NC (1.018 to NC)	NC (1.413 to NC)	NC (NC to NC)	NC (NC to NC)	
Median (95% CI)	NC (NC to NC)	NC (20.534 to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.6760		0.3502	
Hazard ratio (95% CI) vs Kd	-	1.43 (0.26 to 7.83)		1.46 (0.66 to 3.22)	
P-value	-	0.6777		0.3531	

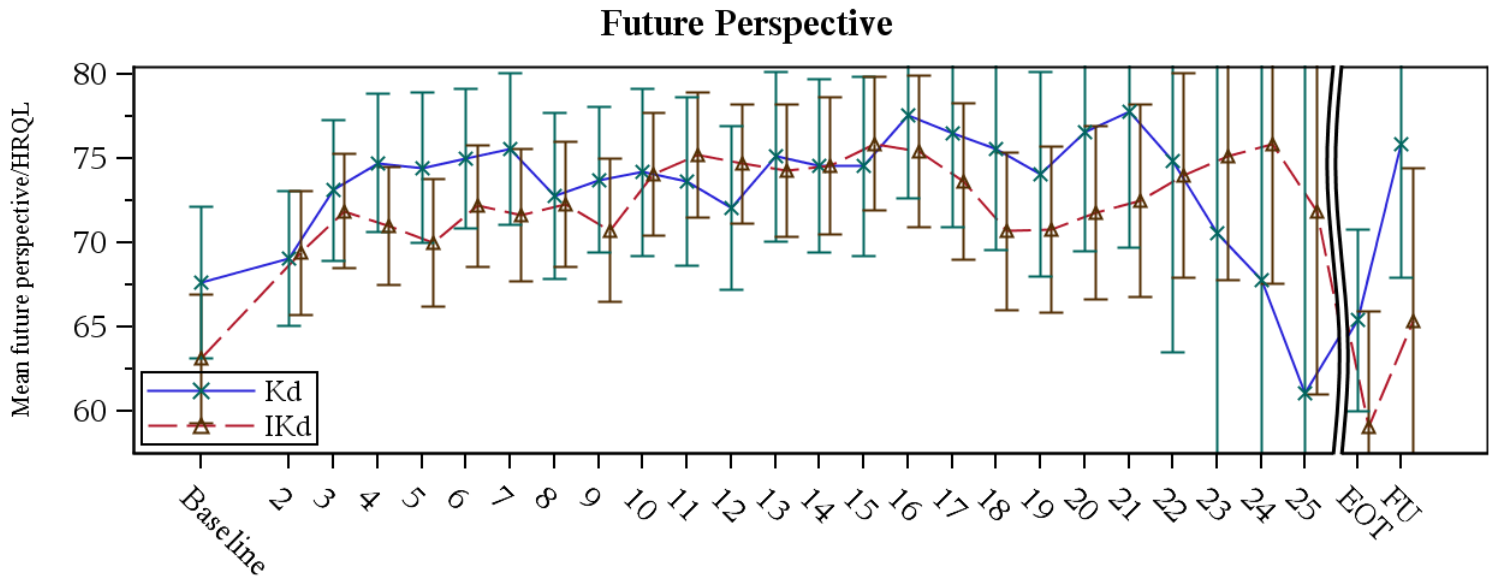
A lower score represents a better level of quality of life. Clinical meaningful improvement change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
PGM=DEVOPS/SAR650984/EFC15246/CIR_RWE/REPORT/PGM/eff_km_subgp_sr_sig_de_i_t.sas OUT=REPORT/OUTPUT/eff_km_my20_eff_imppl_piimid_de_i_t_x.rtf (07APR2021 14:44)

16.2.6.1 Health-related quality-of-life endpoints - QLQ-MY20
16.2.6.1.2 Side-effects of treatment
16.2.6.1.2.17 Efficacy response data - Subgroup analyses by previous treatment with PI and IMiD
16.2.6.1.2.17.6 QLQ-MY20 - Time until permanent deterioration by 10 pt in side-effects of treatment according to previous treatment with PI and IMiD (LOCF) - ITT population

	Yes		No		
	Kd (N=17)	**IKd (N=23)**	**Kd (N=106)**	**IKd (N=156)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	6 (35.3)	6 (26.1)	28 (26.4)	41 (26.3)	0.5833
Number (%) of patients censored	11 (64.7)	17 (73.9)	78 (73.6)	115 (73.7)	
Kaplan-Meier estimates of side-effects of treatment in months					
25% quantile (95% CI)	11.50 (7.786 to 24.016)	19.88 (1.511 to NC)	19.15 (12.189 to NC)	18.79 (13.864 to NC)	
Median (95% CI)	24.02 (9.331 to 24.016)	NC (19.877 to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	24.02 (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.5735		0.9970	
Hazard ratio (95% CI) vs Kd	-	0.72 (0.23 to 2.25)		1.00 (0.62 to 1.62)	
P-value	-	0.5752		0.9970	

A lower score represents a better level of quality of life. Clinical meaningful deterioration change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
PGM=DEVOPS/SAR650984/EFC15246/CIR_RWE/REPORT/PGM/eff_km_subgp_sr_sig_de_i_t.sas OUT=REPORT/OUTPUT/eff_km_my20_eff_detpl_piimid_de_i_t_x.rtf (07APR2021 14:44)

16.2.6.1 Health-related quality-of-life endpoints - QLQ-MY20
16.2.6.1.2 Future perspective
16.2.6.1.2.1 Efficacy response data
16.2.6.1.2.1.1 QLQ-MY20 - Mean and 95% CI for future perspective score over time - ITT population



#patients																									
Kd	114	114	112	110	104	100	95	91	88	84	78	72	67	66	62	57	52	50	45	37	30	23	17	10	6	62	35
IKd	167	170	168	164	161	155	150	146	139	133	130	127	121	118	112	109	105	102	97	91	78	56	38	23	17	60	34

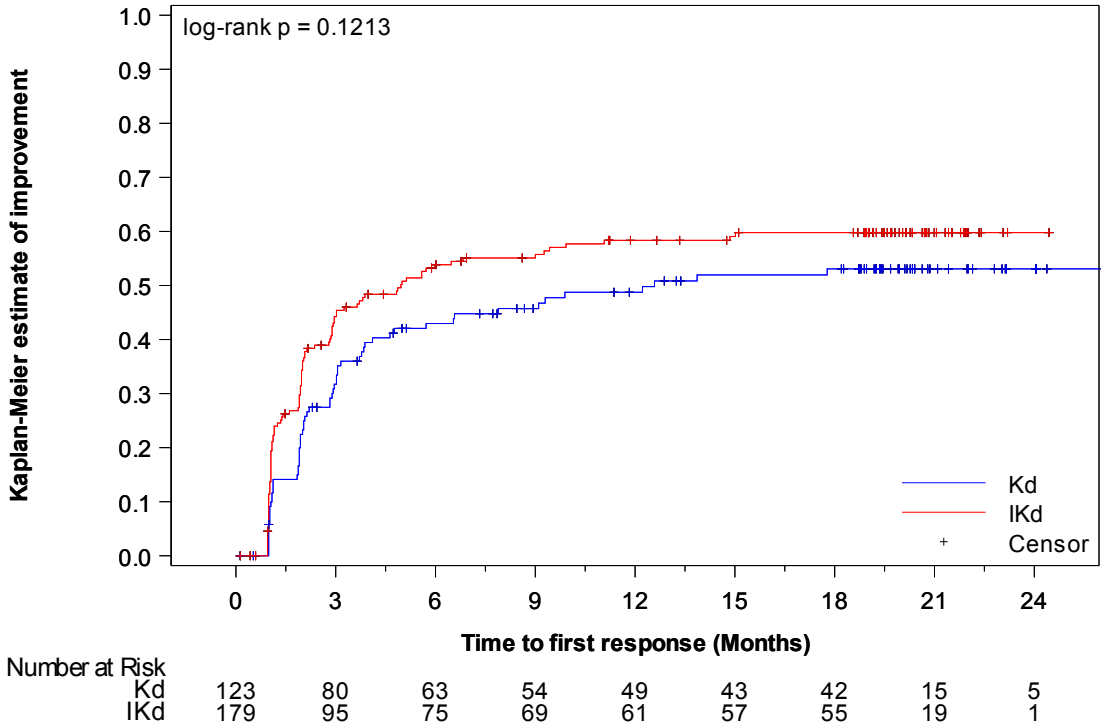
A higher score represents a better level of quality of life. Cycles with less than 20 patients overall are not presented.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
PGM=DEVOPS/SAR650984/EFC15246/CIR_RWE/REPORT/PGM/eff_qlq_line_i_f.sas OUT=REPORT/OUTPUT/eff_qlq_line_my20_per_de_i_f_x.rtf (12FEB2021 15:16)

16.2.6.1 Health-related quality-of-life endpoints - QLQ-MY20
16.2.6.1.2 Future perspective
16.2.6.1.2.1 Efficacy response data
16.2.6.1.2.1.15 QLQ-MY20 - Time to first improvement by 15 pt in future perspective (LOCF) - ITT population

First improvement 15 points Future perspective (%)	**Kd (N=123)**	**IKd (N=179)**
Number (%) of events	61 (49.6)	102 (57.0)
Number (%) of patients censored	62 (50.4)	77 (43.0)
Kaplan-Meier estimates of future perspective in months		
25% quantile (95% CI)	2.07 (1.906 to 3.023)	1.35 (1.051 to 1.938)
Median (95% CI)	12.58 (4.632 to NC)	4.96 (2.891 to 9.922)
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)
Comparison vs. Kd		
Stratified[a] Log-Rank test p-value[b] vs Kd	-	0.1213
Stratified[a] Hazard ratio (95% CI) vs Kd	-	1.29 (0.93 to 1.77)
P-value	-	0.1223
Improvement probability (95% CI)[c]		
3 Months	0.317 (0.236 to 0.401)	0.442 (0.367 to 0.514)
6 Months	0.430 (0.339 to 0.517)	0.538 (0.461 to 0.610)

A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 15 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] Stratified on number of prior lines of therapy (1 vs. >1) and Revised International Staging System (R-ISS) stage (I or II vs. III vs. not classified) according to IRT
[b] One-sided significance level is 0.025
[c] Estimated using the Kaplan-Meier method
NA/NC = Not Applicable / Not Calculable
PGM=DEVOPS/SAR650984/EFC15246/CIR_RWE/REPORT/PGM/eff_km_invhr_sr_i_t.sas OUT=REPORT/OUTPUT/eff_km_my20_per_imp15l_de_i_t_x.rtf (07APR2021 14:23)

16.2.6.1 Health-related quality-of-life endpoints - QLQ-MY20
16.2.6.1.2 Future perspective
16.2.6.1.2.1 Efficacy response data
16.2.6.1.2.1.16 QLQ-MY20 - Time to first improvement by 15 pt in future perspective - Kaplan-Meier curve (LOCF) - ITT population



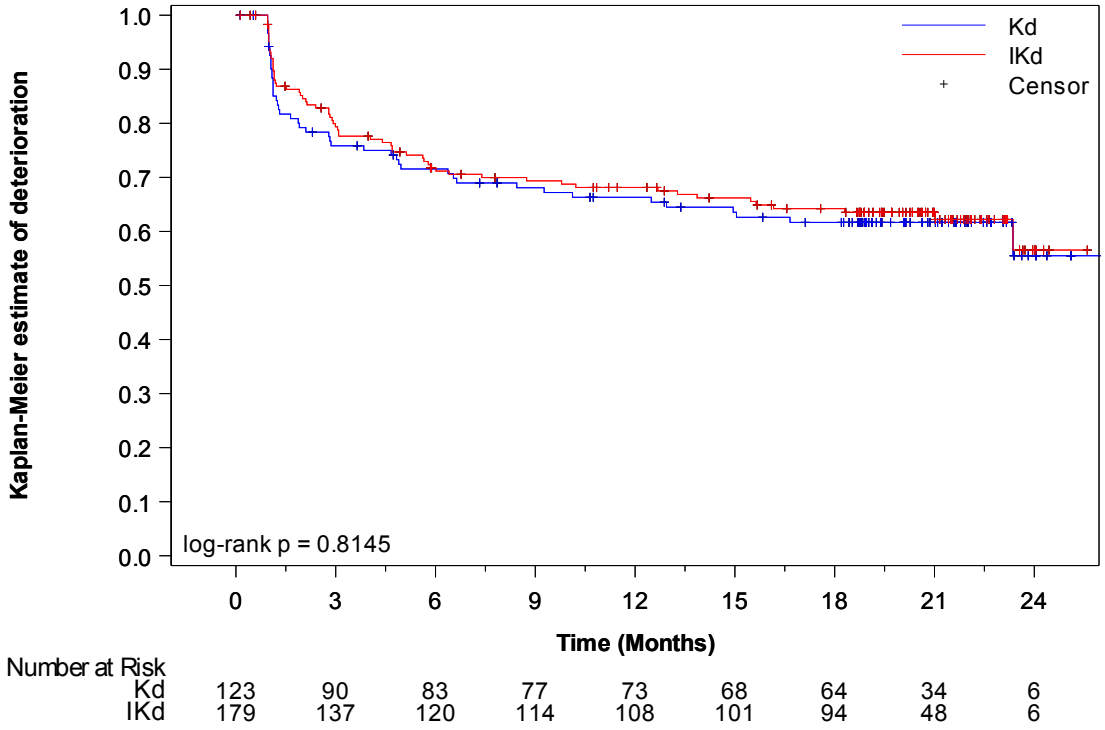
A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 15 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.

16.2.6.1 Health-related quality-of-life endpoints - QLQ-MY20
16.2.6.1.2 Future perspective
16.2.6.1.2.1 Efficacy response data
16.2.6.1.2.1.17 QLQ-MY20 - Time to first deterioration by 15 pt in future perspective (LOCF) - ITT population

First deterioration 15 points Future perspective (%)	**Kd (N=123)**	**IKd (N=179)**
Number (%) of events	46 (37.4)	64 (35.8)
Number (%) of patients censored	77 (62.6)	115 (64.2)
Kaplan-Meier estimates of future perspective in months		
25% quantile (95% CI)	3.84 (1.281 to 9.265)	4.70 (2.825 to 10.218)
Median (95% CI)	NC (23.359 to NC)	NC (23.359 to NC)
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)
Comparison vs. Kd		
Stratified[a] Log-Rank test p-value[b] vs Kd	-	0.8145
Stratified[a] Hazard ratio (95% CI) vs Kd	-	0.96 (0.65 to 1.40)
P-value	-	0.8137
Deterioration probability (95% CI)[c]		
3 Months	0.758 (0.671 to 0.825)	0.794 (0.726 to 0.847)
6 Months	0.716 (0.625 to 0.788)	0.718 (0.644 to 0.779)

A higher score represents a better level of quality of life. Clinical meaningful deterioration change from baseline less than or equal to -15 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] Stratified on number of prior lines of therapy (1 vs. >1) and Revised International Staging System (R-ISS) stage (I or II vs. III vs. not classified) according to IRT
[b] One-sided significance level is 0.025
[c] Estimated using the Kaplan-Meier method
NA/NC = Not Applicable / Not Calculable
PGM=DEVOPS/SAR650984/EFC15246/CIR_RWE/REPORT/PGM/eff_km_invhr_sr_i_t.sas OUT=REPORT/OUTPUT/eff_km_my20_per_det15l_de_i_t_x.rtf (07APR2021 14:23)

16.2.6.1 Health-related quality-of-life endpoints - QLQ-MY20
16.2.6.1.2 Future perspective
16.2.6.1.2.1 Efficacy response data
16.2.6.1.2.1.18 QLQ-MY20 - Time to first deterioration by 15 pt in future perspective - Kaplan-Meier curve (LOCF) - ITT population



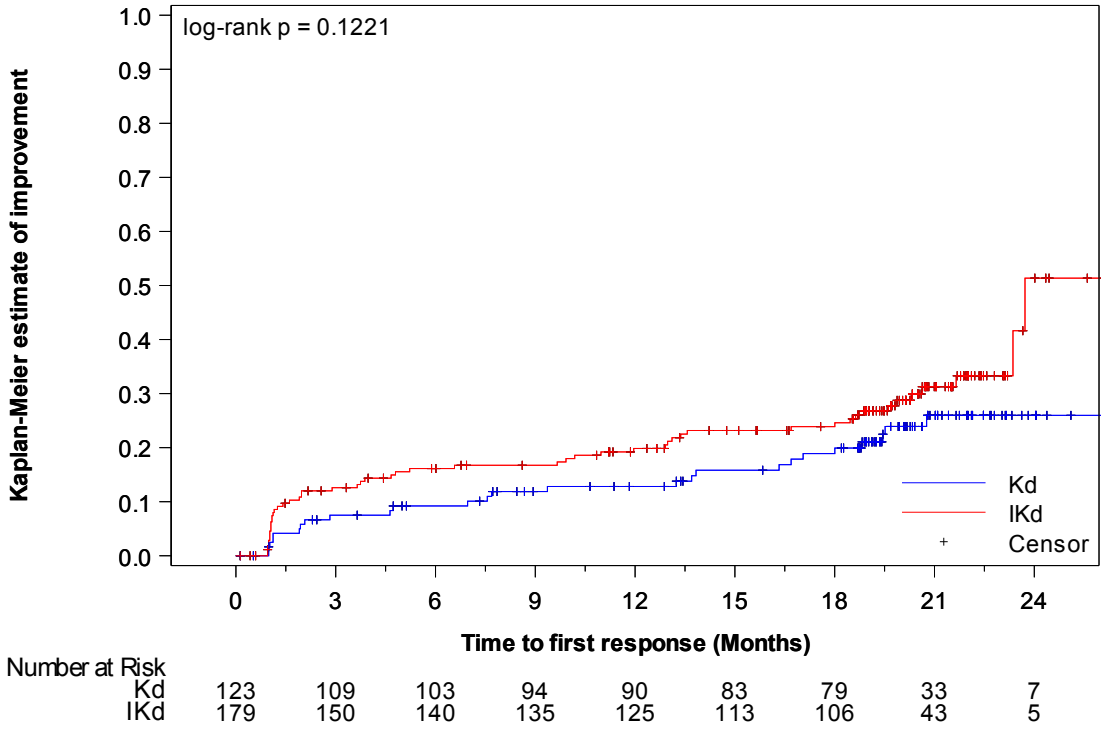
A higher score represents a better level of quality of life. Clinical meaningful deterioration change from baseline less than or equal to -15 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
PGM=DEVOPS/SAR650984/EFC15246/CIR_RWE/REPORT/PGM/eff_qlq_km_i_f.sas OUT=REPORT/OUTPUT/eff_km_my20_per_det15l_de_i_f_x.rtf (07APR2021 14:25)

16.2.6.1 Health-related quality-of-life endpoints - QLQ-MY20
16.2.6.1.2 Future perspective
16.2.6.1.2.1 Efficacy response data
16.2.6.1.2.1.19 QLQ-MY20 - Time until permanent improvement by 15 pt in future perspective (LOCF) - ITT population

First permanent improvement 15 points Future perspective (%)	**Kd (N=123)**	**IKd (N=179)**
Number (%) of events	26 (21.1)	51 (28.5)
Number (%) of patients censored	97 (78.9)	128 (71.5)
Kaplan-Meier estimates of future perspective in months		
25% quantile (95% CI)	20.76 (16.329 to NC)	18.46 (10.185 to 21.651)
Median (95% CI)	NC (NC to NC)	23.72 (23.359 to NC)
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)
Comparison vs. Kd		
Stratified[a] Log-Rank test p-value[b] vs Kd	-	0.1221
Stratified[a] Hazard ratio (95% CI) vs Kd	-	1.45 (0.90 to 2.34)
P-value	-	0.1243
Improvement probability (95% CI)[c]		
3 Months	0.075 (0.037 to 0.131)	0.126 (0.082 to 0.180)
6 Months	0.092 (0.049 to 0.152)	0.161 (0.111 to 0.220)

A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 15 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] Stratified on number of prior lines of therapy (1 vs. >1) and Revised International Staging System (R-ISS) stage (I or II vs. III vs. not classified) according to IRT
[b] One-sided significance level is 0.025
[c] Estimated using the Kaplan-Meier method
NA/NC = Not Applicable / Not Calculable
PGM=DEVOPS/SAR650984/EFC15246/CIR_RWE/REPORT/PGM/eff_km_invhr_sr_i_t.sas OUT=REPORT/OUTPUT/eff_km_my20_per_imp15pl_de_i_t_x.rtf (07APR2021 14:23)

16.2.6.1 Health-related quality-of-life endpoints - QLQ-MY20
16.2.6.1.2 Future perspective
16.2.6.1.2.1 Efficacy response data
16.2.6.1.2.1.20 QLQ-MY20 - Time until permanent improvement by 15 pt in future perspective - Kaplan-Meier curve (LOCF) - ITT population



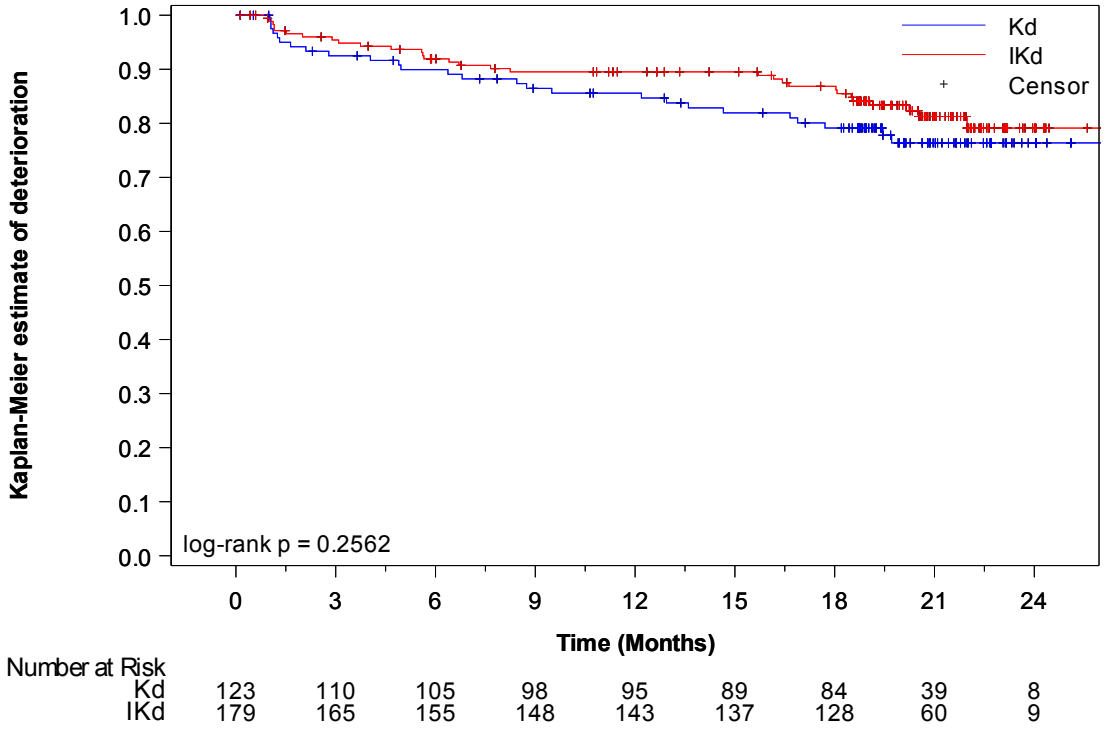
A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 15 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
PGM=DEVOPS/SAR650984/EFC15246/CIR_RWE/REPORT/PGM/eff_qlq_km_i_f.sas OUT=REPORT/OUTPUT/eff_km_my20_per_imp15pl_de_i_f_x.rtf (07APR2021 14:25)

16.2.6.1 Health-related quality-of-life endpoints - QLQ-MY20
16.2.6.1.2 Future perspective
16.2.6.1.2.1 Efficacy response data
16.2.6.1.2.1.21 QLQ-MY20 - Time until permanent deterioration by 15 pt in future perspective (LOCF) - ITT population

First permanent deterioration 15 points Future perspective (%)	**Kd (N=123)**	**IKd (N=179)**
Number (%) of events	26 (21.1)	30 (16.8)
Number (%) of patients censored	97 (78.9)	149 (83.2)
Kaplan-Meier estimates of future perspective in months		
25% quantile (95% CI)	NC (13.602 to NC)	NC (20.534 to NC)
Median (95% CI)	NC (NC to NC)	NC (NC to NC)
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)
Comparison vs. Kd		
Stratified[a] Log-Rank test p-value[b] vs Kd	-	0.2562
Stratified[a] Hazard ratio (95% CI) vs Kd	-	0.74 (0.44 to 1.25)
P-value	-	0.2580
Deterioration probability (95% CI)[c]		
3 Months	0.925 (0.861 to 0.960)	0.954 (0.910 to 0.977)
6 Months	0.899 (0.829 to 0.942)	0.919 (0.867 to 0.951)

A higher score represents a better level of quality of life. Clinical meaningful deterioration change from baseline less than or equal to -15 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] Stratified on number of prior lines of therapy (1 vs. >1) and Revised International Staging System (R-ISS) stage (I or II vs. III vs. not classified) according to IRT
[b] One-sided significance level is 0.025
[c] Estimated using the Kaplan-Meier method
NA/NC = Not Applicable / Not Calculable
PGM=DEVOPS/SAR650984/EFC15246/CIR_RWE/REPORT/PGM/eff_km_invhr_sr_i_t.sas OUT=REPORT/OUTPUT/eff_km_my20_per_det15pl_de_i_t_x.rtf (07APR2021 14:23)

16.2.6.1 Health-related quality-of-life endpoints - QLQ-MY20
16.2.6.1.2 Future perspective
16.2.6.1.2.1 Efficacy response data
16.2.6.1.2.1.22 QLQ-MY20 - Time until permanent deterioration by 15 pt in future perspective - Kaplan-Meier curve (LOCF) - ITT population



A higher score represents a better level of quality of life. Clinical meaningful deterioration change from baseline less than or equal to -15 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
PGM=DEVOPS/SAR650984/EFC15246/CIR_RWE/REPORT/PGM/eff_qlq_km_i_f.sas OUT=REPORT/OUTPUT/eff_km_my20_per_det15pl_de_i_f_x.rtf (07APR2021 14:25)

16.2.6.1 Health-related quality-of-life endpoints - QLQ-MY20
16.2.6.1.2 Future perspective
16.2.6.1.2.2 Efficacy response data - Subgroup analyses by age
16.2.6.1.2.2.3 QLQ-MY20 - Time to first improvement by 10 pt in future perspective according to age (LOCF) - ITT population

	<65 years		>=65 years		
	Kd (N=66)	**IKd (N=88)**	**Kd (N=57)**	**IKd (N=91)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	41 (62.1)	63 (71.6)	38 (66.7)	65 (71.4)	0.2989
Number (%) of patients censored	25 (37.9)	25 (28.4)	19 (33.3)	26 (28.6)	
Kaplan-Meier estimates of future perspective in months					
25% quantile (95% CI)	1.12 (0.986 to 1.938)	1.02 (0.986 to 1.051)	1.05 (0.986 to 1.117)	1.05 (0.986 to 1.150)	
Median (95% CI)	4.11 (1.938 to 15.146)	1.94 (1.084 to 2.136)	2.14 (1.117 to 3.877)	1.97 (1.314 to 2.957)	
75% quantile (95% CI)	26.35 (15.146 to 26.349)	NC (2.825 to NC)	NC (3.877 to NC)	14.46 (4.665 to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.0545		0.5681	
Hazard ratio (95% CI) vs Kd	-	1.47 (0.99 to 2.20)		1.12 (0.75 to 1.68)	
P-value	-	0.0560		0.5683	
Improvement probability (95% CI)[b]					

A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
PGM=DEVOPS/SAR650984/EFC15246/CIR_RWE/REPORT/PGM/eff_km_subgp_sr_sig_de_i_t.sas OUT=REPORT/OUTPUT/eff_km_my20_per_impl_age_de_i_t_x.rtf (07APR2021 14:41)

16.2.6.1 Health-related quality-of-life endpoints - QLQ-MY20
16.2.6.1.2 Future perspective
16.2.6.1.2.2 Efficacy response data - Subgroup analyses by age
16.2.6.1.2.2.4 QLQ-MY20 - Time to first deterioration by 10 pt in future perspective according to age (LOCF) - ITT population

	<65 years		>=65 years		
	Kd (N=66)	**IKd (N=88)**	**Kd (N=57)**	**IKd (N=91)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	38 (57.6)	39 (44.3)	31 (54.4)	55 (60.4)	0.0946
Number (%) of patients censored	28 (42.4)	49 (55.7)	26 (45.6)	36 (39.6)	
Kaplan-Meier estimates of future perspective in months					
25% quantile (95% CI)	1.22 (1.051 to 2.793)	2.83 (1.150 to 4.665)	1.91 (1.084 to 2.957)	1.97 (1.150 to 2.990)	
Median (95% CI)	7.46 (3.055 to NC)	NC (6.111 to NC)	10.12 (2.957 to NC)	6.41 (3.417 to 14.062)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (21.027 to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.1009		0.4847	
Hazard ratio (95% CI) vs Kd	-	0.69 (0.44 to 1.08)		1.17 (0.75 to 1.82)	
P-value	-	0.1029		0.4852	
Deterioration probability (95% CI)[b]					

A higher score represents a better level of quality of life. Clinical meaningful deterioration change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
PGM=DEVOPS/SAR650984/EFC15246/CIR_RWE/REPORT/PGM/eff_km_subgp_sr_sig_de_i_t.sas OUT=REPORT/OUTPUT/eff_km_my20_per_detl_age_de_i_t_x.rtf (07APR2021 14:40)

16.2.6.1 Health-related quality-of-life endpoints - QLQ-MY20
16.2.6.1.2 Future perspective
16.2.6.1.2.2 Efficacy response data - Subgroup analyses by age
16.2.6.1.2.2.5 QLQ-MY20 - Time until permanent improvement by 10 pt in future perspective according to age (LOCF) - ITT population

	<65 years		>=65 years		
	Kd (N=66)	**IKd (N=88)**	**Kd (N=57)**	**IKd (N=91)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	21 (31.8)	43 (48.9)	21 (36.8)	35 (38.5)	0.1887
Number (%) of patients censored	45 (68.2)	45 (51.1)	36 (63.2)	56 (61.5)	
Kaplan-Meier estimates of future perspective in months					
25% quantile (95% CI)	12.78 (1.117 to 26.349)	2.89 (1.051 to 9.035)	8.64 (1.117 to 19.515)	7.06 (1.610 to 15.704)	
Median (95% CI)	26.35 (24.016 to 26.349)	19.84 (12.977 to NC)	24.05 (16.329 to NC)	NC (17.774 to NC)	
75% quantile (95% CI)	26.35 (24.016 to 26.349)	NC (NC to NC)	NC (24.049 to NC)	NC (NC to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.0246		0.8801	
Hazard ratio (95% CI) vs Kd	-	1.83 (1.07 to 3.12)		1.04 (0.61 to 1.79)	
P-value	-	0.0268		0.8807	
Hazard ratio inverted (95% CI) vs IKd		-		0.96 (0.56 to 1.65)	

A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
PGM=DEVOPS/SAR650984/EFC15246/CIR_RWE/REPORT/PGM/eff_km_subgp_sr_sig_de_i_t.sas OUT=REPORT/OUTPUT/eff_km_my20_per_imppl_age_de_i_t_x.rtf (07APR2021 14:41)

16.2.6.1 Health-related quality-of-life endpoints - QLQ-MY20
16.2.6.1.2 Future perspective
16.2.6.1.2.2 Efficacy response data - Subgroup analyses by age
16.2.6.1.2.2.6 QLQ-MY20 - Time until permanent deterioration by 10 pt in future perspective according to age (LOCF) - ITT population

	<65 years		>=65 years		
	Kd (N=66)	**IKd (N=88)**	**Kd (N=57)**	**IKd (N=91)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	22 (33.3)	22 (25.0)	19 (33.3)	28 (30.8)	0.5459
Number (%) of patients censored	44 (66.7)	66 (75.0)	38 (66.7)	63 (69.2)	
Kaplan-Meier estimates of future perspective in months					
25% quantile (95% CI)	9.23 (3.844 to 18.891)	20.57 (4.862 to NC)	12.19 (4.961 to 23.984)	16.62 (7.622 to 20.534)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	23.98 (23.984 to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (23.984 to NC)	NC (NC to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.2606		0.7413	
Hazard ratio (95% CI) vs Kd	-	0.71 (0.40 to 1.29)		0.91 (0.51 to 1.62)	
P-value	-	0.2629		0.7414	
Deterioration probability (95% CI)[b]					

A higher score represents a better level of quality of life. Clinical meaningful deterioration change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
PGM=DEVOPS/SAR650984/EFC15246/CIR_RWE/REPORT/PGM/eff_km_subgp_sr_sig_de_i_t.sas OUT=REPORT/OUTPUT/eff_km_my20_per_detpl_age_de_i_t_x.rtf (07APR2021 14:41)

16.2.6.1 Health-related quality-of-life endpoints - QLQ-MY20
16.2.6.1.2 Future perspective
16.2.6.1.2.3 Efficacy response data - Subgroup analyses by gender
16.2.6.1.2.3.3 QLQ-MY20 - Time to first improvement by 10 pt in future perspective according to gender (LOCF) - ITT population

	Male		Female		
	Kd (N=68)	**IKd (N=101)**	**Kd (N=55)**	**IKd (N=78)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	39 (57.4)	71 (70.3)	40 (72.7)	57 (73.1)	0.1713
Number (%) of patients censored	29 (42.6)	30 (29.7)	15 (27.3)	21 (26.9)	
Kaplan-Meier estimates of future perspective in months					
25% quantile (95% CI)	1.12 (0.986 to 1.971)	1.05 (0.986 to 1.084)	1.02 (0.986 to 1.117)	1.02 (0.986 to 1.051)	
Median (95% CI)	5.62 (2.234 to NC)	1.94 (1.117 to 2.136)	1.99 (1.117 to 2.858)	1.97 (1.150 to 2.136)	
75% quantile (95% CI)	NC (NC to NC)	NC (3.680 to NC)	26.35 (2.858 to 26.349)	NC (2.891 to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.0219		0.7702	
Hazard ratio (95% CI) vs Kd	-	1.58 (1.06 to 2.33)		1.06 (0.71 to 1.60)	
P-value	-	0.0230		0.7714	
Hazard ratio inverted (95% CI) vs IKd		-		0.94 (0.63 to 1.41)	

A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.1 Health-related quality-of-life endpoints - QLQ-MY20
16.2.6.1.2 Future perspective
16.2.6.1.2.3 Efficacy response data - Subgroup analyses by gender
16.2.6.1.2.3.4 QLQ-MY20 - Time to first deterioration by 10 pt in future perspective according to gender (LOCF) - ITT population

	Male		Female		
	Kd (N=68)	**IKd (N=101)**	**Kd (N=55)**	**IKd (N=78)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	40 (58.8)	49 (48.5)	29 (52.7)	45 (57.7)	0.1699
Number (%) of patients censored	28 (41.2)	52 (51.5)	26 (47.3)	33 (42.3)	
Kaplan-Meier estimates of future perspective in months					
25% quantile (95% CI)	1.15 (1.051 to 2.070)	2.00 (1.183 to 3.811)	1.94 (1.051 to 6.341)	2.07 (1.117 to 3.088)	
Median (95% CI)	5.32 (2.793 to 19.614)	14.06 (5.848 to NC)	12.48 (6.341 to NC)	7.62 (3.417 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.1572		0.5857	
Hazard ratio (95% CI) vs Kd	-	0.74 (0.49 to 1.12)		1.14 (0.71 to 1.82)	
P-value	-	0.1588		0.5860	
Deterioration probability (95% CI)[b]					

A higher score represents a better level of quality of life. Clinical meaningful deterioration change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.1 Health-related quality-of-life endpoints - QLQ-MY20
16.2.6.1.2 Future perspective
16.2.6.1.2.3 Efficacy response data - Subgroup analyses by gender
16.2.6.1.2.3.5 QLQ-MY20 - Time until permanent improvement by 10 pt in future perspective according to gender (LOCF) - ITT population

	Male		Female		
	Kd (N=68)	**IKd (N=101)**	**Kd (N=55)**	**IKd (N=78)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	20 (29.4)	43 (42.6)	22 (40.0)	35 (44.9)	0.5834
Number (%) of patients censored	48 (70.6)	58 (57.4)	33 (60.0)	43 (55.1)	
Kaplan-Meier estimates of future perspective in months					
25% quantile (95% CI)	9.36 (1.117 to NC)	3.81 (1.117 to 8.345)	10.22 (1.117 to 17.051)	9.56 (1.248 to 13.372)	
Median (95% CI)	NC (24.016 to NC)	21.45 (18.891 to NC)	24.05 (17.051 to NC)	NC (15.704 to NC)	
75% quantile (95% CI)	NC (24.016 to NC)	NC (NC to NC)	26.35 (24.049 to NC)	NC (NC to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.1038		0.4432	
Hazard ratio (95% CI) vs Kd	-	1.55 (0.91 to 2.64)		1.24 (0.72 to 2.12)	
P-value	-	0.1066		0.4440	
Improvement probability (95% CI)[b]					

A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
PGM=DEVOPS/SAR650984/EFC15246/CIR_RWE/REPORT/PGM/eff_km_subgp_sr_sig_de_i_t.sas OUT=REPORT/OUTPUT/eff_km_my20_per_imppl_sex_de_i_t_x.rtf (07APR2021 14:41)

16.2.6.1 Health-related quality-of-life endpoints - QLQ-MY20
16.2.6.1.2 Future perspective
16.2.6.1.2.3 Efficacy response data - Subgroup analyses by gender
16.2.6.1.2.3.6 QLQ-MY20 - Time until permanent deterioration by 10 pt in future perspective according to gender (LOCF) - ITT population

	Male		Female		
	Kd (N=68)	**IKd (N=101)**	**Kd (N=55)**	**IKd (N=78)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	27 (39.7)	25 (24.8)	14 (25.5)	25 (32.1)	0.0693
Number (%) of patients censored	41 (60.3)	76 (75.2)	41 (74.5)	53 (67.9)	
Kaplan-Meier estimates of future perspective in months					
25% quantile (95% CI)	9.23 (3.844 to 16.657)	19.58 (11.499 to NC)	17.71 (6.538 to NC)	16.16 (6.735 to 21.979)	
Median (95% CI)	23.98 (16.887 to NC)	NC (NC to NC)	NC (NC to NC)	NC (21.979 to NC)	
75% quantile (95% CI)	NC (23.984 to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.0459		0.4672	
Hazard ratio (95% CI) vs Kd	-	0.58 (0.34 to 1.00)		1.27 (0.66 to 2.45)	
P-value	-	0.0486		0.4683	
Deterioration probability (95% CI)[b]					

A higher score represents a better level of quality of life. Clinical meaningful deterioration change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.1 Health-related quality-of-life endpoints - QLQ-MY20
16.2.6.1.2 Future perspective
16.2.6.1.2.4 Efficacy response data - Subgroup analyses by ethnic origin
16.2.6.1.2.4.3 QLQ-MY20 - Time to first improvement by 10 pt in future perspective according to ethnic origin (LOCF) - ITT population

	White		Other		
	Kd (N=83)	**IKd (N=131)**	**Kd (N=28)**	**IKd (N=34)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	55 (66.3)	96 (73.3)	19 (67.9)	24 (70.6)	0.6691
Number (%) of patients censored	28 (33.7)	35 (26.7)	9 (32.1)	10 (29.4)	
Kaplan-Meier estimates of future perspective in months					
25% quantile (95% CI)	1.05 (0.986 to 1.117)	1.05 (0.986 to 1.084)	1.12 (0.986 to 1.150)	0.99 (0.953 to 1.018)	
Median (95% CI)	3.71 (1.938 to 5.815)	1.97 (1.150 to 2.136)	2.04 (1.117 to 9.298)	1.05 (0.986 to 2.070)	
75% quantile (95% CI)	NC (9.101 to NC)	6.05 (3.680 to NC)	26.35 (3.023 to 26.349)	NC (1.906 to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.1107		0.1753	
Hazard ratio (95% CI) vs Kd	-	1.31 (0.94 to 1.83)		1.52 (0.82 to 2.82)	
P-value	-	0.1118		0.1785	
Improvement probability (95% CI)[b]					

A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.1 Health-related quality-of-life endpoints - QLQ-MY20
16.2.6.1.2 Future perspective
16.2.6.1.2.4 Efficacy response data - Subgroup analyses by ethnic origin
16.2.6.1.2.4.4 QLQ-MY20 - Time to first deterioration by 10 pt in future perspective according to ethnic origin (LOCF) - ITT population

	White		Other		
	Kd (N=83)	**IKd (N=131)**	**Kd (N=28)**	**IKd (N=34)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	50 (60.2)	71 (54.2)	13 (46.4)	17 (50.0)	0.5563
Number (%) of patients censored	33 (39.8)	60 (45.8)	15 (53.6)	17 (50.0)	
Kaplan-Meier estimates of future perspective in months					
25% quantile (95% CI)	1.64 (1.051 to 2.004)	2.07 (1.511 to 3.187)	1.15 (1.051 to 3.055)	1.54 (1.018 to 4.698)	
Median (95% CI)	7.46 (3.680 to 13.963)	8.54 (5.552 to NC)	NC (1.281 to NC)	16.16 (2.825 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (21.027 to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.3953		0.8263	
Hazard ratio (95% CI) vs Kd	-	0.85 (0.60 to 1.23)		1.08 (0.53 to 2.23)	
P-value	-	0.3958		0.8270	
Deterioration probability (95% CI)[b]					

A higher score represents a better level of quality of life. Clinical meaningful deterioration change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.1 Health-related quality-of-life endpoints - QLQ-MY20
16.2.6.1.2 Future perspective
16.2.6.1.2.4 Efficacy response data - Subgroup analyses by ethnic origin
16.2.6.1.2.4.5 QLQ-MY20 - Time until permanent improvement by 10 pt in future perspective according to ethnic origin (LOCF) - ITT population

	White		Other		
	Kd (N=83)	**IKd (N=131)**	**Kd (N=28)**	**IKd (N=34)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	24 (28.9)	59 (45.0)	14 (50.0)	13 (38.2)	0.1475
Number (%) of patients censored	59 (71.1)	72 (55.0)	14 (50.0)	21 (61.8)	
Kaplan-Meier estimates of future perspective in months					
25% quantile (95% CI)	12.78 (1.938 to NC)	4.17 (1.610 to 9.035)	7.52 (1.117 to 16.329)	4.83 (1.018 to 20.304)	
Median (95% CI)	NC (24.049 to NC)	20.47 (17.741 to NC)	24.02 (8.641 to NC)	NC (10.349 to NC)	
75% quantile (95% CI)	NC (24.049 to NC)	NC (NC to NC)	26.35 (24.016 to NC)	NC (NC to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.0280		0.7689	
Hazard ratio (95% CI) vs Kd	-	1.69 (1.05 to 2.72)		0.89 (0.41 to 1.93)	
P-value	-	0.0299		0.7684	
Hazard ratio inverted (95% CI) vs IKd		-		1.12 (0.52 to 2.44)	

A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
PGM=DEVOPS/SAR650984/EFC15246/CIR_RWE/REPORT/PGM/eff_km_subgp_sr_sig_de_i_t.sas OUT=REPORT/OUTPUT/eff_km_my20_per_imppl_race_de_i_t_x.rtf (07APR2021 14:41)

16.2.6.1 Health-related quality-of-life endpoints - QLQ-MY20
16.2.6.1.2 Future perspective
16.2.6.1.2.4 Efficacy response data - Subgroup analyses by ethnic origin
16.2.6.1.2.4.6 QLQ-MY20 - Time until permanent deterioration by 10 pt in future perspective according to ethnic origin (LOCF) - ITT population

	White		Other		
	Kd (N=83)	**IKd (N=131)**	**Kd (N=28)**	**IKd (N=34)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	29 (34.9)	37 (28.2)	8 (28.6)	11 (32.4)	0.4627
Number (%) of patients censored	54 (65.1)	94 (71.8)	20 (71.4)	23 (67.6)	
Kaplan-Meier estimates of future perspective in months					
25% quantile (95% CI)	12.94 (5.815 to 18.891)	18.07 (11.499 to 21.979)	11.50 (1.051 to NC)	16.16 (1.117 to NC)	
Median (95% CI)	23.98 (23.984 to NC)	NC (NC to NC)	NC (13.602 to NC)	NC (16.854 to NC)	
75% quantile (95% CI)	NC (23.984 to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.3470		0.7774	
Hazard ratio (95% CI) vs Kd	-	0.79 (0.49 to 1.29)		1.14 (0.46 to 2.84)	
P-value	-	0.3481		0.7776	
Deterioration probability (95% CI)[b]					

A higher score represents a better level of quality of life. Clinical meaningful deterioration change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.1 Health-related quality-of-life endpoints - QLQ-MY20
16.2.6.1.2 Future perspective
16.2.6.1.2.5 Efficacy response data - Subgroup analyses by geographical region
16.2.6.1.2.5.3 QLQ-MY20 - Time to first improvement by 10 pt in future perspective according to geographical region (LOCF) - ITT population

	Europe		America		Asia		Other countries		
	Kd (N=60)	**IKd (N=85)**	**Kd (N=20)**	**IKd (N=24)**	**Kd (N=21)**	**IKd (N=25)**	**Kd (N=22)**	**IKd (N=45)**	**p-value of treatment-by-subgroup interaction[c]**
Number (%) of events	33 (55.0)	58 (68.2)	16 (80.0)	18 (75.0)	14 (66.7)	20 (80.0)	16 (72.7)	32 (71.1)	0.6575
Number (%) of patients censored	27 (45.0)	27 (31.8)	4 (20.0)	6 (25.0)	7 (33.3)	5 (20.0)	6 (27.3)	13 (28.9)	
Kaplan-Meier estimates of event in months									
25% quantile (95% CI)	1.02 (0.986 to 1.938)	1.05 (0.986 to 1.150)	1.00 (0.920 to 1.938)	1.05 (0.986 to 1.117)	1.12 (0.986 to 1.117)	0.99 (0.920 to 1.018)	1.08 (0.986 to 2.136)	1.05 (0.986 to 1.117)	
Median (95% CI)	3.88 (1.938 to NC)	2.10 (1.413 to 3.713)	2.53 (0.986 to 9.101)	1.94 (1.051 to 2.366)	1.59 (1.117 to 26.349)	1.05 (0.986 to 1.906)	3.35 (1.084 to 15.146)	1.94 (1.084 to 2.957)	
75% quantile (95% CI)	NC (NC to NC)	NC (4.961 to NC)	9.10 (2.825 to NC)	2.83 (1.971 to NC)	26.35 (2.037 to 26.349)	2.04 (1.051 to NC)	NC (3.844 to NC)	NC (2.957 to NC)	

A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
PGM=DEVOPS/SAR650984/EFC15246/CIR_RWE/REPORT/PGM/eff_km_subgp_sr_sig_de_i_t.sas OUT=REPORT/OUTPUT/eff_km_my20_per_impl_greg_de_i_t_x.rtf (07APR2021 14:41)

16.2.6.1 Health-related quality-of-life endpoints - QLQ-MY20
16.2.6.1.2 Future perspective
16.2.6.1.2.5 Efficacy response data - Subgroup analyses by geographical region
16.2.6.1.2.5.3 QLQ-MY20 - Time to first improvement by 10 pt in future perspective according to geographical region (LOCF) - ITT population

	Europe		America		Asia		Other countries		
	Kd (N=60)	**IKd (N=85)**	**Kd (N=20)**	**IKd (N=24)**	**Kd (N=21)**	**IKd (N=25)**	**Kd (N=22)**	**IKd (N=45)**	**p-value of treatment-by-subgroup interaction[c]**
Comparison vs. Kd									
Log-Rank test p-value[a] vs Kd	-	0.1572		0.7822		0.0642		0.5008	
Hazard ratio (95% CI) vs Kd	-	1.36 (0.89 to 2.09)		1.10 (0.56 to 2.18)		1.92 (0.95 to 3.88)		1.23 (0.67 to 2.24)	
P-value	-	0.1588		0.7826		0.0689		0.5016	
Improvement probability (95% CI)[b]									
3 Months	0.446 (0.316 to 0.567)	0.580 (0.466 to 0.678)	0.550 (0.313 to 0.735)	0.764 (0.526 to 0.894)	0.550 (0.313 to 0.735)	0.792 (0.570 to 0.908)	0.500 (0.282 to 0.684)	0.644 (0.487 to 0.765)	

A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
PGM=DEVOPS/SAR650984/EFC15246/CIR_RWE/REPORT/PGM/eff_km_subgp_sr_sig_de_i_t.sas OUT=REPORT/OUTPUT/eff_km_my20_per_impl_greg_de_i_t_x.rtf (07APR2021 14:41)

16.2.6.1 Health-related quality-of-life endpoints - QLQ-MY20
16.2.6.1.2 Future perspective
16.2.6.1.2.5 Efficacy response data - Subgroup analyses by geographical region
16.2.6.1.2.5.4 QLQ-MY20 - Time to first deterioration by 10 pt in future perspective according to geographical region (LOCF) - ITT population

	Europe		America		Asia		Other countries		
	Kd (N=60)	**IKd (N=85)**	**Kd (N=20)**	**IKd (N=24)**	**Kd (N=21)**	**IKd (N=25)**	**Kd (N=22)**	**IKd (N=45)**	**p-value of treatment-by-subgroup interaction[c]**
Number (%) of events	31 (51.7)	47 (55.3)	15 (75.0)	9 (37.5)	10 (47.6)	13 (52.0)	13 (59.1)	25 (55.6)	0.3717
Number (%) of patients censored	29 (48.3)	38 (44.7)	5 (25.0)	15 (62.5)	11 (52.4)	12 (48.0)	9 (40.9)	20 (44.4)	
Kaplan-Meier estimates of event in months									
25% quantile (95% CI)	1.91 (1.051 to 2.793)	1.97 (1.150 to 2.924)	1.25 (0.953 to 4.008)	1.58 (0.986 to NC)	1.13 (1.051 to 3.055)	1.99 (0.986 to 6.407)	2.96 (0.953 to 7.721)	3.42 (1.117 to 5.552)	
Median (95% CI)	10.18 (2.825 to NC)	7.39 (3.187 to NC)	6.05 (1.216 to 13.963)	NC (4.041 to NC)	11.50 (1.117 to NC)	16.16 (2.825 to NC)	10.46 (2.957 to NC)	8.02 (4.698 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (6.341 to NC)	NC (NC to NC)	NC (NC to NC)	NC (21.027 to NC)	NC (12.485 to NC)	NC (NC to NC)	

A higher score represents a better level of quality of life. Clinical meaningful deterioration change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
PGM=DEVOPS/SAR650984/EFC15246/CIR_RWE/REPORT/PGM/eff_km_subgp_sr_sig_de_i_t.sas OUT=REPORT/OUTPUT/eff_km_my20_per_detl_greg_de_i_t_x.rtf (07APR2021 14:41)

16.2.6.1 Health-related quality-of-life endpoints - QLQ-MY20
16.2.6.1.2 Future perspective
16.2.6.1.2.5 Efficacy response data - Subgroup analyses by geographical region
16.2.6.1.2.5.4 QLQ-MY20 - Time to first deterioration by 10 pt in future perspective according to geographical region (LOCF) - ITT population

	Europe		America		Asia		Other countries		
	Kd (N=60)	**IKd (N=85)**	**Kd (N=20)**	**IKd (N=24)**	**Kd (N=21)**	**IKd (N=25)**	**Kd (N=22)**	**IKd (N=45)**	**p-value of treatment-by-subgroup interaction[c]**
Comparison vs. Kd									
Log-Rank test p-value[a] vs Kd	-	0.8566		0.0589		0.9768		0.9725	
Hazard ratio (95% CI) vs Kd	-	1.04 (0.66 to 1.64)		0.46 (0.20 to 1.05)		1.01 (0.44 to 2.31)		0.99 (0.51 to 1.93)	
P-value	-	0.8572		0.0653		0.9768		0.9725	
Deterioration probability (95% CI)[b]									
3 Months	0.621 (0.483 to 0.732)	0.639 (0.525 to 0.731)	0.600 (0.357 to 0.776)	0.737 (0.505 to 0.872)	0.600 (0.357 to 0.776)	0.708 (0.484 to 0.849)	0.727 (0.491 to 0.867)	0.756 (0.602 to 0.856)	

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The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.1 Health-related quality-of-life endpoints - QLQ-MY20
16.2.6.1.2 Future perspective
16.2.6.1.2.5 Efficacy response data - Subgroup analyses by geographical region
16.2.6.1.2.5.5 QLQ-MY20 - Time until permanent improvement by 10 pt in future perspective according to geographical region (LOCF) - ITT population

	Europe		America		Asia		Other countries		
	Kd (N=60)	**IKd (N=85)**	**Kd (N=20)**	**IKd (N=24)**	**Kd (N=21)**	**IKd (N=25)**	**Kd (N=22)**	**IKd (N=45)**	**p-value of treatment-by-subgroup interaction[c]**
Number (%) of events	17 (28.3)	36 (42.4)	7 (35.0)	15 (62.5)	9 (42.9)	12 (48.0)	9 (40.9)	15 (33.3)	0.3513
Number (%) of patients censored	43 (71.7)	49 (57.6)	13 (65.0)	9 (37.5)	12 (57.1)	13 (52.0)	13 (59.1)	30 (66.7)	
Kaplan-Meier estimates of event in months									
25% quantile (95% CI)	11.14 (1.117 to NC)	8.51 (1.906 to 16.099)	12.78 (0.986 to NC)	1.61 (0.986 to 5.520)	7.52 (1.018 to 24.016)	1.07 (0.986 to 15.704)	8.64 (0.986 to 24.049)	4.17 (1.084 to NC)	
Median (95% CI)	NC (NC to NC)	NC (18.464 to NC)	NC (12.780 to NC)	8.34 (2.103 to 19.844)	24.02 (7.524 to NC)	20.30 (1.084 to NC)	24.05 (8.641 to 24.049)	NC (18.628 to NC)	

A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
PGM=DEVOPS/SAR650984/EFC15246/CIR_RWE/REPORT/PGM/eff_km_subgp_sr_sig_de_i_t.sas OUT=REPORT/OUTPUT/eff_km_my20_per_imppl_greg_de_i_t_x.rtf (07APR2021 14:41)

16.2.6.1 Health-related quality-of-life endpoints - QLQ-MY20
16.2.6.1.2 Future perspective
16.2.6.1.2.5 Efficacy response data - Subgroup analyses by geographical region
16.2.6.1.2.5.5 QLQ-MY20 - Time until permanent improvement by 10 pt in future perspective according to geographical region (LOCF) - ITT population

	Europe		America		Asia		Other countries		
	Kd (N=60)	**IKd (N=85)**	**Kd (N=20)**	**IKd (N=24)**	**Kd (N=21)**	**IKd (N=25)**	**Kd (N=22)**	**IKd (N=45)**	**p-value of treatment-by-subgroup interaction[c]**
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	19.84 (8.345 to NC)	26.35 (24.016 to NC)	NC (20.304 to NC)	24.05 (NC to NC)	NC (NC to NC)	
Comparison vs. Kd									
Log-Rank test p-value[a] vs Kd	-	0.1859		0.0249		0.3686		0.7247	
Hazard ratio (95% CI) vs Kd	-	1.47 (0.83 to 2.62)		2.72 (1.10 to 6.75)		1.51 (0.61 to 3.73)		0.86 (0.38 to 1.97)	
P-value	-	0.1887		0.0308		0.3718		0.7249	
Hazard ratio inverted (95% CI) vs IKd		-		0.37 (0.15 to 0.91)		0.66 (0.27 to 1.64)		1.16 (0.51 to 2.66)	

A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
PGM=DEVOPS/SAR650984/EFC15246/CIR_RWE/REPORT/PGM/eff_km_subgp_sr_sig_de_i_t.sas OUT=REPORT/OUTPUT/eff_km_my20_per_imppl_greg_de_i_t_x.rtf (07APR2021 14:41)

16.2.6.1 Health-related quality-of-life endpoints - QLQ-MY20
16.2.6.1.2 Future perspective
16.2.6.1.2.5 Efficacy response data - Subgroup analyses by geographical region
16.2.6.1.2.5.6 QLQ-MY20 - Time until permanent deterioration by 10 pt in future perspective according to geographical region (LOCF) - ITT population

	Europe		America		Asia		Other countries		
	Kd (N=60)	**IKd (N=85)**	**Kd (N=20)**	**IKd (N=24)**	**Kd (N=21)**	**IKd (N=25)**	**Kd (N=22)**	**IKd (N=45)**	**p-value of treatment-by-subgroup interaction[c]**
Number (%) of events	18 (30.0)	24 (28.2)	8 (40.0)	4 (16.7)	7 (33.3)	8 (32.0)	8 (36.4)	14 (31.1)	0.7376
Number (%) of patients censored	42 (70.0)	61 (71.8)	12 (60.0)	20 (83.3)	14 (66.7)	17 (68.0)	14 (63.6)	31 (68.9)	
Kaplan-Meier estimates of event in months									
25% quantile (95% CI)	12.19 (5.815 to NC)	16.43 (4.862 to NC)	13.60 (1.216 to NC)	21.98 (0.986 to NC)	2.58 (1.051 to NC)	16.16 (0.986 to NC)	9.23 (1.018 to NC)	19.58 (7.491 to NC)	
Median (95% CI)	23.98 (23.984 to NC)	NC (NC to NC)	NC (13.602 to NC)	NC (21.979 to NC)	NC (1.314 to NC)	NC (16.624 to NC)	NC (9.232 to NC)	NC (20.534 to NC)	

A higher score represents a better level of quality of life. Clinical meaningful deterioration change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.1 Health-related quality-of-life endpoints - QLQ-MY20
16.2.6.1.2 Future perspective
16.2.6.1.2.5 Efficacy response data - Subgroup analyses by geographical region
16.2.6.1.2.5.6 QLQ-MY20 - Time until permanent deterioration by 10 pt in future perspective according to geographical region (LOCF) - ITT population

	Europe		America		Asia		Other countries		
	Kd (N=60)	**IKd (N=85)**	**Kd (N=20)**	**IKd (N=24)**	**Kd (N=21)**	**IKd (N=25)**	**Kd (N=22)**	**IKd (N=45)**	**p-value of treatment-by-subgroup interaction[c]**
75% quantile (95% CI)	NC (23.984 to NC)	NC (NC to NC)	NC (NC to NC)	NC (21.979 to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Kd									
Log-Rank test p-value[a] vs Kd	-	0.7867		0.0901		0.7767		0.7332	
Hazard ratio (95% CI) vs Kd	-	0.92 (0.50 to 1.69)		0.34 (0.09 to 1.26)		0.86 (0.31 to 2.38)		0.86 (0.36 to 2.05)	
P-value	-	0.7868		0.1066		0.7769		0.7334	
Deterioration probability (95% CI)[b]									

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The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.1 Health-related quality-of-life endpoints - QLQ-MY20
16.2.6.1.2 Future perspective
16.2.6.1.2.6 Efficacy response data - Subgroup analyses by regulatory region
16.2.6.1.2.6.3 QLQ-MY20 - Time to first improvement by 10 pt in future perspective according to regulatory region (LOCF) - ITT population

	Western countries		Other countries		
	Kd (N=55)	**IKd (N=97)**	**Kd (N=68)**	**IKd (N=82)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	35 (63.6)	65 (67.0)	44 (64.7)	63 (76.8)	0.0625
Number (%) of patients censored	20 (36.4)	32 (33.0)	24 (35.3)	19 (23.2)	
Kaplan-Meier estimates of future perspective in months					
25% quantile (95% CI)	1.05 (0.986 to 1.873)	1.12 (1.018 to 1.248)	1.08 (0.986 to 1.150)	0.99 (0.986 to 1.051)	
Median (95% CI)	2.86 (1.873 to 6.571)	2.07 (1.938 to 3.680)	3.98 (1.906 to 9.101)	1.08 (1.051 to 1.971)	
75% quantile (95% CI)	NC (4.632 to NC)	NC (4.961 to NC)	26.35 (9.298 to 26.349)	5.13 (2.004 to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.8339		0.0074	
Hazard ratio (95% CI) vs Kd	-	1.04 (0.69 to 1.58)		1.70 (1.15 to 2.51)	
P-value	-	0.8350		0.0080	
Hazard ratio inverted (95% CI) vs IKd		-		0.59 (0.40 to 0.87)	

A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.1 Health-related quality-of-life endpoints - QLQ-MY20
16.2.6.1.2 Future perspective
16.2.6.1.2.6 Efficacy response data - Subgroup analyses by regulatory region
16.2.6.1.2.6.4 QLQ-MY20 - Time to first deterioration by 10 pt in future perspective according to regulatory region (LOCF) - ITT population

	Western countries		Other countries		
	Kd (N=55)	**IKd (N=97)**	**Kd (N=68)**	**IKd (N=82)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	24 (43.6)	44 (45.4)	45 (66.2)	50 (61.0)	0.6602
Number (%) of patients censored	31 (56.4)	53 (54.6)	23 (33.8)	32 (39.0)	
Kaplan-Meier estimates of future perspective in months					
25% quantile (95% CI)	2.07 (1.051 to 6.538)	2.60 (1.906 to 3.778)	1.15 (1.051 to 1.906)	1.51 (1.117 to 3.055)	
Median (95% CI)	NC (6.374 to NC)	NC (6.604 to NC)	5.75 (1.938 to 11.499)	6.11 (3.745 to 16.164)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (13.010 to NC)	NC (21.027 to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.9520		0.5475	
Hazard ratio (95% CI) vs Kd	-	1.02 (0.62 to 1.67)		0.88 (0.59 to 1.32)	
P-value	-	0.9521		0.5478	
Deterioration probability (95% CI)[b]					

A higher score represents a better level of quality of life. Clinical meaningful deterioration change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.1 Health-related quality-of-life endpoints - QLQ-MY20
16.2.6.1.2 Future perspective
16.2.6.1.2.6 Efficacy response data - Subgroup analyses by regulatory region
16.2.6.1.2.6.5 QLQ-MY20 - Time until permanent improvement by 10 pt in future perspective according to regulatory region (LOCF) - ITT population

	Western countries		Other countries		
	Kd (N=55)	**IKd (N=97)**	**Kd (N=68)**	**IKd (N=82)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	24 (43.6)	41 (42.3)	18 (26.5)	37 (45.1)	0.0248
Number (%) of patients censored	31 (56.4)	56 (57.7)	50 (73.5)	45 (54.9)	
Kaplan-Meier estimates of future perspective in months					
25% quantile (95% CI)	1.94 (1.018 to 10.218)	3.81 (1.314 to 13.109)	19.52 (9.363 to 26.349)	4.67 (1.084 to 11.795)	
Median (95% CI)	24.05 (10.185 to 24.049)	NC (18.530 to NC)	26.35 (24.016 to NC)	19.84 (15.704 to NC)	
75% quantile (95% CI)	24.05 (NC to NC)	NC (NC to NC)	NC (26.349 to NC)	NC (NC to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.7136		0.0079	
Hazard ratio (95% CI) vs Kd	-	0.91 (0.55 to 1.51)		2.14 (1.20 to 3.81)	
P-value	-	0.7137		0.0095	
Hazard ratio inverted (95% CI) vs IKd		-		0.47 (0.26 to 0.83)	

A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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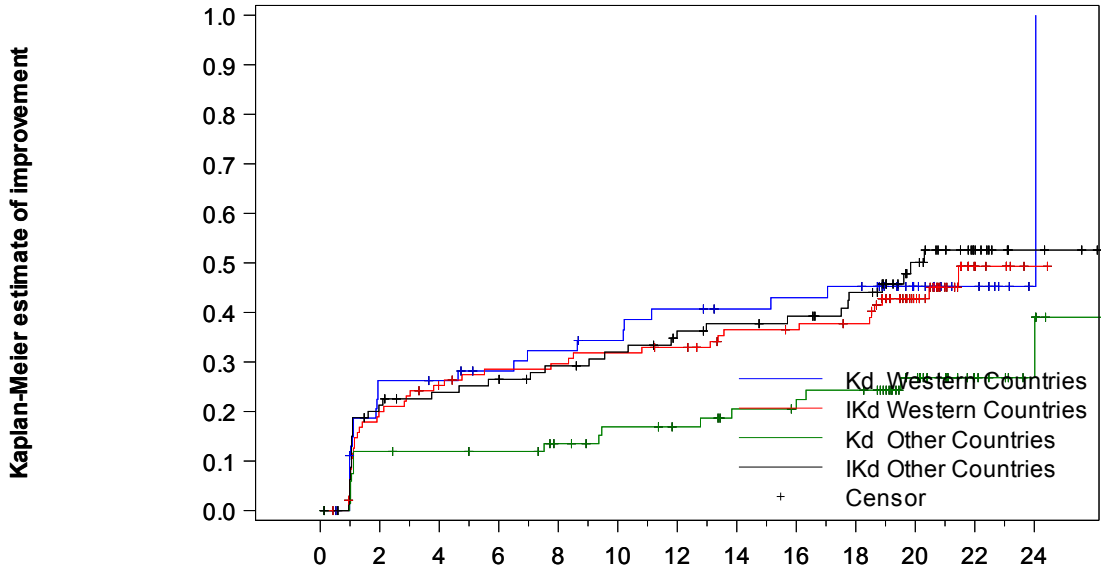
16.2.6.1 Health-related quality-of-life endpoints - QLQ-MY20
16.2.6.1.2 Future perspective
16.2.6.1.2.6 Efficacy response data - Subgroup analyses by regulatory region
16.2.6.1.2.6.6 QLQ-MY20 - Time until permanent improvement by 10 pt in future perspective according to regulatory region - Kaplan-Meier curve (LOCF) - ITT population



Number at Risk									
Kd Western Countries	55	39	35	31	28	26	24	8	1
IKd Western Countries	97	73	65	62	60	53	50	16	1
Kd Other Countries	68	58	57	51	47	43	40	20	6
IKd Other Countries	82	59	56	51	44	41	35	16	3

A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
PGM=DEVOPS/SAR650984/EFC15246/CIR_RWE/REPORT/PGM/eff_qlq_km_subgp_de_i_f.sas OUT=REPORT/OUTPUT/eff_km_my20_per_imppl_rreg_de_i_f_x.rtf (07APR2021 14:37)

16.2.6.1 Health-related quality-of-life endpoints - QLQ-MY20
16.2.6.1.2 Future perspective
16.2.6.1.2.6 Efficacy response data - Subgroup analyses by regulatory region
16.2.6.1.2.6.7 QLQ-MY20 - Time until permanent deterioration by 10 pt in future perspective according to regulatory region (LOCF) - ITT population

	Western countries		Other countries		
	Kd (N=55)	**IKd (N=97)**	**Kd (N=68)**	**IKd (N=82)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	14 (25.5)	24 (24.7)	27 (39.7)	26 (31.7)	0.5391
Number (%) of patients censored	41 (74.5)	73 (75.3)	41 (60.3)	56 (68.3)	
Kaplan-Meier estimates of future perspective in months					
25% quantile (95% CI)	18.30 (6.538 to NC)	19.58 (13.766 to NC)	6.80 (1.314 to 16.657)	15.38 (4.665 to 21.979)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (16.887 to NC)	NC (21.979 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.9308		0.3094	
Hazard ratio (95% CI) vs Kd	-	0.97 (0.50 to 1.88)		0.76 (0.44 to 1.30)	
P-value	-	0.9306		0.3110	
Deterioration probability (95% CI)[b]					

A higher score represents a better level of quality of life. Clinical meaningful deterioration change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
PGM=DEVOPS/SAR650984/EFC15246/CIR_RWE/REPORT/PGM/eff_km_subgp_sr_sig_de_i_t.sas OUT=REPORT/OUTPUT/eff_km_my20_per_detpl_rreg_de_i_t_x.rtf (07APR2021 14:41)

16.2.6.1 Health-related quality-of-life endpoints - QLQ-MY20
16.2.6.1.2 Future perspective
16.2.6.1.2.7 Efficacy response data - Subgroup analyses by baseline ECOG PS
16.2.6.1.2.7.3 QLQ-MY20 - Time to first improvement by 10 pt in future perspective according to baseline ECOG PS (LOCF) - ITT population

	0 or 1		>1		
	Kd (N=118)	**IKd (N=168)**	**Kd (N=5)**	**IKd (N=11)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	76 (64.4)	121 (72.0)	3 (60.0)	7 (63.6)	0.7586
Number (%) of patients censored	42 (35.6)	47 (28.0)	2 (40.0)	4 (36.4)	
Kaplan-Meier estimates of future perspective in months					
25% quantile (95% CI)	1.05 (0.986 to 1.117)	1.05 (0.986 to 1.051)	2.86 (2.825 to NC)	1.05 (0.986 to 4.961)	
Median (95% CI)	3.02 (1.938 to 5.815)	1.94 (1.150 to 2.070)	3.81 (2.825 to NC)	4.96 (0.986 to NC)	
75% quantile (95% CI)	26.35 (15.146 to 26.349)	NC (3.713 to NC)	NC (2.825 to NC)	14.46 (1.610 to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.0774		0.5974	
Hazard ratio (95% CI) vs Kd	-	1.30 (0.97 to 1.73)		1.44 (0.37 to 5.66)	
P-value	-	0.0782		0.5994	
Improvement probability (95% CI)[b]					

A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.1 Health-related quality-of-life endpoints - QLQ-MY20
16.2.6.1.2 Future perspective
16.2.6.1.2.7 Efficacy response data - Subgroup analyses by baseline ECOG PS
16.2.6.1.2.7.4 QLQ-MY20 - Time to first deterioration by 10 pt in future perspective according to baseline ECOG PS (LOCF) - ITT population

	0 or 1		>1		
	Kd (N=118)	**IKd (N=168)**	**Kd (N=5)**	**IKd (N=11)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	65 (55.1)	90 (53.6)	4 (80.0)	4 (36.4)	0.2842
Number (%) of patients censored	53 (44.9)	78 (46.4)	1 (20.0)	7 (63.6)	
Kaplan-Meier estimates of future perspective in months					
25% quantile (95% CI)	1.28 (1.084 to 2.825)	2.07 (1.478 to 3.187)	1.94 (1.906 to 2.793)	1.91 (0.986 to NC)	
Median (95% CI)	10.12 (5.749 to NC)	10.38 (5.848 to NC)	2.07 (1.906 to NC)	NC (0.986 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	2.79 (1.906 to NC)	NC (2.103 to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.6698		0.3777	
Hazard ratio (95% CI) vs Kd	-	0.93 (0.68 to 1.28)		0.54 (0.13 to 2.18)	
P-value	-	0.6679		0.3849	
Deterioration probability (95% CI)[b]					

A higher score represents a better level of quality of life. Clinical meaningful deterioration change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
PGM=DEVOPS/SAR650984/EFC15246/CIR_RWE/REPORT/PGM/eff_km_subgp_sr_sig_de_i_t.sas OUT=REPORT/OUTPUT/eff_km_my20_per_detl_ecog_de_i_t_x.rtf (07APR2021 14:40)

16.2.6.1 Health-related quality-of-life endpoints - QLQ-MY20
16.2.6.1.2 Future perspective
16.2.6.1.2.7 Efficacy response data - Subgroup analyses by baseline ECOG PS
16.2.6.1.2.7.5 QLQ-MY20 - Time until permanent improvement by 10 pt in future perspective according to baseline ECOG PS (LOCF) - ITT population

	0 or 1		>1		
	Kd (N=118)	**IKd (N=168)**	**Kd (N=5)**	**IKd (N=11)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	42 (35.6)	74 (44.0)	0 (0.0)	4 (36.4)	0.9773
Number (%) of patients censored	76 (64.4)	94 (56.0)	5 (100.0)	7 (63.6)	
Kaplan-Meier estimates of future perspective in months					
25% quantile (95% CI)	9.46 (1.906 to 16.329)	4.67 (1.906 to 10.349)	NC (NC to NC)	1.61 (0.986 to NC)	
Median (95% CI)	24.05 (24.016 to NC)	21.45 (18.628 to NC)	NC (NC to NC)	NC (0.986 to NC)	
75% quantile (95% CI)	26.35 (24.049 to NC)	NC (NC to NC)	NC (NC to NC)	NC (7.754 to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.1459		0.1097	
Hazard ratio (95% CI) vs Kd	-	1.33 (0.91 to 1.94)			
P-value	-	0.1472		0.9969	

A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.1 Health-related quality-of-life endpoints - QLQ-MY20
16.2.6.1.2 Future perspective
16.2.6.1.2.7 Efficacy response data - Subgroup analyses by baseline ECOG PS
16.2.6.1.2.7.6 QLQ-MY20 - Time until permanent deterioration by 10 pt in future perspective according to baseline ECOG PS (LOCF) - ITT population

	0 or 1		>1		
	Kd (N=118)	**IKd (N=168)**	**Kd (N=5)**	**IKd (N=11)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	37 (31.4)	47 (28.0)	4 (80.0)	3 (27.3)	0.1965
Number (%) of patients censored	81 (68.6)	121 (72.0)	1 (20.0)	8 (72.7)	
Kaplan-Meier estimates of future perspective in months					
25% quantile (95% CI)	13.60 (5.815 to 23.984)	18.04 (11.499 to 21.979)	6.80 (2.793 to 10.776)	19.38 (0.986 to NC)	
Median (95% CI)	NC (23.984 to NC)	NC (NC to NC)	9.30 (2.793 to NC)	NC (0.986 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	10.78 (2.793 to NC)	NC (19.384 to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.5031		0.0637	
Hazard ratio (95% CI) vs Kd	-	0.86 (0.56 to 1.33)		0.26 (0.05 to 1.19)	
P-value	-	0.5035		0.0826	
Deterioration probability (95% CI)[b]					

A higher score represents a better level of quality of life. Clinical meaningful deterioration change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.1 Health-related quality-of-life endpoints - QLQ-MY20
16.2.6.1.2 Future perspective
16.2.6.1.2.8 Efficacy response data - Subgroup analyses by ISS staging at SE
16.2.6.1.2.8.3 QLQ-MY20 - Time to first improvement by 10 pt in future perspective according to ISS staging at SE (LOCF) - ITT population

	I		II		III		
	Kd (N=71)	**IKd (N=89)**	**Kd (N=31)**	**IKd (N=63)**	**Kd (N=20)**	**IKd (N=26)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	50 (70.4)	68 (76.4)	19 (61.3)	43 (68.3)	9 (45.0)	16 (61.5)	0.6529
Number (%) of patients censored	21 (29.6)	21 (23.6)	12 (38.7)	20 (31.7)	11 (55.0)	10 (38.5)	
Kaplan-Meier estimates of future perspective in months							
25% quantile (95% CI)	1.05 (0.986 to 1.117)	1.02 (0.986 to 1.051)	1.12 (0.986 to 2.234)	1.05 (0.986 to 1.610)	1.12 (0.953 to 4.107)	1.05 (0.953 to 1.084)	
Median (95% CI)	2.09 (1.117 to 4.632)	1.25 (1.084 to 2.070)	3.81 (1.906 to 26.349)	2.00 (1.906 to 4.698)	6.57 (1.117 to NC)	1.97 (1.051 to 4.961)	
75% quantile (95% CI)	NC (5.815 to NC)	5.52 (2.136 to NC)	26.35 (6.571 to 26.349)	NC (5.651 to NC)	NC (6.571 to NC)	NC (2.004 to NC)	
Comparison vs. Kd							
Log-Rank test p-value[a] vs Kd	-	0.2042		0.3451		0.1298	
Hazard ratio (95% CI) vs Kd	-	1.27 (0.88 to 1.83)		1.30 (0.75 to 2.26)		1.87 (0.82 to 4.26)	

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The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.1 Health-related quality-of-life endpoints - QLQ-MY20
16.2.6.1.2 Future perspective
16.2.6.1.2.8 Efficacy response data - Subgroup analyses by ISS staging at SE
16.2.6.1.2.8.4 QLQ-MY20 - Time to first deterioration by 10 pt in future perspective according to ISS staging at SE (LOCF) - ITT population

	I		II		III		
	Kd (N=71)	**IKd (N=89)**	**Kd (N=31)**	**IKd (N=63)**	**Kd (N=20)**	**IKd (N=26)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	38 (53.5)	47 (52.8)	18 (58.1)	39 (61.9)	12 (60.0)	7 (26.9)	0.1263
Number (%) of patients censored	33 (46.5)	42 (47.2)	13 (41.9)	24 (38.1)	8 (40.0)	19 (73.1)	
Kaplan-Meier estimates of future perspective in months							
25% quantile (95% CI)	1.64 (1.051 to 3.680)	2.92 (1.150 to 3.778)	1.91 (1.051 to 3.055)	1.94 (1.051 to 2.793)	1.12 (0.953 to 2.793)	3.81 (0.986 to NC)	
Median (95% CI)	13.40 (4.830 to NC)	14.06 (5.782 to NC)	10.18 (2.070 to NC)	5.85 (2.825 to 18.300)	5.32 (1.117 to NC)	NC (3.811 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (12.485 to NC)	NC (NC to NC)	NC (6.538 to NC)	NC (NC to NC)	
Comparison vs. Kd							
Log-Rank test p-value[a] vs Kd	-	0.7790		0.7491		0.0359	
Hazard ratio (95% CI) vs Kd	-	0.94 (0.61 to 1.44)		1.10 (0.63 to 1.92)		0.38 (0.15 to 0.97)	
P-value	-	0.7782		0.7492		0.0433	

A higher score represents a better level of quality of life. Clinical meaningful deterioration change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
PGM=DEVOPS/SAR650984/EFC15246/CIR_RWE/REPORT/PGM/eff_km_subgp_sr_sig_de_i_t.sas OUT=REPORT/OUTPUT/eff_km_my20_per_detl_seiss_de_i_t_x.rtf (07APR2021 14:41)

16.2.6.1 Health-related quality-of-life endpoints - QLQ-MY20
16.2.6.1.2 Future perspective
16.2.6.1.2.8 Efficacy response data - Subgroup analyses by ISS staging at SE
16.2.6.1.2.8.5 QLQ-MY20 - Time until permanent improvement by 10 pt in future perspective according to ISS staging at SE (LOCF) - ITT population

	I		II		III		
	Kd (N=71)	**IKd (N=89)**	**Kd (N=31)**	**IKd (N=63)**	**Kd (N=20)**	**IKd (N=26)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	29 (40.8)	44 (49.4)	10 (32.3)	23 (36.5)	3 (15.0)	10 (38.5)	0.3559
Number (%) of patients censored	42 (59.2)	45 (50.6)	21 (67.7)	40 (63.5)	17 (85.0)	16 (61.5)	
Kaplan-Meier estimates of future perspective in months							
25% quantile (95% CI)	4.63 (1.117 to 16.000)	3.02 (1.051 to 10.349)	13.83 (0.986 to 26.349)	7.06 (1.971 to 18.891)	NC (1.018 to NC)	1.41 (0.953 to 7.754)	
Median (95% CI)	24.05 (16.329 to NC)	19.84 (15.704 to NC)	24.02 (24.016 to 26.349)	NC (18.891 to NC)	NC (NC to NC)	NC (2.103 to NC)	
75% quantile (95% CI)	NC (24.049 to NC)	NC (NC to NC)	26.35 (24.016 to 26.349)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Kd							
Log-Rank test p-value[a] vs Kd	-	0.3305		0.3671		0.0693	

A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.1 Health-related quality-of-life endpoints - QLQ-MY20
16.2.6.1.2 Future perspective
16.2.6.1.2.8 Efficacy response data - Subgroup analyses by ISS staging at SE
16.2.6.1.2.8.6 QLQ-MY20 - Time until permanent deterioration by 10 pt in future perspective according to ISS staging at SE (LOCF) - ITT population

	I		II		III		
	Kd (N=71)	**IKd (N=89)**	**Kd (N=31)**	**IKd (N=63)**	**Kd (N=20)**	**IKd (N=26)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	21 (29.6)	23 (25.8)	11 (35.5)	24 (38.1)	8 (40.0)	3 (11.5)	0.2129
Number (%) of patients censored	50 (70.4)	66 (74.2)	20 (64.5)	39 (61.9)	12 (60.0)	23 (88.5)	
Kaplan-Meier estimates of future perspective in months							
25% quantile (95% CI)	13.96 (4.862 to NC)	19.38 (11.499 to NC)	11.50 (2.004 to NC)	15.38 (3.285 to 20.238)	6.54 (1.051 to 16.657)	NC (0.986 to NC)	
Median (95% CI)	NC (23.984 to NC)	NC (NC to NC)	NC (12.189 to NC)	NC (20.238 to NC)	NC (6.538 to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (16.657 to NC)	NC (NC to NC)	
Comparison vs. Kd							
Log-Rank test p-value[a] vs Kd	-	0.5632		0.9148		0.0498	
Hazard ratio (95% CI) vs Kd	-	0.84 (0.46 to 1.52)		1.04 (0.51 to 2.12)		0.29 (0.08 to 1.08)	
P-value	-	0.5637		0.9154		0.0656	

A higher score represents a better level of quality of life. Clinical meaningful deterioration change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.1 Health-related quality-of-life endpoints - QLQ-MY20
16.2.6.1.2 Future perspective
16.2.6.1.2.9 Efficacy response data - Subgroup analyses by R-ISS stage at SE
16.2.6.1.2.9.3 QLQ-MY20 - Time to first improvement by 10 pt in future perspective according to R-ISS stage at SE (LOCF) - ITT population

	I or II		III		Not classified		
	Kd (N=103)	**IKd (N=155)**	**Kd (N=8)**	**IKd (N=16)**	**Kd (N=12)**	**IKd (N=8)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	68 (66.0)	114 (73.5)	3 (37.5)	10 (62.5)	8 (66.7)	4 (50.0)	0.7350
Number (%) of patients censored	35 (34.0)	41 (26.5)	5 (62.5)	6 (37.5)	4 (33.3)	4 (50.0)	
Kaplan-Meier estimates of future perspective in months							
25% quantile (95% CI)	1.05 (0.986 to 1.117)	1.02 (0.986 to 1.051)	1.08 (0.986 to NC)	1.08 (0.953 to 2.004)	1.53 (0.953 to 3.713)	1.08 (1.018 to 5.125)	
Median (95% CI)	2.86 (1.938 to 5.618)	1.94 (1.150 to 2.070)	NC (0.986 to NC)	2.00 (1.018 to 4.961)	4.17 (0.986 to NC)	3.60 (1.018 to NC)	
75% quantile (95% CI)	26.35 (12.583 to 26.349)	NC (3.713 to NC)	NC (1.117 to NC)	4.96 (2.004 to NC)	NC (3.713 to NC)	NC (1.084 to NC)	
Comparison vs. Kd							
Log-Rank test p-value[a] vs Kd	-	0.1076		0.3009		0.9622	
Hazard ratio (95% CI) vs Kd	-	1.28 (0.95 to 1.73)		1.96 (0.54 to 7.16)		1.03 (0.31 to 3.43)	
P-value	-	0.1085		0.3097		0.9620	

A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
PGM=DEVOPS/SAR650984/EFC15246/CIR_RWE/REPORT/PGM/eff_km_subgp_sr_sig_de_i_t.sas OUT=REPORT/OUTPUT/eff_km_my20_per_impl_seriss_de_i_t_x.rtf (07APR2021 14:41)

16.2.6.1 Health-related quality-of-life endpoints - QLQ-MY20
16.2.6.1.2 Future perspective
16.2.6.1.2.9 Efficacy response data - Subgroup analyses by R-ISS stage at SE
16.2.6.1.2.9.4 QLQ-MY20 - Time to first deterioration by 10 pt in future perspective according to R-ISS stage at SE (LOCF) - ITT population

	I or II		III		Not classified		
	Kd (N=103)	**IKd (N=155)**	**Kd (N=8)**	**IKd (N=16)**	**Kd (N=12)**	**IKd (N=8)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	57 (55.3)	87 (56.1)	5 (62.5)	4 (25.0)	7 (58.3)	3 (37.5)	0.2326
Number (%) of patients censored	46 (44.7)	68 (43.9)	3 (37.5)	12 (75.0)	5 (41.7)	5 (62.5)	
Kaplan-Meier estimates of future perspective in months							
25% quantile (95% CI)	1.91 (1.117 to 2.825)	2.04 (1.216 to 3.088)	1.05 (0.953 to 2.793)	3.81 (0.986 to NC)	1.48 (0.986 to 7.721)	1.02 (0.986 to NC)	
Median (95% CI)	10.12 (4.830 to NC)	8.54 (5.552 to NC)	2.79 (0.953 to NC)	NC (2.103 to NC)	10.84 (0.986 to NC)	NC (0.986 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (1.117 to NC)	NC (NC to NC)	NC (7.721 to NC)	NC (1.018 to NC)	
Comparison vs. Kd							
Log-Rank test p-value[a] vs Kd	-	0.8193		0.0802		0.9997	
Hazard ratio (95% CI) vs Kd	-	0.96 (0.69 to 1.34)		0.33 (0.09 to 1.22)		1.00 (0.26 to 3.88)	
P-value	-	0.8185		0.0963		1.0000	

A higher score represents a better level of quality of life. Clinical meaningful deterioration change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
PGM=DEVOPS/SAR650984/EFC15246/CIR_RWE/REPORT/PGM/eff_km_subgp_sr_sig_de_i_t.sas OUT=REPORT/OUTPUT/eff_km_my20_per_detl_seriss_de_i_t_x.rtf (07APR2021 14:41)

16.2.6.1 Health-related quality-of-life endpoints - QLQ-MY20
16.2.6.1.2 Future perspective
16.2.6.1.2.9 Efficacy response data - Subgroup analyses by R-ISS stage at SE
16.2.6.1.2.9.5 QLQ-MY20 - Time until permanent improvement by 10 pt in future perspective according to R-ISS stage at SE (LOCF) - ITT population

	I or II		III		Not classified		
	Kd (N=103)	**IKd (N=155)**	**Kd (N=8)**	**IKd (N=16)**	**Kd (N=12)**	**IKd (N=8)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	38 (36.9)	68 (43.9)	1 (12.5)	7 (43.8)	3 (25.0)	3 (37.5)	0.2566
Number (%) of patients censored	65 (63.1)	87 (56.1)	7 (87.5)	9 (56.3)	9 (75.0)	5 (62.5)	
Kaplan-Meier estimates of future perspective in months							
25% quantile (95% CI)	9.36 (1.117 to 16.329)	4.76 (1.906 to 11.992)	NC (7.524 to NC)	1.41 (0.953 to 7.754)	NC (1.117 to NC)	1.08 (1.018 to NC)	
Median (95% CI)	24.05 (24.016 to NC)	NC (18.891 to NC)	NC (7.524 to NC)	7.75 (1.084 to NC)	NC (4.632 to NC)	10.81 (1.018 to NC)	
75% quantile (95% CI)	26.35 (24.049 to NC)	NC (NC to NC)	NC (7.524 to NC)	NC (7.754 to NC)	NC (NC to NC)	NC (1.084 to NC)	
Comparison vs. Kd							
Log-Rank test p-value[a] vs Kd	-	0.3412		0.1399		0.2051	
Hazard ratio (95% CI) vs Kd	-	1.21 (0.81 to 1.81)		4.26 (0.52 to 34.70)		2.71 (0.54 to 13.51)	

A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.1 Health-related quality-of-life endpoints - QLQ-MY20
16.2.6.1.2 Future perspective
16.2.6.1.2.9 Efficacy response data - Subgroup analyses by R-ISS stage at SE
16.2.6.1.2.9.6 QLQ-MY20 - Time until permanent deterioration by 10 pt in future perspective according to R-ISS stage at SE (LOCF) - ITT population

	I or II		III		Not classified		
	Kd (N=103)	**IKd (N=155)**	**Kd (N=8)**	**IKd (N=16)**	**Kd (N=12)**	**IKd (N=8)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	33 (32.0)	47 (30.3)	3 (37.5)	1 (6.3)	5 (41.7)	2 (25.0)	0.3308
Number (%) of patients censored	70 (68.0)	108 (69.7)	5 (62.5)	15 (93.8)	7 (58.3)	6 (75.0)	
Kaplan-Meier estimates of future perspective in months							
25% quantile (95% CI)	11.50 (5.815 to 18.891)	16.62 (8.246 to 21.979)	1.12 (1.051 to NC)	NC (0.986 to NC)	13.45 (1.084 to 23.984)	19.38 (3.745 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (1.051 to NC)	NC (NC to NC)	23.98 (6.538 to 23.984)	NC (3.745 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (2.793 to NC)	NC (NC to NC)	23.98 (NC to NC)	NC (19.384 to NC)	
Comparison vs. Kd							
Log-Rank test p-value[a] vs Kd	-	0.6095		0.0743		0.9480	

A higher score represents a better level of quality of life. Clinical meaningful deterioration change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.1 Health-related quality-of-life endpoints - QLQ-MY20
16.2.6.1.2 Future perspective
16.2.6.1.2.10 Efficacy response data - Subgroup analyses by nb of prior lines
16.2.6.1.2.10.3 QLQ-MY20 - Time to first improvement by 10 pt in future perspective according to nb of prior lines (LOCF) - ITT population

	1		>1		
	Kd (N=55)	**IKd (N=79)**	**Kd (N=68)**	**IKd (N=100)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	32 (58.2)	56 (70.9)	47 (69.1)	72 (72.0)	0.2150
Number (%) of patients censored	23 (41.8)	23 (29.1)	21 (30.9)	28 (28.0)	
Kaplan-Meier estimates of future perspective in months					
25% quantile (95% CI)	1.12 (0.986 to 2.136)	1.02 (0.986 to 1.051)	1.02 (0.986 to 1.117)	1.05 (0.986 to 1.084)	
Median (95% CI)	5.62 (2.136 to 26.349)	1.97 (1.117 to 2.957)	2.14 (1.117 to 3.713)	1.94 (1.150 to 2.070)	
75% quantile (95% CI)	26.35 (NC to NC)	NC (4.698 to NC)	NC (3.811 to NC)	14.46 (2.891 to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.0397		0.5209	
Hazard ratio (95% CI) vs Kd	-	1.58 (1.02 to 2.46)		1.13 (0.78 to 1.63)	
P-value	-	0.0414		0.5212	
Hazard ratio inverted (95% CI) vs IKd		-		0.89 (0.61 to 1.28)	

A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.1 Health-related quality-of-life endpoints - QLQ-MY20
16.2.6.1.2 Future perspective
16.2.6.1.2.10 Efficacy response data - Subgroup analyses by nb of prior lines
16.2.6.1.2.10.4 QLQ-MY20 - Time to first deterioration by 10 pt in future perspective according to nb of prior lines (LOCF) - ITT population

	1		>1		
	Kd (N=55)	**IKd (N=79)**	**Kd (N=68)**	**IKd (N=100)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	35 (63.6)	41 (51.9)	34 (50.0)	53 (53.0)	0.1239
Number (%) of patients censored	20 (36.4)	38 (48.1)	34 (50.0)	47 (47.0)	
Kaplan-Meier estimates of future perspective in months					
25% quantile (95% CI)	1.12 (0.986 to 1.314)	2.60 (1.117 to 4.041)	2.07 (1.281 to 6.538)	2.00 (1.150 to 2.990)	
Median (95% CI)	4.42 (1.314 to 13.963)	8.54 (4.698 to NC)	12.48 (7.425 to NC)	10.61 (3.778 to NC)	
75% quantile (95% CI)	NC (13.963 to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.1166		0.5962	
Hazard ratio (95% CI) vs Kd	-	0.70 (0.44 to 1.10)		1.12 (0.73 to 1.73)	
P-value	-	0.1186		0.5965	
Deterioration probability (95% CI)[b]					

A higher score represents a better level of quality of life. Clinical meaningful deterioration change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.6.1 Health-related quality-of-life endpoints - QLQ-MY20
16.2.6.1.2 Future perspective
16.2.6.1.2.10 Efficacy response data - Subgroup analyses by nb of prior lines
16.2.6.1.2.10.5 QLQ-MY20 - Time until permanent improvement by 10 pt in future perspective according to nb of prior lines (LOCF) - ITT population

	1		>1		
	Kd (N=55)	**IKd (N=79)**	**Kd (N=68)**	**IKd (N=100)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	17 (30.9)	33 (41.8)	25 (36.8)	45 (45.0)	0.6192
Number (%) of patients censored	38 (69.1)	46 (58.2)	43 (63.2)	55 (55.0)	
Kaplan-Meier estimates of future perspective in months					
25% quantile (95% CI)	19.52 (1.117 to 24.049)	9.03 (1.150 to 16.099)	7.52 (1.117 to 16.000)	2.89 (1.117 to 7.754)	
Median (95% CI)	24.05 (24.016 to 26.349)	NC (18.464 to NC)	NC (16.000 to NC)	20.30 (15.704 to NC)	
75% quantile (95% CI)	26.35 (24.016 to 26.349)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.1056		0.4015	
Hazard ratio (95% CI) vs Kd	-	1.63 (0.90 to 2.97)		1.23 (0.76 to 2.01)	
P-value	-	0.1090		0.4024	
Improvement probability (95% CI)[b]					

A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.1 Health-related quality-of-life endpoints - QLQ-MY20
16.2.6.1.2 Future perspective
16.2.6.1.2.10 Efficacy response data - Subgroup analyses by nb of prior lines
16.2.6.1.2.10.6 QLQ-MY20 - Time until permanent deterioration by 10 pt in future perspective according to nb of prior lines (LOCF) - ITT population

	1		>1		
	Kd (N=55)	**IKd (N=79)**	**Kd (N=68)**	**IKd (N=100)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	20 (36.4)	25 (31.6)	21 (30.9)	25 (25.0)	0.8760
Number (%) of patients censored	35 (63.6)	54 (68.4)	47 (69.1)	75 (75.0)	
Kaplan-Meier estimates of future perspective in months					
25% quantile (95% CI)	9.23 (2.004 to 23.984)	16.62 (7.491 to 20.567)	11.50 (6.374 to NC)	20.24 (6.407 to NC)	
Median (95% CI)	23.98 (23.984 to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (23.984 to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.5683		0.4144	
Hazard ratio (95% CI) vs Kd	-	0.84 (0.47 to 1.52)		0.79 (0.44 to 1.40)	
P-value	-	0.5688		0.4156	
Deterioration probability (95% CI)[b]					

A higher score represents a better level of quality of life. Clinical meaningful deterioration change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.1 Health-related quality-of-life endpoints - QLQ-MY20
16.2.6.1.2 Future perspective
16.2.6.1.2.11 Efficacy response data - Subgroup analyses by cytogenetic abnormality
16.2.6.1.2.11.3 QLQ-MY20 - Time to first improvement by 10 pt in future perspective according to cytogenetic abnormality (LOCF) - ITT population

	At least one		None		
	Kd (N=31)	**IKd (N=42)**	**Kd (N=77)**	**IKd (N=114)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	17 (54.8)	31 (73.8)	52 (67.5)	81 (71.1)	0.2979
Number (%) of patients censored	14 (45.2)	11 (26.2)	25 (32.5)	33 (28.9)	
Kaplan-Meier estimates of future perspective in months					
25% quantile (95% CI)	1.08 (0.986 to 1.150)	0.99 (0.953 to 1.051)	1.05 (0.986 to 1.117)	1.05 (0.986 to 1.084)	
Median (95% CI)	3.84 (1.117 to NC)	1.28 (1.051 to 2.004)	2.83 (1.906 to 6.571)	1.97 (1.183 to 2.793)	
75% quantile (95% CI)	NC (5.618 to NC)	NC (1.971 to NC)	26.35 (9.101 to 26.349)	NC (3.713 to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.1102		0.3614	
Hazard ratio (95% CI) vs Kd	-	1.61 (0.89 to 2.92)		1.18 (0.83 to 1.67)	
P-value	-	0.1136		0.3619	
Improvement probability (95% CI)[b]					

A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.1 Health-related quality-of-life endpoints - QLQ-MY20
16.2.6.1.2 Future perspective
16.2.6.1.2.11 Efficacy response data - Subgroup analyses by cytogenetic abnormality
16.2.6.1.2.11.4 QLQ-MY20 - Time to first deterioration by 10 pt in future perspective according to cytogenetic abnormality (LOCF) - ITT population

	At least one		None		
	Kd (N=31)	**IKd (N=42)**	**Kd (N=77)**	**IKd (N=114)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	18 (58.1)	23 (54.8)	43 (55.8)	62 (54.4)	0.6964
Number (%) of patients censored	13 (41.9)	19 (45.2)	34 (44.2)	52 (45.6)	
Kaplan-Meier estimates of future perspective in months					
25% quantile (95% CI)	1.12 (0.986 to 2.103)	2.04 (0.986 to 4.041)	1.91 (1.117 to 3.055)	2.00 (1.183 to 3.088)	
Median (95% CI)	5.60 (1.938 to NC)	11.10 (3.811 to NC)	8.44 (5.322 to NC)	10.15 (4.698 to NC)	
75% quantile (95% CI)	NC (11.499 to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.5432		0.8294	
Hazard ratio (95% CI) vs Kd	-	0.83 (0.45 to 1.53)		0.96 (0.65 to 1.41)	
P-value	-	0.5438		0.8287	
Deterioration probability (95% CI)[b]					

A higher score represents a better level of quality of life. Clinical meaningful deterioration change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.1 Health-related quality-of-life endpoints - QLQ-MY20
16.2.6.1.2 Future perspective
16.2.6.1.2.11 Efficacy response data - Subgroup analyses by cytogenetic abnormality
16.2.6.1.2.11.5 QLQ-MY20 - Time until permanent improvement by 10 pt in future perspective according to cytogenetic abnormality (LOCF) - ITT population

	At least one		None		
	Kd (N=31)	**IKd (N=42)**	**Kd (N=77)**	**IKd (N=114)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	11 (35.5)	21 (50.0)	28 (36.4)	46 (40.4)	0.6230
Number (%) of patients censored	20 (64.5)	21 (50.0)	49 (63.6)	68 (59.6)	
Kaplan-Meier estimates of future perspective in months					
25% quantile (95% CI)	1.94 (1.018 to NC)	1.41 (1.018 to 9.561)	11.14 (1.938 to 19.515)	7.75 (2.103 to 17.741)	
Median (95% CI)	NC (7.524 to NC)	18.63 (7.556 to NC)	24.05 (24.016 to NC)	NC (19.614 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	26.35 (24.049 to NC)	NC (NC to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.3564		0.5139	
Hazard ratio (95% CI) vs Kd	-	1.41 (0.68 to 2.92)		1.17 (0.73 to 1.89)	
P-value	-	0.3587		0.5144	
Improvement probability (95% CI)[b]					

A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.1 Health-related quality-of-life endpoints - QLQ-MY20
16.2.6.1.2 Future perspective
16.2.6.1.2.11 Efficacy response data - Subgroup analyses by cytogenetic abnormality
16.2.6.1.2.11.6 QLQ-MY20 - Time until permanent deterioration by 10 pt in future perspective according to cytogenetic abnormality (LOCF) - ITT population

	At least one		None		
	Kd (N=31)	**IKd (N=42)**	**Kd (N=77)**	**IKd (N=114)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	12 (38.7)	12 (28.6)	24 (31.2)	33 (28.9)	0.5533
Number (%) of patients censored	19 (61.3)	30 (71.4)	53 (68.8)	81 (71.1)	
Kaplan-Meier estimates of future perspective in months					
25% quantile (95% CI)	6.37 (1.051 to 18.300)	16.43 (3.745 to NC)	13.60 (4.961 to NC)	18.07 (11.499 to 21.979)	
Median (95% CI)	NC (10.776 to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.3274		0.6832	
Hazard ratio (95% CI) vs Kd	-	0.67 (0.30 to 1.50)		0.90 (0.53 to 1.52)	
P-value	-	0.3305		0.6833	
Deterioration probability (95% CI)[b]					

A higher score represents a better level of quality of life. Clinical meaningful deterioration change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
PGM=DEVOPS/SAR650984/EFC15246/CIR_RWE/REPORT/PGM/eff_km_subgp_sr_sig_de_i_t.sas OUT=REPORT/OUTPUT/eff_km_my20_per_detpl_cyto_de_i_t_x.rtf (07APR2021 14:41)

16.2.6.1 Health-related quality-of-life endpoints - QLQ-MY20
16.2.6.1.2 Future perspective
16.2.6.1.2.12 Efficacy response data - Subgroup analyses by MM type at SE
16.2.6.1.2.12.3 QLQ-MY20 - Time to first improvement by 10 pt in future perspective according to MM type at SE (LOCF) - ITT population

	IgG		Non-IgG		
	Kd (N=85)	**IKd (N=126)**	**Kd (N=38)**	**IKd (N=53)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	55 (64.7)	92 (73.0)	24 (63.2)	36 (67.9)	0.3553
Number (%) of patients censored	30 (35.3)	34 (27.0)	14 (36.8)	17 (32.1)	
Kaplan-Meier estimates of future perspective in months					
25% quantile (95% CI)	1.12 (1.018 to 1.150)	1.02 (0.986 to 1.051)	1.03 (0.986 to 1.117)	1.08 (0.986 to 1.906)	
Median (95% CI)	3.71 (1.938 to 8.575)	1.61 (1.117 to 2.004)	2.48 (1.084 to 26.349)	2.07 (1.380 to 4.698)	
75% quantile (95% CI)	NC (12.583 to NC)	11.33 (2.957 to NC)	26.35 (4.107 to 26.349)	NC (4.665 to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.0369		0.7642	
Hazard ratio (95% CI) vs Kd	-	1.43 (1.02 to 1.99)		1.08 (0.64 to 1.83)	
P-value	-	0.0379		0.7642	
Hazard ratio inverted (95% CI) vs IKd		-		0.92 (0.55 to 1.56)	

A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.1 Health-related quality-of-life endpoints - QLQ-MY20
16.2.6.1.2 Future perspective
16.2.6.1.2.12 Efficacy response data - Subgroup analyses by MM type at SE
16.2.6.1.2.12.4 QLQ-MY20 - Time to first deterioration by 10 pt in future perspective according to MM type at SE (LOCF) - ITT population

	IgG		Non-IgG		
	Kd (N=85)	**IKd (N=126)**	**Kd (N=38)**	**IKd (N=53)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	50 (58.8)	59 (46.8)	19 (50.0)	35 (66.0)	0.0544
Number (%) of patients censored	35 (41.2)	67 (53.2)	19 (50.0)	18 (34.0)	
Kaplan-Meier estimates of future perspective in months					
25% quantile (95% CI)	1.25 (1.051 to 2.004)	2.79 (1.511 to 3.745)	2.35 (1.051 to 5.322)	1.91 (0.986 to 3.187)	
Median (95% CI)	7.89 (2.957 to 19.614)	21.03 (7.392 to NC)	11.50 (3.055 to NC)	5.78 (2.825 to 10.382)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (10.382 to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.1042		0.2072	
Hazard ratio (95% CI) vs Kd	-	0.73 (0.50 to 1.07)		1.43 (0.82 to 2.50)	
P-value	-	0.1056		0.2096	
Deterioration probability (95% CI)[b]					

A higher score represents a better level of quality of life. Clinical meaningful deterioration change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
PGM=DEVOPS/SAR650984/EFC15246/CIR_RWE/REPORT/PGM/eff_km_subgp_sr_sig_de_i_t.sas OUT=REPORT/OUTPUT/eff_km_my20_per_detl_semm_de_i_t_x.rtf (07APR2021 14:41)

16.2.6.1 Health-related quality-of-life endpoints - QLQ-MY20
16.2.6.1.2 Future perspective
16.2.6.1.2.12 Efficacy response data - Subgroup analyses by MM type at SE
16.2.6.1.2.12.5 QLQ-MY20 - Time until permanent improvement by 10 pt in future perspective according to MM type at SE (LOCF) - ITT population

	IgG		Non-IgG		
	Kd (N=85)	**IKd (N=126)**	**Kd (N=38)**	**IKd (N=53)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	29 (34.1)	59 (46.8)	13 (34.2)	19 (35.8)	0.4111
Number (%) of patients censored	56 (65.9)	67 (53.2)	25 (65.8)	34 (64.2)	
Kaplan-Meier estimates of future perspective in months					
25% quantile (95% CI)	10.18 (1.117 to 19.515)	2.89 (1.150 to 9.035)	7.52 (0.986 to 26.349)	7.06 (1.084 to 18.530)	
Median (95% CI)	24.05 (24.049 to NC)	20.30 (16.099 to NC)	24.02 (13.832 to 26.349)	NC (18.464 to NC)	
75% quantile (95% CI)	NC (24.049 to NC)	NC (NC to NC)	26.35 (24.016 to 26.349)	NC (NC to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.0726		0.6298	
Hazard ratio (95% CI) vs Kd	-	1.50 (0.96 to 2.34)		1.20 (0.57 to 2.52)	
P-value	-	0.0746		0.6302	

A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.1 Health-related quality-of-life endpoints - QLQ-MY20
16.2.6.1.2 Future perspective
16.2.6.1.2.12 Efficacy response data - Subgroup analyses by MM type at SE
16.2.6.1.2.12.6 QLQ-MY20 - Time until permanent deterioration by 10 pt in future perspective according to MM type at SE (LOCF) - ITT population

	IgG		Non-IgG		
	Kd (N=85)	**IKd (N=126)**	**Kd (N=38)**	**IKd (N=53)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	29 (34.1)	30 (23.8)	12 (31.6)	20 (37.7)	0.2298
Number (%) of patients censored	56 (65.9)	96 (76.2)	26 (68.4)	33 (62.3)	
Kaplan-Meier estimates of future perspective in months					
25% quantile (95% CI)	12.94 (4.238 to 18.891)	20.53 (14.817 to NC)	9.23 (2.793 to NC)	14.00 (3.745 to 19.581)	
Median (95% CI)	NC (23.984 to NC)	NC (NC to NC)	NC (16.624 to NC)	NC (16.854 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.1327		0.7037	
Hazard ratio (95% CI) vs Kd	-	0.68 (0.41 to 1.13)		1.15 (0.56 to 2.35)	
P-value	-	0.1351		0.7039	

A higher score represents a better level of quality of life. Clinical meaningful deterioration change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.1 Health-related quality-of-life endpoints - QLQ-MY20
16.2.6.1.2 Future perspective
16.2.6.1.2.13 Efficacy response data - Subgroup analyses by previous autologous stem-cell
16.2.6.1.2.13.3 QLQ-MY20 - Time to first improvement by 10 pt in future perspective according to previous autologous stem-cell (LOCF) - ITT population

	Yes		No		
	Kd (N=69)	**IKd (N=116)**	**Kd (N=54)**	**IKd (N=63)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	43 (62.3)	81 (69.8)	36 (66.7)	47 (74.6)	0.7488
Number (%) of patients censored	26 (37.7)	35 (30.2)	18 (33.3)	16 (25.4)	
Kaplan-Meier estimates of future perspective in months					
25% quantile (95% CI)	1.05 (0.986 to 1.117)	1.02 (0.986 to 1.051)	1.08 (1.018 to 2.037)	1.05 (0.986 to 1.150)	
Median (95% CI)	3.71 (1.873 to 9.298)	1.97 (1.117 to 2.825)	2.86 (1.906 to 5.815)	1.94 (1.150 to 2.004)	
75% quantile (95% CI)	NC (12.583 to NC)	NC (4.698 to NC)	26.35 (5.618 to 26.349)	5.65 (2.004 to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.2038		0.1083	
Hazard ratio (95% CI) vs Kd	-	1.27 (0.88 to 1.84)		1.43 (0.92 to 2.22)	
P-value	-	0.2048		0.1101	
Improvement probability (95% CI)[b]					

A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.1 Health-related quality-of-life endpoints - QLQ-MY20
16.2.6.1.2 Future perspective
16.2.6.1.2.13 Efficacy response data - Subgroup analyses by previous autologous stem-cell
16.2.6.1.2.13.4 QLQ-MY20 - Time to first deterioration by 10 pt in future perspective according to previous autologous stem-cell (LOCF) - ITT population

	Yes		No		
	Kd (N=69)	**IKd (N=116)**	**Kd (N=54)**	**IKd (N=63)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	36 (52.2)	61 (52.6)	33 (61.1)	33 (52.4)	0.3944
Number (%) of patients censored	33 (47.8)	55 (47.4)	21 (38.9)	30 (47.6)	
Kaplan-Meier estimates of future perspective in months					
25% quantile (95% CI)	1.46 (1.051 to 4.961)	1.97 (1.150 to 2.825)	1.87 (1.051 to 2.103)	3.09 (1.150 to 4.698)	
Median (95% CI)	13.01 (5.815 to NC)	10.15 (4.665 to NC)	6.34 (2.103 to 13.405)	11.40 (4.698 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (13.405 to NC)	NC (NC to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.9659		0.2766	
Hazard ratio (95% CI) vs Kd	-	1.01 (0.67 to 1.52)		0.77 (0.47 to 1.24)	
P-value	-	0.9660		0.2780	
Deterioration probability (95% CI)[b]					

A higher score represents a better level of quality of life. Clinical meaningful deterioration change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.1 Health-related quality-of-life endpoints - QLQ-MY20
16.2.6.1.2 Future perspective
16.2.6.1.2.13 Efficacy response data - Subgroup analyses by previous autologous stem-cell
16.2.6.1.2.13.5 QLQ-MY20 - Time until permanent improvement by 10 pt in future perspective according to previous autologous stem-cell (LOCF) - ITT population

	Yes		No		
	Kd (N=69)	**IKd (N=116)**	**Kd (N=54)**	**IKd (N=63)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	19 (27.5)	52 (44.8)	23 (42.6)	26 (41.3)	0.1658
Number (%) of patients censored	50 (72.5)	64 (55.2)	31 (57.4)	37 (58.7)	
Kaplan-Meier estimates of future perspective in months					
25% quantile (95% CI)	10.18 (1.117 to NC)	3.81 (1.150 to 11.992)	7.52 (1.117 to 16.329)	4.17 (1.117 to 13.109)	
Median (95% CI)	NC (NC to NC)	21.45 (17.741 to NC)	24.02 (15.146 to 26.349)	NC (13.109 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	26.35 (24.016 to 26.349)	NC (NC to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.0391		0.8291	
Hazard ratio (95% CI) vs Kd	-	1.73 (1.02 to 2.92)		1.06 (0.60 to 1.88)	
P-value	-	0.0417		0.8295	
Hazard ratio inverted (95% CI) vs IKd		-		0.94 (0.53 to 1.66)	

A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.1 Health-related quality-of-life endpoints - QLQ-MY20
16.2.6.1.2 Future perspective
16.2.6.1.2.13 Efficacy response data - Subgroup analyses by previous autologous stem-cell
16.2.6.1.2.13.6 QLQ-MY20 - Time until permanent deterioration by 10 pt in future perspective according to previous autologous stem-cell (LOCF) - ITT population

	Yes		No		
	Kd (N=69)	**IKd (N=116)**	**Kd (N=54)**	**IKd (N=63)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	22 (31.9)	33 (28.4)	19 (35.2)	17 (27.0)	0.8430
Number (%) of patients censored	47 (68.1)	83 (71.6)	35 (64.8)	46 (73.0)	
Kaplan-Meier estimates of future perspective in months					
25% quantile (95% CI)	9.30 (3.844 to NC)	18.56 (13.273 to NC)	11.50 (4.238 to 23.984)	16.16 (6.407 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (18.300 to NC)	NC (21.979 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.5428		0.4632	
Hazard ratio (95% CI) vs Kd	-	0.85 (0.49 to 1.45)		0.78 (0.41 to 1.51)	
P-value	-	0.5432		0.4643	
Deterioration probability (95% CI)[b]					

A higher score represents a better level of quality of life. Clinical meaningful deterioration change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.1 Health-related quality-of-life endpoints - QLQ-MY20
16.2.6.1.2 Future perspective
16.2.6.1.2.14 Efficacy response data - Subgroup analyses by baseline eGFR (MDRD)
16.2.6.1.2.14.3 QLQ-MY20 - Time to first improvement by 10 pt in future perspective according to baseline eGFR (MDRD) (LOCF) - ITT population

	>=60 mL/min/1.73m2		<60 mL/min/1.73m2		
	Kd (N=93)	**IKd (N=122)**	**Kd (N=18)**	**IKd (N=43)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	63 (67.7)	88 (72.1)	11 (61.1)	32 (74.4)	0.4551
Number (%) of patients censored	30 (32.3)	34 (27.9)	7 (38.9)	11 (25.6)	
Kaplan-Meier estimates of future perspective in months					
25% quantile (95% CI)	1.08 (1.018 to 1.117)	0.99 (0.986 to 1.051)	1.02 (0.920 to 1.906)	1.05 (0.986 to 1.610)	
Median (95% CI)	2.94 (1.938 to 5.815)	1.91 (1.084 to 2.103)	2.14 (0.986 to NC)	1.97 (1.084 to 2.366)	
75% quantile (95% CI)	26.35 (9.298 to 26.349)	5.65 (2.957 to NC)	NC (2.136 to NC)	14.46 (2.070 to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.0448		0.9223	
Hazard ratio (95% CI) vs Kd	-	1.39 (1.01 to 1.93)		1.03 (0.52 to 2.06)	
P-value	-	0.0458		0.9229	
Hazard ratio inverted (95% CI) vs IKd		-		0.97 (0.49 to 1.92)	

A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.1 Health-related quality-of-life endpoints - QLQ-MY20
16.2.6.1.2 Future perspective
16.2.6.1.2.14 Efficacy response data - Subgroup analyses by baseline eGFR (MDRD)
16.2.6.1.2.14.4 QLQ-MY20 - Time to first deterioration by 10 pt in future perspective according to baseline eGFR (MDRD) (LOCF) - ITT population

	>=60 mL/min/1.73m2		<60 mL/min/1.73m2		
	Kd (N=93)	**IKd (N=122)**	**Kd (N=18)**	**IKd (N=43)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	50 (53.8)	68 (55.7)	13 (72.2)	20 (46.5)	0.0823
Number (%) of patients censored	43 (46.2)	54 (44.3)	5 (27.8)	23 (53.5)	
Kaplan-Meier estimates of future perspective in months					
25% quantile (95% CI)	1.23 (1.051 to 1.938)	2.79 (1.183 to 3.285)	2.07 (1.051 to 5.322)	1.91 (0.986 to 6.111)	
Median (95% CI)	11.60 (3.055 to NC)	8.54 (4.698 to 21.027)	5.54 (1.314 to 11.499)	NC (2.793 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	11.50 (5.322 to NC)	NC (NC to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.8461		0.0628	
Hazard ratio (95% CI) vs Kd	-	1.04 (0.72 to 1.49)		0.52 (0.26 to 1.05)	
P-value	-	0.8465		0.0675	
Deterioration probability (95% CI)[b]					

A higher score represents a better level of quality of life. Clinical meaningful deterioration change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
PGM=DEVOPS/SAR650984/EFC15246/CIR_RWE/REPORT/PGM/eff_km_subgp_sr_sig_de_i_t.sas OUT=REPORT/OUTPUT/eff_km_my20_per_detl_crcl_de_i_t_x.rtf (07APR2021 14:40)

16.2.6.1 Health-related quality-of-life endpoints - QLQ-MY20
16.2.6.1.2 Future perspective
16.2.6.1.2.14 Efficacy response data - Subgroup analyses by baseline eGFR (MDRD)
16.2.6.1.2.14.5 QLQ-MY20 - Time until permanent improvement by 10 pt in future perspective according to baseline eGFR (MDRD) (LOCF) - ITT population

	>=60 mL/min/1.73m2		<60 mL/min/1.73m2		
	Kd (N=93)	**IKd (N=122)**	**Kd (N=18)**	**IKd (N=43)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	36 (38.7)	50 (41.0)	2 (11.1)	22 (51.2)	0.0682
Number (%) of patients censored	57 (61.3)	72 (59.0)	16 (88.9)	21 (48.8)	
Kaplan-Meier estimates of future perspective in months					
25% quantile (95% CI)	7.52 (1.117 to 16.000)	4.67 (1.248 to 13.109)	NC (1.018 to NC)	1.91 (1.018 to 11.795)	
Median (95% CI)	24.05 (24.016 to NC)	NC (18.464 to NC)	NC (NC to NC)	19.84 (7.556 to NC)	
75% quantile (95% CI)	26.35 (24.049 to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.4392		0.0190	
Hazard ratio (95% CI) vs Kd	-	1.19 (0.77 to 1.83)		4.80 (1.13 to 20.41)	
P-value	-	0.4397		0.0338	
Hazard ratio inverted (95% CI) vs IKd		-		0.21 (0.05 to 0.89)	

A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.1 Health-related quality-of-life endpoints - QLQ-MY20
16.2.6.1.2 Future perspective
16.2.6.1.2.14 Efficacy response data - Subgroup analyses by baseline eGFR (MDRD)
16.2.6.1.2.14.6 QLQ-MY20 - Time until permanent deterioration by 10 pt in future perspective according to baseline eGFR (MDRD) (LOCF) - ITT population

	>=60 mL/min/1.73m2		<60 mL/min/1.73m2		
	Kd (N=93)	**IKd (N=122)**	**Kd (N=18)**	**IKd (N=43)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	29 (31.2)	36 (29.5)	8 (44.4)	12 (27.9)	0.1085
Number (%) of patients censored	64 (68.8)	86 (70.5)	10 (55.6)	31 (72.1)	
Kaplan-Meier estimates of future perspective in months					
25% quantile (95% CI)	13.60 (5.815 to NC)	16.43 (6.735 to 21.979)	8.23 (1.051 to 16.624)	18.07 (3.745 to NC)	
Median (95% CI)	NC (23.984 to NC)	NC (NC to NC)	17.71 (4.961 to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (16.624 to NC)	NC (NC to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.9917		0.0453	
Hazard ratio (95% CI) vs Kd	-	1.00 (0.61 to 1.63)		0.41 (0.16 to 1.01)	
P-value	-	0.9917		0.0525	
Deterioration probability (95% CI)[b]					

A higher score represents a better level of quality of life. Clinical meaningful deterioration change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.1 Health-related quality-of-life endpoints - QLQ-MY20
16.2.6.1.2 Future perspective
16.2.6.1.2.15 Efficacy response data - Subgroup analyses by previous treatment with PI
16.2.6.1.2.15.3 QLQ-MY20 - Time to first improvement by 10 pt in future perspective according to previous treatment with PI (LOCF) - ITT population

	Yes		No		
	Kd (N=47)	**IKd (N=81)**	**Kd (N=76)**	**IKd (N=98)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	32 (68.1)	53 (65.4)	47 (61.8)	75 (76.5)	0.3969
Number (%) of patients censored	15 (31.9)	28 (34.6)	29 (38.2)	23 (23.5)	
Kaplan-Meier estimates of future perspective in months					
25% quantile (95% CI)	1.12 (1.018 to 1.938)	1.05 (0.986 to 1.117)	1.05 (0.986 to 1.117)	1.02 (0.986 to 1.051)	
Median (95% CI)	3.71 (1.906 to 6.571)	1.97 (1.150 to 3.417)	2.86 (1.873 to 9.298)	1.91 (1.117 to 2.070)	
75% quantile (95% CI)	26.35 (5.618 to 26.349)	NC (4.961 to NC)	NC (15.146 to NC)	5.52 (2.825 to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.5545		0.0406	
Hazard ratio (95% CI) vs Kd	-	1.14 (0.73 to 1.78)		1.46 (1.01 to 2.11)	
P-value	-	0.5548		0.0418	
Hazard ratio inverted (95% CI) vs IKd		-		0.68 (0.47 to 0.99)	

A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.1 Health-related quality-of-life endpoints - QLQ-MY20
16.2.6.1.2 Future perspective
16.2.6.1.2.15 Efficacy response data - Subgroup analyses by previous treatment with PI
16.2.6.1.2.15.4 QLQ-MY20 - Time to first deterioration by 10 pt in future perspective according to previous treatment with PI (LOCF) - ITT population

	Yes		No		
	Kd (N=47)	**IKd (N=81)**	**Kd (N=76)**	**IKd (N=98)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	26 (55.3)	40 (49.4)	43 (56.6)	54 (55.1)	0.7359
Number (%) of patients censored	21 (44.7)	41 (50.6)	33 (43.4)	44 (44.9)	
Kaplan-Meier estimates of future perspective in months					
25% quantile (95% CI)	1.91 (1.051 to 2.891)	2.60 (1.216 to 3.811)	1.22 (1.051 to 2.957)	1.97 (1.051 to 3.055)	
Median (95% CI)	10.12 (2.070 to NC)	11.10 (4.698 to NC)	7.89 (4.008 to NC)	10.38 (3.778 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.5068		0.7978	
Hazard ratio (95% CI) vs Kd	-	0.85 (0.52 to 1.39)		0.95 (0.64 to 1.42)	
P-value	-	0.5073		0.7971	
Deterioration probability (95% CI)[b]					

A higher score represents a better level of quality of life. Clinical meaningful deterioration change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.1 Health-related quality-of-life endpoints - QLQ-MY20
16.2.6.1.2 Future perspective
16.2.6.1.2.15 Efficacy response data - Subgroup analyses by previous treatment with PI
16.2.6.1.2.15.5 QLQ-MY20 - Time until permanent improvement by 10 pt in future perspective according to previous treatment with PI (LOCF) - ITT population

	Yes		No		
	Kd (N=47)	**IKd (N=81)**	**Kd (N=76)**	**IKd (N=98)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	18 (38.3)	35 (43.2)	24 (31.6)	43 (43.9)	0.6925
Number (%) of patients censored	29 (61.7)	46 (56.8)	52 (68.4)	55 (56.1)	
Kaplan-Meier estimates of future perspective in months					
25% quantile (95% CI)	6.97 (1.117 to 24.016)	3.02 (1.150 to 13.109)	11.14 (1.873 to 24.049)	4.67 (1.117 to 11.795)	
Median (95% CI)	24.02 (16.329 to 26.349)	21.45 (15.704 to NC)	24.05 (24.049 to NC)	20.47 (17.741 to NC)	
75% quantile (95% CI)	26.35 (24.016 to 26.349)	NC (NC to NC)	NC (24.049 to NC)	NC (NC to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.3363		0.1376	
Hazard ratio (95% CI) vs Kd	-	1.34 (0.74 to 2.41)		1.46 (0.88 to 2.40)	
P-value	-	0.3380		0.1400	
Improvement probability (95% CI)[b]					

A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.1 Health-related quality-of-life endpoints - QLQ-MY20
16.2.6.1.2 Future perspective
16.2.6.1.2.15 Efficacy response data - Subgroup analyses by previous treatment with PI
16.2.6.1.2.15.6 QLQ-MY20 - Time until permanent deterioration by 10 pt in future perspective according to previous treatment with PI (LOCF) - ITT population

	Yes		No		
	Kd (N=47)	**IKd (N=81)**	**Kd (N=76)**	**IKd (N=98)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	12 (25.5)	24 (29.6)	29 (38.2)	26 (26.5)	0.0879
Number (%) of patients censored	35 (74.5)	57 (70.4)	47 (61.8)	72 (73.5)	
Kaplan-Meier estimates of future perspective in months					
25% quantile (95% CI)	23.98 (6.374 to NC)	15.38 (4.698 to NC)	8.44 (3.844 to 16.624)	19.38 (13.766 to NC)	
Median (95% CI)	NC (23.984 to NC)	NC (NC to NC)	NC (17.708 to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.4333		0.0642	
Hazard ratio (95% CI) vs Kd	-	1.32 (0.66 to 2.65)		0.61 (0.36 to 1.04)	
P-value	-	0.4347		0.0670	
Deterioration probability (95% CI)[b]					

A higher score represents a better level of quality of life. Clinical meaningful deterioration change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.1 Health-related quality-of-life endpoints - QLQ-MY20
16.2.6.1.2 Future perspective
16.2.6.1.2.16 Efficacy response data - Subgroup analyses by previous treatment with IMiD
16.2.6.1.2.16.3 QLQ-MY20 - Time to first improvement by 10 pt in future perspective according to previous treatment with IMiD (LOCF) - ITT population

	Yes		No		
	Kd (N=62)	**IKd (N=81)**	**Kd (N=61)**	**IKd (N=98)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	40 (64.5)	58 (71.6)	39 (63.9)	70 (71.4)	0.6198
Number (%) of patients censored	22 (35.5)	23 (28.4)	22 (36.1)	28 (28.6)	
Kaplan-Meier estimates of future perspective in months					
25% quantile (95% CI)	1.08 (0.986 to 1.117)	1.05 (0.986 to 1.117)	1.07 (0.986 to 1.906)	1.02 (0.986 to 1.051)	
Median (95% CI)	2.86 (1.873 to 9.101)	2.00 (1.183 to 2.957)	3.84 (1.906 to 6.571)	1.91 (1.084 to 2.004)	
75% quantile (95% CI)	26.35 (12.583 to 26.349)	NC (3.713 to NC)	NC (8.575 to NC)	NC (2.825 to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.3269		0.0949	
Hazard ratio (95% CI) vs Kd	-	1.22 (0.82 to 1.84)		1.40 (0.94 to 2.07)	
P-value	-	0.3278		0.0964	
Improvement probability (95% CI)[b]					

A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.1 Health-related quality-of-life endpoints - QLQ-MY20
16.2.6.1.2 Future perspective
16.2.6.1.2.16 Efficacy response data - Subgroup analyses by previous treatment with IMiD
16.2.6.1.2.16.4 QLQ-MY20 - Time to first deterioration by 10 pt in future perspective according to previous treatment with IMiD (LOCF) - ITT population

	Yes		No		
	Kd (N=62)	**IKd (N=81)**	**Kd (N=61)**	**IKd (N=98)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	36 (58.1)	40 (49.4)	33 (54.1)	54 (55.1)	0.2838
Number (%) of patients censored	26 (41.9)	41 (50.6)	28 (45.9)	44 (44.9)	
Kaplan-Meier estimates of future perspective in months					
25% quantile (95% CI)	1.64 (1.084 to 2.825)	2.10 (1.511 to 3.778)	1.56 (1.051 to 4.830)	2.00 (1.117 to 3.187)	
Median (95% CI)	6.34 (2.825 to NC)	18.30 (5.552 to NC)	13.01 (4.830 to NC)	7.49 (4.041 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.2097		0.7955	
Hazard ratio (95% CI) vs Kd	-	0.75 (0.48 to 1.18)		1.06 (0.69 to 1.63)	
P-value	-	0.2112		0.7968	
Deterioration probability (95% CI)[b]					

A higher score represents a better level of quality of life. Clinical meaningful deterioration change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.1 Health-related quality-of-life endpoints - QLQ-MY20
16.2.6.1.2 Future perspective
16.2.6.1.2.16 Efficacy response data - Subgroup analyses by previous treatment with IMiD
16.2.6.1.2.16.5 QLQ-MY20 - Time until permanent improvement by 10 pt in future perspective according to previous treatment with IMiD (LOCF) - ITT population

	Yes		No		
	Kd (N=62)	**IKd (N=81)**	**Kd (N=61)**	**IKd (N=98)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	23 (37.1)	34 (42.0)	19 (31.1)	44 (44.9)	0.4962
Number (%) of patients censored	39 (62.9)	47 (58.0)	42 (68.9)	54 (55.1)	
Kaplan-Meier estimates of future perspective in months					
25% quantile (95% CI)	10.22 (1.873 to 24.016)	3.75 (1.413 to 12.977)	7.52 (1.117 to NC)	4.67 (1.084 to 11.795)	
Median (95% CI)	24.02 (19.515 to 26.349)	NC (18.891 to NC)	NC (NC to NC)	19.61 (13.569 to NC)	
75% quantile (95% CI)	26.35 (24.016 to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.4382		0.1033	
Hazard ratio (95% CI) vs Kd	-	1.24 (0.72 to 2.12)		1.56 (0.91 to 2.67)	
P-value	-	0.4391		0.1062	

A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.1 Health-related quality-of-life endpoints - QLQ-MY20
16.2.6.1.2 Future perspective
16.2.6.1.2.16 Efficacy response data - Subgroup analyses by previous treatment with IMiD
16.2.6.1.2.16.6 QLQ-MY20 - Time until permanent deterioration by 10 pt in future perspective according to previous treatment with IMiD (LOCF) - ITT population

	Yes		No		
	Kd (N=62)	**IKd (N=81)**	**Kd (N=61)**	**IKd (N=98)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	23 (37.1)	20 (24.7)	18 (29.5)	30 (30.6)	0.1753
Number (%) of patients censored	39 (62.9)	61 (75.3)	43 (70.5)	68 (69.4)	
Kaplan-Meier estimates of future perspective in months					
25% quantile (95% CI)	9.30 (4.008 to 13.963)	19.58 (8.246 to NC)	16.66 (4.238 to NC)	16.43 (4.862 to 20.567)	
Median (95% CI)	NC (16.887 to NC)	NC (NC to NC)	NC (23.984 to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (23.984 to NC)	NC (NC to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.0879		0.8165	
Hazard ratio (95% CI) vs Kd	-	0.60 (0.33 to 1.09)		1.07 (0.60 to 1.92)	
P-value	-	0.0914		0.8165	
Deterioration probability (95% CI)[b]					

A higher score represents a better level of quality of life. Clinical meaningful deterioration change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.1 Health-related quality-of-life endpoints - QLQ-MY20
16.2.6.1.2 Future perspective
16.2.6.1.2.17 Efficacy response data - Subgroup analyses by previous treatment with PI and IMiD
16.2.6.1.2.17.3 QLQ-MY20 - Time to first improvement by 10 pt in future perspective according to previous treatment with PI and IMiD (LOCF) - ITT population

	Yes		No		
	Kd (N=17)	**IKd (N=23)**	**Kd (N=106)**	**IKd (N=156)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	12 (70.6)	15 (65.2)	67 (63.2)	113 (72.4)	0.3055
Number (%) of patients censored	5 (29.4)	8 (34.8)	39 (36.8)	43 (27.6)	
Kaplan-Meier estimates of future perspective in months					
25% quantile (95% CI)	1.07 (0.953 to 1.938)	1.08 (0.986 to 1.971)	1.08 (1.018 to 1.117)	1.05 (0.986 to 1.051)	
Median (95% CI)	2.87 (1.018 to 26.349)	3.42 (1.150 to NC)	3.71 (1.938 to 6.571)	1.94 (1.150 to 2.004)	
75% quantile (95% CI)	26.35 (1.938 to 26.349)	NC (3.417 to NC)	NC (15.146 to NC)	NC (3.680 to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.8170		0.0338	
Hazard ratio (95% CI) vs Kd	-	0.91 (0.42 to 1.99)		1.39 (1.02 to 1.88)	
P-value	-	0.8171		0.0345	
Hazard ratio inverted (95% CI) vs IKd		-		0.72 (0.53 to 0.98)	

A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.1 Health-related quality-of-life endpoints - QLQ-MY20
16.2.6.1.2 Future perspective
16.2.6.1.2.17 Efficacy response data - Subgroup analyses by previous treatment with PI and IMiD
16.2.6.1.2.17.4 QLQ-MY20 - Time to first deterioration by 10 pt in future perspective according to previous treatment with PI and IMiD (LOCF) - ITT population

	Yes		No		
	Kd (N=17)	**IKd (N=23)**	**Kd (N=106)**	**IKd (N=156)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	10 (58.8)	8 (34.8)	59 (55.7)	86 (55.1)	0.1519
Number (%) of patients censored	7 (41.2)	15 (65.2)	47 (44.3)	70 (44.9)	
Kaplan-Meier estimates of future perspective in months					
25% quantile (95% CI)	2.02 (0.953 to 3.055)	3.29 (1.117 to NC)	1.28 (1.084 to 2.103)	1.97 (1.150 to 2.990)	
Median (95% CI)	5.26 (1.971 to NC)	NC (3.285 to NC)	10.12 (5.322 to NC)	8.54 (5.552 to 21.027)	
75% quantile (95% CI)	NC (3.055 to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.1106		0.9122	
Hazard ratio (95% CI) vs Kd	-	0.48 (0.19 to 1.21)		0.98 (0.70 to 1.37)	
P-value	-	0.1189		0.9121	
Deterioration probability (95% CI)[b]					

A higher score represents a better level of quality of life. Clinical meaningful deterioration change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.1 Health-related quality-of-life endpoints - QLQ-MY20
16.2.6.1.2 Future perspective
16.2.6.1.2.17 Efficacy response data - Subgroup analyses by previous treatment with PI and IMiD
16.2.6.1.2.17.5 QLQ-MY20 - Time until permanent improvement by 10 pt in future perspective according to previous treatment with PI and IMiD (LOCF) - ITT population

	Yes		No		
	Kd (N=17)	**IKd (N=23)**	**Kd (N=106)**	**IKd (N=156)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	7 (41.2)	10 (43.5)	35 (33.0)	68 (43.6)	0.6969
Number (%) of patients censored	10 (58.8)	13 (56.5)	71 (67.0)	88 (56.4)	
Kaplan-Meier estimates of future perspective in months					
25% quantile (95% CI)	6.06 (0.986 to 26.349)	2.83 (1.084 to 21.454)	10.22 (1.906 to 17.051)	4.67 (1.314 to 10.349)	
Median (95% CI)	24.02 (1.938 to 26.349)	21.45 (2.825 to NC)	NC (24.049 to NC)	NC (18.530 to NC)	
75% quantile (95% CI)	26.35 (24.016 to 26.349)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.5266		0.0994	
Hazard ratio (95% CI) vs Kd	-	1.41 (0.48 to 4.14)		1.41 (0.94 to 2.12)	
P-value	-	0.5287		0.1010	

A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.1 Health-related quality-of-life endpoints - QLQ-MY20
16.2.6.1.2 Future perspective
16.2.6.1.2.17 Efficacy response data - Subgroup analyses by previous treatment with PI and IMiD
16.2.6.1.2.17.6 QLQ-MY20 - Time until permanent deterioration by 10 pt in future perspective according to previous treatment with PI and IMiD (LOCF) - ITT population

	Yes		No		
	Kd (N=17)	**IKd (N=23)**	**Kd (N=106)**	**IKd (N=156)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	4 (23.5)	6 (26.1)	37 (34.9)	44 (28.2)	0.5225
Number (%) of patients censored	13 (76.5)	17 (73.9)	69 (65.1)	112 (71.8)	
Kaplan-Meier estimates of future perspective in months					
25% quantile (95% CI)	NC (1.314 to NC)	18.04 (1.511 to NC)	9.30 (4.862 to 17.708)	18.07 (11.499 to 21.979)	
Median (95% CI)	NC (11.499 to NC)	NC (18.037 to NC)	NC (23.984 to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.8113		0.2382	
Hazard ratio (95% CI) vs Kd	-	1.17 (0.33 to 4.14)		0.77 (0.50 to 1.19)	
P-value	-	0.8115		0.2395	

A higher score represents a better level of quality of life. Clinical meaningful deterioration change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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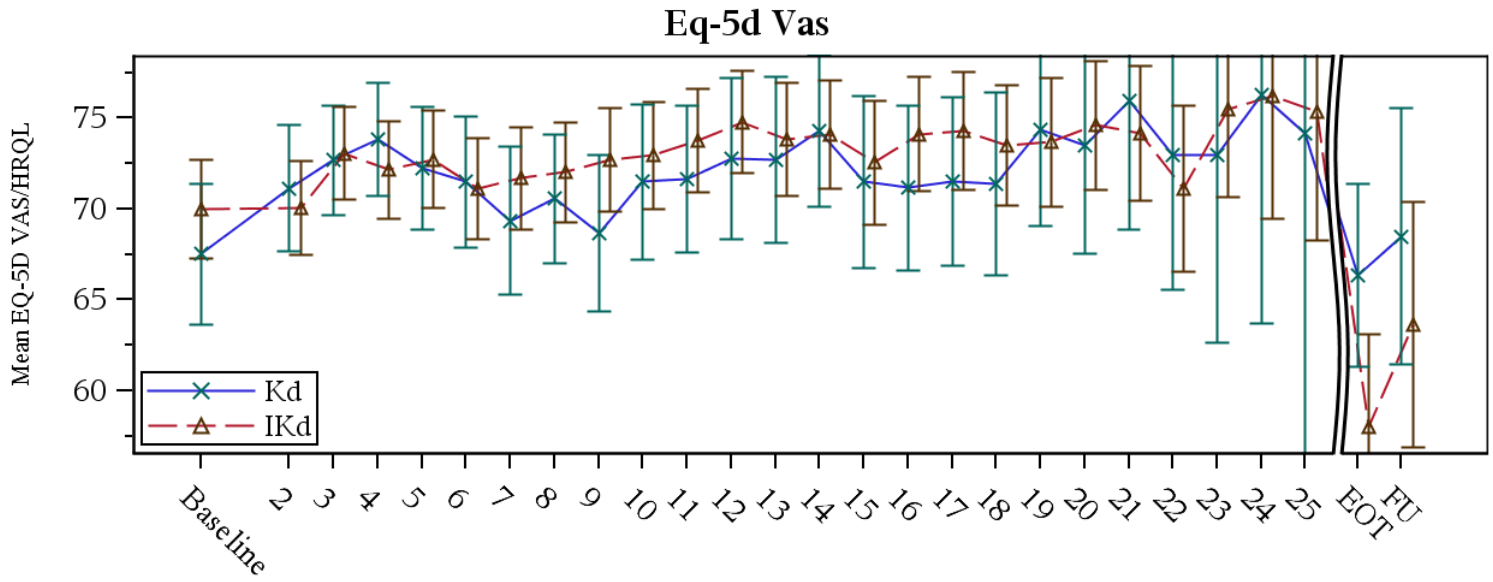
16.2.6.1 Health-related quality-of-life endpoints - EQ-5D
16.2.6.1.2 EQ-5D VAS
16.2.6.1.2.1 Efficacy response data
16.2.6.1.2.1.1 EQ-5D - Mean and 95% CI for EQ-5D VAS score over time (LOCF) - ITT population



#patients																										
Kd	112	114	112	110	104	100	95	91	88	84	78	72	67	66	62	57	52	50	45	37	30	23	17	10	6	62	34
IKd	164	168	168	164	161	155	150	145	138	133	130	127	121	118	112	108	105	102	97	91	78	56	38	23	17	59	34

A higher score represents a better level of quality of life. Cycles with less than 20 patients overall are not presented.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
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16.2.6.1 Health-related quality-of-life endpoints - EQ-5D
16.2.6.1.2 EQ-5D VAS
16.2.6.1.2.1 Efficacy response data
16.2.6.1.2.1.15 EQ-5D - Time to first improvement by 15 pt in EQ-5D VAS (LOCF) - ITT population

First improvement 15 points EQ VAS Score	**Kd (N=123)**	**IKd (N=179)**
Number (%) of events	43 (35.0)	64 (35.8)
Number (%) of patients censored	80 (65.0)	115 (64.2)
Kaplan-Meier estimates of EQ-5D VAS in months		
25% quantile (95% CI)	3.06 (1.873 to 5.552)	2.96 (2.070 to 4.830)
Median (95% CI)	NC (NC to NC)	NC (NC to NC)
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)
Comparison vs. Kd		
Stratified[a] Log-Rank test p-value[b] vs Kd	-	0.9161
Stratified[a] Hazard ratio (95% CI) vs Kd	-	1.02 (0.69 to 1.51)
P-value	-	0.9162
Improvement probability (95% CI)[c]		
3 Months	0.242 (0.169 to 0.321)	0.253 (0.191 to 0.319)
6 Months	0.328 (0.246 to 0.413)	0.329 (0.260 to 0.399)

A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 15 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] Stratified on number of prior lines of therapy (1 vs. >1) and Revised International Staging System (R-ISS) stage (I or II vs. III vs. not classified) according to IRT
[b] One-sided significance level is 0.025
[c] Estimated using the Kaplan-Meier method
NA/NC = Not Applicable / Not Calculable
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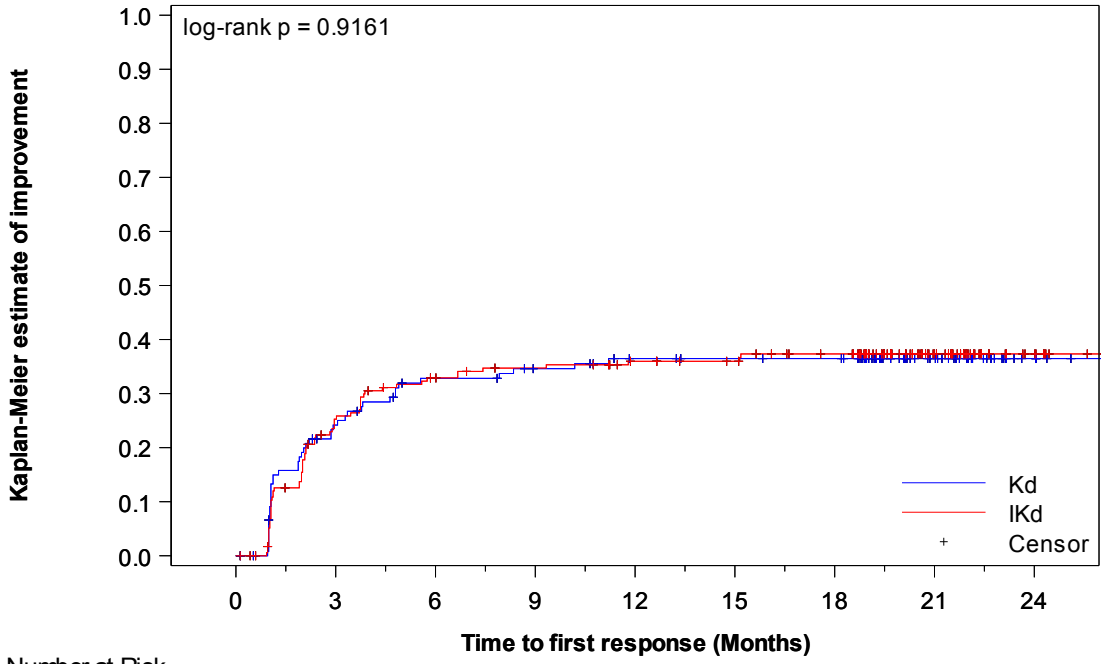
16.2.6.1 Health-related quality-of-life endpoints - EQ-5D
16.2.6.1.2 EQ-5D VAS
16.2.6.1.2.1 Efficacy response data
16.2.6.1.2.1.16 EQ-5D - Time to first improvement by 15 pt in EQ-5D VAS - Kaplan-Meier curve (LOCF) - ITT population



Number at Risk

Kd	123	89	76	71	65	63	62	32	6
IKd	179	128	112	106	99	95	87	41	8

A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 15 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
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16.2.6.1 Health-related quality-of-life endpoints - EQ-5D
16.2.6.1.2 EQ-5D VAS
16.2.6.1.2.1 Efficacy response data
16.2.6.1.2.1.17 EQ-5D - Time to first deterioration by 15 pt in EQ-5D VAS (LOCF) - ITT population

First deterioration 15 points EQ VAS Score	**Kd (N=123)**	**IKd (N=179)**
Number (%) of events	58 (47.2)	79 (44.1)
Number (%) of patients censored	65 (52.8)	100 (55.9)
Kaplan-Meier estimates of EQ-5D VAS in months		
25% quantile (95% CI)	4.76 (2.825 to 5.618)	4.24 (2.825 to 6.012)
Median (95% CI)	16.82 (7.458 to NC)	NC (13.240 to NC)
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)
Comparison vs. Kd		
Stratified[a] Log-Rank test p-value[b] vs Kd	-	0.4504
Stratified[a] Hazard ratio (95% CI) vs Kd	-	0.88 (0.62 to 1.23)
P-value	-	0.4507
Deterioration probability (95% CI)[c]		
3 Months	0.800 (0.716 to 0.861)	0.805 (0.738 to 0.857)
6 Months	0.662 (0.569 to 0.740)	0.689 (0.614 to 0.752)

A higher score represents a better level of quality of life. Clinical meaningful deterioration change from baseline less than or equal to -15 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] Stratified on number of prior lines of therapy (1 vs. >1) and Revised International Staging System (R-ISS) stage (I or II vs. III vs. not classified) according to IRT
[b] One-sided significance level is 0.025
[c] Estimated using the Kaplan-Meier method
NA/NC = Not Applicable / Not Calculable
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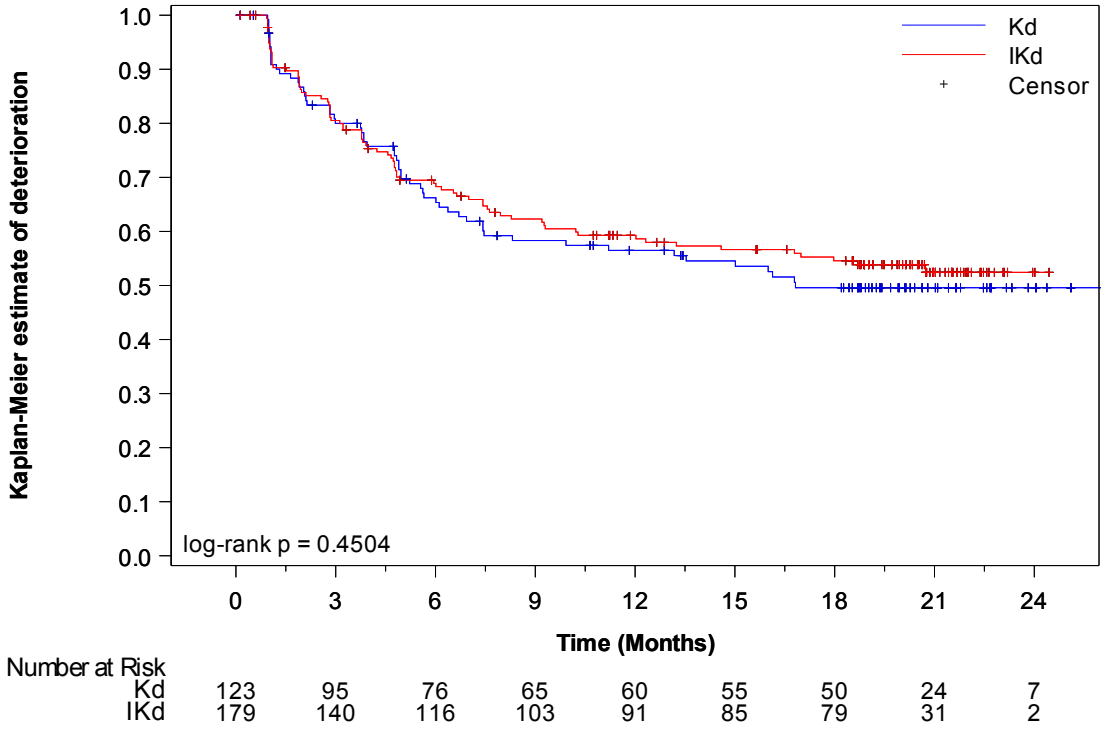
16.2.6.1 Health-related quality-of-life endpoints - EQ-5D
16.2.6.1.2 EQ-5D VAS
16.2.6.1.2.1 Efficacy response data
16.2.6.1.2.1.18 EQ-5D - Time to first deterioration by 15 pt in EQ-5D VAS - Kaplan-Meier curve (LOCF) - ITT population



A higher score represents a better level of quality of life. Clinical meaningful deterioration change from baseline less than or equal to -15 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
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16.2.6.1 Health-related quality-of-life endpoints - EQ-5D
16.2.6.1.2 EQ-5D VAS
16.2.6.1.2.1 Efficacy response data
16.2.6.1.2.1.19 EQ-5D - Time until permanent improvement by 15 pt in EQ-5D VAS (LOCF) - ITT population

First permanent improvement 15 points EQ VAS Score	**Kd (N=123)**	**IKd (N=179)**
Number (%) of events	23 (18.7)	27 (15.1)
Number (%) of patients censored	100 (81.3)	152 (84.9)
Kaplan-Meier estimates of EQ-5D VAS in months		
25% quantile (95% CI)	NC (14.226 to NC)	NC (21.257 to NC)
Median (95% CI)	NC (NC to NC)	NC (NC to NC)
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)
Comparison vs. Kd		
Stratified[a] Log-Rank test p-value[b] vs Kd	-	0.3710
Stratified[a] Hazard ratio (95% CI) vs Kd	-	0.78 (0.44 to 1.36)
P-value	-	0.3723
Improvement probability (95% CI)[c]		
3 Months	0.066 (0.031 to 0.120)	0.057 (0.029 to 0.099)
6 Months	0.092 (0.049 to 0.152)	0.069 (0.038 to 0.113)

A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 15 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] Stratified on number of prior lines of therapy (1 vs. >1) and Revised International Staging System (R-ISS) stage (I or II vs. III vs. not classified) according to IRT
[b] One-sided significance level is 0.025
[c] Estimated using the Kaplan-Meier method
NA/NC = Not Applicable / Not Calculable
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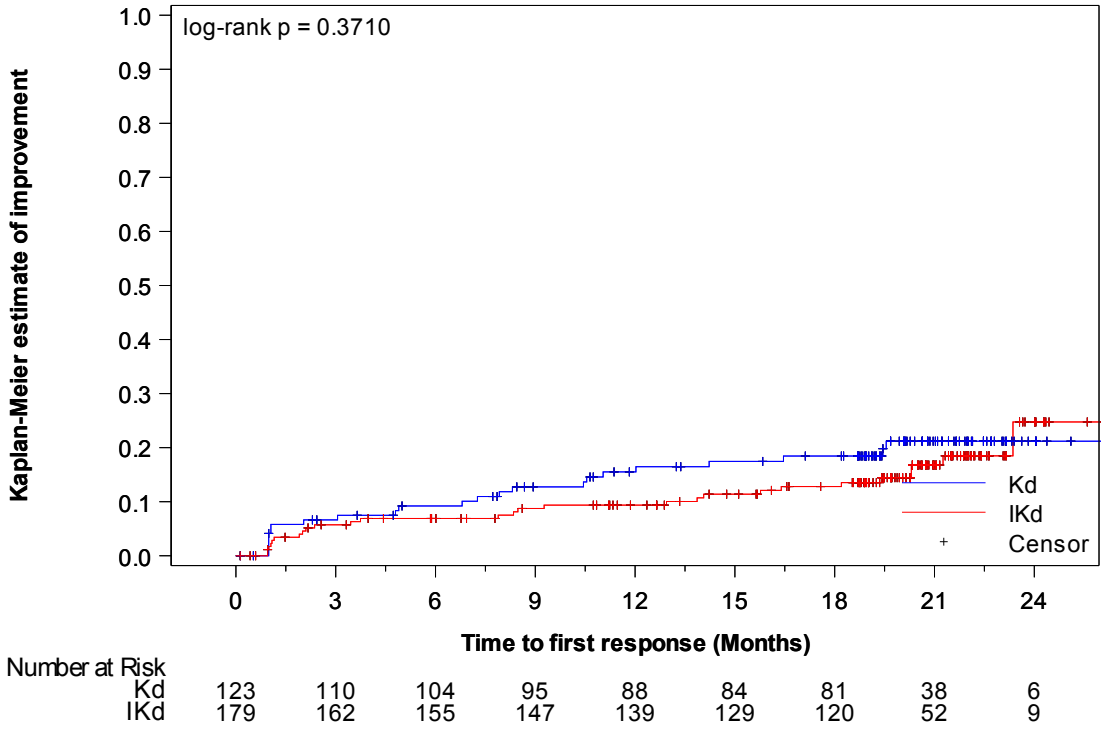
16.2.6.1 Health-related quality-of-life endpoints - EQ-5D
16.2.6.1.2 EQ-5D VAS
16.2.6.1.2.1 Efficacy response data
16.2.6.1.2.1.20 EQ-5D - Time until permanent improvement by 15 pt in EQ-5D VAS - Kaplan-Meier curve (LOCF) - ITT population



A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 15 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.

16.2.6.1 Health-related quality-of-life endpoints - EQ-5D
16.2.6.1.2 EQ-5D VAS
16.2.6.1.2.1 Efficacy response data
16.2.6.1.2.1.21 EQ-5D - Time until permanent deterioration by 15 pt in EQ-5D VAS (LOCF) - ITT population

First permanent deterioration 15 points EQ VAS Score	**Kd (N=123)**	**IKd (N=179)**
Number (%) of events	23 (18.7)	31 (17.3)
Number (%) of patients censored	100 (81.3)	148 (82.7)
Kaplan-Meier estimates of EQ-5D VAS in months		
25% quantile (95% CI)	NC (16.821 to NC)	NC (17.018 to NC)
Median (95% CI)	NC (NC to NC)	NC (NC to NC)
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)
Comparison vs. Kd		
Stratified[a] Log-Rank test p-value[b] vs Kd	-	0.7298
Stratified[a] Hazard ratio (95% CI) vs Kd	-	0.91 (0.53 to 1.56)
P-value	-	0.7299
Deterioration probability (95% CI)[c]		
3 Months	0.983 (0.935 to 0.996)	0.954 (0.910 to 0.977)
6 Months	0.940 (0.879 to 0.971)	0.907 (0.853 to 0.942)

A higher score represents a better level of quality of life. Clinical meaningful deterioration change from baseline less than or equal to -15 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] Stratified on number of prior lines of therapy (1 vs. >1) and Revised International Staging System (R-ISS) stage (I or II vs. III vs. not classified) according to IRT
[b] One-sided significance level is 0.025
[c] Estimated using the Kaplan-Meier method
NA/NC = Not Applicable / Not Calculable
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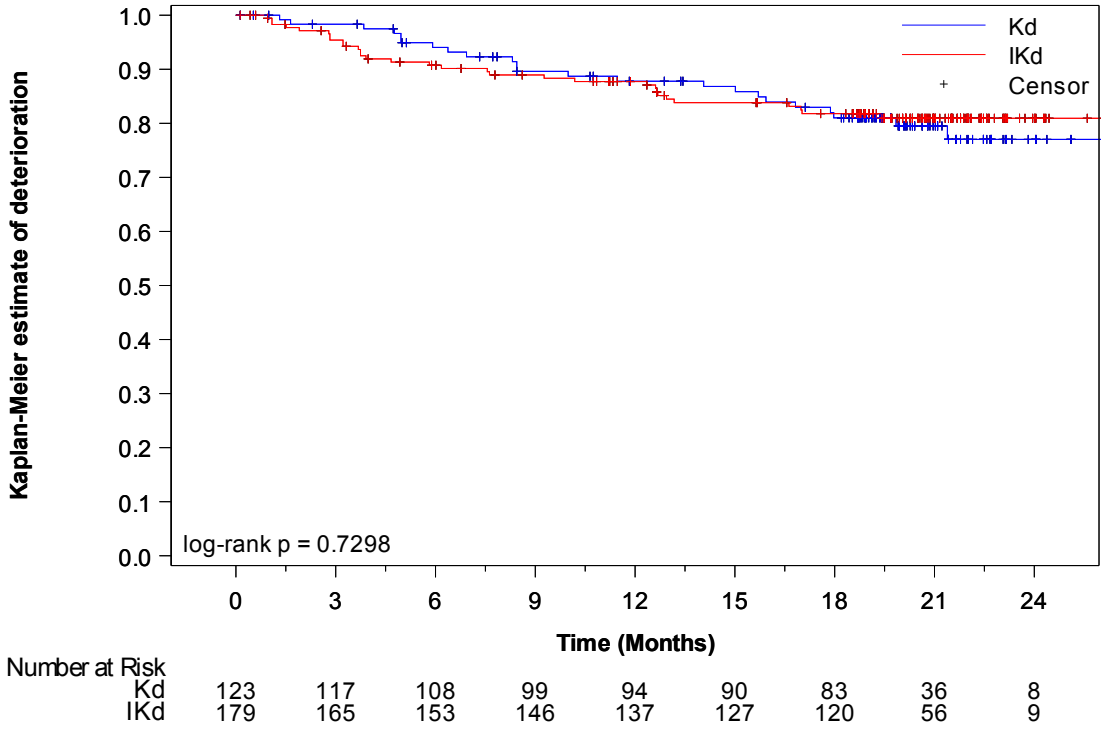
16.2.6.1 Health-related quality-of-life endpoints - EQ-5D
16.2.6.1.2 EQ-5D VAS
16.2.6.1.2.1 Efficacy response data
16.2.6.1.2.1.22 EQ-5D - Time until permanent deterioration by 15 pt in EQ-5D VAS - Kaplan-Meier curve (LOCF) - ITT population



A higher score represents a better level of quality of life. Clinical meaningful deterioration change from baseline less than or equal to -15 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
PGM=DEVOPS/SAR650984/EFC15246/CIR_RWE/REPORT/PGM/eff_qlq_km_i_f.sas OUT=REPORT/OUTPUT/eff_km_eq5d_vas_det15pl_de_i_f_x.rtf (07APR2021 14:25)

16.2.6.1 Health-related quality-of-life endpoints - EQ-5D
16.2.6.1.2 EQ-5D VAS
16.2.6.1.2.2 Efficacy response data - Subgroup analyses by age
16.2.6.1.2.2.3 EQ-5D - Time to first improvement by 10 pt in EQ-5D VAS according to age (LOCF) - ITT population

	<65 years		>=65 years		
	Kd (N=66)	**IKd (N=88)**	**Kd (N=57)**	**IKd (N=91)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	33 (50.0)	42 (47.7)	24 (42.1)	50 (54.9)	0.1346
Number (%) of patients censored	33 (50.0)	46 (52.3)	33 (57.9)	41 (45.1)	
Kaplan-Meier estimates of EQ-5D VAS in months					
25% quantile (95% CI)	1.05 (1.018 to 1.906)	1.91 (1.051 to 2.891)	2.89 (1.117 to 3.811)	1.56 (1.051 to 2.136)	
Median (95% CI)	11.20 (2.431 to NC)	NC (3.745 to NC)	NC (3.811 to NC)	8.71 (2.825 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.6053		0.1155	
Hazard ratio (95% CI) vs Kd	-	0.89 (0.56 to 1.40)		1.47 (0.91 to 2.40)	
P-value	-	0.6055		0.1179	
Improvement probability (95% CI)[b]					

A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
PGM=DEVOPS/SAR650984/EFC15246/CIR_RWE/REPORT/PGM/eff_km_subgp_sr_sig_de_i_t.sas OUT=REPORT/OUTPUT/eff_km_eq5d_vas_impl_age_de_i_t_x.rtf (07APR2021 14:45)

16.2.6.1 Health-related quality-of-life endpoints - EQ-5D
16.2.6.1.2 EQ-5D VAS
16.2.6.1.2.2 Efficacy response data - Subgroup analyses by age
16.2.6.1.2.2.4 EQ-5D - Time to first deterioration by 10 pt in EQ-5D VAS according to age (LOCF) - ITT population

	<65 years		>=65 years		
	Kd (N=66)	**IKd (N=88)**	**Kd (N=57)**	**IKd (N=91)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	32 (48.5)	54 (61.4)	39 (68.4)	49 (53.8)	0.0600
Number (%) of patients censored	34 (51.5)	34 (38.6)	18 (31.6)	42 (46.2)	
Kaplan-Meier estimates of EQ-5D VAS in months					
25% quantile (95% CI)	2.83 (1.216 to 4.895)	2.00 (1.084 to 2.858)	2.14 (1.117 to 3.844)	1.89 (1.051 to 3.220)	
Median (95% CI)	21.22 (4.961 to NC)	7.43 (3.910 to 12.320)	5.65 (3.844 to 7.556)	8.51 (4.764 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (7.556 to NC)	NC (NC to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.1707		0.1820	
Hazard ratio (95% CI) vs Kd	-	1.36 (0.88 to 2.10)		0.75 (0.49 to 1.15)	
P-value	-	0.1723		0.1834	
Deterioration probability (95% CI)[b]					

A higher score represents a better level of quality of life. Clinical meaningful deterioration change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
PGM=DEVOPS/SAR650984/EFC15246/CIR_RWE/REPORT/PGM/eff_km_subgp_sr_sig_de_i_t.sas OUT=REPORT/OUTPUT/eff_km_eq5d_vas_detl_age_de_i_t_x.rtf (07APR2021 14:44)

16.2.6.1 Health-related quality-of-life endpoints - EQ-5D
16.2.6.1.2 EQ-5D VAS
16.2.6.1.2.2 Efficacy response data - Subgroup analyses by age
16.2.6.1.2.2.5 EQ-5D - Time until permanent improvement by 10 pt in EQ-5D VAS according to age (LOCF) - ITT population

	<65 years		>=65 years		
	Kd (N=66)	**IKd (N=88)**	**Kd (N=57)**	**IKd (N=91)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	17 (25.8)	27 (30.7)	12 (21.1)	21 (23.1)	0.8375
Number (%) of patients censored	49 (74.2)	61 (69.3)	45 (78.9)	70 (76.9)	
Kaplan-Meier estimates of EQ-5D VAS in months					
25% quantile (95% CI)	16.46 (4.895 to NC)	14.49 (7.458 to 21.257)	22.21 (11.039 to NC)	19.88 (14.554 to NC)	
Median (95% CI)	NC (NC to NC)	NC (21.257 to NC)	NC (22.209 to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.5408		0.7953	
Hazard ratio (95% CI) vs Kd	-	1.21 (0.66 to 2.22)		1.10 (0.54 to 2.23)	
P-value	-	0.5415		0.7954	
Improvement probability (95% CI)[b]					

A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
PGM=DEVOPS/SAR650984/EFC15246/CIR_RWE/REPORT/PGM/eff_km_subgp_sr_sig_de_i_t.sas OUT=REPORT/OUTPUT/eff_km_eq5d_vas_imppl_age_de_i_t_x.rtf (07APR2021 14:45)

16.2.6.1 Health-related quality-of-life endpoints - EQ-5D
16.2.6.1.2 EQ-5D VAS
16.2.6.1.2.2 Efficacy response data - Subgroup analyses by age
16.2.6.1.2.2.6 EQ-5D - Time until permanent deterioration by 10 pt in EQ-5D VAS according to age (LOCF) - ITT population

	<65 years		>=65 years		
	Kd (N=66)	**IKd (N=88)**	**Kd (N=57)**	**IKd (N=91)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	13 (19.7)	26 (29.5)	16 (28.1)	24 (26.4)	0.2380
Number (%) of patients censored	53 (80.3)	62 (70.5)	41 (71.9)	67 (73.6)	
Kaplan-Meier estimates of EQ-5D VAS in months					
25% quantile (95% CI)	21.39 (14.094 to NC)	12.65 (5.322 to NC)	17.97 (6.374 to NC)	21.19 (12.682 to 23.129)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	24.44 (23.097 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (23.129 to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.1696		0.8224	
Hazard ratio (95% CI) vs Kd	-	1.59 (0.82 to 3.09)		0.93 (0.49 to 1.75)	
P-value	-	0.1734		0.8225	
Deterioration probability (95% CI)[b]					

A higher score represents a better level of quality of life. Clinical meaningful deterioration change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
PGM=DEVOPS/SAR650984/EFC15246/CIR_RWE/REPORT/PGM/eff_km_subgp_sr_sig_de_i_t.sas OUT=REPORT/OUTPUT/eff_km_eq5d_vas_detpl_age_de_i_t_x.rtf (07APR2021 14:45)

16.2.6.1 Health-related quality-of-life endpoints - EQ-5D
16.2.6.1.2 EQ-5D VAS
16.2.6.1.2.3 Efficacy response data - Subgroup analyses by gender
16.2.6.1.2.3.3 EQ-5D - Time to first improvement by 10 pt in EQ-5D VAS according to gender (LOCF) - ITT population

	Male		Female		
	Kd (N=68)	**IKd (N=101)**	**Kd (N=55)**	**IKd (N=78)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	26 (38.2)	51 (50.5)	31 (56.4)	41 (52.6)	0.1994
Number (%) of patients censored	42 (61.8)	50 (49.5)	24 (43.6)	37 (47.4)	
Kaplan-Meier estimates of EQ-5D VAS in months					
25% quantile (95% CI)	1.91 (1.051 to 3.975)	1.91 (1.051 to 2.103)	1.12 (1.018 to 2.858)	1.97 (1.051 to 2.398)	
Median (95% CI)	NC (4.632 to NC)	10.25 (3.745 to NC)	6.19 (2.858 to NC)	10.18 (2.891 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.1698		0.7054	
Hazard ratio (95% CI) vs Kd	-	1.39 (0.87 to 2.23)		0.91 (0.57 to 1.46)	
P-value	-	0.1717		0.7054	
Improvement probability (95% CI)[b]					

A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
PGM=DEVOPS/SAR650984/EFC15246/CIR_RWE/REPORT/PGM/eff_km_subgp_sr_sig_de_i_t.sas OUT=REPORT/OUTPUT/eff_km_eq5d_vas_impl_sex_de_i_t_x.rtf (07APR2021 14:45)

16.2.6.1 Health-related quality-of-life endpoints - EQ-5D
16.2.6.1.2 EQ-5D VAS
16.2.6.1.2.3 Efficacy response data - Subgroup analyses by gender
16.2.6.1.2.3.4 EQ-5D - Time to first deterioration by 10 pt in EQ-5D VAS according to gender (LOCF) - ITT population

	Male		Female		
	Kd (N=68)	**IKd (N=101)**	**Kd (N=55)**	**IKd (N=78)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	39 (57.4)	61 (60.4)	32 (58.2)	42 (53.8)	0.4527
Number (%) of patients censored	29 (42.6)	40 (39.6)	23 (41.8)	36 (46.2)	
Kaplan-Meier estimates of EQ-5D VAS in months					
25% quantile (95% CI)	2.43 (1.314 to 4.632)	1.87 (1.084 to 2.793)	2.14 (1.018 to 4.764)	2.86 (1.051 to 4.830)	
Median (95% CI)	6.01 (4.764 to NC)	5.59 (3.220 to 12.025)	7.43 (4.764 to NC)	11.10 (6.538 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.5652		0.6062	
Hazard ratio (95% CI) vs Kd	-	1.13 (0.75 to 1.68)		0.89 (0.56 to 1.40)	
P-value	-	0.5654		0.6065	
Deterioration probability (95% CI)[b]					

A higher score represents a better level of quality of life. Clinical meaningful deterioration change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
PGM=DEVOPS/SAR650984/EFC15246/CIR_RWE/REPORT/PGM/eff_km_subgp_sr_sig_de_i_t.sas OUT=REPORT/OUTPUT/eff_km_eq5d_vas_detl_sex_de_i_t_x.rtf (07APR2021 14:45)

16.2.6.1 Health-related quality-of-life endpoints - EQ-5D
16.2.6.1.2 EQ-5D VAS
16.2.6.1.2.3 Efficacy response data - Subgroup analyses by gender
16.2.6.1.2.3.5 EQ-5D - Time until permanent improvement by 10 pt in EQ-5D VAS according to gender (LOCF) - ITT population

	Male		Female		
	Kd (N=68)	**IKd (N=101)**	**Kd (N=55)**	**IKd (N=78)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	11 (16.2)	27 (26.7)	18 (32.7)	21 (26.9)	0.0929
Number (%) of patients censored	57 (83.8)	74 (73.3)	37 (67.3)	57 (73.1)	
Kaplan-Meier estimates of EQ-5D VAS in months					
25% quantile (95% CI)	NC (14.226 to NC)	14.55 (12.025 to NC)	15.70 (7.261 to 22.209)	19.88 (12.977 to NC)	
Median (95% CI)	NC (NC to NC)	NC (22.341 to NC)	NC (22.209 to NC)	NC (21.257 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.1220		0.4374	
Hazard ratio (95% CI) vs Kd	-	1.73 (0.86 to 3.48)		0.78 (0.42 to 1.46)	
P-value	-	0.1268		0.4386	
Improvement probability (95% CI)[b]					

A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
PGM=DEVOPS/SAR650984/EFC15246/CIR_RWE/REPORT/PGM/eff_km_subgp_sr_sig_de_i_t.sas OUT=REPORT/OUTPUT/eff_km_eq5d_vas_imppl_sex_de_i_t_x.rtf (07APR2021 14:45)

16.2.6.1 Health-related quality-of-life endpoints - EQ-5D
16.2.6.1.2 EQ-5D VAS
16.2.6.1.2.3 Efficacy response data - Subgroup analyses by gender
16.2.6.1.2.3.6 EQ-5D - Time until permanent deterioration by 10 pt in EQ-5D VAS according to gender (LOCF) - ITT population

	Male		Female		
	Kd (N=68)	**IKd (N=101)**	**Kd (N=55)**	**IKd (N=78)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	16 (23.5)	27 (26.7)	13 (23.6)	23 (29.5)	0.8609
Number (%) of patients censored	52 (76.5)	74 (73.3)	42 (76.4)	55 (70.5)	
Kaplan-Meier estimates of EQ-5D VAS in months					
25% quantile (95% CI)	17.97 (6.374 to NC)	19.25 (5.815 to NC)	20.57 (14.062 to NC)	17.05 (10.415 to 24.444)	
Median (95% CI)	NC (NC to NC)	NC (23.129 to NC)	NC (21.388 to NC)	24.44 (23.097 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (24.444 to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.6139		0.4804	
Hazard ratio (95% CI) vs Kd	-	1.17 (0.63 to 2.18)		1.28 (0.65 to 2.53)	
P-value	-	0.6143		0.4815	
Deterioration probability (95% CI)[b]					

A higher score represents a better level of quality of life. Clinical meaningful deterioration change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
PGM=DEVOPS/SAR650984/EFC15246/CIR_RWE/REPORT/PGM/eff_km_subgp_sr_sig_de_i_t.sas OUT=REPORT/OUTPUT/eff_km_eq5d_vas_detpl_sex_de_i_t_x.rtf (07APR2021 14:45)

16.2.6.1 Health-related quality-of-life endpoints - EQ-5D
16.2.6.1.2 EQ-5D VAS
16.2.6.1.2.4 Efficacy response data - Subgroup analyses by ethnic origin
16.2.6.1.2.4.3 EQ-5D - Time to first improvement by 10 pt in EQ-5D VAS according to ethnic origin (LOCF) - ITT population

	White		Other		
	Kd (N=83)	**IKd (N=131)**	**Kd (N=28)**	**IKd (N=34)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	42 (50.6)	70 (53.4)	12 (42.9)	16 (47.1)	0.7626
Number (%) of patients censored	41 (49.4)	61 (46.6)	16 (57.1)	18 (52.9)	
Kaplan-Meier estimates of EQ-5D VAS in months					
25% quantile (95% CI)	1.12 (1.018 to 2.891)	1.91 (1.051 to 2.136)	1.28 (1.051 to 2.924)	1.87 (1.018 to 2.136)	
Median (95% CI)	9.79 (3.055 to NC)	10.18 (3.811 to NC)	NC (1.873 to NC)	NC (2.004 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.7862		0.6289	
Hazard ratio (95% CI) vs Kd	-	1.05 (0.72 to 1.55)		1.20 (0.57 to 2.54)	
P-value	-	0.7875		0.6294	
Improvement probability (95% CI)[b]					

A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
PGM=DEVOPS/SAR650984/EFC15246/CIR_RWE/REPORT/PGM/eff_km_subgp_sr_sig_de_i_t.sas OUT=REPORT/OUTPUT/eff_km_eq5d_vas_impl_race_de_i_t_x.rtf (07APR2021 14:45)

16.2.6.1 Health-related quality-of-life endpoints - EQ-5D
16.2.6.1.2 EQ-5D VAS
16.2.6.1.2.4 Efficacy response data - Subgroup analyses by ethnic origin
16.2.6.1.2.4.4 EQ-5D - Time to first deterioration by 10 pt in EQ-5D VAS according to ethnic origin (LOCF) - ITT population

	White		Other		
	Kd (N=83)	**IKd (N=131)**	**Kd (N=28)**	**IKd (N=34)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	47 (56.6)	78 (59.5)	18 (64.3)	19 (55.9)	0.4476
Number (%) of patients censored	36 (43.4)	53 (40.5)	10 (35.7)	15 (44.1)	
Kaplan-Meier estimates of EQ-5D VAS in months					
25% quantile (95% CI)	2.43 (1.216 to 3.844)	1.87 (1.051 to 2.760)	2.00 (1.051 to 4.961)	2.97 (0.986 to 5.552)	
Median (95% CI)	7.39 (4.764 to NC)	7.39 (3.844 to 11.105)	6.01 (2.037 to NC)	7.46 (3.811 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (7.556 to NC)	NC (14.587 to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.5432		0.5648	
Hazard ratio (95% CI) vs Kd	-	1.12 (0.78 to 1.61)		0.83 (0.43 to 1.58)	
P-value	-	0.5434		0.5654	
Deterioration probability (95% CI)[b]					

A higher score represents a better level of quality of life. Clinical meaningful deterioration change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
PGM=DEVOPS/SAR650984/EFC15246/CIR_RWE/REPORT/PGM/eff_km_subgp_sr_sig_de_i_t.sas OUT=REPORT/OUTPUT/eff_km_eq5d_vas_detl_race_de_i_t_x.rtf (07APR2021 14:45)

16.2.6.1 Health-related quality-of-life endpoints - EQ-5D
16.2.6.1.2 EQ-5D VAS
16.2.6.1.2.4 Efficacy response data - Subgroup analyses by ethnic origin
16.2.6.1.2.4.5 EQ-5D - Time until permanent improvement by 10 pt in EQ-5D VAS according to ethnic origin (LOCF) - ITT population

	White		Other		
	Kd (N=83)	**IKd (N=131)**	**Kd (N=28)**	**IKd (N=34)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	21 (25.3)	36 (27.5)	6 (21.4)	9 (26.5)	0.8208
Number (%) of patients censored	62 (74.7)	95 (72.5)	22 (78.6)	25 (73.5)	
Kaplan-Meier estimates of EQ-5D VAS in months					
25% quantile (95% CI)	19.45 (10.448 to NC)	17.94 (12.945 to NC)	17.91 (1.051 to NC)	20.67 (7.458 to 22.341)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (20.665 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (22.341 to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.7445		0.6354	
Hazard ratio (95% CI) vs Kd	-	1.09 (0.64 to 1.87)		1.28 (0.46 to 3.61)	
P-value	-	0.7446		0.6363	
Improvement probability (95% CI)[b]					

A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
PGM=DEVOPS/SAR650984/EFC15246/CIR_RWE/REPORT/PGM/eff_km_subgp_sr_sig_de_i_t.sas OUT=REPORT/OUTPUT/eff_km_eq5d_vas_imppl_race_de_i_t_x.rtf (07APR2021 14:45)

16.2.6.1 Health-related quality-of-life endpoints - EQ-5D
16.2.6.1.2 EQ-5D VAS
16.2.6.1.2.4 Efficacy response data - Subgroup analyses by ethnic origin
16.2.6.1.2.4.6 EQ-5D - Time until permanent deterioration by 10 pt in EQ-5D VAS according to ethnic origin (LOCF) - ITT population

	White		Other		
	Kd (N=83)	**IKd (N=131)**	**Kd (N=28)**	**IKd (N=34)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	20 (24.1)	41 (31.3)	7 (25.0)	6 (17.6)	0.2921
Number (%) of patients censored	63 (75.9)	90 (68.7)	21 (75.0)	28 (82.4)	
Kaplan-Meier estimates of EQ-5D VAS in months					
25% quantile (95% CI)	20.57 (13.634 to NC)	12.94 (8.181 to 21.191)	17.97 (3.877 to NC)	23.13 (6.505 to NC)	
Median (95% CI)	NC (NC to NC)	24.44 (23.097 to NC)	NC (17.971 to NC)	NC (23.129 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (24.444 to NC)	NC (NC to NC)	NC (23.129 to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.2446		0.5161	
Hazard ratio (95% CI) vs Kd	-	1.37 (0.80 to 2.34)		0.70 (0.23 to 2.08)	
P-value	-	0.2466		0.5183	
Deterioration probability (95% CI)[b]					

A higher score represents a better level of quality of life. Clinical meaningful deterioration change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.1 Health-related quality-of-life endpoints - EQ-5D
16.2.6.1.2 EQ-5D VAS
16.2.6.1.2.5 Efficacy response data - Subgroup analyses by geographical region
16.2.6.1.2.5.3 EQ-5D - Time to first improvement by 10 pt in EQ-5D VAS according to geographical region (LOCF) - ITT population

	Europe		America		Asia		Other countries		
	Kd (N=60)	**IKd (N=85)**	**Kd (N=20)**	**IKd (N=24)**	**Kd (N=21)**	**IKd (N=25)**	**Kd (N=22)**	**IKd (N=45)**	**p-value of treatment-by-subgroup interaction[c]**
Number (%) of events	27 (45.0)	44 (51.8)	12 (60.0)	15 (62.5)	9 (42.9)	12 (48.0)	9 (40.9)	21 (46.7)	0.9764
Number (%) of patients censored	33 (55.0)	41 (48.2)	8 (40.0)	9 (37.5)	12 (57.1)	13 (52.0)	13 (59.1)	24 (53.3)	
Kaplan-Meier estimates of event in months									
25% quantile (95% CI)	1.12 (0.986 to 2.957)	2.00 (1.051 to 2.825)	1.05 (0.986 to 2.103)	1.08 (0.986 to 2.103)	1.12 (1.051 to 3.975)	1.12 (0.920 to 2.070)	3.88 (1.051 to NC)	1.91 (1.051 to 3.877)	
Median (95% CI)	NC (3.055 to NC)	10.18 (3.713 to NC)	3.33 (1.051 to NC)	2.53 (1.906 to NC)	NC (1.117 to NC)	NC (1.117 to NC)	NC (3.877 to NC)	NC (3.844 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (3.811 to NC)	NC (2.957 to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Kd									

A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.1 Health-related quality-of-life endpoints - EQ-5D
16.2.6.1.2 EQ-5D VAS
16.2.6.1.2.5 Efficacy response data - Subgroup analyses by geographical region
16.2.6.1.2.5.3 EQ-5D - Time to first improvement by 10 pt in EQ-5D VAS according to geographical region (LOCF) - ITT population

	Europe		America		Asia		Other countries		
	Kd (N=60)	**IKd (N=85)**	**Kd (N=20)**	**IKd (N=24)**	**Kd (N=21)**	**IKd (N=25)**	**Kd (N=22)**	**IKd (N=45)**	**p-value of treatment-by-subgroup interaction[c]**
Log-Rank test p-value[a] vs Kd	-	0.6675		0.8190		0.6523		0.4803	
Hazard ratio (95% CI) vs Kd	-	1.11 (0.69 to 1.79)		1.09 (0.51 to 2.34)		1.22 (0.51 to 2.89)		1.32 (0.61 to 2.89)	
P-value	-	0.6677		0.8197		0.6528		0.4818	
Improvement probability (95% CI)[b]									
3 Months	0.361 (0.240 to 0.483)	0.363 (0.261 to 0.465)	0.500 (0.271 to 0.692)	0.584 (0.355 to 0.757)	0.404 (0.194 to 0.606)	0.458 (0.256 to 0.640)	0.091 (0.016 to 0.251)	0.289 (0.166 to 0.424)	
6 Months	0.452 (0.321 to 0.575)	0.452 (0.342 to 0.556)	0.550 (0.313 to 0.735)	0.630 (0.397 to 0.794)	0.458 (0.235 to 0.657)	0.500 (0.291 to 0.678)	0.273 (0.111 to 0.464)	0.378 (0.239 to 0.516)	

A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.1 Health-related quality-of-life endpoints - EQ-5D
16.2.6.1.2 EQ-5D VAS
16.2.6.1.2.5 Efficacy response data - Subgroup analyses by geographical region
16.2.6.1.2.5.4 EQ-5D - Time to first deterioration by 10 pt in EQ-5D VAS according to geographical region (LOCF) - ITT population

	Europe		America		Asia		Other countries		
	Kd (N=60)	**IKd (N=85)**	**Kd (N=20)**	**IKd (N=24)**	**Kd (N=21)**	**IKd (N=25)**	**Kd (N=22)**	**IKd (N=45)**	**p-value of treatment-by-subgroup interaction[c]**
Number (%) of events	28 (46.7)	45 (52.9)	13 (65.0)	12 (50.0)	12 (57.1)	15 (60.0)	18 (81.8)	31 (68.9)	0.8599
Number (%) of patients censored	32 (53.3)	40 (47.1)	7 (35.0)	12 (50.0)	9 (42.9)	10 (40.0)	4 (18.2)	14 (31.1)	
Kaplan-Meier estimates of event in months									
25% quantile (95% CI)	3.78 (1.643 to 6.571)	2.79 (1.413 to 6.538)	1.94 (0.953 to 3.910)	1.08 (0.986 to 3.811)	2.02 (1.051 to 4.961)	2.48 (0.986 to 4.830)	1.87 (0.986 to 3.943)	1.08 (1.018 to 1.938)	
Median (95% CI)	21.22 (6.571 to NC)	11.10 (6.965 to NC)	4.99 (1.906 to NC)	12.32 (1.577 to NC)	7.13 (2.004 to NC)	6.11 (2.825 to NC)	4.80 (1.873 to 6.012)	4.01 (1.906 to 8.181)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (5.224 to NC)	NC (12.320 to NC)	NC (7.556 to NC)	NC (8.279 to NC)	6.37 (4.830 to NC)	NC (7.425 to NC)	

A higher score represents a better level of quality of life. Clinical meaningful deterioration change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.1 Health-related quality-of-life endpoints - EQ-5D
16.2.6.1.2 EQ-5D VAS
16.2.6.1.2.5 Efficacy response data - Subgroup analyses by geographical region
16.2.6.1.2.5.4 EQ-5D - Time to first deterioration by 10 pt in EQ-5D VAS according to geographical region (LOCF) - ITT population

	Europe		America		Asia		Other countries		
	Kd (N=60)	**IKd (N=85)**	**Kd (N=20)**	**IKd (N=24)**	**Kd (N=21)**	**IKd (N=25)**	**Kd (N=22)**	**IKd (N=45)**	**p-value of treatment-by-subgroup interaction[c]**
Comparison vs. Kd									
Log-Rank test p-value[a] vs Kd	-	0.6836		0.6135		0.9057		0.6934	
Hazard ratio (95% CI) vs Kd	-	1.10 (0.69 to 1.77)		0.82 (0.37 to 1.79)		1.05 (0.49 to 2.24)		0.89 (0.50 to 1.59)	
P-value	-	0.6837		0.6141		0.9059		0.6935	
Deterioration probability (95% CI)[b]									
3 Months	0.776 (0.645 to 0.863)	0.735 (0.626 to 0.817)	0.600 (0.357 to 0.776)	0.647 (0.416 to 0.806)	0.600 (0.357 to 0.776)	0.708 (0.484 to 0.849)	0.636 (0.403 to 0.799)	0.556 (0.400 to 0.686)	
6 Months	0.647 (0.507 to 0.756)	0.662 (0.550 to 0.753)	0.450 (0.231 to 0.647)	0.508 (0.289 to 0.691)	0.550 (0.313 to 0.735)	0.500 (0.291 to 0.678)	0.318 (0.142 to 0.511)	0.394 (0.251 to 0.533)	

A higher score represents a better level of quality of life. Clinical meaningful deterioration change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.1 Health-related quality-of-life endpoints - EQ-5D
16.2.6.1.2 EQ-5D VAS
16.2.6.1.2.5 Efficacy response data - Subgroup analyses by geographical region
16.2.6.1.2.5.5 EQ-5D - Time until permanent improvement by 10 pt in EQ-5D VAS according to geographical region (LOCF) - ITT population

	Europe		America		Asia		Other countries		
	Kd (N=60)	**IKd (N=85)**	**Kd (N=20)**	**IKd (N=24)**	**Kd (N=21)**	**IKd (N=25)**	**Kd (N=22)**	**IKd (N=45)**	**p-value of treatment-by-subgroup interaction[c]**
Number (%) of events	12 (20.0)	23 (27.1)	9 (45.0)	9 (37.5)	4 (19.0)	6 (24.0)	4 (18.2)	10 (22.2)	0.9155
Number (%) of patients censored	48 (80.0)	62 (72.9)	11 (55.0)	15 (62.5)	17 (81.0)	19 (76.0)	18 (81.8)	35 (77.8)	
Kaplan-Meier estimates of event in months									
25% quantile (95% CI)	NC (8.312 to NC)	19.42 (12.715 to NC)	10.55 (0.986 to 19.450)	7.46 (0.986 to NC)	NC (1.051 to NC)	21.26 (1.084 to NC)	22.21 (3.055 to NC)	NC (3.745 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	19.45 (10.546 to NC)	NC (7.458 to NC)	NC (17.906 to NC)	NC (20.665 to NC)	NC (22.209 to NC)	NC (NC to NC)	

A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.1 Health-related quality-of-life endpoints - EQ-5D
16.2.6.1.2 EQ-5D VAS
16.2.6.1.2.5 Efficacy response data - Subgroup analyses by geographical region
16.2.6.1.2.5.5 EQ-5D - Time until permanent improvement by 10 pt in EQ-5D VAS according to geographical region (LOCF) - ITT population

	Europe		**America**		**Asia**		**Other countries**		
	Kd (N=60)	**IKd (N=85)**	**Kd (N=20)**	**IKd (N=24)**	**Kd (N=21)**	**IKd (N=25)**	**Kd (N=22)**	**IKd (N=45)**	**p-value of treatment-by-subgroup interaction[c]**
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (19.450 to NC)	NC (NC to NC)	NC (NC to NC)	NC (22.341 to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Kd									
Log-Rank test p-value[a] vs Kd	-	0.4763		0.9406		0.8519		0.5415	
Hazard ratio (95% CI) vs Kd	-	1.29 (0.64 to 2.59)		0.97 (0.38 to 2.43)		1.13 (0.32 to 4.00)		1.44 (0.45 to 4.64)	
P-value	-	0.4775		0.9406		0.8520		0.5436	
Improvement probability (95% CI)[b]									

A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.1 Health-related quality-of-life endpoints - EQ-5D
16.2.6.1.2 EQ-5D VAS
16.2.6.1.2.5 Efficacy response data - Subgroup analyses by geographical region
16.2.6.1.2.5.6 EQ-5D - Time until permanent deterioration by 10 pt in EQ-5D VAS according to geographical region (LOCF) - ITT population

	Europe		America		Asia		Other countries		
	Kd (N=60)	**IKd (N=85)**	**Kd (N=20)**	**IKd (N=24)**	**Kd (N=21)**	**IKd (N=25)**	**Kd (N=22)**	**IKd (N=45)**	**p-value of treatment-by-subgroup interaction[c]**
Number (%) of events	12 (20.0)	23 (27.1)	4 (20.0)	7 (29.2)	6 (28.6)	6 (24.0)	7 (31.8)	14 (31.1)	0.7693
Number (%) of patients censored	48 (80.0)	62 (72.9)	16 (80.0)	17 (70.8)	15 (71.4)	19 (76.0)	15 (68.2)	31 (68.9)	
Kaplan-Meier estimates of event in months									
25% quantile (95% CI)	NC (13.634 to NC)	19.42 (9.265 to 24.444)	21.39 (4.764 to NC)	14.00 (0.986 to NC)	10.55 (1.314 to NC)	23.13 (3.910 to NC)	17.97 (2.136 to NC)	10.41 (4.665 to NC)	
Median (95% CI)	NC (NC to NC)	24.44 (NC to NC)	21.39 (21.388 to NC)	NC (13.996 to NC)	NC (10.546 to NC)	NC (23.129 to NC)	NC (17.971 to NC)	NC (23.097 to NC)	

A higher score represents a better level of quality of life. Clinical meaningful deterioration change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.1 Health-related quality-of-life endpoints - EQ-5D
16.2.6.1.2 EQ-5D VAS
16.2.6.1.2.5 Efficacy response data - Subgroup analyses by geographical region
16.2.6.1.2.5.6 EQ-5D - Time until permanent deterioration by 10 pt in EQ-5D VAS according to geographical region (LOCF) - ITT population

	Europe		America		Asia		Other countries		
	Kd (N=60)	**IKd (N=85)**	**Kd (N=20)**	**IKd (N=24)**	**Kd (N=21)**	**IKd (N=25)**	**Kd (N=22)**	**IKd (N=45)**	**p-value of treatment-by-subgroup interaction[c]**
75% quantile (95% CI)	NC (NC to NC)	24.44 (NC to NC)	NC (21.388 to NC)	NC (NC to NC)	NC (NC to NC)	NC (23.129 to NC)	NC (NC to NC)	NC (23.097 to NC)	
Comparison vs. Kd									
Log-Rank test p-value[a] vs Kd	-	0.5246		0.2800		0.6626		0.9123	
Hazard ratio (95% CI) vs Kd	-	1.26 (0.62 to 2.54)		1.95 (0.57 to 6.71)		0.78 (0.25 to 2.42)		1.05 (0.42 to 2.61)	
P-value	-	0.5255		0.2887		0.6635		0.9130	
Deterioration probability (95% CI)[b]									

A higher score represents a better level of quality of life. Clinical meaningful deterioration change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.1 Health-related quality-of-life endpoints - EQ-5D
16.2.6.1.2 EQ-5D VAS
16.2.6.1.2.6 Efficacy response data - Subgroup analyses by regulatory region
16.2.6.1.2.6.3 EQ-5D - Time to first improvement by 10 pt in EQ-5D VAS according to regulatory region (LOCF) - ITT population

	Western countries		Other countries		
	Kd (N=55)	**IKd (N=97)**	**Kd (N=68)**	**IKd (N=82)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	24 (43.6)	49 (50.5)	33 (48.5)	43 (52.4)	0.9391
Number (%) of patients censored	31 (56.4)	48 (49.5)	35 (51.5)	39 (47.6)	
Kaplan-Meier estimates of EQ-5D VAS in months					
25% quantile (95% CI)	1.91 (1.051 to 4.632)	1.97 (1.117 to 2.891)	1.12 (1.051 to 2.891)	1.17 (1.018 to 2.070)	
Median (95% CI)	NC (3.877 to NC)	14.00 (4.731 to NC)	NC (2.924 to NC)	4.70 (2.366 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.6179		0.4992	
Hazard ratio (95% CI) vs Kd	-	1.13 (0.69 to 1.85)		1.17 (0.74 to 1.84)	
P-value	-	0.6181		0.4996	
Improvement probability (95% CI)[b]					

A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
PGM=DEVOPS/SAR650984/EFC15246/CIR_RWE/REPORT/PGM/eff_km_subgp_sr_sig_de_i_t.sas OUT=REPORT/OUTPUT/eff_km_eq5d_vas_impl_rreg_de_i_t_x.rtf (07APR2021 14:45)

16.2.6.1 Health-related quality-of-life endpoints - EQ-5D
16.2.6.1.2 EQ-5D VAS
16.2.6.1.2.6 Efficacy response data - Subgroup analyses by regulatory region
16.2.6.1.2.6.4 EQ-5D - Time to first deterioration by 10 pt in EQ-5D VAS according to regulatory region (LOCF) - ITT population

	Western countries		Other countries		
	Kd (N=55)	**IKd (N=97)**	**Kd (N=68)**	**IKd (N=82)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	30 (54.5)	55 (56.7)	41 (60.3)	48 (58.5)	0.8740
Number (%) of patients censored	25 (45.5)	42 (43.3)	27 (39.7)	34 (41.5)	
Kaplan-Meier estimates of EQ-5D VAS in months					
25% quantile (95% CI)	3.78 (1.051 to 4.961)	1.94 (1.084 to 3.220)	2.00 (1.216 to 2.990)	1.94 (1.051 to 3.121)	
Median (95% CI)	6.93 (4.961 to NC)	8.87 (4.008 to NC)	6.70 (3.023 to 11.203)	7.39 (4.665 to 13.207)	
75% quantile (95% CI)	NC (21.224 to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.8359		0.9894	
Hazard ratio (95% CI) vs Kd	-	1.05 (0.67 to 1.64)		1.00 (0.66 to 1.51)	
P-value	-	0.8370		0.9894	
Deterioration probability (95% CI)[b]					

A higher score represents a better level of quality of life. Clinical meaningful deterioration change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.1 Health-related quality-of-life endpoints - EQ-5D
16.2.6.1.2 EQ-5D VAS
16.2.6.1.2.6 Efficacy response data - Subgroup analyses by regulatory region
16.2.6.1.2.6.5 EQ-5D - Time until permanent improvement by 10 pt in EQ-5D VAS according to regulatory region (LOCF) - ITT population

	Western countries		Other countries		
	Kd (N=55)	**IKd (N=97)**	**Kd (N=68)**	**IKd (N=82)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	13 (23.6)	23 (23.7)	16 (23.5)	25 (30.5)	0.5190
Number (%) of patients censored	42 (76.4)	74 (76.3)	52 (76.5)	57 (69.5)	
Kaplan-Meier estimates of EQ-5D VAS in months					
25% quantile (95% CI)	22.21 (7.918 to NC)	19.88 (12.945 to NC)	19.45 (12.025 to NC)	17.84 (7.885 to 21.257)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (21.257 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.9498		0.3672	
Hazard ratio (95% CI) vs Kd	-	0.98 (0.49 to 1.94)		1.33 (0.71 to 2.50)	
P-value	-	0.9496		0.3689	
Improvement probability (95% CI)[b]					

A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.1 Health-related quality-of-life endpoints - EQ-5D
16.2.6.1.2 EQ-5D VAS
16.2.6.1.2.6 Efficacy response data - Subgroup analyses by regulatory region
16.2.6.1.2.6.6 EQ-5D - Time until permanent deterioration by 10 pt in EQ-5D VAS according to regulatory region (LOCF) - ITT population

	Western countries		Other countries		
	Kd (N=55)	**IKd (N=97)**	**Kd (N=68)**	**IKd (N=82)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	12 (21.8)	25 (25.8)	17 (25.0)	25 (30.5)	0.9521
Number (%) of patients censored	43 (78.2)	72 (74.2)	51 (75.0)	57 (69.5)	
Kaplan-Meier estimates of EQ-5D VAS in months					
25% quantile (95% CI)	20.57 (8.312 to NC)	19.42 (9.265 to NC)	19.15 (10.546 to NC)	12.94 (6.505 to 24.444)	
Median (95% CI)	NC (NC to NC)	NC (23.097 to NC)	NC (NC to NC)	24.44 (23.129 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (24.444 to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.5841		0.4434	
Hazard ratio (95% CI) vs Kd	-	1.21 (0.61 to 2.41)		1.27 (0.69 to 2.36)	
P-value	-	0.5847		0.4445	
Deterioration probability (95% CI)[b]					

A higher score represents a better level of quality of life. Clinical meaningful deterioration change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.1 Health-related quality-of-life endpoints - EQ-5D
16.2.6.1.2 EQ-5D VAS
16.2.6.1.2.7 Efficacy response data - Subgroup analyses by baseline ECOG PS
16.2.6.1.2.7.3 EQ-5D - Time to first improvement by 10 pt in EQ-5D VAS according to baseline ECOG PS (LOCF) - ITT population

	0 or 1		>1		
	Kd (N=118)	**IKd (N=168)**	**Kd (N=5)**	**IKd (N=11)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	54 (45.8)	88 (52.4)	3 (60.0)	4 (36.4)	0.2634
Number (%) of patients censored	64 (54.2)	80 (47.6)	2 (40.0)	7 (63.6)	
Kaplan-Meier estimates of EQ-5D VAS in months					
25% quantile (95% CI)	1.91 (1.117 to 2.957)	1.91 (1.084 to 2.103)	0.99 (0.986 to NC)	2.10 (0.986 to NC)	
Median (95% CI)	NC (4.632 to NC)	10.18 (3.811 to NC)	1.05 (0.986 to NC)	NC (0.986 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (0.986 to NC)	NC (2.530 to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.3578		0.4070	
Hazard ratio (95% CI) vs Kd	-	1.17 (0.84 to 1.64)		0.53 (0.12 to 2.42)	
P-value	-	0.3583		0.4141	
Improvement probability (95% CI)[b]					

A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.1 Health-related quality-of-life endpoints - EQ-5D
16.2.6.1.2 EQ-5D VAS
16.2.6.1.2.7 Efficacy response data - Subgroup analyses by baseline ECOG PS
16.2.6.1.2.7.4 EQ-5D - Time to first deterioration by 10 pt in EQ-5D VAS according to baseline ECOG PS (LOCF) - ITT population

	0 or 1		>1		
	Kd (N=118)	**IKd (N=168)**	**Kd (N=5)**	**IKd (N=11)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	70 (59.3)	98 (58.3)	1 (20.0)	5 (45.5)	0.2921
Number (%) of patients censored	48 (40.7)	70 (41.7)	4 (80.0)	6 (54.5)	
Kaplan-Meier estimates of EQ-5D VAS in months					
25% quantile (95% CI)	2.14 (1.314 to 3.778)	1.94 (1.084 to 2.825)	NC (2.070 to NC)	3.12 (0.986 to 8.181)	
Median (95% CI)	6.57 (4.895 to 10.185)	8.28 (4.830 to 12.780)	NC (2.070 to NC)	8.18 (0.986 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (2.070 to NC)	NC (6.965 to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.9120		0.3076	
Hazard ratio (95% CI) vs Kd	-	0.98 (0.72 to 1.34)		2.91 (0.34 to 24.93)	
P-value	-	0.9118		0.3303	
Deterioration probability (95% CI)[b]					

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The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.1 Health-related quality-of-life endpoints - EQ-5D
16.2.6.1.2 EQ-5D VAS
16.2.6.1.2.7 Efficacy response data - Subgroup analyses by baseline ECOG PS
16.2.6.1.2.7.5 EQ-5D - Time until permanent improvement by 10 pt in EQ-5D VAS according to baseline ECOG PS (LOCF) - ITT population

	0 or 1		>1		
	Kd (N=118)	**IKd (N=168)**	**Kd (N=5)**	**IKd (N=11)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	26 (22.0)	45 (26.8)	3 (60.0)	3 (27.3)	0.1672
Number (%) of patients censored	92 (78.0)	123 (73.2)	2 (40.0)	8 (72.7)	
Kaplan-Meier estimates of EQ-5D VAS in months					
25% quantile (95% CI)	22.21 (14.226 to NC)	19.42 (13.766 to 22.341)	0.99 (0.986 to NC)	14.55 (1.906 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	1.05 (0.986 to NC)	NC (1.906 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (0.986 to NC)	NC (NC to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.4163		0.1891	
Hazard ratio (95% CI) vs Kd	-	1.22 (0.75 to 1.98)		0.35 (0.07 to 1.79)	
P-value	-	0.4171		0.2077	
Improvement probability (95% CI)[b]					

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The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.1 Health-related quality-of-life endpoints - EQ-5D
16.2.6.1.2 EQ-5D VAS
16.2.6.1.2.7 Efficacy response data - Subgroup analyses by baseline ECOG PS
16.2.6.1.2.7.6 EQ-5D - Time until permanent deterioration by 10 pt in EQ-5D VAS according to baseline ECOG PS (LOCF) - ITT population

	0 or 1		>1		
	Kd (N=118)	**IKd (N=168)**	**Kd (N=5)**	**IKd (N=11)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	28 (23.7)	47 (28.0)	1 (20.0)	3 (27.3)	0.9961
Number (%) of patients censored	90 (76.3)	121 (72.0)	4 (80.0)	8 (72.7)	
Kaplan-Meier estimates of EQ-5D VAS in months					
25% quantile (95% CI)	20.57 (14.062 to NC)	19.25 (9.265 to 23.129)	NC (4.764 to NC)	12.62 (5.191 to NC)	
Median (95% CI)	NC (NC to NC)	24.44 (23.129 to NC)	NC (4.764 to NC)	NC (5.191 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (24.444 to NC)	NC (4.764 to NC)	NC (NC to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.4131		0.8158	
Hazard ratio (95% CI) vs Kd	-	1.22 (0.76 to 1.94)		1.31 (0.13 to 12.70)	
P-value	-	0.4139		0.8164	
Deterioration probability (95% CI)[b]					

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The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.1 Health-related quality-of-life endpoints - EQ-5D
16.2.6.1.2 EQ-5D VAS
16.2.6.1.2.8 Efficacy response data - Subgroup analyses by ISS staging at SE
16.2.6.1.2.8.3 EQ-5D - Time to first improvement by 10 pt in EQ-5D VAS according to ISS staging at SE (LOCF) - ITT population

	I		II		III		
	Kd (N=71)	**IKd (N=89)**	**Kd (N=31)**	**IKd (N=63)**	**Kd (N=20)**	**IKd (N=26)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	37 (52.1)	43 (48.3)	13 (41.9)	36 (57.1)	7 (35.0)	13 (50.0)	0.1831
Number (%) of patients censored	34 (47.9)	46 (51.7)	18 (58.1)	27 (42.9)	13 (65.0)	13 (50.0)	
Kaplan-Meier estimates of EQ-5D VAS in months							
25% quantile (95% CI)	1.12 (1.051 to 3.055)	1.91 (1.117 to 2.957)	1.87 (0.986 to 3.975)	1.97 (1.051 to 2.530)	2.92 (0.986 to NC)	1.05 (0.953 to 2.004)	
Median (95% CI)	6.74 (3.285 to NC)	NC (5.782 to NC)	NC (1.906 to NC)	4.73 (2.825 to NC)	NC (2.924 to NC)	2.10 (1.051 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (2.366 to NC)	
Comparison vs. Kd							
Log-Rank test p-value[a] vs Kd	-	0.5480		0.3866		0.0962	
Hazard ratio (95% CI) vs Kd	-	0.87 (0.56 to 1.36)		1.32 (0.70 to 2.49)		2.16 (0.85 to 5.47)	
P-value	-	0.5483		0.3882		0.1040	

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The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.1 Health-related quality-of-life endpoints - EQ-5D
16.2.6.1.2 EQ-5D VAS
16.2.6.1.2.8 Efficacy response data - Subgroup analyses by ISS staging at SE
16.2.6.1.2.8.3 EQ-5D - Time to first improvement by 10 pt in EQ-5D VAS according to ISS staging at SE (LOCF) - ITT population

	I		II		III		
	Kd (N=71)	**IKd (N=89)**	**Kd (N=31)**	**IKd (N=63)**	**Kd (N=20)**	**IKd (N=26)**	**p-value of treatment-by-sub group interaction[c]**
Improvement probability (95% CI)[b]							
3 Months	0.343 (0.235 to 0.454)	0.340 (0.244 to 0.439)	0.394 (0.223 to 0.560)	0.382 (0.264 to 0.500)	0.276 (0.100 to 0.486)	0.581 (0.352 to 0.754)	
6 Months	0.472 (0.352 to 0.583)	0.397 (0.295 to 0.497)	0.430 (0.252 to 0.596)	0.515 (0.384 to 0.631)	0.331 (0.135 to 0.543)	0.581 (0.352 to 0.754)	
9 Months	0.501 (0.379 to 0.611)	0.445 (0.339 to 0.545)	0.430 (0.252 to 0.596)	0.532 (0.400 to 0.647)	0.392 (0.175 to 0.604)	0.581 (0.352 to 0.754)	
12 Months	0.532 (0.408 to 0.641)	0.468 (0.361 to 0.568)	0.430 (0.252 to 0.596)	0.549 (0.417 to 0.664)	0.392 (0.175 to 0.604)	0.581 (0.352 to 0.754)	
15 Months	0.532 (0.408 to 0.641)	0.481 (0.373 to 0.581)	0.430 (0.252 to 0.596)	0.567 (0.433 to 0.680)	0.392 (0.175 to 0.604)	0.581 (0.352 to 0.754)	
18 Months	0.532 (0.408 to 0.641)	0.494 (0.385 to 0.595)	0.430 (0.252 to 0.596)	0.585 (0.451 to 0.697)	0.392 (0.175 to 0.604)	0.581 (0.352 to 0.754)	
21 Months	0.532 (0.408 to 0.641)	0.494 (0.385 to 0.595)	0.430 (0.252 to 0.596)	0.585 (0.451 to 0.697)	0.392 (0.175 to 0.604)	0.581 (0.352 to 0.754)	
24 Months	0.532 (0.408 to 0.641)	0.494 (0.385 to 0.595)	0.430 (0.252 to 0.596)	0.585 (0.451 to 0.697)	0.392 (0.175 to 0.604)	0.581 (0.352 to 0.754)	

A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
PGM=DEVOPS/SAR650984/EFC15246/CIR_RWE/REPORT/PGM/eff_km_subgp_sr_sig_de_i_t.sas OUT=REPORT/OUTPUT/eff_km_eq5d_vas_impl_seiss_de_i_t_x.rtf (07APR2021 14:45)

16.2.6.1 Health-related quality-of-life endpoints - EQ-5D
16.2.6.1.2 EQ-5D VAS
16.2.6.1.2.8 Efficacy response data - Subgroup analyses by ISS staging at SE
16.2.6.1.2.8.3 EQ-5D - Time to first improvement by 10 pt in EQ-5D VAS according to ISS staging at SE (LOCF) - ITT population

	I		II		III		
	Kd (N=71)	**IKd (N=89)**	**Kd (N=31)**	**IKd (N=63)**	**Kd (N=20)**	**IKd (N=26)**	**p-value of treatment-by-sub group interaction[c]**
Number of patients at risk[b]							
3 Months	46	58	17	38	13	8	
6 Months	36	52	16	28	11	8	
9 Months	33	47	15	27	9	7	
12 Months	29	42	13	26	9	7	
15 Months	29	40	12	25	8	6	
18 Months	29	37	12	23	7	4	
21 Months	14	17	6	10	5	1	
24 Months	3	5	0	1	0	0	

A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
PGM=DEVOPS/SAR650984/EFC15246/CIR_RWE/REPORT/PGM/eff_km_subgp_sr_sig_de_i_t.sas OUT=REPORT/OUTPUT/eff_km_eq5d_vas_impl_seiss_de_i_t_x.rtf (07APR2021 14:45)

16.2.6.1 Health-related quality-of-life endpoints - EQ-5D
16.2.6.1.2 EQ-5D VAS
16.2.6.1.2.8 Efficacy response data - Subgroup analyses by ISS staging at SE
16.2.6.1.2.8.4 EQ-5D - Time to first deterioration by 10 pt in EQ-5D VAS according to ISS staging at SE (LOCF) - ITT population

	I		II		III		
	Kd (N=71)	**IKd (N=89)**	**Kd (N=31)**	**IKd (N=63)**	**Kd (N=20)**	**IKd (N=26)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	40 (56.3)	54 (60.7)	18 (58.1)	37 (58.7)	12 (60.0)	12 (46.2)	0.6342
Number (%) of patients censored	31 (43.7)	35 (39.3)	13 (41.9)	26 (41.3)	8 (40.0)	14 (53.8)	
Kaplan-Meier estimates of EQ-5D VAS in months							
25% quantile (95% CI)	2.96 (1.906 to 4.830)	3.12 (1.873 to 4.008)	1.31 (1.018 to 4.895)	1.08 (0.986 to 1.971)	1.97 (0.953 to 4.764)	1.41 (0.986 to 4.764)	
Median (95% CI)	7.43 (4.961 to NC)	8.51 (5.552 to 16.986)	7.39 (2.793 to NC)	6.97 (2.267 to NC)	4.96 (1.971 to NC)	8.87 (2.103 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (8.312 to NC)	NC (NC to NC)	NC (4.961 to NC)	NC (8.871 to NC)	
Comparison vs. Kd							
Log-Rank test p-value[a] vs Kd	-	0.6453		0.7964		0.4437	
Hazard ratio (95% CI) vs Kd	-	1.10 (0.73 to 1.66)		1.08 (0.61 to 1.89)		0.73 (0.33 to 1.63)	
P-value	-	0.6455		0.7965		0.4455	

A higher score represents a better level of quality of life. Clinical meaningful deterioration change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.1 Health-related quality-of-life endpoints - EQ-5D
16.2.6.1.2 EQ-5D VAS
16.2.6.1.2.8 Efficacy response data - Subgroup analyses by ISS staging at SE
16.2.6.1.2.8.5 EQ-5D - Time until permanent improvement by 10 pt in EQ-5D VAS according to ISS staging at SE (LOCF) - ITT population

	I		II		III		
	Kd (N=71)	**IKd (N=89)**	**Kd (N=31)**	**IKd (N=63)**	**Kd (N=20)**	**IKd (N=26)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	20 (28.2)	19 (21.3)	6 (19.4)	21 (33.3)	3 (15.0)	8 (30.8)	0.1413
Number (%) of patients censored	51 (71.8)	70 (78.7)	25 (80.6)	42 (66.7)	17 (85.0)	18 (69.2)	
Kaplan-Meier estimates of EQ-5D VAS in months							
25% quantile (95% CI)	16.46 (10.448 to NC)	21.26 (14.752 to NC)	NC (0.986 to NC)	15.70 (8.476 to 20.665)	NC (0.986 to NC)	7.46 (1.051 to NC)	
Median (95% CI)	NC (22.209 to NC)	NC (NC to NC)	NC (NC to NC)	NC (20.665 to NC)	NC (NC to NC)	NC (7.458 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Kd							
Log-Rank test p-value[a] vs Kd	-	0.3404		0.2472		0.2070	
Hazard ratio (95% CI) vs Kd	-	0.74 (0.39 to 1.38)		1.70 (0.68 to 4.22)		2.30 (0.61 to 8.68)	
P-value	-	0.3422		0.2526		0.2200	

A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.1 Health-related quality-of-life endpoints - EQ-5D
16.2.6.1.2 EQ-5D VAS
16.2.6.1.2.8 Efficacy response data - Subgroup analyses by ISS staging at SE
16.2.6.1.2.8.6 EQ-5D - Time until permanent deterioration by 10 pt in EQ-5D VAS according to ISS staging at SE (LOCF) - ITT population

	I		II		III		
	Kd (N=71)	**IKd (N=89)**	**Kd (N=31)**	**IKd (N=63)**	**Kd (N=20)**	**IKd (N=26)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	10 (14.1)	26 (29.2)	11 (35.5)	18 (28.6)	7 (35.0)	6 (23.1)	0.0654
Number (%) of patients censored	61 (85.9)	63 (70.8)	20 (64.5)	45 (71.4)	13 (65.0)	20 (76.9)	
Kaplan-Meier estimates of EQ-5D VAS in months							
25% quantile (95% CI)	NC (20.567 to NC)	19.25 (8.641 to 23.097)	14.06 (1.314 to NC)	17.05 (3.877 to NC)	9.43 (4.764 to 17.971)	9.26 (0.986 to NC)	
Median (95% CI)	NC (NC to NC)	24.44 (23.097 to NC)	NC (14.094 to NC)	NC (23.129 to NC)	17.97 (9.429 to NC)	NC (9.265 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (24.444 to NC)	NC (NC to NC)	NC (NC to NC)	NC (17.971 to NC)	NC (NC to NC)	
Comparison vs. Kd							
Log-Rank test p-value[a] vs Kd	-	0.0241		0.5092		0.4345	
Hazard ratio (95% CI) vs Kd	-	2.26 (1.09 to 4.70)		0.78 (0.37 to 1.65)		0.65 (0.22 to 1.93)	
P-value	-	0.0282		0.5103		0.4381	

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The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.6.1 Health-related quality-of-life endpoints - EQ-5D
16.2.6.1.2 EQ-5D VAS
16.2.6.1.2.9 Efficacy response data - Subgroup analyses by R-ISS stage at SE
16.2.6.1.2.9.3 EQ-5D - Time to first improvement by 10 pt in EQ-5D VAS according to R-ISS stage at SE (LOCF) - ITT population

	I or II		III		Not classified		
	Kd (N=103)	**IKd (N=155)**	**Kd (N=8)**	**IKd (N=16)**	**Kd (N=12)**	**IKd (N=8)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	45 (43.7)	83 (53.5)	4 (50.0)	8 (50.0)	8 (66.7)	1 (12.5)	0.2461
Number (%) of patients censored	58 (56.3)	72 (46.5)	4 (50.0)	8 (50.0)	4 (33.3)	7 (87.5)	
Kaplan-Meier estimates of EQ-5D VAS in months							
25% quantile (95% CI)	1.87 (1.051 to 2.858)	1.91 (1.051 to 2.136)	2.89 (1.051 to 3.055)	1.91 (0.986 to 2.103)	2.87 (0.953 to 6.571)	NC (2.004 to NC)	
Median (95% CI)	NC (3.811 to NC)	10.18 (3.811 to NC)	3.06 (1.051 to NC)	2.10 (1.084 to NC)	6.65 (0.986 to NC)	NC (2.004 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (2.924 to NC)	NC (2.103 to NC)	NC (6.571 to NC)	NC (NC to NC)	
Comparison vs. Kd							
Log-Rank test p-value[a] vs Kd	-	0.2851		0.5473		0.0836	
Hazard ratio (95% CI) vs Kd	-	1.22 (0.85 to 1.75)		1.45 (0.43 to 4.85)		0.19 (0.02 to 1.54)	
P-value	-	0.2859		0.5495		0.1210	

A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.1 Health-related quality-of-life endpoints - EQ-5D
16.2.6.1.2 EQ-5D VAS
16.2.6.1.2.9 Efficacy response data - Subgroup analyses by R-ISS stage at SE
16.2.6.1.2.9.4 EQ-5D - Time to first deterioration by 10 pt in EQ-5D VAS according to R-ISS stage at SE (LOCF) - ITT population

	I or II		III		Not classified		
	Kd (N=103)	**IKd (N=155)**	**Kd (N=8)**	**IKd (N=16)**	**Kd (N=12)**	**IKd (N=8)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	56 (54.4)	93 (60.0)	6 (75.0)	8 (50.0)	9 (75.0)	2 (25.0)	0.2102
Number (%) of patients censored	47 (45.6)	62 (40.0)	2 (25.0)	8 (50.0)	3 (25.0)	6 (75.0)	
Kaplan-Meier estimates of EQ-5D VAS in months							
25% quantile (95% CI)	2.79 (1.248 to 3.910)	1.94 (1.084 to 2.858)	1.05 (0.953 to 4.961)	1.41 (0.986 to 8.181)	2.56 (1.873 to 5.552)	6.97 (1.018 to NC)	
Median (95% CI)	7.39 (4.895 to NC)	7.43 (4.797 to 12.780)	4.96 (0.953 to 11.203)	8.18 (1.084 to NC)	6.24 (2.004 to NC)	NC (1.018 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	7.89 (2.037 to 11.203)	NC (8.181 to NC)	NC (5.552 to NC)	NC (6.965 to NC)	
Comparison vs. Kd							
Log-Rank test p-value[a] vs Kd	-	0.5027		0.2562		0.1461	
Hazard ratio (95% CI) vs Kd	-	1.12 (0.80 to 1.56)		0.54 (0.18 to 1.59)		0.34 (0.07 to 1.57)	

A higher score represents a better level of quality of life. Clinical meaningful deterioration change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.6.1 Health-related quality-of-life endpoints - EQ-5D
16.2.6.1.2 EQ-5D VAS
16.2.6.1.2.9 Efficacy response data - Subgroup analyses by R-ISS stage at SE
16.2.6.1.2.9.5 EQ-5D - Time until permanent improvement by 10 pt in EQ-5D VAS according to R-ISS stage at SE (LOCF) - ITT population

	I or II		III		Not classified		
	Kd (N=103)	**IKd (N=155)**	**Kd (N=8)**	**IKd (N=16)**	**Kd (N=12)**	**IKd (N=8)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	24 (23.3)	43 (27.7)	1 (12.5)	5 (31.3)	4 (33.3)	0 (0.0)	0.6242
Number (%) of patients censored	79 (76.7)	112 (72.3)	7 (87.5)	11 (68.8)	8 (66.7)	8 (100.0)	
Kaplan-Meier estimates of EQ-5D VAS in months							
25% quantile (95% CI)	19.45 (11.039 to NC)	19.42 (13.766 to 22.341)	NC (1.051 to NC)	2.37 (1.084 to NC)	13.86 (7.918 to NC)	NC (NC to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (1.051 to NC)	NC (2.103 to NC)	NC (8.312 to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Kd							
Log-Rank test p-value[a] vs Kd	-	0.6073		0.3253		0.1903	
Hazard ratio (95% CI) vs Kd	-	1.14 (0.69 to 1.88)		2.82 (0.33 to 24.27)			

A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.1 Health-related quality-of-life endpoints - EQ-5D
16.2.6.1.2 EQ-5D VAS
16.2.6.1.2.9 Efficacy response data - Subgroup analyses by R-ISS stage at SE
16.2.6.1.2.9.6 EQ-5D - Time until permanent deterioration by 10 pt in EQ-5D VAS according to R-ISS stage at SE (LOCF) - ITT population

	I or II		III		Not classified		
	Kd (N=103)	**IKd (N=155)**	**Kd (N=8)**	**IKd (N=16)**	**Kd (N=12)**	**IKd (N=8)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	23 (22.3)	46 (29.7)	3 (37.5)	3 (18.8)	3 (25.0)	1 (12.5)	0.3870
Number (%) of patients censored	80 (77.7)	109 (70.3)	5 (62.5)	13 (81.3)	9 (75.0)	7 (87.5)	
Kaplan-Meier estimates of EQ-5D VAS in months							
25% quantile (95% CI)	21.39 (14.062 to NC)	17.05 (9.265 to 23.097)	9.43 (4.961 to NC)	9.26 (6.637 to NC)	NC (2.136 to NC)	NC (1.018 to NC)	
Median (95% CI)	NC (NC to NC)	24.44 (23.129 to NC)	15.01 (4.961 to NC)	NC (8.181 to NC)	NC (6.932 to NC)	NC (1.018 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (24.444 to NC)	NC (9.429 to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Kd							
Log-Rank test p-value[a] vs Kd	-	0.2408		0.3054		0.8065	
Hazard ratio (95% CI) vs Kd	-	1.35 (0.82 to 2.23)		0.44 (0.09 to 2.20)		0.75 (0.08 to 7.26)	
P-value	-	0.2426		0.3186		0.8072	

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CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.1 Health-related quality-of-life endpoints - EQ-5D
16.2.6.1.2 EQ-5D VAS
16.2.6.1.2.10 Efficacy response data - Subgroup analyses by nb of prior lines
16.2.6.1.2.10.3 EQ-5D - Time to first improvement by 10 pt in EQ-5D VAS according to nb of prior lines (LOCF) - ITT population

	1		>1		
	Kd (N=55)	**IKd (N=79)**	**Kd (N=68)**	**IKd (N=100)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	24 (43.6)	38 (48.1)	33 (48.5)	54 (54.0)	0.8597
Number (%) of patients censored	31 (56.4)	41 (51.9)	35 (51.5)	46 (46.0)	
Kaplan-Meier estimates of EQ-5D VAS in months					
25% quantile (95% CI)	1.12 (1.051 to 4.632)	1.97 (1.051 to 3.811)	1.91 (1.018 to 2.891)	1.87 (1.051 to 2.037)	
Median (95% CI)	NC (4.632 to NC)	NC (4.797 to NC)	7.92 (2.924 to NC)	3.84 (2.530 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.7181		0.4856	
Hazard ratio (95% CI) vs Kd	-	1.10 (0.66 to 1.83)		1.17 (0.76 to 1.80)	
P-value	-	0.7182		0.4860	
Improvement probability (95% CI)[b]					

A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.1 Health-related quality-of-life endpoints - EQ-5D
16.2.6.1.2 EQ-5D VAS
16.2.6.1.2.10 Efficacy response data - Subgroup analyses by nb of prior lines
16.2.6.1.2.10.4 EQ-5D - Time to first deterioration by 10 pt in EQ-5D VAS according to nb of prior lines (LOCF) - ITT population

	1		>1		
	Kd (N=55)	**IKd (N=79)**	**Kd (N=68)**	**IKd (N=100)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	30 (54.5)	46 (58.2)	41 (60.3)	57 (57.0)	0.4728
Number (%) of patients censored	25 (45.5)	33 (41.8)	27 (39.7)	43 (43.0)	
Kaplan-Meier estimates of EQ-5D VAS in months					
25% quantile (95% CI)	2.83 (1.216 to 4.895)	2.10 (1.051 to 3.680)	2.07 (1.051 to 3.844)	1.94 (1.084 to 3.121)	
Median (95% CI)	6.82 (4.895 to NC)	6.97 (3.975 to NC)	7.39 (3.910 to 11.203)	8.51 (4.238 to 19.253)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (11.203 to NC)	NC (NC to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.5714		0.6626	
Hazard ratio (95% CI) vs Kd	-	1.14 (0.72 to 1.81)		0.91 (0.61 to 1.37)	
P-value	-	0.5717		0.6627	
Deterioration probability (95% CI)[b]					

A higher score represents a better level of quality of life. Clinical meaningful deterioration change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
PGM=DEVOPS/SAR650984/EFC15246/CIR_RWE/REPORT/PGM/eff_km_subgp_sr_sig_de_i_t.sas OUT=REPORT/OUTPUT/eff_km_eq5d_vas_detl_plne_de_i_t_x.rtf (07APR2021 14:45)

16.2.6.1 Health-related quality-of-life endpoints - EQ-5D
16.2.6.1.2 EQ-5D VAS
16.2.6.1.2.10 Efficacy response data - Subgroup analyses by nb of prior lines
16.2.6.1.2.10.5 EQ-5D - Time until permanent improvement by 10 pt in EQ-5D VAS according to nb of prior lines (LOCF) - ITT population

	1		>1		
	Kd (N=55)	**IKd (N=79)**	**Kd (N=68)**	**IKd (N=100)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	13 (23.6)	21 (26.6)	16 (23.5)	27 (27.0)	0.8853
Number (%) of patients censored	42 (76.4)	58 (73.4)	52 (76.5)	73 (73.0)	
Kaplan-Meier estimates of EQ-5D VAS in months					
25% quantile (95% CI)	22.21 (4.895 to NC)	19.81 (14.554 to NC)	17.91 (11.039 to NC)	16.39 (12.025 to NC)	
Median (95% CI)	NC (22.209 to NC)	NC (NC to NC)	NC (NC to NC)	NC (22.341 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.7644		0.6093	
Hazard ratio (95% CI) vs Kd	-	1.11 (0.56 to 2.22)		1.17 (0.63 to 2.18)	
P-value	-	0.7645		0.6097	
Improvement probability (95% CI)[b]					

A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
PGM=DEVOPS/SAR650984/EFC15246/CIR_RWE/REPORT/PGM/eff_km_subgp_sr_sig_de_i_t.sas OUT=REPORT/OUTPUT/eff_km_eq5d_vas_imppl_plne_de_i_t_x.rtf (07APR2021 14:45)

16.2.6.1 Health-related quality-of-life endpoints - EQ-5D
16.2.6.1.2 EQ-5D VAS
16.2.6.1.2.10 Efficacy response data - Subgroup analyses by nb of prior lines
16.2.6.1.2.10.6 EQ-5D - Time until permanent deterioration by 10 pt in EQ-5D VAS according to nb of prior lines (LOCF) - ITT population

	1		>1		
	Kd (N=55)	**IKd (N=79)**	**Kd (N=68)**	**IKd (N=100)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	13 (23.6)	22 (27.8)	16 (23.5)	28 (28.0)	0.8852
Number (%) of patients censored	42 (76.4)	57 (72.2)	52 (76.5)	72 (72.0)	
Kaplan-Meier estimates of EQ-5D VAS in months					
25% quantile (95% CI)	20.57 (6.932 to NC)	19.42 (6.735 to 24.444)	19.15 (10.546 to NC)	16.99 (9.265 to 23.129)	
Median (95% CI)	NC (NC to NC)	24.44 (24.444 to NC)	NC (NC to NC)	NC (23.097 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (24.444 to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.5143		0.6056	
Hazard ratio (95% CI) vs Kd	-	1.26 (0.63 to 2.49)		1.18 (0.64 to 2.17)	
P-value	-	0.5152		0.6060	
Deterioration probability (95% CI)[b]					

A higher score represents a better level of quality of life. Clinical meaningful deterioration change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
PGM=DEVOPS/SAR650984/EFC15246/CIR_RWE/REPORT/PGM/eff_km_subgp_sr_sig_de_i_t.sas OUT=REPORT/OUTPUT/eff_km_eq5d_vas_detpl_plne_de_i_t_x.rtf (07APR2021 14:45)

16.2.6.1 Health-related quality-of-life endpoints - EQ-5D
16.2.6.1.2 EQ-5D VAS
16.2.6.1.2.11 Efficacy response data - Subgroup analyses by cytogenetic abnormality
16.2.6.1.2.11.3 EQ-5D - Time to first improvement by 10 pt in EQ-5D VAS according to cytogenetic abnormality (LOCF) - ITT population

	At least one		None		
	Kd (N=31)	**IKd (N=42)**	**Kd (N=77)**	**IKd (N=114)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	12 (38.7)	20 (47.6)	35 (45.5)	62 (54.4)	0.9826
Number (%) of patients censored	19 (61.3)	22 (52.4)	42 (54.5)	52 (45.6)	
Kaplan-Meier estimates of EQ-5D VAS in months					
25% quantile (95% CI)	1.91 (1.018 to 3.811)	1.91 (1.084 to 2.136)	1.87 (1.051 to 3.055)	1.22 (1.051 to 2.136)	
Median (95% CI)	NC (2.924 to NC)	NC (2.070 to NC)	NC (3.745 to NC)	7.03 (3.023 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.5788		0.2876	
Hazard ratio (95% CI) vs Kd	-	1.22 (0.60 to 2.51)		1.25 (0.83 to 1.89)	
P-value	-	0.5794		0.2886	
Improvement probability (95% CI)[b]					

A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
PGM=DEVOPS/SAR650984/EFC15246/CIR_RWE/REPORT/PGM/eff_km_subgp_sr_sig_de_i_t.sas OUT=REPORT/OUTPUT/eff_km_eq5d_vas_impl_cyto_de_i_t_x.rtf (07APR2021 14:45)

16.2.6.1 Health-related quality-of-life endpoints - EQ-5D
16.2.6.1.2 EQ-5D VAS
16.2.6.1.2.11 Efficacy response data - Subgroup analyses by cytogenetic abnormality
16.2.6.1.2.11.4 EQ-5D - Time to first deterioration by 10 pt in EQ-5D VAS according to cytogenetic abnormality (LOCF) - ITT population

	At least one		None		
	Kd (N=31)	**IKd (N=42)**	**Kd (N=77)**	**IKd (N=114)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	19 (61.3)	29 (69.0)	43 (55.8)	61 (53.5)	0.3501
Number (%) of patients censored	12 (38.7)	13 (31.0)	34 (44.2)	53 (46.5)	
Kaplan-Meier estimates of EQ-5D VAS in months					
25% quantile (95% CI)	2.83 (1.018 to 4.961)	1.05 (0.986 to 2.103)	2.14 (1.183 to 3.844)	1.97 (1.084 to 3.811)	
Median (95% CI)	6.37 (2.957 to NC)	4.45 (2.004 to 8.279)	6.57 (4.632 to NC)	11.10 (5.585 to NC)	
75% quantile (95% CI)	NC (7.425 to NC)	NC (7.392 to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.4384		0.7026	
Hazard ratio (95% CI) vs Kd	-	1.26 (0.70 to 2.24)		0.93 (0.63 to 1.37)	
P-value	-	0.4394		0.7026	
Deterioration probability (95% CI)[b]					

A higher score represents a better level of quality of life. Clinical meaningful deterioration change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.1 Health-related quality-of-life endpoints - EQ-5D
16.2.6.1.2 EQ-5D VAS
16.2.6.1.2.11 Efficacy response data - Subgroup analyses by cytogenetic abnormality
16.2.6.1.2.11.5 EQ-5D - Time until permanent improvement by 10 pt in EQ-5D VAS according to cytogenetic abnormality (LOCF) - ITT population

	At least one		None		
	Kd (N=31)	**IKd (N=42)**	**Kd (N=77)**	**IKd (N=114)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	5 (16.1)	12 (28.6)	21 (27.3)	33 (28.9)	0.3093
Number (%) of patients censored	26 (83.9)	30 (71.4)	56 (72.7)	81 (71.1)	
Kaplan-Meier estimates of EQ-5D VAS in months					
25% quantile (95% CI)	NC (1.117 to NC)	17.84 (2.366 to NC)	16.46 (7.261 to NC)	18.20 (12.977 to 22.341)	
Median (95% CI)	NC (NC to NC)	NC (20.665 to NC)	NC (22.209 to NC)	NC (22.341 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.2689		0.9594	
Hazard ratio (95% CI) vs Kd	-	1.79 (0.63 to 5.08)		1.01 (0.59 to 1.75)	
P-value	-	0.2758		0.9594	
Improvement probability (95% CI)[b]					

A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.1 Health-related quality-of-life endpoints - EQ-5D
16.2.6.1.2 EQ-5D VAS
16.2.6.1.2.11 Efficacy response data - Subgroup analyses by cytogenetic abnormality
16.2.6.1.2.11.6 EQ-5D - Time until permanent deterioration by 10 pt in EQ-5D VAS according to cytogenetic abnormality (LOCF) - ITT population

	At least one		None		
	Kd (N=31)	**IKd (N=42)**	**Kd (N=77)**	**IKd (N=114)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	7 (22.6)	14 (33.3)	18 (23.4)	29 (25.4)	0.5942
Number (%) of patients censored	24 (77.4)	28 (66.7)	59 (76.6)	85 (74.6)	
Kaplan-Meier estimates of EQ-5D VAS in months					
25% quantile (95% CI)	19.15 (4.961 to NC)	9.26 (3.910 to NC)	20.57 (13.634 to NC)	21.26 (12.682 to 24.444)	
Median (95% CI)	NC (NC to NC)	NC (17.051 to NC)	NC (NC to NC)	24.44 (23.097 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (24.444 to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.3719		0.7306	
Hazard ratio (95% CI) vs Kd	-	1.51 (0.61 to 3.74)		1.11 (0.61 to 2.00)	
P-value	-	0.3753		0.7307	
Deterioration probability (95% CI)[b]					

A higher score represents a better level of quality of life. Clinical meaningful deterioration change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
PGM=DEVOPS/SAR650984/EFC15246/CIR_RWE/REPORT/PGM/eff_km_subgp_sr_sig_de_i_t.sas OUT=REPORT/OUTPUT/eff_km_eq5d_vas_detpl_cyto_de_i_t_x.rtf (07APR2021 14:45)

16.2.6.1 Health-related quality-of-life endpoints - EQ-5D
16.2.6.1.2 EQ-5D VAS
16.2.6.1.2.12 Efficacy response data - Subgroup analyses by MM type at SE
16.2.6.1.2.12.3 EQ-5D - Time to first improvement by 10 pt in EQ-5D VAS according to MM type at SE (LOCF) - ITT population

	IgG		Non-IgG		
	Kd (N=85)	**IKd (N=126)**	**Kd (N=38)**	**IKd (N=53)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	38 (44.7)	62 (49.2)	19 (50.0)	30 (56.6)	0.8792
Number (%) of patients censored	47 (55.3)	64 (50.8)	19 (50.0)	23 (43.4)	
Kaplan-Meier estimates of EQ-5D VAS in months					
25% quantile (95% CI)	1.87 (1.051 to 3.055)	2.00 (1.117 to 2.398)	1.89 (1.051 to 3.055)	1.12 (1.018 to 2.004)	
Median (95% CI)	NC (3.877 to NC)	14.00 (3.877 to NC)	5.65 (2.924 to NC)	4.73 (1.906 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.5931		0.6082	
Hazard ratio (95% CI) vs Kd	-	1.12 (0.75 to 1.67)		1.16 (0.65 to 2.06)	
P-value	-	0.5933		0.6085	
Improvement probability (95% CI)[b]					

A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.1 Health-related quality-of-life endpoints - EQ-5D
16.2.6.1.2 EQ-5D VAS
16.2.6.1.2.12 Efficacy response data - Subgroup analyses by MM type at SE
16.2.6.1.2.12.4 EQ-5D - Time to first deterioration by 10 pt in EQ-5D VAS according to MM type at SE (LOCF) - ITT population

	IgG		Non-IgG		
	Kd (N=85)	**IKd (N=126)**	**Kd (N=38)**	**IKd (N=53)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	50 (58.8)	69 (54.8)	21 (55.3)	34 (64.2)	0.3773
Number (%) of patients censored	35 (41.2)	57 (45.2)	17 (44.7)	19 (35.8)	
Kaplan-Meier estimates of EQ-5D VAS in months					
25% quantile (95% CI)	2.14 (1.248 to 3.844)	2.79 (1.117 to 3.778)	2.86 (1.051 to 5.585)	1.08 (0.986 to 2.136)	
Median (95% CI)	6.57 (4.764 to 21.224)	9.20 (5.552 to NC)	7.39 (3.943 to NC)	5.59 (2.004 to 12.025)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (11.203 to NC)	NC (12.025 to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.6905		0.4699	
Hazard ratio (95% CI) vs Kd	-	0.93 (0.65 to 1.34)		1.22 (0.71 to 2.11)	
P-value	-	0.6906		0.4707	
Deterioration probability (95% CI)[b]					

A higher score represents a better level of quality of life. Clinical meaningful deterioration change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.1 Health-related quality-of-life endpoints - EQ-5D
16.2.6.1.2 EQ-5D VAS
16.2.6.1.2.12 Efficacy response data - Subgroup analyses by MM type at SE
16.2.6.1.2.12.5 EQ-5D - Time until permanent improvement by 10 pt in EQ-5D VAS according to MM type at SE (LOCF) - ITT population

	IgG		Non-IgG		
	Kd (N=85)	**IKd (N=126)**	**Kd (N=38)**	**IKd (N=53)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	20 (23.5)	29 (23.0)	9 (23.7)	19 (35.8)	0.4304
Number (%) of patients censored	65 (76.5)	97 (77.0)	29 (76.3)	34 (64.2)	
Kaplan-Meier estimates of EQ-5D VAS in months					
25% quantile (95% CI)	22.21 (12.025 to NC)	19.88 (14.489 to NC)	16.46 (1.051 to NC)	14.06 (3.745 to 20.304)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	22.34 (19.811 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (22.341 to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.9819		0.3328	
Hazard ratio (95% CI) vs Kd	-	0.99 (0.56 to 1.76)		1.48 (0.67 to 3.27)	
P-value	-	0.9819		0.3359	

A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.1 Health-related quality-of-life endpoints - EQ-5D
16.2.6.1.2 EQ-5D VAS
16.2.6.1.2.12 Efficacy response data - Subgroup analyses by MM type at SE
16.2.6.1.2.12.6 EQ-5D - Time until permanent deterioration by 10 pt in EQ-5D VAS according to MM type at SE (LOCF) - ITT population

	IgG		Non-IgG		
	Kd (N=85)	**IKd (N=126)**	**Kd (N=38)**	**IKd (N=53)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	20 (23.5)	36 (28.6)	9 (23.7)	14 (26.4)	0.7903
Number (%) of patients censored	65 (76.5)	90 (71.4)	29 (76.3)	39 (73.6)	
Kaplan-Meier estimates of EQ-5D VAS in months					
25% quantile (95% CI)	21.39 (14.062 to NC)	19.42 (9.265 to 23.097)	20.57 (6.374 to NC)	12.94 (3.877 to NC)	
Median (95% CI)	NC (NC to NC)	24.44 (23.097 to NC)	NC (20.567 to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (24.444 to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.3888		0.8174	
Hazard ratio (95% CI) vs Kd	-	1.27 (0.74 to 2.20)		1.10 (0.48 to 2.55)	
P-value	-	0.3899		0.8174	
Deterioration probability (95% CI)[b]					

A higher score represents a better level of quality of life. Clinical meaningful deterioration change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
PGM=DEVOPS/SAR650984/EFC15246/CIR_RWE/REPORT/PGM/eff_km_subgp_sr_sig_de_i_t.sas OUT=REPORT/OUTPUT/eff_km_eq5d_vas_detpl_semm_de_i_t_x.rtf (07APR2021 14:45)

16.2.6.1 Health-related quality-of-life endpoints - EQ-5D
16.2.6.1.2 EQ-5D VAS
16.2.6.1.2.13 Efficacy response data - Subgroup analyses by previous autologous stem-cell
16.2.6.1.2.13.3 EQ-5D - Time to first improvement by 10 pt in EQ-5D VAS according to previous autologous stem-cell (LOCF) - ITT population

	Yes		No		
	Kd (N=69)	**IKd (N=116)**	**Kd (N=54)**	**IKd (N=63)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	29 (42.0)	54 (46.6)	28 (51.9)	38 (60.3)	0.6113
Number (%) of patients censored	40 (58.0)	62 (53.4)	26 (48.1)	25 (39.7)	
Kaplan-Meier estimates of EQ-5D VAS in months					
25% quantile (95% CI)	1.20 (1.018 to 3.055)	1.91 (1.117 to 2.825)	2.10 (1.051 to 2.957)	1.15 (1.051 to 2.004)	
Median (95% CI)	NC (4.632 to NC)	NC (4.698 to NC)	6.74 (2.957 to NC)	3.81 (2.004 to 13.996)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (13.996 to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.7208		0.3100	
Hazard ratio (95% CI) vs Kd	-	1.09 (0.69 to 1.71)		1.29 (0.79 to 2.10)	
P-value	-	0.7209		0.3113	
Improvement probability (95% CI)[b]					

A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.1 Health-related quality-of-life endpoints - EQ-5D
16.2.6.1.2 EQ-5D VAS
16.2.6.1.2.13 Efficacy response data - Subgroup analyses by previous autologous stem-cell
16.2.6.1.2.13.4 EQ-5D - Time to first deterioration by 10 pt in EQ-5D VAS according to previous autologous stem-cell (LOCF) - ITT population

	Yes		No		
	Kd (N=69)	**IKd (N=116)**	**Kd (N=54)**	**IKd (N=63)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	39 (56.5)	72 (62.1)	32 (59.3)	31 (49.2)	0.2031
Number (%) of patients censored	30 (43.5)	44 (37.9)	22 (40.7)	32 (50.8)	
Kaplan-Meier estimates of EQ-5D VAS in months					
25% quantile (95% CI)	2.79 (1.183 to 4.632)	1.51 (1.051 to 2.793)	2.14 (1.216 to 3.943)	3.27 (1.413 to 5.585)	
Median (95% CI)	6.01 (4.895 to NC)	6.54 (3.844 to 11.105)	7.39 (3.943 to NC)	12.32 (5.585 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (13.536 to NC)	NC (NC to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.4314		0.3018	
Hazard ratio (95% CI) vs Kd	-	1.17 (0.79 to 1.73)		0.77 (0.47 to 1.26)	
P-value	-	0.4318		0.3032	
Deterioration probability (95% CI)[b]					

A higher score represents a better level of quality of life. Clinical meaningful deterioration change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
PGM=DEVOPS/SAR650984/EFC15246/CIR_RWE/REPORT/PGM/eff_km_subgp_sr_sig_de_i_t.sas OUT=REPORT/OUTPUT/eff_km_eq5d_vas_detl_auto_de_i_t_x.rtf (07APR2021 14:45)

16.2.6.1 Health-related quality-of-life endpoints - EQ-5D
16.2.6.1.2 EQ-5D VAS
16.2.6.1.2.13 Efficacy response data - Subgroup analyses by previous autologous stem-cell
16.2.6.1.2.13.5 EQ-5D - Time until permanent improvement by 10 pt in EQ-5D VAS according to previous autologous stem-cell (LOCF) - ITT population

	Yes		No		
	Kd (N=69)	**IKd (N=116)**	**Kd (N=54)**	**IKd (N=63)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	14 (20.3)	32 (27.6)	15 (27.8)	16 (25.4)	0.3004
Number (%) of patients censored	55 (79.7)	84 (72.4)	39 (72.2)	47 (74.6)	
Kaplan-Meier estimates of EQ-5D VAS in months					
25% quantile (95% CI)	NC (12.025 to NC)	18.20 (8.476 to 22.341)	15.70 (3.877 to NC)	19.42 (12.945 to NC)	
Median (95% CI)	NC (NC to NC)	NC (22.341 to NC)	NC (22.209 to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.2703		0.6896	
Hazard ratio (95% CI) vs Kd	-	1.42 (0.76 to 2.67)		0.87 (0.43 to 1.75)	
P-value	-	0.2728		0.6899	
Improvement probability (95% CI)[b]					

A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
PGM=DEVOPS/SAR650984/EFC15246/CIR_RWE/REPORT/PGM/eff_km_subgp_sr_sig_de_i_t.sas OUT=REPORT/OUTPUT/eff_km_eq5d_vas_imppl_auto_de_i_t_x.rtf (07APR2021 14:45)

16.2.6.1 Health-related quality-of-life endpoints - EQ-5D
16.2.6.1.2 EQ-5D VAS
16.2.6.1.2.13 Efficacy response data - Subgroup analyses by previous autologous stem-cell
16.2.6.1.2.13.6 EQ-5D - Time until permanent deterioration by 10 pt in EQ-5D VAS according to previous autologous stem-cell (LOCF) - ITT population

	Yes		No		
	Kd (N=69)	**IKd (N=116)**	**Kd (N=54)**	**IKd (N=63)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	15 (21.7)	38 (32.8)	14 (25.9)	12 (19.0)	0.1017
Number (%) of patients censored	54 (78.3)	78 (67.2)	40 (74.1)	51 (81.0)	
Kaplan-Meier estimates of EQ-5D VAS in months					
25% quantile (95% CI)	19.15 (10.546 to NC)	12.65 (5.815 to 21.257)	20.57 (6.374 to NC)	23.10 (16.624 to NC)	
Median (95% CI)	NC (NC to NC)	24.44 (23.129 to 24.444)	NC (21.388 to NC)	NC (23.097 to NC)	
75% quantile (95% CI)	NC (NC to NC)	24.44 (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.1098		0.3434	
Hazard ratio (95% CI) vs Kd	-	1.62 (0.89 to 2.95)		0.69 (0.32 to 1.49)	
P-value	-	0.1134		0.3461	
Deterioration probability (95% CI)[b]					

A higher score represents a better level of quality of life. Clinical meaningful deterioration change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.1 Health-related quality-of-life endpoints - EQ-5D
16.2.6.1.2 EQ-5D VAS
16.2.6.1.2.14 Efficacy response data - Subgroup analyses by baseline eGFR (MDRD)
16.2.6.1.2.14.3 EQ-5D - Time to first improvement by 10 pt in EQ-5D VAS according to baseline eGFR (MDRD) (LOCF) - ITT population

	>=60 mL/min/1.73m2		<60 mL/min/1.73m2		
	Kd (N=93)	**IKd (N=122)**	**Kd (N=18)**	**IKd (N=43)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	48 (51.6)	62 (50.8)	6 (33.3)	24 (55.8)	0.3270
Number (%) of patients censored	45 (48.4)	60 (49.2)	12 (66.7)	19 (44.2)	
Kaplan-Meier estimates of EQ-5D VAS in months					
25% quantile (95% CI)	1.12 (1.051 to 2.103)	1.91 (1.051 to 2.136)	2.86 (0.986 to NC)	1.12 (1.051 to 2.398)	
Median (95% CI)	8.26 (3.055 to NC)	10.25 (3.745 to NC)	NC (2.858 to NC)	6.67 (2.004 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.9704		0.2839	
Hazard ratio (95% CI) vs Kd	-	1.01 (0.69 to 1.47)		1.62 (0.66 to 3.97)	
P-value	-	0.9704		0.2886	
Improvement probability (95% CI)[b]					

A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.1 Health-related quality-of-life endpoints - EQ-5D
16.2.6.1.2 EQ-5D VAS
16.2.6.1.2.14 Efficacy response data - Subgroup analyses by baseline eGFR (MDRD)
16.2.6.1.2.14.4 EQ-5D - Time to first deterioration by 10 pt in EQ-5D VAS according to baseline eGFR (MDRD) (LOCF) - ITT population

	>=60 mL/min/1.73m2		<60 mL/min/1.73m2		
	Kd (N=93)	**IKd (N=122)**	**Kd (N=18)**	**IKd (N=43)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	52 (55.9)	76 (62.3)	13 (72.2)	21 (48.8)	0.0091
Number (%) of patients censored	41 (44.1)	46 (37.7)	5 (27.8)	22 (51.2)	
Kaplan-Meier estimates of EQ-5D VAS in months					
25% quantile (95% CI)	2.81 (1.643 to 3.943)	1.94 (1.084 to 2.825)	1.31 (0.986 to 3.023)	1.08 (0.986 to 4.830)	
Median (95% CI)	7.43 (5.224 to NC)	6.64 (3.910 to 10.875)	3.91 (1.051 to 7.556)	NC (3.220 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (19.253 to NC)	7.56 (3.023 to NC)	NC (NC to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.1833		0.0402	
Hazard ratio (95% CI) vs Kd	-	1.27 (0.89 to 1.81)		0.49 (0.24 to 0.98)	
P-value	-	0.1843		0.0445	
Deterioration probability (95% CI)[b]					

A higher score represents a better level of quality of life. Clinical meaningful deterioration change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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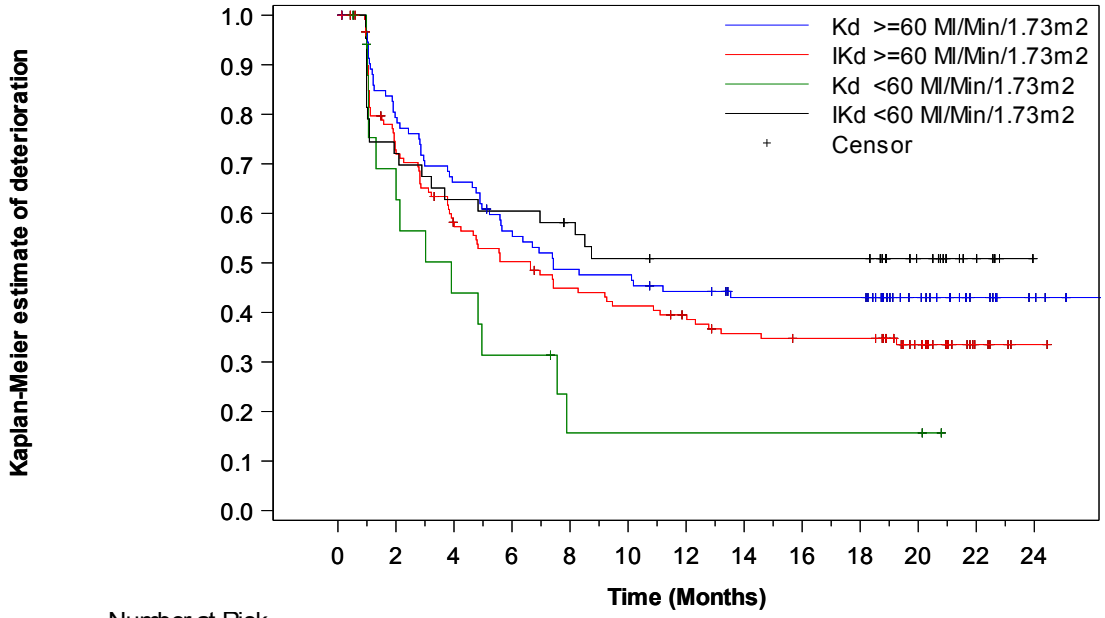
16.2.6.1 Health-related quality-of-life endpoints - EQ-5D
16.2.6.1.2 EQ-5D VAS
16.2.6.1.2.14 Efficacy response data - Subgroup analyses by baseline eGFR (MDRD)
16.2.6.1.2.14.5 EQ-5D - Time to first deterioration by 10 pt in EQ-5D VAS according to baseline eGFR (MDRD) - Kaplan-Meier curve (LOCF) - ITT population



Number at Risk

Kd >=60 Ml/Min/1.73m2	93	64	51	43	39	35	35	18	6
lKd >=60 Ml/Min/1.73m2	122	76	57	49	42	36	35	12	1
Kd <60 Ml/Min/1.73m2	18	9	5	2	2	2	2	0	0
lKd <60 Ml/Min/1.73m2	43	29	26	21	20	20	20	7	0

A higher score represents a better level of quality of life. Clinical meaningful deterioration change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
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16.2.6.1 Health-related quality-of-life endpoints - EQ-5D
16.2.6.1.2 EQ-5D VAS
16.2.6.1.2.14 Efficacy response data - Subgroup analyses by baseline eGFR (MDRD)
16.2.6.1.2.14.6 EQ-5D - Time until permanent improvement by 10 pt in EQ-5D VAS according to baseline eGFR (MDRD) (LOCF) - ITT population

	>=60 mL/min/1.73m2		<60 mL/min/1.73m2		
	Kd (N=93)	**IKd (N=122)**	**Kd (N=18)**	**IKd (N=43)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	26 (28.0)	30 (24.6)	1 (5.6)	15 (34.9)	0.0833
Number (%) of patients censored	67 (72.0)	92 (75.4)	17 (94.4)	28 (65.1)	
Kaplan-Meier estimates of EQ-5D VAS in months					
25% quantile (95% CI)	16.85 (10.546 to NC)	19.81 (12.945 to NC)	NC (0.986 to NC)	17.84 (2.530 to 20.665)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (19.877 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.7400		0.0535	
Hazard ratio (95% CI) vs Kd	-	0.91 (0.54 to 1.55)		5.81 (0.77 to 44.02)	
P-value	-	0.7390		0.0885	
Improvement probability (95% CI)[b]					

A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
PGM=DEVOPS/SAR650984/EFC15246/CIR_RWE/REPORT/PGM/eff_km_subgp_sr_sig_de_i_t.sas OUT=REPORT/OUTPUT/eff_km_eq5d_vas_imppl_crcl_de_i_t_x.rtf (07APR2021 14:45)

16.2.6.1 Health-related quality-of-life endpoints - EQ-5D
16.2.6.1.2 EQ-5D VAS
16.2.6.1.2.14 Efficacy response data - Subgroup analyses by baseline eGFR (MDRD)
16.2.6.1.2.14.7 EQ-5D - Time until permanent deterioration by 10 pt in EQ-5D VAS according to baseline eGFR (MDRD) (LOCF) - ITT population

	>=60 mL/min/1.73m2		<60 mL/min/1.73m2		
	Kd (N=93)	**IKd (N=122)**	**Kd (N=18)**	**IKd (N=43)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	18 (19.4)	35 (28.7)	9 (50.0)	12 (27.9)	0.0046
Number (%) of patients censored	75 (80.6)	87 (71.3)	9 (50.0)	31 (72.1)	
Kaplan-Meier estimates of EQ-5D VAS in months					
25% quantile (95% CI)	NC (14.094 to NC)	16.62 (6.735 to 23.097)	5.91 (1.314 to 16.033)	19.61 (6.637 to 24.444)	
Median (95% CI)	NC (NC to NC)	NC (23.097 to NC)	16.03 (5.914 to 21.388)	24.44 (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	21.39 (16.033 to 21.388)	24.44 (NC to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.0747		0.0134	
Hazard ratio (95% CI) vs Kd	-	1.67 (0.94 to 2.94)		0.34 (0.14 to 0.83)	
P-value	-	0.0780		0.0181	
Deterioration probability (95% CI)[b]					

A higher score represents a better level of quality of life. Clinical meaningful deterioration change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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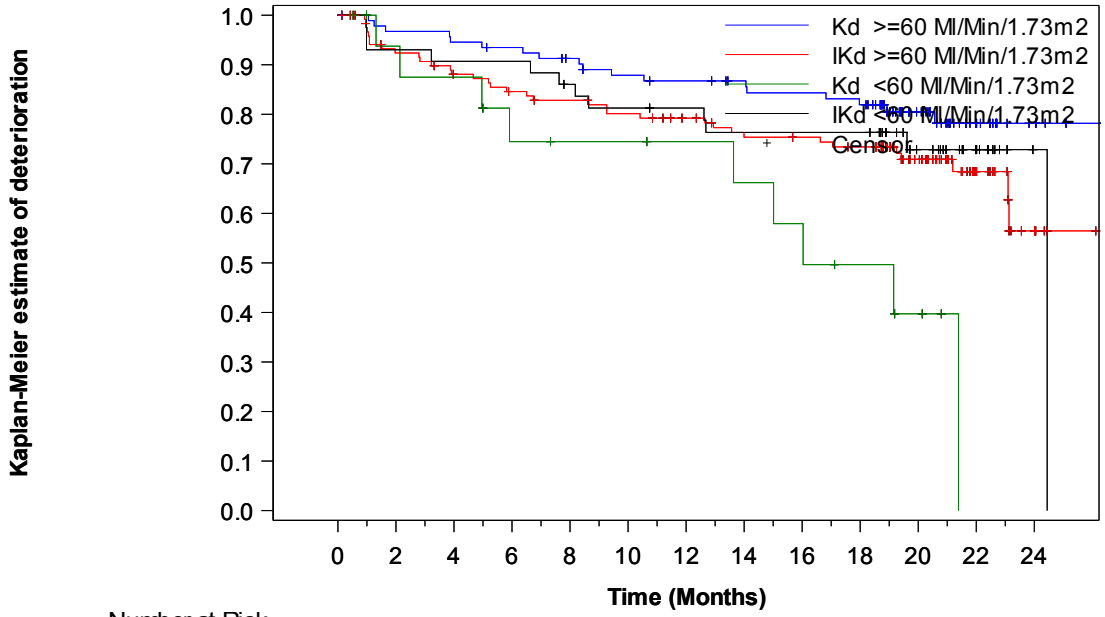
16.2.6.1 Health-related quality-of-life endpoints - EQ-5D
16.2.6.1.2 EQ-5D VAS
16.2.6.1.2.14 Efficacy response data - Subgroup analyses by baseline eGFR (MDRD)
16.2.6.1.2.14.8 EQ-5D - Time until permanent deterioration by 10 pt in EQ-5D VAS according to baseline eGFR (MDRD) - Kaplan-Meier curve (LOCF) - ITT population



Number at Risk

Kd >=60 Ml/Min/1.73m2	93	89	85	78	75	70	68	30	8
lKd >=60 Ml/Min/1.73m2	122	106	96	91	84	78	74	32	6
Kd <60 Ml/Min/1.73m2	18	14	11	10	9	8	5	1	0
lKd <60 Ml/Min/1.73m2	43	40	39	34	33	31	31	14	1

A higher score represents a better level of quality of life. Clinical meaningful deterioration change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
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16.2.6.1 Health-related quality-of-life endpoints - EQ-5D
16.2.6.1.2 EQ-5D VAS
16.2.6.1.2.15 Efficacy response data - Subgroup analyses by previous treatment with PI
16.2.6.1.2.15.3 EQ-5D - Time to first improvement by 10 pt in EQ-5D VAS according to previous treatment with PI (LOCF) - ITT population

	Yes		No		
	Kd (N=47)	**IKd (N=81)**	**Kd (N=76)**	**IKd (N=98)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	21 (44.7)	43 (53.1)	36 (47.4)	49 (50.0)	0.4849
Number (%) of patients censored	26 (55.3)	38 (46.9)	40 (52.6)	49 (50.0)	
Kaplan-Meier estimates of EQ-5D VAS in months					
25% quantile (95% CI)	2.10 (1.051 to 3.811)	1.91 (1.051 to 2.070)	1.28 (1.051 to 2.924)	1.91 (1.051 to 2.530)	
Median (95% CI)	NC (3.285 to NC)	5.78 (2.398 to NC)	NC (3.055 to NC)	15.64 (3.844 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.3130		0.8961	
Hazard ratio (95% CI) vs Kd	-	1.31 (0.78 to 2.20)		1.03 (0.67 to 1.58)	
P-value	-	0.3145		0.8963	
Improvement probability (95% CI)[b]					

A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
PGM=DEVOPS/SAR650984/EFC15246/CIR_RWE/REPORT/PGM/eff_km_subgp_sr_sig_de_i_t.sas OUT=REPORT/OUTPUT/eff_km_eq5d_vas_impl_pi_de_i_t_x.rtf (07APR2021 14:45)

16.2.6.1 Health-related quality-of-life endpoints - EQ-5D
16.2.6.1.2 EQ-5D VAS
16.2.6.1.2.15 Efficacy response data - Subgroup analyses by previous treatment with PI
16.2.6.1.2.15.4 EQ-5D - Time to first deterioration by 10 pt in EQ-5D VAS according to previous treatment with PI (LOCF) - ITT population

	Yes		No		
	Kd (N=47)	**IKd (N=81)**	**Kd (N=76)**	**IKd (N=98)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	28 (59.6)	44 (54.3)	43 (56.6)	59 (60.2)	0.6464
Number (%) of patients censored	19 (40.4)	37 (45.7)	33 (43.4)	39 (39.8)	
Kaplan-Meier estimates of EQ-5D VAS in months					
25% quantile (95% CI)	2.14 (1.216 to 3.943)	1.97 (1.051 to 3.220)	2.83 (1.183 to 4.764)	1.94 (1.084 to 3.220)	
Median (95% CI)	7.00 (2.858 to NC)	7.43 (4.008 to NC)	6.93 (4.895 to 21.224)	8.18 (4.238 to 13.207)	
75% quantile (95% CI)	NC (13.536 to NC)	NC (NC to NC)	NC (21.224 to NC)	NC (NC to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.7650		0.7303	
Hazard ratio (95% CI) vs Kd	-	0.93 (0.58 to 1.49)		1.07 (0.72 to 1.59)	
P-value	-	0.7650		0.7316	
Deterioration probability (95% CI)[b]					

A higher score represents a better level of quality of life. Clinical meaningful deterioration change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.1 Health-related quality-of-life endpoints - EQ-5D
16.2.6.1.2 EQ-5D VAS
16.2.6.1.2.15 Efficacy response data - Subgroup analyses by previous treatment with PI
16.2.6.1.2.15.5 EQ-5D - Time until permanent improvement by 10 pt in EQ-5D VAS according to previous treatment with PI (LOCF) - ITT population

	Yes		No		
	Kd (N=47)	**IKd (N=81)**	**Kd (N=76)**	**IKd (N=98)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	9 (19.1)	21 (25.9)	20 (26.3)	27 (27.6)	0.4728
Number (%) of patients censored	38 (80.9)	60 (74.1)	56 (73.7)	71 (72.4)	
Kaplan-Meier estimates of EQ-5D VAS in months					
25% quantile (95% CI)	NC (14.226 to NC)	18.20 (14.062 to NC)	16.85 (7.261 to NC)	19.81 (12.090 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (22.209 to NC)	NC (22.341 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.3724		0.9696	
Hazard ratio (95% CI) vs Kd	-	1.42 (0.65 to 3.11)		1.01 (0.57 to 1.80)	
P-value	-	0.3749		0.9697	
Improvement probability (95% CI)[b]					

A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.1 Health-related quality-of-life endpoints - EQ-5D
16.2.6.1.2 EQ-5D VAS
16.2.6.1.2.15 Efficacy response data - Subgroup analyses by previous treatment with PI
16.2.6.1.2.15.6 EQ-5D - Time until permanent deterioration by 10 pt in EQ-5D VAS according to previous treatment with PI (LOCF) - ITT population

	Yes		No		
	Kd (N=47)	**IKd (N=81)**	**Kd (N=76)**	**IKd (N=98)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	8 (17.0)	25 (30.9)	21 (27.6)	25 (25.5)	0.0756
Number (%) of patients censored	39 (83.0)	56 (69.1)	55 (72.4)	73 (74.5)	
Kaplan-Meier estimates of EQ-5D VAS in months					
25% quantile (95% CI)	NC (8.312 to NC)	16.62 (6.505 to 21.257)	16.82 (9.429 to NC)	19.61 (9.265 to NC)	
Median (95% CI)	NC (NC to NC)	23.10 (21.257 to NC)	NC (NC to NC)	24.44 (23.129 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (23.097 to NC)	NC (NC to NC)	NC (24.444 to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.0680		0.6591	
Hazard ratio (95% CI) vs Kd	-	2.07 (0.93 to 4.61)		0.88 (0.49 to 1.57)	
P-value	-	0.0740		0.6593	
Deterioration probability (95% CI)[b]					

A higher score represents a better level of quality of life. Clinical meaningful deterioration change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.1 Health-related quality-of-life endpoints - EQ-5D
16.2.6.1.2 EQ-5D VAS
16.2.6.1.2.16 Efficacy response data - Subgroup analyses by previous treatment with IMiD
16.2.6.1.2.16.2 EQ-5D - Change from baseline in EQ-5D VAS according to previous treatment with IMiD (LOCF) - ITT population

	Yes		No		
	Kd (N=62)	**IKd (N=81)**	**Kd (N=61)**	**IKd (N=98)**	**p-value of treatment-by-subgroup interaction[b]**
Cycle 1 (Baseline)					
Number	58	74	54	90	
Mean (SD)	67.16 (21.03)	68.95 (18.68)	67.91 (20.41)	70.86 (16.93)	
Median	70.00	70.00	70.00	74.50	
Q1 : Q3	59.00 : 80.00	51.00 : 83.00	51.00 : 86.00	60.00 : 81.00	
Min : Max	12.00 : 100.00	25.00 : 100.00	25.00 : 100.00	29.00 : 100.00	
Cycle 2					
Number	54	72	51	89	
Mean (SD)	70.09 (17.92)	68.92 (18.14)	72.20 (19.80)	71.79 (16.16)	
Median	72.50	75.00	75.00	75.00	
Q1 : Q3	60.00 : 80.00	55.00 : 80.00	60.00 : 85.00	60.00 : 80.00	
Min : Max	18.00 : 98.00	24.00 : 100.00	0.00 : 100.00	10.00 : 100.00	
Change from baseline[a]					
LS Mean (SE)	0.45 (2.10)	-0.20 (1.81)	3.59 (2.16)	1.68 (1.63)	0.7434

A higher score represents a better level of quality of life. Cycles with less than 20 patients overall are not presented.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
[a] Derived from MMRM model with change from baseline values as the response variable, and treatment, visit, treatment by-visit interaction, baseline value and baseline-by-visit interaction as covariates.
Covariance structure of the R matrix in the MMRM is AR(1).
[b] Derived from MMRM model with change from baseline values as the response variable, and treatment, visit, treatment-by-visit interaction, baseline-by-visit interaction, subgroup, subgroup-by-treatment interaction as covariates.
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16.2.6.1 Health-related quality-of-life endpoints - EQ-5D
16.2.6.1.2 EQ-5D VAS
16.2.6.1.2.16 Efficacy response data - Subgroup analyses by previous treatment with IMiD
16.2.6.1.2.16.2 EQ-5D - Change from baseline in EQ-5D VAS according to previous treatment with IMiD (LOCF) - ITT population

	Yes		No		
	Kd (N=62)	**IKd (N=81)**	**Kd (N=61)**	**IKd (N=98)**	**p-value of treatment-by-subgroup interaction[b]**
LS mean difference (SE) vs Kd		-0.65 (2.77)		-1.92 (2.71)	
95% CI		(-6.08 to 4.79)		(-7.22 to 3.39)	
P-value vs Kd		0.8152		0.4788	
Hedges' G					
Hedges' G (SE) vs Kd		-0.04 (0.18)		-0.12 (0.18)	
95% CI		(-0.39 to 0.31)		(-0.47 to 0.22)	
Cycle 3					
Number	52	71	51	86	
Mean (SD)	72.52 (16.91)	73.11 (17.30)	73.76 (15.81)	73.44 (16.71)	
Median	72.50	76.00	75.00	79.00	
Q1 : Q3	60.50 : 88.00	62.00 : 86.00	60.00 : 86.00	66.00 : 85.00	
Min : Max	18.00 : 100.00	23.00 : 100.00	39.00 : 100.00	20.00 : 100.00	
Change from baseline[a]					
LS Mean (SE)	3.11 (2.12)	4.11 (1.82)	5.16 (2.16)	3.25 (1.65)	0.4539
LS mean difference (SE) vs Kd		1.00 (2.79)		-1.92 (2.71)	

A higher score represents a better level of quality of life. Cycles with less than 20 patients overall are not presented.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
[a] Derived from MMRM model with change from baseline values as the response variable, and treatment, visit, treatment by-visit interaction, baseline value and baseline-by-visit interaction as covariates.
Covariance structure of the R matrix in the MMRM is AR(1).
[b] Derived from MMRM model with change from baseline values as the response variable, and treatment, visit, treatment-by-visit interaction, baseline-by-visit interaction, subgroup, subgroup-by-treatment interaction as covariates.

16.2.6.1 Health-related quality-of-life endpoints - EQ-5D
16.2.6.1.2 EQ-5D VAS
16.2.6.1.2.16 Efficacy response data - Subgroup analyses by previous treatment with IMiD
16.2.6.1.2.16.2 EQ-5D - Change from baseline in EQ-5D VAS according to previous treatment with IMiD (LOCF) - ITT population

	Yes		No		
	Kd (N=62)	**IKd (N=81)**	**Kd (N=61)**	**IKd (N=98)**	**p-value of treatment-by-subgroup interaction[b]**
95% CI		(-4.48 to 6.48)		(-7.24 to 3.41)	
P-value vs Kd		0.7201		0.4802	
Hedges' G					
Hedges' G (SE) vs Kd		0.07 (0.18)		-0.13 (0.18)	
95% CI		(-0.29 to 0.42)		(-0.47 to 0.22)	
Cycle 4					
Number	50	69	51	85	
Mean (SD)	75.48 (15.28)	72.39 (17.74)	73.35 (17.70)	72.44 (17.25)	
Median	79.00	80.00	80.00	75.00	
Q1 : Q3	68.00 : 88.00	60.00 : 85.00	69.00 : 85.00	60.00 : 83.00	
Min : Max	26.00 : 100.00	30.00 : 100.00	20.00 : 100.00	20.00 : 100.00	
Change from baseline[a]					
LS Mean (SE)	5.63 (2.15)	3.24 (1.84)	4.75 (2.16)	2.18 (1.66)	0.9629
LS mean difference (SE) vs Kd		-2.39 (2.83)		-2.57 (2.72)	
95% CI		(-7.94 to 3.16)		(-7.91 to 2.77)	

A higher score represents a better level of quality of life. Cycles with less than 20 patients overall are not presented.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
[a] Derived from MMRM model with change from baseline values as the response variable, and treatment, visit, treatment by-visit interaction, baseline value and baseline-by-visit interaction as covariates.
Covariance structure of the R matrix in the MMRM is AR(1).
[b] Derived from MMRM model with change from baseline values as the response variable, and treatment, visit, treatment-by-visit interaction, baseline-by-visit interaction, subgroup, subgroup-by-treatment interaction as covariates.
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16.2.6.1 Health-related quality-of-life endpoints - EQ-5D
16.2.6.1.2 EQ-5D VAS
16.2.6.1.2.16 Efficacy response data - Subgroup analyses by previous treatment with IMiD
16.2.6.1.2.16.2 EQ-5D - Change from baseline in EQ-5D VAS according to previous treatment with IMiD (LOCF) - ITT population

	Yes		No		
	Kd (N=62)	**IKd (N=81)**	**Kd (N=61)**	**IKd (N=98)**	**p-value of treatment-by-subgroup interaction[b]**
P-value vs Kd		0.3982		0.3447	
Hedges' G					
Hedges' G (SE) vs Kd		-0.16 (0.19)		-0.17 (0.18)	
95% CI		(-0.52 to 0.21)		(-0.52 to 0.18)	
Cycle 5					
Number	49	67	46	84	
Mean (SD)	72.24 (17.29)	72.66 (16.52)	72.78 (18.20)	73.06 (18.24)	
Median	70.00	75.00	73.50	79.00	
Q1 : Q3	65.00 : 85.00	60.00 : 86.00	60.00 : 85.00	65.00 : 85.00	
Min : Max	20.00 : 100.00	24.00 : 99.00	30.00 : 100.00	10.00 : 100.00	
Change from baseline[a]					
LS Mean (SE)	2.37 (2.18)	2.86 (1.86)	4.59 (2.22)	2.81 (1.67)	0.5710
LS mean difference (SE) vs Kd		0.49 (2.86)		-1.77 (2.78)	
95% CI		(-5.13 to 6.10)		(-7.22 to 3.67)	
P-value vs Kd		0.8647		0.5233	

A higher score represents a better level of quality of life. Cycles with less than 20 patients overall are not presented.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
[a] Derived from MMRM model with change from baseline values as the response variable, and treatment, visit, treatment by-visit interaction, baseline value and baseline-by-visit interaction as covariates.
Covariance structure of the R matrix in the MMRM is AR(1).
[b] Derived from MMRM model with change from baseline values as the response variable, and treatment, visit, treatment-by-visit interaction, baseline-by-visit interaction, subgroup, subgroup-by-treatment interaction as covariates.

16.2.6.1 Health-related quality-of-life endpoints - EQ-5D
16.2.6.1.2 EQ-5D VAS
16.2.6.1.2.16 Efficacy response data - Subgroup analyses by previous treatment with IMiD
16.2.6.1.2.16.2 EQ-5D - Change from baseline in EQ-5D VAS according to previous treatment with IMiD (LOCF) - ITT population

	Yes		No		
	Kd (N=62)	**IKd (N=81)**	**Kd (N=61)**	**IKd (N=98)**	**p-value of treatment-by-subgroup interaction[b]**
Hedges' G					
Hedges' G (SE) vs Kd		0.03 (0.19)		-0.12 (0.18)	
95% CI		(-0.34 to 0.40)		(-0.47 to 0.24)	
Cycle 6					
Number	46	65	46	81	
Mean (SD)	71.35 (19.36)	71.28 (17.33)	72.41 (17.02)	71.78 (17.65)	
Median	73.50	71.00	74.50	75.00	
Q1 : Q3	60.00 : 85.00	60.00 : 84.00	61.00 : 84.00	66.00 : 81.00	
Min : Max	11.00 : 100.00	30.00 : 100.00	31.00 : 100.00	19.00 : 100.00	
Change from baseline[a]					
LS Mean (SE)	0.68 (2.23)	1.55 (1.89)	4.08 (2.25)	0.73 (1.69)	0.2992
LS mean difference (SE) vs Kd		0.87 (2.92)		-3.34 (2.81)	
95% CI		(-4.86 to 6.59)		(-8.86 to 2.17)	
P-value vs Kd		0.7663		0.2349	
Hedges' G					

A higher score represents a better level of quality of life. Cycles with less than 20 patients overall are not presented.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
[a] Derived from MMRM model with change from baseline values as the response variable, and treatment, visit, treatment by-visit interaction, baseline value and baseline-by-visit interaction as covariates.
Covariance structure of the R matrix in the MMRM is AR(1).
[b] Derived from MMRM model with change from baseline values as the response variable, and treatment, visit, treatment-by-visit interaction, baseline-by-visit interaction, subgroup, subgroup-by-treatment interaction as covariates.
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16.2.6.1 Health-related quality-of-life endpoints - EQ-5D
16.2.6.1.2 EQ-5D VAS
16.2.6.1.2.16 Efficacy response data - Subgroup analyses by previous treatment with IMiD
16.2.6.1.2.16.2 EQ-5D - Change from baseline in EQ-5D VAS according to previous treatment with IMiD (LOCF) - ITT population

	Yes		No		
	Kd (N=62)	**IKd (N=81)**	**Kd (N=61)**	**IKd (N=98)**	**p-value of treatment-by-subgroup interaction[b]**
Hedges' G (SE) vs Kd		0.06 (0.19)		-0.22 (0.19)	
95% CI		(-0.32 to 0.43)		(-0.58 to 0.14)	
Cycle 7					
Number	44	64	43	77	
Mean (SD)	71.80 (19.26)	71.17 (19.91)	66.65 (21.05)	73.74 (14.17)	
Median	73.50	74.00	70.00	76.00	
Q1 : Q3	62.50 : 82.00	59.00 : 85.00	50.00 : 84.00	67.00 : 81.00	
Min : Max	2.00 : 100.00	10.00 : 100.00	0.00 : 98.00	29.00 : 98.00	
Change from baseline[a]					
LS Mean (SE)	1.16 (2.28)	1.63 (1.91)	-1.80 (2.30)	2.42 (1.73)	0.3641
LS mean difference (SE) vs Kd		0.47 (2.97)		4.22 (2.88)	
95% CI		(-5.36 to 6.29)		(-1.42 to 9.86)	
P-value vs Kd		0.8748		0.1424	
Hedges' G					
Hedges' G (SE) vs Kd		0.03 (0.20)		0.28 (0.19)	

A higher score represents a better level of quality of life. Cycles with less than 20 patients overall are not presented.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
[a] Derived from MMRM model with change from baseline values as the response variable, and treatment, visit, treatment by-visit interaction, baseline value and baseline-by-visit interaction as covariates.
Covariance structure of the R matrix in the MMRM is AR(1).
[b] Derived from MMRM model with change from baseline values as the response variable, and treatment, visit, treatment-by-visit interaction, baseline-by-visit interaction, subgroup, subgroup-by-treatment interaction as covariates.
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16.2.6.1 Health-related quality-of-life endpoints - EQ-5D
16.2.6.1.2 EQ-5D VAS
16.2.6.1.2.16 Efficacy response data - Subgroup analyses by previous treatment with IMiD
16.2.6.1.2.16.2 EQ-5D - Change from baseline in EQ-5D VAS according to previous treatment with IMiD (LOCF) - ITT population

	Yes		No		
	Kd (N=62)	**IKd (N=81)**	**Kd (N=61)**	**IKd (N=98)**	**p-value of treatment-by-subgroup interaction[b]**
95% CI		(-0.35 to 0.41)		(-0.09 to 0.65)	
Cycle 8					
Number	43	62	40	74	
Mean (SD)	69.86 (16.44)	72.03 (18.31)	70.78 (17.98)	73.22 (14.71)	
Median	70.00	72.00	75.00	71.00	
Q1 : Q3	59.00 : 80.00	60.00 : 83.00	52.50 : 81.00	61.00 : 83.00	
Min : Max	41.00 : 100.00	20.00 : 100.00	29.00 : 100.00	35.00 : 100.00	
Change from baseline[a]					
LS Mean (SE)	0.00 (2.31)	2.60 (1.93)	3.26 (2.37)	2.14 (1.76)	0.3781
LS mean difference (SE) vs Kd		2.60 (3.02)		-1.12 (2.95)	
95% CI		(-3.31 to 8.52)		(-6.91 to 4.68)	
P-value vs Kd		0.3881		0.7049	
Hedges' G					
Hedges' G (SE) vs Kd		0.17 (0.20)		-0.07 (0.20)	
95% CI		(-0.22 to 0.56)		(-0.46 to 0.31)	

A higher score represents a better level of quality of life. Cycles with less than 20 patients overall are not presented.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
[a] Derived from MMRM model with change from baseline values as the response variable, and treatment, visit, treatment by-visit interaction, baseline value and baseline-by-visit interaction as covariates.
Covariance structure of the R matrix in the MMRM is AR(1).
[b] Derived from MMRM model with change from baseline values as the response variable, and treatment, visit, treatment-by-visit interaction, baseline-by-visit interaction, subgroup, subgroup-by-treatment interaction as covariates.
PGM=DEVOPS/SAR650984/EFC15246/CIR_RWE/REPORT/PGM/eff_qlq_mmrm_subgp_hg_i_t.sas OUT=REPORT/OUTPUT/eff_mmrm_eq5d_vas_imid_de_i_t_x.rtf (27APR2021 16:19)

16.2.6.1 Health-related quality-of-life endpoints - EQ-5D
16.2.6.1.2 EQ-5D VAS
16.2.6.1.2.16 Efficacy response data - Subgroup analyses by previous treatment with IMiD
16.2.6.1.2.16.2 EQ-5D - Change from baseline in EQ-5D VAS according to previous treatment with IMiD (LOCF) - ITT population

	Yes		No		
	Kd (N=62)	**IKd (N=81)**	**Kd (N=61)**	**IKd (N=98)**	**p-value of treatment-by-subgroup interaction[b]**
Cycle 9					
Number	43	60	37	70	
Mean (SD)	68.91 (22.22)	73.43 (16.87)	69.76 (18.90)	72.93 (17.08)	
Median	70.00	75.50	74.00	75.00	
Q1 : Q3	60.00 : 89.00	60.00 : 85.00	56.00 : 84.00	60.00 : 85.00	
Min : Max	1.00 : 100.00	29.00 : 100.00	30.00 : 100.00	29.00 : 100.00	
Change from baseline[a]					
LS Mean (SE)	-0.88 (2.33)	2.89 (1.96)	1.78 (2.46)	1.90 (1.80)	0.3964
LS mean difference (SE) vs Kd		3.77 (3.05)		0.11 (3.05)	
95% CI		(-2.21 to 9.75)		(-5.86 to 6.09)	
P-value vs Kd		0.2161		0.9700	
Hedges' G					
Hedges' G (SE) vs Kd		0.25 (0.20)		0.01 (0.20)	
95% CI		(-0.14 to 0.64)		(-0.39 to 0.41)	

A higher score represents a better level of quality of life. Cycles with less than 20 patients overall are not presented.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
[a] Derived from MMRM model with change from baseline values as the response variable, and treatment, visit, treatment by-visit interaction, baseline value and baseline-by-visit interaction as covariates.
Covariance structure of the R matrix in the MMRM is AR(1).
[b] Derived from MMRM model with change from baseline values as the response variable, and treatment, visit, treatment-by-visit interaction, baseline-by-visit interaction, subgroup, subgroup-by-treatment interaction as covariates.
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16.2.6.1 Health-related quality-of-life endpoints - EQ-5D
16.2.6.1.2 EQ-5D VAS
16.2.6.1.2.16 Efficacy response data - Subgroup analyses by previous treatment with IMiD
16.2.6.1.2.16.2 EQ-5D - Change from baseline in EQ-5D VAS according to previous treatment with IMiD (LOCF) - ITT population

	Yes		No		
	Kd (N=62)	**IKd (N=81)**	**Kd (N=61)**	**IKd (N=98)**	**p-value of treatment-by-subgroup interaction[b]**
Cycle 10					
Number	40	58	36	67	
Mean (SD)	73.20 (19.25)	72.72 (17.38)	69.00 (20.37)	74.30 (16.70)	
Median	78.50	75.00	70.00	79.00	
Q1 : Q3	64.50 : 89.00	60.00 : 85.00	51.00 : 86.50	64.00 : 88.00	
Min : Max	1.00 : 100.00	30.00 : 100.00	15.00 : 99.00	30.00 : 100.00	
Change from baseline[a]					
LS Mean (SE)	3.49 (2.39)	1.94 (1.99)	1.42 (2.52)	2.80 (1.84)	0.5060
LS mean difference (SE) vs Kd		-1.55 (3.11)		1.38 (3.12)	
95% CI		(-7.65 to 4.55)		(-4.74 to 7.50)	
P-value vs Kd		0.6178		0.6587	
Hedges' G					
Hedges' G (SE) vs Kd		-0.10 (0.21)		0.09 (0.21)	
95% CI		(-0.50 to 0.30)		(-0.31 to 0.50)	
Cycle 11					

A higher score represents a better level of quality of life. Cycles with less than 20 patients overall are not presented.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
[a] Derived from MMRM model with change from baseline values as the response variable, and treatment, visit, treatment by-visit interaction, baseline value and baseline-by-visit interaction as covariates.
Covariance structure of the R matrix in the MMRM is AR(1).
[b] Derived from MMRM model with change from baseline values as the response variable, and treatment, visit, treatment-by-visit interaction, baseline-by-visit interaction, subgroup, subgroup-by-treatment interaction as covariates.
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16.2.6.1 Health-related quality-of-life endpoints - EQ-5D
16.2.6.1.2 EQ-5D VAS
16.2.6.1.2.16 Efficacy response data - Subgroup analyses by previous treatment with IMiD
16.2.6.1.2.16.2 EQ-5D - Change from baseline in EQ-5D VAS according to previous treatment with IMiD (LOCF) - ITT population

	Yes		No		
	Kd (N=62)	**IKd (N=81)**	**Kd (N=61)**	**IKd (N=98)**	**p-value of treatment-by-subgroup interaction[b]**
Number	36	57	34	65	
Mean (SD)	72.25 (17.47)	72.72 (16.77)	70.82 (18.07)	75.75 (15.74)	
Median	73.50	75.00	70.00	79.00	
Q1 : Q3	57.00 : 87.00	60.00 : 85.00	56.00 : 86.00	70.00 : 85.00	
Min : Max	35.00 : 100.00	30.00 : 100.00	40.00 : 100.00	30.00 : 100.00	
Change from baseline[a]					
LS Mean (SE)	2.14 (2.48)	2.45 (2.02)	1.50 (2.58)	4.13 (1.88)	0.6085
LS mean difference (SE) vs Kd		0.31 (3.20)		2.63 (3.20)	
95% CI		(-5.97 to 6.58)		(-3.64 to 8.89)	
P-value vs Kd		0.9231		0.4114	
Hedges' G					
Hedges' G (SE) vs Kd		0.02 (0.21)		0.17 (0.21)	
95% CI		(-0.39 to 0.44)		(-0.24 to 0.59)	
Cycle 12					
Number	34	54	30	65	

A higher score represents a better level of quality of life. Cycles with less than 20 patients overall are not presented.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
[a] Derived from MMRM model with change from baseline values as the response variable, and treatment, visit, treatment by-visit interaction, baseline value and baseline-by-visit interaction as covariates.
Covariance structure of the R matrix in the MMRM is AR(1).
[b] Derived from MMRM model with change from baseline values as the response variable, and treatment, visit, treatment-by-visit interaction, baseline-by-visit interaction, subgroup, subgroup-by-treatment interaction as covariates.
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16.2.6.1 Health-related quality-of-life endpoints - EQ-5D
16.2.6.1.2 EQ-5D VAS
16.2.6.1.2.16 Efficacy response data - Subgroup analyses by previous treatment with IMiD
16.2.6.1.2.16.2 EQ-5D - Change from baseline in EQ-5D VAS according to previous treatment with IMiD (LOCF) - ITT population

	Yes		No		
	Kd (N=62)	**IKd (N=81)**	**Kd (N=61)**	**IKd (N=98)**	**p-value of treatment-by-subgroup interaction[b]**
Mean (SD)	76.74 (15.72)	74.28 (16.70)	67.83 (21.61)	75.75 (15.25)	
Median	78.50	73.00	71.50	79.00	
Q1 : Q3	69.00 : 90.00	62.00 : 90.00	50.00 : 86.00	68.00 : 90.00	
Min : Max	49.00 : 100.00	30.00 : 100.00	35.00 : 98.00	29.00 : 100.00	
Change from baseline[a]					
LS Mean (SE)	6.74 (2.57)	3.26 (2.06)	0.24 (2.71)	4.49 (1.90)	0.0977
LS mean difference (SE) vs Kd		-3.48 (3.29)		4.25 (3.31)	
95% CI		(-9.93 to 2.98)		(-2.23 to 10.73)	
P-value vs Kd		0.2905		0.1988	
Hedges' G					
Hedges' G (SE) vs Kd		-0.23 (0.22)		0.28 (0.22)	
95% CI		(-0.66 to 0.20)		(-0.15 to 0.71)	
Cycle 13					
Number	31	53	29	60	
Mean (SD)	76.35 (16.24)	73.08 (17.89)	68.62 (21.79)	76.62 (15.37)	

A higher score represents a better level of quality of life. Cycles with less than 20 patients overall are not presented.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
[a] Derived from MMRM model with change from baseline values as the response variable, and treatment, visit, treatment by-visit interaction, baseline value and baseline-by-visit interaction as covariates.
Covariance structure of the R matrix in the MMRM is AR(1).
[b] Derived from MMRM model with change from baseline values as the response variable, and treatment, visit, treatment-by-visit interaction, baseline-by-visit interaction, subgroup, subgroup-by-treatment interaction as covariates.
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16.2.6.1 Health-related quality-of-life endpoints - EQ-5D
16.2.6.1.2 EQ-5D VAS
16.2.6.1.2.16 Efficacy response data - Subgroup analyses by previous treatment with IMiD
16.2.6.1.2.16.2 EQ-5D - Change from baseline in EQ-5D VAS according to previous treatment with IMiD (LOCF) - ITT population

	Yes		No		
	Kd (N=62)	**IKd (N=81)**	**Kd (N=61)**	**IKd (N=98)**	**p-value of treatment-by-subgroup interaction[b]**
Median	80.00	80.00	71.00	79.50	
Q1 : Q3	64.00 : 90.00	60.00 : 85.00	59.00 : 85.00	67.00 : 90.00	
Min : Max	40.00 : 97.00	19.00 : 100.00	20.00 : 99.00	35.00 : 100.00	
Change from baseline[a]					
LS Mean (SE)	7.00 (2.67)	2.36 (2.09)	1.60 (2.79)	5.99 (1.95)	0.0601
LS mean difference (SE) vs Kd		-4.64 (3.39)		4.39 (3.40)	
95% CI		(-11.30 to 2.01)		(-2.28 to 11.07)	
P-value vs Kd		0.1712		0.1966	
Hedges' G					
Hedges' G (SE) vs Kd		-0.31 (0.23)		0.29 (0.23)	
95% CI		(-0.75 to 0.13)		(-0.15 to 0.73)	
Cycle 14					
Number	31	51	28	59	
Mean (SD)	76.84 (12.61)	73.69 (17.48)	72.07 (16.77)	76.29 (14.46)	
Median	77.00	75.00	75.00	77.00	

A higher score represents a better level of quality of life. Cycles with less than 20 patients overall are not presented.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
[a] Derived from MMRM model with change from baseline values as the response variable, and treatment, visit, treatment by-visit interaction, baseline value and baseline-by-visit interaction as covariates.
Covariance structure of the R matrix in the MMRM is AR(1).
[b] Derived from MMRM model with change from baseline values as the response variable, and treatment, visit, treatment-by-visit interaction, baseline-by-visit interaction, subgroup, subgroup-by-treatment interaction as covariates.

16.2.6.1 Health-related quality-of-life endpoints - EQ-5D
16.2.6.1.2 EQ-5D VAS
16.2.6.1.2.16 Efficacy response data - Subgroup analyses by previous treatment with IMiD
16.2.6.1.2.16.2 EQ-5D - Change from baseline in EQ-5D VAS according to previous treatment with IMiD (LOCF) - ITT population

	Yes		No		
	Kd (N=62)	**IKd (N=81)**	**Kd (N=61)**	**IKd (N=98)**	**p-value of treatment-by-subgroup interaction[b]**
Q1 : Q3	70.00 : 89.00	60.00 : 90.00	60.00 : 85.00	68.00 : 90.00	
Min : Max	50.00 : 96.00	39.00 : 100.00	40.00 : 99.00	36.00 : 100.00	
Change from baseline[a]					
LS Mean (SE)	7.58 (2.72)	2.96 (2.12)	4.18 (2.85)	5.59 (1.98)	0.2176
LS mean difference (SE) vs Kd		-4.63 (3.45)		1.42 (3.47)	
95% CI		(-11.40 to 2.15)		(-5.40 to 8.23)	
P-value vs Kd		0.1806		0.6838	
Hedges' G					
Hedges' G (SE) vs Kd		-0.30 (0.23)		0.09 (0.23)	
95% CI		(-0.75 to 0.14)		(-0.36 to 0.54)	
Cycle 15					
Number	29	49	28	55	
Mean (SD)	75.21 (16.85)	73.00 (19.03)	66.46 (19.91)	73.65 (17.53)	
Median	75.00	80.00	67.50	76.00	
Q1 : Q3	64.00 : 90.00	60.00 : 90.00	50.00 : 82.00	69.00 : 85.00	

A higher score represents a better level of quality of life. Cycles with less than 20 patients overall are not presented.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
[a] Derived from MMRM model with change from baseline values as the response variable, and treatment, visit, treatment by-visit interaction, baseline value and baseline-by-visit interaction as covariates.
Covariance structure of the R matrix in the MMRM is AR(1).
[b] Derived from MMRM model with change from baseline values as the response variable, and treatment, visit, treatment-by-visit interaction, baseline-by-visit interaction, subgroup, subgroup-by-treatment interaction as covariates.
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16.2.6.1 Health-related quality-of-life endpoints - EQ-5D
16.2.6.1.2 EQ-5D VAS
16.2.6.1.2.16 Efficacy response data - Subgroup analyses by previous treatment with IMiD
16.2.6.1.2.16.2 EQ-5D - Change from baseline in EQ-5D VAS according to previous treatment with IMiD (LOCF) - ITT population

	Yes		No		
	Kd (N=62)	**IKd (N=81)**	**Kd (N=61)**	**IKd (N=98)**	**p-value of treatment-by-subgroup interaction[b]**
Min : Max	30.00 : 97.00	30.00 : 100.00	30.00 : 100.00	11.00 : 99.00	
Change from baseline[a]					
LS Mean (SE)	6.38 (2.80)	2.71 (2.16)	-1.07 (2.89)	3.08 (2.03)	0.1178
LS mean difference (SE) vs Kd		-3.67 (3.54)		4.15 (3.53)	
95% CI		(-10.60 to 3.27)		(-2.77 to 11.07)	
P-value vs Kd		0.2997		0.2400	
Hedges' G					
Hedges' G (SE) vs Kd		-0.24 (0.23)		0.27 (0.23)	
95% CI		(-0.70 to 0.22)		(-0.18 to 0.73)	
Cycle 16					
Number	26	47	26	53	
Mean (SD)	71.50 (15.63)	74.83 (18.65)	69.54 (19.34)	75.62 (13.62)	
Median	70.50	80.00	70.00	78.00	
Q1 : Q3	60.00 : 84.00	60.00 : 90.00	58.00 : 85.00	70.00 : 84.00	
Min : Max	40.00 : 95.00	15.00 : 100.00	30.00 : 100.00	40.00 : 99.00	

A higher score represents a better level of quality of life. Cycles with less than 20 patients overall are not presented.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
[a] Derived from MMRM model with change from baseline values as the response variable, and treatment, visit, treatment by-visit interaction, baseline value and baseline-by-visit interaction as covariates.
Covariance structure of the R matrix in the MMRM is AR(1).
[b] Derived from MMRM model with change from baseline values as the response variable, and treatment, visit, treatment-by-visit interaction, baseline-by-visit interaction, subgroup, subgroup-by-treatment interaction as covariates.
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16.2.6.1 Health-related quality-of-life endpoints - EQ-5D
16.2.6.1.2 EQ-5D VAS
16.2.6.1.2.16 Efficacy response data - Subgroup analyses by previous treatment with IMiD
16.2.6.1.2.16.2 EQ-5D - Change from baseline in EQ-5D VAS according to previous treatment with IMiD (LOCF) - ITT population

	Yes		No		
	Kd (N=62)	**IKd (N=81)**	**Kd (N=61)**	**IKd (N=98)**	**p-value of treatment-by-subgroup interaction[b]**
Change from baseline[a]					
LS Mean (SE)	2.03 (2.92)	4.41 (2.21)	1.78 (2.96)	4.54 (2.08)	0.9397
LS mean difference (SE) vs Kd		2.37 (3.66)		2.76 (3.62)	
95% CI		(-4.80 to 9.55)		(-4.33 to 9.85)	
P-value vs Kd		0.5165		0.4450	
Hedges' G					
Hedges' G (SE) vs Kd		0.16 (0.24)		0.18 (0.24)	
95% CI		(-0.32 to 0.63)		(-0.29 to 0.65)	
Cycle 17					
Number	23	46	25	52	
Mean (SD)	76.52 (14.15)	75.46 (17.83)	66.76 (18.53)	76.23 (13.95)	
Median	78.00	80.00	60.00	75.00	
Q1 : Q3	70.00 : 89.00	60.00 : 90.00	58.00 : 78.00	70.00 : 86.50	
Min : Max	50.00 : 97.00	35.00 : 100.00	40.00 : 99.00	48.00 : 100.00	
Change from baseline[a]					

A higher score represents a better level of quality of life. Cycles with less than 20 patients overall are not presented.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
[a] Derived from MMRM model with change from baseline values as the response variable, and treatment, visit, treatment by-visit interaction, baseline value and baseline-by-visit interaction as covariates.
Covariance structure of the R matrix in the MMRM is AR(1).
[b] Derived from MMRM model with change from baseline values as the response variable, and treatment, visit, treatment-by-visit interaction, baseline-by-visit interaction, subgroup, subgroup-by-treatment interaction as covariates.
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16.2.6.1 Health-related quality-of-life endpoints - EQ-5D
16.2.6.1.2 EQ-5D VAS
16.2.6.1.2.16 Efficacy response data - Subgroup analyses by previous treatment with IMiD
16.2.6.1.2.16.2 EQ-5D - Change from baseline in EQ-5D VAS according to previous treatment with IMiD (LOCF) - ITT population

	Yes		No		
	Kd (N=62)	**IKd (N=81)**	**Kd (N=61)**	**IKd (N=98)**	**p-value of treatment-by-subgroup interaction[b]**
LS Mean (SE)	5.69 (3.07)	5.63 (2.24)	-0.60 (3.02)	5.10 (2.11)	0.2769
LS mean difference (SE) vs Kd		-0.07 (3.80)		5.70 (3.69)	
95% CI		(-7.53 to 7.40)		(-1.54 to 12.93)	
P-value vs Kd		0.9861		0.1226	
Hedges' G					
Hedges' G (SE) vs Kd		0.00 (0.26)		0.38 (0.25)	
95% CI		(-0.50 to 0.49)		(-0.10 to 0.85)	
Cycle 18					
Number	21	46	25	49	
Mean (SD)	71.71 (16.66)	73.89 (18.41)	69.48 (19.01)	74.73 (15.43)	
Median	73.00	80.00	65.00	79.00	
Q1 : Q3	65.00 : 80.00	60.00 : 90.00	60.00 : 90.00	65.00 : 89.00	
Min : Max	40.00 : 95.00	29.00 : 100.00	36.00 : 100.00	39.00 : 100.00	
Change from baseline[a]					
LS Mean (SE)	2.26 (3.23)	4.15 (2.26)	2.10 (3.05)	3.71 (2.16)	0.9591

A higher score represents a better level of quality of life. Cycles with less than 20 patients overall are not presented.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
[a] Derived from MMRM model with change from baseline values as the response variable, and treatment, visit, treatment by-visit interaction, baseline value and baseline-by-visit interaction as covariates.
Covariance structure of the R matrix in the MMRM is AR(1).
[b] Derived from MMRM model with change from baseline values as the response variable, and treatment, visit, treatment-by-visit interaction, baseline-by-visit interaction, subgroup, subgroup-by-treatment interaction as covariates.
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16.2.6.1 Health-related quality-of-life endpoints - EQ-5D
16.2.6.1.2 EQ-5D VAS
16.2.6.1.2.16 Efficacy response data - Subgroup analyses by previous treatment with IMiD
16.2.6.1.2.16.2 EQ-5D - Change from baseline in EQ-5D VAS according to previous treatment with IMiD (LOCF) - ITT population

	Yes		No		
	Kd (N=62)	**IKd (N=81)**	**Kd (N=61)**	**IKd (N=98)**	**p-value of treatment-by-subgroup interaction[b]**
LS mean difference (SE) vs Kd		1.89 (3.94)		1.61 (3.74)	
95% CI		(-5.83 to 9.61)		(-5.72 to 8.95)	
P-value vs Kd		0.6313		0.6667	
Hedges' G					
Hedges' G (SE) vs Kd		0.12 (0.26)		0.11 (0.25)	
95% CI		(-0.38 to 0.63)		(-0.38 to 0.59)	
Cycle 19					
Number	19	44	22	47	
Mean (SD)	75.53 (15.53)	72.45 (19.42)	72.50 (19.75)	76.26 (14.30)	
Median	75.00	77.00	72.50	76.00	
Q1 : Q3	63.00 : 90.00	60.00 : 89.00	59.00 : 91.00	69.00 : 89.00	
Min : Max	45.00 : 97.00	29.00 : 100.00	32.00 : 100.00	39.00 : 100.00	
Change from baseline[a]					
LS Mean (SE)	6.37 (3.39)	2.60 (2.29)	4.68 (3.18)	4.78 (2.20)	0.4920
LS mean difference (SE) vs Kd		-3.77 (4.09)		0.10 (3.87)	

A higher score represents a better level of quality of life. Cycles with less than 20 patients overall are not presented.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
[a] Derived from MMRM model with change from baseline values as the response variable, and treatment, visit, treatment by-visit interaction, baseline value and baseline-by-visit interaction as covariates.
Covariance structure of the R matrix in the MMRM is AR(1).
[b] Derived from MMRM model with change from baseline values as the response variable, and treatment, visit, treatment-by-visit interaction, baseline-by-visit interaction, subgroup, subgroup-by-treatment interaction as covariates.
PGM=DEVOPS/SAR650984/EFC15246/CIR_RWE/REPORT/PGM/eff_qlq_mmrm_subgp_hg_i_t.sas OUT=REPORT/OUTPUT/eff_mmrm_eq5d_vas_imid_de_i_t_x.rtf (27APR2021 16:19)

16.2.6.1 Health-related quality-of-life endpoints - EQ-5D
16.2.6.1.2 EQ-5D VAS
16.2.6.1.2.16 Efficacy response data - Subgroup analyses by previous treatment with IMiD
16.2.6.1.2.16.2 EQ-5D - Change from baseline in EQ-5D VAS according to previous treatment with IMiD (LOCF) - ITT population

	Yes		No		
	Kd (N=62)	**IKd (N=81)**	**Kd (N=61)**	**IKd (N=98)**	**p-value of treatment-by-subgroup interaction[b]**
95% CI		(-11.79 to 4.26)		(-7.48 to 7.69)	
P-value vs Kd		0.3576		0.9787	
Hedges' G					
Hedges' G (SE) vs Kd		-0.25 (0.28)		0.01 (0.26)	
95% CI		(-0.78 to 0.28)		(-0.50 to 0.51)	
Cycle 20					
Number	16	41	18	44	
Mean (SD)	72.31 (15.70)	74.00 (19.42)	74.56 (20.71)	76.25 (13.90)	
Median	75.00	80.00	80.00	79.00	
Q1 : Q3	62.50 : 85.00	60.00 : 90.00	62.00 : 92.00	63.00 : 87.00	
Min : Max	40.00 : 94.00	20.00 : 100.00	35.00 : 100.00	48.00 : 99.00	
Change from baseline[a]					
LS Mean (SE)	4.50 (3.64)	3.80 (2.35)	3.90 (3.42)	5.59 (2.27)	0.6884
LS mean difference (SE) vs Kd		-0.70 (4.33)		1.69 (4.11)	
95% CI		(-9.20 to 7.79)		(-6.36 to 9.74)	

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The last observation carried forward (LOCF) procedure was applied to impute missing data.
[a] Derived from MMRM model with change from baseline values as the response variable, and treatment, visit, treatment by-visit interaction, baseline value and baseline-by-visit interaction as covariates.
Covariance structure of the R matrix in the MMRM is AR(1).
[b] Derived from MMRM model with change from baseline values as the response variable, and treatment, visit, treatment-by-visit interaction, baseline-by-visit interaction, subgroup, subgroup-by-treatment interaction as covariates.

16.2.6.1 Health-related quality-of-life endpoints - EQ-5D
16.2.6.1.2 EQ-5D VAS
16.2.6.1.2.16 Efficacy response data - Subgroup analyses by previous treatment with IMiD
16.2.6.1.2.16.2 EQ-5D - Change from baseline in EQ-5D VAS according to previous treatment with IMiD (LOCF) - ITT population

	Yes		No		
	Kd (N=62)	**IKd (N=81)**	**Kd (N=61)**	**IKd (N=98)**	**p-value of treatment-by-subgroup interaction[b]**
P-value vs Kd		0.8713		0.6804	
Hedges' G					
Hedges' G (SE) vs Kd		-0.05 (0.29)		0.11 (0.28)	
95% CI		(-0.62 to 0.52)		(-0.43 to 0.65)	
Cycle 21					
Number	15	36	13	36	
Mean (SD)	74.47 (18.68)	75.36 (18.40)	77.62 (20.34)	74.83 (13.93)	
Median	80.00	80.00	85.00	75.00	
Q1 : Q3	55.00 : 90.00	60.00 : 90.00	59.00 : 95.00	62.00 : 86.00	
Min : Max	40.00 : 94.00	40.00 : 99.00	50.00 : 99.00	48.00 : 99.00	
Change from baseline[a]					
LS Mean (SE)	5.92 (3.82)	4.63 (2.47)	5.73 (3.89)	4.99 (2.43)	0.9323
LS mean difference (SE) vs Kd		-1.29 (4.55)		-0.74 (4.59)	
95% CI		(-10.21 to 7.62)		(-9.74 to 8.26)	
P-value vs Kd		0.7763		0.8714	

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Covariance structure of the R matrix in the MMRM is AR(1).
[b] Derived from MMRM model with change from baseline values as the response variable, and treatment, visit, treatment-by-visit interaction, baseline-by-visit interaction, subgroup, subgroup-by-treatment interaction as covariates.
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16.2.6.1 Health-related quality-of-life endpoints - EQ-5D
16.2.6.1.2 EQ-5D VAS
16.2.6.1.2.16 Efficacy response data - Subgroup analyses by previous treatment with IMiD
16.2.6.1.2.16.2 EQ-5D - Change from baseline in EQ-5D VAS according to previous treatment with IMiD (LOCF) - ITT population

	Yes		No		
	Kd (N=62)	**IKd (N=81)**	**Kd (N=61)**	**IKd (N=98)**	**p-value of treatment-by-subgroup interaction[b]**
Hedges' G					
Hedges' G (SE) vs Kd		-0.09 (0.31)		-0.05 (0.32)	
95% CI		(-0.69 to 0.52)		(-0.67 to 0.57)	
Cycle 22					
Number	13	31	8	21	
Mean (SD)	71.46 (14.54)	70.87 (17.43)	74.50 (21.49)	72.38 (17.27)	
Median	70.00	75.00	72.50	70.00	
Q1 : Q3	67.00 : 80.00	59.00 : 85.00	55.00 : 96.50	60.00 : 90.00	
Min : Max	39.00 : 95.00	39.00 : 99.00	50.00 : 98.00	36.00 : 99.00	
Change from baseline[a]					
LS Mean (SE)	4.88 (4.06)	2.51 (2.63)	5.64 (4.78)	2.42 (2.95)	0.9073
LS mean difference (SE) vs Kd		-2.36 (4.83)		-3.23 (5.62)	
95% CI		(-11.85 to 7.12)		(-14.24 to 7.78)	
P-value vs Kd		0.6248		0.5656	
Hedges' G					

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Covariance structure of the R matrix in the MMRM is AR(1).
[b] Derived from MMRM model with change from baseline values as the response variable, and treatment, visit, treatment-by-visit interaction, baseline-by-visit interaction, subgroup, subgroup-by-treatment interaction as covariates.
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16.2.6.1 Health-related quality-of-life endpoints - EQ-5D
16.2.6.1.2 EQ-5D VAS
16.2.6.1.2.16 Efficacy response data - Subgroup analyses by previous treatment with IMiD
16.2.6.1.2.16.2 EQ-5D - Change from baseline in EQ-5D VAS according to previous treatment with IMiD (LOCF) - ITT population

	Yes		No		
	Kd (N=62)	**IKd (N=81)**	**Kd (N=61)**	**IKd (N=98)**	**p-value of treatment-by-subgroup interaction[b]**
Hedges' G (SE) vs Kd		-0.16 (0.33)		-0.24 (0.42)	
95% CI		(-0.81 to 0.49)		(-1.05 to 0.58)	
Cycle 23					
Number	7	21	8	15	
Mean (SD)	75.00 (17.32)	74.29 (15.54)	71.00 (24.71)	77.40 (13.89)	
Median	80.00	80.00	72.00	80.00	
Q1 : Q3	70.00 : 85.00	70.00 : 82.00	48.00 : 95.00	70.00 : 90.00	
Min : Max	40.00 : 95.00	41.00 : 95.00	42.00 : 96.00	50.00 : 94.00	
Change from baseline[a]					
LS Mean (SE)	6.77 (5.07)	4.79 (3.03)	2.25 (5.14)	4.86 (3.53)	0.5927
LS mean difference (SE) vs Kd		-1.98 (5.90)		2.61 (6.24)	
95% CI		(-13.56 to 9.59)		(-9.62 to 14.84)	
P-value vs Kd		0.7371		0.6755	
Hedges' G					
Hedges' G (SE) vs Kd		-0.14 (0.44)		0.19 (0.44)	

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[a] Derived from MMRM model with change from baseline values as the response variable, and treatment, visit, treatment by-visit interaction, baseline value and baseline-by-visit interaction as covariates.
Covariance structure of the R matrix in the MMRM is AR(1).
[b] Derived from MMRM model with change from baseline values as the response variable, and treatment, visit, treatment-by-visit interaction, baseline-by-visit interaction, subgroup, subgroup-by-treatment interaction as covariates.

16.2.6.1 Health-related quality-of-life endpoints - EQ-5D
16.2.6.1.2 EQ-5D VAS
16.2.6.1.2.16 Efficacy response data - Subgroup analyses by previous treatment with IMiD
16.2.6.1.2.16.2 EQ-5D - Change from baseline in EQ-5D VAS according to previous treatment with IMiD (LOCF) - ITT population

	Yes		No		
	Kd (N=62)	**IKd (N=81)**	**Kd (N=61)**	**IKd (N=98)**	**p-value of treatment-by-subgroup interaction[b]**
95% CI		(-0.98 to 0.70)		(-0.69 to 1.06)	
Cycle 24					
Number	5	11	4	11	
Mean (SD)	73.80 (20.51)	74.36 (17.78)	76.75 (17.91)	78.00 (14.66)	
Median	80.00	80.00	74.50	80.00	
Q1 : Q3	65.00 : 85.00	50.00 : 85.00	62.00 : 91.50	61.00 : 90.00	
Min : Max	43.00 : 96.00	45.00 : 97.00	60.00 : 98.00	57.00 : 99.00	
Change from baseline[a]					
LS Mean (SE)	3.83 (6.09)	4.17 (3.96)	10.68 (6.62)	5.96 (4.16)	0.6356
LS mean difference (SE) vs Kd		0.34 (7.27)		-4.72 (7.81)	
95% CI		(-13.92 to 14.59)		(-20.04 to 10.60)	
P-value vs Kd		0.9630		0.5458	
Hedges' G					
Hedges' G (SE) vs Kd		0.03 (0.54)		-0.35 (0.59)	
95% CI		(-1.05 to 1.10)		(-1.47 to 0.78)	

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[a] Derived from MMRM model with change from baseline values as the response variable, and treatment, visit, treatment by-visit interaction, baseline value and baseline-by-visit interaction as covariates.
Covariance structure of the R matrix in the MMRM is AR(1).
[b] Derived from MMRM model with change from baseline values as the response variable, and treatment, visit, treatment-by-visit interaction, baseline-by-visit interaction, subgroup, subgroup-by-treatment interaction as covariates.

16.2.6.1 Health-related quality-of-life endpoints - EQ-5D
16.2.6.1.2 EQ-5D VAS
16.2.6.1.2.16 Efficacy response data - Subgroup analyses by previous treatment with IMiD
16.2.6.1.2.16.2 EQ-5D - Change from baseline in EQ-5D VAS according to previous treatment with IMiD (LOCF) - ITT population

	Yes		No		
	Kd (N=62)	**IKd (N=81)**	**Kd (N=61)**	**IKd (N=98)**	**p-value of treatment-by-subgroup interaction[b]**
Cycle 25					
Number	3	8	2	8	
Mean (SD)	70.00 (30.41)	81.25 (8.36)	74.50 (27.58)	72.63 (14.83)	
Median	85.00	80.50	74.50	74.50	
Q1 : Q3	35.00 : 90.00	74.50 : 90.00	55.00 : 94.00	61.00 : 82.50	
Min : Max	35.00 : 90.00	70.00 : 90.00	55.00 : 94.00	50.00 : 95.00	
Change from baseline[a]					
LS Mean (SE)	3.78 (7.70)	7.90 (4.80)	6.24 (9.13)	3.45 (4.88)	0.6158
LS mean difference (SE) vs Kd		4.12 (9.07)		-2.79 (10.35)	
95% CI		(-13.67 to 21.91)		(-23.08 to 17.50)	
P-value vs Kd		0.6500		0.7876	
Hedges' G					
Hedges' G (SE) vs Kd		0.30 (0.68)		-0.20 (0.79)	
95% CI		(-1.01 to 1.62)		(-1.69 to 1.28)	

A higher score represents a better level of quality of life. Cycles with less than 20 patients overall are not presented.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
[a] Derived from MMRM model with change from baseline values as the response variable, and treatment, visit, treatment by-visit interaction, baseline value and baseline-by-visit interaction as covariates.
Covariance structure of the R matrix in the MMRM is AR(1).
[b] Derived from MMRM model with change from baseline values as the response variable, and treatment, visit, treatment-by-visit interaction, baseline-by-visit interaction, subgroup, subgroup-by-treatment interaction as covariates.
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16.2.6.1 Health-related quality-of-life endpoints - EQ-5D
16.2.6.1.2 EQ-5D VAS
16.2.6.1.2.16 Efficacy response data - Subgroup analyses by previous treatment with IMiD
16.2.6.1.2.16.3 EQ-5D - Time to first improvement by 10 pt in EQ-5D VAS according to previous treatment with IMiD (LOCF) - ITT population

	Yes		No		
	Kd (N=62)	**IKd (N=81)**	**Kd (N=61)**	**IKd (N=98)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	29 (46.8)	46 (56.8)	28 (45.9)	46 (46.9)	0.4623
Number (%) of patients censored	33 (53.2)	35 (43.2)	33 (54.1)	52 (53.1)	
Kaplan-Meier estimates of EQ-5D VAS in months					
25% quantile (95% CI)	1.91 (1.051 to 3.745)	1.91 (1.051 to 2.136)	1.12 (0.986 to 2.924)	1.97 (1.117 to 2.530)	
Median (95% CI)	NC (3.745 to NC)	5.78 (2.366 to NC)	NC (2.924 to NC)	NC (4.698 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.2850		0.9659	
Hazard ratio (95% CI) vs Kd	-	1.29 (0.81 to 2.05)		1.01 (0.63 to 1.62)	
P-value	-	0.2863		0.9659	
Improvement probability (95% CI)[b]					

A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.1 Health-related quality-of-life endpoints - EQ-5D
16.2.6.1.2 EQ-5D VAS
16.2.6.1.2.16 Efficacy response data - Subgroup analyses by previous treatment with IMiD
16.2.6.1.2.16.4 EQ-5D - Time to first deterioration by 10 pt in EQ-5D VAS according to previous treatment with IMiD (LOCF) - ITT population

	Yes		No		
	Kd (N=62)	**IKd (N=81)**	**Kd (N=61)**	**IKd (N=98)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	35 (56.5)	46 (56.8)	36 (59.0)	57 (58.2)	0.7462
Number (%) of patients censored	27 (43.5)	35 (43.2)	25 (41.0)	41 (41.8)	
Kaplan-Meier estimates of EQ-5D VAS in months					
25% quantile (95% CI)	2.07 (1.084 to 3.844)	1.51 (1.051 to 3.220)	2.84 (1.906 to 4.830)	2.14 (1.084 to 3.220)	
Median (95% CI)	5.65 (3.844 to NC)	9.20 (4.238 to NC)	7.56 (4.830 to 21.224)	6.97 (3.975 to 19.253)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (21.224 to NC)	NC (NC to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.8627		0.7876	
Hazard ratio (95% CI) vs Kd	-	0.96 (0.62 to 1.49)		1.06 (0.70 to 1.61)	
P-value	-	0.8623		0.7888	
Deterioration probability (95% CI)[b]					

A higher score represents a better level of quality of life. Clinical meaningful deterioration change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.6.1 Health-related quality-of-life endpoints - EQ-5D
16.2.6.1.2 EQ-5D VAS
16.2.6.1.2.16 Efficacy response data - Subgroup analyses by previous treatment with IMiD
16.2.6.1.2.16.5 EQ-5D - Time until permanent improvement by 10 pt in EQ-5D VAS according to previous treatment with IMiD (LOCF) - ITT population

	Yes		No		
	Kd (N=62)	**IKd (N=81)**	**Kd (N=61)**	**IKd (N=98)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	16 (25.8)	24 (29.6)	13 (21.3)	24 (24.5)	0.8482
Number (%) of patients censored	46 (74.2)	57 (70.4)	48 (78.7)	74 (75.5)	
Kaplan-Meier estimates of EQ-5D VAS in months					
25% quantile (95% CI)	17.91 (7.261 to NC)	16.39 (12.025 to 22.341)	NC (12.025 to NC)	19.81 (12.715 to NC)	
Median (95% CI)	NC (22.209 to NC)	NC (22.341 to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.7505		0.6117	
Hazard ratio (95% CI) vs Kd	-	1.11 (0.59 to 2.09)		1.19 (0.61 to 2.34)	
P-value	-	0.7506		0.6122	
Improvement probability (95% CI)[b]					

A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.1 Health-related quality-of-life endpoints - EQ-5D
16.2.6.1.2 EQ-5D VAS
16.2.6.1.2.16 Efficacy response data - Subgroup analyses by previous treatment with IMiD
16.2.6.1.2.16.6 EQ-5D - Time until permanent deterioration by 10 pt in EQ-5D VAS according to previous treatment with IMiD (LOCF) - ITT population

	Yes		No		
	Kd (N=62)	**IKd (N=81)**	**Kd (N=61)**	**IKd (N=98)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	16 (25.8)	22 (27.2)	13 (21.3)	28 (28.6)	0.5054
Number (%) of patients censored	46 (74.2)	59 (72.8)	48 (78.7)	70 (71.4)	
Kaplan-Meier estimates of EQ-5D VAS in months					
25% quantile (95% CI)	19.15 (4.961 to NC)	16.99 (6.735 to 23.129)	20.57 (10.546 to NC)	19.25 (8.181 to 24.444)	
Median (95% CI)	NC (NC to NC)	NC (23.097 to NC)	NC (NC to NC)	24.44 (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	24.44 (NC to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.9366		0.3016	
Hazard ratio (95% CI) vs Kd	-	1.03 (0.54 to 1.96)		1.41 (0.73 to 2.73)	
P-value	-	0.9368		0.3040	
Deterioration probability (95% CI)[b]					

A higher score represents a better level of quality of life. Clinical meaningful deterioration change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.1 Health-related quality-of-life endpoints - EQ-5D
16.2.6.1.2 EQ-5D VAS
16.2.6.1.2.17 Efficacy response data - Subgroup analyses by previous treatment with PI and IMiD
16.2.6.1.2.17.3 EQ-5D - Time to first improvement by 10 pt in EQ-5D VAS according to previous treatment with PI and IMiD (LOCF) - ITT population

	Yes		No		
	Kd (N=17)	**IKd (N=23)**	**Kd (N=106)**	**IKd (N=156)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	8 (47.1)	12 (52.2)	49 (46.2)	80 (51.3)	0.9729
Number (%) of patients censored	9 (52.9)	11 (47.8)	57 (53.8)	76 (48.7)	
Kaplan-Meier estimates of EQ-5D VAS in months					
25% quantile (95% CI)	2.00 (1.018 to 5.651)	1.97 (0.986 to 2.891)	1.87 (1.051 to 2.891)	1.91 (1.084 to 2.103)	
Median (95% CI)	5.65 (1.051 to NC)	3.42 (2.103 to NC)	NC (3.811 to NC)	10.25 (3.844 to NC)	
75% quantile (95% CI)	NC (5.651 to NC)	NC (5.782 to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.7533		0.4853	
Hazard ratio (95% CI) vs Kd	-	1.15 (0.47 to 2.83)		1.13 (0.80 to 1.62)	
P-value	-	0.7535		0.4856	

A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
PGM=DEVOPS/SAR650984/EFC15246/CIR_RWE/REPORT/PGM/eff_km_subgp_sr_sig_de_i_t.sas OUT=REPORT/OUTPUT/eff_km_eq5d_vas_impl_piimid_de_i_t_x.rtf (07APR2021 14:45)

16.2.6.1 Health-related quality-of-life endpoints - EQ-5D
16.2.6.1.2 EQ-5D VAS
16.2.6.1.2.17 Efficacy response data - Subgroup analyses by previous treatment with PI and IMiD
16.2.6.1.2.17.4 EQ-5D - Time to first deterioration by 10 pt in EQ-5D VAS according to previous treatment with PI and IMiD (LOCF) - ITT population

	Yes		No		
	Kd (N=17)	**IKd (N=23)**	**Kd (N=106)**	**IKd (N=156)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	9 (52.9)	12 (52.2)	62 (58.5)	91 (58.3)	0.9196
Number (%) of patients censored	8 (47.1)	11 (47.8)	44 (41.5)	65 (41.7)	
Kaplan-Meier estimates of EQ-5D VAS in months					
25% quantile (95% CI)	2.43 (0.953 to 6.571)	1.51 (0.986 to 5.552)	2.43 (1.643 to 3.910)	1.97 (1.084 to 2.825)	
Median (95% CI)	7.44 (2.070 to NC)	9.20 (2.858 to NC)	6.93 (4.895 to 13.536)	8.18 (4.830 to 12.780)	
75% quantile (95% CI)	NC (6.571 to NC)	NC (9.199 to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.9176		0.9196	
Hazard ratio (95% CI) vs Kd	-	0.96 (0.40 to 2.27)		1.02 (0.74 to 1.40)	
P-value	-	0.9173		0.9198	
Deterioration probability (95% CI)[b]					

A higher score represents a better level of quality of life. Clinical meaningful deterioration change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.6.1 Health-related quality-of-life endpoints - EQ-5D
16.2.6.1.2 EQ-5D VAS
16.2.6.1.2.17 Efficacy response data - Subgroup analyses by previous treatment with PI and IMiD
16.2.6.1.2.17.5 EQ-5D - Time until permanent improvement by 10 pt in EQ-5D VAS according to previous treatment with PI and IMiD (LOCF) - ITT population

	Yes		No		
	Kd (N=17)	**IKd (N=23)**	**Kd (N=106)**	**IKd (N=156)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	3 (17.6)	7 (30.4)	26 (24.5)	41 (26.3)	0.4965
Number (%) of patients censored	14 (82.4)	16 (69.6)	80 (75.5)	115 (73.7)	
Kaplan-Meier estimates of EQ-5D VAS in months					
25% quantile (95% CI)	NC (1.051 to NC)	17.84 (1.906 to NC)	19.45 (11.959 to NC)	19.42 (12.977 to 22.341)	
Median (95% CI)	NC (NC to NC)	NC (17.840 to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.3921		0.7756	
Hazard ratio (95% CI) vs Kd	-	1.79 (0.46 to 6.93)		1.07 (0.66 to 1.76)	
P-value	-	0.3990		0.7757	

A higher score represents a better level of quality of life. Clinical meaningful improvement change from baseline greater than or equal to 10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
PGM=DEVOPS/SAR650984/EFC15246/CIR_RWE/REPORT/PGM/eff_km_subgp_sr_sig_de_i_t.sas OUT=REPORT/OUTPUT/eff_km_eq5d_vas_imppl_piimid_de_i_t_x.rtf (07APR2021 14:45)

16.2.6.1 Health-related quality-of-life endpoints - EQ-5D
16.2.6.1.2 EQ-5D VAS
16.2.6.1.2.17 Efficacy response data - Subgroup analyses by previous treatment with PI and IMiD
16.2.6.1.2.17.6 EQ-5D - Time until permanent deterioration by 10 pt in EQ-5D VAS according to previous treatment with PI and IMiD (LOCF) - ITT population

	Yes		No		
	Kd (N=17)	**IKd (N=23)**	**Kd (N=106)**	**IKd (N=156)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	3 (17.6)	8 (34.8)	26 (24.5)	42 (26.9)	0.3366
Number (%) of patients censored	14 (82.4)	15 (65.2)	80 (75.5)	114 (73.1)	
Kaplan-Meier estimates of EQ-5D VAS in months					
25% quantile (95% CI)	NC (1.314 to NC)	12.94 (1.511 to 23.097)	19.15 (13.634 to NC)	19.25 (9.265 to 24.444)	
Median (95% CI)	NC (NC to NC)	23.10 (12.945 to NC)	NC (NC to NC)	24.44 (23.129 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (23.097 to NC)	NC (NC to NC)	NC (24.444 to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.2495		0.6632	
Hazard ratio (95% CI) vs Kd	-	2.15 (0.57 to 8.16)		1.11 (0.68 to 1.82)	
P-value	-	0.2607		0.6633	

A higher score represents a better level of quality of life. Clinical meaningful deterioration change from baseline less than or equal to -10 pt.
The last observation carried forward (LOCF) procedure was applied to impute missing data.
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
NA/NC = Not Applicable / Not Calculable
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16.2.7.1 Safety endpoints

16.2.7.1.3 Non-progression treatment emergent adverse event by treatment group - Safety population

Any treatment emergent adverse event without progression events	**Kd (N=122)**	**IKd (N=177)**
Number (%) of events	117 (95.9)	172 (97.2)
Number (%) of patients censored	5 (4.1)	5 (2.8)
Kaplan-Meier estimates of TEAE in months		
25% quantile (95% CI)	0.20 (0.131 to 0.230)	0.07 (0.066 to 0.099)
Median (95% CI)	0.43 (0.329 to 0.591)	0.20 (0.131 to 0.230)
75% quantile (95% CI)	1.02 (0.657 to 1.478)	0.69 (0.427 to 1.117)
Comparison vs. Kd		
Log-Rank test p-value[a] vs Kd	-	0.0253
Hazard ratio (95% CI) vs Kd	-	1.31 (1.03 to 1.65)
P-value	-	0.0257
Hazard ratio inverted (95% CI) vs IKd	0.76 (0.60 to 0.97)	-
probability (95% CI)[b]		
3 Months	0.090 (0.048 to 0.149)	0.073 (0.041 to 0.118)
6 Months	0.049 (0.020 to 0.098)	0.045 (0.021 to 0.083)
9 Months	0.049 (0.020 to 0.098)	0.034 (0.014 to 0.068)
12 Months	0.049 (0.020 to 0.098)	0.028 (0.011 to 0.061)

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable

CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley

[a] One-sided significance level is 0.025

[b] Estimated using the Kaplan-Meier method

Note : Non-progression related TEAE (excluding the Neoplasms benign, malignant and unspecified)

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16.2.7.1 Safety endpoints

16.2.7.1.3 Non-progression treatment emergent adverse event by treatment group - Safety population

Any treatment emergent adverse event without progression events	**Kd (N=122)**	**IKd (N=177)**
15 Months	0.041 (0.015 to 0.087)	0.028 (0.011 to 0.061)
18 Months	0.041 (0.015 to 0.087)	0.028 (0.011 to 0.061)
21 Months	0.041 (0.015 to 0.087)	0.028 (0.011 to 0.061)
24 Months	0.041 (0.015 to 0.087)	0.028 (0.011 to 0.061)
27 Months	0.041 (0.015 to 0.087)	0.028 (0.011 to 0.061)
30 Months	0.041 (0.015 to 0.087)	0.028 (0.011 to 0.061)
Number of patients at risk[b]		
3 Months	11	13
6 Months	6	8
9 Months	6	6
12 Months	6	5
15 Months	5	5
18 Months	5	5
21 Months	3	5
24 Months	1	1
27 Months	0	0
30 Months	0	0

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable

CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley

[a] One-sided significance level is 0.025

[b] Estimated using the Kaplan-Meier method

Note : Non-progression related TEAE (excluding the Neoplasms benign, malignant and unspecified)

PGM=DEVOPS/SAR650984/EFC15246/CIR_RWE/REPORT/PGM/eff_km_sr_de_s_t.sas OUT=REPORT/OUTPUT/eff_km_de_teaenp_s_t_x.rtf (09FEB2021 15:16)

16.2.7.1 Safety endpoints

16.2.7.1.6 Non-progression treatment emergent serious adverse event by treatment group - Safety population

Treatment emergent serious adverse event without progression events	**Kd (N=122)**	**IKd (N=177)**
Number (%) of events	69 (56.6)	102 (57.6)
Number (%) of patients censored	53 (43.4)	75 (42.4)
Kaplan-Meier estimates of TEAE in months		
25% quantile (95% CI)	4.96 (2.957 to 5.848)	3.06 (1.314 to 5.618)
Median (95% CI)	13.86 (9.199 to NC)	12.55 (9.626 to 18.103)
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)
Comparison vs. Kd		
Log-Rank test p-value[a] vs Kd	-	0.6781
Hazard ratio (95% CI) vs Kd	-	1.07 (0.79 to 1.45)
P-value	-	0.6798
probability (95% CI)[b]		
3 Months	0.828 (0.748 to 0.884)	0.757 (0.687 to 0.814)
6 Months	0.662 (0.571 to 0.739)	0.671 (0.596 to 0.735)
9 Months	0.596 (0.503 to 0.677)	0.597 (0.520 to 0.665)
12 Months	0.545 (0.452 to 0.629)	0.522 (0.446 to 0.593)
15 Months	0.477 (0.385 to 0.563)	0.457 (0.381 to 0.529)

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable

CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley

[a] One-sided significance level is 0.025

[b] Estimated using the Kaplan-Meier method

Note : Non-progression related TEAE (excluding the Neoplasms benign, malignant and unspecified)

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16.2.7.1 Safety endpoints

16.2.7.1.6 Non-progression treatment emergent serious adverse event by treatment group - Safety population

Treatment emergent serious adverse event without progression events	**Kd (N=122)**	**IKd (N=177)**
18 Months	0.442 (0.351 to 0.528)	0.431 (0.356 to 0.504)
21 Months	0.433 (0.343 to 0.520)	0.425 (0.350 to 0.497)
24 Months	0.418 (0.327 to 0.507)	0.410 (0.335 to 0.483)
27 Months	0.418 (0.327 to 0.507)	0.410 (0.335 to 0.483)
30 Months	0.418 (0.327 to 0.507)	0.410 (0.335 to 0.483)
Number of patients at risk[b]		
3 Months	100	133
6 Months	80	117
9 Months	71	104
12 Months	65	91
15 Months	55	73
18 Months	50	66
21 Months	37	58
24 Months	10	19
27 Months	2	1
30 Months	0	0

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable

CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley

[a] One-sided significance level is 0.025

[b] Estimated using the Kaplan-Meier method

Note : Non-progression related TEAE (excluding the Neoplasms benign, malignant and unspecified)

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16.2.7.1 Safety endpoints

16.2.7.1.9 Non-progression treatment emergent adverse event leading to discontinuation of treatment by treatment group - Safety population

Any treatment emergent leading to discontinuation of treatment without progression events	**Kd (N=122)**	**IKd (N=177)**
Number (%) of events	16 (13.1)	12 (6.8)
Number (%) of patients censored	106 (86.9)	165 (93.2)
Kaplan-Meier estimates of TEAE in months		
25% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)
Median (95% CI)	NC (NC to NC)	NC (NC to NC)
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)
Comparison vs. Kd		
Log-Rank test p-value[a] vs Kd	-	0.0598
Hazard ratio (95% CI) vs Kd	-	0.49 (0.23 to 1.05)
P-value	-	0.0652
probability (95% CI)[b]		
3 Months	0.967 (0.915 to 0.988)	0.989 (0.955 to 0.997)
6 Months	0.942 (0.881 to 0.972)	0.965 (0.924 to 0.984)
9 Months	0.889 (0.816 to 0.934)	0.947 (0.901 to 0.972)
12 Months	0.889 (0.816 to 0.934)	0.947 (0.901 to 0.972)
15 Months	0.889 (0.816 to 0.934)	0.935 (0.885 to 0.963)

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable

CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley

[a] One-sided significance level is 0.025

[b] Estimated using the Kaplan-Meier method

Note : Non-progression related TEAE (excluding the Neoplasms benign, malignant and unspecified)

PGM=DEVOPS/SAR650984/EFC15246/CIR_RWE/REPORT/PGM/eff_km_sr_de_s_t.sas OUT=REPORT/OUTPUT/eff_km_de_tediscnp_s_t_x.rtf (09FEB2021 15:16)

16.2.7.1 Safety endpoints

16.2.7.1.9 Non-progression treatment emergent adverse event leading to discontinuation of treatment by treatment group - Safety population

Any treatment emergent leading to discontinuation of treatment without progression events	**Kd (N=122)**	**IKd (N=177)**
18 Months	0.869 (0.793 to 0.919)	0.935 (0.885 to 0.963)
21 Months	0.860 (0.781 to 0.912)	0.927 (0.876 to 0.958)
24 Months	0.860 (0.781 to 0.912)	0.927 (0.876 to 0.958)
27 Months	0.860 (0.781 to 0.912)	0.927 (0.876 to 0.958)
30 Months	0.860 (0.781 to 0.912)	0.927 (0.876 to 0.958)
Number of patients at risk[b]		
3 Months	116	172
6 Months	108	163
9 Months	99	156
12 Months	97	153
15 Months	92	141
18 Months	89	134
21 Months	73	118
24 Months	26	40
27 Months	4	2
30 Months	0	0

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable

CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley

[a] One-sided significance level is 0.025

[b] Estimated using the Kaplan-Meier method

Note : Non-progression related TEAE (excluding the Neoplasms benign, malignant and unspecified)

PGM=DEVOPS/SAR650984/EFC15246/CIR_RWE/REPORT/PGM/eff_km_sr_de_s_t.sas OUT=REPORT/OUTPUT/eff_km_de_tediscnp_s_t_x.rtf (09FEB2021 15:16)

16.2.7.1 Safety endpoints
16.2.7.1.10 Treatment emergent mild adverse event by treatment group - Safety population

Any treatment emergent by severity (Grade 1,2)	**Kd (N=122)**	**IKd (N=177)**
Number (%) of events	115 (94.3)	167 (94.4)
Number (%) of patients censored	7 (5.7)	10 (5.6)
Kaplan-Meier estimates of TEAE in months		
25% quantile (95% CI)	0.20 (0.131 to 0.263)	0.07 (0.066 to 0.099)
Median (95% CI)	0.53 (0.361 to 0.624)	0.20 (0.131 to 0.263)
75% quantile (95% CI)	1.18 (0.821 to 1.906)	0.99 (0.493 to 1.478)
Comparison vs. Kd		
Log-Rank test p-value[a] vs Kd	-	0.0513
Hazard ratio (95% CI) vs Kd	-	1.27 (1.00 to 1.61)
P-value	-	0.0519
probability (95% CI)[b]		
3 Months	0.117 (0.067 to 0.181)	0.109 (0.069 to 0.161)
6 Months	0.067 (0.031 to 0.121)	0.073 (0.040 to 0.118)
9 Months	0.067 (0.031 to 0.121)	0.053 (0.026 to 0.095)
12 Months	0.067 (0.031 to 0.121)	0.046 (0.021 to 0.087)
15 Months	0.048 (0.019 to 0.098)	0.046 (0.021 to 0.087)
18 Months	0.048 (0.019 to 0.098)	0.046 (0.021 to 0.087)

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
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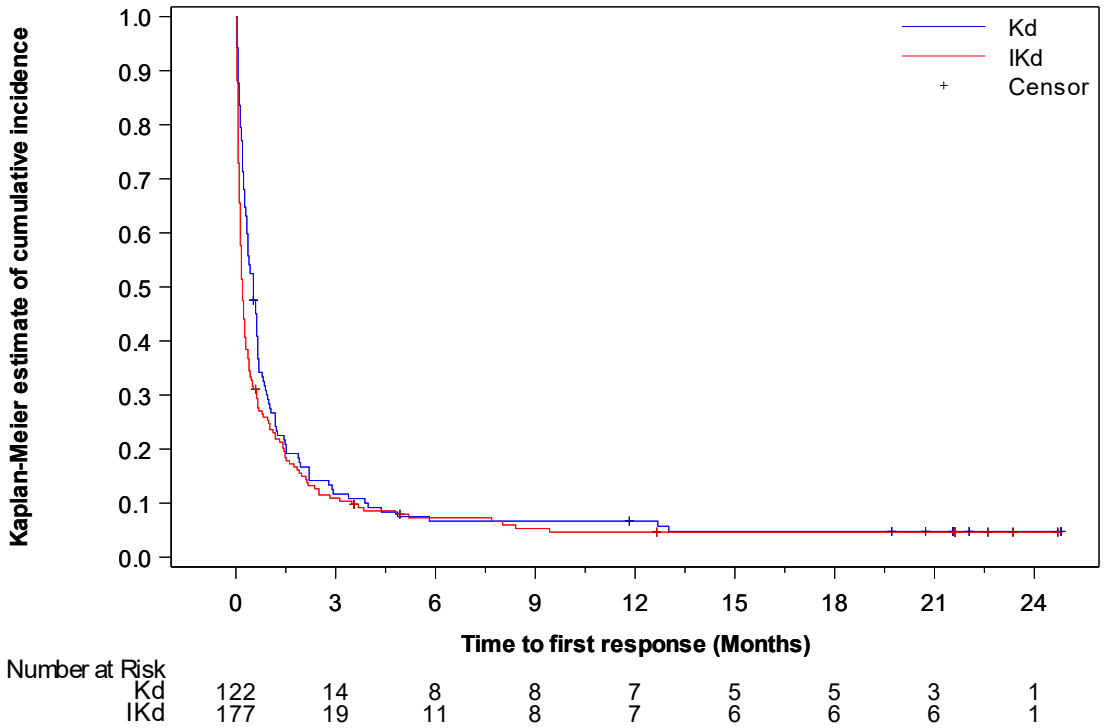
16.2.7.1 Safety endpoints
16.2.7.1.10 Treatment emergent mild adverse event by treatment group - Safety population

Any treatment emergent by severity (Grade 1,2)	**Kd (N=122)**	**IKd (N=177)**
21 Months	0.048 (0.019 to 0.098)	0.046 (0.021 to 0.087)
24 Months	0.048 (0.019 to 0.098)	0.046 (0.021 to 0.087)
27 Months	0.048 (0.019 to 0.098)	0.046 (0.021 to 0.087)
30 Months	0.048 (0.019 to 0.098)	0.046 (0.021 to 0.087)
Number of patients at risk[b]		
3 Months	14	19
6 Months	8	11
9 Months	8	8
12 Months	7	7
15 Months	5	6
18 Months	5	6
21 Months	3	6
24 Months	1	1
27 Months	0	0
30 Months	0	0

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
PGM=DEVOPS/SAR650984/EFC15246/CIR_RWE/REPORT/PGM/eff_km_sr_de_s_t.sas OUT=REPORT/OUTPUT/eff_km_de_tesev12_s_t_x.rtf (09FEB2021 15:16)

16.2.7.1 Safety endpoints

16.2.7.1.11 Kaplan-Meier cumulative incidence curve of treatment emergent mild adverse event by treatment group - Safety population



16.2.7.1 Safety endpoints
16.2.7.1.12 Non-progression treatment emergent mild adverse event by treatment group - Safety population

Any treatment emergent by severity (Grade 1,2) without progression events	**Kd (N=122)**	**IKd (N=177)**
Number (%) of events	115 (94.3)	167 (94.4)
Number (%) of patients censored	7 (5.7)	10 (5.6)
Kaplan-Meier estimates of TEAE in months		
25% quantile (95% CI)	0.20 (0.131 to 0.263)	0.07 (0.066 to 0.099)
Median (95% CI)	0.53 (0.361 to 0.624)	0.20 (0.131 to 0.263)
75% quantile (95% CI)	1.18 (0.821 to 1.906)	0.99 (0.493 to 1.478)
Comparison vs. Kd		
Log-Rank test p-value[a] vs Kd	-	0.0513
Hazard ratio (95% CI) vs Kd	-	1.27 (1.00 to 1.61)
P-value	-	0.0519
probability (95% CI)[b]		
3 Months	0.117 (0.067 to 0.181)	0.109 (0.069 to 0.161)
6 Months	0.067 (0.031 to 0.121)	0.073 (0.040 to 0.118)
9 Months	0.067 (0.031 to 0.121)	0.053 (0.026 to 0.095)
12 Months	0.067 (0.031 to 0.121)	0.046 (0.021 to 0.087)
15 Months	0.048 (0.019 to 0.098)	0.046 (0.021 to 0.087)

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
Note : Non-progression related TEAE (excluding the Neoplasms benign, malignant and unspecified)
PGM=DEVOPS/SAR650984/EFC15246/CIR_RWE/REPORT/PGM/eff_km_sr_de_s_t.sas OUT=REPORT/OUTPUT/eff_km_de_tesev12np_s_t_x.rtf (09FEB2021 15:16)

16.2.7.1 Safety endpoints

16.2.7.1.12 Non-progression treatment emergent mild adverse event by treatment group - Safety population

Any treatment emergent by severity (Grade 1,2) without progression events	**Kd (N=122)**	**IKd (N=177)**
18 Months	0.048 (0.019 to 0.098)	0.046 (0.021 to 0.087)
21 Months	0.048 (0.019 to 0.098)	0.046 (0.021 to 0.087)
24 Months	0.048 (0.019 to 0.098)	0.046 (0.021 to 0.087)
27 Months	0.048 (0.019 to 0.098)	0.046 (0.021 to 0.087)
30 Months	0.048 (0.019 to 0.098)	0.046 (0.021 to 0.087)
Number of patients at risk[b]		
3 Months	14	19
6 Months	8	11
9 Months	8	8
12 Months	7	7
15 Months	5	6
18 Months	5	6
21 Months	3	6
24 Months	1	1
27 Months	0	0
30 Months	0	0

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable

CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley

[a] One-sided significance level is 0.025

[b] Estimated using the Kaplan-Meier method

Note : Non-progression related TEAE (excluding the Neoplasms benign, malignant and unspecified)

PGM=DEVOPS/SAR650984/EFC15246/CIR_RWE/REPORT/PGM/eff_km_sr_de_s_t.sas OUT=REPORT/OUTPUT/eff_km_de_tesev12np_s_t_x.rtf (09FEB2021 15:16)

16.2.7.1 Safety endpoints
16.2.7.1.15 Non-progression treatment emergent severe adverse event by treatment group - Safety population

Any treatment emergent by severity (Grade 3,4) without progression events	**Kd (N=122)**	**IKd (N=177)**
Number (%) of events	81 (66.4)	131 (74.0)
Number (%) of patients censored	41 (33.6)	46 (26.0)
Kaplan-Meier estimates of TEAE in months		
25% quantile (95% CI)	2.07 (0.821 to 3.877)	1.31 (0.690 to 2.004)
Median (95% CI)	6.74 (4.961 to 10.809)	5.95 (4.797 to 7.819)
75% quantile (95% CI)	NC (16.854 to NC)	17.31 (11.499 to NC)
Comparison vs. Kd		
Log-Rank test p-value[a] vs Kd	-	0.1641
Hazard ratio (95% CI) vs Kd	-	1.22 (0.92 to 1.61)
P-value	-	0.1648
probability (95% CI)[b]		
3 Months	0.703 (0.613 to 0.776)	0.653 (0.578 to 0.719)
6 Months	0.544 (0.451 to 0.628)	0.491 (0.415 to 0.563)
9 Months	0.443 (0.353 to 0.529)	0.399 (0.326 to 0.471)
12 Months	0.400 (0.312 to 0.487)	0.306 (0.240 to 0.376)
15 Months	0.357 (0.272 to 0.443)	0.275 (0.211 to 0.343)

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
Note : Non-progression related TEAE (excluding the Neoplasms benign, malignant and unspecified)
PGM=DEVOPS/SAR650984/EFC15246/CIR_RWE/REPORT/PGM/eff_km_sr_de_s_t.sas OUT=REPORT/OUTPUT/eff_km_de_tesev34np_s_t_x.rtf (09FEB2021 15:16)

16.2.7.1 Safety endpoints

16.2.7.1.15 Non-progression treatment emergent severe adverse event by treatment group - Safety population

Any treatment emergent by severity (Grade 3,4) without progression events	**Kd (N=122)**	**IKd (N=177)**
18 Months	0.331 (0.248 to 0.416)	0.247 (0.185 to 0.315)
21 Months	0.331 (0.248 to 0.416)	0.240 (0.178 to 0.308)
24 Months	0.316 (0.232 to 0.402)	0.240 (0.178 to 0.308)
27 Months	0.316 (0.232 to 0.402)	0.240 (0.178 to 0.308)
30 Months	0.316 (0.232 to 0.402)	0.240 (0.178 to 0.308)
Number of patients at risk[b]		
3 Months	84	113
6 Months	65	85
9 Months	52	69
12 Months	47	53
15 Months	41	41
18 Months	37	35
21 Months	27	32
24 Months	8	10
27 Months	1	0
30 Months	0	0

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable

CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley

[a] One-sided significance level is 0.025

[b] Estimated using the Kaplan-Meier method

Note : Non-progression related TEAE (excluding the Neoplasms benign, malignant and unspecified)

PGM=DEVOPS/SAR650984/EFC15246/CIR_RWE/REPORT/PGM/eff_km_sr_de_s_t.sas OUT=REPORT/OUTPUT/eff_km_de_tesev34np_s_t_x.rtf (09FEB2021 15:16)

16.2.7.1 Safety endpoints

16.2.7.1.18 Non-progression treatment emergent severe adverse event including death by treatment group - Safety population

Any treatment emergent by severity (Grade 3,4,5) without progression events	**Kd (N=122)**	**IKd (N=177)**
Number (%) of events	82 (67.2)	133 (75.1)
Number (%) of patients censored	40 (32.8)	44 (24.9)
Kaplan-Meier estimates of TEAE in months		
25% quantile (95% CI)	1.87 (0.821 to 3.285)	1.28 (0.657 to 1.971)
Median (95% CI)	6.57 (4.928 to 10.480)	5.95 (4.764 to 7.819)
75% quantile (95% CI)	NC (16.854 to NC)	16.76 (11.433 to NC)
Comparison vs. Kd		
Log-Rank test p-value[a] vs Kd	-	0.1541
Hazard ratio (95% CI) vs Kd	-	1.22 (0.93 to 1.61)
P-value	-	0.1548
probability (95% CI)[b]		
3 Months	0.696 (0.606 to 0.770)	0.649 (0.574 to 0.714)
6 Months	0.539 (0.446 to 0.623)	0.488 (0.412 to 0.560)
9 Months	0.439 (0.349 to 0.525)	0.396 (0.324 to 0.468)
12 Months	0.396 (0.309 to 0.482)	0.304 (0.238 to 0.373)
15 Months	0.354 (0.269 to 0.439)	0.268 (0.204 to 0.335)

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable

CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley

[a] One-sided significance level is 0.025

[b] Estimated using the Kaplan-Meier method

Note : Non-progression related TEAE (excluding the Neoplasms benign, malignant and unspecified)

PGM=DEVOPS/SAR650984/EFC15246/CIR_RWE/REPORT/PGM/eff_km_sr_de_s_t.sas OUT=REPORT/OUTPUT/eff_km_de_tesev345np_s_t_x.rtf (09FEB2021 15:16)

16.2.7.1 Safety endpoints

16.2.7.1.18 Non-progression treatment emergent severe adverse event including death by treatment group - Safety population

Any treatment emergent by severity (Grade 3,4,5) without progression events	**Kd (N=122)**	**IKd (N=177)**
18 Months	0.327 (0.245 to 0.412)	0.241 (0.179 to 0.308)
21 Months	0.327 (0.245 to 0.412)	0.234 (0.173 to 0.300)
24 Months	0.313 (0.230 to 0.399)	0.234 (0.173 to 0.300)
27 Months	0.313 (0.230 to 0.399)	0.234 (0.173 to 0.300)
30 Months	0.313 (0.230 to 0.399)	0.234 (0.173 to 0.300)
Number of patients at risk[b]		
3 Months	84	113
6 Months	65	85
9 Months	52	69
12 Months	47	53
15 Months	41	41
18 Months	37	35
21 Months	27	32
24 Months	8	10
27 Months	1	0
30 Months	0	0

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable

CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley

[a] One-sided significance level is 0.025

[b] Estimated using the Kaplan-Meier method

Note : Non-progression related TEAE (excluding the Neoplasms benign, malignant and unspecified)

PGM=DEVOPS/SAR650984/EFC15246/CIR_RWE/REPORT/PGM/eff_km_sr_de_s_t.sas OUT=REPORT/OUTPUT/eff_km_de_tesev345np_s_t_x.rtf (09FEB2021 15:16)

16.2.7.1 Safety endpoints
16.2.7.1.19 Treatment emergent mild (grade 1) adverse event by treatment group - Safety population

Any treatment emergent by severity (Grade 1)	**Kd (N=122)**	**IKd (N=177)**
Number (%) of events	105 (86.1)	155 (87.6)
Number (%) of patients censored	17 (13.9)	22 (12.4)
Kaplan-Meier estimates of TEAE in months		
25% quantile (95% CI)	0.36 (0.197 to 0.526)	0.16 (0.099 to 0.197)
Median (95% CI)	1.02 (0.624 to 1.741)	0.62 (0.361 to 1.018)
75% quantile (95% CI)	4.37 (2.168 to 9.495)	2.96 (1.774 to 5.224)
Comparison vs. Kd		
Log-Rank test p-value[a] vs Kd	-	0.1068
Hazard ratio (95% CI) vs Kd	-	1.23 (0.96 to 1.57)
P-value	-	0.1074
probability (95% CI)[b]		
3 Months	0.307 (0.227 to 0.390)	0.245 (0.184 to 0.310)
6 Months	0.211 (0.143 to 0.288)	0.171 (0.119 to 0.232)
9 Months	0.193 (0.127 to 0.269)	0.126 (0.081 to 0.181)
12 Months	0.165 (0.104 to 0.238)	0.112 (0.070 to 0.166)
15 Months	0.146 (0.088 to 0.217)	0.105 (0.064 to 0.159)
18 Months	0.116 (0.065 to 0.183)	0.105 (0.064 to 0.159)

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
PGM=DEVOPS/SAR650984/EFC15246/CIR_RWE/REPORT/PGM/eff_km_sr_de_s_t.sas OUT=REPORT/OUTPUT/eff_km_de_tesev1_s_t_x.rtf (09FEB2021 15:16)

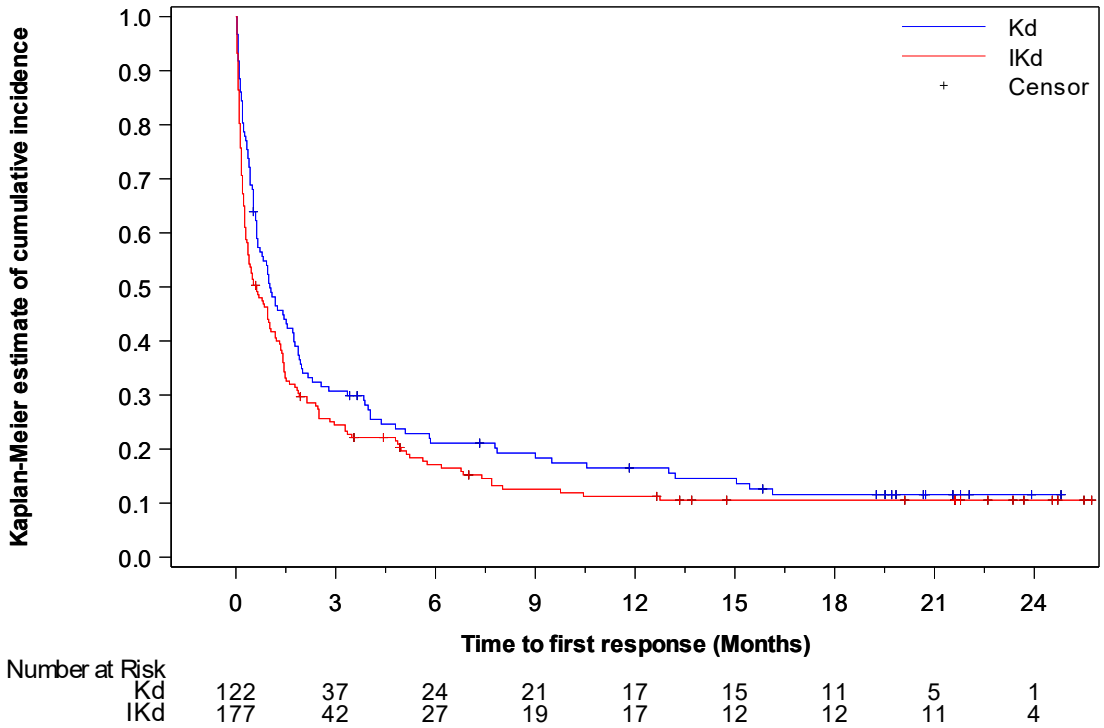
16.2.7.1 Safety endpoints
16.2.7.1.19 Treatment emergent mild (grade 1) adverse event by treatment group - Safety population

Any treatment emergent by severity (Grade 1)	**Kd (N=122)**	**IKd (N=177)**
21 Months	0.116 (0.065 to 0.183)	0.105 (0.064 to 0.159)
24 Months	0.116 (0.065 to 0.183)	0.105 (0.064 to 0.159)
27 Months	0.116 (0.065 to 0.183)	0.105 (0.064 to 0.159)
30 Months	0.116 (0.065 to 0.183)	0.105 (0.064 to 0.159)
Number of patients at risk[b]		
3 Months	37	42
6 Months	24	27
9 Months	21	19
12 Months	17	17
15 Months	15	12
18 Months	11	12
21 Months	5	11
24 Months	1	4
27 Months	0	0
30 Months	0	0

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
PGM=DEVOPS/SAR650984/EFC15246/CIR_RWE/REPORT/PGM/eff_km_sr_de_s_t.sas OUT=REPORT/OUTPUT/eff_km_de_tesev1_s_t_x.rtf (09FEB2021 15:16)

16.2.7.1 Safety endpoints

16.2.7.1.20 Kaplan-Meier cumulative incidence curve of treatment emergent mild (grade 1) adverse event by treatment group - Safety population



16.2.7.1 Safety endpoints
16.2.7.1.21 Non-progression treatment emergent mild (grade 1) adverse event by treatment group - Safety population

Any treatment emergent by severity (Grade 1) without progression events	**Kd (N=122)**	**IKd (N=177)**
Number (%) of events	105 (86.1)	155 (87.6)
Number (%) of patients censored	17 (13.9)	22 (12.4)
Kaplan-Meier estimates of TEAE in months		
25% quantile (95% CI)	0.36 (0.197 to 0.526)	0.16 (0.099 to 0.197)
Median (95% CI)	1.02 (0.624 to 1.741)	0.62 (0.361 to 1.018)
75% quantile (95% CI)	4.37 (2.168 to 9.495)	2.96 (1.774 to 5.224)
Comparison vs. Kd		
Log-Rank test p-value[a] vs Kd	-	0.1068
Hazard ratio (95% CI) vs Kd	-	1.23 (0.96 to 1.57)
P-value	-	0.1074
probability (95% CI)[b]		
3 Months	0.307 (0.227 to 0.390)	0.245 (0.184 to 0.310)
6 Months	0.211 (0.143 to 0.288)	0.171 (0.119 to 0.232)
9 Months	0.193 (0.127 to 0.269)	0.126 (0.081 to 0.181)
12 Months	0.165 (0.104 to 0.238)	0.112 (0.070 to 0.166)
15 Months	0.146 (0.088 to 0.217)	0.105 (0.064 to 0.159)

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
Note : Non-progression related TEAE (excluding the Neoplasms benign, malignant and unspecified)
PGM=DEVOPS/SAR650984/EFC15246/CIR_RWE/REPORT/PGM/eff_km_sr_de_s_t.sas OUT=REPORT/OUTPUT/eff_km_de_tesev1np_s_t_x.rtf (09FEB2021 15:16)

16.2.7.1 Safety endpoints
16.2.7.1.21 Non-progression treatment emergent mild (grade 1) adverse event by treatment group - Safety population

Any treatment emergent by severity (Grade 1) without progression events	**Kd (N=122)**	**IKd (N=177)**
18 Months	0.116 (0.065 to 0.183)	0.105 (0.064 to 0.159)
21 Months	0.116 (0.065 to 0.183)	0.105 (0.064 to 0.159)
24 Months	0.116 (0.065 to 0.183)	0.105 (0.064 to 0.159)
27 Months	0.116 (0.065 to 0.183)	0.105 (0.064 to 0.159)
30 Months	0.116 (0.065 to 0.183)	0.105 (0.064 to 0.159)
Number of patients at risk[b]		
3 Months	37	42
6 Months	24	27
9 Months	21	19
12 Months	17	17
15 Months	15	12
18 Months	11	12
21 Months	5	11
24 Months	1	4
27 Months	0	0
30 Months	0	0

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
Note : Non-progression related TEAE (excluding the Neoplasms benign, malignant and unspecified)
PGM=DEVOPS/SAR650984/EFC15246/CIR_RWE/REPORT/PGM/eff_km_sr_de_s_t.sas OUT=REPORT/OUTPUT/eff_km_de_tesev1np_s_t_x.rtf (09FEB2021 15:16)

16.2.7.1 Safety endpoints
16.2.7.1.22 Treatment emergent moderate (grade 2) adverse event by treatment group - Safety population

Any treatment emergent by severity (Grade 2)	**Kd (N=122)**	**IKd (N=177)**
Number (%) of events	108 (88.5)	164 (92.7)
Number (%) of patients censored	14 (11.5)	13 (7.3)
Kaplan-Meier estimates of TEAE in months		
25% quantile (95% CI)	0.36 (0.263 to 0.624)	0.13 (0.066 to 0.164)
Median (95% CI)	1.18 (0.723 to 1.774)	0.62 (0.394 to 1.051)
75% quantile (95% CI)	3.75 (2.201 to 7.524)	2.63 (1.840 to 4.172)
Comparison vs. Kd		
Log-Rank test p-value[a] vs Kd	-	0.0163
Hazard ratio (95% CI) vs Kd	-	1.35 (1.06 to 1.72)
P-value	-	0.0167
Hazard ratio inverted (95% CI) vs IKd	0.74 (0.58 to 0.95)	-
probability (95% CI)[b]		
3 Months	0.298 (0.219 to 0.381)	0.242 (0.182 to 0.308)
6 Months	0.204 (0.137 to 0.280)	0.129 (0.084 to 0.184)
9 Months	0.162 (0.102 to 0.233)	0.092 (0.054 to 0.142)
12 Months	0.135 (0.080 to 0.203)	0.061 (0.032 to 0.105)
15 Months	0.093 (0.048 to 0.157)	0.055 (0.027 to 0.097)

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
PGM=DEVOPS/SAR650984/EFC15246/CIR_RWE/REPORT/PGM/eff_km_sr_de_s_t.sas OUT=REPORT/OUTPUT/eff_km_de_tesev2_s_t_x.rtf (09FEB2021 15:16)

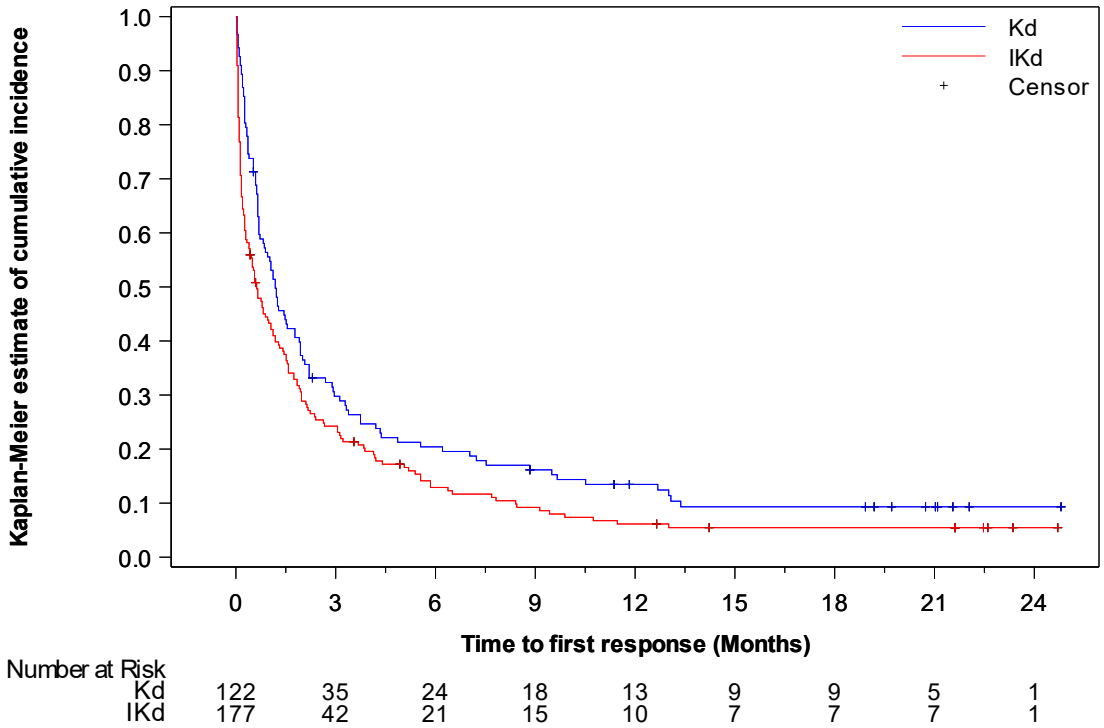
16.2.7.1 Safety endpoints
16.2.7.1.22 Treatment emergent moderate (grade 2) adverse event by treatment group - Safety population

Any treatment emergent by severity (Grade 2)	**Kd (N=122)**	**IKd (N=177)**
18 Months	0.093 (0.048 to 0.157)	0.055 (0.027 to 0.097)
21 Months	0.093 (0.048 to 0.157)	0.055 (0.027 to 0.097)
24 Months	0.093 (0.048 to 0.157)	0.055 (0.027 to 0.097)
27 Months	0.093 (0.048 to 0.157)	0.055 (0.027 to 0.097)
30 Months	0.093 (0.048 to 0.157)	0.055 (0.027 to 0.097)
Number of patients at risk[b]		
3 Months	35	42
6 Months	24	21
9 Months	18	15
12 Months	13	10
15 Months	9	7
18 Months	9	7
21 Months	5	7
24 Months	1	1
27 Months	0	0
30 Months	0	0

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
PGM=DEVOPS/SAR650984/EFC15246/CIR_RWE/REPORT/PGM/eff_km_sr_de_s_t.sas OUT=REPORT/OUTPUT/eff_km_de_tesev2_s_t_x.rtf (09FEB2021 15:16)

16.2.7.1 Safety endpoints

16.2.7.1.23 Kaplan-Meier cumulative incidence curve of treatment emergent moderate (grade 2) adverse event by treatment group - Safety population



16.2.7.1 Safety endpoints
16.2.7.1.24 Non-progression treatment emergent moderate (grade 2) adverse event by treatment group - Safety population

Any treatment emergent by severity (Grade 2) without progression events	**Kd (N=122)**	**IKd (N=177)**
Number (%) of events	108 (88.5)	164 (92.7)
Number (%) of patients censored	14 (11.5)	13 (7.3)
Kaplan-Meier estimates of TEAE in months		
25% quantile (95% CI)	0.36 (0.263 to 0.624)	0.13 (0.066 to 0.164)
Median (95% CI)	1.18 (0.723 to 1.774)	0.62 (0.394 to 1.051)
75% quantile (95% CI)	3.75 (2.201 to 7.524)	2.63 (1.840 to 4.172)
Comparison vs. Kd		
Log-Rank test p-value[a] vs Kd	-	0.0154
Hazard ratio (95% CI) vs Kd	-	1.35 (1.06 to 1.72)
P-value	-	0.0158
Hazard ratio inverted (95% CI) vs IKd	0.74 (0.58 to 0.95)	-
probability (95% CI)[b]		
3 Months	0.298 (0.219 to 0.381)	0.242 (0.182 to 0.308)
6 Months	0.204 (0.137 to 0.280)	0.129 (0.084 to 0.184)
9 Months	0.162 (0.102 to 0.233)	0.092 (0.054 to 0.142)
12 Months	0.135 (0.080 to 0.203)	0.061 (0.032 to 0.105)

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
Note : Non-progression related TEAE (excluding the Neoplasms benign, malignant and unspecified)
PGM=DEVOPS/SAR650984/EFC15246/CIR_RWE/REPORT/PGM/eff_km_sr_de_s_t.sas OUT=REPORT/OUTPUT/eff_km_de_tesev2np_s_t_x.rtf (09FEB2021 15:16)

16.2.7.1 Safety endpoints

16.2.7.1.24 Non-progression treatment emergent moderate (grade 2) adverse event by treatment group - Safety population

Any treatment emergent by severity (Grade 2) without progression events	**Kd (N=122)**	**IKd (N=177)**
15 Months	0.093 (0.048 to 0.157)	0.055 (0.027 to 0.097)
18 Months	0.093 (0.048 to 0.157)	0.055 (0.027 to 0.097)
21 Months	0.093 (0.048 to 0.157)	0.055 (0.027 to 0.097)
24 Months	0.093 (0.048 to 0.157)	0.055 (0.027 to 0.097)
27 Months	0.093 (0.048 to 0.157)	0.055 (0.027 to 0.097)
30 Months	0.093 (0.048 to 0.157)	0.055 (0.027 to 0.097)
Number of patients at risk[b]		
3 Months	35	42
6 Months	24	21
9 Months	18	15
12 Months	13	10
15 Months	9	7
18 Months	9	7
21 Months	5	7
24 Months	1	1
27 Months	0	0
30 Months	0	0

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable

CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley

[a] One-sided significance level is 0.025

[b] Estimated using the Kaplan-Meier method

Note : Non-progression related TEAE (excluding the Neoplasms benign, malignant and unspecified)

PGM=DEVOPS/SAR650984/EFC15246/CIR_RWE/REPORT/PGM/eff_km_sr_de_s_t.sas OUT=REPORT/OUTPUT/eff_km_de_tesev2np_s_t_x.rtf (09FEB2021 15:16)

16.2.7.1 Safety endpoints
16.2.7.1.25 Treatment emergent severe (grade 3) adverse event by treatment group - Safety population

Any treatment emergent by severity (Grade 3)	**Kd (N=122)**	**IKd (N=177)**
Number (%) of events	76 (62.3)	129 (72.9)
Number (%) of patients censored	46 (37.7)	48 (27.1)
Kaplan-Meier estimates of TEAE in months		
25% quantile (95% CI)	2.40 (1.117 to 4.041)	1.31 (0.723 to 2.103)
Median (95% CI)	7.85 (5.487 to 13.240)	6.41 (4.928 to 8.444)
75% quantile (95% CI)	NC (NC to NC)	19.12 (12.912 to NC)
Comparison vs. Kd		
Log-Rank test p-value[a] vs Kd	-	0.0525
Hazard ratio (95% CI) vs Kd	-	1.32 (1.00 to 1.76)
P-value	-	0.0532
probability (95% CI)[b]		
3 Months	0.728 (0.640 to 0.798)	0.653 (0.578 to 0.718)
6 Months	0.577 (0.484 to 0.660)	0.503 (0.426 to 0.574)
9 Months	0.476 (0.384 to 0.562)	0.415 (0.341 to 0.487)
12 Months	0.442 (0.352 to 0.529)	0.326 (0.257 to 0.396)
15 Months	0.390 (0.303 to 0.477)	0.287 (0.221 to 0.356)
18 Months	0.363 (0.277 to 0.450)	0.259 (0.195 to 0.327)

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
PGM=DEVOPS/SAR650984/EFC15246/CIR_RWE/REPORT/PGM/eff_km_sr_de_s_t.sas OUT=REPORT/OUTPUT/eff_km_de_tesev3_s_t_x.rtf (09FEB2021 15:16)

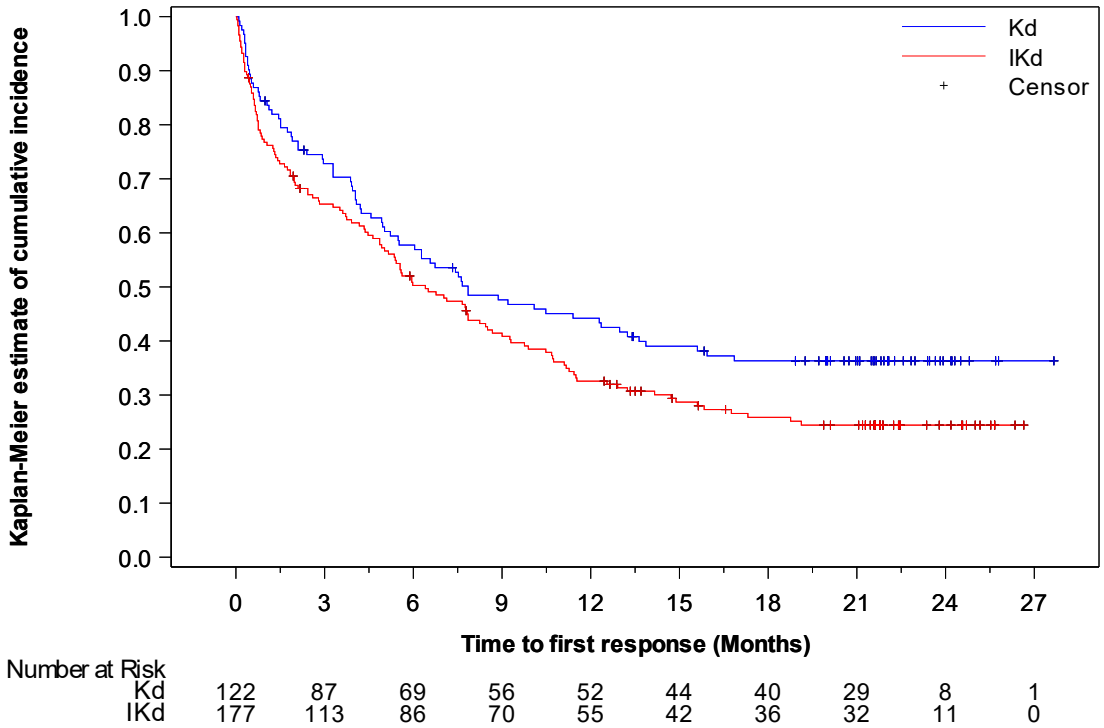
16.2.7.1 Safety endpoints
16.2.7.1.25 Treatment emergent severe (grade 3) adverse event by treatment group - Safety population

Any treatment emergent by severity (Grade 3)	**Kd (N=122)**	**IKd (N=177)**
21 Months	0.363 (0.277 to 0.450)	0.244 (0.181 to 0.313)
24 Months	0.363 (0.277 to 0.450)	0.244 (0.181 to 0.313)
27 Months	0.363 (0.277 to 0.450)	0.244 (0.181 to 0.313)
30 Months	0.363 (0.277 to 0.450)	0.244 (0.181 to 0.313)
Number of patients at risk[b]		
3 Months	87	113
6 Months	69	86
9 Months	56	70
12 Months	52	55
15 Months	44	42
18 Months	40	36
21 Months	29	32
24 Months	8	11
27 Months	1	0
30 Months	0	0

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
PGM=DEVOPS/SAR650984/EFC15246/CIR_RWE/REPORT/PGM/eff_km_sr_de_s_t.sas OUT=REPORT/OUTPUT/eff_km_de_tesev3_s_t_x.rtf (09FEB2021 15:16)

16.2.7.1 Safety endpoints

16.2.7.1.26 Kaplan-Meier cumulative incidence curve of treatment emergent severe (grade 3) adverse event by treatment group - Safety population



16.2.7.1 Safety endpoints
16.2.7.1.27 Non-progression treatment emergent severe (grade 3) adverse event by treatment group - Safety population

Any treatment emergent by severity (Grade 3) without progression events	**Kd (N=122)**	**IKd (N=177)**
Number (%) of events	76 (62.3)	127 (71.8)
Number (%) of patients censored	46 (37.7)	50 (28.2)
Kaplan-Meier estimates of TEAE in months		
25% quantile (95% CI)	2.92 (1.117 to 4.041)	1.31 (0.723 to 2.103)
Median (95% CI)	7.85 (5.520 to 13.240)	6.51 (5.027 to 8.509)
75% quantile (95% CI)	NC (NC to NC)	NC (13.240 to NC)
Comparison vs. Kd		
Log-Rank test p-value[a] vs Kd	-	0.0748
Hazard ratio (95% CI) vs Kd	-	1.29 (0.97 to 1.72)
P-value	-	0.0756
probability (95% CI)[b]		
3 Months	0.736 (0.648 to 0.806)	0.659 (0.584 to 0.724)
6 Months	0.586 (0.492 to 0.668)	0.509 (0.432 to 0.580)
9 Months	0.476 (0.384 to 0.562)	0.420 (0.346 to 0.492)
12 Months	0.442 (0.352 to 0.528)	0.332 (0.262 to 0.402)
15 Months	0.390 (0.303 to 0.477)	0.300 (0.233 to 0.370)

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
Note : Non-progression related TEAE (excluding the Neoplasms benign, malignant and unspecified)
PGM=DEVOPS/SAR650984/EFC15246/CIR_RWE/REPORT/PGM/eff_km_sr_de_s_t.sas OUT=REPORT/OUTPUT/eff_km_de_tesev3np_s_t_x.rtf (09FEB2021 15:16)

16.2.7.1 Safety endpoints

16.2.7.1.27 Non-progression treatment emergent severe (grade 3) adverse event by treatment group - Safety population

Any treatment emergent by severity (Grade 3) without progression events	**Kd (N=122)**	**IKd (N=177)**
18 Months	0.363 (0.277 to 0.449)	0.272 (0.206 to 0.341)
21 Months	0.363 (0.277 to 0.449)	0.257 (0.193 to 0.326)
24 Months	0.363 (0.277 to 0.449)	0.257 (0.193 to 0.326)
27 Months	0.363 (0.277 to 0.449)	0.257 (0.193 to 0.326)
30 Months	0.363 (0.277 to 0.449)	0.257 (0.193 to 0.326)
Number of patients at risk[b]		
3 Months	88	114
6 Months	70	87
9 Months	56	71
12 Months	52	56
15 Months	44	44
18 Months	40	38
21 Months	29	33
24 Months	8	11
27 Months	1	0
30 Months	0	0

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable

CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley

[a] One-sided significance level is 0.025

[b] Estimated using the Kaplan-Meier method

Note : Non-progression related TEAE (excluding the Neoplasms benign, malignant and unspecified)

PGM=DEVOPS/SAR650984/EFC15246/CIR_RWE/REPORT/PGM/eff_km_sr_de_s_t.sas OUT=REPORT/OUTPUT/eff_km_de_tesev3np_s_t_x.rtf (09FEB2021 15:16)

16.2.7.1 Safety endpoints
16.2.7.1.28 Treatment emergent severe (grade 4) adverse event by treatment group - Safety population

Any treatment emergent by severity (Grade 4)	**Kd (N=122)**	**IKd (N=177)**
Number (%) of events	19 (15.6)	21 (11.9)
Number (%) of patients censored	103 (84.4)	156 (88.1)
Kaplan-Meier estimates of TEAE in months		
25% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)
Median (95% CI)	NC (NC to NC)	NC (NC to NC)
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)
Comparison vs. Kd		
Log-Rank test p-value[a] vs Kd	-	0.3089
Hazard ratio (95% CI) vs Kd	-	0.73 (0.39 to 1.35)
P-value	-	0.3110
probability (95% CI)[b]		
3 Months	0.918 (0.852 to 0.955)	0.960 (0.918 to 0.981)
6 Months	0.867 (0.791 to 0.916)	0.925 (0.875 to 0.956)
9 Months	0.858 (0.781 to 0.909)	0.913 (0.860 to 0.947)
12 Months	0.849 (0.771 to 0.902)	0.895 (0.839 to 0.933)
15 Months	0.849 (0.771 to 0.902)	0.877 (0.817 to 0.918)
18 Months	0.849 (0.771 to 0.902)	0.877 (0.817 to 0.918)

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
PGM=DEVOPS/SAR650984/EFC15246/CIR_RWE/REPORT/PGM/eff_km_sr_de_s_t.sas OUT=REPORT/OUTPUT/eff_km_de_tesev4_s_t_x.rtf (09FEB2021 15:16)

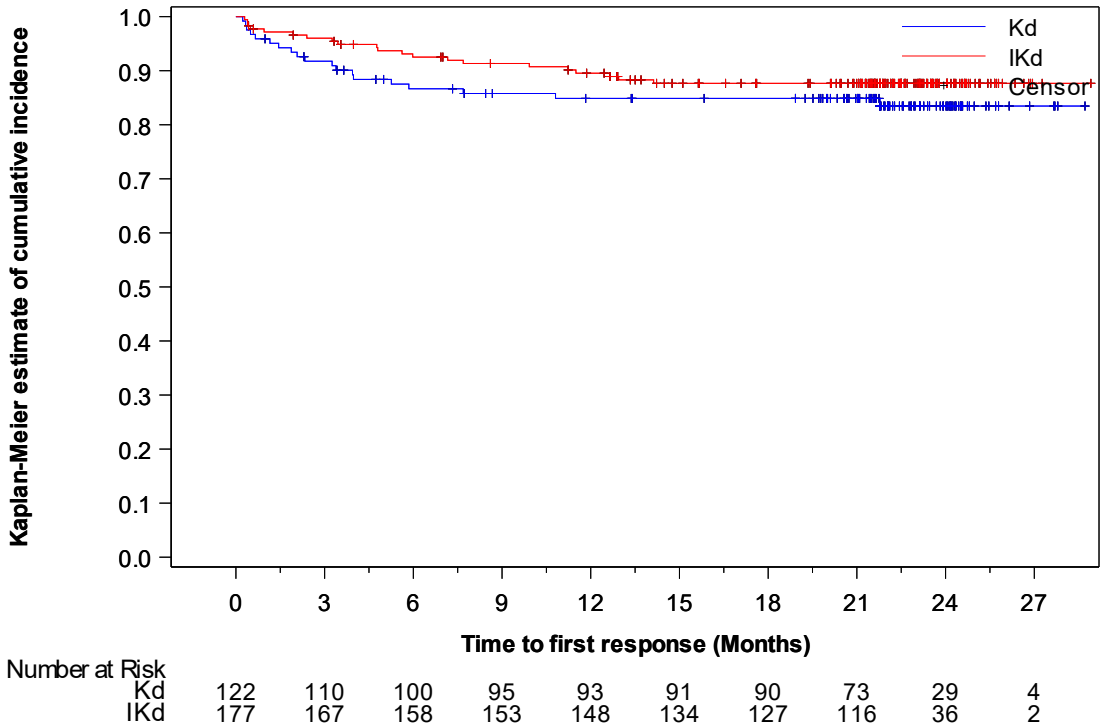
16.2.7.1 Safety endpoints
16.2.7.1.28 Treatment emergent severe (grade 4) adverse event by treatment group - Safety population

Any treatment emergent by severity (Grade 4)	**Kd (N=122)**	**IKd (N=177)**
21 Months	0.849 (0.771 to 0.902)	0.877 (0.817 to 0.918)
24 Months	0.835 (0.751 to 0.892)	0.877 (0.817 to 0.918)
27 Months	0.835 (0.751 to 0.892)	0.877 (0.817 to 0.918)
30 Months	0.835 (0.751 to 0.892)	0.877 (0.817 to 0.918)
Number of patients at risk[b]		
3 Months	110	167
6 Months	100	158
9 Months	95	153
12 Months	93	148
15 Months	91	134
18 Months	90	127
21 Months	73	116
24 Months	29	36
27 Months	4	2
30 Months	0	0

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
PGM=DEVOPS/SAR650984/EFC15246/CIR_RWE/REPORT/PGM/eff_km_sr_de_s_t.sas OUT=REPORT/OUTPUT/eff_km_de_tesev4_s_t_x.rtf (09FEB2021 15:16)

16.2.7.1 Safety endpoints

16.2.7.1.29 Kaplan-Meier cumulative incidence curve of treatment emergent severe (grade 4) adverse event by treatment group - Safety population



16.2.7.1 Safety endpoints
16.2.7.1.30 Non-progression treatment emergent severe (grade 4) adverse event by treatment group - Safety population

Any treatment emergent by severity (Grade 4) without progression events	**Kd (N=122)**	**IKd (N=177)**
Number (%) of events	19 (15.6)	20 (11.3)
Number (%) of patients censored	103 (84.4)	157 (88.7)
Kaplan-Meier estimates of TEAE in months		
25% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)
Median (95% CI)	NC (NC to NC)	NC (NC to NC)
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)
Comparison vs. Kd		
Log-Rank test p-value[a] vs Kd	-	0.2436
Hazard ratio (95% CI) vs Kd	-	0.69 (0.37 to 1.29)
P-value	-	0.2463
probability (95% CI)[b]		
3 Months	0.918 (0.852 to 0.955)	0.966 (0.926 to 0.985)
6 Months	0.867 (0.791 to 0.916)	0.931 (0.881 to 0.960)
9 Months	0.858 (0.781 to 0.909)	0.919 (0.867 to 0.951)
12 Months	0.849 (0.771 to 0.902)	0.901 (0.845 to 0.937)
15 Months	0.849 (0.771 to 0.902)	0.882 (0.823 to 0.922)

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
Note : Non-progression related TEAE (excluding the Neoplasms benign, malignant and unspecified)
PGM=DEVOPS/SAR650984/EFC15246/CIR_RWE/REPORT/PGM/eff_km_sr_de_s_t.sas OUT=REPORT/OUTPUT/eff_km_de_tesev4np_s_t_x.rtf (09FEB2021 15:16)

16.2.7.1 Safety endpoints

16.2.7.1.30 Non-progression treatment emergent severe (grade 4) adverse event by treatment group - Safety population

Any treatment emergent by severity (Grade 4) without progression events	**Kd (N=122)**	**IKd (N=177)**
18 Months	0.849 (0.771 to 0.902)	0.882 (0.823 to 0.922)
21 Months	0.849 (0.771 to 0.902)	0.882 (0.823 to 0.922)
24 Months	0.835 (0.751 to 0.892)	0.882 (0.823 to 0.922)
27 Months	0.835 (0.751 to 0.892)	0.882 (0.823 to 0.922)
30 Months	0.835 (0.751 to 0.892)	0.882 (0.823 to 0.922)
Number of patients at risk[b]		
3 Months	110	167
6 Months	100	158
9 Months	95	153
12 Months	93	148
15 Months	91	134
18 Months	90	127
21 Months	73	116
24 Months	29	36
27 Months	4	2
30 Months	0	0

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable

CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley

[a] One-sided significance level is 0.025

[b] Estimated using the Kaplan-Meier method

Note : Non-progression related TEAE (excluding the Neoplasms benign, malignant and unspecified)

PGM=DEVOPS/SAR650984/EFC15246/CIR_RWE/REPORT/PGM/eff_km_sr_de_s_t.sas OUT=REPORT/OUTPUT/eff_km_de_tesev4np_s_t_x.rtf (09FEB2021 15:16)

16.2.7.1 Safety endpoints
16.2.7.1.31 Treatment emergent severe (grade 5) adverse event by treatment group - Safety population

Any treatment emergent by severity (Grade 5)	**Kd (N=122)**	**IKd (N=177)**
Number (%) of events	4 (3.3)	6 (3.4)
Number (%) of patients censored	118 (96.7)	171 (96.6)
Kaplan-Meier estimates of TEAE in months		
25% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)
Median (95% CI)	NC (NC to NC)	NC (NC to NC)
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)
Comparison vs. Kd		
Log-Rank test p-value[a] vs Kd	-	0.9687
Hazard ratio (95% CI) vs Kd	-	1.03 (0.29 to 3.63)
P-value	-	0.9687
probability (95% CI)[b]		
3 Months	0.984 (0.936 to 0.996)	0.989 (0.956 to 0.997)
6 Months	0.984 (0.936 to 0.996)	0.977 (0.940 to 0.991)
9 Months	0.966 (0.912 to 0.987)	0.977 (0.940 to 0.991)
12 Months	0.966 (0.912 to 0.987)	0.971 (0.932 to 0.988)
15 Months	0.966 (0.912 to 0.987)	0.965 (0.923 to 0.984)
18 Months	0.966 (0.912 to 0.987)	0.965 (0.923 to 0.984)

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
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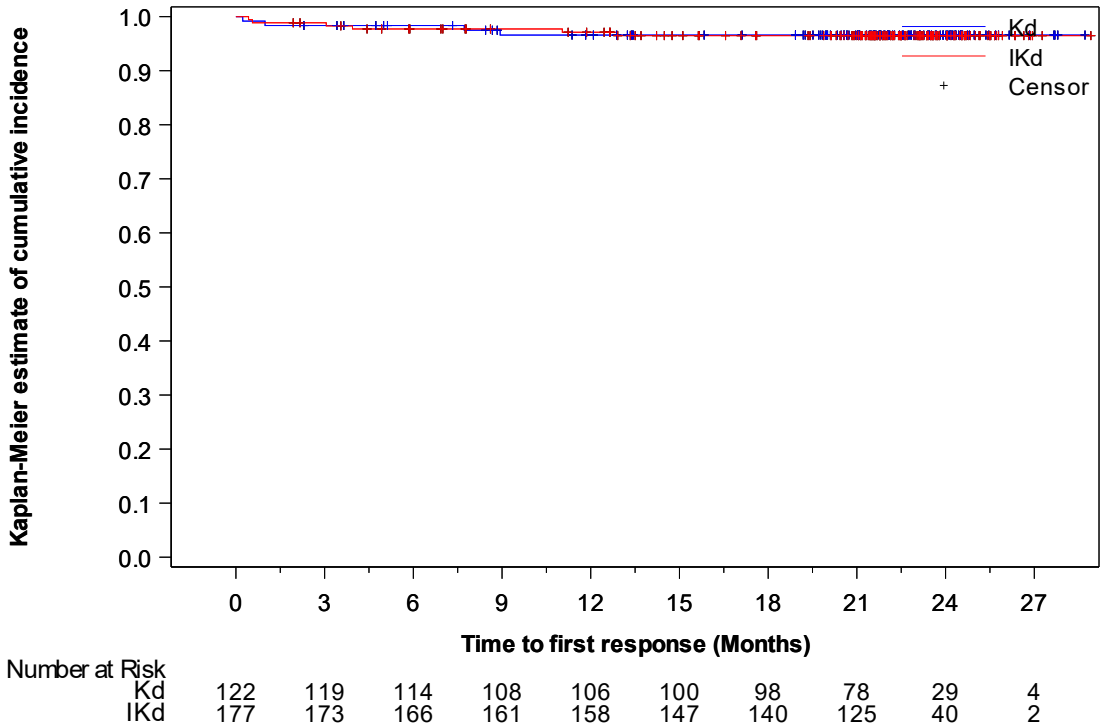
16.2.7.1 Safety endpoints
16.2.7.1.31 Treatment emergent severe (grade 5) adverse event by treatment group - Safety population

Any treatment emergent by severity (Grade 5)	**Kd (N=122)**	**IKd (N=177)**
21 Months	0.966 (0.912 to 0.987)	0.965 (0.923 to 0.984)
24 Months	0.966 (0.912 to 0.987)	0.965 (0.923 to 0.984)
27 Months	0.966 (0.912 to 0.987)	0.965 (0.923 to 0.984)
30 Months	0.966 (0.912 to 0.987)	0.965 (0.923 to 0.984)
Number of patients at risk[b]		
3 Months	119	173
6 Months	114	166
9 Months	108	161
12 Months	106	158
15 Months	100	147
18 Months	98	140
21 Months	78	125
24 Months	29	40
27 Months	4	2
30 Months	0	0

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
PGM=DEVOPS/SAR650984/EFC15246/CIR_RWE/REPORT/PGM/eff_km_sr_de_s_t.sas OUT=REPORT/OUTPUT/eff_km_de_tesev5_s_t_x.rtf (09FEB2021 15:16)

16.2.7.1 Safety endpoints

16.2.7.1.32 Kaplan-Meier cumulative incidence curve of treatment emergent severe (grade 5) adverse event by treatment group - Safety population



16.2.7.1 Safety endpoints

16.2.7.1.33 Non-progression treatment emergent severe (grade 5) adverse event by treatment group - Safety population

Any treatment emergent by severity (Grade 5) without progression events	**Kd (N=122)**	**IKd (N=177)**
Number (%) of events	4 (3.3)	6 (3.4)
Number (%) of patients censored	118 (96.7)	171 (96.6)
Kaplan-Meier estimates of TEAE in months		
25% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)
Median (95% CI)	NC (NC to NC)	NC (NC to NC)
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)
Comparison vs. Kd		
Log-Rank test p-value[a] vs Kd	-	0.9687
Hazard ratio (95% CI) vs Kd	-	1.03 (0.29 to 3.63)
P-value	-	0.9687
probability (95% CI)[b]		
3 Months	0.984 (0.936 to 0.996)	0.989 (0.956 to 0.997)
6 Months	0.984 (0.936 to 0.996)	0.977 (0.940 to 0.991)
9 Months	0.966 (0.912 to 0.987)	0.977 (0.940 to 0.991)
12 Months	0.966 (0.912 to 0.987)	0.971 (0.932 to 0.988)
15 Months	0.966 (0.912 to 0.987)	0.965 (0.923 to 0.984)

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable

CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley

[a] One-sided significance level is 0.025

[b] Estimated using the Kaplan-Meier method

Note : Non-progression related TEAE (excluding the Neoplasms benign, malignant and unspecified)

PGM=DEVOPS/SAR650984/EFC15246/CIR_RWE/REPORT/PGM/eff_km_sr_de_s_t.sas OUT=REPORT/OUTPUT/eff_km_de_tesev5np_s_t_x.rtf (09FEB2021 15:16)

16.2.7.1 Safety endpoints

16.2.7.1.33 Non-progression treatment emergent severe (grade 5) adverse event by treatment group - Safety population

Any treatment emergent by severity (Grade 5) without progression events	**Kd (N=122)**	**IKd (N=177)**
18 Months	0.966 (0.912 to 0.987)	0.965 (0.923 to 0.984)
21 Months	0.966 (0.912 to 0.987)	0.965 (0.923 to 0.984)
24 Months	0.966 (0.912 to 0.987)	0.965 (0.923 to 0.984)
27 Months	0.966 (0.912 to 0.987)	0.965 (0.923 to 0.984)
30 Months	0.966 (0.912 to 0.987)	0.965 (0.923 to 0.984)
Number of patients at risk[b]		
3 Months	119	173
6 Months	114	166
9 Months	108	161
12 Months	106	158
15 Months	100	147
18 Months	98	140
21 Months	78	125
24 Months	29	40
27 Months	4	2
30 Months	0	0

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable

CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley

[a] One-sided significance level is 0.025

[b] Estimated using the Kaplan-Meier method

Note : Non-progression related TEAE (excluding the Neoplasms benign, malignant and unspecified)

PGM=DEVOPS/SAR650984/EFC15246/CIR_RWE/REPORT/PGM/eff_km_sr_de_s_t.sas OUT=REPORT/OUTPUT/eff_km_de_tesev5np_s_t_x.rtf (09FEB2021 15:16)

16.2.7.1 Safety endpoints
16.2.7.1.40 Treatment emergent not severe (grade 1) adverse event of interest by treatment group - Safety population

Any treatment emergent AESI by severity (Grade 1)	**Kd (N=122)**	**IKd (N=177)**
Number (%) of events	0 (0.0)	0 (0.0)
Number (%) of patients censored	122 (100.0)	177 (100.0)
Kaplan-Meier estimates of AESI in months		
25% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)
Median (95% CI)	NC (NC to NC)	NC (NC to NC)
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)
Comparison vs. Kd		
Hazard ratio (95% CI) vs Kd	-	NC (NC to NC)
probability (95% CI)[b]		
3 Months	1.000 (1.000 to 1.000)	1.000 (1.000 to 1.000)
6 Months	1.000 (1.000 to 1.000)	1.000 (1.000 to 1.000)
9 Months	1.000 (1.000 to 1.000)	1.000 (1.000 to 1.000)
12 Months	1.000 (1.000 to 1.000)	1.000 (1.000 to 1.000)
15 Months	1.000 (1.000 to 1.000)	1.000 (1.000 to 1.000)
18 Months	1.000 (1.000 to 1.000)	1.000 (1.000 to 1.000)
21 Months	1.000 (1.000 to 1.000)	1.000 (1.000 to 1.000)

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
Note : AESI include IR of grade 3 or 4, pregnancy, overdose and second primary malignancy
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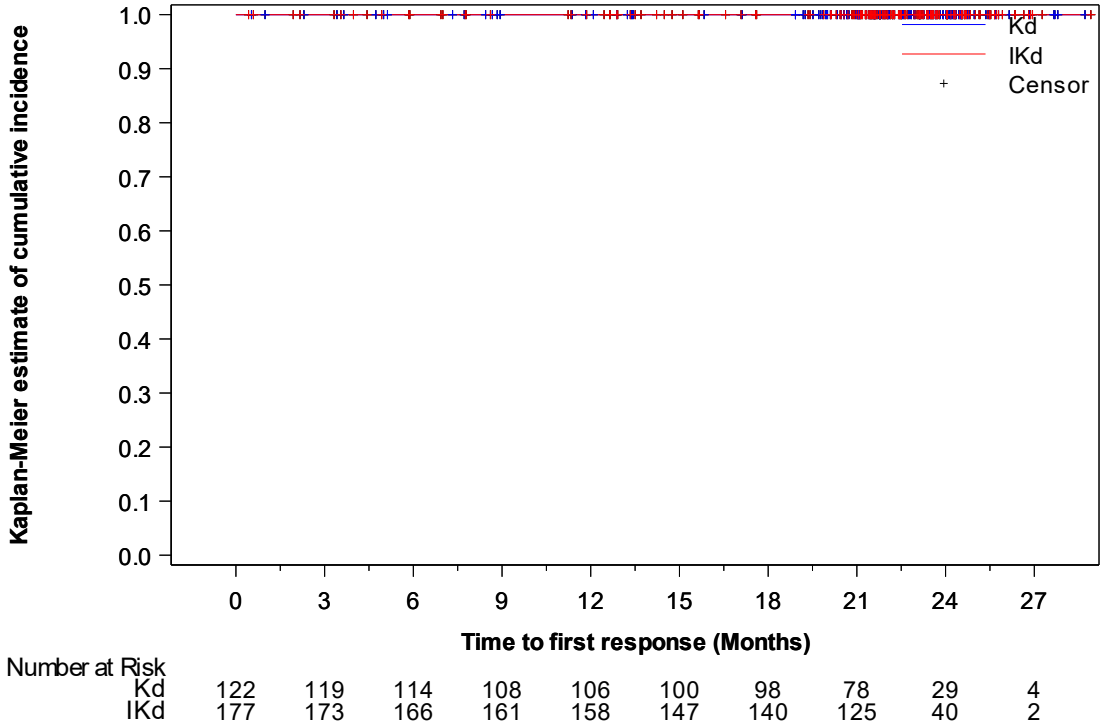
16.2.7.1 Safety endpoints
16.2.7.1.40 Treatment emergent not severe (grade 1) adverse event of interest by treatment group - Safety population

Any treatment emergent AESI by severity (Grade 1)	**Kd (N=122)**	**IKd (N=177)**
24 Months	1.000 (1.000 to 1.000)	1.000 (1.000 to 1.000)
27 Months	1.000 (1.000 to 1.000)	1.000 (1.000 to 1.000)
30 Months	1.000 (1.000 to 1.000)	1.000 (1.000 to 1.000)
Number of patients at risk[b]		
3 Months	119	173
6 Months	114	166
9 Months	108	161
12 Months	106	158
15 Months	100	147
18 Months	98	140
21 Months	78	125
24 Months	29	40
27 Months	4	2
30 Months	0	0

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
Note : AESI include IR of grade 3 or 4, pregnancy, overdose and second primary malignancy
PGM=DEVOPS/SAR650984/EFC15246/CIR_RWE/REPORT/PGM/eff_km_sr_de_s_t.sas OUT=REPORT/OUTPUT/eff_km_de_tsisv1_s_t_x.rtf (09FEB2021 15:16)

16.2.7.1 Safety endpoints

16.2.7.1.41 Kaplan-Meier cumulative incidence curve of treatment emergent not severe (grade 1) adverse event of interest by treatment group - Safety population



16.2.7.1 Safety endpoints
16.2.7.1.42 Treatment emergent not severe (grade 2) adverse event of interest by treatment group - Safety population

Any treatment emergent AESI by severity (Grade 2)	**Kd (N=122)**	**IKd (N=177)**
Number (%) of events	0 (0.0)	0 (0.0)
Number (%) of patients censored	122 (100.0)	177 (100.0)
Kaplan-Meier estimates of AESI in months		
25% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)
Median (95% CI)	NC (NC to NC)	NC (NC to NC)
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)
Comparison vs. Kd		
Hazard ratio (95% CI) vs Kd	-	NC (NC to NC)
probability (95% CI)[b]		
3 Months	1.000 (1.000 to 1.000)	1.000 (1.000 to 1.000)
6 Months	1.000 (1.000 to 1.000)	1.000 (1.000 to 1.000)
9 Months	1.000 (1.000 to 1.000)	1.000 (1.000 to 1.000)
12 Months	1.000 (1.000 to 1.000)	1.000 (1.000 to 1.000)
15 Months	1.000 (1.000 to 1.000)	1.000 (1.000 to 1.000)
18 Months	1.000 (1.000 to 1.000)	1.000 (1.000 to 1.000)
21 Months	1.000 (1.000 to 1.000)	1.000 (1.000 to 1.000)

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
Note : AESI include IR of grade 3 or 4, pregnancy, overdose and second primary malignancy
PGM=DEVOPS/SAR650984/EFC15246/CIR_RWE/REPORT/PGM/eff_km_sr_de_s_t.sas OUT=REPORT/OUTPUT/eff_km_de_tsisv2_s_t_x.rtf (09FEB2021 15:16)

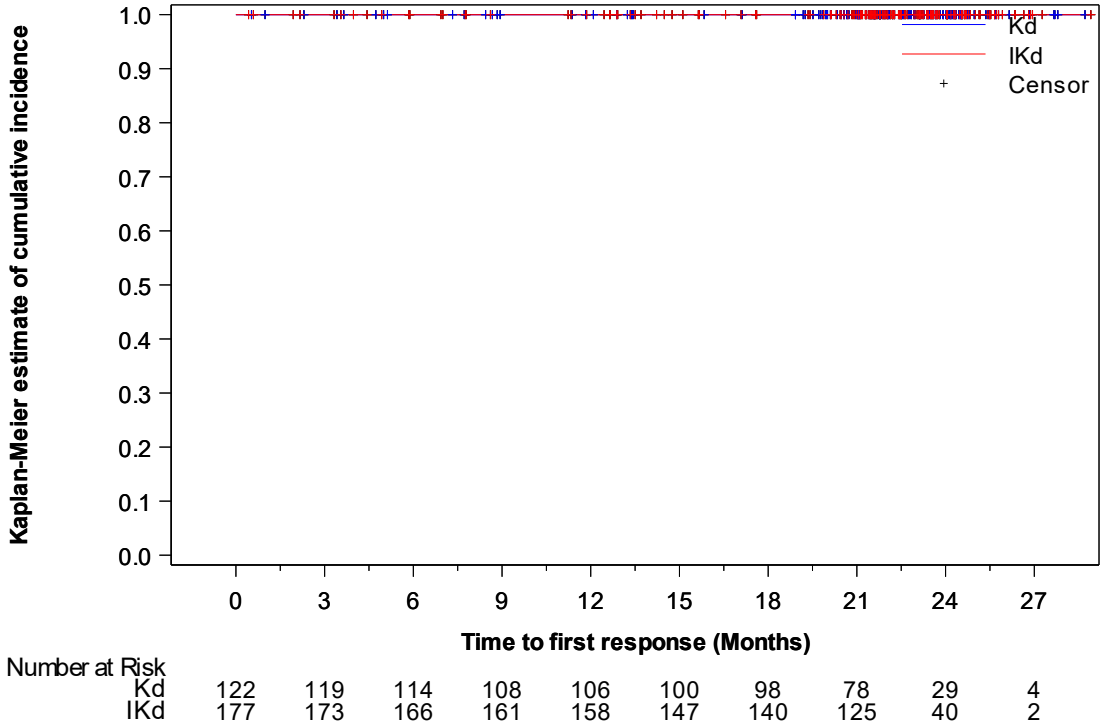
16.2.7.1 Safety endpoints
16.2.7.1.42 Treatment emergent not severe (grade 2) adverse event of interest by treatment group - Safety population

Any treatment emergent AESI by severity (Grade 2)	**Kd (N=122)**	**IKd (N=177)**
24 Months	1.000 (1.000 to 1.000)	1.000 (1.000 to 1.000)
27 Months	1.000 (1.000 to 1.000)	1.000 (1.000 to 1.000)
30 Months	1.000 (1.000 to 1.000)	1.000 (1.000 to 1.000)
Number of patients at risk[b]		
3 Months	119	173
6 Months	114	166
9 Months	108	161
12 Months	106	158
15 Months	100	147
18 Months	98	140
21 Months	78	125
24 Months	29	40
27 Months	4	2
30 Months	0	0

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
Note : AESI include IR of grade 3 or 4, pregnancy, overdose and second primary malignancy
PGM=DEVOPS/SAR650984/EFC15246/CIR_RWE/REPORT/PGM/eff_km_sr_de_s_t.sas OUT=REPORT/OUTPUT/eff_km_de_tsisv2_s_t_x.rtf (09FEB2021 15:16)

16.2.7.1 Safety endpoints

16.2.7.1.43 Kaplan-Meier cumulative incidence curve of treatment emergent not severe (grade 2) adverse event of interest by treatment group - Safety population



16.2.7.1 Safety endpoints
16.2.7.1.44 Treatment emergent severe (grade 3) adverse event of interest by treatment group - Safety population

Any treatment emergent AESI by severity (Grade 3)	**Kd (N=122)**	**IKd (N=177)**
Number (%) of events	0 (0.0)	1 (0.6)
Number (%) of patients censored	122 (100.0)	176 (99.4)
Kaplan-Meier estimates of AESI in months		
25% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)
Median (95% CI)	NC (NC to NC)	NC (NC to NC)
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)
Comparison vs. Kd		
Log-Rank test p-value[a] vs Kd	-	0.4054
Hazard ratio (95% CI) vs Kd	-	NC (NC to NC)
P-value	-	0.9976
probability (95% CI)[b]		
3 Months	1.000 (1.000 to 1.000)	1.000 (1.000 to 1.000)
6 Months	1.000 (1.000 to 1.000)	0.994 (0.959 to 0.999)
9 Months	1.000 (1.000 to 1.000)	0.994 (0.959 to 0.999)
12 Months	1.000 (1.000 to 1.000)	0.994 (0.959 to 0.999)
15 Months	1.000 (1.000 to 1.000)	0.994 (0.959 to 0.999)

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
Note : AESI include IR of grade 3 or 4, pregnancy, overdose and second primary malignancy
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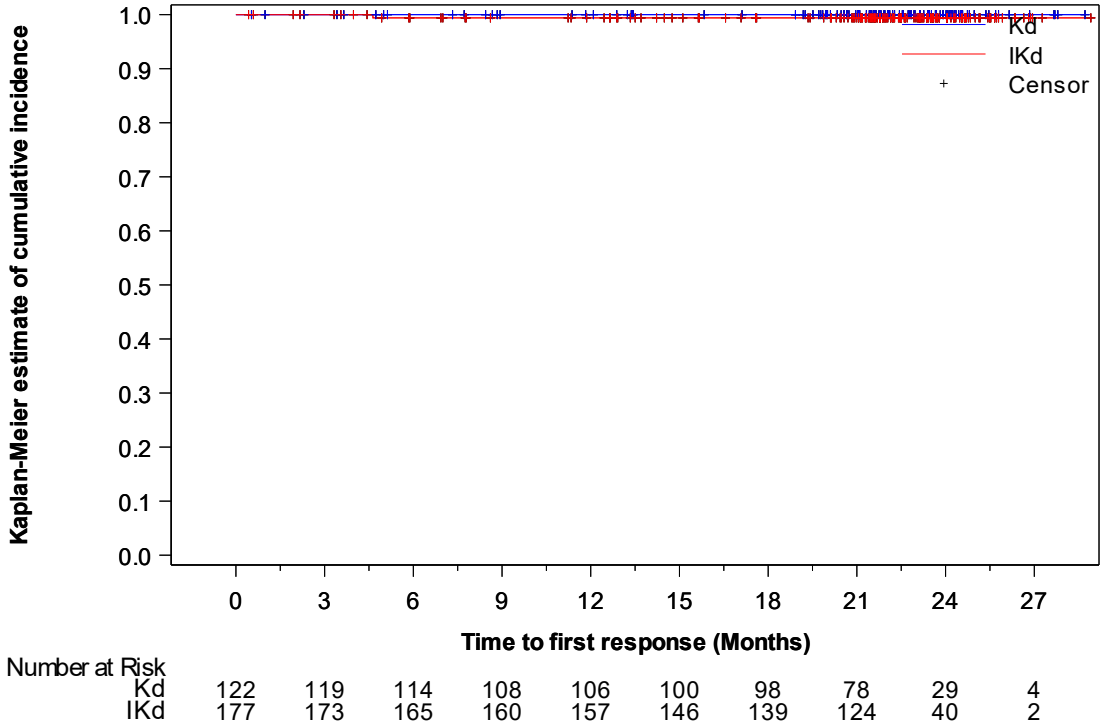
16.2.7.1 Safety endpoints
16.2.7.1.44 Treatment emergent severe (grade 3) adverse event of interest by treatment group - Safety population

Any treatment emergent AESI by severity (Grade 3)	**Kd (N=122)**	**IKd (N=177)**
18 Months	1.000 (1.000 to 1.000)	0.994 (0.959 to 0.999)
21 Months	1.000 (1.000 to 1.000)	0.994 (0.959 to 0.999)
24 Months	1.000 (1.000 to 1.000)	0.994 (0.959 to 0.999)
27 Months	1.000 (1.000 to 1.000)	0.994 (0.959 to 0.999)
30 Months	1.000 (1.000 to 1.000)	0.994 (0.959 to 0.999)
Number of patients at risk[b]		
3 Months	119	173
6 Months	114	165
9 Months	108	160
12 Months	106	157
15 Months	100	146
18 Months	98	139
21 Months	78	124
24 Months	29	40
27 Months	4	2
30 Months	0	0

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
Note : AESI include IR of grade 3 or 4, pregnancy, overdose and second primary malignancy
PGM=DEVOPS/SAR650984/EFC15246/CIR_RWE/REPORT/PGM/eff_km_sr_de_s_t.sas OUT=REPORT/OUTPUT/eff_km_de_tsisv3_s_t_x.rtf (09FEB2021 15:16)

16.2.7.1 Safety endpoints

16.2.7.1.45 Kaplan-Meier cumulative incidence curve of treatment emergent severe (grade 3) adverse event of interest by treatment group - Safety population



16.2.7.1 Safety endpoints
16.2.7.1.46 Treatment emergent severe (grade 4) adverse event of interest by treatment group - Safety population

Any treatment emergent AESI by severity (Grade 4)	**Kd (N=122)**	**IKd (N=177)**
Number (%) of events	0 (0.0)	0 (0.0)
Number (%) of patients censored	122 (100.0)	177 (100.0)
Kaplan-Meier estimates of AESI in months		
25% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)
Median (95% CI)	NC (NC to NC)	NC (NC to NC)
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)
Comparison vs. Kd		
Hazard ratio (95% CI) vs Kd	-	NC (NC to NC)
probability (95% CI)[b]		
3 Months	1.000 (1.000 to 1.000)	1.000 (1.000 to 1.000)
6 Months	1.000 (1.000 to 1.000)	1.000 (1.000 to 1.000)
9 Months	1.000 (1.000 to 1.000)	1.000 (1.000 to 1.000)
12 Months	1.000 (1.000 to 1.000)	1.000 (1.000 to 1.000)
15 Months	1.000 (1.000 to 1.000)	1.000 (1.000 to 1.000)
18 Months	1.000 (1.000 to 1.000)	1.000 (1.000 to 1.000)
21 Months	1.000 (1.000 to 1.000)	1.000 (1.000 to 1.000)

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
Note : AESI include IR of grade 3 or 4, pregnancy, overdose and second primary malignancy
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16.2.7.1 Safety endpoints

16.2.7.1.46 Treatment emergent severe (grade 4) adverse event of interest by treatment group - Safety population

Any treatment emergent AESI by severity (Grade 4)	**Kd (N=122)**	**IKd (N=177)**
24 Months	1.000 (1.000 to 1.000)	1.000 (1.000 to 1.000)
27 Months	1.000 (1.000 to 1.000)	1.000 (1.000 to 1.000)
30 Months	1.000 (1.000 to 1.000)	1.000 (1.000 to 1.000)
Number of patients at risk[b]		
3 Months	119	173
6 Months	114	166
9 Months	108	161
12 Months	106	158
15 Months	100	147
18 Months	98	140
21 Months	78	125
24 Months	29	40
27 Months	4	2
30 Months	0	0

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable

CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley

[a] One-sided significance level is 0.025

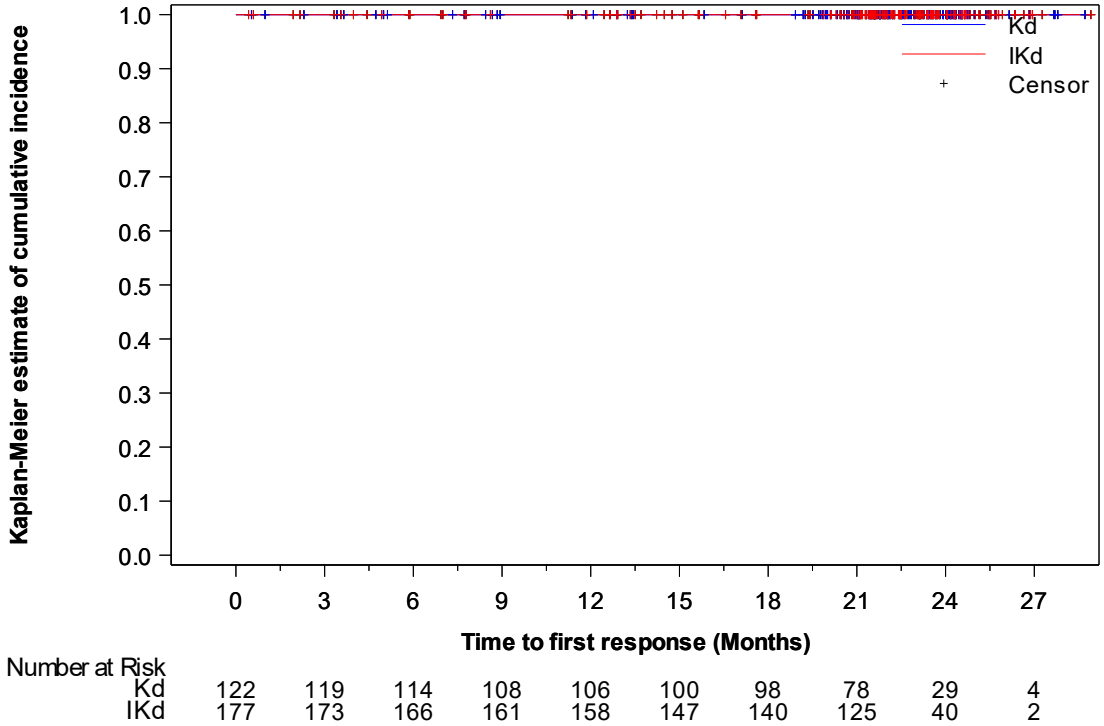
[b] Estimated using the Kaplan-Meier method

Note : AESI include IR of grade 3 or 4, pregnancy, overdose and second primary malignancy

PGM=DEVOPS/SAR650984/EFC15246/CIR_RWE/REPORT/PGM/eff_km_sr_de_s_t.sas OUT=REPORT/OUTPUT/eff_km_de_tsisv4_s_t_x.rtf (09FEB2021 15:16)

16.2.7.1 Safety endpoints

16.2.7.1.47 Kaplan-Meier cumulative incidence curve of treatment emergent severe (grade 4) adverse event of interest by treatment group - Safety population



16.2.7.1 Safety endpoints
16.2.7.1.49 Subgroup analysis by age
16.2.7.1.49.1 Treatment emergent adverse event by treatment group according to age - Safety population

	<65 years		>=65 years		
	Kd (N=65)	**IKd (N=87)**	**Kd (N=57)**	**IKd (N=90)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	61 (93.8)	83 (95.4)	56 (98.2)	89 (98.9)	0.4516
Number (%) of patients censored	4 (6.2)	4 (4.6)	1 (1.8)	1 (1.1)	
Kaplan-Meier estimates of TEAE in months					
25% quantile (95% CI)	0.1643 (0.0986 to 0.1971)	0.0657 (0.0657 to 0.0986)	0.2300 (0.0657 to 0.2957)	0.0657 (0.0657 to 0.1314)	
Median (95% CI)	0.5257 (0.2300 to 0.6571)	0.1643 (0.1314 to 0.2300)	0.3943 (0.2957 to 0.5914)	0.2300 (0.1314 to 0.3614)	
75% quantile (95% CI)	1.4784 (0.6571 to 2.9240)	0.6571 (0.2628 to 1.1828)	0.6899 (0.5914 to 1.1828)	0.7228 (0.4271 to 1.4784)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd		0.0583		0.4156	
Hazard ratio (95% CI) vs Kd		1.3774 (0.9875 to 1.9211)		1.1507 (0.8205 to 1.6139)	
P-value		0.0593		0.4160	

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
PGM=DEVOPS/SAR650984/EFC15246/CIR_RWE/REPORT/PGM/eff_km_sr_subgrp_sig_s_t.sas OUT=REPORT/OUTPUT/eff_km_de_teae_age_s_t_x.rtf (12FEB2021 8:08)

16.2.7.1 Safety endpoints
16.2.7.1.49 Subgroup analysis by age
16.2.7.1.49.1 Treatment emergent adverse event by treatment group according to age - Safety population

	<65 years		>=65 years		
	Kd (N=65)	**IKd (N=87)**	**Kd (N=57)**	**IKd (N=90)**	**p-value of treatment-by-sub group interaction[c]**
probability (95% CI)[b]					
3 Months	0.1231 (0.0575 to 0.2150)	0.1149 (0.0589 to 0.1916)	0.0526 (0.0138 to 0.1319)	0.0333 (0.0089 to 0.0861)	
6 Months	0.0615 (0.0199 to 0.1376)	0.0805 (0.0354 to 0.1494)	0.0351 (0.0065 to 0.1074)	0.0111 (0.0010 to 0.0540)	
9 Months	0.0615 (0.0199 to 0.1376)	0.0575 (0.0213 to 0.1200)	0.0351 (0.0065 to 0.1074)	0.0111 (0.0010 to 0.0540)	
12 Months	0.0615 (0.0199 to 0.1376)	0.0460 (0.0150 to 0.1047)	0.0351 (0.0065 to 0.1074)	0.0111 (0.0010 to 0.0540)	
15 Months	0.0615 (0.0199 to 0.1376)	0.0460 (0.0150 to 0.1047)	0.0175 (0.0014 to 0.0820)	0.0111 (0.0010 to 0.0540)	
18 Months	0.0615 (0.0199 to 0.1376)	0.0460 (0.0150 to 0.1047)	0.0175 (0.0014 to 0.0820)	0.0111 (0.0010 to 0.0540)	
21 Months	0.0615 (0.0199 to 0.1376)	0.0460 (0.0150 to 0.1047)	0.0175 (0.0014 to 0.0820)	0.0111 (0.0010 to 0.0540)	
24 Months	0.0615 (0.0199 to 0.1376)	0.0460 (0.0150 to 0.1047)	0.0175 (0.0014 to 0.0820)	0.0111 (0.0010 to 0.0540)	
27 Months	0.0615 (0.0199 to 0.1376)	0.0460 (0.0150 to 0.1047)	0.0175 (0.0014 to 0.0820)	0.0111 (0.0010 to 0.0540)	

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.49 Subgroup analysis by age
16.2.7.1.49.1 Treatment emergent adverse event by treatment group according to age - Safety population

	<65 years		>=65 years		
	Kd (N=65)	**IKd (N=87)**	**Kd (N=57)**	**IKd (N=90)**	**p-value of treatment-by-sub group interaction[c]**
30 Months	0.0615 (0.0199 to 0.1376)	0.0460 (0.0150 to 0.1047)	0.0175 (0.0014 to 0.0820)	0.0111 (0.0010 to 0.0540)	
Number of patients at risk[b]					
3 Months	8	10	3	3	
6 Months	4	7	2	1	
9 Months	4	5	2	1	
12 Months	4	4	2	1	
15 Months	4	4	1	1	
18 Months	4	4	1	1	
21 Months	3	4	0	1	
24 Months	1	1	0	0	
27 Months	0	0	0	0	
30 Months	0	0	0	0	

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
PGM=DEVOPS/SAR650984/EFC15246/CIR_RWE/REPORT/PGM/eff_km_sr_subgrp_sig_s_t.sas OUT=REPORT/OUTPUT/eff_km_de_teae_age_s_t_x.rtf (12FEB2021 8:08)

16.2.7.1 Safety endpoints
16.2.7.1.49 Subgroup analysis by age
16.2.7.1.49.2 Treatment emergent serious adverse event by treatment group according to age - Safety population

	<65 years		>=65 years		
	Kd (N=65)	**IKd (N=87)**	**Kd (N=57)**	**IKd (N=90)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	32 (49.2)	46 (52.9)	38 (66.7)	59 (65.6)	0.8317
Number (%) of patients censored	33 (50.8)	41 (47.1)	19 (33.3)	31 (34.4)	
Kaplan-Meier estimates of TEAE in months					
25% quantile (95% CI)	5.5195 (3.3183 to 9.1992)	5.6181 (1.4784 to 9.2977)	3.8768 (0.9856 to 5.5852)	1.7413 (0.4600 to 3.8439)	
Median (95% CI)	16.7228 (10.4805 to NC)	13.4045 (11.2361 to NC)	12.3532 (5.5852 to 15.4415)	8.8542 (5.1253 to 14.8830)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (15.4415 to NC)	NC (21.1253 to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd		0.6589		0.8802	
Hazard ratio (95% CI) vs Kd		1.1070 (0.7048 to 1.7386)		1.0318 (0.6861 to 1.5516)	
P-value		0.6591		0.8806	
probability (95% CI)[b]					

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
PGM=DEVOPS/SAR650984/EFC15246/CIR_RWE/REPORT/PGM/eff_km_sr_subgrp_sig_s_t.sas OUT=REPORT/OUTPUT/eff_km_de_tesae_age_s_t_x.rtf (12FEB2021 8:12)

16.2.7.1 Safety endpoints
16.2.7.1.49 Subgroup analysis by age
16.2.7.1.49.2 Treatment emergent serious adverse event by treatment group according to age - Safety population

	<65 years		>=65 years		
	Kd (N=65)	**IKd (N=87)**	**Kd (N=57)**	**IKd (N=90)**	**p-value of treatment-by-sub group interaction[c]**
3 Months	0.8764 (0.7680 to 0.9362)	0.7931 (0.6919 to 0.8642)	0.7544 (0.6208 to 0.8465)	0.7000 (0.5938 to 0.7834)	
6 Months	0.7042 (0.5763 to 0.8001)	0.7468 (0.6414 to 0.8253)	0.6140 (0.4753 to 0.7263)	0.5778 (0.4691 to 0.6720)	
9 Months	0.6566 (0.5266 to 0.7588)	0.6768 (0.5673 to 0.7642)	0.5263 (0.3898 to 0.6458)	0.5000 (0.3930 to 0.5978)	
12 Months	0.5765 (0.4459 to 0.6869)	0.5834 (0.4723 to 0.6791)	0.5088 (0.3732 to 0.6292)	0.4444 (0.3402 to 0.5434)	
15 Months	0.5440 (0.4140 to 0.6569)	0.4849 (0.3750 to 0.5862)	0.3826 (0.2574 to 0.5065)	0.3994 (0.2982 to 0.4985)	
18 Months	0.4935 (0.3650 to 0.6096)	0.4568 (0.3473 to 0.5596)	0.3644 (0.2414 to 0.4881)	0.3762 (0.2768 to 0.4752)	
21 Months	0.4935 (0.3650 to 0.6096)	0.4568 (0.3473 to 0.5596)	0.3462 (0.2256 to 0.4696)	0.3645 (0.2660 to 0.4633)	
24 Months	0.4935 (0.3650 to 0.6096)	0.4568 (0.3473 to 0.5596)	0.3077 (0.1838 to 0.4404)	0.3375 (0.2408 to 0.4366)	
27 Months	0.4935 (0.3650 to 0.6096)	0.4568 (0.3473 to 0.5596)	0.3077 (0.1838 to 0.4404)	0.3375 (0.2408 to 0.4366)	
30 Months	0.4935 (0.3650 to 0.6096)	0.4568 (0.3473 to 0.5596)	0.3077 (0.1838 to 0.4404)	0.3375 (0.2408 to 0.4366)	

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
PGM=DEVOPS/SAR650984/EFC15246/CIR_RWE/REPORT/PGM/eff_km_sr_subgrp_sig_s_t.sas OUT=REPORT/OUTPUT/eff_km_de_tesae_age_s_t_x.rtf (12FEB2021 8:12)

16.2.7.1 Safety endpoints
16.2.7.1.49 Subgroup analysis by age
16.2.7.1.49.2 Treatment emergent serious adverse event by treatment group according to age - Safety population

	<65 years		>=65 years		
	Kd (N=65)	**IKd (N=87)**	**Kd (N=57)**	**IKd (N=90)**	**p-value of treatment-by-sub group interaction[c]**
Number of patients at risk[b]					
3 Months	56	69	43	63	
6 Months	45	64	35	52	
9 Months	41	58	30	45	
12 Months	36	50	29	40	
15 Months	33	36	21	35	
18 Months	29	32	20	32	
21 Months	22	30	14	27	
24 Months	8	12	1	7	
27 Months	1	0	1	1	
30 Months	0	0	0	0	

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
PGM=DEVOPS/SAR650984/EFC15246/CIR_RWE/REPORT/PGM/eff_km_sr_subgrp_sig_s_t.sas OUT=REPORT/OUTPUT/eff_km_de_tesae_age_s_t_x.rtf (12FEB2021 8:12)

16.2.7.1 Safety endpoints
16.2.7.1.49 Subgroup analysis by age
16.2.7.1.49.3 Treatment emergent adverse event leading to discontinuation of treatment by treatment group according to age - Safety population

	<65 years		>=65 years		
	Kd (N=65)	**IKd (N=87)**	**Kd (N=57)**	**IKd (N=90)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	5 (7.7)	6 (6.9)	12 (21.1)	9 (10.0)	0.3794
Number (%) of patients censored	60 (92.3)	81 (93.1)	45 (78.9)	81 (90.0)	
Kaplan-Meier estimates of TEAE in months					
25% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (7.3922 to NC)	NC (NC to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd		0.8094		0.0650	
Hazard ratio (95% CI) vs Kd		0.8642 (0.2637 to 2.8321)		0.4526 (0.1907 to 1.0743)	
P-value		0.8096		0.0722	
probability (95% CI)[b]					
3 Months	1.0000 (1.0000 to 1.0000)	0.9885 (0.9212 to 0.9984)	0.9116 (0.8006 to 0.9622)	0.9551 (0.8847 to 0.9829)	

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
PGM=DEVOPS/SAR650984/EFC15246/CIR_RWE/REPORT/PGM/eff_km_sr_subgrp_sig_s_t.sas OUT=REPORT/OUTPUT/eff_km_de_tedisc_age_s_t_x.rtf (12FEB2021 8:09)

16.2.7.1 Safety endpoints
16.2.7.1.49 Subgroup analysis by age
16.2.7.1.49.3 Treatment emergent adverse event leading to discontinuation of treatment by treatment group according to age - Safety population

	<65 years		>=65 years		
	Kd (N=65)	**IKd (N=87)**	**Kd (N=57)**	**IKd (N=90)**	**p-value of treatment-by-sub group interaction[c]**
6 Months	0.9680 (0.8779 to 0.9919)	0.9650 (0.8953 to 0.9886)	0.8937 (0.7786 to 0.9508)	0.9319 (0.8547 to 0.9688)	
9 Months	0.9349 (0.8356 to 0.9751)	0.9529 (0.8793 to 0.9821)	0.8204 (0.6917 to 0.8991)	0.9083 (0.8249 to 0.9531)	
12 Months	0.9349 (0.8356 to 0.9751)	0.9529 (0.8793 to 0.9821)	0.8204 (0.6917 to 0.8991)	0.9083 (0.8249 to 0.9531)	
15 Months	0.9349 (0.8356 to 0.9751)	0.9278 (0.8462 to 0.9669)	0.8204 (0.6917 to 0.8991)	0.9083 (0.8249 to 0.9531)	
18 Months	0.9165 (0.8106 to 0.9645)	0.9278 (0.8462 to 0.9669)	0.8004 (0.6681 to 0.8843)	0.9083 (0.8249 to 0.9531)	
21 Months	0.9165 (0.8106 to 0.9645)	0.9278 (0.8462 to 0.9669)	0.7804 (0.6451 to 0.8691)	0.8950 (0.8075 to 0.9440)	
24 Months	0.9165 (0.8106 to 0.9645)	0.9278 (0.8462 to 0.9669)	0.7804 (0.6451 to 0.8691)	0.8950 (0.8075 to 0.9440)	
27 Months	0.9165 (0.8106 to 0.9645)	0.9278 (0.8462 to 0.9669)	0.7804 (0.6451 to 0.8691)	0.8950 (0.8075 to 0.9440)	
30 Months	0.9165 (0.8106 to 0.9645)	0.9278 (0.8462 to 0.9669)	0.7804 (0.6451 to 0.8691)	0.8950 (0.8075 to 0.9440)	

Number of patients at risk[b]

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
PGM=DEVOPS/SAR650984/EFC15246/CIR_RWE/REPORT/PGM/eff_km_sr_subgrp_sig_s_t.sas OUT=REPORT/OUTPUT/eff_km_de_tedisc_age_s_t_x.rtf (12FEB2021 8:09)

16.2.7.1 Safety endpoints
16.2.7.1.49 Subgroup analysis by age
16.2.7.1.49.3 Treatment emergent adverse event leading to discontinuation of treatment by treatment group according to age - Safety population

	<65 years		>=65 years		
	Kd (N=65)	**IKd (N=87)**	**Kd (N=57)**	**IKd (N=90)**	**p-value of treatment-by-sub group interaction[c]**
3 Months	64	85	51	85	
6 Months	59	82	49	79	
9 Months	55	79	44	76	
12 Months	54	78	43	74	
15 Months	51	69	41	71	
18 Months	49	65	40	68	
21 Months	37	60	36	58	
24 Months	18	20	8	20	
27 Months	1	0	3	2	
30 Months	0	0	0	0	

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
PGM=DEVOPS/SAR650984/EFC15246/CIR_RWE/REPORT/PGM/eff_km_sr_subgrp_sig_s_t.sas OUT=REPORT/OUTPUT/eff_km_de_tedisc_age_s_t_x.rtf (12FEB2021 8:09)

16.2.7.1 Safety endpoints
16.2.7.1.49 Subgroup analysis by age
16.2.7.1.49.4 Treatment emergent mild adverse event by treatment group according to age - Safety population

	<65 years		>=65 years		
	Kd (N=65)	**IKd (N=87)**	**Kd (N=57)**	**IKd (N=90)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	61 (93.8)	82 (94.3)	54 (94.7)	85 (94.4)	0.5921
Number (%) of patients censored	4 (6.2)	5 (5.7)	3 (5.3)	5 (5.6)	
Kaplan-Meier estimates of TEAE in months					
25% quantile (95% CI)	0.1643 (0.0986 to 0.1971)	0.0657 (0.0657 to 0.0986)	0.2628 (0.0657 to 0.3614)	0.0657 (0.0657 to 0.1314)	
Median (95% CI)	0.5257 (0.2300 to 0.6571)	0.1643 (0.1314 to 0.2300)	0.5257 (0.3614 to 0.6899)	0.2628 (0.1643 to 0.3943)	
75% quantile (95% CI)	1.8727 (0.6571 to 2.9240)	0.7885 (0.2628 to 1.7413)	0.9856 (0.6899 to 1.4456)	1.1828 (0.4928 to 1.8398)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd		0.0913		0.3979	
Hazard ratio (95% CI) vs Kd		1.3311 (0.9540 to 1.8573)		1.1597 (0.8223 to 1.6356)	
P-value		0.0924		0.3983	

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
PGM=DEVOPS/SAR650984/EFC15246/CIR_RWE/REPORT/PGM/eff_km_sr_subgrp_sig_s_t.sas OUT=REPORT/OUTPUT/eff_km_de_tesev12_age_s_t_x.rtf (12FEB2021 8:12)

16.2.7.1 Safety endpoints
16.2.7.1.49 Subgroup analysis by age
16.2.7.1.49.4 Treatment emergent mild adverse event by treatment group according to age - Safety population

	<65 years		>=65 years		
	Kd (N=65)	**IKd (N=87)**	**Kd (N=57)**	**IKd (N=90)**	**p-value of treatment-by-sub group interaction[c]**
probability (95% CI)[b]					
3 Months	0.1385 (0.0681 to 0.2334)	0.1379 (0.0756 to 0.2188)	0.0910 (0.0335 to 0.1840)	0.0804 (0.0355 to 0.1491)	
6 Months	0.0769 (0.0284 to 0.1577)	0.0920 (0.0430 to 0.1637)	0.0546 (0.0144 to 0.1363)	0.0551 (0.0195 to 0.1183)	
9 Months	0.0769 (0.0284 to 0.1577)	0.0690 (0.0282 to 0.1349)	0.0546 (0.0144 to 0.1363)	0.0367 (0.0087 to 0.1001)	
12 Months	0.0769 (0.0284 to 0.1577)	0.0575 (0.0213 to 0.1200)	0.0546 (0.0144 to 0.1363)	0.0367 (0.0087 to 0.1001)	
15 Months	0.0615 (0.0199 to 0.1376)	0.0575 (0.0213 to 0.1200)	0.0273 (0.0028 to 0.1104)	0.0367 (0.0087 to 0.1001)	
18 Months	0.0615 (0.0199 to 0.1376)	0.0575 (0.0213 to 0.1200)	0.0273 (0.0028 to 0.1104)	0.0367 (0.0087 to 0.1001)	
21 Months	0.0615 (0.0199 to 0.1376)	0.0575 (0.0213 to 0.1200)	0.0273 (0.0028 to 0.1104)	0.0367 (0.0087 to 0.1001)	
24 Months	0.0615 (0.0199 to 0.1376)	0.0575 (0.0213 to 0.1200)	0.0273 (0.0028 to 0.1104)	0.0367 (0.0087 to 0.1001)	
27 Months	0.0615 (0.0199 to 0.1376)	0.0575 (0.0213 to 0.1200)	0.0273 (0.0028 to 0.1104)	0.0367 (0.0087 to 0.1001)	

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
PGM=DEVOPS/SAR650984/EFC15246/CIR_RWE/REPORT/PGM/eff_km_sr_subgrp_sig_s_t.sas OUT=REPORT/OUTPUT/eff_km_de_tesev12_age_s_t_x.rtf (12FEB2021 8:12)

16.2.7.1 Safety endpoints
16.2.7.1.49 Subgroup analysis by age
16.2.7.1.49.4 Treatment emergent mild adverse event by treatment group according to age - Safety population

	<65 years		>=65 years		
	Kd (N=65)	**IKd (N=87)**	**Kd (N=57)**	**IKd (N=90)**	**p-value of treatment-by-sub group interaction[c]**
30 Months	0.0615 (0.0199 to 0.1376)	0.0575 (0.0213 to 0.1200)	0.0273 (0.0028 to 0.1104)	0.0367 (0.0087 to 0.1001)	
Number of patients at risk[b]					
3 Months	9	12	5	7	
6 Months	5	8	3	3	
9 Months	5	6	3	2	
12 Months	5	5	2	2	
15 Months	4	4	1	2	
18 Months	4	4	1	2	
21 Months	3	4	0	2	
24 Months	1	1	0	0	
27 Months	0	0	0	0	
30 Months	0	0	0	0	

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
PGM=DEVOPS/SAR650984/EFC15246/CIR_RWE/REPORT/PGM/eff_km_sr_subgrp_sig_s_t.sas OUT=REPORT/OUTPUT/eff_km_de_tesev12_age_s_t_x.rtf (12FEB2021 8:12)

16.2.7.1 Safety endpoints
16.2.7.1.49 Subgroup analysis by age
16.2.7.1.49.5 Treatment emergent severe adverse event by treatment group according to age - Safety population

	<65 years		>=65 years		
	Kd (N=65)	**IKd (N=87)**	**Kd (N=57)**	**IKd (N=90)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	41 (63.1)	59 (67.8)	40 (70.2)	75 (83.3)	0.2663
Number (%) of patients censored	24 (36.9)	28 (32.2)	17 (29.8)	15 (16.7)	
Kaplan-Meier estimates of TEAE in months					
25% quantile (95% CI)	2.9240 (1.1499 to 4.0411)	1.9713 (0.8871 to 4.4682)	1.5113 (0.4600 to 3.8768)	0.6899 (0.3614 to 1.6427)	
Median (95% CI)	7.6550 (4.0739 to 15.6057)	8.4435 (5.1581 to 11.4333)	6.2752 (3.8768 to 12.9774)	4.7639 (2.0041 to 5.9466)	
75% quantile (95% CI)	NC (15.9343 to NC)	NC (14.7187 to NC)	NC (12.9774 to NC)	10.7105 (7.7864 to 16.7556)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd		0.7641		0.0540	
Hazard ratio (95% CI) vs Kd		1.0626 (0.7131 to 1.5834)		1.4572 (0.9914 to 2.1418)	
P-value		0.7653		0.0554	

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
PGM=DEVOPS/SAR650984/EFC15246/CIR_RWE/REPORT/PGM/eff_km_sr_subgrp_sig_s_t.sas OUT=REPORT/OUTPUT/eff_km_de_tesev34_age_s_t_x.rtf (12FEB2021 8:13)

16.2.7.1 Safety endpoints
16.2.7.1.49 Subgroup analysis by age
16.2.7.1.49.5 Treatment emergent severe adverse event by treatment group according to age - Safety population

	<65 years		>=65 years		
	Kd (N=65)	**IKd (N=87)**	**Kd (N=57)**	**IKd (N=90)**	**p-value of treatment-by-sub group interaction[c]**
probability (95% CI)[b]					
3 Months	0.7218 (0.5954 to 0.8147)	0.7119 (0.6042 to 0.7952)	0.6639 (0.5249 to 0.7708)	0.5745 (0.4653 to 0.6693)	
6 Months	0.5335 (0.4048 to 0.6463)	0.5836 (0.4724 to 0.6792)	0.5383 (0.4001 to 0.6578)	0.3830 (0.2827 to 0.4824)	
9 Months	0.4689 (0.3430 to 0.5849)	0.4902 (0.3812 to 0.5904)	0.4127 (0.2837 to 0.5370)	0.2929 (0.2024 to 0.3891)	
12 Months	0.3880 (0.2689 to 0.5054)	0.3851 (0.2830 to 0.4862)	0.4127 (0.2837 to 0.5370)	0.2140 (0.1358 to 0.3041)	
15 Months	0.3880 (0.2689 to 0.5054)	0.3456 (0.2463 to 0.4468)	0.3211 (0.2037 to 0.4444)	0.1781 (0.1065 to 0.2647)	
18 Months	0.3550 (0.2395 to 0.4721)	0.3167 (0.2196 to 0.4182)	0.3022 (0.1877 to 0.4248)	0.1527 (0.0863 to 0.2365)	
21 Months	0.3550 (0.2395 to 0.4721)	0.3017 (0.2057 to 0.4032)	0.3022 (0.1877 to 0.4248)	0.1527 (0.0863 to 0.2365)	
24 Months	0.3550 (0.2395 to 0.4721)	0.3017 (0.2057 to 0.4032)	0.2686 (0.1543 to 0.3967)	0.1527 (0.0863 to 0.2365)	
27 Months	0.3550 (0.2395 to 0.4721)	0.3017 (0.2057 to 0.4032)	0.2686 (0.1543 to 0.3967)	0.1527 (0.0863 to 0.2365)	

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
PGM=DEVOPS/SAR650984/EFC15246/CIR_RWE/REPORT/PGM/eff_km_sr_subgrp_sig_s_t.sas OUT=REPORT/OUTPUT/eff_km_de_tesev34_age_s_t_x.rtf (12FEB2021 8:13)

16.2.7.1 Safety endpoints
16.2.7.1.49 Subgroup analysis by age
16.2.7.1.49.5 Treatment emergent severe adverse event by treatment group according to age - Safety population

	<65 years		>=65 years		
	Kd (N=65)	**IKd (N=87)**	**Kd (N=57)**	**IKd (N=90)**	**p-value of treatment-by-sub group interaction[c]**
30 Months	0.3550 (0.2395 to 0.4721)	0.3017 (0.2057 to 0.4032)	0.2686 (0.1543 to 0.3967)	0.1527 (0.0863 to 0.2365)	
Number of patients at risk[b]					
3 Months	46	61	37	51	
6 Months	34	50	30	34	
9 Months	29	42	23	26	
12 Months	24	33	23	19	
15 Months	24	25	17	14	
18 Months	21	21	16	12	
21 Months	15	19	12	12	
24 Months	7	6	1	4	
27 Months	0	0	1	0	
30 Months	0	0	0	0	

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
PGM=DEVOPS/SAR650984/EFC15246/CIR_RWE/REPORT/PGM/eff_km_sr_subgrp_sig_s_t.sas OUT=REPORT/OUTPUT/eff_km_de_tesev34_age_s_t_x.rtf (12FEB2021 8:13)

16.2.7.1 Safety endpoints
16.2.7.1.49 Subgroup analysis by age
16.2.7.1.49.6 Treatment emergent severe adverse event including death by treatment group according to age - Safety population

	<65 years		>=65 years		
	Kd (N=65)	**IKd (N=87)**	**Kd (N=57)**	**IKd (N=90)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	41 (63.1)	60 (69.0)	41 (71.9)	76 (84.4)	0.3079
Number (%) of patients censored	24 (36.9)	27 (31.0)	16 (28.1)	14 (15.6)	
Kaplan-Meier estimates of TEAE in months					
25% quantile (95% CI)	2.9240 (1.1499 to 4.0411)	1.9713 (0.8871 to 4.4682)	1.1170 (0.4600 to 3.2854)	0.6571 (0.3614 to 1.4127)	
Median (95% CI)	7.6550 (4.0739 to 15.6057)	8.4435 (5.1581 to 11.4333)	6.2752 (3.2854 to 12.3532)	4.5667 (2.0041 to 5.6181)	
75% quantile (95% CI)	NC (15.9343 to NC)	NC (13.2402 to NC)	NC (12.3532 to NC)	10.7105 (7.6879 to 15.8357)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd		0.6991		0.0604	
Hazard ratio (95% CI) vs Kd		1.0815 (0.7268 to 1.6094)		1.4379 (0.9822 to 2.1051)	
P-value		0.6992		0.0618	

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
PGM=DEVOPS/SAR650984/EFC15246/CIR_RWE/REPORT/PGM/eff_km_sr_subgrp_sig_s_t.sas OUT=REPORT/OUTPUT/eff_km_de_tesev345_age_s_t_x.rtf (12FEB2021 8:13)

16.2.7.1 Safety endpoints
16.2.7.1.49 Subgroup analysis by age
16.2.7.1.49.6 Treatment emergent severe adverse event including death by treatment group according to age - Safety population

	<65 years		>=65 years		
	Kd (N=65)	**IKd (N=87)**	**Kd (N=57)**	**IKd (N=90)**	**p-value of treatment-by-sub group interaction[c]**
probability (95% CI)[b]					
3 Months	0.7218 (0.5954 to 0.8147)	0.7119 (0.6042 to 0.7952)	0.6491 (0.5106 to 0.7574)	0.5667 (0.4581 to 0.6615)	
6 Months	0.5335 (0.4048 to 0.6463)	0.5836 (0.4724 to 0.6792)	0.5263 (0.3898 to 0.6458)	0.3778 (0.2785 to 0.4765)	
9 Months	0.4689 (0.3430 to 0.5849)	0.4902 (0.3812 to 0.5904)	0.4035 (0.2766 to 0.5268)	0.2889 (0.1995 to 0.3843)	
12 Months	0.3880 (0.2689 to 0.5054)	0.3851 (0.2830 to 0.4862)	0.4035 (0.2766 to 0.5268)	0.2111 (0.1339 to 0.3002)	
15 Months	0.3880 (0.2689 to 0.5054)	0.3345 (0.2366 to 0.4352)	0.3139 (0.1988 to 0.4357)	0.1757 (0.1050 to 0.2613)	
18 Months	0.3550 (0.2395 to 0.4721)	0.3065 (0.2110 to 0.4071)	0.2955 (0.1832 to 0.4165)	0.1506 (0.0851 to 0.2335)	
21 Months	0.3550 (0.2395 to 0.4721)	0.2919 (0.1978 to 0.3924)	0.2955 (0.1832 to 0.4165)	0.1506 (0.0851 to 0.2335)	
24 Months	0.3550 (0.2395 to 0.4721)	0.2919 (0.1978 to 0.3924)	0.2626 (0.1507 to 0.3889)	0.1506 (0.0851 to 0.2335)	
27 Months	0.3550 (0.2395 to 0.4721)	0.2919 (0.1978 to 0.3924)	0.2626 (0.1507 to 0.3889)	0.1506 (0.0851 to 0.2335)	

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.49 Subgroup analysis by age
16.2.7.1.49.6 Treatment emergent severe adverse event including death by treatment group according to age - Safety population

	<65 years		>=65 years		
	Kd (N=65)	**IKd (N=87)**	**Kd (N=57)**	**IKd (N=90)**	**p-value of treatment-by-sub group interaction[c]**
30 Months	0.3550 (0.2395 to 0.4721)	0.2919 (0.1978 to 0.3924)	0.2626 (0.1507 to 0.3889)	0.1506 (0.0851 to 0.2335)	
Number of patients at risk[b]					
3 Months	46	61	37	51	
6 Months	34	50	30	34	
9 Months	29	42	23	26	
12 Months	24	33	23	19	
15 Months	24	25	17	14	
18 Months	21	21	16	12	
21 Months	15	19	12	12	
24 Months	7	6	1	4	
27 Months	0	0	1	0	
30 Months	0	0	0	0	

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
PGM=DEVOPS/SAR650984/EFC15246/CIR_RWE/REPORT/PGM/eff_km_sr_subgrp_sig_s_t.sas OUT=REPORT/OUTPUT/eff_km_de_tesev345_age_s_t_x.rtf (12FEB2021 8:13)

16.2.7.1 Safety endpoints
16.2.7.1.50 Subgroup analysis by gender
16.2.7.1.50.1 Treatment emergent adverse event by treatment group according to gender - Safety population

	Male		Female		
	Kd (N=68)	**IKd (N=99)**	**Kd (N=54)**	**IKd (N=78)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	65 (95.6)	98 (99.0)	52 (96.3)	74 (94.9)	0.1476
Number (%) of patients censored	3 (4.4)	1 (1.0)	2 (3.7)	4 (5.1)	
Kaplan-Meier estimates of TEAE in months					
25% quantile (95% CI)	0.1643 (0.0657 to 0.2628)	0.0657 (0.0329 to 0.0986)	0.1971 (0.1314 to 0.3285)	0.0986 (0.0657 to 0.1314)	
Median (95% CI)	0.4107 (0.2628 to 0.6242)	0.1643 (0.1314 to 0.2300)	0.4600 (0.3285 to 0.6242)	0.2300 (0.1314 to 0.3943)	
75% quantile (95% CI)	0.8542 (0.6571 to 1.5113)	0.6242 (0.3614 to 0.7885)	1.1828 (0.6242 to 2.2012)	1.4456 (0.4928 to 2.1355)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd		0.0086		0.5280	
Hazard ratio (95% CI) vs Kd		1.5231 (1.1105 to 2.0891)		1.1216 (0.7852 to 1.6019)	
P-value		0.0091		0.5282	

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.

16.2.7.1 Safety endpoints
16.2.7.1.50 Subgroup analysis by gender
16.2.7.1.50.1 Treatment emergent adverse event by treatment group according to gender - Safety population

	Male		Female		
	Kd (N=68)	**IKd (N=99)**	**Kd (N=54)**	**IKd (N=78)**	**p-value of treatment-by-sub group interaction[c]**
Hazard ratio inverted (95% CI) vs IKd	0.6566 (0.4787 to 0.9005)				
probability (95% CI)[b]					
3 Months	0.0882 (0.0359 to 0.1699)	0.0505 (0.0188 to 0.1062)	0.0926 (0.0341 to 0.1872)	0.1026 (0.0479 to 0.1814)	
6 Months	0.0588 (0.0190 to 0.1319)	0.0404 (0.0132 to 0.0926)	0.0370 (0.0069 to 0.1129)	0.0513 (0.0166 to 0.1160)	
9 Months	0.0588 (0.0190 to 0.1319)	0.0202 (0.0039 to 0.0642)	0.0370 (0.0069 to 0.1129)	0.0513 (0.0166 to 0.1160)	
12 Months	0.0588 (0.0190 to 0.1319)	0.0101 (0.0009 to 0.0495)	0.0370 (0.0069 to 0.1129)	0.0513 (0.0166 to 0.1160)	
15 Months	0.0441 (0.0117 to 0.1120)	0.0101 (0.0009 to 0.0495)	0.0370 (0.0069 to 0.1129)	0.0513 (0.0166 to 0.1160)	
18 Months	0.0441 (0.0117 to 0.1120)	0.0101 (0.0009 to 0.0495)	0.0370 (0.0069 to 0.1129)	0.0513 (0.0166 to 0.1160)	
21 Months	0.0441 (0.0117 to 0.1120)	0.0101 (0.0009 to 0.0495)	0.0370 (0.0069 to 0.1129)	0.0513 (0.0166 to 0.1160)	
24 Months	0.0441 (0.0117 to 0.1120)	0.0101 (0.0009 to 0.0495)	0.0370 (0.0069 to 0.1129)	0.0513 (0.0166 to 0.1160)	

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.50 Subgroup analysis by gender
16.2.7.1.50.1 Treatment emergent adverse event by treatment group according to gender - Safety population

	Male		Female		
	Kd (N=68)	**IKd (N=99)**	**Kd (N=54)**	**IKd (N=78)**	**p-value of treatment-by-sub group interaction[c]**
27 Months	0.0441 (0.0117 to 0.1120)	0.0101 (0.0009 to 0.0495)	0.0370 (0.0069 to 0.1129)	0.0513 (0.0166 to 0.1160)	
30 Months	0.0441 (0.0117 to 0.1120)	0.0101 (0.0009 to 0.0495)	0.0370 (0.0069 to 0.1129)	0.0513 (0.0166 to 0.1160)	
Number of patients at risk[b]					
3 Months	6	5	5	8	
6 Months	4	4	2	4	
9 Months	4	2	2	4	
12 Months	4	1	2	4	
15 Months	3	1	2	4	
18 Months	3	1	2	4	
21 Months	2	1	1	4	
24 Months	1	0	0	1	
27 Months	0	0	0	0	
30 Months	0	0	0	0	

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.50 Subgroup analysis by gender
16.2.7.1.50.2 Treatment emergent serious adverse event by treatment group according to gender - Safety population

	Male		Female		
	Kd (N=68)	**IKd (N=99)**	**Kd (N=54)**	**IKd (N=78)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	39 (57.4)	61 (61.6)	31 (57.4)	44 (56.4)	0.9767
Number (%) of patients censored	29 (42.6)	38 (38.4)	23 (42.6)	34 (43.6)	
Kaplan-Meier estimates of TEAE in months					
25% quantile (95% CI)	3.9425 (1.5113 to 5.5524)	3.8439 (1.2485 to 6.7680)	5.5195 (3.3183 to 7.7864)	1.8398 (0.4271 to 4.6324)	
Median (95% CI)	13.8645 (6.5051 to NC)	12.5503 (9.6263 to 17.9384)	13.6345 (7.7864 to NC)	13.2895 (6.5051 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd		0.6756		0.7108	
Hazard ratio (95% CI) vs Kd		1.0896 (0.7288 to 1.6290)		1.0909 (0.6886 to 1.7282)	
P-value		0.6757		0.7109	
probability (95% CI)[b]					

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.50 Subgroup analysis by gender
16.2.7.1.50.2 Treatment emergent serious adverse event by treatment group according to gender - Safety population

	Male		Female		
	Kd (N=68)	**IKd (N=99)**	**Kd (N=54)**	**IKd (N=78)**	**p-value of treatment-by-sub group interaction[c]**
3 Months	0.7644 (0.6446 to 0.8485)	0.7778 (0.6824 to 0.8476)	0.8889 (0.7693 to 0.9485)	0.7051 (0.5905 to 0.7932)	
6 Months	0.6295 (0.5028 to 0.7324)	0.6860 (0.5845 to 0.7677)	0.7037 (0.5627 to 0.8068)	0.6282 (0.5111 to 0.7247)	
9 Months	0.5846 (0.4577 to 0.6915)	0.6348 (0.5316 to 0.7213)	0.6095 (0.4663 to 0.7253)	0.5256 (0.4096 to 0.6292)	
12 Months	0.5396 (0.4137 to 0.6497)	0.5120 (0.4093 to 0.6055)	0.5524 (0.4101 to 0.6736)	0.5128 (0.3972 to 0.6169)	
15 Months	0.4942 (0.3701 to 0.6067)	0.4174 (0.3187 to 0.5129)	0.4346 (0.2990 to 0.5625)	0.4722 (0.3580 to 0.5781)	
18 Months	0.4313 (0.3108 to 0.5460)	0.3936 (0.2959 to 0.4896)	0.4346 (0.2990 to 0.5625)	0.4444 (0.3315 to 0.5512)	
21 Months	0.4154 (0.2961 to 0.5304)	0.3816 (0.2846 to 0.4778)	0.4346 (0.2990 to 0.5625)	0.4444 (0.3315 to 0.5512)	
24 Months	0.4154 (0.2961 to 0.5304)	0.3675 (0.2708 to 0.4644)	0.3984 (0.2592 to 0.5340)	0.4291 (0.3167 to 0.5366)	
27 Months	0.4154 (0.2961 to 0.5304)	0.3675 (0.2708 to 0.4644)	0.3984 (0.2592 to 0.5340)	0.4291 (0.3167 to 0.5366)	
30 Months	0.4154 (0.2961 to 0.5304)	0.3675 (0.2708 to 0.4644)	0.3984 (0.2592 to 0.5340)	0.4291 (0.3167 to 0.5366)	

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.50 Subgroup analysis by gender
16.2.7.1.50.2 Treatment emergent serious adverse event by treatment group according to gender - Safety population

	Male		Female		
	Kd (N=68)	**IKd (N=99)**	**Kd (N=54)**	**IKd (N=78)**	**p-value of treatment-by-sub group interaction[c]**
Number of patients at risk[b]					
3 Months	51	77	48	55	
6 Months	42	67	38	49	
9 Months	39	62	32	41	
12 Months	36	50	29	40	
15 Months	32	37	22	34	
18 Months	27	33	22	31	
21 Months	18	28	18	29	
24 Months	7	10	2	9	
27 Months	1	0	1	1	
30 Months	0	0	0	0	

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.50 Subgroup analysis by gender
16.2.7.1.50.3 Treatment emergent adverse event leading to discontinuation of treatment by treatment group according to gender - Safety population

	Male		Female		
	Kd (N=68)	**IKd (N=99)**	**Kd (N=54)**	**IKd (N=78)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	12 (17.6)	8 (8.1)	5 (9.3)	7 (9.0)	0.2523
Number (%) of patients censored	56 (82.4)	91 (91.9)	49 (90.7)	71 (91.0)	
Kaplan-Meier estimates of TEAE in months					
25% quantile (95% CI)	NC (8.9363 to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd		0.0517		0.9970	
Hazard ratio (95% CI) vs Kd		0.4226 (0.1727 to 1.0342)		0.9978 (0.3167 to 3.1439)	
P-value		0.0592		0.9970	
probability (95% CI)[b]					
3 Months	0.9407 (0.8497 to 0.9773)	0.9798 (0.9216 to 0.9949)	0.9815 (0.8757 to 0.9974)	0.9610 (0.8841 to 0.9873)	

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.50 Subgroup analysis by gender
16.2.7.1.50.3 Treatment emergent adverse event leading to discontinuation of treatment by treatment group according to gender - Safety population

	Male		Female		
	Kd (N=68)	**IKd (N=99)**	**Kd (N=54)**	**IKd (N=78)**	**p-value of treatment-by-sub group interaction[c]**
6 Months	0.9101 (0.8108 to 0.9586)	0.9585 (0.8931 to 0.9842)	0.9630 (0.8599 to 0.9906)	0.9351 (0.8510 to 0.9724)	
9 Months	0.8448 (0.7303 to 0.9135)	0.9475 (0.8783 to 0.9778)	0.9256 (0.8137 to 0.9714)	0.9089 (0.8184 to 0.9555)	
12 Months	0.8448 (0.7303 to 0.9135)	0.9475 (0.8783 to 0.9778)	0.9256 (0.8137 to 0.9714)	0.9089 (0.8184 to 0.9555)	
15 Months	0.8448 (0.7303 to 0.9135)	0.9250 (0.8490 to 0.9636)	0.9256 (0.8137 to 0.9714)	0.9089 (0.8184 to 0.9555)	
18 Months	0.8096 (0.6883 to 0.8874)	0.9250 (0.8490 to 0.9636)	0.9256 (0.8137 to 0.9714)	0.9089 (0.8184 to 0.9555)	
21 Months	0.8096 (0.6883 to 0.8874)	0.9120 (0.8312 to 0.9552)	0.9045 (0.7853 to 0.9592)	0.9089 (0.8184 to 0.9555)	
24 Months	0.8096 (0.6883 to 0.8874)	0.9120 (0.8312 to 0.9552)	0.9045 (0.7853 to 0.9592)	0.9089 (0.8184 to 0.9555)	
27 Months	0.8096 (0.6883 to 0.8874)	0.9120 (0.8312 to 0.9552)	0.9045 (0.7853 to 0.9592)	0.9089 (0.8184 to 0.9555)	
30 Months	0.8096 (0.6883 to 0.8874)	0.9120 (0.8312 to 0.9552)	0.9045 (0.7853 to 0.9592)	0.9089 (0.8184 to 0.9555)	

Number of patients at risk[b]

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.50 Subgroup analysis by gender
16.2.7.1.50.3 Treatment emergent adverse event leading to discontinuation of treatment by treatment group according to gender - Safety population

	Male		Female		
	Kd (N=68)	**IKd (N=99)**	**Kd (N=54)**	**IKd (N=78)**	**p-value of treatment-by-sub group interaction[c]**
3 Months	62	96	53	74	
6 Months	56	89	52	72	
9 Months	51	86	48	69	
12 Months	50	85	47	67	
15 Months	48	77	44	63	
18 Months	45	72	44	61	
21 Months	36	63	37	55	
24 Months	14	21	12	19	
27 Months	1	1	3	1	
30 Months	0	0	0	0	

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
PGM=DEVOPS/SAR650984/EFC15246/CIR_RWE/REPORT/PGM/eff_km_sr_subgrp_sig_s_t.sas OUT=REPORT/OUTPUT/eff_km_de_tedisc_sex_s_t_x.rtf (12FEB2021 8:12)

16.2.7.1 Safety endpoints
16.2.7.1.50 Subgroup analysis by gender
16.2.7.1.50.4 Treatment emergent mild adverse event by treatment group according to gender - Safety population

	Male		Female		
	Kd (N=68)	**IKd (N=99)**	**Kd (N=54)**	**IKd (N=78)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	64 (94.1)	95 (96.0)	51 (94.4)	72 (92.3)	0.4479
Number (%) of patients censored	4 (5.9)	4 (4.0)	3 (5.6)	6 (7.7)	
Kaplan-Meier estimates of TEAE in months					
25% quantile (95% CI)	0.1643 (0.0657 to 0.2628)	0.0657 (0.0329 to 0.0986)	0.1971 (0.1314 to 0.3285)	0.0986 (0.0657 to 0.1314)	
Median (95% CI)	0.5257 (0.2957 to 0.6571)	0.1643 (0.1314 to 0.2300)	0.5257 (0.3285 to 0.9199)	0.2464 (0.1643 to 0.3943)	
75% quantile (95% CI)	0.8871 (0.6571 to 1.5113)	0.6571 (0.3614 to 1.1170)	1.5113 (0.9199 to 2.9240)	1.4784 (0.6242 to 2.1684)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd		0.0477		0.3648	
Hazard ratio (95% CI) vs Kd		1.3786 (1.0019 to 1.8969)		1.1806 (0.8241 to 1.6914)	
P-value		0.0487		0.3654	

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
PGM=DEVOPS/SAR650984/EFC15246/CIR_RWE/REPORT/PGM/eff_km_sr_subgrp_sig_s_t.sas OUT=REPORT/OUTPUT/eff_km_de_tesev12_sex_s_t_x.rtf (12FEB2021 8:13)

16.2.7.1 Safety endpoints
16.2.7.1.50 Subgroup analysis by gender
16.2.7.1.50.4 Treatment emergent mild adverse event by treatment group according to gender - Safety population

	Male		Female		
	Kd (N=68)	**IKd (N=99)**	**Kd (N=54)**	**IKd (N=78)**	**p-value of treatment-by-sub group interaction[c]**
Hazard ratio inverted (95% CI) vs IKd	0.7254 (0.5272 to 0.9981)				
probability (95% CI)[b]					
3 Months	0.1063 (0.0468 to 0.1937)	0.1049 (0.0539 to 0.1753)	0.1296 (0.0570 to 0.2330)	0.1154 (0.0567 to 0.1970)	
6 Months	0.0607 (0.0196 to 0.1358)	0.0708 (0.0303 to 0.1347)	0.0741 (0.0238 to 0.1634)	0.0769 (0.0314 to 0.1495)	
9 Months	0.0607 (0.0196 to 0.1358)	0.0283 (0.0059 to 0.0843)	0.0741 (0.0238 to 0.1634)	0.0769 (0.0314 to 0.1495)	
12 Months	0.0607 (0.0196 to 0.1358)	0.0142 (0.0013 to 0.0656)	0.0741 (0.0238 to 0.1634)	0.0769 (0.0314 to 0.1495)	
15 Months	0.0455 (0.0121 to 0.1153)	0.0142 (0.0013 to 0.0656)	0.0494 (0.0107 to 0.1361)	0.0769 (0.0314 to 0.1495)	
18 Months	0.0455 (0.0121 to 0.1153)	0.0142 (0.0013 to 0.0656)	0.0494 (0.0107 to 0.1361)	0.0769 (0.0314 to 0.1495)	
21 Months	0.0455 (0.0121 to 0.1153)	0.0142 (0.0013 to 0.0656)	0.0494 (0.0107 to 0.1361)	0.0769 (0.0314 to 0.1495)	
24 Months	0.0455 (0.0121 to 0.1153)	0.0142 (0.0013 to 0.0656)	0.0494 (0.0107 to 0.1361)	0.0769 (0.0314 to 0.1495)	

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
PGM=DEVOPS/SAR650984/EFC15246/CIR_RWE/REPORT/PGM/eff_km_sr_subgrp_sig_s_t.sas OUT=REPORT/OUTPUT/eff_km_de_tesev12_sex_s_t_x.rtf (12FEB2021 8:13)

16.2.7.1 Safety endpoints
16.2.7.1.50 Subgroup analysis by gender
16.2.7.1.50.4 Treatment emergent mild adverse event by treatment group according to gender - Safety population

	Male		Female		
	Kd (N=68)	**IKd (N=99)**	**Kd (N=54)**	**IKd (N=78)**	**p-value of treatment-by-sub group interaction[c]**
27 Months	0.0455 (0.0121 to 0.1153)	0.0142 (0.0013 to 0.0656)	0.0494 (0.0107 to 0.1361)	0.0769 (0.0314 to 0.1495)	
30 Months	0.0455 (0.0121 to 0.1153)	0.0142 (0.0013 to 0.0656)	0.0494 (0.0107 to 0.1361)	0.0769 (0.0314 to 0.1495)	
Number of patients at risk[b]					
3 Months	7	10	7	9	
6 Months	4	5	4	6	
9 Months	4	2	4	6	
12 Months	4	1	3	6	
15 Months	3	1	2	5	
18 Months	3	1	2	5	
21 Months	2	1	1	5	
24 Months	1	0	0	1	
27 Months	0	0	0	0	
30 Months	0	0	0	0	

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
PGM=DEVOPS/SAR650984/EFC15246/CIR_RWE/REPORT/PGM/eff_km_sr_subgrp_sig_s_t.sas OUT=REPORT/OUTPUT/eff_km_de_tesev12_sex_s_t_x.rtf (12FEB2021 8:13)

16.2.7.1 Safety endpoints
16.2.7.1.50 Subgroup analysis by gender
16.2.7.1.50.5 Treatment emergent severe adverse event by treatment group according to gender - Safety population

	Male		Female		
	Kd (N=68)	**IKd (N=99)**	**Kd (N=54)**	**IKd (N=78)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	42 (61.8)	79 (79.8)	39 (72.2)	55 (70.5)	0.1939
Number (%) of patients censored	26 (38.2)	20 (20.2)	15 (27.8)	23 (29.5)	
Kaplan-Meier estimates of TEAE in months					
25% quantile (95% CI)	2.1027 (1.0513 to 4.0411)	0.9528 (0.6242 to 2.0041)	1.1499 (0.3943 to 3.8768)	1.4127 (0.3943 to 3.2854)	
Median (95% CI)	7.6222 (4.0739 to 15.6057)	6.4066 (4.3368 to 9.0021)	6.2752 (3.8768 to 10.8090)	5.3881 (3.7125 to 7.8193)	
75% quantile (95% CI)	NC (NC to NC)	14.7187 (10.6776 to NC)	21.7823 (10.8090 to NC)	NC (9.7577 to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd		0.0317		0.9152	
Hazard ratio (95% CI) vs Kd		1.5055 (1.0338 to 2.1925)		1.0225 (0.6783 to 1.5414)	
P-value		0.0329		0.9153	
Hazard ratio inverted (95% CI) vs IKd	0.6642 (0.4561 to 0.9674)				

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
PGM=DEVOPS/SAR650984/EFC15246/CIR_RWE/REPORT/PGM/eff_km_sr_subgrp_sig_s_t.sas OUT=REPORT/OUTPUT/eff_km_de_tesev34_sex_s_t_x.rtf (12FEB2021 8:13)

16.2.7.1 Safety endpoints
16.2.7.1.50 Subgroup analysis by gender
16.2.7.1.50.5 Treatment emergent severe adverse event by treatment group according to gender - Safety population

	Male		Female		
	Kd (N=68)	**IKd (N=99)**	**Kd (N=54)**	**IKd (N=78)**	**p-value of treatment-by-sub group interaction[c]**
probability (95% CI)[b]					
3 Months	0.7022 (0.5772 to 0.7966)	0.6254 (0.5221 to 0.7124)	0.6852 (0.5434 to 0.7911)	0.6639 (0.5469 to 0.7572)	
6 Months	0.5495 (0.4225 to 0.6597)	0.5023 (0.4000 to 0.5961)	0.5185 (0.3786 to 0.6414)	0.4556 (0.3422 to 0.5620)	
9 Months	0.4732 (0.3495 to 0.5871)	0.4101 (0.3124 to 0.5051)	0.4051 (0.2741 to 0.5321)	0.3645 (0.2587 to 0.4708)	
12 Months	0.4427 (0.3211 to 0.5573)	0.2973 (0.2103 to 0.3892)	0.3472 (0.2234 to 0.4740)	0.2994 (0.2017 to 0.4032)	
15 Months	0.3969 (0.2794 to 0.5119)	0.2288 (0.1501 to 0.3176)	0.3074 (0.1895 to 0.4333)	0.2994 (0.2017 to 0.4032)	
18 Months	0.3657 (0.2514 to 0.4805)	0.1913 (0.1182 to 0.2778)	0.2869 (0.1723 to 0.4121)	0.2836 (0.1875 to 0.3873)	
21 Months	0.3657 (0.2514 to 0.4805)	0.1785 (0.1076 to 0.2641)	0.2869 (0.1723 to 0.4121)	0.2836 (0.1875 to 0.3873)	
24 Months	0.3657 (0.2514 to 0.4805)	0.1785 (0.1076 to 0.2641)	0.2459 (0.1304 to 0.3807)	0.2836 (0.1875 to 0.3873)	
27 Months	0.3657 (0.2514 to 0.4805)	0.1785 (0.1076 to 0.2641)	0.2459 (0.1304 to 0.3807)	0.2836 (0.1875 to 0.3873)	

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
PGM=DEVOPS/SAR650984/EFC15246/CIR_RWE/REPORT/PGM/eff_km_sr_subgrp_sig_s_t.sas OUT=REPORT/OUTPUT/eff_km_de_tesev34_sex_s_t_x.rtf (12FEB2021 8:13)

16.2.7.1 Safety endpoints
16.2.7.1.50 Subgroup analysis by gender
16.2.7.1.50.5 Treatment emergent severe adverse event by treatment group according to gender - Safety population

	Male		Female		
	Kd (N=68)	**IKd (N=99)**	**Kd (N=54)**	**IKd (N=78)**	**p-value of treatment-by-sub group interaction[c]**
30 Months	0.3657 (0.2514 to 0.4805)	0.1785 (0.1076 to 0.2641)	0.2459 (0.1304 to 0.3807)	0.2836 (0.1875 to 0.3873)	
Number of patients at risk[b]					
3 Months	46	61	37	51	
6 Months	36	49	28	35	
9 Months	31	40	21	28	
12 Months	29	29	18	23	
15 Months	26	19	15	20	
18 Months	23	15	14	18	
21 Months	17	13	10	18	
24 Months	7	6	1	4	
27 Months	1	0	0	0	
30 Months	0	0	0	0	

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
PGM=DEVOPS/SAR650984/EFC15246/CIR_RWE/REPORT/PGM/eff_km_sr_subgrp_sig_s_t.sas OUT=REPORT/OUTPUT/eff_km_de_tesev34_sex_s_t_x.rtf (12FEB2021 8:13)

16.2.7.1 Safety endpoints
16.2.7.1.50 Subgroup analysis by gender
16.2.7.1.50.6 Treatment emergent severe adverse event including death by treatment group according to gender - Safety population

	Male		Female		
	Kd (N=68)	**IKd (N=99)**	**Kd (N=54)**	**IKd (N=78)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	43 (63.2)	80 (80.8)	39 (72.2)	56 (71.8)	0.2270
Number (%) of patients censored	25 (36.8)	19 (19.2)	15 (27.8)	22 (28.2)	
Kaplan-Meier estimates of TEAE in months					
25% quantile (95% CI)	2.0862 (0.9856 to 4.0411)	0.9528 (0.6242 to 2.0041)	1.1499 (0.3943 to 3.8768)	1.3142 (0.3943 to 2.5955)	
Median (95% CI)	7.5236 (4.0739 to 15.6057)	6.4066 (4.3368 to 9.0021)	6.2752 (3.8768 to 10.8090)	5.2074 (3.5154 to 7.8193)	
75% quantile (95% CI)	NC (15.9343 to NC)	14.1602 (10.6776 to NC)	21.7823 (10.8090 to NC)	NC (9.7577 to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd		0.0339		0.8474	
Hazard ratio (95% CI) vs Kd		1.4922 (1.0284 to 2.1651)		1.0408 (0.6915 to 1.5666)	
P-value		0.0351		0.8479	
Hazard ratio inverted (95% CI) vs IKd	0.6702 (0.4619 to 0.9724)				

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
PGM=DEVOPS/SAR650984/EFC15246/CIR_RWE/REPORT/PGM/eff_km_sr_subgrp_sig_s_t.sas OUT=REPORT/OUTPUT/eff_km_de_tesev345_sex_s_t_x.rtf (12FEB2021 8:13)

16.2.7.1 Safety endpoints
16.2.7.1.50 Subgroup analysis by gender
16.2.7.1.50.6 Treatment emergent severe adverse event including death by treatment group according to gender - Safety population

	Male		Female		
	Kd (N=68)	**IKd (N=99)**	**Kd (N=54)**	**IKd (N=78)**	**p-value of treatment-by-sub group interaction[c]**
probability (95% CI)[b]					
3 Months	0.6903 (0.5655 to 0.7858)	0.6254 (0.5221 to 0.7124)	0.6852 (0.5434 to 0.7911)	0.6538 (0.5372 to 0.7479)	
6 Months	0.5402 (0.4144 to 0.6502)	0.5023 (0.4000 to 0.5961)	0.5185 (0.3786 to 0.6414)	0.4487 (0.3365 to 0.5546)	
9 Months	0.4652 (0.3429 to 0.5785)	0.4101 (0.3124 to 0.5051)	0.4051 (0.2741 to 0.5321)	0.3590 (0.2545 to 0.4644)	
12 Months	0.4352 (0.3151 to 0.5491)	0.2973 (0.2103 to 0.3892)	0.3472 (0.2234 to 0.4740)	0.2949 (0.1984 to 0.3977)	
15 Months	0.3902 (0.2742 to 0.5042)	0.2204 (0.1434 to 0.3079)	0.3074 (0.1895 to 0.4333)	0.2949 (0.1984 to 0.3977)	
18 Months	0.3595 (0.2468 to 0.4733)	0.1842 (0.1130 to 0.2691)	0.2869 (0.1723 to 0.4121)	0.2794 (0.1845 to 0.3820)	
21 Months	0.3595 (0.2468 to 0.4733)	0.1719 (0.1029 to 0.2557)	0.2869 (0.1723 to 0.4121)	0.2794 (0.1845 to 0.3820)	
24 Months	0.3595 (0.2468 to 0.4733)	0.1719 (0.1029 to 0.2557)	0.2459 (0.1304 to 0.3807)	0.2794 (0.1845 to 0.3820)	
27 Months	0.3595 (0.2468 to 0.4733)	0.1719 (0.1029 to 0.2557)	0.2459 (0.1304 to 0.3807)	0.2794 (0.1845 to 0.3820)	

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
PGM=DEVOPS/SAR650984/EFC15246/CIR_RWE/REPORT/PGM/eff_km_sr_subgrp_sig_s_t.sas OUT=REPORT/OUTPUT/eff_km_de_tesev345_sex_s_t_x.rtf (12FEB2021 8:13)

16.2.7.1 Safety endpoints
16.2.7.1.50 Subgroup analysis by gender
16.2.7.1.50.6 Treatment emergent severe adverse event including death by treatment group according to gender - Safety population

	Male		Female		
	Kd (N=68)	**IKd (N=99)**	**Kd (N=54)**	**IKd (N=78)**	**p-value of treatment-by-sub group interaction[c]**
30 Months	0.3595 (0.2468 to 0.4733)	0.1719 (0.1029 to 0.2557)	0.2459 (0.1304 to 0.3807)	0.2794 (0.1845 to 0.3820)	
Number of patients at risk[b]					
3 Months	46	61	37	51	
6 Months	36	49	28	35	
9 Months	31	40	21	28	
12 Months	29	29	18	23	
15 Months	26	19	15	20	
18 Months	23	15	14	18	
21 Months	17	13	10	18	
24 Months	7	6	1	4	
27 Months	1	0	0	0	
30 Months	0	0	0	0	

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
PGM=DEVOPS/SAR650984/EFC15246/CIR_RWE/REPORT/PGM/eff_km_sr_subgrp_sig_s_t.sas OUT=REPORT/OUTPUT/eff_km_de_tesev345_sex_s_t_x.rtf (12FEB2021 8:13)

16.2.7.1 Safety endpoints
16.2.7.1.51 Subgroup analysis by ethnic origin
16.2.7.1.51.1 Treatment emergent adverse event by treatment group according to ethnic origin - Safety population

	White		Other		
	Kd (N=83)	**IKd (N=130)**	**Kd (N=27)**	**IKd (N=33)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	78 (94.0)	125 (96.2)	27 (100.0)	33 (100.0)	0.9617
Number (%) of patients censored	5 (6.0)	5 (3.8)	0 (0.0)	0 (0.0)	
Kaplan-Meier estimates of TEAE in months					
25% quantile (95% CI)	0.1643 (0.0986 to 0.2300)	0.0657 (0.0657 to 0.0986)	0.2300 (0.0986 to 0.3943)	0.0657 (0.0329 to 0.0986)	
Median (95% CI)	0.3614 (0.2628 to 0.6242)	0.1971 (0.1314 to 0.2628)	0.5257 (0.2628 to 0.6571)	0.1643 (0.0986 to 0.2957)	
75% quantile (95% CI)	1.1828 (0.6571 to 2.2012)	0.6899 (0.4600 to 1.1170)	0.6899 (0.5257 to 1.2485)	0.5257 (0.1971 to 2.1684)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd		0.0685		0.4220	
Hazard ratio (95% CI) vs Kd		1.3004 (0.9794 to 1.7264)		1.2408 (0.7322 to 2.1028)	
P-value		0.0693		0.4227	

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
PGM=DEVOPS/SAR650984/EFC15246/CIR_RWE/REPORT/PGM/eff_km_sr_subgrp_sig_s_t.sas OUT=REPORT/OUTPUT/eff_km_de_teae_race_s_t_x.rtf (12FEB2021 8:09)

16.2.7.1 Safety endpoints
16.2.7.1.51 Subgroup analysis by ethnic origin
16.2.7.1.51.1 Treatment emergent adverse event by treatment group according to ethnic origin - Safety population

	White		Other		
	Kd (N=83)	**IKd (N=130)**	**Kd (N=27)**	**IKd (N=33)**	**p-value of treatment-by-sub group interaction[c]**
probability (95% CI)[b]					
3 Months	0.1084 (0.0533 to 0.1858)	0.0846 (0.0448 to 0.1403)	0.0370 (0.0027 to 0.1590)	0.0606 (0.0108 to 0.1762)	
6 Months	0.0723 (0.0295 to 0.1410)	0.0538 (0.0238 to 0.1020)	0.0370 (0.0027 to 0.1590)	0.0303 (0.0023 to 0.1335)	
9 Months	0.0723 (0.0295 to 0.1410)	0.0462 (0.0190 to 0.0920)	0.0370 (0.0027 to 0.1590)	0.0303 (0.0023 to 0.1335)	
12 Months	0.0723 (0.0295 to 0.1410)	0.0385 (0.0144 to 0.0819)	0.0370 (0.0027 to 0.1590)	0.0303 (0.0023 to 0.1335)	
15 Months	0.0602 (0.0223 to 0.1254)	0.0385 (0.0144 to 0.0819)	0.0370 (0.0027 to 0.1590)	0.0303 (0.0023 to 0.1335)	
18 Months	0.0602 (0.0223 to 0.1254)	0.0385 (0.0144 to 0.0819)	0.0370 (0.0027 to 0.1590)	0.0303 (0.0023 to 0.1335)	
21 Months	0.0602 (0.0223 to 0.1254)	0.0385 (0.0144 to 0.0819)	0.0370 (0.0027 to 0.1590)	0.0303 (0.0023 to 0.1335)	
24 Months	0.0602 (0.0223 to 0.1254)	0.0385 (0.0144 to 0.0819)	0.0370 (0.0027 to 0.1590)	0.0303 (0.0023 to 0.1335)	
27 Months	0.0602 (0.0223 to 0.1254)	0.0385 (0.0144 to 0.0819)	0.0370 (0.0027 to 0.1590)	0.0303 (0.0023 to 0.1335)	

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
PGM=DEVOPS/SAR650984/EFC15246/CIR_RWE/REPORT/PGM/eff_km_sr_subgrp_sig_s_t.sas OUT=REPORT/OUTPUT/eff_km_de_teae_race_s_t_x.rtf (12FEB2021 8:09)

16.2.7.1 Safety endpoints
16.2.7.1.51 Subgroup analysis by ethnic origin
16.2.7.1.51.1 Treatment emergent adverse event by treatment group according to ethnic origin - Safety population

	White		Other		
	Kd (N=83)	**IKd (N=130)**	**Kd (N=27)**	**IKd (N=33)**	**p-value of treatment-by-sub group interaction[c]**
30 Months	0.0602 (0.0223 to 0.1254)	0.0385 (0.0144 to 0.0819)	0.0370 (0.0027 to 0.1590)	0.0303 (0.0023 to 0.1335)	
Number of patients at risk[b]					
3 Months	9	11	1	2	
6 Months	6	7	0	1	
9 Months	6	6	0	0	
12 Months	6	5	0	0	
15 Months	5	5	0	0	
18 Months	5	5	0	0	
21 Months	3	5	0	0	
24 Months	1	1	0	0	
27 Months	0	0	0	0	
30 Months	0	0	0	0	

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
PGM=DEVOPS/SAR650984/EFC15246/CIR_RWE/REPORT/PGM/eff_km_sr_subgrp_sig_s_t.sas OUT=REPORT/OUTPUT/eff_km_de_teae_race_s_t_x.rtf (12FEB2021 8:09)

16.2.7.1 Safety endpoints
16.2.7.1.51 Subgroup analysis by ethnic origin
16.2.7.1.51.2 Treatment emergent serious adverse event by treatment group according to ethnic origin - Safety population

	White		Other		
	Kd (N=83)	**IKd (N=130)**	**Kd (N=27)**	**IKd (N=33)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	50 (60.2)	82 (63.1)	14 (51.9)	16 (48.5)	0.5481
Number (%) of patients censored	33 (39.8)	48 (36.9)	13 (48.1)	17 (51.5)	
Kaplan-Meier estimates of TEAE in months					
25% quantile (95% CI)	4.6324 (2.0698 to 5.8480)	1.9713 (0.8871 to 4.5010)	5.5195 (0.4600 to 10.4805)	6.4066 (0.0986 to 11.4333)	
Median (95% CI)	13.8316 (7.6879 to 21.7823)	11.2361 (7.6879 to 13.4045)	15.4415 (5.5524 to NC)	18.1027 (8.4435 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd		0.4007		0.8210	
Hazard ratio (95% CI) vs Kd		1.1627 (0.8178 to 1.6531)		0.9201 (0.4487 to 1.8869)	
P-value		0.4011		0.8203	
probability (95% CI)[b]					

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
PGM=DEVOPS/SAR650984/EFC15246/CIR_RWE/REPORT/PGM/eff_km_sr_subgrp_sig_s_t.sas OUT=REPORT/OUTPUT/eff_km_de_tesae_race_s_t_x.rtf (12FEB2021 8:12)

16.2.7.1 Safety endpoints
16.2.7.1.51 Subgroup analysis by ethnic origin
16.2.7.1.51.2 Treatment emergent serious adverse event by treatment group according to ethnic origin - Safety population

	White		Other		
	Kd (N=83)	**IKd (N=130)**	**Kd (N=27)**	**IKd (N=33)**	**p-value of treatment-by-sub group interaction[c]**
3 Months	0.8072 (0.7048 to 0.8772)	0.7231 (0.6375 to 0.7917)	0.8519 (0.6520 to 0.9417)	0.7879 (0.6059 to 0.8927)	
6 Months	0.6506 (0.5378 to 0.7424)	0.6302 (0.5410 to 0.7067)	0.7037 (0.4940 to 0.8394)	0.7576 (0.5733 to 0.8706)	
9 Months	0.6022 (0.4886 to 0.6982)	0.5524 (0.4626 to 0.6332)	0.6296 (0.4212 to 0.7807)	0.6667 (0.4794 to 0.7996)	
12 Months	0.5653 (0.4518 to 0.6640)	0.4823 (0.3939 to 0.5652)	0.5185 (0.3191 to 0.6855)	0.6061 (0.4201 to 0.7489)	
15 Months	0.4547 (0.3450 to 0.5579)	0.3859 (0.3017 to 0.4693)	0.5185 (0.3191 to 0.6855)	0.6061 (0.4201 to 0.7489)	
18 Months	0.4171 (0.3098 to 0.5208)	0.3777 (0.2940 to 0.4610)	0.4753 (0.2791 to 0.6482)	0.5348 (0.3491 to 0.6892)	
21 Months	0.4045 (0.2981 to 0.5082)	0.3777 (0.2940 to 0.4610)	0.4753 (0.2791 to 0.6482)	0.4991 (0.3155 to 0.6580)	
24 Months	0.3820 (0.2738 to 0.4892)	0.3573 (0.2741 to 0.4411)	0.4753 (0.2791 to 0.6482)	0.4991 (0.3155 to 0.6580)	
27 Months	0.3820 (0.2738 to 0.4892)	0.3573 (0.2741 to 0.4411)	0.4753 (0.2791 to 0.6482)	0.4991 (0.3155 to 0.6580)	
30 Months	0.3820 (0.2738 to 0.4892)	0.3573 (0.2741 to 0.4411)	0.4753 (0.2791 to 0.6482)	0.4991 (0.3155 to 0.6580)	

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
PGM=DEVOPS/SAR650984/EFC15246/CIR_RWE/REPORT/PGM/eff_km_sr_subgrp_sig_s_t.sas OUT=REPORT/OUTPUT/eff_km_de_tesae_race_s_t_x.rtf (12FEB2021 8:12)

16.2.7.1 Safety endpoints
16.2.7.1.51 Subgroup analysis by ethnic origin
16.2.7.1.51.2 Treatment emergent serious adverse event by treatment group according to ethnic origin - Safety population

	White		Other		
	Kd (N=83)	**IKd (N=130)**	**Kd (N=27)**	**IKd (N=33)**	**p-value of treatment-by-sub group interaction[c]**
Number of patients at risk[b]					
3 Months	67	94	23	26	
6 Months	54	81	19	25	
9 Months	49	71	17	22	
12 Months	46	62	14	20	
15 Months	37	47	12	17	
18 Months	33	43	11	15	
21 Months	22	38	10	14	
24 Months	4	11	4	6	
27 Months	0	1	2	0	
30 Months	0	0	0	0	

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.51 Subgroup analysis by ethnic origin
16.2.7.1.51.3 Treatment emergent adverse event leading to discontinuation of treatment by treatment group according to ethnic origin - Safety population

	White		Other		
	Kd (N=83)	**IKd (N=130)**	**Kd (N=27)**	**IKd (N=33)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	10 (12.0)	14 (10.8)	4 (14.8)	1 (3.0)	0.2217
Number (%) of patients censored	73 (88.0)	116 (89.2)	23 (85.2)	32 (97.0)	
Kaplan-Meier estimates of TEAE in months					
25% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (7.3922 to NC)	NC (NC to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd		0.7396		0.1163	
Hazard ratio (95% CI) vs Kd		0.8715 (0.3871 to 1.9621)		0.2050 (0.0229 to 1.8342)	
P-value		0.7398		0.1564	
probability (95% CI)[b]					
3 Months	0.9517 (0.8763 to 0.9816)	0.9612 (0.9094 to 0.9837)	0.9630 (0.7649 to 0.9947)	1.0000 (1.0000 to 1.0000)	

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
PGM=DEVOPS/SAR650984/EFC15246/CIR_RWE/REPORT/PGM/eff_km_sr_subgrp_sig_s_t.sas OUT=REPORT/OUTPUT/eff_km_de_tedisc_race_s_t_x.rtf (12FEB2021 8:12)

16.2.7.1 Safety endpoints
16.2.7.1.51 Subgroup analysis by ethnic origin
16.2.7.1.51.3 Treatment emergent adverse event leading to discontinuation of treatment by treatment group according to ethnic origin - Safety population

	White		Other		
	Kd (N=83)	**IKd (N=130)**	**Kd (N=27)**	**IKd (N=33)**	**p-value of treatment-by-sub group interaction[c]**
6 Months	0.9147 (0.8294 to 0.9584)	0.9374 (0.8787 to 0.9682)	0.9630 (0.7649 to 0.9947)	0.9688 (0.7982 to 0.9955)	
9 Months	0.8895 (0.7983 to 0.9409)	0.9132 (0.8486 to 0.9510)	0.8889 (0.6939 to 0.9627)	0.9688 (0.7982 to 0.9955)	
12 Months	0.8895 (0.7983 to 0.9409)	0.9132 (0.8486 to 0.9510)	0.8889 (0.6939 to 0.9627)	0.9688 (0.7982 to 0.9955)	
15 Months	0.8895 (0.7983 to 0.9409)	0.8966 (0.8286 to 0.9387)	0.8889 (0.6939 to 0.9627)	0.9688 (0.7982 to 0.9955)	
18 Months	0.8895 (0.7983 to 0.9409)	0.8966 (0.8286 to 0.9387)	0.8444 (0.6351 to 0.9390)	0.9688 (0.7982 to 0.9955)	
21 Months	0.8756 (0.7808 to 0.9311)	0.8875 (0.8172 to 0.9318)	0.8444 (0.6351 to 0.9390)	0.9688 (0.7982 to 0.9955)	
24 Months	0.8756 (0.7808 to 0.9311)	0.8875 (0.8172 to 0.9318)	0.8444 (0.6351 to 0.9390)	0.9688 (0.7982 to 0.9955)	
27 Months	0.8756 (0.7808 to 0.9311)	0.8875 (0.8172 to 0.9318)	0.8444 (0.6351 to 0.9390)	0.9688 (0.7982 to 0.9955)	
30 Months	0.8756 (0.7808 to 0.9311)	0.8875 (0.8172 to 0.9318)	0.8444 (0.6351 to 0.9390)	0.9688 (0.7982 to 0.9955)	

Number of patients at risk[b]

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
PGM=DEVOPS/SAR650984/EFC15246/CIR_RWE/REPORT/PGM/eff_km_sr_subgrp_sig_s_t.sas OUT=REPORT/OUTPUT/eff_km_de_tedisc_race_s_t_x.rtf (12FEB2021 8:12)

16.2.7.1 Safety endpoints
16.2.7.1.51 Subgroup analysis by ethnic origin
16.2.7.1.51.3 Treatment emergent adverse event leading to discontinuation of treatment by treatment group according to ethnic origin - Safety population

	White		Other		
	Kd (N=83)	**IKd (N=130)**	**Kd (N=27)**	**IKd (N=33)**	**p-value of treatment-by-sub group interaction[c]**
3 Months	78	124	26	32	
6 Months	73	117	26	31	
9 Months	69	112	23	30	
12 Months	67	112	23	29	
15 Months	65	105	20	25	
18 Months	64	99	19	24	
21 Months	49	85	18	24	
24 Months	17	30	7	8	
27 Months	1	1	3	1	
30 Months	0	0	0	0	

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
PGM=DEVOPS/SAR650984/EFC15246/CIR_RWE/REPORT/PGM/eff_km_sr_subgrp_sig_s_t.sas OUT=REPORT/OUTPUT/eff_km_de_tedisc_race_s_t_x.rtf (12FEB2021 8:12)

16.2.7.1 Safety endpoints
16.2.7.1.51 Subgroup analysis by ethnic origin
16.2.7.1.51.4 Treatment emergent mild adverse event by treatment group according to ethnic origin - Safety population

	White		Other		
	Kd (N=83)	**IKd (N=130)**	**Kd (N=27)**	**IKd (N=33)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	76 (91.6)	121 (93.1)	27 (100.0)	33 (100.0)	0.8451
Number (%) of patients censored	7 (8.4)	9 (6.9)	0 (0.0)	0 (0.0)	
Kaplan-Meier estimates of TEAE in months					
25% quantile (95% CI)	0.1643 (0.0986 to 0.2628)	0.0657 (0.0657 to 0.0986)	0.2300 (0.0986 to 0.3943)	0.0657 (0.0329 to 0.1314)	
Median (95% CI)	0.5257 (0.3285 to 0.6571)	0.2136 (0.1643 to 0.2957)	0.5257 (0.2628 to 0.6899)	0.1643 (0.0986 to 0.2957)	
75% quantile (95% CI)	1.5113 (0.6899 to 2.8912)	0.9528 (0.4928 to 1.4784)	0.9528 (0.6242 to 1.2485)	1.4456 (0.1971 to 2.8255)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd		0.0705		0.7938	
Hazard ratio (95% CI) vs Kd		1.3028 (0.9773 to 1.7367)		1.0744 (0.6269 to 1.8414)	
P-value		0.0713		0.7939	

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
PGM=DEVOPS/SAR650984/EFC15246/CIR_RWE/REPORT/PGM/eff_km_sr_subgrp_sig_s_t.sas OUT=REPORT/OUTPUT/eff_km_de_tesev12_race_s_t_x.rtf (12FEB2021 8:12)

16.2.7.1 Safety endpoints
16.2.7.1.51 Subgroup analysis by ethnic origin
16.2.7.1.51.4 Treatment emergent mild adverse event by treatment group according to ethnic origin - Safety population

	White		Other		
	Kd (N=83)	**IKd (N=130)**	**Kd (N=27)**	**IKd (N=33)**	**p-value of treatment-by-sub group interaction[c]**
probability (95% CI)[b]					
3 Months	0.1483 (0.0815 to 0.2339)	0.1182 (0.0696 to 0.1808)	0.0370 (0.0027 to 0.1590)	0.0909 (0.0233 to 0.2167)	
6 Months	0.0989 (0.0463 to 0.1751)	0.0849 (0.0444 to 0.1418)	0.0370 (0.0027 to 0.1590)	0.0303 (0.0023 to 0.1335)	
9 Months	0.0989 (0.0463 to 0.1751)	0.0679 (0.0324 to 0.1213)	0.0370 (0.0027 to 0.1590)	0.0303 (0.0023 to 0.1335)	
12 Months	0.0989 (0.0463 to 0.1751)	0.0594 (0.0267 to 0.1108)	0.0370 (0.0027 to 0.1590)	0.0303 (0.0023 to 0.1335)	
15 Months	0.0706 (0.0275 to 0.1416)	0.0594 (0.0267 to 0.1108)	0.0370 (0.0027 to 0.1590)	0.0303 (0.0023 to 0.1335)	
18 Months	0.0706 (0.0275 to 0.1416)	0.0594 (0.0267 to 0.1108)	0.0370 (0.0027 to 0.1590)	0.0303 (0.0023 to 0.1335)	
21 Months	0.0706 (0.0275 to 0.1416)	0.0594 (0.0267 to 0.1108)	0.0370 (0.0027 to 0.1590)	0.0303 (0.0023 to 0.1335)	
24 Months	0.0706 (0.0275 to 0.1416)	0.0594 (0.0267 to 0.1108)	0.0370 (0.0027 to 0.1590)	0.0303 (0.0023 to 0.1335)	
27 Months	0.0706 (0.0275 to 0.1416)	0.0594 (0.0267 to 0.1108)	0.0370 (0.0027 to 0.1590)	0.0303 (0.0023 to 0.1335)	

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
PGM=DEVOPS/SAR650984/EFC15246/CIR_RWE/REPORT/PGM/eff_km_sr_subgrp_sig_s_t.sas OUT=REPORT/OUTPUT/eff_km_de_tesev12_race_s_t_x.rtf (12FEB2021 8:12)

16.2.7.1 Safety endpoints
16.2.7.1.51 Subgroup analysis by ethnic origin
16.2.7.1.51.4 Treatment emergent mild adverse event by treatment group according to ethnic origin - Safety population

	White		Other		
	Kd (N=83)	**IKd (N=130)**	**Kd (N=27)**	**IKd (N=33)**	**p-value of treatment-by-sub group interaction[c]**
30 Months	0.0706 (0.0275 to 0.1416)	0.0594 (0.0267 to 0.1108)	0.0370 (0.0027 to 0.1590)	0.0303 (0.0023 to 0.1335)	
Number of patients at risk[b]					
3 Months	12	15	1	3	
6 Months	8	10	0	1	
9 Months	8	8	0	0	
12 Months	7	7	0	0	
15 Months	5	6	0	0	
18 Months	5	6	0	0	
21 Months	3	6	0	0	
24 Months	1	1	0	0	
27 Months	0	0	0	0	
30 Months	0	0	0	0	

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
PGM=DEVOPS/SAR650984/EFC15246/CIR_RWE/REPORT/PGM/eff_km_sr_subgrp_sig_s_t.sas OUT=REPORT/OUTPUT/eff_km_de_tesev12_race_s_t_x.rtf (12FEB2021 8:12)

16.2.7.1 Safety endpoints
16.2.7.1.51 Subgroup analysis by ethnic origin
16.2.7.1.51.5 Treatment emergent severe adverse event by treatment group according to ethnic origin - Safety population

	White		Other		
	Kd (N=83)	**IKd (N=130)**	**Kd (N=27)**	**IKd (N=33)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	57 (68.7)	99 (76.2)	16 (59.3)	26 (78.8)	0.4650
Number (%) of patients censored	26 (31.3)	31 (23.8)	11 (40.7)	7 (21.2)	
Kaplan-Meier estimates of TEAE in months					
25% quantile (95% CI)	2.0698 (0.5257 to 3.9097)	1.3142 (0.6571 to 2.1027)	1.9055 (0.4600 to 5.5195)	1.6427 (0.0986 to 2.7926)	
Median (95% CI)	6.2752 (4.2053 to 12.3532)	5.5524 (4.1725 to 7.6550)	7.5236 (3.2854 to NC)	7.7536 (1.9713 to 11.4333)	
75% quantile (95% CI)	NC (13.8645 to NC)	15.8357 (10.7433 to NC)	NC (10.4805 to NC)	14.7187 (8.2464 to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd		0.2181		0.1521	
Hazard ratio (95% CI) vs Kd		1.2272 (0.8855 to 1.7008)		1.5731 (0.8418 to 2.9398)	
P-value		0.2189		0.1556	
probability (95% CI)[b]					

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
PGM=DEVOPS/SAR650984/EFC15246/CIR_RWE/REPORT/PGM/eff_km_sr_subgrp_sig_s_t.sas OUT=REPORT/OUTPUT/eff_km_de_tesev34_race_s_t_x.rtf (12FEB2021 8:13)

16.2.7.1 Safety endpoints
16.2.7.1.51 Subgroup analysis by ethnic origin
16.2.7.1.51.5 Treatment emergent severe adverse event by treatment group according to ethnic origin - Safety population

	White		Other		
	Kd (N=83)	**IKd (N=130)**	**Kd (N=27)**	**IKd (N=33)**	**p-value of treatment-by-sub group interaction[c]**
3 Months	0.6848 (0.5726 to 0.7732)	0.6518 (0.5630 to 0.7270)	0.7407 (0.5319 to 0.8670)	0.6019 (0.4146 to 0.7463)	
6 Months	0.5258 (0.4128 to 0.6269)	0.4501 (0.3628 to 0.5333)	0.5926 (0.3863 to 0.7499)	0.5702 (0.3842 to 0.7190)	
9 Months	0.4515 (0.3416 to 0.5550)	0.3802 (0.2969 to 0.4630)	0.4815 (0.2869 to 0.6519)	0.3802 (0.2168 to 0.5424)	
12 Months	0.4139 (0.3065 to 0.5178)	0.2949 (0.2188 to 0.3748)	0.4074 (0.2253 to 0.5821)	0.2851 (0.1429 to 0.4452)	
15 Months	0.3512 (0.2494 to 0.4544)	0.2533 (0.1815 to 0.3313)	0.4074 (0.2253 to 0.5821)	0.2444 (0.1108 to 0.4056)	
18 Months	0.3126 (0.2151 to 0.4147)	0.2349 (0.1649 to 0.3121)	0.4074 (0.2253 to 0.5821)	0.1629 (0.0555 to 0.3202)	
21 Months	0.3126 (0.2151 to 0.4147)	0.2255 (0.1566 to 0.3023)	0.4074 (0.2253 to 0.5821)	0.1629 (0.0555 to 0.3202)	
24 Months	0.2865 (0.1872 to 0.3936)	0.2255 (0.1566 to 0.3023)	0.4074 (0.2253 to 0.5821)	0.1629 (0.0555 to 0.3202)	
27 Months	0.2865 (0.1872 to 0.3936)	0.2255 (0.1566 to 0.3023)	0.4074 (0.2253 to 0.5821)	0.1629 (0.0555 to 0.3202)	
30 Months	0.2865 (0.1872 to 0.3936)	0.2255 (0.1566 to 0.3023)	0.4074 (0.2253 to 0.5821)	0.1629 (0.0555 to 0.3202)	

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
PGM=DEVOPS/SAR650984/EFC15246/CIR_RWE/REPORT/PGM/eff_km_sr_subgrp_sig_s_t.sas OUT=REPORT/OUTPUT/eff_km_de_tesev34_race_s_t_x.rtf (12FEB2021 8:13)

16.2.7.1 Safety endpoints
16.2.7.1.51 Subgroup analysis by ethnic origin
16.2.7.1.51.5 Treatment emergent severe adverse event by treatment group according to ethnic origin - Safety population

	White		Other		
	Kd (N=83)	**IKd (N=130)**	**Kd (N=27)**	**IKd (N=33)**	**p-value of treatment-by-sub group interaction[c]**
Number of patients at risk[b]					
3 Months	56	84	20	19	
6 Months	43	58	16	18	
9 Months	36	49	13	12	
12 Months	33	38	11	9	
15 Months	28	29	10	6	
18 Months	24	25	10	4	
21 Months	15	23	9	4	
24 Months	4	7	3	1	
27 Months	0	0	1	0	
30 Months	0	0	0	0	

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.51 Subgroup analysis by ethnic origin
16.2.7.1.51.6 Treatment emergent severe adverse event including death by treatment group according to ethnic origin - Safety population

	White		Other		
	Kd (N=83)	**IKd (N=130)**	**Kd (N=27)**	**IKd (N=33)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	58 (69.9)	101 (77.7)	16 (59.3)	26 (78.8)	0.4669
Number (%) of patients censored	25 (30.1)	29 (22.3)	11 (40.7)	7 (21.2)	
Kaplan-Meier estimates of TEAE in months					
25% quantile (95% CI)	1.8727 (0.5257 to 3.8768)	1.2813 (0.6571 to 2.0041)	1.9055 (0.4600 to 5.5195)	1.6427 (0.0986 to 2.7926)	
Median (95% CI)	6.2752 (4.2053 to 12.2875)	5.4867 (4.1725 to 7.1622)	7.5236 (3.2854 to NC)	7.7536 (1.9713 to 11.4333)	
75% quantile (95% CI)	NC (13.8645 to NC)	14.8830 (10.7433 to NC)	NC (10.4805 to NC)	14.7187 (8.2464 to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd		0.2073		0.1521	
Hazard ratio (95% CI) vs Kd		1.2309 (0.8908 to 1.7008)		1.5731 (0.8418 to 2.9398)	
P-value		0.2081		0.1556	
probability (95% CI)[b]					

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
PGM=DEVOPS/SAR650984/EFC15246/CIR_RWE/REPORT/PGM/eff_km_sr_subgrp_sig_s_t.sas OUT=REPORT/OUTPUT/eff_km_de_tesev345_race_s_t_x.rtf (12FEB2021 8:13)

16.2.7.1 Safety endpoints
16.2.7.1.51 Subgroup analysis by ethnic origin
16.2.7.1.51.6 Treatment emergent severe adverse event including death by treatment group according to ethnic origin - Safety population

	White		Other		
	Kd (N=83)	**IKd (N=130)**	**Kd (N=27)**	**IKd (N=33)**	**p-value of treatment-by-sub group interaction[c]**
3 Months	0.6747 (0.5626 to 0.7640)	0.6462 (0.5574 to 0.7215)	0.7407 (0.5319 to 0.8670)	0.6019 (0.4146 to 0.7463)	
6 Months	0.5181 (0.4059 to 0.6190)	0.4462 (0.3594 to 0.5291)	0.5926 (0.3863 to 0.7499)	0.5702 (0.3842 to 0.7190)	
9 Months	0.4449 (0.3361 to 0.5479)	0.3769 (0.2941 to 0.4593)	0.4815 (0.2869 to 0.6519)	0.3802 (0.2168 to 0.5424)	
12 Months	0.4078 (0.3016 to 0.5111)	0.2923 (0.2168 to 0.3717)	0.4074 (0.2253 to 0.5821)	0.2851 (0.1429 to 0.4452)	
15 Months	0.3460 (0.2455 to 0.4485)	0.2441 (0.1739 to 0.3209)	0.4074 (0.2253 to 0.5821)	0.2444 (0.1108 to 0.4056)	
18 Months	0.3080 (0.2117 to 0.4092)	0.2264 (0.1581 to 0.3023)	0.4074 (0.2253 to 0.5821)	0.1629 (0.0555 to 0.3202)	
21 Months	0.3080 (0.2117 to 0.4092)	0.2173 (0.1501 to 0.2927)	0.4074 (0.2253 to 0.5821)	0.1629 (0.0555 to 0.3202)	
24 Months	0.2823 (0.1843 to 0.3883)	0.2173 (0.1501 to 0.2927)	0.4074 (0.2253 to 0.5821)	0.1629 (0.0555 to 0.3202)	
27 Months	0.2823 (0.1843 to 0.3883)	0.2173 (0.1501 to 0.2927)	0.4074 (0.2253 to 0.5821)	0.1629 (0.0555 to 0.3202)	
30 Months	0.2823 (0.1843 to 0.3883)	0.2173 (0.1501 to 0.2927)	0.4074 (0.2253 to 0.5821)	0.1629 (0.0555 to 0.3202)	

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.51 Subgroup analysis by ethnic origin
16.2.7.1.51.6 Treatment emergent severe adverse event including death by treatment group according to ethnic origin - Safety population

	White		Other		
	Kd (N=83)	**IKd (N=130)**	**Kd (N=27)**	**IKd (N=33)**	**p-value of treatment-by-sub group interaction[c]**
Number of patients at risk[b]					
3 Months	56	84	20	19	
6 Months	43	58	16	18	
9 Months	36	49	13	12	
12 Months	33	38	11	9	
15 Months	28	29	10	6	
18 Months	24	25	10	4	
21 Months	15	23	9	4	
24 Months	4	7	3	1	
27 Months	0	0	1	0	
30 Months	0	0	0	0	

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.52 Subgroup analysis by geographical region
16.2.7.1.52.1 Treatment emergent adverse event by treatment group according to geographical region - Safety population

	Europe		America	
	Kd (N=60)	**IKd (N=85)**	**Kd (N=20)**	**IKd (N=23)**
Number (%) of events	56 (93.3)	80 (94.1)	20 (100.0)	23 (100.0)
Number (%) of patients censored	4 (6.7)	5 (5.9)	0 (0.0)	0 (0.0)
Kaplan-Meier estimates of TEAE in months				
25% quantile (95% CI)	0.0986 (0.0657 to 0.2628)	0.0657 (0.0657 to 0.0986)	0.1807 (0.0329 to 0.2300)	0.0986 (0.0329 to 0.1314)
Median (95% CI)	0.4107 (0.2628 to 0.7885)	0.2628 (0.1643 to 0.4928)	0.3450 (0.1643 to 0.6899)	0.1643 (0.1314 to 0.3614)
75% quantile (95% CI)	1.6756 (0.7885 to 4.2053)	1.1170 (0.6899 to 2.1027)	0.8706 (0.3614 to 2.2012)	0.6571 (0.1971 to 1.0185)
Comparison vs. Kd				
Log-Rank test p-value[a] vs Kd		0.3834		0.1167
Hazard ratio (95% CI) vs Kd		1.1642 (0.8269 to 1.6390)		1.6379 (0.8790 to 3.0520)
P-value		0.3838		0.1202
Hazard ratio inverted (95% CI) vs IKd				

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.52 Subgroup analysis by geographical region
16.2.7.1.52.1 Treatment emergent adverse event by treatment group according to geographical region - Safety population

	Europe		America	
	Kd (N=60)	**IKd (N=85)**	**Kd (N=20)**	**IKd (N=23)**
probability (95% CI)[b]				
3 Months	0.1500 (0.0738 to 0.2513)	0.1176 (0.0603 to 0.1959)	0.0500 (0.0035 to 0.2053)	0.0435 (0.0031 to 0.1824)
6 Months	0.0833 (0.0307 to 0.1699)	0.0824 (0.0362 to 0.1527)	0.0500 (0.0035 to 0.2053)	0.0435 (0.0031 to 0.1824)
9 Months	0.0833 (0.0307 to 0.1699)	0.0706 (0.0288 to 0.1378)	0.0500 (0.0035 to 0.2053)	0.0435 (0.0031 to 0.1824)
12 Months	0.0833 (0.0307 to 0.1699)	0.0588 (0.0218 to 0.1226)	0.0500 (0.0035 to 0.2053)	0.0435 (0.0031 to 0.1824)
15 Months	0.0667 (0.0215 to 0.1482)	0.0588 (0.0218 to 0.1226)	0.0500 (0.0035 to 0.2053)	0.0435 (0.0031 to 0.1824)
18 Months	0.0667 (0.0215 to 0.1482)	0.0588 (0.0218 to 0.1226)	0.0500 (0.0035 to 0.2053)	0.0435 (0.0031 to 0.1824)
21 Months	0.0667 (0.0215 to 0.1482)	0.0588 (0.0218 to 0.1226)	0.0500 (0.0035 to 0.2053)	0.0435 (0.0031 to 0.1824)
24 Months	0.0667 (0.0215 to 0.1482)	0.0588 (0.0218 to 0.1226)	0.0500 (0.0035 to 0.2053)	0.0435 (0.0031 to 0.1824)
27 Months	0.0667 (0.0215 to 0.1482)	0.0588 (0.0218 to 0.1226)	0.0500 (0.0035 to 0.2053)	0.0435 (0.0031 to 0.1824)

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.52 Subgroup analysis by geographical region
16.2.7.1.52.1 Treatment emergent adverse event by treatment group according to geographical region - Safety population

	Europe		America	
	Kd (N=60)	**IKd (N=85)**	**Kd (N=20)**	**IKd (N=23)**
30 Months	0.0667 (0.0215 to 0.1482)	0.0588 (0.0218 to 0.1226)	0.0500 (0.0035 to 0.2053)	0.0435 (0.0031 to 0.1824)
Number of patients at risk[b]				
3 Months	9	10	0	0
6 Months	5	7	0	0
9 Months	5	6	0	0
12 Months	5	5	0	0
15 Months	4	5	0	0
18 Months	4	5	0	0
21 Months	3	5	0	0
24 Months	1	1	0	0
27 Months	0	0	0	0
30 Months	0	0	0	0

Asia		Other countries		
Kd (N=20)	**IKd (N=24)**	**Kd (N=22)**	**IKd (N=45)**	**p-value of treatment-by-sub group interaction[c]**

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.52 Subgroup analysis by geographical region
16.2.7.1.52.1 Treatment emergent adverse event by treatment group according to geographical region - Safety population

Asia		Other countries		
Kd (N=20)	**IKd (N=24)**	**Kd (N=22)**	**IKd (N=45)**	**p-value of treatment-by-sub group interaction[c]**
20 (100.0)	24 (100.0)	21 (95.5)	45 (100.0)	0.4527
0 (0.0)	0 (0.0)	1 (4.5)	0 (0.0)	
0.2793 (0.0986 to 0.4271)	0.0986 (0.0329 to 0.1643)	0.1971 (0.0657 to 0.2628)	0.0657 (0.0329 to 0.0657)	
0.5257 (0.2628 to 0.6571)	0.1807 (0.0986 to 0.5257)	0.4271 (0.1971 to 0.6571)	0.1314 (0.0657 to 0.1643)	
0.6735 (0.5257 to 1.5113)	1.1828 (0.2957 to 2.8255)	0.6899 (0.5257 to 1.5113)	0.2300 (0.1643 to 0.4271)	
	0.7265		0.0195	
	1.1162 (0.6024 to 2.0681)		1.8599 (1.0966 to 3.1548)	
	0.7269		0.0213	
		0.5376 (0.3170 to 0.9119)		

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.52 Subgroup analysis by geographical region
16.2.7.1.52.1 Treatment emergent adverse event by treatment group according to geographical region - Safety population

Asia		Other countries		
Kd (N=20)	**IKd (N=24)**	**Kd (N=22)**	**IKd (N=45)**	**p-value of treatment-by-subgroup interaction[c]**
0.0500 (0.0035 to 0.2053)	0.0833 (0.0144 to 0.2330)	0.0455 (0.0032 to 0.1894)	0.0222 (0.0018 to 0.1015)	
0.0500 (0.0035 to 0.2053)	0.0417 (0.0030 to 0.1759)	0.0455 (0.0032 to 0.1894)	0.0222 (0.0018 to 0.1015)	
0.0500 (0.0035 to 0.2053)	0.0417 (0.0030 to 0.1759)	0.0455 (0.0032 to 0.1894)	0.0222 (0.0018 to 0.1015)	
0.0500 (0.0035 to 0.2053)	0.0417 (0.0030 to 0.1759)	0.0455 (0.0032 to 0.1894)	0.0222 (0.0018 to 0.1015)	
0.0500 (0.0035 to 0.2053)	0.0417 (0.0030 to 0.1759)	0.0455 (0.0032 to 0.1894)	0.0222 (0.0018 to 0.1015)	
0.0500 (0.0035 to 0.2053)	0.0417 (0.0030 to 0.1759)	0.0455 (0.0032 to 0.1894)	0.0222 (0.0018 to 0.1015)	
0.0500 (0.0035 to 0.2053)	0.0417 (0.0030 to 0.1759)	0.0455 (0.0032 to 0.1894)	0.0222 (0.0018 to 0.1015)	
0.0500 (0.0035 to 0.2053)	0.0417 (0.0030 to 0.1759)	0.0455 (0.0032 to 0.1894)	0.0222 (0.0018 to 0.1015)	
0.0500 (0.0035 to 0.2053)	0.0417 (0.0030 to 0.1759)	0.0455 (0.0032 to 0.1894)	0.0222 (0.0018 to 0.1015)	

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.52 Subgroup analysis by geographical region
16.2.7.1.52.1 Treatment emergent adverse event by treatment group according to geographical region - Safety population

Asia		Other countries		
Kd (N=20)	**IKd (N=24)**	**Kd (N=22)**	**IKd (N=45)**	**p-value of treatment-by-sub group interaction[c]**
0.0500 (0.0035 to 0.2053)	0.0417 (0.0030 to 0.1759)	0.0455 (0.0032 to 0.1894)	0.0222 (0.0018 to 0.1015)	
1	2	1	1	
0	1	1	0	
0	0	1	0	
0	0	1	0	
0	0	1	0	
0	0	1	0	
0	0	0	0	
0	0	0	0	
0	0	0	0	
0	0	0	0	

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
PGM=DEVOPS/SAR650984/EFC15246/CIR_RWE/REPORT/PGM/eff_km_sr_subgrp_sig_s_t.sas OUT=REPORT/OUTPUT/eff_km_de_teae_greg_s_t_x.rtf (12FEB2021 8:09)

16.2.7.1 Safety endpoints
16.2.7.1.52 Subgroup analysis by geographical region
16.2.7.1.52.2 Treatment emergent serious adverse event by treatment group according to geographical region - Safety population

	Europe		America	
	Kd (N=60)	**IKd (N=85)**	**Kd (N=20)**	**IKd (N=23)**
Number (%) of events	31 (51.7)	51 (60.0)	10 (50.0)	13 (56.5)
Number (%) of patients censored	29 (48.3)	34 (40.0)	10 (50.0)	10 (43.5)
Kaplan-Meier estimates of TEAE in months				
25% quantile (95% CI)	5.0267 (1.4456 to 7.8522)	3.8111 (0.7228 to 6.5051)	5.1253 (0.3285 to 11.2361)	10.4805 (0.2300 to 12.0575)
Median (95% CI)	18.0041 (7.8522 to NC)	12.8131 (7.6879 to 21.1253)	16.7228 (4.9610 to NC)	12.5503 (11.2361 to NC)
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (13.4045 to NC)
Comparison vs. Kd				
Log-Rank test p-value[a] vs Kd		0.3191		0.8822
Hazard ratio (95% CI) vs Kd		1.2543 (0.8025 to 1.9606)		1.0642 (0.4658 to 2.4317)
P-value		0.3201		0.8826

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.52 Subgroup analysis by geographical region
16.2.7.1.52.2 Treatment emergent serious adverse event by treatment group according to geographical region - Safety population

	Europe		America	
	Kd (N=60)	**IKd (N=85)**	**Kd (N=20)**	**IKd (N=23)**
probability (95% CI)[b]				
3 Months	0.7993 (0.6737 to 0.8807)	0.7647 (0.6594 to 0.8413)	0.9000 (0.6560 to 0.9740)	0.8696 (0.6481 to 0.9560)
6 Months	0.6973 (0.5633 to 0.7973)	0.6696 (0.5586 to 0.7587)	0.6500 (0.4030 to 0.8153)	0.8261 (0.6006 to 0.9309)
9 Months	0.6284 (0.4922 to 0.7374)	0.5859 (0.4734 to 0.6824)	0.6500 (0.4030 to 0.8153)	0.8261 (0.6006 to 0.9309)
12 Months	0.6109 (0.4746 to 0.7219)	0.5142 (0.4030 to 0.6146)	0.5500 (0.3134 to 0.7349)	0.6087 (0.3827 to 0.7737)
15 Months	0.5062 (0.3723 to 0.6255)	0.4280 (0.3208 to 0.5309)	0.5500 (0.3134 to 0.7349)	0.4304 (0.2277 to 0.6186)
18 Months	0.5062 (0.3723 to 0.6255)	0.4025 (0.2968 to 0.5056)	0.4950 (0.2650 to 0.6891)	0.4304 (0.2277 to 0.6186)
21 Months	0.4887 (0.3558 to 0.6089)	0.4025 (0.2968 to 0.5056)	0.4950 (0.2650 to 0.6891)	0.4304 (0.2277 to 0.6186)
24 Months	0.4561 (0.3186 to 0.5835)	0.3876 (0.2825 to 0.4912)	0.4950 (0.2650 to 0.6891)	0.4304 (0.2277 to 0.6186)
27 Months	0.4561 (0.3186 to 0.5835)	0.3876 (0.2825 to 0.4912)	0.4950 (0.2650 to 0.6891)	0.4304 (0.2277 to 0.6186)
30 Months	0.4561 (0.3186 to 0.5835)	0.3876 (0.2825 to 0.4912)	0.4950 (0.2650 to 0.6891)	0.4304 (0.2277 to 0.6186)

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.52 Subgroup analysis by geographical region
16.2.7.1.52.2 Treatment emergent serious adverse event by treatment group according to geographical region - Safety population

	Europe		America		Asia		Other countries		
	Kd (N=60)	**IKd (N=85)**	**Kd (N=20)**	**IKd (N=23)**	**Kd (N=20)**	**IKd (N=24)**	**Kd (N=22)**	**IKd (N=45)**	**p-value of treatment-by-sub group interaction[c]**
Number of patients at risk[b]									
3 Months	47	65	18	20	10 (50.0)	11 (45.8)	19 (86.4)	30 (66.7)	0.6484
6 Months	41	56	13	19					
9 Months	36	49	13	19					
12 Months	35	43	11	14					
15 Months	29	34	11	9					
18 Months	29	31	9	8					
21 Months	22	27	6	7					
24 Months	4	9	0	0					
27 Months	0	1	0	0					
30 Months	0	0	0	0	10 (50.0)	13 (54.2)	3 (13.6)	15 (33.3)	

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.52 Subgroup analysis by geographical region
16.2.7.1.52.2 Treatment emergent serious adverse event by treatment group according to geographical region - Safety population

Asia		Other countries		
Kd (N=20)	**IKd (N=24)**	**Kd (N=22)**	**IKd (N=45)**	**p-value of treatment-by-sub group interaction[c]**
4.7310 (0.3614 to 10.4805)	7.4251 (0.0986 to 17.3142)	3.3183 (0.4600 to 6.2752)	1.2813 (0.3614 to 2.5955)	
NC (3.9425 to NC)	NC (8.4435 to NC)	7.1294 (3.3183 to 14.0945)	5.6181 (1.9713 to 14.1273)	
NC (NC to NC)	NC (NC to NC)	15.4415 (7.6879 to NC)	NC (9.2649 to NC)	
	0.7083		0.5190	
	0.8491 (0.3602 to 2.0019)		0.8269 (0.4636 to 1.4748)	
	0.7086		0.5196	
0.8500 (0.6038 to 0.9490)	0.8333 (0.6148 to 0.9339)	0.7727 (0.5374 to 0.8985)	0.6000 (0.4427 to 0.7260)	

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.52 Subgroup analysis by geographical region
16.2.7.1.52.2 Treatment emergent serious adverse event by treatment group according to geographical region - Safety population

Asia		Other countries		
Kd (N=20)	**IKd (N=24)**	**Kd (N=22)**	**IKd (N=45)**	**p-value of treatment-by-sub group interaction[c]**
0.6500 (0.4030 to 0.8153)	0.7917 (0.5698 to 0.9075)	0.5909 (0.3610 to 0.7621)	0.4889 (0.3374 to 0.6241)	
0.6000 (0.3573 to 0.7760)	0.7083 (0.4838 to 0.8489)	0.4545 (0.2444 to 0.6433)	0.4000 (0.2582 to 0.5379)	
0.5000 (0.2713 to 0.6919)	0.6667 (0.4428 to 0.8173)	0.4091 (0.2085 to 0.6007)	0.3778 (0.2391 to 0.5157)	
0.5000 (0.2713 to 0.6919)	0.6667 (0.4428 to 0.8173)	0.2727 (0.1112 to 0.4637)	0.3542 (0.2188 to 0.4922)	
0.5000 (0.2713 to 0.6919)	0.5641 (0.3381 to 0.7392)	0.1364 (0.0341 to 0.3087)	0.3542 (0.2188 to 0.4922)	
0.5000 (0.2713 to 0.6919)	0.5128 (0.2908 to 0.6969)	0.1364 (0.0341 to 0.3087)	0.3542 (0.2188 to 0.4922)	
0.5000 (0.2713 to 0.6919)	0.5128 (0.2908 to 0.6969)	0.1364 (0.0341 to 0.3087)	0.3269 (0.1947 to 0.4658)	
0.5000 (0.2713 to 0.6919)	0.5128 (0.2908 to 0.6969)	0.1364 (0.0341 to 0.3087)	0.3269 (0.1947 to 0.4658)	
0.5000 (0.2713 to 0.6919)	0.5128 (0.2908 to 0.6969)	0.1364 (0.0341 to 0.3087)	0.3269 (0.1947 to 0.4658)	

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.52 Subgroup analysis by geographical region
16.2.7.1.52.2 Treatment emergent serious adverse event by treatment group according to geographical region - Safety population

Asia		Other countries		
Kd (N=20)	**IKd (N=24)**	**Kd (N=22)**	**IKd (N=45)**	**p-value of treatment-by-sub group interaction[c]**
17	20	17	27	
13	19	13	22	
12	17	10	18	
10	16	9	17	
8	13	6	15	
8	11	3	14	
7	10	1	13	
4	6	1	4	
2	0	0	0	
0	0	0	0	

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.52 Subgroup analysis by geographical region
16.2.7.1.52.3 Treatment emergent adverse event leading to discontinuation of treatment by treatment group according to geographical region - Safety population

	Europe		America	
	Kd (N=60)	**IKd (N=85)**	**Kd (N=20)**	**IKd (N=23)**
Number (%) of events	8 (13.3)	10 (11.8)	4 (20.0)	1 (4.3)
Number (%) of patients censored	52 (86.7)	75 (88.2)	16 (80.0)	22 (95.7)
Kaplan-Meier estimates of TEAE in months				
25% quantile (95% CI)	NC (15.3758 to NC)	NC (NC to NC)	NC (0.3285 to NC)	NC (5.9795 to NC)
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)
Comparison vs. Kd				
Log-Rank test p-value[a] vs Kd		0.6897		0.1332
Hazard ratio (95% CI) vs Kd		0.8276 (0.3265 to 2.0976)		0.2173 (0.0243 to 1.9446)
P-value		0.6901		0.1722
probability (95% CI)[b]				

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.52 Subgroup analysis by geographical region
16.2.7.1.52.3 Treatment emergent adverse event leading to discontinuation of treatment by treatment group according to geographical region - Safety population

	Europe		America	
	Kd (N=60)	**IKd (N=85)**	**Kd (N=20)**	**IKd (N=23)**
3 Months	0.9833 (0.8875 to 0.9976)	0.9643 (0.8934 to 0.9883)	0.9500 (0.6947 to 0.9928)	1.0000 (1.0000 to 1.0000)
6 Months	0.9661 (0.8711 to 0.9914)	0.9399 (0.8615 to 0.9745)	0.9000 (0.6560 to 0.9740)	0.9545 (0.7187 to 0.9935)
9 Months	0.8910 (0.7730 to 0.9496)	0.9151 (0.8301 to 0.9586)	0.8500 (0.6038 to 0.9490)	0.9545 (0.7187 to 0.9935)
12 Months	0.8910 (0.7730 to 0.9496)	0.9151 (0.8301 to 0.9586)	0.8500 (0.6038 to 0.9490)	0.9545 (0.7187 to 0.9935)
15 Months	0.8910 (0.7730 to 0.9496)	0.8895 (0.7983 to 0.9410)	0.8500 (0.6038 to 0.9490)	0.9545 (0.7187 to 0.9935)
18 Months	0.8703 (0.7463 to 0.9362)	0.8895 (0.7983 to 0.9410)	0.8000 (0.5511 to 0.9198)	0.9545 (0.7187 to 0.9935)
21 Months	0.8496 (0.7207 to 0.9221)	0.8758 (0.7812 to 0.9313)	0.8000 (0.5511 to 0.9198)	0.9545 (0.7187 to 0.9935)
24 Months	0.8496 (0.7207 to 0.9221)	0.8758 (0.7812 to 0.9313)	0.8000 (0.5511 to 0.9198)	0.9545 (0.7187 to 0.9935)
27 Months	0.8496 (0.7207 to 0.9221)	0.8758 (0.7812 to 0.9313)	0.8000 (0.5511 to 0.9198)	0.9545 (0.7187 to 0.9935)
30 Months	0.8496 (0.7207 to 0.9221)	0.8758 (0.7812 to 0.9313)	0.8000 (0.5511 to 0.9198)	0.9545 (0.7187 to 0.9935)

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.52 Subgroup analysis by geographical region
16.2.7.1.52.3 Treatment emergent adverse event leading to discontinuation of treatment by treatment group according to geographical region - Safety population

	Europe		America		Asia		Other countries		
	Kd (N=60)	**IKd (N=85)**	**Kd (N=20)**	**IKd (N=23)**	**Kd (N=20)**	**IKd (N=24)**	**Kd (N=22)**	**IKd (N=45)**	**p-value of treatment-by-sub group interaction[c]**
Number of patients at risk[b]									
3 Months	57	81	19	22	2 (10.0)	1 (4.2)	3 (13.6)	3 (6.7)	0.6756
6 Months	52	76	18	21	18 (90.0)	23 (95.8)	19 (86.4)	42 (93.3)	
9 Months	47	74	17	21					
12 Months	45	72	17	21					
15 Months	43	68	17	18					
18 Months	42	65	15	17					
21 Months	35	57	10	13					
24 Months	12	20	2	1					
27 Months	0	1	0	0					
30 Months	0	0	0	0					

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.52 Subgroup analysis by geographical region
16.2.7.1.52.3 Treatment emergent adverse event leading to discontinuation of treatment by treatment group according to geographical region - Safety population

	Asia		Other countries		
	Kd (N=20)	IKd (N=24)	Kd (N=22)	IKd (N=45)	p-value of treatment-by-sub group interaction[c]
Median (95% CI) [a]	NC (2.2012 to NC)	NC (4.7967 to NC)	NC (0.6571 to NC)	NC (NC to NC)	
Q1 (95% CI) [b]	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Q3 (95% CI) [b]	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Hazard ratio (95% CI)		0.4497		0.3452	
Hazard ratio (95% CI)		0.4084 (0.0370 to 4.5044)		0.4711 (0.0951 to 2.3342)	
p-value		0.4647		0.3566	
6 months (95% CI) [b]	0.9500 (0.6947 to 0.9928)	1.0000 (1.0000 to 1.0000)	0.9091 (0.6830 to 0.9765)	0.9556 (0.8338 to 0.9887)	
12 months (95% CI) [b]	0.9500 (0.6947 to 0.9928)	0.9583 (0.7392 to 0.9940)	0.8636 (0.6344 to 0.9539)	0.9556 (0.8338 to 0.9887)	
18 months (95% CI) [b]	0.9000 (0.6560 to 0.9740)	0.9583 (0.7392 to 0.9940)	0.8636 (0.6344 to 0.9539)	0.9322 (0.8043 to 0.9776)	

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.

16.2.7.1 Safety endpoints
16.2.7.1.52 Subgroup analysis by geographical region
16.2.7.1.52.3 Treatment emergent adverse event leading to discontinuation of treatment by treatment group according to geographical region - Safety population

Asia		Other countries		
Kd (N=20)	IKd (N=24)	Kd (N=22)	IKd (N=45)	p-value of treatment-by-sub group interaction[c]
0.9000 (0.6560 to 0.9740)	0.9583 (0.7392 to 0.9940)	0.8636 (0.6344 to 0.9539)	0.9322 (0.8043 to 0.9776)	
0.9000 (0.6560 to 0.9740)	0.9583 (0.7392 to 0.9940)	0.8636 (0.6344 to 0.9539)	0.9322 (0.8043 to 0.9776)	
0.9000 (0.6560 to 0.9740)	0.9583 (0.7392 to 0.9940)	0.8636 (0.6344 to 0.9539)	0.9322 (0.8043 to 0.9776)	
0.9000 (0.6560 to 0.9740)	0.9583 (0.7392 to 0.9940)	0.8636 (0.6344 to 0.9539)	0.9322 (0.8043 to 0.9776)	
0.9000 (0.6560 to 0.9740)	0.9583 (0.7392 to 0.9940)	0.8636 (0.6344 to 0.9539)	0.9322 (0.8043 to 0.9776)	
0.9000 (0.6560 to 0.9740)	0.9583 (0.7392 to 0.9940)	0.8636 (0.6344 to 0.9539)	0.9322 (0.8043 to 0.9776)	
0.9000 (0.6560 to 0.9740)	0.9583 (0.7392 to 0.9940)	0.8636 (0.6344 to 0.9539)	0.9322 (0.8043 to 0.9776)	
19	24	20	43	
19	23	19	41	
17	22	18	38	
17	21	18	38	

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.52 Subgroup analysis by geographical region
16.2.7.1.52.3 Treatment emergent adverse event leading to discontinuation of treatment by treatment group according to geographical region - Safety population

Asia		Other countries		
Kd (N=20)	**IKd (N=24)**	**Kd (N=22)**	**IKd (N=45)**	**p-value of treatment-by-sub group interaction[c]**
14	18	18	36	
14	17	18	34	
13	17	15	31	
7	8	5	11	
3	1	1	0	
0	0	0	0	

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
PGM=DEVOPS/SAR650984/EFC15246/CIR_RWE/REPORT/PGM/eff_km_sr_subgrp_sig_s_t.sas OUT=REPORT/OUTPUT/eff_km_de_tedisc_greg_s_t_x.rtf (12FEB2021 8:12)

16.2.7.1 Safety endpoints
16.2.7.1.52 Subgroup analysis by geographical region
16.2.7.1.52.4 Treatment emergent mild adverse event by treatment group according to geographical region - Safety population

	Europe		America	
	Kd (N=60)	**IKd (N=85)**	**Kd (N=20)**	**IKd (N=23)**
Number (%) of events	54 (90.0)	75 (88.2)	20 (100.0)	23 (100.0)
Number (%) of patients censored	6 (10.0)	10 (11.8)	0 (0.0)	0 (0.0)
Kaplan-Meier estimates of TEAE in months				
25% quantile (95% CI)	0.0986 (0.0657 to 0.3285)	0.0657 (0.0657 to 0.0986)	0.1807 (0.0329 to 0.2300)	0.0986 (0.0329 to 0.1314)
Median (95% CI)	0.5914 (0.3285 to 0.8214)	0.2957 (0.1643 to 0.6242)	0.3450 (0.1643 to 0.9528)	0.1643 (0.1314 to 0.3614)
75% quantile (95% CI)	2.2012 (0.9856 to 4.8624)	1.7413 (0.9528 to 3.6797)	1.0021 (0.3614 to 2.2012)	0.6571 (0.1971 to 1.0185)
Comparison vs. Kd				
Log-Rank test p-value[a] vs Kd		0.5990		0.0925
Hazard ratio (95% CI) vs Kd		1.0984 (0.7740 to 1.5589)		1.6966 (0.9102 to 3.1625)
P-value		0.5991		0.0961
Hazard ratio inverted (95% CI) vs IKd				

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
PGM=DEVOPS/SAR650984/EFC15246/CIR_RWE/REPORT/PGM/eff_km_sr_subgrp_sig_s_t.sas OUT=REPORT/OUTPUT/eff_km_de_tesev12_greg_s_t_x.rtf (12FEB2021 8:12)

16.2.7.1 Safety endpoints
16.2.7.1.52 Subgroup analysis by geographical region
16.2.7.1.52.4 Treatment emergent mild adverse event by treatment group according to geographical region - Safety population

	Europe		America	
	Kd (N=60)	**IKd (N=85)**	**Kd (N=20)**	**IKd (N=23)**
probability (95% CI)[b]				
3 Months	0.1894 (0.1015 to 0.2983)	0.1817 (0.1077 to 0.2710)	0.0500 (0.0035 to 0.2053)	0.0435 (0.0031 to 0.1824)
6 Months	0.1206 (0.0531 to 0.2177)	0.1435 (0.0781 to 0.2279)	0.0500 (0.0035 to 0.2053)	0.0435 (0.0031 to 0.1824)
9 Months	0.1206 (0.0531 to 0.2177)	0.1148 (0.0565 to 0.1957)	0.0500 (0.0035 to 0.2053)	0.0435 (0.0031 to 0.1824)
12 Months	0.1206 (0.0531 to 0.2177)	0.1004 (0.0463 to 0.1791)	0.0500 (0.0035 to 0.2053)	0.0435 (0.0031 to 0.1824)
15 Months	0.0804 (0.0275 to 0.1707)	0.1004 (0.0463 to 0.1791)	0.0500 (0.0035 to 0.2053)	0.0435 (0.0031 to 0.1824)
18 Months	0.0804 (0.0275 to 0.1707)	0.1004 (0.0463 to 0.1791)	0.0500 (0.0035 to 0.2053)	0.0435 (0.0031 to 0.1824)
21 Months	0.0804 (0.0275 to 0.1707)	0.1004 (0.0463 to 0.1791)	0.0500 (0.0035 to 0.2053)	0.0435 (0.0031 to 0.1824)
24 Months	0.0804 (0.0275 to 0.1707)	0.1004 (0.0463 to 0.1791)	0.0500 (0.0035 to 0.2053)	0.0435 (0.0031 to 0.1824)
27 Months	0.0804 (0.0275 to 0.1707)	0.1004 (0.0463 to 0.1791)	0.0500 (0.0035 to 0.2053)	0.0435 (0.0031 to 0.1824)

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
PGM=DEVOPS/SAR650984/EFC15246/CIR_RWE/REPORT/PGM/eff_km_sr_subgrp_sig_s_t.sas OUT=REPORT/OUTPUT/eff_km_de_tesev12_greg_s_t_x.rtf (12FEB2021 8:12)

16.2.7.1 Safety endpoints
16.2.7.1.52 Subgroup analysis by geographical region
16.2.7.1.52.4 Treatment emergent mild adverse event by treatment group according to geographical region - Safety population

	Europe		America	
	Kd (N=60)	**IKd (N=85)**	**Kd (N=20)**	**IKd (N=23)**
30 Months	0.0804 (0.0275 to 0.1707)	0.1004 (0.0463 to 0.1791)	0.0500 (0.0035 to 0.2053)	0.0435 (0.0031 to 0.1824)
Number of patients at risk[b]				
3 Months	11	15	0	0
6 Months	7	10	0	0
9 Months	7	8	0	0
12 Months	6	7	0	0
15 Months	4	6	0	0
18 Months	4	6	0	0
21 Months	3	6	0	0
24 Months	1	1	0	0
27 Months	0	0	0	0
30 Months	0	0	0	0

Asia		Other countries		
Kd (N=20)	**IKd (N=24)**	**Kd (N=22)**	**IKd (N=45)**	**p-value of treatment-by-sub group interaction[c]**

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
PGM=DEVOPS/SAR650984/EFC15246/CIR_RWE/REPORT/PGM/eff_km_sr_subgrp_sig_s_t.sas OUT=REPORT/OUTPUT/eff_km_de_tesev12_greg_s_t_x.rtf (12FEB2021 8:12)

16.2.7.1 Safety endpoints
16.2.7.1.52 Subgroup analysis by geographical region
16.2.7.1.52.4 Treatment emergent mild adverse event by treatment group according to geographical region - Safety population

Asia		Other countries		
Kd (N=20)	**IKd (N=24)**	**Kd (N=22)**	**IKd (N=45)**	**p-value of treatment-by-sub group interaction[c]**
20 (100.0)	24 (100.0)	21 (95.5)	45 (100.0)	0.1788
0 (0.0)	0 (0.0)	1 (4.5)	0 (0.0)	
0.2793 (0.0986 to 0.4271)	0.1150 (0.0329 to 0.1643)	0.1971 (0.0657 to 0.3614)	0.0657 (0.0329 to 0.0657)	
0.5257 (0.2628 to 0.6571)	0.1807 (0.1314 to 1.4456)	0.5257 (0.1971 to 0.8542)	0.1314 (0.0657 to 0.1643)	
0.6735 (0.5257 to 1.5113)	1.7248 (0.2957 to 3.1211)	0.8871 (0.5257 to 3.9754)	0.2300 (0.1643 to 0.4271)	
	0.8209		0.0084	
	0.9294 (0.4933 to 1.7509)		2.0102 (1.1844 to 3.4118)	
	0.8208		0.0097	
		0.4975 (0.2931 to 0.8443)		

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
PGM=DEVOPS/SAR650984/EFC15246/CIR_RWE/REPORT/PGM/eff_km_sr_subgrp_sig_s_t.sas OUT=REPORT/OUTPUT/eff_km_de_tesev12_greg_s_t_x.rtf (12FEB2021 8:12)

16.2.7.1 Safety endpoints
16.2.7.1.52 Subgroup analysis by geographical region
16.2.7.1.52.4 Treatment emergent mild adverse event by treatment group according to geographical region - Safety population

Asia		Other countries		
Kd (N=20)	**IKd (N=24)**	**Kd (N=22)**	**IKd (N=45)**	**p-value of treatment-by-subgroup interaction[c]**
0.0500 (0.0035 to 0.2053)	0.1250 (0.0314 to 0.2865)	0.0909 (0.0156 to 0.2511)	0.0222 (0.0018 to 0.1015)	
0.0500 (0.0035 to 0.2053)	0.0417 (0.0030 to 0.1759)	0.0455 (0.0032 to 0.1894)	0.0222 (0.0018 to 0.1015)	
0.0500 (0.0035 to 0.2053)	0.0417 (0.0030 to 0.1759)	0.0455 (0.0032 to 0.1894)	0.0222 (0.0018 to 0.1015)	
0.0500 (0.0035 to 0.2053)	0.0417 (0.0030 to 0.1759)	0.0455 (0.0032 to 0.1894)	0.0222 (0.0018 to 0.1015)	
0.0500 (0.0035 to 0.2053)	0.0417 (0.0030 to 0.1759)	0.0455 (0.0032 to 0.1894)	0.0222 (0.0018 to 0.1015)	
0.0500 (0.0035 to 0.2053)	0.0417 (0.0030 to 0.1759)	0.0455 (0.0032 to 0.1894)	0.0222 (0.0018 to 0.1015)	
0.0500 (0.0035 to 0.2053)	0.0417 (0.0030 to 0.1759)	0.0455 (0.0032 to 0.1894)	0.0222 (0.0018 to 0.1015)	
0.0500 (0.0035 to 0.2053)	0.0417 (0.0030 to 0.1759)	0.0455 (0.0032 to 0.1894)	0.0222 (0.0018 to 0.1015)	
0.0500 (0.0035 to 0.2053)	0.0417 (0.0030 to 0.1759)	0.0455 (0.0032 to 0.1894)	0.0222 (0.0018 to 0.1015)	

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.52 Subgroup analysis by geographical region
16.2.7.1.52.4 Treatment emergent mild adverse event by treatment group according to geographical region - Safety population

Asia		Other countries		
Kd (N=20)	**IKd (N=24)**	**Kd (N=22)**	**IKd (N=45)**	**p-value of treatment-by-sub group interaction[c]**
0.0500 (0.0035 to 0.2053)	0.0417 (0.0030 to 0.1759)	0.0455 (0.0032 to 0.1894)	0.0222 (0.0018 to 0.1015)	
1	3	2	1	
0	1	1	0	
0	0	1	0	
0	0	1	0	
0	0	1	0	
0	0	1	0	
0	0	0	0	
0	0	0	0	
0	0	0	0	
0	0	0	0	

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
PGM=DEVOPS/SAR650984/EFC15246/CIR_RWE/REPORT/PGM/eff_km_sr_subgrp_sig_s_t.sas OUT=REPORT/OUTPUT/eff_km_de_tesev12_greg_s_t_x.rtf (12FEB2021 8:12)

16.2.7.1 Safety endpoints
16.2.7.1.52 Subgroup analysis by geographical region
16.2.7.1.52.5 Treatment emergent severe adverse event by treatment group according to geographical region - Safety population

	Europe		America	
	Kd (N=60)	**IKd (N=85)**	**Kd (N=20)**	**IKd (N=23)**
Number (%) of events	34 (56.7)	59 (69.4)	17 (85.0)	20 (87.0)
Number (%) of patients censored	26 (43.3)	26 (30.6)	3 (15.0)	3 (13.0)
Kaplan-Meier estimates of TEAE in months				
25% quantile (95% CI)	2.9240 (0.7885 to 6.0452)	1.2485 (0.4600 to 3.6140)	0.7721 (0.2957 to 3.2854)	2.1027 (0.4600 to 5.1581)
Median (95% CI)	12.3532 (6.0452 to NC)	5.9466 (4.3696 to 8.5092)	4.1396 (0.4928 to 10.0862)	7.8193 (2.4312 to 10.7105)
75% quantile (95% CI)	NC (NC to NC)	NC (10.6776 to NC)	10.4476 (4.2382 to NC)	11.2690 (7.8193 to NC)
Comparison vs. Kd				
Log-Rank test p-value[a] vs Kd		0.1082		0.6413
Hazard ratio (95% CI) vs Kd		1.4116 (0.9250 to 2.1543)		0.8574 (0.4485 to 1.6391)
P-value		0.1099		0.6416

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.52 Subgroup analysis by geographical region
16.2.7.1.52.5 Treatment emergent severe adverse event by treatment group according to geographical region - Safety population

	Europe		America	
	Kd (N=60)	**IKd (N=85)**	**Kd (N=20)**	**IKd (N=23)**
probability (95% CI)[b]				
3 Months	0.7305 (0.5982 to 0.8254)	0.6920 (0.5815 to 0.7787)	0.6000 (0.3573 to 0.7760)	0.6445 (0.4125 to 0.8042)
6 Months	0.6436 (0.5071 to 0.7512)	0.4772 (0.3675 to 0.5789)	0.3000 (0.1225 to 0.5014)	0.5064 (0.2875 to 0.6897)
9 Months	0.5192 (0.3839 to 0.6385)	0.3937 (0.2896 to 0.4960)	0.3000 (0.1225 to 0.5014)	0.4143 (0.2124 to 0.6059)
12 Months	0.5192 (0.3839 to 0.6385)	0.3221 (0.2254 to 0.4226)	0.1500 (0.0373 to 0.3347)	0.1381 (0.0346 to 0.3118)
15 Months	0.4476 (0.3166 to 0.5702)	0.2968 (0.2030 to 0.3964)	0.1500 (0.0373 to 0.3347)	0.0921 (0.0158 to 0.2537)
18 Months	0.4297 (0.3002 to 0.5527)	0.2968 (0.2030 to 0.3964)	0.1500 (0.0373 to 0.3347)	0.0921 (0.0158 to 0.2537)
21 Months	0.4297 (0.3002 to 0.5527)	0.2968 (0.2030 to 0.3964)	0.1500 (0.0373 to 0.3347)	0.0921 (0.0158 to 0.2537)
24 Months	0.3939 (0.2598 to 0.5252)	0.2968 (0.2030 to 0.3964)	0.1500 (0.0373 to 0.3347)	0.0921 (0.0158 to 0.2537)
27 Months	0.3939 (0.2598 to 0.5252)	0.2968 (0.2030 to 0.3964)	0.1500 (0.0373 to 0.3347)	0.0921 (0.0158 to 0.2537)
30 Months	0.3939 (0.2598 to 0.5252)	0.2968 (0.2030 to 0.3964)	0.1500 (0.0373 to 0.3347)	0.0921 (0.0158 to 0.2537)

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.52 Subgroup analysis by geographical region
16.2.7.1.52.5 Treatment emergent severe adverse event by treatment group according to geographical region - Safety population

	Europe		America		Asia		Other countries		
	Kd (N=60)	**IKd (N=85)**	**Kd (N=20)**	**IKd (N=23)**	**Kd (N=20)**	**IKd (N=24)**	**Kd (N=22)**	**IKd (N=45)**	**p-value of treatment-by-sub group interaction[c]**
Number of patients at risk[b]									
3 Months	42	58	12	14	11 (55.0)	19 (79.2)	19 (86.4)	36 (80.0)	0.3409
6 Months	37	40	6	11	9 (45.0)	5 (20.8)	3 (13.6)	9 (20.0)	
9 Months	29	33	6	9					
12 Months	29	27	3	3					
15 Months	25	23	3	1					
18 Months	24	22	2	1					
21 Months	17	21	1	1					
24 Months	4	7	0	0					
27 Months	0	0	0	0					
30 Months	0	0	0	0					

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
PGM=DEVOPS/SAR650984/EFC15246/CIR_RWE/REPORT/PGM/eff_km_sr_subgrp_sig_s_t.sas OUT=REPORT/OUTPUT/eff_km_de_tesev34_greg_s_t_x.rtf (12FEB2021 8:13)

16.2.7.1 Safety endpoints
16.2.7.1.52 Subgroup analysis by geographical region
16.2.7.1.52.5 Treatment emergent severe adverse event by treatment group according to geographical region - Safety population

Asia		Other countries		
Kd (N=20)	**IKd (N=24)**	**Kd (N=22)**	**IKd (N=45)**	**p-value of treatment-by-sub group interaction[c]**
3.6140 (0.5914 to 6.7351)	1.9055 (0.0986 to 4.7967)	1.1170 (0.1971 to 3.8768)	0.9528 (0.2628 to 1.8398)	
9.0021 (3.2854 to NC)	7.2608 (1.9713 to 14.7187)	4.4189 (1.1170 to 9.1992)	4.7639 (1.4784 to 8.2464)	
NC (10.4805 to NC)	15.6057 (8.6735 to NC)	13.6345 (4.9281 to NC)	15.8357 (7.8522 to NC)	
	0.1592		0.7693	
	1.6985 (0.8056 to 3.5808)		0.9201 (0.5274 to 1.6052)	
	0.1639		0.7693	
0.8000 (0.5511 to 0.9198)	0.6250 (0.4030 to 0.7842)	0.5909 (0.3610 to 0.7621)	0.5556 (0.3998 to 0.6860)	

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints

16.2.7.1.52 Subgroup analysis by geographical region

16.2.7.1.52.5 Treatment emergent severe adverse event by treatment group according to geographical region - Safety population

Asia		Other countries		
Kd (N=20)	**IKd (N=24)**	**Kd (N=22)**	**IKd (N=45)**	**p-value of treatment-by-subgroup interaction[c]**
0.6000 (0.3573 to 0.7760)	0.5833 (0.3645 to 0.7499)	0.4091 (0.2085 to 0.6007)	0.4222 (0.2776 to 0.5599)	
0.5000 (0.2713 to 0.6919)	0.4167 (0.2224 to 0.6006)	0.3182 (0.1418 to 0.5111)	0.3556 (0.2203 to 0.4932)	
0.4500 (0.2311 to 0.6471)	0.3333 (0.1590 to 0.5187)	0.2727 (0.1112 to 0.4637)	0.3111 (0.1837 to 0.4473)	
0.4500 (0.2311 to 0.6471)	0.2778 (0.1153 to 0.4679)	0.2273 (0.0827 to 0.4145)	0.2632 (0.1451 to 0.3975)	
0.4500 (0.2311 to 0.6471)	0.1667 (0.0452 to 0.3545)	0.1364 (0.0341 to 0.3087)	0.2073 (0.1006 to 0.3402)	
0.4500 (0.2311 to 0.6471)	0.1667 (0.0452 to 0.3545)	0.1364 (0.0341 to 0.3087)	0.1777 (0.0787 to 0.3091)	
0.4500 (0.2311 to 0.6471)	0.1667 (0.0452 to 0.3545)	0.1364 (0.0341 to 0.3087)	0.1777 (0.0787 to 0.3091)	
0.4500 (0.2311 to 0.6471)	0.1667 (0.0452 to 0.3545)	0.1364 (0.0341 to 0.3087)	0.1777 (0.0787 to 0.3091)	
0.4500 (0.2311 to 0.6471)	0.1667 (0.0452 to 0.3545)	0.1364 (0.0341 to 0.3087)	0.1777 (0.0787 to 0.3091)	

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable

CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley

[a] One-sided significance level is 0.025

[b] Estimated using the Kaplan-Meier method

[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.

PGM=DEVOPS/SAR650984/EFC15246/CIR_RWE/REPORT/PGM/eff_km_sr_subgrp_sig_s_t.sas OUT=REPORT/OUTPUT/eff_km_de_tesev34_greg_s_t_x.rtf (12FEB2021 8:13)

16.2.7.1 Safety endpoints
16.2.7.1.52 Subgroup analysis by geographical region
16.2.7.1.52.5 Treatment emergent severe adverse event by treatment group according to geographical region - Safety population

Asia		Other countries		
Kd (N=20)	**IKd (N=24)**	**Kd (N=22)**	**IKd (N=45)**	**p-value of treatment-by-sub group interaction[c]**
16	15	13	25	
12	14	9	19	
10	10	7	16	
9	8	6	14	
8	5	5	10	
8	3	3	7	
7	3	2	6	
3	1	1	2	
1	0	0	0	
0	0	0	0	

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.52 Subgroup analysis by geographical region
16.2.7.1.52.6 Treatment emergent severe adverse event including death by treatment group according to geographical region - Safety population

	Europe		America	
	Kd (N=60)	**IKd (N=85)**	**Kd (N=20)**	**IKd (N=23)**
Number (%) of events	35 (58.3)	61 (71.8)	17 (85.0)	20 (87.0)
Number (%) of patients censored	25 (41.7)	24 (28.2)	3 (15.0)	3 (13.0)
Kaplan-Meier estimates of TEAE in months				
25% quantile (95% CI)	2.5133 (0.7885 to 5.4867)	0.9528 (0.4271 to 3.5154)	0.7721 (0.2957 to 3.2854)	2.1027 (0.4600 to 5.1581)
Median (95% CI)	12.2875 (5.4867 to NC)	5.6181 (4.3368 to 8.5092)	4.1396 (0.4928 to 10.0862)	7.8193 (2.4312 to 10.7105)
75% quantile (95% CI)	NC (NC to NC)	NC (10.6776 to NC)	10.4476 (4.2382 to NC)	11.2690 (7.8193 to NC)
Comparison vs. Kd				
Log-Rank test p-value[a] vs Kd		0.0975		0.6413
Hazard ratio (95% CI) vs Kd		1.4194 (0.9360 to 2.1523)		0.8574 (0.4485 to 1.6391)
P-value		0.0992		0.6416

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.52 Subgroup analysis by geographical region
16.2.7.1.52.6 Treatment emergent severe adverse event including death by treatment group according to geographical region - Safety population

	Europe		America	
	Kd (N=60)	**IKd (N=85)**	**Kd (N=20)**	**IKd (N=23)**
probability (95% CI)[b]				
3 Months	0.7159 (0.5834 to 0.8128)	0.6824 (0.5720 to 0.7699)	0.6000 (0.3573 to 0.7760)	0.6445 (0.4125 to 0.8042)
6 Months	0.6307 (0.4951 to 0.7392)	0.4706 (0.3618 to 0.5718)	0.3000 (0.1225 to 0.5014)	0.5064 (0.2875 to 0.6897)
9 Months	0.5089 (0.3752 to 0.6278)	0.3882 (0.2852 to 0.4899)	0.3000 (0.1225 to 0.5014)	0.4143 (0.2124 to 0.6059)
12 Months	0.5089 (0.3752 to 0.6278)	0.3176 (0.2221 to 0.4173)	0.1500 (0.0373 to 0.3347)	0.1381 (0.0346 to 0.3118)
15 Months	0.4387 (0.3096 to 0.5604)	0.2819 (0.1909 to 0.3797)	0.1500 (0.0373 to 0.3347)	0.0921 (0.0158 to 0.2537)
18 Months	0.4211 (0.2936 to 0.5432)	0.2819 (0.1909 to 0.3797)	0.1500 (0.0373 to 0.3347)	0.0921 (0.0158 to 0.2537)
21 Months	0.4211 (0.2936 to 0.5432)	0.2819 (0.1909 to 0.3797)	0.1500 (0.0373 to 0.3347)	0.0921 (0.0158 to 0.2537)
24 Months	0.3860 (0.2542 to 0.5161)	0.2819 (0.1909 to 0.3797)	0.1500 (0.0373 to 0.3347)	0.0921 (0.0158 to 0.2537)
27 Months	0.3860 (0.2542 to 0.5161)	0.2819 (0.1909 to 0.3797)	0.1500 (0.0373 to 0.3347)	0.0921 (0.0158 to 0.2537)
30 Months	0.3860 (0.2542 to 0.5161)	0.2819 (0.1909 to 0.3797)	0.1500 (0.0373 to 0.3347)	0.0921 (0.0158 to 0.2537)

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.52 Subgroup analysis by geographical region
16.2.7.1.52.6 Treatment emergent severe adverse event including death by treatment group according to geographical region - Safety population

	Europe		America		Asia		Other countries		
	Kd (N=60)	**IKd (N=85)**	**Kd (N=20)**	**IKd (N=23)**	**Kd (N=20)**	**IKd (N=24)**	**Kd (N=22)**	**IKd (N=45)**	**p-value of treatment-by-sub group interaction[c]**
Number of patients at risk[b]									
3 Months	42	58	12	14	11 (55.0)	19 (79.2)	19 (86.4)	36 (80.0)	0.3349
6 Months	37	40	6	11					
9 Months	29	33	6	9					
12 Months	29	27	3	3					
15 Months	25	23	3	1					
18 Months	24	22	2	1					
21 Months	17	21	1	1					
24 Months	4	7	0	0					
27 Months	0	0	0	0					
30 Months	0	0	0	0	9 (45.0)	5 (20.8)	3 (13.6)	9 (20.0)	

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.52 Subgroup analysis by geographical region
16.2.7.1.52.6 Treatment emergent severe adverse event including death by treatment group according to geographical region - Safety population

Asia		Other countries		
Kd (N=20)	**IKd (N=24)**	**Kd (N=22)**	**IKd (N=45)**	**p-value of treatment-by-sub group interaction[c]**
3.6140 (0.5914 to 6.7351)	1.9055 (0.0986 to 4.7967)	1.1170 (0.1971 to 3.8768)	0.9528 (0.2628 to 1.8398)	
9.0021 (3.2854 to NC)	7.2608 (1.9713 to 14.7187)	4.4189 (1.1170 to 9.1992)	4.7639 (1.4784 to 8.2464)	
NC (10.4805 to NC)	15.6057 (8.6735 to NC)	13.6345 (4.9281 to NC)	15.8357 (7.8522 to NC)	
	0.1592		0.7693	
	1.6985 (0.8056 to 3.5808)		0.9201 (0.5274 to 1.6052)	
	0.1639		0.7693	
0.8000 (0.5511 to 0.9198)	0.6250 (0.4030 to 0.7842)	0.5909 (0.3610 to 0.7621)	0.5556 (0.3998 to 0.6860)	

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints

16.2.7.1.52 Subgroup analysis by geographical region

16.2.7.1.52.6 Treatment emergent severe adverse event including death by treatment group according to geographical region - Safety population

Asia		Other countries		
Kd (N=20)	**IKd (N=24)**	**Kd (N=22)**	**IKd (N=45)**	**p-value of treatment-by-sub group interaction[c]**
0.6000 (0.3573 to 0.7760)	0.5833 (0.3645 to 0.7499)	0.4091 (0.2085 to 0.6007)	0.4222 (0.2776 to 0.5599)	
0.5000 (0.2713 to 0.6919)	0.4167 (0.2224 to 0.6006)	0.3182 (0.1418 to 0.5111)	0.3556 (0.2203 to 0.4932)	
0.4500 (0.2311 to 0.6471)	0.3333 (0.1590 to 0.5187)	0.2727 (0.1112 to 0.4637)	0.3111 (0.1837 to 0.4473)	
0.4500 (0.2311 to 0.6471)	0.2778 (0.1153 to 0.4679)	0.2273 (0.0827 to 0.4145)	0.2632 (0.1451 to 0.3975)	
0.4500 (0.2311 to 0.6471)	0.1667 (0.0452 to 0.3545)	0.1364 (0.0341 to 0.3087)	0.2073 (0.1006 to 0.3402)	
0.4500 (0.2311 to 0.6471)	0.1667 (0.0452 to 0.3545)	0.1364 (0.0341 to 0.3087)	0.1777 (0.0787 to 0.3091)	
0.4500 (0.2311 to 0.6471)	0.1667 (0.0452 to 0.3545)	0.1364 (0.0341 to 0.3087)	0.1777 (0.0787 to 0.3091)	
0.4500 (0.2311 to 0.6471)	0.1667 (0.0452 to 0.3545)	0.1364 (0.0341 to 0.3087)	0.1777 (0.0787 to 0.3091)	
0.4500 (0.2311 to 0.6471)	0.1667 (0.0452 to 0.3545)	0.1364 (0.0341 to 0.3087)	0.1777 (0.0787 to 0.3091)	

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable

CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley

[a] One-sided significance level is 0.025

[b] Estimated using the Kaplan-Meier method

[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.

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16.2.7.1 Safety endpoints
16.2.7.1.52 Subgroup analysis by geographical region
16.2.7.1.52.6 Treatment emergent severe adverse event including death by treatment group according to geographical region - Safety population

Asia		Other countries		
Kd (N=20)	**IKd (N=24)**	**Kd (N=22)**	**IKd (N=45)**	**p-value of treatment-by-sub group interaction[c]**
16	15	13	25	
12	14	9	19	
10	10	7	16	
9	8	6	14	
8	5	5	10	
8	3	3	7	
7	3	2	6	
3	1	1	2	
1	0	0	0	
0	0	0	0	

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.53 Subgroup analysis by regulatory region
16.2.7.1.53.1 Treatment emergent adverse event by treatment group according to regulatory region - Safety population

	Western countries		Other countries		
	Kd (N=55)	**IKd (N=97)**	**Kd (N=67)**	**IKd (N=80)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	51 (92.7)	93 (95.9)	66 (98.5)	79 (98.8)	0.7111
Number (%) of patients censored	4 (7.3)	4 (4.1)	1 (1.5)	1 (1.3)	
Kaplan-Meier estimates of TEAE in months					
25% quantile (95% CI)	0.0657 (0.0657 to 0.1971)	0.0657 (0.0657 to 0.0986)	0.2300 (0.1643 to 0.3285)	0.0986 (0.0657 to 0.1314)	
Median (95% CI)	0.3285 (0.1971 to 0.5914)	0.1643 (0.0986 to 0.2300)	0.5257 (0.3614 to 0.6571)	0.1971 (0.1314 to 0.3943)	
75% quantile (95% CI)	0.9856 (0.5914 to 2.9569)	0.6242 (0.2957 to 1.2485)	1.0513 (0.6571 to 1.5113)	0.9692 (0.4271 to 1.4784)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd		0.1187		0.1708	
Hazard ratio (95% CI) vs Kd		1.3126 (0.9317 to 1.8494)		1.2570 (0.9050 to 1.7460)	
P-value		0.1198		0.1723	

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.53 Subgroup analysis by regulatory region
16.2.7.1.53.1 Treatment emergent adverse event by treatment group according to regulatory region - Safety population

	Western countries		Other countries		
	Kd (N=55)	**IKd (N=97)**	**Kd (N=67)**	**IKd (N=80)**	**p-value of treatment-by-sub group interaction[c]**
probability (95% CI)[b]					
3 Months	0.1273 (0.0559 to 0.2291)	0.0722 (0.0318 to 0.1348)	0.0597 (0.0193 to 0.1338)	0.0750 (0.0306 to 0.1459)	
6 Months	0.0727 (0.0234 to 0.1606)	0.0515 (0.0192 to 0.1082)	0.0299 (0.0056 to 0.0925)	0.0375 (0.0100 to 0.0962)	
9 Months	0.0727 (0.0234 to 0.1606)	0.0515 (0.0192 to 0.1082)	0.0299 (0.0056 to 0.0925)	0.0125 (0.0011 to 0.0602)	
12 Months	0.0727 (0.0234 to 0.1606)	0.0412 (0.0135 to 0.0944)	0.0299 (0.0056 to 0.0925)	0.0125 (0.0011 to 0.0602)	
15 Months	0.0727 (0.0234 to 0.1606)	0.0412 (0.0135 to 0.0944)	0.0149 (0.0013 to 0.0708)	0.0125 (0.0011 to 0.0602)	
18 Months	0.0727 (0.0234 to 0.1606)	0.0412 (0.0135 to 0.0944)	0.0149 (0.0013 to 0.0708)	0.0125 (0.0011 to 0.0602)	
21 Months	0.0727 (0.0234 to 0.1606)	0.0412 (0.0135 to 0.0944)	0.0149 (0.0013 to 0.0708)	0.0125 (0.0011 to 0.0602)	
24 Months	0.0727 (0.0234 to 0.1606)	0.0412 (0.0135 to 0.0944)	0.0149 (0.0013 to 0.0708)	0.0125 (0.0011 to 0.0602)	
27 Months	0.0727 (0.0234 to 0.1606)	0.0412 (0.0135 to 0.0944)	0.0149 (0.0013 to 0.0708)	0.0125 (0.0011 to 0.0602)	

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.53 Subgroup analysis by regulatory region
16.2.7.1.53.1 Treatment emergent adverse event by treatment group according to regulatory region - Safety population

	Western countries		Other countries		
	Kd (N=55)	**IKd (N=97)**	**Kd (N=67)**	**IKd (N=80)**	**p-value of treatment-by-sub group interaction[c]**
30 Months	0.0727 (0.0234 to 0.1606)	0.0412 (0.0135 to 0.0944)	0.0149 (0.0013 to 0.0708)	0.0125 (0.0011 to 0.0602)	
Number of patients at risk[b]					
3 Months	7	7	4	6	
6 Months	4	5	2	3	
9 Months	4	5	2	1	
12 Months	4	4	2	1	
15 Months	4	4	1	1	
18 Months	4	4	1	1	
21 Months	3	4	0	1	
24 Months	1	1	0	0	
27 Months	0	0	0	0	
30 Months	0	0	0	0	

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.53 Subgroup analysis by regulatory region
16.2.7.1.53.2 Treatment emergent serious adverse event by treatment group according to regulatory region - Safety population

	Western countries		Other countries		
	Kd (N=55)	**IKd (N=97)**	**Kd (N=67)**	**IKd (N=80)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	31 (56.4)	61 (62.9)	39 (58.2)	44 (55.0)	0.3595
Number (%) of patients censored	24 (43.6)	36 (37.1)	28 (41.8)	36 (45.0)	
Kaplan-Meier estimates of TEAE in months					
25% quantile (95% CI)	5.2567 (0.9856 to 7.7864)	1.8398 (0.6242 to 4.8953)	4.0739 (2.1027 to 5.8480)	3.4333 (1.5441 to 6.5380)	
Median (95% CI)	15.4415 (7.7864 to NC)	11.4333 (7.7864 to 14.8830)	12.3532 (6.2752 to NC)	13.1417 (8.2464 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd		0.3287		0.7884	
Hazard ratio (95% CI) vs Kd		1.2402 (0.8045 to 1.9118)		0.9425 (0.6123 to 1.4509)	
P-value		0.3296		0.7880	
probability (95% CI)[b]					

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.53 Subgroup analysis by regulatory region
16.2.7.1.53.2 Treatment emergent serious adverse event by treatment group according to regulatory region - Safety population

	Western countries		Other countries		
	Kd (N=55)	**IKd (N=97)**	**Kd (N=67)**	**IKd (N=80)**	**p-value of treatment-by-sub group interaction[c]**
3 Months	0.7996 (0.6674 to 0.8837)	0.7320 (0.6319 to 0.8089)	0.8358 (0.7232 to 0.9055)	0.7625 (0.6533 to 0.8414)	
6 Months	0.6880 (0.5469 to 0.7932)	0.6383 (0.5341 to 0.7251)	0.6418 (0.5149 to 0.7436)	0.6875 (0.5736 to 0.7768)	
9 Months	0.6136 (0.4711 to 0.7284)	0.5859 (0.4811 to 0.6767)	0.5817 (0.4546 to 0.6891)	0.5875 (0.4718 to 0.6862)	
12 Months	0.5950 (0.4527 to 0.7118)	0.4813 (0.3786 to 0.5766)	0.5052 (0.3800 to 0.6176)	0.5500 (0.4348 to 0.6511)	
15 Months	0.5021 (0.3632 to 0.6258)	0.4025 (0.3033 to 0.4995)	0.4409 (0.3189 to 0.5560)	0.4875 (0.3745 to 0.5912)	
18 Months	0.4463 (0.3116 to 0.5722)	0.3788 (0.2810 to 0.4760)	0.4239 (0.3029 to 0.5397)	0.4600 (0.3479 to 0.5649)	
21 Months	0.4463 (0.3116 to 0.5722)	0.3788 (0.2810 to 0.4760)	0.4070 (0.2872 to 0.5232)	0.4461 (0.3345 to 0.5515)	
24 Months	0.4091 (0.2695 to 0.5438)	0.3507 (0.2540 to 0.4489)	0.4070 (0.2872 to 0.5232)	0.4461 (0.3345 to 0.5515)	
27 Months	0.4091 (0.2695 to 0.5438)	0.3507 (0.2540 to 0.4489)	0.4070 (0.2872 to 0.5232)	0.4461 (0.3345 to 0.5515)	
30 Months	0.4091 (0.2695 to 0.5438)	0.3507 (0.2540 to 0.4489)	0.4070 (0.2872 to 0.5232)	0.4461 (0.3345 to 0.5515)	

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
PGM=DEVOPS/SAR650984/EFC15246/CIR_RWE/REPORT/PGM/eff_km_sr_subgrp_sig_s_t.sas OUT=REPORT/OUTPUT/eff_km_de_tesae_rreg_s_t_x.rtf (12FEB2021 8:12)

16.2.7.1 Safety endpoints
16.2.7.1.53 Subgroup analysis by regulatory region
16.2.7.1.53.2 Treatment emergent serious adverse event by treatment group according to regulatory region - Safety population

	Western countries		Other countries		
	Kd (N=55)	**IKd (N=97)**	**Kd (N=67)**	**IKd (N=80)**	**p-value of treatment-by-sub group interaction[c]**
Number of patients at risk[b]					
3 Months	43	71	56	61	
6 Months	37	61	43	55	
9 Months	33	56	38	47	
12 Months	32	46	33	44	
15 Months	27	35	27	36	
18 Months	24	31	25	33	
21 Months	18	27	18	30	
24 Months	2	6	7	13	
27 Months	0	0	2	1	
30 Months	0	0	0	0	

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
PGM=DEVOPS/SAR650984/EFC15246/CIR_RWE/REPORT/PGM/eff_km_sr_subgrp_sig_s_t.sas OUT=REPORT/OUTPUT/eff_km_de_tesae_rreg_s_t_x.rtf (12FEB2021 8:12)

16.2.7.1 Safety endpoints
16.2.7.1.53 Subgroup analysis by regulatory region
16.2.7.1.53.3 Treatment emergent adverse event leading to discontinuation of treatment by treatment group according to regulatory region - Safety population

	Western countries		Other countries		
	Kd (N=55)	**IKd (N=97)**	**Kd (N=67)**	**IKd (N=80)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	8 (14.5)	7 (7.2)	9 (13.4)	8 (10.0)	0.5302
Number (%) of patients censored	47 (85.5)	90 (92.8)	58 (86.6)	72 (90.0)	
Kaplan-Meier estimates of TEAE in months					
25% quantile (95% CI)	NC (15.3758 to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd		0.1326		0.5164	
Hazard ratio (95% CI) vs Kd		0.4677 (0.1696 to 1.2898)		0.7305 (0.2818 to 1.8935)	
P-value		0.1420		0.5182	
probability (95% CI)[b]					
3 Months	0.9633 (0.8611 to 0.9907)	0.9895 (0.9276 to 0.9985)	0.9552 (0.8676 to 0.9853)	0.9500 (0.8722 to 0.9809)	

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
PGM=DEVOPS/SAR650984/EFC15246/CIR_RWE/REPORT/PGM/eff_km_sr_subgrp_sig_s_t.sas OUT=REPORT/OUTPUT/eff_km_de_tedisc_rreg_s_t_x.rtf (12FEB2021 8:12)

16.2.7.1 Safety endpoints
16.2.7.1.53 Subgroup analysis by regulatory region
16.2.7.1.53.3 Treatment emergent adverse event leading to discontinuation of treatment by treatment group according to regulatory region - Safety population

	Western countries		Other countries		
	Kd (N=55)	**IKd (N=97)**	**Kd (N=67)**	**IKd (N=80)**	**p-value of treatment-by-sub group interaction[c]**
6 Months	0.9444 (0.8374 to 0.9817)	0.9570 (0.8893 to 0.9836)	0.9251 (0.8294 to 0.9681)	0.9373 (0.8560 to 0.9734)	
9 Months	0.8841 (0.7598 to 0.9463)	0.9350 (0.8609 to 0.9703)	0.8786 (0.7718 to 0.9374)	0.9241 (0.8388 to 0.9652)	
12 Months	0.8841 (0.7598 to 0.9463)	0.9350 (0.8609 to 0.9703)	0.8786 (0.7718 to 0.9374)	0.9241 (0.8388 to 0.9652)	
15 Months	0.8841 (0.7598 to 0.9463)	0.9350 (0.8609 to 0.9703)	0.8786 (0.7718 to 0.9374)	0.8973 (0.8050 to 0.9473)	
18 Months	0.8626 (0.7326 to 0.9322)	0.9350 (0.8609 to 0.9703)	0.8614 (0.7502 to 0.9255)	0.8973 (0.8050 to 0.9473)	
21 Months	0.8410 (0.7063 to 0.9174)	0.9222 (0.8433 to 0.9622)	0.8614 (0.7502 to 0.9255)	0.8973 (0.8050 to 0.9473)	
24 Months	0.8410 (0.7063 to 0.9174)	0.9222 (0.8433 to 0.9622)	0.8614 (0.7502 to 0.9255)	0.8973 (0.8050 to 0.9473)	
27 Months	0.8410 (0.7063 to 0.9174)	0.9222 (0.8433 to 0.9622)	0.8614 (0.7502 to 0.9255)	0.8973 (0.8050 to 0.9473)	
30 Months	0.8410 (0.7063 to 0.9174)	0.9222 (0.8433 to 0.9622)	0.8614 (0.7502 to 0.9255)	0.8973 (0.8050 to 0.9473)	

Number of patients at risk[b]

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
PGM=DEVOPS/SAR650984/EFC15246/CIR_RWE/REPORT/PGM/eff_km_sr_subgrp_sig_s_t.sas OUT=REPORT/OUTPUT/eff_km_de_tedisc_rreg_s_t_x.rtf (12FEB2021 8:12)

16.2.7.1 Safety endpoints
16.2.7.1.53 Subgroup analysis by regulatory region
16.2.7.1.53.3 Treatment emergent adverse event leading to discontinuation of treatment by treatment group according to regulatory region - Safety population

	Western countries		Other countries		
	Kd (N=55)	**IKd (N=97)**	**Kd (N=67)**	**IKd (N=80)**	**p-value of treatment-by-sub group interaction[c]**
3 Months	51	94	64	76	
6 Months	47	87	61	74	
9 Months	43	85	56	70	
12 Months	43	83	54	69	
15 Months	41	77	51	63	
18 Months	40	73	49	60	
21 Months	34	62	39	56	
24 Months	9	20	17	20	
27 Months	1	0	3	2	
30 Months	0	0	0	0	

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
PGM=DEVOPS/SAR650984/EFC15246/CIR_RWE/REPORT/PGM/eff_km_sr_subgrp_sig_s_t.sas OUT=REPORT/OUTPUT/eff_km_de_tedisc_rreg_s_t_x.rtf (12FEB2021 8:12)

16.2.7.1 Safety endpoints
16.2.7.1.53 Subgroup analysis by regulatory region
16.2.7.1.53.4 Treatment emergent mild adverse event by treatment group according to regulatory region - Safety population

	Western countries		Other countries		
	Kd (N=55)	**IKd (N=97)**	**Kd (N=67)**	**IKd (N=80)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	50 (90.9)	90 (92.8)	65 (97.0)	77 (96.3)	0.6299
Number (%) of patients censored	5 (9.1)	7 (7.2)	2 (3.0)	3 (3.8)	
Kaplan-Meier estimates of TEAE in months					
25% quantile (95% CI)	0.0657 (0.0657 to 0.1971)	0.0657 (0.0657 to 0.0986)	0.2300 (0.1971 to 0.3614)	0.0986 (0.0657 to 0.1314)	
Median (95% CI)	0.3614 (0.1971 to 0.6571)	0.1643 (0.0986 to 0.2300)	0.5257 (0.3614 to 0.6571)	0.2300 (0.1643 to 0.4271)	
75% quantile (95% CI)	0.9856 (0.6571 to 3.3840)	0.6242 (0.2957 to 1.4127)	1.2156 (0.6899 to 2.2012)	1.4456 (0.6571 to 2.1684)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd		0.1324		0.2935	
Hazard ratio (95% CI) vs Kd		1.3043 (0.9218 to 1.8455)		1.1940 (0.8567 to 1.6641)	
P-value		0.1335		0.2952	

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
PGM=DEVOPS/SAR650984/EFC15246/CIR_RWE/REPORT/PGM/eff_km_sr_subgrp_sig_s_t.sas OUT=REPORT/OUTPUT/eff_km_de_tesev12_rreg_s_t_x.rtf (12FEB2021 8:13)

16.2.7.1 Safety endpoints
16.2.7.1.53 Subgroup analysis by regulatory region
16.2.7.1.53.4 Treatment emergent mild adverse event by treatment group according to regulatory region - Safety population

	Western countries		Other countries		
	Kd (N=55)	**IKd (N=97)**	**Kd (N=67)**	**IKd (N=80)**	**p-value of treatment-by-sub group interaction[c]**
probability (95% CI)[b]					
3 Months	0.1513 (0.0710 to 0.2596)	0.0928 (0.0456 to 0.1604)	0.0896 (0.0365 to 0.1723)	0.1295 (0.0666 to 0.2138)	
6 Months	0.0945 (0.0349 to 0.1906)	0.0825 (0.0386 to 0.1477)	0.0448 (0.0119 to 0.1135)	0.0592 (0.0201 to 0.1294)	
9 Months	0.0945 (0.0349 to 0.1906)	0.0825 (0.0386 to 0.1477)	0.0448 (0.0119 to 0.1135)	0.0148 (0.0013 to 0.0695)	
12 Months	0.0945 (0.0349 to 0.1906)	0.0707 (0.0305 to 0.1337)	0.0448 (0.0119 to 0.1135)	0.0148 (0.0013 to 0.0695)	
15 Months	0.0756 (0.0243 to 0.1664)	0.0707 (0.0305 to 0.1337)	0.0224 (0.0023 to 0.0923)	0.0148 (0.0013 to 0.0695)	
18 Months	0.0756 (0.0243 to 0.1664)	0.0707 (0.0305 to 0.1337)	0.0224 (0.0023 to 0.0923)	0.0148 (0.0013 to 0.0695)	
21 Months	0.0756 (0.0243 to 0.1664)	0.0707 (0.0305 to 0.1337)	0.0224 (0.0023 to 0.0923)	0.0148 (0.0013 to 0.0695)	
24 Months	0.0756 (0.0243 to 0.1664)	0.0707 (0.0305 to 0.1337)	0.0224 (0.0023 to 0.0923)	0.0148 (0.0013 to 0.0695)	
27 Months	0.0756 (0.0243 to 0.1664)	0.0707 (0.0305 to 0.1337)	0.0224 (0.0023 to 0.0923)	0.0148 (0.0013 to 0.0695)	

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.53 Subgroup analysis by regulatory region
16.2.7.1.53.4 Treatment emergent mild adverse event by treatment group according to regulatory region - Safety population

	Western countries		Other countries		
	Kd (N=55)	**IKd (N=97)**	**Kd (N=67)**	**IKd (N=80)**	**p-value of treatment-by-sub group interaction[c]**
30 Months	0.0756 (0.0243 to 0.1664)	0.0707 (0.0305 to 0.1337)	0.0224 (0.0023 to 0.0923)	0.0148 (0.0013 to 0.0695)	
Number of patients at risk[b]					
3 Months	8	9	6	10	
6 Months	5	7	3	4	
9 Months	5	7	3	1	
12 Months	5	6	2	1	
15 Months	4	5	1	1	
18 Months	4	5	1	1	
21 Months	3	5	0	1	
24 Months	1	1	0	0	
27 Months	0	0	0	0	
30 Months	0	0	0	0	

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
PGM=DEVOPS/SAR650984/EFC15246/CIR_RWE/REPORT/PGM/eff_km_sr_subgrp_sig_s_t.sas OUT=REPORT/OUTPUT/eff_km_de_tesev12_rreg_s_t_x.rtf (12FEB2021 8:13)

16.2.7.1 Safety endpoints
16.2.7.1.53 Subgroup analysis by regulatory region
16.2.7.1.53.5 Treatment emergent severe adverse event by treatment group according to regulatory region - Safety population

	Western countries		Other countries		
	Kd (N=55)	**IKd (N=97)**	**Kd (N=67)**	**IKd (N=80)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	36 (65.5)	71 (73.2)	45 (67.2)	63 (78.8)	0.7549
Number (%) of patients censored	19 (34.5)	26 (26.8)	22 (32.8)	17 (21.3)	
Kaplan-Meier estimates of TEAE in months					
25% quantile (95% CI)	1.2156 (0.3943 to 3.8768)	1.2813 (0.5914 to 2.8255)	2.1027 (0.8214 to 4.0411)	1.3470 (0.6899 to 2.4312)	
Median (95% CI)	6.5708 (3.8768 to 15.9343)	5.9466 (4.3368 to 9.0021)	6.7351 (4.0411 to 10.8090)	5.3717 (3.2854 to 7.8193)	
75% quantile (95% CI)	NC (15.9343 to NC)	16.7556 (11.1704 to NC)	NC (12.3532 to NC)	14.7187 (9.7577 to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd		0.3579		0.1622	
Hazard ratio (95% CI) vs Kd		1.2072 (0.8076 to 1.8044)		1.3129 (0.8952 to 1.9255)	
P-value		0.3586		0.1635	
probability (95% CI)[b]					

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
PGM=DEVOPS/SAR650984/EFC15246/CIR_RWE/REPORT/PGM/eff_km_sr_subgrp_sig_s_t.sas OUT=REPORT/OUTPUT/eff_km_de_tesev34_rreg_s_t_x.rtf (12FEB2021 8:13)

16.2.7.1 Safety endpoints
16.2.7.1.53 Subgroup analysis by regulatory region
16.2.7.1.53.5 Treatment emergent severe adverse event by treatment group according to regulatory region - Safety population

	Western countries		Other countries		
	Kd (N=55)	**IKd (N=97)**	**Kd (N=67)**	**IKd (N=80)**	**p-value of treatment-by-sub group interaction[c]**
3 Months	0.6688 (0.5267 to 0.7769)	0.6570 (0.5529 to 0.7424)	0.7164 (0.5922 to 0.8087)	0.6250 (0.5094 to 0.7207)	
6 Months	0.5350 (0.3933 to 0.6575)	0.4874 (0.3840 to 0.5830)	0.5373 (0.4114 to 0.6477)	0.4750 (0.3626 to 0.5791)	
9 Months	0.4586 (0.3216 to 0.5852)	0.4133 (0.3138 to 0.5098)	0.4310 (0.3108 to 0.5453)	0.3625 (0.2589 to 0.4667)	
12 Months	0.4395 (0.3042 to 0.5666)	0.3285 (0.2365 to 0.4233)	0.3694 (0.2551 to 0.4838)	0.2625 (0.1720 to 0.3619)	
15 Months	0.4013 (0.2700 to 0.5290)	0.2713 (0.1855 to 0.3641)	0.3218 (0.2132 to 0.4354)	0.2479 (0.1593 to 0.3468)	
18 Months	0.3439 (0.2202 to 0.4710)	0.2466 (0.1639 to 0.3384)	0.3218 (0.2132 to 0.4354)	0.2158 (0.1314 to 0.3139)	
21 Months	0.3439 (0.2202 to 0.4710)	0.2466 (0.1639 to 0.3384)	0.3218 (0.2132 to 0.4354)	0.1992 (0.1174 to 0.2967)	
24 Months	0.3095 (0.1852 to 0.4424)	0.2466 (0.1639 to 0.3384)	0.3218 (0.2132 to 0.4354)	0.1992 (0.1174 to 0.2967)	
27 Months	0.3095 (0.1852 to 0.4424)	0.2466 (0.1639 to 0.3384)	0.3218 (0.2132 to 0.4354)	0.1992 (0.1174 to 0.2967)	
30 Months	0.3095 (0.1852 to 0.4424)	0.2466 (0.1639 to 0.3384)	0.3218 (0.2132 to 0.4354)	0.1992 (0.1174 to 0.2967)	

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
PGM=DEVOPS/SAR650984/EFC15246/CIR_RWE/REPORT/PGM/eff_km_sr_subgrp_sig_s_t.sas OUT=REPORT/OUTPUT/eff_km_de_tesev34_rreg_s_t_x.rtf (12FEB2021 8:13)

16.2.7.1 Safety endpoints
16.2.7.1.53 Subgroup analysis by regulatory region
16.2.7.1.53.5 Treatment emergent severe adverse event by treatment group according to regulatory region - Safety population

	Western countries		Other countries		
	Kd (N=55)	**IKd (N=97)**	**Kd (N=67)**	**IKd (N=80)**	**p-value of treatment-by-sub group interaction[c]**
Number of patients at risk[b]					
3 Months	35	62	48	50	
6 Months	28	46	36	38	
9 Months	24	39	28	29	
12 Months	23	31	24	21	
15 Months	21	23	20	16	
18 Months	18	20	19	13	
21 Months	14	19	13	12	
24 Months	2	5	6	5	
27 Months	0	0	1	0	
30 Months	0	0	0	0	

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
PGM=DEVOPS/SAR650984/EFC15246/CIR_RWE/REPORT/PGM/eff_km_sr_subgrp_sig_s_t.sas OUT=REPORT/OUTPUT/eff_km_de_tesev34_rreg_s_t_x.rtf (12FEB2021 8:13)

16.2.7.1 Safety endpoints
16.2.7.1.53 Subgroup analysis by regulatory region
16.2.7.1.53.6 Treatment emergent severe adverse event including death by treatment group according to regulatory region - Safety population

	Western countries		Other countries		
	Kd (N=55)	**IKd (N=97)**	**Kd (N=67)**	**IKd (N=80)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	37 (67.3)	72 (74.2)	45 (67.2)	64 (80.0)	0.6769
Number (%) of patients censored	18 (32.7)	25 (25.8)	22 (32.8)	16 (20.0)	
Kaplan-Meier estimates of TEAE in months					
25% quantile (95% CI)	1.1499 (0.3943 to 3.2854)	1.2485 (0.5257 to 2.0041)	2.1027 (0.8214 to 4.0411)	1.3470 (0.6899 to 2.4312)	
Median (95% CI)	6.5708 (3.2854 to 15.6057)	5.9466 (4.3368 to 9.0021)	6.7351 (4.0411 to 10.8090)	5.3717 (3.2854 to 7.8193)	
75% quantile (95% CI)	NC (15.6057 to NC)	16.7556 (11.1704 to NC)	NC (12.3532 to NC)	13.7988 (9.7577 to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd		0.3906		0.1358	
Hazard ratio (95% CI) vs Kd		1.1899 (0.7997 to 1.7704)		1.3357 (0.9119 to 1.9566)	
P-value		0.3912		0.1371	
probability (95% CI)[b]					

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
PGM=DEVOPS/SAR650984/EFC15246/CIR_RWE/REPORT/PGM/eff_km_sr_subgrp_sig_s_t.sas OUT=REPORT/OUTPUT/eff_km_de_tesev345_rreg_s_t_x.rtf (12FEB2021 8:13)

16.2.7.1 Safety endpoints
16.2.7.1.53 Subgroup analysis by regulatory region
16.2.7.1.53.6 Treatment emergent severe adverse event including death by treatment group according to regulatory region - Safety population

	Western countries		Other countries		
	Kd (N=55)	**IKd (N=97)**	**Kd (N=67)**	**IKd (N=80)**	**p-value of treatment-by-sub group interaction[c]**
3 Months	0.6536 (0.5121 to 0.7632)	0.6492 (0.5453 to 0.7350)	0.7164 (0.5922 to 0.8087)	0.6250 (0.5094 to 0.7207)	
6 Months	0.5229 (0.3830 to 0.6452)	0.4816 (0.3790 to 0.5769)	0.5373 (0.4114 to 0.6477)	0.4750 (0.3626 to 0.5791)	
9 Months	0.4482 (0.3134 to 0.5739)	0.4083 (0.3098 to 0.5043)	0.4310 (0.3108 to 0.5453)	0.3625 (0.2589 to 0.4667)	
12 Months	0.4295 (0.2965 to 0.5557)	0.3246 (0.2335 to 0.4187)	0.3694 (0.2551 to 0.4838)	0.2625 (0.1720 to 0.3619)	
15 Months	0.3921 (0.2632 to 0.5187)	0.2680 (0.1832 to 0.3601)	0.3218 (0.2132 to 0.4354)	0.2361 (0.1498 to 0.3338)	
18 Months	0.3361 (0.2148 to 0.4617)	0.2437 (0.1618 to 0.3347)	0.3218 (0.2132 to 0.4354)	0.2055 (0.1237 to 0.3018)	
21 Months	0.3361 (0.2148 to 0.4617)	0.2437 (0.1618 to 0.3347)	0.3218 (0.2132 to 0.4354)	0.1897 (0.1106 to 0.2851)	
24 Months	0.3025 (0.1807 to 0.4336)	0.2437 (0.1618 to 0.3347)	0.3218 (0.2132 to 0.4354)	0.1897 (0.1106 to 0.2851)	
27 Months	0.3025 (0.1807 to 0.4336)	0.2437 (0.1618 to 0.3347)	0.3218 (0.2132 to 0.4354)	0.1897 (0.1106 to 0.2851)	
30 Months	0.3025 (0.1807 to 0.4336)	0.2437 (0.1618 to 0.3347)	0.3218 (0.2132 to 0.4354)	0.1897 (0.1106 to 0.2851)	

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
PGM=DEVOPS/SAR650984/EFC15246/CIR_RWE/REPORT/PGM/eff_km_sr_subgrp_sig_s_t.sas OUT=REPORT/OUTPUT/eff_km_de_tesev345_rreg_s_t_x.rtf (12FEB2021 8:13)

16.2.7.1 Safety endpoints
16.2.7.1.53 Subgroup analysis by regulatory region
16.2.7.1.53.6 Treatment emergent severe adverse event including death by treatment group according to regulatory region - Safety population

	Western countries		Other countries		
	Kd (N=55)	**IKd (N=97)**	**Kd (N=67)**	**IKd (N=80)**	**p-value of treatment-by-sub group interaction[c]**
Number of patients at risk[b]					
3 Months	35	62	48	50	
6 Months	28	46	36	38	
9 Months	24	39	28	29	
12 Months	23	31	24	21	
15 Months	21	23	20	16	
18 Months	18	20	19	13	
21 Months	14	19	13	12	
24 Months	2	5	6	5	
27 Months	0	0	1	0	
30 Months	0	0	0	0	

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.54 Subgroup analysis by baseline ECOG PS
16.2.7.1.54.1 Treatment emergent adverse event by treatment group according to baseline ECOG PS - Safety population

	0 or 1		>1		
	Kd (N=117)	**IKd (N=167)**	**Kd (N=5)**	**IKd (N=10)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	112 (95.7)	162 (97.0)	5 (100.0)	10 (100.0)	0.8417
Number (%) of patients censored	5 (4.3)	5 (3.0)	0 (0.0)	0 (0.0)	
Kaplan-Meier estimates of TEAE in months					
25% quantile (95% CI)	0.1971 (0.1314 to 0.2300)	0.0657 (0.0657 to 0.0986)	0.1314 (0.0986 to 0.3614)	0.0657 (0.0329 to 0.2957)	
Median (95% CI)	0.4928 (0.3285 to 0.6242)	0.1971 (0.1314 to 0.2300)	0.3614 (0.0986 to 1.1828)	0.2136 (0.0329 to 0.3943)	
75% quantile (95% CI)	1.0185 (0.6571 to 1.5113)	0.7885 (0.4600 to 1.1828)	0.3614 (0.0986 to 1.1828)	0.3943 (0.1314 to 1.4784)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd		0.0301		0.8681	
Hazard ratio (95% CI) vs Kd		1.3055 (1.0253 to 1.6622)		1.0977 (0.3651 to 3.3001)	
P-value		0.0306		0.8682	

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
PGM=DEVOPS/SAR650984/EFC15246/CIR_RWE/REPORT/PGM/eff_km_sr_subgrp_sig_s_t.sas OUT=REPORT/OUTPUT/eff_km_de_teae_ecog_s_t_x.rtf (12FEB2021 8:09)

16.2.7.1 Safety endpoints
16.2.7.1.54 Subgroup analysis by baseline ECOG PS
16.2.7.1.54.1 Treatment emergent adverse event by treatment group according to baseline ECOG PS - Safety population

	0 or 1		>1		
	Kd (N=117)	**IKd (N=167)**	**Kd (N=5)**	**IKd (N=10)**	**p-value of treatment-by-sub group interaction[c]**
Hazard ratio inverted (95% CI) vs IKd	0.7660 (0.6016 to 0.9753)				
probability (95% CI)[b]					
3 Months	0.0940 (0.0498 to 0.1551)	0.0778 (0.0436 to 0.1248)	0.2000 (0.0084 to 0.5819)	0.1000 (0.0057 to 0.3581)	
6 Months	0.0513 (0.0210 to 0.1018)	0.0479 (0.0225 to 0.0878)	0.2000 (0.0084 to 0.5819)	0.1000 (0.0057 to 0.3581)	
9 Months	0.0513 (0.0210 to 0.1018)	0.0359 (0.0148 to 0.0723)	0.2000 (0.0084 to 0.5819)	0.1000 (0.0057 to 0.3581)	
12 Months	0.0513 (0.0210 to 0.1018)	0.0299 (0.0113 to 0.0644)	0.2000 (0.0084 to 0.5819)	0.1000 (0.0057 to 0.3581)	
15 Months	0.0427 (0.0159 to 0.0905)	0.0299 (0.0113 to 0.0644)	0.2000 (0.0084 to 0.5819)	0.1000 (0.0057 to 0.3581)	
18 Months	0.0427 (0.0159 to 0.0905)	0.0299 (0.0113 to 0.0644)	0.2000 (0.0084 to 0.5819)	0.1000 (0.0057 to 0.3581)	
21 Months	0.0427 (0.0159 to 0.0905)	0.0299 (0.0113 to 0.0644)	0.2000 (0.0084 to 0.5819)	0.1000 (0.0057 to 0.3581)	
24 Months	0.0427 (0.0159 to 0.0905)	0.0299 (0.0113 to 0.0644)	0.2000 (0.0084 to 0.5819)	0.1000 (0.0057 to 0.3581)	

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.54 Subgroup analysis by baseline ECOG PS
16.2.7.1.54.1 Treatment emergent adverse event by treatment group according to baseline ECOG PS - Safety population

	0 or 1		>1		
	Kd (N=117)	**IKd (N=167)**	**Kd (N=5)**	**IKd (N=10)**	**p-value of treatment-by-sub group interaction[c]**
27 Months	0.0427 (0.0159 to 0.0905)	0.0299 (0.0113 to 0.0644)	0.2000 (0.0084 to 0.5819)	0.1000 (0.0057 to 0.3581)	
30 Months	0.0427 (0.0159 to 0.0905)	0.0299 (0.0113 to 0.0644)	0.2000 (0.0084 to 0.5819)	0.1000 (0.0057 to 0.3581)	
Number of patients at risk[b]					
3 Months	11	13	0	0	
6 Months	6	8	0	0	
9 Months	6	6	0	0	
12 Months	6	5	0	0	
15 Months	5	5	0	0	
18 Months	5	5	0	0	
21 Months	3	5	0	0	
24 Months	1	1	0	0	
27 Months	0	0	0	0	
30 Months	0	0	0	0	

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.54 Subgroup analysis by baseline ECOG PS
16.2.7.1.54.2 Treatment emergent serious adverse event by treatment group according to baseline ECOG PS - Safety population

	0 or 1		>1		
	Kd (N=117)	**IKd (N=167)**	**Kd (N=5)**	**IKd (N=10)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	66 (56.4)	98 (58.7)	4 (80.0)	7 (70.0)	0.3619
Number (%) of patients censored	51 (43.6)	69 (41.3)	1 (20.0)	3 (30.0)	
Kaplan-Meier estimates of TEAE in months					
25% quantile (95% CI)	4.9610 (2.9569 to 6.5051)	3.0554 (1.2813 to 5.1253)	0.3614 (0.0986 to 5.8480)	1.3142 (0.3943 to 9.9548)	
Median (95% CI)	13.8645 (10.8090 to NC)	12.8131 (9.2649 to 17.9384)	5.0267 (0.0986 to NC)	9.9384 (0.3943 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	5.8480 (0.0986 to NC)	NC (9.9220 to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd		0.5263		0.3863	
Hazard ratio (95% CI) vs Kd		1.1061 (0.8095 to 1.5114)		0.5808 (0.1675 to 2.0144)	
P-value		0.5265		0.3918	
probability (95% CI)[b]					

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
PGM=DEVOPS/SAR650984/EFC15246/CIR_RWE/REPORT/PGM/eff_km_sr_subgrp_sig_s_t.sas OUT=REPORT/OUTPUT/eff_km_de_tesae_ecog_s_t_x.rtf (12FEB2021 8:12)

16.2.7.1 Safety endpoints
16.2.7.1.54 Subgroup analysis by baseline ECOG PS
16.2.7.1.54.2 Treatment emergent serious adverse event by treatment group according to baseline ECOG PS - Safety population

	0 or 1		>1		
	Kd (N=117)	**IKd (N=167)**	**Kd (N=5)**	**IKd (N=10)**	**p-value of treatment-by-sub group interaction[c]**
3 Months	0.8289 (0.7474 to 0.8860)	0.7545 (0.6818 to 0.8128)	0.6000 (0.1257 to 0.8818)	0.6000 (0.2527 to 0.8272)	
6 Months	0.6821 (0.5891 to 0.7584)	0.6642 (0.5870 to 0.7303)	0.2000 (0.0084 to 0.5819)	0.6000 (0.2527 to 0.8272)	
9 Months	0.6127 (0.5178 to 0.6945)	0.5857 (0.5070 to 0.6562)	0.2000 (0.0084 to 0.5819)	0.6000 (0.2527 to 0.8272)	
12 Months	0.5602 (0.4650 to 0.6450)	0.5193 (0.4408 to 0.5920)	0.2000 (0.0084 to 0.5819)	0.4000 (0.1227 to 0.6702)	
15 Months	0.4796 (0.3857 to 0.5674)	0.4499 (0.3727 to 0.5240)	0.2000 (0.0084 to 0.5819)	0.3000 (0.0711 to 0.5779)	
18 Months	0.4430 (0.3505 to 0.5315)	0.4230 (0.3464 to 0.4974)	0.2000 (0.0084 to 0.5819)	0.3000 (0.0711 to 0.5779)	
21 Months	0.4338 (0.3416 to 0.5224)	0.4161 (0.3397 to 0.4907)	0.2000 (0.0084 to 0.5819)	0.3000 (0.0711 to 0.5779)	
24 Months	0.4178 (0.3241 to 0.5085)	0.4007 (0.3245 to 0.4757)	0.2000 (0.0084 to 0.5819)	0.3000 (0.0711 to 0.5779)	
27 Months	0.4178 (0.3241 to 0.5085)	0.4007 (0.3245 to 0.4757)	0.2000 (0.0084 to 0.5819)	0.3000 (0.0711 to 0.5779)	
30 Months	0.4178 (0.3241 to 0.5085)	0.4007 (0.3245 to 0.4757)	0.2000 (0.0084 to 0.5819)	0.3000 (0.0711 to 0.5779)	

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
PGM=DEVOPS/SAR650984/EFC15246/CIR_RWE/REPORT/PGM/eff_km_sr_subgrp_sig_s_t.sas OUT=REPORT/OUTPUT/eff_km_de_tesae_ecog_s_t_x.rtf (12FEB2021 8:12)

16.2.7.1 Safety endpoints
16.2.7.1.54 Subgroup analysis by baseline ECOG PS
16.2.7.1.54.2 Treatment emergent serious adverse event by treatment group according to baseline ECOG PS - Safety population

	0 or 1		>1		
	Kd (N=117)	**IKd (N=167)**	**Kd (N=5)**	**IKd (N=10)**	**p-value of treatment-by-sub group interaction[c]**
Number of patients at risk[b]					
3 Months	96	126	3	6	
6 Months	79	110	1	6	
9 Months	70	97	1	6	
12 Months	64	86	1	4	
15 Months	53	68	1	3	
18 Months	48	62	1	2	
21 Months	35	55	1	2	
24 Months	9	19	0	0	
27 Months	2	1	0	0	
30 Months	0	0	0	0	

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
PGM=DEVOPS/SAR650984/EFC15246/CIR_RWE/REPORT/PGM/eff_km_sr_subgrp_sig_s_t.sas OUT=REPORT/OUTPUT/eff_km_de_tesae_ecog_s_t_x.rtf (12FEB2021 8:12)

16.2.7.1 Safety endpoints
16.2.7.1.54 Subgroup analysis by baseline ECOG PS
16.2.7.1.54.3 Treatment emergent adverse event leading to discontinuation of treatment by treatment group according to baseline ECOG PS - Safety population

	0 or 1		>1		
	Kd (N=117)	**IKd (N=167)**	**Kd (N=5)**	**IKd (N=10)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	15 (12.8)	15 (9.0)	2 (40.0)	0 (0.0)	0.9883
Number (%) of patients censored	102 (87.2)	152 (91.0)	3 (60.0)	10 (100.0)	
Kaplan-Meier estimates of TEAE in months					
25% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	10.6119 (5.8480 to NC)	NC (NC to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	15.3758 (5.8480 to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (5.8480 to NC)	NC (NC to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd		0.2881		0.0145	
Hazard ratio (95% CI) vs Kd		0.6801 (0.3324 to 1.3912)		NC (NC to NC)	
P-value		0.2910		0.9983	
probability (95% CI)[b]					
3 Months	0.9571 (0.9000 to 0.9819)	0.9700 (0.9294 to 0.9874)	1.0000 (1.0000 to 1.0000)	1.0000 (1.0000 to 1.0000)	

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.54 Subgroup analysis by baseline ECOG PS
16.2.7.1.54.3 Treatment emergent adverse event leading to discontinuation of treatment by treatment group according to baseline ECOG PS - Safety population

	0 or 1		>1		
	Kd (N=117)	**IKd (N=167)**	**Kd (N=5)**	**IKd (N=10)**	**p-value of treatment-by-sub group interaction[c]**
6 Months	0.9396 (0.8775 to 0.9708)	0.9453 (0.8976 to 0.9712)	0.7500 (0.1279 to 0.9605)	1.0000 (1.0000 to 1.0000)	
9 Months	0.8854 (0.8107 to 0.9318)	0.9265 (0.8742 to 0.9576)	0.7500 (0.1279 to 0.9605)	1.0000 (1.0000 to 1.0000)	
12 Months	0.8854 (0.8107 to 0.9318)	0.9265 (0.8742 to 0.9576)	0.7500 (0.1279 to 0.9605)	1.0000 (1.0000 to 1.0000)	
15 Months	0.8854 (0.8107 to 0.9318)	0.9135 (0.8582 to 0.9478)	0.7500 (0.1279 to 0.9605)	1.0000 (1.0000 to 1.0000)	
18 Months	0.8756 (0.7987 to 0.9244)	0.9135 (0.8582 to 0.9478)	0.3750 (0.0110 to 0.8080)	1.0000 (1.0000 to 1.0000)	
21 Months	0.8656 (0.7867 to 0.9168)	0.9062 (0.8490 to 0.9424)	0.3750 (0.0110 to 0.8080)	1.0000 (1.0000 to 1.0000)	
24 Months	0.8656 (0.7867 to 0.9168)	0.9062 (0.8490 to 0.9424)	0.3750 (0.0110 to 0.8080)	1.0000 (1.0000 to 1.0000)	
27 Months	0.8656 (0.7867 to 0.9168)	0.9062 (0.8490 to 0.9424)	0.3750 (0.0110 to 0.8080)	1.0000 (1.0000 to 1.0000)	
30 Months	0.8656 (0.7867 to 0.9168)	0.9062 (0.8490 to 0.9424)	0.3750 (0.0110 to 0.8080)	1.0000 (1.0000 to 1.0000)	

Number of patients at risk[b]

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
PGM=DEVOPS/SAR650984/EFC15246/CIR_RWE/REPORT/PGM/eff_km_sr_subgrp_sig_s_t.sas OUT=REPORT/OUTPUT/eff_km_de_tedisc_ecog_s_t_x.rtf (12FEB2021 8:12)

16.2.7.1 Safety endpoints
16.2.7.1.54 Subgroup analysis by baseline ECOG PS
16.2.7.1.54.3 Treatment emergent adverse event leading to discontinuation of treatment by treatment group according to baseline ECOG PS - Safety population

	0 or 1		>1		
	Kd (N=117)	**IKd (N=167)**	**Kd (N=5)**	**IKd (N=10)**	**p-value of treatment-by-sub group interaction[c]**
3 Months	110	161	5	9	
6 Months	105	152	3	9	
9 Months	96	146	3	9	
12 Months	94	144	3	8	
15 Months	90	132	2	8	
18 Months	88	126	1	7	
21 Months	72	112	1	6	
24 Months	26	40	0	0	
27 Months	4	2	0	0	
30 Months	0	0	0	0	

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
PGM=DEVOPS/SAR650984/EFC15246/CIR_RWE/REPORT/PGM/eff_km_sr_subgrp_sig_s_t.sas OUT=REPORT/OUTPUT/eff_km_de_tedisc_ecog_s_t_x.rtf (12FEB2021 8:12)

16.2.7.1 Safety endpoints
16.2.7.1.54 Subgroup analysis by baseline ECOG PS
16.2.7.1.54.4 Treatment emergent mild adverse event by treatment group according to baseline ECOG PS - Safety population

	0 or 1		>1		
	Kd (N=117)	**IKd (N=167)**	**Kd (N=5)**	**IKd (N=10)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	110 (94.0)	157 (94.0)	5 (100.0)	10 (100.0)	0.9710
Number (%) of patients censored	7 (6.0)	10 (6.0)	0 (0.0)	0 (0.0)	
Kaplan-Meier estimates of TEAE in months					
25% quantile (95% CI)	0.1971 (0.1314 to 0.2628)	0.0657 (0.0657 to 0.0986)	0.1314 (0.0986 to 0.5914)	0.0657 (0.0329 to 0.2957)	
Median (95% CI)	0.5257 (0.3614 to 0.6571)	0.1971 (0.1643 to 0.2628)	0.3614 (0.0986 to 1.1828)	0.2136 (0.0329 to 0.3943)	
75% quantile (95% CI)	1.2156 (0.8214 to 1.9384)	1.0185 (0.5257 to 1.6099)	0.5914 (0.0986 to 1.1828)	0.3943 (0.1314 to 1.4784)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd		0.0635		0.7746	
Hazard ratio (95% CI) vs Kd		1.2598 (0.9866 to 1.6087)		1.1741 (0.3910 to 3.5251)	
P-value		0.0641		0.7748	

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
PGM=DEVOPS/SAR650984/EFC15246/CIR_RWE/REPORT/PGM/eff_km_sr_subgrp_sig_s_t.sas OUT=REPORT/OUTPUT/eff_km_de_tesev12_ecog_s_t_x.rtf (12FEB2021 8:12)

16.2.7.1 Safety endpoints
16.2.7.1.54 Subgroup analysis by baseline ECOG PS
16.2.7.1.54.4 Treatment emergent mild adverse event by treatment group according to baseline ECOG PS - Safety population

	0 or 1		>1		
	Kd (N=117)	**IKd (N=167)**	**Kd (N=5)**	**IKd (N=10)**	**p-value of treatment-by-sub group interaction[c]**
probability (95% CI)[b]					
3 Months	0.1218 (0.0702 to 0.1887)	0.1160 (0.0728 to 0.1701)	0.2000 (0.0084 to 0.5819)	0.1000 (0.0057 to 0.3581)	
6 Months	0.0696 (0.0326 to 0.1257)	0.0773 (0.0426 to 0.1252)	0.2000 (0.0084 to 0.5819)	0.1000 (0.0057 to 0.3581)	
9 Months	0.0696 (0.0326 to 0.1257)	0.0562 (0.0272 to 0.1002)	0.2000 (0.0084 to 0.5819)	0.1000 (0.0057 to 0.3581)	
12 Months	0.0696 (0.0326 to 0.1257)	0.0492 (0.0225 to 0.0916)	0.2000 (0.0084 to 0.5819)	0.1000 (0.0057 to 0.3581)	
15 Months	0.0497 (0.0195 to 0.1016)	0.0492 (0.0225 to 0.0916)	0.2000 (0.0084 to 0.5819)	0.1000 (0.0057 to 0.3581)	
18 Months	0.0497 (0.0195 to 0.1016)	0.0492 (0.0225 to 0.0916)	0.2000 (0.0084 to 0.5819)	0.1000 (0.0057 to 0.3581)	
21 Months	0.0497 (0.0195 to 0.1016)	0.0492 (0.0225 to 0.0916)	0.2000 (0.0084 to 0.5819)	0.1000 (0.0057 to 0.3581)	
24 Months	0.0497 (0.0195 to 0.1016)	0.0492 (0.0225 to 0.0916)	0.2000 (0.0084 to 0.5819)	0.1000 (0.0057 to 0.3581)	
27 Months	0.0497 (0.0195 to 0.1016)	0.0492 (0.0225 to 0.0916)	0.2000 (0.0084 to 0.5819)	0.1000 (0.0057 to 0.3581)	

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
PGM=DEVOPS/SAR650984/EFC15246/CIR_RWE/REPORT/PGM/eff_km_sr_subgrp_sig_s_t.sas OUT=REPORT/OUTPUT/eff_km_de_tesev12_ecog_s_t_x.rtf (12FEB2021 8:12)

16.2.7.1 Safety endpoints
16.2.7.1.54 Subgroup analysis by baseline ECOG PS
16.2.7.1.54.4 Treatment emergent mild adverse event by treatment group according to baseline ECOG PS - Safety population

	0 or 1		>1		
	Kd (N=117)	**IKd (N=167)**	**Kd (N=5)**	**IKd (N=10)**	**p-value of treatment-by-sub group interaction[c]**
30 Months	0.0497 (0.0195 to 0.1016)	0.0492 (0.0225 to 0.0916)	0.2000 (0.0084 to 0.5819)	0.1000 (0.0057 to 0.3581)	
Number of patients at risk[b]					
3 Months	14	19	0	0	
6 Months	8	11	0	0	
9 Months	8	8	0	0	
12 Months	7	7	0	0	
15 Months	5	6	0	0	
18 Months	5	6	0	0	
21 Months	3	6	0	0	
24 Months	1	1	0	0	
27 Months	0	0	0	0	
30 Months	0	0	0	0	

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
PGM=DEVOPS/SAR650984/EFC15246/CIR_RWE/REPORT/PGM/eff_km_sr_subgrp_sig_s_t.sas OUT=REPORT/OUTPUT/eff_km_de_tesev12_ecog_s_t_x.rtf (12FEB2021 8:12)

16.2.7.1 Safety endpoints
16.2.7.1.54 Subgroup analysis by baseline ECOG PS
16.2.7.1.54.5 Treatment emergent severe adverse event by treatment group according to baseline ECOG PS - Safety population

	0 or 1		>1		
	Kd (N=117)	**IKd (N=167)**	**Kd (N=5)**	**IKd (N=10)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	77 (65.8)	126 (75.4)	4 (80.0)	8 (80.0)	0.7486
Number (%) of patients censored	40 (34.2)	41 (24.6)	1 (20.0)	2 (20.0)	
Kaplan-Meier estimates of TEAE in months					
25% quantile (95% CI)	2.0698 (1.0513 to 3.8768)	1.2485 (0.6899 to 1.9713)	0.3614 (0.0986 to 5.8480)	1.3142 (0.0657 to 3.9097)	
Median (95% CI)	7.4251 (4.5667 to 11.4004)	5.9466 (4.7639 to 7.8193)	5.0267 (0.0986 to NC)	3.9097 (0.0657 to 12.5503)	
75% quantile (95% CI)	NC (21.7823 to NC)	16.7556 (11.4333 to NC)	5.8480 (0.0986 to NC)	9.9220 (2.4312 to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd		0.1107		0.9526	
Hazard ratio (95% CI) vs Kd		1.2592 (0.9481 to 1.6726)		1.0372 (0.3096 to 3.4747)	
P-value		0.1115		0.9528	
probability (95% CI)[b]					

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
PGM=DEVOPS/SAR650984/EFC15246/CIR_RWE/REPORT/PGM/eff_km_sr_subgrp_sig_s_t.sas OUT=REPORT/OUTPUT/eff_km_de_tesev34_ecog_s_t_x.rtf (12FEB2021 8:13)

16.2.7.1 Safety endpoints
16.2.7.1.54 Subgroup analysis by baseline ECOG PS
16.2.7.1.54.5 Treatment emergent severe adverse event by treatment group according to baseline ECOG PS - Safety population

	0 or 1		>1		
	Kd (N=117)	**IKd (N=167)**	**Kd (N=5)**	**IKd (N=10)**	**p-value of treatment-by-sub group interaction[c]**
3 Months	0.6990 (0.6067 to 0.7737)	0.6463 (0.5686 to 0.7136)	0.6000 (0.1257 to 0.8818)	0.5714 (0.2172 to 0.8146)	
6 Months	0.5505 (0.4553 to 0.6358)	0.4892 (0.4113 to 0.5626)	0.2000 (0.0084 to 0.5819)	0.3429 (0.0817 to 0.6328)	
9 Months	0.4535 (0.3607 to 0.5415)	0.3926 (0.3183 to 0.4660)	0.2000 (0.0084 to 0.5819)	0.3429 (0.0817 to 0.6328)	
12 Months	0.4090 (0.3185 to 0.4972)	0.3020 (0.2340 to 0.3727)	0.2000 (0.0084 to 0.5819)	0.2286 (0.0349 to 0.5223)	
15 Months	0.3641 (0.2767 to 0.4518)	0.2683 (0.2028 to 0.3379)	0.2000 (0.0084 to 0.5819)	0.1143 (0.0063 to 0.3952)	
18 Months	0.3363 (0.2511 to 0.4235)	0.2395 (0.1764 to 0.3081)	0.2000 (0.0084 to 0.5819)	0.1143 (0.0063 to 0.3952)	
21 Months	0.3363 (0.2511 to 0.4235)	0.2322 (0.1698 to 0.3005)	0.2000 (0.0084 to 0.5819)	0.1143 (0.0063 to 0.3952)	
24 Months	0.3203 (0.2344 to 0.4093)	0.2322 (0.1698 to 0.3005)	0.2000 (0.0084 to 0.5819)	0.1143 (0.0063 to 0.3952)	
27 Months	0.3203 (0.2344 to 0.4093)	0.2322 (0.1698 to 0.3005)	0.2000 (0.0084 to 0.5819)	0.1143 (0.0063 to 0.3952)	
30 Months	0.3203 (0.2344 to 0.4093)	0.2322 (0.1698 to 0.3005)	0.2000 (0.0084 to 0.5819)	0.1143 (0.0063 to 0.3952)	

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
PGM=DEVOPS/SAR650984/EFC15246/CIR_RWE/REPORT/PGM/eff_km_sr_subgrp_sig_s_t.sas OUT=REPORT/OUTPUT/eff_km_de_tesev34_ecog_s_t_x.rtf (12FEB2021 8:13)

16.2.7.1 Safety endpoints
16.2.7.1.54 Subgroup analysis by baseline ECOG PS
16.2.7.1.54.5 Treatment emergent severe adverse event by treatment group according to baseline ECOG PS - Safety population

	0 or 1		>1		
	Kd (N=117)	**IKd (N=167)**	**Kd (N=5)**	**IKd (N=10)**	**p-value of treatment-by-sub group interaction[c]**
Number of patients at risk[b]					
3 Months	80	107	3	5	
6 Months	63	81	1	3	
9 Months	51	65	1	3	
12 Months	46	50	1	2	
15 Months	40	38	1	1	
18 Months	36	33	1	0	
21 Months	26	31	1	0	
24 Months	8	10	0	0	
27 Months	1	0	0	0	
30 Months	0	0	0	0	

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
PGM=DEVOPS/SAR650984/EFC15246/CIR_RWE/REPORT/PGM/eff_km_sr_subgrp_sig_s_t.sas OUT=REPORT/OUTPUT/eff_km_de_tesev34_ecog_s_t_x.rtf (12FEB2021 8:13)

16.2.7.1 Safety endpoints
16.2.7.1.54 Subgroup analysis by baseline ECOG PS
16.2.7.1.54.6 Treatment emergent severe adverse event including death by treatment group according to baseline ECOG PS - Safety population

	0 or 1		>1		
	Kd (N=117)	**IKd (N=167)**	**Kd (N=5)**	**IKd (N=10)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	78 (66.7)	127 (76.0)	4 (80.0)	9 (90.0)	0.8977
Number (%) of patients censored	39 (33.3)	40 (24.0)	1 (20.0)	1 (10.0)	
Kaplan-Meier estimates of TEAE in months					
25% quantile (95% CI)	1.9055 (0.9856 to 3.2854)	1.2485 (0.6899 to 1.9713)	0.3614 (0.0986 to 5.8480)	0.4271 (0.0657 to 3.9097)	
Median (95% CI)	7.4251 (4.5667 to 11.4004)	5.9466 (4.7639 to 7.8193)	5.0267 (0.0986 to NC)	3.1704 (0.0657 to 9.9220)	
75% quantile (95% CI)	NC (16.8542 to NC)	15.8357 (11.4333 to NC)	5.8480 (0.0986 to NC)	9.9220 (2.4312 to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd		0.1152		0.8269	
Hazard ratio (95% CI) vs Kd		1.2541 (0.9456 to 1.6631)		1.1415 (0.3485 to 3.7388)	
P-value		0.1160		0.8270	
probability (95% CI)[b]					

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.54 Subgroup analysis by baseline ECOG PS
16.2.7.1.54.6 Treatment emergent severe adverse event including death by treatment group according to baseline ECOG PS - Safety population

	0 or 1		>1		
	Kd (N=117)	**IKd (N=167)**	**Kd (N=5)**	**IKd (N=10)**	**p-value of treatment-by-sub group interaction[c]**
3 Months	0.6919 (0.5995 to 0.7671)	0.6463 (0.5686 to 0.7136)	0.6000 (0.1257 to 0.8818)	0.5000 (0.1836 to 0.7532)	
6 Months	0.5449 (0.4501 to 0.6301)	0.4892 (0.4113 to 0.5626)	0.2000 (0.0084 to 0.5819)	0.3000 (0.0711 to 0.5779)	
9 Months	0.4488 (0.3567 to 0.5365)	0.3926 (0.3183 to 0.4660)	0.2000 (0.0084 to 0.5819)	0.3000 (0.0711 to 0.5779)	
12 Months	0.4048 (0.3150 to 0.4926)	0.3020 (0.2340 to 0.3727)	0.2000 (0.0084 to 0.5819)	0.2000 (0.0309 to 0.4747)	
15 Months	0.3604 (0.2737 to 0.4476)	0.2627 (0.1979 to 0.3319)	0.2000 (0.0084 to 0.5819)	0.1000 (0.0057 to 0.3581)	
18 Months	0.3329 (0.2484 to 0.4195)	0.2345 (0.1722 to 0.3025)	0.2000 (0.0084 to 0.5819)	0.1000 (0.0057 to 0.3581)	
21 Months	0.3329 (0.2484 to 0.4195)	0.2274 (0.1658 to 0.2951)	0.2000 (0.0084 to 0.5819)	0.1000 (0.0057 to 0.3581)	
24 Months	0.3170 (0.2318 to 0.4054)	0.2274 (0.1658 to 0.2951)	0.2000 (0.0084 to 0.5819)	0.1000 (0.0057 to 0.3581)	
27 Months	0.3170 (0.2318 to 0.4054)	0.2274 (0.1658 to 0.2951)	0.2000 (0.0084 to 0.5819)	0.1000 (0.0057 to 0.3581)	
30 Months	0.3170 (0.2318 to 0.4054)	0.2274 (0.1658 to 0.2951)	0.2000 (0.0084 to 0.5819)	0.1000 (0.0057 to 0.3581)	

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.54 Subgroup analysis by baseline ECOG PS
16.2.7.1.54.6 Treatment emergent severe adverse event including death by treatment group according to baseline ECOG PS - Safety population

	0 or 1		>1		
	Kd (N=117)	**IKd (N=167)**	**Kd (N=5)**	**IKd (N=10)**	**p-value of treatment-by-sub group interaction[c]**
Number of patients at risk[b]					
3 Months	80	107	3	5	
6 Months	63	81	1	3	
9 Months	51	65	1	3	
12 Months	46	50	1	2	
15 Months	40	38	1	1	
18 Months	36	33	1	0	
21 Months	26	31	1	0	
24 Months	8	10	0	0	
27 Months	1	0	0	0	
30 Months	0	0	0	0	

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
PGM=DEVOPS/SAR650984/EFC15246/CIR_RWE/REPORT/PGM/eff_km_sr_subgrp_sig_s_t.sas OUT=REPORT/OUTPUT/eff_km_de_tesev345_ecog_s_t_x.rtf (12FEB2021 8:13)

16.2.7.1 Safety endpoints
16.2.7.1.55 Subgroup analysis by ISS staging at study entry
16.2.7.1.55.1 Treatment emergent adverse event by treatment group according to ISS staging at study entry - Safety population

	I		II		III		
	Kd (N=70)	**IKd (N=89)**	**Kd (N=31)**	**IKd (N=63)**	**Kd (N=20)**	**IKd (N=24)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	68 (97.1)	85 (95.5)	29 (93.5)	62 (98.4)	19 (95.0)	24 (100.0)	0.0209
Number (%) of patients censored	2 (2.9)	4 (4.5)	2 (6.5)	1 (1.6)	1 (5.0)	0 (0.0)	
Kaplan-Meier estimates of TEAE in months							
25% quantile (95% CI)	0.1643 (0.0986 to 0.2300)	0.0986 (0.0657 to 0.0986)	0.2628 (0.0657 to 0.5257)	0.0657 (0.0329 to 0.0986)	0.1971 (0.0329 to 0.3614)	0.0657 (0.0329 to 0.1314)	
Median (95% CI)	0.3614 (0.2300 to 0.5257)	0.2300 (0.1643 to 0.4271)	0.6242 (0.3285 to 1.0185)	0.1314 (0.0986 to 0.1971)	0.4600 (0.1971 to 0.8214)	0.1643 (0.0657 to 0.3943)	
75% quantile (95% CI)	0.6899 (0.5257 to 1.5113)	1.1828 (0.6242 to 2.1355)	1.5113 (0.7885 to 5.8152)	0.3943 (0.2300 to 0.9528)	0.9363 (0.5257 to 2.8912)	0.5421 (0.1971 to 1.1170)	
Comparison vs. Kd							
Log-Rank test p-value[a] vs Kd		0.9572		0.0021		0.1687	
Hazard ratio (95% CI) vs Kd		0.9912 (0.7189 to 1.3668)		2.0078 (1.2766 to 3.1580)		1.5262 (0.8323 to 2.7983)	
P-value		0.9572		0.0026		0.1717	

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
PGM=DEVOPS/SAR650984/EFC15246/CIR_RWE/REPORT/PGM/eff_km_sr_subgrp_sig_s_t.sas OUT=REPORT/OUTPUT/eff_km_de_teae_seiss_s_t_x.rtf (12FEB2021 8:09)

16.2.7.1 Safety endpoints
16.2.7.1.55 Subgroup analysis by ISS staging at study entry
16.2.7.1.55.1 Treatment emergent adverse event by treatment group according to ISS staging at study entry - Safety population

	I		II		III		
	Kd (N=70)	**IKd (N=89)**	**Kd (N=31)**	**IKd (N=63)**	**Kd (N=20)**	**IKd (N=24)**	**p-value of treatment-by-sub group interaction[c]**
Hazard ratio inverted (95% CI) vs IKd			0.4980 (0.3167 to 0.7834)				
probability (95% CI)[b]							
3 Months	0.0714 (0.0264 to 0.1472)	0.1124 (0.0575 to 0.1876)	0.1613 (0.0588 to 0.3088)	0.0317 (0.0060 to 0.0979)	0.0500 (0.0035 to 0.2053)	0.0417 (0.0030 to 0.1759)	
6 Months	0.0286 (0.0054 to 0.0888)	0.0787 (0.0346 to 0.1463)	0.0968 (0.0247 to 0.2291)	0.0159 (0.0013 to 0.0749)	0.0500 (0.0035 to 0.2053)	0.0417 (0.0030 to 0.1759)	
9 Months	0.0286 (0.0054 to 0.0888)	0.0562 (0.0209 to 0.1174)	0.0968 (0.0247 to 0.2291)	0.0159 (0.0013 to 0.0749)	0.0500 (0.0035 to 0.2053)	0.0417 (0.0030 to 0.1759)	
12 Months	0.0286 (0.0054 to 0.0888)	0.0449 (0.0146 to 0.1025)	0.0968 (0.0247 to 0.2291)	0.0159 (0.0013 to 0.0749)	0.0500 (0.0035 to 0.2053)	0.0417 (0.0030 to 0.1759)	
15 Months	0.0286 (0.0054 to 0.0888)	0.0449 (0.0146 to 0.1025)	0.0645 (0.0115 to 0.1862)	0.0159 (0.0013 to 0.0749)	0.0500 (0.0035 to 0.2053)	0.0417 (0.0030 to 0.1759)	
18 Months	0.0286 (0.0054 to 0.0888)	0.0449 (0.0146 to 0.1025)	0.0645 (0.0115 to 0.1862)	0.0159 (0.0013 to 0.0749)	0.0500 (0.0035 to 0.2053)	0.0417 (0.0030 to 0.1759)	
21 Months	0.0286 (0.0054 to 0.0888)	0.0449 (0.0146 to 0.1025)	0.0645 (0.0115 to 0.1862)	0.0159 (0.0013 to 0.0749)	0.0500 (0.0035 to 0.2053)	0.0417 (0.0030 to 0.1759)	
24 Months	0.0286 (0.0054 to 0.0888)	0.0449 (0.0146 to 0.1025)	0.0645 (0.0115 to 0.1862)	0.0159 (0.0013 to 0.0749)	0.0500 (0.0035 to 0.2053)	0.0417 (0.0030 to 0.1759)	

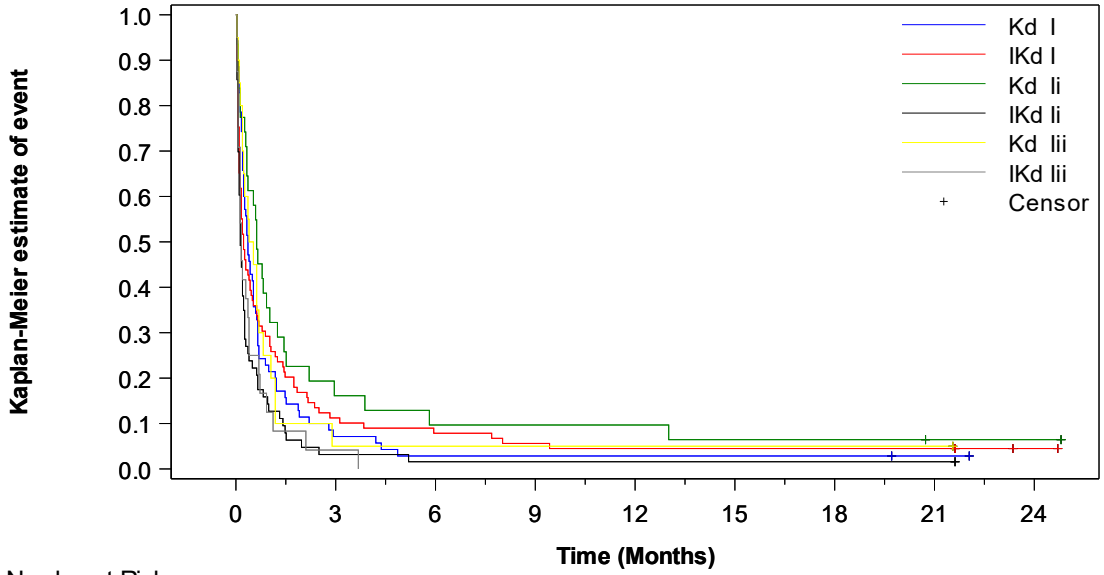
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
PGM=DEVOPS/SAR650984/EFC15246/CIR_RWE/REPORT/PGM/eff_km_sr_subgrp_sig_s_t.sas OUT=REPORT/OUTPUT/eff_km_de_teae_seiss_s_t_x.rtf (12FEB2021 8:09)

16.2.7.1 Safety endpoints
16.2.7.1.55 Subgroup analysis by ISS staging at study entry
16.2.7.1.55.1 Treatment emergent adverse event by treatment group according to ISS staging at study entry - Safety population

	I		II		III		
	Kd (N=70)	**IKd (N=89)**	**Kd (N=31)**	**IKd (N=63)**	**Kd (N=20)**	**IKd (N=24)**	**p-value of treatment-by-sub group interaction[c]**
27 Months	0.0286 (0.0054 to 0.0888)	0.0449 (0.0146 to 0.1025)	0.0645 (0.0115 to 0.1862)	0.0159 (0.0013 to 0.0749)	0.0500 (0.0035 to 0.2053)	0.0417 (0.0030 to 0.1759)	
30 Months	0.0286 (0.0054 to 0.0888)	0.0449 (0.0146 to 0.1025)	0.0645 (0.0115 to 0.1862)	0.0159 (0.0013 to 0.0749)	0.0500 (0.0035 to 0.2053)	0.0417 (0.0030 to 0.1759)	
Number of patients at risk[b]							
3 Months	5	10	5	2	1	1	
6 Months	2	7	3	1	1	0	
9 Months	2	5	3	1	1	0	
12 Months	2	4	3	1	1	0	
15 Months	2	4	2	1	1	0	
18 Months	2	4	2	1	1	0	
21 Months	1	4	1	1	1	0	
24 Months	0	1	1	0	0	0	
27 Months	0	0	0	0	0	0	
30 Months	0	0	0	0	0	0	

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
PGM=DEVOPS/SAR650984/EFC15246/CIR_RWE/REPORT/PGM/eff_km_sr_subgrp_sig_s_t.sas OUT=REPORT/OUTPUT/eff_km_de_teae_seiss_s_t_x.rtf (12FEB2021 8:09)

16.2.7.1 Safety endpoints
16.2.7.1.55 Subgroup analysis by ISS staging at study entry
16.2.7.1.55.2 Kaplan-Meier cumulative incidence curve of treatment emergent adverse event by treatment group according to ISS staging at study entry - Safety population



Number at Risk

Kd I	70	5	2	2	2	2	2	1	0
IKd I	89	10	7	5	4	4	4	4	1
Kd Ii	31	5	3	3	3	2	2	1	1
IKd Ii	63	2	1	1	1	1	1	1	0
Kd Iii	20	1	1	1	1	1	1	1	0
IKd Iii	24	1	0	0	0	0	0	0	0

16.2.7.1 Safety endpoints
16.2.7.1.55 Subgroup analysis by ISS staging at study entry
16.2.7.1.55.3 Treatment emergent serious adverse event by treatment group according to ISS staging at study entry - Safety population

	I		II		III		
	Kd (N=70)	**IKd (N=89)**	**Kd (N=31)**	**IKd (N=63)**	**Kd (N=20)**	**IKd (N=24)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	39 (55.7)	46 (51.7)	16 (51.6)	41 (65.1)	14 (70.0)	18 (75.0)	0.3124
Number (%) of patients censored	31 (44.3)	43 (48.3)	15 (48.4)	22 (34.9)	6 (30.0)	6 (25.0)	
Kaplan-Meier estimates of TEAE in months							
25% quantile (95% CI)	4.9610 (3.3183 to 6.5708)	7.1622 (2.4312 to 9.9548)	5.5852 (1.7413 to 13.6345)	1.9713 (0.4600 to 4.6324)	0.3614 (0.0986 to 4.6324)	0.5914 (0.0657 to 0.7228)	
Median (95% CI)	13.2731 (7.8522 to NC)	18.1027 (12.0575 to NC)	14.0945 (6.5051 to NC)	8.7392 (4.7639 to 14.1273)	12.5832 (0.3614 to 18.0041)	3.3840 (0.6571 to 12.5503)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (14.4559 to NC)	NC (14.6858 to NC)	NC (7.6879 to NC)	
Comparison vs. Kd							
Log-Rank test p-value[a] vs Kd		0.5866		0.1707		0.5134	
Hazard ratio (95% CI) vs Kd		0.8884 (0.5797 to 1.3614)		1.4937 (0.8380 to 2.6625)		1.2654 (0.6238 to 2.5667)	
P-value		0.5868		0.1737		0.5143	

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
PGM=DEVOPS/SAR650984/EFC15246/CIR_RWE/REPORT/PGM/eff_km_sr_subgrp_sig_s_t.sas OUT=REPORT/OUTPUT/eff_km_de_tesae_seiss_s_t_x.rtf (12FEB2021 8:12)

16.2.7.1 Safety endpoints
16.2.7.1.55 Subgroup analysis by ISS staging at study entry
16.2.7.1.55.3 Treatment emergent serious adverse event by treatment group according to ISS staging at study entry - Safety population

	I		II		III		
	Kd (N=70)	**IKd (N=89)**	**Kd (N=31)**	**IKd (N=63)**	**Kd (N=20)**	**IKd (N=24)**	**p-value of treatment-by-sub group interaction[c]**
probability (95% CI)[b]							
3 Months	0.8571 (0.7508 to 0.9205)	0.8315 (0.7361 to 0.8948)	0.8375 (0.6525 to 0.9290)	0.7143 (0.5855 to 0.8093)	0.6500 (0.4030 to 0.8153)	0.5000 (0.2910 to 0.6776)	
6 Months	0.6714 (0.5482 to 0.7680)	0.7753 (0.6737 to 0.8487)	0.7035 (0.5071 to 0.8334)	0.5694 (0.4380 to 0.6811)	0.5500 (0.3134 to 0.7349)	0.4583 (0.2561 to 0.6397)	
9 Months	0.6143 (0.4901 to 0.7168)	0.6966 (0.5897 to 0.7808)	0.6011 (0.4051 to 0.7507)	0.4881 (0.3596 to 0.6047)	0.5500 (0.3134 to 0.7349)	0.4167 (0.2224 to 0.6006)	
12 Months	0.5429 (0.4196 to 0.6507)	0.6180 (0.5088 to 0.7098)	0.6011 (0.4051 to 0.7507)	0.4230 (0.2994 to 0.5413)	0.5000 (0.2713 to 0.6919)	0.3333 (0.1590 to 0.5187)	
15 Months	0.4714 (0.3514 to 0.5823)	0.5471 (0.4374 to 0.6441)	0.4884 (0.2983 to 0.6541)	0.3579 (0.2413 to 0.4759)	0.4444 (0.2245 to 0.6439)	0.2500 (0.1017 to 0.4313)	
18 Months	0.4571 (0.3380 to 0.5684)	0.5092 (0.3997 to 0.6086)	0.4508 (0.2652 to 0.6199)	0.3417 (0.2272 to 0.4592)	0.3241 (0.1310 to 0.5355)	0.2500 (0.1017 to 0.4313)	
21 Months	0.4571 (0.3380 to 0.5684)	0.4965 (0.3872 to 0.5965)	0.4508 (0.2652 to 0.6199)	0.3417 (0.2272 to 0.4592)	0.2593 (0.0876 to 0.4731)	0.2500 (0.1017 to 0.4313)	
24 Months	0.4331 (0.3121 to 0.5480)	0.4655 (0.3555 to 0.5681)	0.4508 (0.2652 to 0.6199)	0.3417 (0.2272 to 0.4592)	0.2593 (0.0876 to 0.4731)	0.2500 (0.1017 to 0.4313)	
27 Months	0.4331 (0.3121 to 0.5480)	0.4655 (0.3555 to 0.5681)	0.4508 (0.2652 to 0.6199)	0.3417 (0.2272 to 0.4592)	0.2593 (0.0876 to 0.4731)	0.2500 (0.1017 to 0.4313)	

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
PGM=DEVOPS/SAR650984/EFC15246/CIR_RWE/REPORT/PGM/eff_km_sr_subgrp_sig_s_t.sas OUT=REPORT/OUTPUT/eff_km_de_tesae_seiss_s_t_x.rtf (12FEB2021 8:12)

16.2.7.1 Safety endpoints
16.2.7.1.55 Subgroup analysis by ISS staging at study entry
16.2.7.1.55.3 Treatment emergent serious adverse event by treatment group according to ISS staging at study entry - Safety population

	I		II		III		
	Kd (N=70)	**IKd (N=89)**	**Kd (N=31)**	**IKd (N=63)**	**Kd (N=20)**	**IKd (N=24)**	**p-value of treatment-by-sub group interaction[c]**
30 Months	0.4331 (0.3121 to 0.5480)	0.4655 (0.3555 to 0.5681)	0.4508 (0.2652 to 0.6199)	0.3417 (0.2272 to 0.4592)	0.2593 (0.0876 to 0.4731)	0.2500 (0.1017 to 0.4313)	
Number of patients at risk[b]							
3 Months	60	74	25	45	13	12	
6 Months	47	69	21	35	11	11	
9 Months	43	62	17	30	11	10	
12 Months	38	55	17	26	10	8	
15 Months	33	44	13	22	8	4	
18 Months	32	40	12	20	5	3	
21 Months	24	33	9	20	3	3	
24 Months	6	13	3	6	0	0	
27 Months	1	1	1	0	0	0	
30 Months	0	0	0	0	0	0	

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
PGM=DEVOPS/SAR650984/EFC15246/CIR_RWE/REPORT/PGM/eff_km_sr_subgrp_sig_s_t.sas OUT=REPORT/OUTPUT/eff_km_de_tesae_seiss_s_t_x.rtf (12FEB2021 8:12)

16.2.7.1 Safety endpoints
16.2.7.1.55 Subgroup analysis by ISS staging at study entry
16.2.7.1.55.4 Treatment emergent adverse event leading to discontinuation of treatment by treatment group according to ISS staging at study entry - Safety population

	I		II		III		
	Kd (N=70)	**IKd (N=89)**	**Kd (N=31)**	**IKd (N=63)**	**Kd (N=20)**	**IKd (N=24)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	6 (8.6)	7 (7.9)	8 (25.8)	6 (9.5)	3 (15.0)	2 (8.3)	0.4258
Number (%) of patients censored	64 (91.4)	82 (92.1)	23 (74.2)	57 (90.5)	17 (85.0)	22 (91.7)	
Kaplan-Meier estimates of TEAE in months							
25% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	15.3758 (5.8480 to NC)	NC (NC to NC)	NC (0.2300 to NC)	NC (0.5585 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Kd							
Log-Rank test p-value[a] vs Kd		0.8816		0.0345		0.4746	
Hazard ratio (95% CI) vs Kd		0.9201 (0.3092 to 2.7382)		0.3365 (0.1166 to 0.9714)		0.5264 (0.0879 to 3.1509)	
P-value		0.8811		0.0441		0.4821	
probability (95% CI)[b]							

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
PGM=DEVOPS/SAR650984/EFC15246/CIR_RWE/REPORT/PGM/eff_km_sr_subgrp_sig_s_t.sas OUT=REPORT/OUTPUT/eff_km_de_tedisc_seiss_s_t_x.rtf (12FEB2021 8:12)

16.2.7.1 Safety endpoints
16.2.7.1.55 Subgroup analysis by ISS staging at study entry
16.2.7.1.55.4 Treatment emergent adverse event leading to discontinuation of treatment by treatment group according to ISS staging at study entry - Safety population

	I		II		III		
	Kd (N=70)	**IKd (N=89)**	**Kd (N=31)**	**IKd (N=63)**	**Kd (N=20)**	**IKd (N=24)**	**p-value of treatment-by-sub group interaction[c]**
3 Months	0.9714 (0.8906 to 0.9928)	0.9774 (0.9126 to 0.9943)	0.9677 (0.7923 to 0.9954)	0.9683 (0.8790 to 0.9920)	0.9000 (0.6560 to 0.9740)	0.9565 (0.7293 to 0.9938)	
6 Months	0.9571 (0.8730 to 0.9860)	0.9547 (0.8837 to 0.9827)	0.9010 (0.7236 to 0.9670)	0.9357 (0.8376 to 0.9754)	0.9000 (0.6560 to 0.9740)	0.9565 (0.7293 to 0.9938)	
9 Months	0.9281 (0.8359 to 0.9694)	0.9433 (0.8691 to 0.9760)	0.7995 (0.6068 to 0.9046)	0.9023 (0.7952 to 0.9549)	0.8357 (0.5680 to 0.9447)	0.9565 (0.7293 to 0.9938)	
12 Months	0.9281 (0.8359 to 0.9694)	0.9433 (0.8691 to 0.9760)	0.7995 (0.6068 to 0.9046)	0.9023 (0.7952 to 0.9549)	0.8357 (0.5680 to 0.9447)	0.9565 (0.7293 to 0.9938)	
15 Months	0.9281 (0.8359 to 0.9694)	0.9314 (0.8535 to 0.9686)	0.7995 (0.6068 to 0.9046)	0.9023 (0.7952 to 0.9549)	0.8357 (0.5680 to 0.9447)	0.9003 (0.6524 to 0.9745)	
18 Months	0.9281 (0.8359 to 0.9694)	0.9314 (0.8535 to 0.9686)	0.7153 (0.5070 to 0.8477)	0.9023 (0.7952 to 0.9549)	0.8357 (0.5680 to 0.9447)	0.9003 (0.6524 to 0.9745)	
21 Months	0.9129 (0.8163 to 0.9599)	0.9179 (0.8351 to 0.9601)	0.7153 (0.5070 to 0.8477)	0.9023 (0.7952 to 0.9549)	0.8357 (0.5680 to 0.9447)	0.9003 (0.6524 to 0.9745)	
24 Months	0.9129 (0.8163 to 0.9599)	0.9179 (0.8351 to 0.9601)	0.7153 (0.5070 to 0.8477)	0.9023 (0.7952 to 0.9549)	0.8357 (0.5680 to 0.9447)	0.9003 (0.6524 to 0.9745)	
27 Months	0.9129 (0.8163 to 0.9599)	0.9179 (0.8351 to 0.9601)	0.7153 (0.5070 to 0.8477)	0.9023 (0.7952 to 0.9549)	0.8357 (0.5680 to 0.9447)	0.9003 (0.6524 to 0.9745)	
30 Months	0.9129 (0.8163 to 0.9599)	0.9179 (0.8351 to 0.9601)	0.7153 (0.5070 to 0.8477)	0.9023 (0.7952 to 0.9549)	0.8357 (0.5680 to 0.9447)	0.9003 (0.6524 to 0.9745)	

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
PGM=DEVOPS/SAR650984/EFC15246/CIR_RWE/REPORT/PGM/eff_km_sr_subgrp_sig_s_t.sas OUT=REPORT/OUTPUT/eff_km_de_tedisc_seiss_s_t_x.rtf (12FEB2021 8:12)

16.2.7.1 Safety endpoints
16.2.7.1.55 Subgroup analysis by ISS staging at study entry
16.2.7.1.55.4 Treatment emergent adverse event leading to discontinuation of treatment by treatment group according to ISS staging at study entry - Safety population

	I		II		III		
	Kd (N=70)	**IKd (N=89)**	**Kd (N=31)**	**IKd (N=63)**	**Kd (N=20)**	**IKd (N=24)**	**p-value of treatment-by-sub group interaction[c]**
Number of patients at risk[b]							
3 Months	68	86	29	61	17	22	
6 Months	66	84	27	56	14	20	
9 Months	63	82	22	54	13	18	
12 Months	62	80	21	54	13	17	
15 Months	61	74	19	52	11	13	
18 Months	61	70	17	51	10	11	
21 Months	48	62	16	46	8	9	
24 Months	17	22	7	17	2	1	
27 Months	3	2	1	0	0	0	
30 Months	0	0	0	0	0	0	

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
PGM=DEVOPS/SAR650984/EFC15246/CIR_RWE/REPORT/PGM/eff_km_sr_subgrp_sig_s_t.sas OUT=REPORT/OUTPUT/eff_km_de_tedisc_seiss_s_t_x.rtf (12FEB2021 8:12)

16.2.7.1 Safety endpoints
16.2.7.1.55 Subgroup analysis by ISS staging at study entry
16.2.7.1.55.5 Treatment emergent mild adverse event by treatment group according to ISS staging at study entry - Safety population

	I		II		III		
	Kd (N=70)	**IKd (N=89)**	**Kd (N=31)**	**IKd (N=63)**	**Kd (N=20)**	**IKd (N=24)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	68 (97.1)	83 (93.3)	28 (90.3)	62 (98.4)	18 (90.0)	21 (87.5)	0.0059
Number (%) of patients censored	2 (2.9)	6 (6.7)	3 (9.7)	1 (1.6)	2 (10.0)	3 (12.5)	
Kaplan-Meier estimates of TEAE in months							
25% quantile (95% CI)	0.1643 (0.0986 to 0.2300)	0.0986 (0.0657 to 0.1314)	0.2957 (0.0657 to 0.5914)	0.0657 (0.0329 to 0.0986)	0.1971 (0.0329 to 0.5257)	0.0657 (0.0329 to 0.1314)	
Median (95% CI)	0.3614 (0.2300 to 0.5257)	0.2300 (0.1643 to 0.4600)	0.6571 (0.3614 to 1.4456)	0.1314 (0.0986 to 0.2300)	0.5914 (0.1971 to 0.8214)	0.1643 (0.0657 to 1.1170)	
75% quantile (95% CI)	0.8871 (0.6242 to 1.8727)	1.4456 (0.6571 to 2.3655)	2.2012 (0.9199 to 13.0103)	0.3943 (0.2300 to 0.9528)	1.0513 (0.6242 to 2.8912)	2.1027 (0.2957 to 8.4107)	
Comparison vs. Kd							
Log-Rank test p-value[a] vs Kd		0.7707		0.0004		0.8310	
Hazard ratio (95% CI) vs Kd		0.9530 (0.6899 to 1.3164)		2.2505 (1.4177 to 3.5724)		1.0722 (0.5645 to 2.0368)	
P-value		0.7701		0.0006		0.8313	

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
PGM=DEVOPS/SAR650984/EFC15246/CIR_RWE/REPORT/PGM/eff_km_sr_subgrp_sig_s_t.sas OUT=REPORT/OUTPUT/eff_km_de_tesev12_seiss_s_t_x.rtf (12FEB2021 8:13)

16.2.7.1 Safety endpoints
16.2.7.1.55 Subgroup analysis by ISS staging at study entry
16.2.7.1.55.5 Treatment emergent mild adverse event by treatment group according to ISS staging at study entry - Safety population

	I		II		III		
	Kd (N=70)	**IKd (N=89)**	**Kd (N=31)**	**IKd (N=63)**	**Kd (N=20)**	**IKd (N=24)**	**p-value of treatment-by-sub group interaction[c]**
Hazard ratio inverted (95% CI) vs IKd			0.4444 (0.2799 to 0.7054)				
probability (95% CI)[b]							
3 Months	0.0714 (0.0264 to 0.1472)	0.1348 (0.0739 to 0.2142)	0.2258 (0.0997 to 0.3828)	0.0317 (0.0060 to 0.0979)	0.0550 (0.0037 to 0.2218)	0.2381 (0.0912 to 0.4231)	
6 Months	0.0429 (0.0114 to 0.1090)	0.1011 (0.0497 to 0.1740)	0.1290 (0.0407 to 0.2698)	0.0159 (0.0013 to 0.0749)	0.0550 (0.0037 to 0.2218)	0.1190 (0.0227 to 0.3021)	
9 Months	0.0429 (0.0114 to 0.1090)	0.0787 (0.0346 to 0.1463)	0.1290 (0.0407 to 0.2698)	0.0159 (0.0013 to 0.0749)	0.0550 (0.0037 to 0.2218)	0.1190 (0.0227 to 0.3021)	
12 Months	0.0429 (0.0114 to 0.1090)	0.0674 (0.0276 to 0.1320)	0.1290 (0.0407 to 0.2698)	0.0159 (0.0013 to 0.0749)	0.0550 (0.0037 to 0.2218)	0.1190 (0.0227 to 0.3021)	
15 Months	0.0286 (0.0054 to 0.0888)	0.0674 (0.0276 to 0.1320)	0.0860 (0.0178 to 0.2243)	0.0159 (0.0013 to 0.0749)	0.0550 (0.0037 to 0.2218)	0.1190 (0.0227 to 0.3021)	
18 Months	0.0286 (0.0054 to 0.0888)	0.0674 (0.0276 to 0.1320)	0.0860 (0.0178 to 0.2243)	0.0159 (0.0013 to 0.0749)	0.0550 (0.0037 to 0.2218)	0.1190 (0.0227 to 0.3021)	
21 Months	0.0286 (0.0054 to 0.0888)	0.0674 (0.0276 to 0.1320)	0.0860 (0.0178 to 0.2243)	0.0159 (0.0013 to 0.0749)	0.0550 (0.0037 to 0.2218)	0.1190 (0.0227 to 0.3021)	
24 Months	0.0286 (0.0054 to 0.0888)	0.0674 (0.0276 to 0.1320)	0.0860 (0.0178 to 0.2243)	0.0159 (0.0013 to 0.0749)	0.0550 (0.0037 to 0.2218)	0.1190 (0.0227 to 0.3021)	

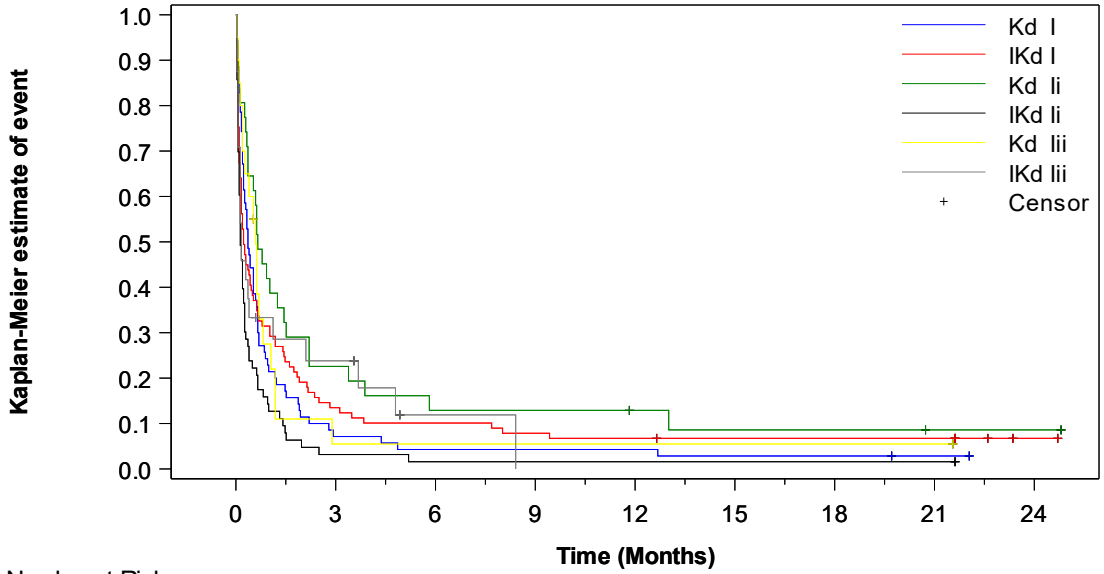
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
PGM=DEVOPS/SAR650984/EFC15246/CIR_RWE/REPORT/PGM/eff_km_sr_subgrp_sig_s_t.sas OUT=REPORT/OUTPUT/eff_km_de_tesev12_seiss_s_t_x.rtf (12FEB2021 8:13)

16.2.7.1 Safety endpoints
16.2.7.1.55 Subgroup analysis by ISS staging at study entry
16.2.7.1.55.5 Treatment emergent mild adverse event by treatment group according to ISS staging at study entry - Safety population

	I		II		III		
	Kd (N=70)	**IKd (N=89)**	**Kd (N=31)**	**IKd (N=63)**	**Kd (N=20)**	**IKd (N=24)**	**p-value of treatment-by-sub group interaction[c]**
27 Months	0.0286 (0.0054 to 0.0888)	0.0674 (0.0276 to 0.1320)	0.0860 (0.0178 to 0.2243)	0.0159 (0.0013 to 0.0749)	0.0550 (0.0037 to 0.2218)	0.1190 (0.0227 to 0.3021)	
30 Months	0.0286 (0.0054 to 0.0888)	0.0674 (0.0276 to 0.1320)	0.0860 (0.0178 to 0.2243)	0.0159 (0.0013 to 0.0749)	0.0550 (0.0037 to 0.2218)	0.1190 (0.0227 to 0.3021)	
Number of patients at risk[b]							
3 Months	5	12	7	2	1	5	
6 Months	3	9	4	1	1	1	
9 Months	3	7	4	1	1	0	
12 Months	3	6	3	1	1	0	
15 Months	2	5	2	1	1	0	
18 Months	2	5	2	1	1	0	
21 Months	1	5	1	1	1	0	
24 Months	0	1	1	0	0	0	
27 Months	0	0	0	0	0	0	
30 Months	0	0	0	0	0	0	

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
PGM=DEVOPS/SAR650984/EFC15246/CIR_RWE/REPORT/PGM/eff_km_sr_subgrp_sig_s_t.sas OUT=REPORT/OUTPUT/eff_km_de_tesev12_seiss_s_t_x.rtf (12FEB2021 8:13)

16.2.7.1 Safety endpoints
16.2.7.1.55 Subgroup analysis by ISS staging at study entry
16.2.7.1.55.6 Kaplan-Meier cumulative incidence curve of treatment emergent mild adverse event by treatment group according to ISS staging at study entry - Safety population



Number at Risk

Kd I	70	5	3	3	3	2	2	1	0
IKd I	89	12	9	7	6	5	5	5	1
Kd Ii	31	7	4	4	3	2	2	1	1
IKd Ii	63	2	1	1	1	1	1	1	0
Kd Iii	20	1	1	1	1	1	1	1	0
IKd Iii	24	5	1	0	0	0	0	0	0

16.2.7.1 Safety endpoints
16.2.7.1.55 Subgroup analysis by ISS staging at study entry
16.2.7.1.55.7 Treatment emergent severe adverse event by treatment group according to ISS staging at study entry - Safety population

	I		II		III		
	Kd (N=70)	**IKd (N=89)**	**Kd (N=31)**	**IKd (N=63)**	**Kd (N=20)**	**IKd (N=24)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	45 (64.3)	63 (70.8)	22 (71.0)	52 (82.5)	13 (65.0)	19 (79.2)	0.8425
Number (%) of patients censored	25 (35.7)	26 (29.2)	9 (29.0)	11 (17.5)	7 (35.0)	5 (20.8)	
Kaplan-Meier estimates of TEAE in months							
25% quantile (95% CI)	2.3984 (1.2156 to 4.2053)	1.8398 (0.8542 to 4.4682)	1.9055 (0.4928 to 5.0267)	0.8214 (0.2957 to 2.5955)	0.4764 (0.0986 to 4.0411)	0.6571 (0.0657 to 1.3142)	
Median (95% CI)	7.6386 (4.5667 to 15.6057)	7.7864 (5.5852 to 10.6776)	6.0452 (2.9569 to 13.6345)	4.7639 (2.7926 to 6.5051)	6.2752 (0.3614 to NC)	1.9713 (0.6899 to 7.7536)	
75% quantile (95% CI)	NC (21.7823 to NC)	NC (13.2402 to NC)	15.9343 (7.8522 to NC)	11.5318 (7.6550 to NC)	NC (7.5236 to NC)	11.4333 (3.7454 to NC)	
Comparison vs. Kd							
Log-Rank test p-value[a] vs Kd		0.4038		0.2591		0.4708	
Hazard ratio (95% CI) vs Kd		1.1771 (0.8024 to 1.7268)		1.3313 (0.8085 to 2.1923)		1.2960 (0.6393 to 2.6275)	
P-value		0.4043		0.2608		0.4721	

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.55 Subgroup analysis by ISS staging at study entry
16.2.7.1.55.7 Treatment emergent severe adverse event by treatment group according to ISS staging at study entry - Safety population

	I		II		III		
	Kd (N=70)	**IKd (N=89)**	**Kd (N=31)**	**IKd (N=63)**	**Kd (N=20)**	**IKd (N=24)**	**p-value of treatment-by-sub group interaction[c]**
probability (95% CI)[b]							
3 Months	0.7429 (0.6234 to 0.8295)	0.7073 (0.6008 to 0.7904)	0.6745 (0.4792 to 0.8099)	0.6032 (0.4717 to 0.7116)	0.5958 (0.3514 to 0.7739)	0.4838 (0.2731 to 0.6662)	
6 Months	0.5571 (0.4335 to 0.6641)	0.5590 (0.4494 to 0.6552)	0.5059 (0.3186 to 0.6663)	0.3968 (0.2767 to 0.5143)	0.5417 (0.3027 to 0.7301)	0.3958 (0.2021 to 0.5844)	
9 Months	0.4857 (0.3648 to 0.5962)	0.4564 (0.3503 to 0.5562)	0.3995 (0.2259 to 0.5678)	0.3175 (0.2074 to 0.4331)	0.3792 (0.1726 to 0.5855)	0.3079 (0.1374 to 0.4969)	
12 Months	0.4429 (0.3248 to 0.5544)	0.3537 (0.2556 to 0.4530)	0.3632 (0.1962 to 0.5327)	0.2381 (0.1419 to 0.3482)	0.3250 (0.1346 to 0.5327)	0.2199 (0.0803 to 0.4028)	
15 Months	0.4000 (0.2856 to 0.5117)	0.3152 (0.2205 to 0.4141)	0.2825 (0.1322 to 0.4539)	0.2063 (0.1171 to 0.3131)	0.3250 (0.1346 to 0.5327)	0.1759 (0.0552 to 0.3527)	
18 Months	0.3714 (0.2600 to 0.4828)	0.2758 (0.1854 to 0.3736)	0.2421 (0.1033 to 0.4122)	0.1876 (0.1021 to 0.2931)	0.3250 (0.1346 to 0.5327)	0.1759 (0.0552 to 0.3527)	
21 Months	0.3714 (0.2600 to 0.4828)	0.2758 (0.1854 to 0.3736)	0.2421 (0.1033 to 0.4122)	0.1688 (0.0876 to 0.2727)	0.3250 (0.1346 to 0.5327)	0.1759 (0.0552 to 0.3527)	
24 Months	0.3482 (0.2364 to 0.4623)	0.2758 (0.1854 to 0.3736)	0.2421 (0.1033 to 0.4122)	0.1688 (0.0876 to 0.2727)	0.3250 (0.1346 to 0.5327)	0.1759 (0.0552 to 0.3527)	
27 Months	0.3482 (0.2364 to 0.4623)	0.2758 (0.1854 to 0.3736)	0.2421 (0.1033 to 0.4122)	0.1688 (0.0876 to 0.2727)	0.3250 (0.1346 to 0.5327)	0.1759 (0.0552 to 0.3527)	

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.55 Subgroup analysis by ISS staging at study entry
16.2.7.1.55.7 Treatment emergent severe adverse event by treatment group according to ISS staging at study entry - Safety population

	I		II		III		
	Kd (N=70)	**IKd (N=89)**	**Kd (N=31)**	**IKd (N=63)**	**Kd (N=20)**	**IKd (N=24)**	**p-value of treatment-by-sub group interaction[c]**
30 Months	0.3482 (0.2364 to 0.4623)	0.2758 (0.1854 to 0.3736)	0.2421 (0.1033 to 0.4122)	0.1688 (0.0876 to 0.2727)	0.3250 (0.1346 to 0.5327)	0.1759 (0.0552 to 0.3527)	
Number of patients at risk[b]							
3 Months	52	62	20	38	11	11	
6 Months	39	49	15	25	10	9	
9 Months	34	40	11	20	7	7	
12 Months	31	31	10	15	6	5	
15 Months	28	24	7	12	6	2	
18 Months	26	21	6	10	5	1	
21 Months	19	20	4	9	4	1	
24 Months	7	7	1	3	0	0	
27 Months	1	0	0	0	0	0	
30 Months	0	0	0	0	0	0	

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.55 Subgroup analysis by ISS staging at study entry
16.2.7.1.55.8 Treatment emergent severe adverse event including death by treatment group according to ISS staging at study entry - Safety population

	I		II		III		
	Kd (N=70)	**IKd (N=89)**	**Kd (N=31)**	**IKd (N=63)**	**Kd (N=20)**	**IKd (N=24)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	45 (64.3)	63 (70.8)	22 (71.0)	52 (82.5)	14 (70.0)	21 (87.5)	0.8079
Number (%) of patients censored	25 (35.7)	26 (29.2)	9 (29.0)	11 (17.5)	6 (30.0)	3 (12.5)	
Kaplan-Meier estimates of TEAE in months							
25% quantile (95% CI)	2.3984 (1.2156 to 4.2053)	1.8398 (0.8542 to 4.4682)	1.9055 (0.4928 to 5.0267)	0.8214 (0.2957 to 2.5955)	0.4764 (0.0986 to 1.0513)	0.5421 (0.0657 to 0.7228)	
Median (95% CI)	7.6386 (4.5667 to 15.6057)	7.7864 (5.5852 to 10.6776)	6.0452 (2.9569 to 13.6345)	4.7639 (2.7926 to 6.5051)	5.1581 (0.3614 to NC)	1.9548 (0.6571 to 7.7536)	
75% quantile (95% CI)	NC (21.7823 to NC)	NC (13.2402 to NC)	15.9343 (7.8522 to NC)	11.5318 (7.6550 to NC)	NC (6.2752 to NC)	11.3511 (3.7454 to NC)	
Comparison vs. Kd							
Log-Rank test p-value[a] vs Kd		0.4038		0.2591		0.3858	
Hazard ratio (95% CI) vs Kd		1.1771 (0.8024 to 1.7268)		1.3313 (0.8085 to 2.1923)		1.3484 (0.6845 to 2.6565)	
P-value		0.4043		0.2608		0.3875	

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
PGM=DEVOPS/SAR650984/EFC15246/CIR_RWE/REPORT/PGM/eff_km_sr_subgrp_sig_s_t.sas OUT=REPORT/OUTPUT/eff_km_de_tesev345_seiss_s_t_x.rtf (12FEB2021 8:13)

16.2.7.1 Safety endpoints
16.2.7.1.55 Subgroup analysis by ISS staging at study entry
16.2.7.1.55.8 Treatment emergent severe adverse event including death by treatment group according to ISS staging at study entry - Safety population

	I		II		III		
	Kd (N=70)	**IKd (N=89)**	**Kd (N=31)**	**IKd (N=63)**	**Kd (N=20)**	**IKd (N=24)**	**p-value of treatment-by-sub group interaction[c]**
probability (95% CI)[b]							
3 Months	0.7429 (0.6234 to 0.8295)	0.7073 (0.6008 to 0.7904)	0.6745 (0.4792 to 0.8099)	0.6032 (0.4717 to 0.7116)	0.5500 (0.3134 to 0.7349)	0.4583 (0.2561 to 0.6397)	
6 Months	0.5571 (0.4335 to 0.6641)	0.5590 (0.4494 to 0.6552)	0.5059 (0.3186 to 0.6663)	0.3968 (0.2767 to 0.5143)	0.5000 (0.2713 to 0.6919)	0.3750 (0.1900 to 0.5603)	
9 Months	0.4857 (0.3648 to 0.5962)	0.4564 (0.3503 to 0.5562)	0.3995 (0.2259 to 0.5678)	0.3175 (0.2074 to 0.4331)	0.3500 (0.1566 to 0.5519)	0.2917 (0.1295 to 0.4758)	
12 Months	0.4429 (0.3248 to 0.5544)	0.3537 (0.2556 to 0.4530)	0.3632 (0.1962 to 0.5327)	0.2381 (0.1419 to 0.3482)	0.3000 (0.1225 to 0.5014)	0.2083 (0.0759 to 0.3852)	
15 Months	0.4000 (0.2856 to 0.5117)	0.3152 (0.2205 to 0.4141)	0.2825 (0.1322 to 0.4539)	0.2063 (0.1171 to 0.3131)	0.3000 (0.1225 to 0.5014)	0.1250 (0.0314 to 0.2865)	
18 Months	0.3714 (0.2600 to 0.4828)	0.2758 (0.1854 to 0.3736)	0.2421 (0.1033 to 0.4122)	0.1876 (0.1021 to 0.2931)	0.3000 (0.1225 to 0.5014)	0.1250 (0.0314 to 0.2865)	
21 Months	0.3714 (0.2600 to 0.4828)	0.2758 (0.1854 to 0.3736)	0.2421 (0.1033 to 0.4122)	0.1688 (0.0876 to 0.2727)	0.3000 (0.1225 to 0.5014)	0.1250 (0.0314 to 0.2865)	
24 Months	0.3482 (0.2364 to 0.4623)	0.2758 (0.1854 to 0.3736)	0.2421 (0.1033 to 0.4122)	0.1688 (0.0876 to 0.2727)	0.3000 (0.1225 to 0.5014)	0.1250 (0.0314 to 0.2865)	
27 Months	0.3482 (0.2364 to 0.4623)	0.2758 (0.1854 to 0.3736)	0.2421 (0.1033 to 0.4122)	0.1688 (0.0876 to 0.2727)	0.3000 (0.1225 to 0.5014)	0.1250 (0.0314 to 0.2865)	

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
PGM=DEVOPS/SAR650984/EFC15246/CIR_RWE/REPORT/PGM/eff_km_sr_subgrp_sig_s_t.sas OUT=REPORT/OUTPUT/eff_km_de_tesev345_seiss_s_t_x.rtf (12FEB2021 8:13)

16.2.7.1 Safety endpoints
16.2.7.1.55 Subgroup analysis by ISS staging at study entry
16.2.7.1.55.8 Treatment emergent severe adverse event including death by treatment group according to ISS staging at study entry - Safety population

	I		II		III		
	Kd (N=70)	**IKd (N=89)**	**Kd (N=31)**	**IKd (N=63)**	**Kd (N=20)**	**IKd (N=24)**	**p-value of treatment-by-sub group interaction[c]**
30 Months	0.3482 (0.2364 to 0.4623)	0.2758 (0.1854 to 0.3736)	0.2421 (0.1033 to 0.4122)	0.1688 (0.0876 to 0.2727)	0.3000 (0.1225 to 0.5014)	0.1250 (0.0314 to 0.2865)	
Number of patients at risk[b]							
3 Months	52	62	20	38	11	11	
6 Months	39	49	15	25	10	9	
9 Months	34	40	11	20	7	7	
12 Months	31	31	10	15	6	5	
15 Months	28	24	7	12	6	2	
18 Months	26	21	6	10	5	1	
21 Months	19	20	4	9	4	1	
24 Months	7	7	1	3	0	0	
27 Months	1	0	0	0	0	0	
30 Months	0	0	0	0	0	0	

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
PGM=DEVOPS/SAR650984/EFC15246/CIR_RWE/REPORT/PGM/eff_km_sr_subgrp_sig_s_t.sas OUT=REPORT/OUTPUT/eff_km_de_tesev345_seiss_s_t_x.rtf (12FEB2021 8:13)

16.2.7.1 Safety endpoints
16.2.7.1.56 Subgroup analysis by R-ISS staging
16.2.7.1.56.1 Treatment emergent adverse event by treatment group according to R-ISS staging - Safety population

	I or II		III		Not classified		
	Kd (N=102)	**IKd (N=155)**	**Kd (N=8)**	**IKd (N=15)**	**Kd (N=12)**	**IKd (N=7)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	99 (97.1)	150 (96.8)	7 (87.5)	15 (100.0)	11 (91.7)	7 (100.0)	0.6821
Number (%) of patients censored	3 (2.9)	5 (3.2)	1 (12.5)	0 (0.0)	1 (8.3)	0 (0.0)	
Kaplan-Meier estimates of TEAE in months							
25% quantile (95% CI)	0.1971 (0.1314 to 0.2300)	0.0657 (0.0657 to 0.0986)	0.1478 (0.0657 to 0.6242)	0.0657 (0.0329 to 0.1314)	0.1807 (0.0329 to 0.2957)	0.0657 (0.0657 to 0.2300)	
Median (95% CI)	0.5092 (0.3285 to 0.6242)	0.1971 (0.1314 to 0.2628)	0.5092 (0.0657 to 0.8214)	0.1643 (0.0329 to 0.3614)	0.3285 (0.0329 to 1.1828)	0.2300 (0.0657 to 0.4600)	
75% quantile (95% CI)	1.0513 (0.6899 to 1.5113)	0.8214 (0.4928 to 1.3142)	0.7228 (0.1971 to NC)	0.3943 (0.1643 to 3.6797)	0.8542 (0.2957 to NC)	0.4600 (0.1643 to 2.8255)	
Comparison vs. Kd							
Log-Rank test p-value[a] vs Kd		0.0719		0.2287		0.5474	
Hazard ratio (95% CI) vs Kd		1.2627 (0.9789 to 1.6289)		1.7330 (0.7003 to 4.2887)		1.3415 (0.5136 to 3.5039)	
P-value		0.0726		0.2343		0.5487	

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
PGM=DEVOPS/SAR650984/EFC15246/CIR_RWE/REPORT/PGM/eff_km_sr_subgrp_sig_s_t.sas OUT=REPORT/OUTPUT/eff_km_de_teae_seriss_s_t_x.rtf (12FEB2021 8:09)

16.2.7.1 Safety endpoints
16.2.7.1.56 Subgroup analysis by R-ISS staging
16.2.7.1.56.1 Treatment emergent adverse event by treatment group according to R-ISS staging - Safety population

	I or II		III		Not classified		
	Kd (N=102)	**IKd (N=155)**	**Kd (N=8)**	**IKd (N=15)**	**Kd (N=12)**	**IKd (N=7)**	**p-value of treatment-by-sub group interaction[c]**
probability (95% CI)[b]							
3 Months	0.0882 (0.0433 to 0.1530)	0.0774 (0.0423 to 0.1263)	0.1250 (0.0066 to 0.4227)	0.0667 (0.0043 to 0.2603)	0.0833 (0.0051 to 0.3111)	0.1429 (0.0071 to 0.4649)	
6 Months	0.0392 (0.0128 to 0.0900)	0.0516 (0.0242 to 0.0944)	0.1250 (0.0066 to 0.4227)	0.0667 (0.0043 to 0.2603)	0.0833 (0.0051 to 0.3111)	0.1429 (0.0071 to 0.4649)	
9 Months	0.0392 (0.0128 to 0.0900)	0.0387 (0.0159 to 0.0777)	0.1250 (0.0066 to 0.4227)	0.0667 (0.0043 to 0.2603)	0.0833 (0.0051 to 0.3111)	0.1429 (0.0071 to 0.4649)	
12 Months	0.0392 (0.0128 to 0.0900)	0.0323 (0.0121 to 0.0692)	0.1250 (0.0066 to 0.4227)	0.0667 (0.0043 to 0.2603)	0.0833 (0.0051 to 0.3111)	0.1429 (0.0071 to 0.4649)	
15 Months	0.0294 (0.0079 to 0.0765)	0.0323 (0.0121 to 0.0692)	0.1250 (0.0066 to 0.4227)	0.0667 (0.0043 to 0.2603)	0.0833 (0.0051 to 0.3111)	0.1429 (0.0071 to 0.4649)	
18 Months	0.0294 (0.0079 to 0.0765)	0.0323 (0.0121 to 0.0692)	0.1250 (0.0066 to 0.4227)	0.0667 (0.0043 to 0.2603)	0.0833 (0.0051 to 0.3111)	0.1429 (0.0071 to 0.4649)	
21 Months	0.0294 (0.0079 to 0.0765)	0.0323 (0.0121 to 0.0692)	0.1250 (0.0066 to 0.4227)	0.0667 (0.0043 to 0.2603)	0.0833 (0.0051 to 0.3111)	0.1429 (0.0071 to 0.4649)	
24 Months	0.0294 (0.0079 to 0.0765)	0.0323 (0.0121 to 0.0692)	0.1250 (0.0066 to 0.4227)	0.0667 (0.0043 to 0.2603)	0.0833 (0.0051 to 0.3111)	0.1429 (0.0071 to 0.4649)	
27 Months	0.0294 (0.0079 to 0.0765)	0.0323 (0.0121 to 0.0692)	0.1250 (0.0066 to 0.4227)	0.0667 (0.0043 to 0.2603)	0.0833 (0.0051 to 0.3111)	0.1429 (0.0071 to 0.4649)	

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
PGM=DEVOPS/SAR650984/EFC15246/CIR_RWE/REPORT/PGM/eff_km_sr_subgrp_sig_s_t.sas OUT=REPORT/OUTPUT/eff_km_de_teae_seriss_s_t_x.rtf (12FEB2021 8:09)

16.2.7.1 Safety endpoints
16.2.7.1.56 Subgroup analysis by R-ISS staging
16.2.7.1.56.1 Treatment emergent adverse event by treatment group according to R-ISS staging - Safety population

	I or II		III		Not classified		
	Kd (N=102)	**IKd (N=155)**	**Kd (N=8)**	**IKd (N=15)**	**Kd (N=12)**	**IKd (N=7)**	**p-value of treatment-by-sub group interaction[c]**
30 Months	0.0294 (0.0079 to 0.0765)	0.0323 (0.0121 to 0.0692)	0.1250 (0.0066 to 0.4227)	0.0667 (0.0043 to 0.2603)	0.0833 (0.0051 to 0.3111)	0.1429 (0.0071 to 0.4649)	
Number of patients at risk[b]							
3 Months	9	12	1	1	1	0	
6 Months	4	8	1	0	1	0	
9 Months	4	6	1	0	1	0	
12 Months	4	5	1	0	1	0	
15 Months	3	5	1	0	1	0	
18 Months	3	5	1	0	1	0	
21 Months	1	5	1	0	1	0	
24 Months	1	1	0	0	0	0	
27 Months	0	0	0	0	0	0	
30 Months	0	0	0	0	0	0	

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
PGM=DEVOPS/SAR650984/EFC15246/CIR_RWE/REPORT/PGM/eff_km_sr_subgrp_sig_s_t.sas OUT=REPORT/OUTPUT/eff_km_de_teae_seriss_s_t_x.rtf (12FEB2021 8:09)

16.2.7.1 Safety endpoints
16.2.7.1.56 Subgroup analysis by R-ISS staging
16.2.7.1.56.2 Treatment emergent serious adverse event by treatment group according to R-ISS staging - Safety population

	I or II		III		Not classified		
	Kd (N=102)	**IKd (N=155)**	**Kd (N=8)**	**IKd (N=15)**	**Kd (N=12)**	**IKd (N=7)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	59 (57.8)	90 (58.1)	6 (75.0)	11 (73.3)	5 (41.7)	4 (57.1)	0.6536
Number (%) of patients censored	43 (42.2)	65 (41.9)	2 (25.0)	4 (26.7)	7 (58.3)	3 (42.9)	
Kaplan-Meier estimates of TEAE in months							
25% quantile (95% CI)	4.0739 (2.1027 to 5.5852)	3.8439 (1.7413 to 6.5051)	0.6735 (0.0986 to 10.4805)	0.4271 (0.0657 to 0.7228)	7.7700 (5.5524 to NC)	0.6571 (0.2300 to 12.5503)	
Median (95% CI)	13.8316 (7.7864 to 21.7823)	12.9446 (9.6263 to 21.0924)	7.5565 (0.0986 to NC)	1.3142 (0.3943 to 12.5503)	NC (6.2752 to NC)	12.5503 (0.2300 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (0.9856 to NC)	NC (1.3142 to NC)	NC (NC to NC)	NC (9.9548 to NC)	
Comparison vs. Kd							
Log-Rank test p-value[a] vs Kd		0.9550		0.7349		0.5176	
Hazard ratio (95% CI) vs Kd		1.0095 (0.7269 to 1.4020)		1.1890 (0.4359 to 3.2437)		1.5397 (0.4125 to 5.7472)	
P-value		0.9550		0.7352		0.5208	

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
PGM=DEVOPS/SAR650984/EFC15246/CIR_RWE/REPORT/PGM/eff_km_sr_subgrp_sig_s_t.sas OUT=REPORT/OUTPUT/eff_km_de_tesae_seriss_s_t_x.rtf (12FEB2021 8:12)

16.2.7.1 Safety endpoints
16.2.7.1.56 Subgroup analysis by R-ISS staging
16.2.7.1.56.2 Treatment emergent serious adverse event by treatment group according to R-ISS staging - Safety population

	I or II		III		Not classified		
	Kd (N=102)	**IKd (N=155)**	**Kd (N=8)**	**IKd (N=15)**	**Kd (N=12)**	**IKd (N=7)**	**p-value of treatment-by-sub group interaction[c]**
probability (95% CI)[b]							
3 Months	0.8135 (0.7233 to 0.8767)	0.7806 (0.7069 to 0.8380)	0.6250 (0.2293 to 0.8607)	0.4000 (0.1649 to 0.6276)	1.0000 (1.0000 to 1.0000)	0.7143 (0.2582 to 0.9198)	
6 Months	0.6448 (0.5434 to 0.7294)	0.6899 (0.6105 to 0.7563)	0.5000 (0.1520 to 0.7749)	0.3333 (0.1215 to 0.5640)	0.9167 (0.5390 to 0.9878)	0.7143 (0.2582 to 0.9198)	
9 Months	0.5951 (0.4928 to 0.6833)	0.6053 (0.5236 to 0.6773)	0.5000 (0.1520 to 0.7749)	0.3333 (0.1215 to 0.5640)	0.6667 (0.3370 to 0.8597)	0.7143 (0.2582 to 0.9198)	
12 Months	0.5446 (0.4425 to 0.6358)	0.5272 (0.4455 to 0.6023)	0.3750 (0.0870 to 0.6744)	0.3333 (0.1215 to 0.5640)	0.6667 (0.3370 to 0.8597)	0.5714 (0.1719 to 0.8371)	
15 Months	0.4720 (0.3715 to 0.5660)	0.4597 (0.3793 to 0.5364)	0.2500 (0.0371 to 0.5581)	0.2667 (0.0826 to 0.4963)	0.5833 (0.2701 to 0.8009)	0.4286 (0.0978 to 0.7344)	
18 Months	0.4296 (0.3309 to 0.5243)	0.4318 (0.3521 to 0.5088)	0.2500 (0.0371 to 0.5581)	0.2667 (0.0826 to 0.4963)	0.5833 (0.2701 to 0.8009)	0.4286 (0.0978 to 0.7344)	
21 Months	0.4188 (0.3207 to 0.5137)	0.4247 (0.3452 to 0.5018)	0.2500 (0.0371 to 0.5581)	0.2667 (0.0826 to 0.4963)	0.5833 (0.2701 to 0.8009)	0.4286 (0.0978 to 0.7344)	
24 Months	0.4014 (0.3022 to 0.4984)	0.4086 (0.3295 to 0.4861)	0.2500 (0.0371 to 0.5581)	0.2667 (0.0826 to 0.4963)	0.5833 (0.2701 to 0.8009)	0.4286 (0.0978 to 0.7344)	
27 Months	0.4014 (0.3022 to 0.4984)	0.4086 (0.3295 to 0.4861)	0.2500 (0.0371 to 0.5581)	0.2667 (0.0826 to 0.4963)	0.5833 (0.2701 to 0.8009)	0.4286 (0.0978 to 0.7344)	

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
PGM=DEVOPS/SAR650984/EFC15246/CIR_RWE/REPORT/PGM/eff_km_sr_subgrp_sig_s_t.sas OUT=REPORT/OUTPUT/eff_km_de_tesae_seriss_s_t_x.rtf (12FEB2021 8:12)

16.2.7.1 Safety endpoints
16.2.7.1.56 Subgroup analysis by R-ISS staging
16.2.7.1.56.2 Treatment emergent serious adverse event by treatment group according to R-ISS staging - Safety population

	I or II		III		Not classified		
	Kd (N=102)	**IKd (N=155)**	**Kd (N=8)**	**IKd (N=15)**	**Kd (N=12)**	**IKd (N=7)**	**p-value of treatment-by-sub group interaction[c]**
30 Months	0.4014 (0.3022 to 0.4984)	0.4086 (0.3295 to 0.4861)	0.2500 (0.0371 to 0.5581)	0.2667 (0.0826 to 0.4963)	0.5833 (0.2701 to 0.8009)	0.4286 (0.0978 to 0.7344)	
Number of patients at risk[b]							
3 Months	82	121	5	6	12	5	
6 Months	65	106	4	5	11	5	
9 Months	59	93	4	5	8	5	
12 Months	54	81	3	5	8	4	
15 Months	45	67	2	2	7	2	
18 Months	40	61	2	1	7	2	
21 Months	30	54	1	1	5	2	
24 Months	8	19	0	0	1	0	
27 Months	2	1	0	0	0	0	
30 Months	0	0	0	0	0	0	

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
PGM=DEVOPS/SAR650984/EFC15246/CIR_RWE/REPORT/PGM/eff_km_sr_subgrp_sig_s_t.sas OUT=REPORT/OUTPUT/eff_km_de_tesae_seriss_s_t_x.rtf (12FEB2021 8:12)

16.2.7.1 Safety endpoints
16.2.7.1.56 Subgroup analysis by R-ISS staging
16.2.7.1.56.3 Treatment emergent adverse event leading to discontinuation of treatment by treatment group according to R-ISS staging - Safety population

	I or II		III		Not classified		
	Kd (N=102)	**IKd (N=155)**	**Kd (N=8)**	**IKd (N=15)**	**Kd (N=12)**	**IKd (N=7)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	17 (16.7)	13 (8.4)	0 (0.0)	1 (6.7)	0 (0.0)	1 (14.3)	0.9998
Number (%) of patients censored	85 (83.3)	142 (91.6)	8 (100.0)	14 (93.3)	12 (100.0)	6 (85.7)	
Kaplan-Meier estimates of TEAE in months							
25% quantile (95% CI)	NC (15.3758 to NC)	NC (NC to NC)	NC (NC to NC)	NC (0.5585 to NC)	NC (NC to NC)	NC (12.5503 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (12.5503 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (12.5503 to NC)	
Comparison vs. Kd							
Log-Rank test p-value[a] vs Kd		0.0383		0.4497		0.1213	
Hazard ratio (95% CI) vs Kd		0.4742 (0.2303 to 0.9765)		NC (NC to NC)		NC (NC to NC)	
P-value		0.0429		0.9985		0.9986	
probability (95% CI)[b]							

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
PGM=DEVOPS/SAR650984/EFC15246/CIR_RWE/REPORT/PGM/eff_km_sr_subgrp_sig_s_t.sas OUT=REPORT/OUTPUT/eff_km_de_tedisc_seriss_s_t_x.rtf (12FEB2021 8:12)

16.2.7.1 Safety endpoints
16.2.7.1.56 Subgroup analysis by R-ISS staging
16.2.7.1.56.3 Treatment emergent adverse event leading to discontinuation of treatment by treatment group according to R-ISS staging - Safety population

	I or II		III		Not classified		
	Kd (N=102)	**IKd (N=155)**	**Kd (N=8)**	**IKd (N=15)**	**Kd (N=12)**	**IKd (N=7)**	**p-value of treatment-by-sub group interaction[c]**
3 Months	0.9510 (0.8862 to 0.9793)	0.9742 (0.9327 to 0.9902)	1.0000 (1.0000 to 1.0000)	0.9286 (0.5908 to 0.9896)	1.0000 (1.0000 to 1.0000)	1.0000 (1.0000 to 1.0000)	
6 Months	0.9209 (0.8481 to 0.9597)	0.9479 (0.8984 to 0.9736)	1.0000 (1.0000 to 1.0000)	0.9286 (0.5908 to 0.9896)	1.0000 (1.0000 to 1.0000)	1.0000 (1.0000 to 1.0000)	
9 Months	0.8595 (0.7742 to 0.9143)	0.9279 (0.8736 to 0.9594)	1.0000 (1.0000 to 1.0000)	0.9286 (0.5908 to 0.9896)	1.0000 (1.0000 to 1.0000)	1.0000 (1.0000 to 1.0000)	
12 Months	0.8595 (0.7742 to 0.9143)	0.9279 (0.8736 to 0.9594)	1.0000 (1.0000 to 1.0000)	0.9286 (0.5908 to 0.9896)	1.0000 (1.0000 to 1.0000)	1.0000 (1.0000 to 1.0000)	
15 Months	0.8595 (0.7742 to 0.9143)	0.9210 (0.8650 to 0.9544)	1.0000 (1.0000 to 1.0000)	0.9286 (0.5908 to 0.9896)	1.0000 (1.0000 to 1.0000)	0.8000 (0.2038 to 0.9692)	
18 Months	0.8366 (0.7468 to 0.8967)	0.9210 (0.8650 to 0.9544)	1.0000 (1.0000 to 1.0000)	0.9286 (0.5908 to 0.9896)	1.0000 (1.0000 to 1.0000)	0.8000 (0.2038 to 0.9692)	
21 Months	0.8250 (0.7331 to 0.8876)	0.9135 (0.8556 to 0.9489)	1.0000 (1.0000 to 1.0000)	0.9286 (0.5908 to 0.9896)	1.0000 (1.0000 to 1.0000)	0.8000 (0.2038 to 0.9692)	
24 Months	0.8250 (0.7331 to 0.8876)	0.9135 (0.8556 to 0.9489)	1.0000 (1.0000 to 1.0000)	0.9286 (0.5908 to 0.9896)	1.0000 (1.0000 to 1.0000)	0.8000 (0.2038 to 0.9692)	
27 Months	0.8250 (0.7331 to 0.8876)	0.9135 (0.8556 to 0.9489)	1.0000 (1.0000 to 1.0000)	0.9286 (0.5908 to 0.9896)	1.0000 (1.0000 to 1.0000)	0.8000 (0.2038 to 0.9692)	
30 Months	0.8250 (0.7331 to 0.8876)	0.9135 (0.8556 to 0.9489)	1.0000 (1.0000 to 1.0000)	0.9286 (0.5908 to 0.9896)	1.0000 (1.0000 to 1.0000)	0.8000 (0.2038 to 0.9692)	

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
PGM=DEVOPS/SAR650984/EFC15246/CIR_RWE/REPORT/PGM/eff_km_sr_subgrp_sig_s_t.sas OUT=REPORT/OUTPUT/eff_km_de_tedisc_seriss_s_t_x.rtf (12FEB2021 8:12)

16.2.7.1 Safety endpoints
16.2.7.1.56 Subgroup analysis by R-ISS staging
16.2.7.1.56.3 Treatment emergent adverse event leading to discontinuation of treatment by treatment group according to R-ISS staging - Safety population

	I or II		III		Not classified		
	Kd (N=102)	**IKd (N=155)**	**Kd (N=8)**	**IKd (N=15)**	**Kd (N=12)**	**IKd (N=7)**	**p-value of treatment-by-sub group interaction[c]**
Number of patients at risk[b]							
3 Months	96	151	7	13	12	6	
6 Months	91	143	5	12	12	6	
9 Months	82	139	5	11	12	5	
12 Months	80	137	5	10	12	5	
15 Months	75	129	5	8	12	3	
18 Months	72	124	5	6	12	3	
21 Months	59	111	4	4	10	3	
24 Months	22	40	1	0	3	0	
27 Months	4	2	0	0	0	0	
30 Months	0	0	0	0	0	0	

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
PGM=DEVOPS/SAR650984/EFC15246/CIR_RWE/REPORT/PGM/eff_km_sr_subgrp_sig_s_t.sas OUT=REPORT/OUTPUT/eff_km_de_tedisc_seriss_s_t_x.rtf (12FEB2021 8:12)

16.2.7.1 Safety endpoints
16.2.7.1.56 Subgroup analysis by R-ISS staging
16.2.7.1.56.4 Treatment emergent mild adverse event by treatment group according to R-ISS staging - Safety population

	I or II		III		Not classified		
	Kd (N=102)	**IKd (N=155)**	**Kd (N=8)**	**IKd (N=15)**	**Kd (N=12)**	**IKd (N=7)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	97 (95.1)	147 (94.8)	7 (87.5)	13 (86.7)	11 (91.7)	7 (100.0)	0.8928
Number (%) of patients censored	5 (4.9)	8 (5.2)	1 (12.5)	2 (13.3)	1 (8.3)	0 (0.0)	
Kaplan-Meier estimates of TEAE in months							
25% quantile (95% CI)	0.1971 (0.1314 to 0.2628)	0.0657 (0.0657 to 0.0986)	0.1478 (0.0657 to 0.6242)	0.0657 (0.0329 to 0.1314)	0.1807 (0.0329 to 0.2957)	0.0657 (0.0657 to 0.2300)	
Median (95% CI)	0.5257 (0.3614 to 0.6571)	0.1971 (0.1314 to 0.2628)	0.5092 (0.0657 to 0.8214)	0.1643 (0.0329 to 0.3943)	0.3285 (0.0329 to 1.9055)	0.2300 (0.0657 to 0.4600)	
75% quantile (95% CI)	1.2156 (0.7885 to 1.9384)	1.0185 (0.6242 to 1.4784)	0.7228 (0.1971 to NC)	3.6797 (0.1643 to NC)	1.5441 (0.2957 to NC)	0.4600 (0.1643 to 2.8255)	
Comparison vs. Kd							
Log-Rank test p-value[a] vs Kd		0.0836		0.5301		0.3756	
Hazard ratio (95% CI) vs Kd		1.2543 (0.9698 to 1.6222)		1.3454 (0.5312 to 3.4079)		1.5491 (0.5841 to 4.1083)	
P-value		0.0843		0.5315		0.3792	

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
PGM=DEVOPS/SAR650984/EFC15246/CIR_RWE/REPORT/PGM/eff_km_sr_subgrp_sig_s_t.sas OUT=REPORT/OUTPUT/eff_km_de_tesev12_seriss_s_t_x.rtf (12FEB2021 8:13)

16.2.7.1 Safety endpoints
16.2.7.1.56 Subgroup analysis by R-ISS staging
16.2.7.1.56.4 Treatment emergent mild adverse event by treatment group according to R-ISS staging - Safety population

	I or II		III		Not classified		
	Kd (N=102)	**IKd (N=155)**	**Kd (N=8)**	**IKd (N=15)**	**Kd (N=12)**	**IKd (N=7)**	**p-value of treatment-by-sub group interaction[c]**
probability (95% CI)[b]							
3 Months	0.1100 (0.0584 to 0.1800)	0.1032 (0.0617 to 0.1571)	0.1250 (0.0066 to 0.4227)	0.2667 (0.0826 to 0.4963)	0.1667 (0.0265 to 0.4130)	0.1429 (0.0071 to 0.4649)	
6 Months	0.0600 (0.0246 to 0.1182)	0.0764 (0.0414 to 0.1255)	0.1250 (0.0066 to 0.4227)	0.0889 (0.0061 to 0.3175)	0.0833 (0.0051 to 0.3111)	0.1429 (0.0071 to 0.4649)	
9 Months	0.0600 (0.0246 to 0.1182)	0.0556 (0.0265 to 0.1002)	0.1250 (0.0066 to 0.4227)	0.0889 (0.0061 to 0.3175)	0.0833 (0.0051 to 0.3111)	0.1429 (0.0071 to 0.4649)	
12 Months	0.0600 (0.0246 to 0.1182)	0.0486 (0.0219 to 0.0915)	0.1250 (0.0066 to 0.4227)	0.0889 (0.0061 to 0.3175)	0.0833 (0.0051 to 0.3111)	0.1429 (0.0071 to 0.4649)	
15 Months	0.0360 (0.0104 to 0.0889)	0.0486 (0.0219 to 0.0915)	0.1250 (0.0066 to 0.4227)	0.0889 (0.0061 to 0.3175)	0.0833 (0.0051 to 0.3111)	0.1429 (0.0071 to 0.4649)	
18 Months	0.0360 (0.0104 to 0.0889)	0.0486 (0.0219 to 0.0915)	0.1250 (0.0066 to 0.4227)	0.0889 (0.0061 to 0.3175)	0.0833 (0.0051 to 0.3111)	0.1429 (0.0071 to 0.4649)	
21 Months	0.0360 (0.0104 to 0.0889)	0.0486 (0.0219 to 0.0915)	0.1250 (0.0066 to 0.4227)	0.0889 (0.0061 to 0.3175)	0.0833 (0.0051 to 0.3111)	0.1429 (0.0071 to 0.4649)	
24 Months	0.0360 (0.0104 to 0.0889)	0.0486 (0.0219 to 0.0915)	0.1250 (0.0066 to 0.4227)	0.0889 (0.0061 to 0.3175)	0.0833 (0.0051 to 0.3111)	0.1429 (0.0071 to 0.4649)	
27 Months	0.0360 (0.0104 to 0.0889)	0.0486 (0.0219 to 0.0915)	0.1250 (0.0066 to 0.4227)	0.0889 (0.0061 to 0.3175)	0.0833 (0.0051 to 0.3111)	0.1429 (0.0071 to 0.4649)	

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.56 Subgroup analysis by R-ISS staging
16.2.7.1.56.4 Treatment emergent mild adverse event by treatment group according to R-ISS staging - Safety population

	I or II		III		Not classified		
	Kd (N=102)	**IKd (N=155)**	**Kd (N=8)**	**IKd (N=15)**	**Kd (N=12)**	**IKd (N=7)**	**p-value of treatment-by-sub group interaction[c]**
30 Months	0.0360 (0.0104 to 0.0889)	0.0486 (0.0219 to 0.0915)	0.1250 (0.0066 to 0.4227)	0.0889 (0.0061 to 0.3175)	0.0833 (0.0051 to 0.3111)	0.1429 (0.0071 to 0.4649)	
Number of patients at risk[b]							
3 Months	11	16	1	3	2	0	
6 Months	6	11	1	0	1	0	
9 Months	6	8	1	0	1	0	
12 Months	5	7	1	0	1	0	
15 Months	3	6	1	0	1	0	
18 Months	3	6	1	0	1	0	
21 Months	1	6	1	0	1	0	
24 Months	1	1	0	0	0	0	
27 Months	0	0	0	0	0	0	
30 Months	0	0	0	0	0	0	

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
PGM=DEVOPS/SAR650984/EFC15246/CIR_RWE/REPORT/PGM/eff_km_sr_subgrp_sig_s_t.sas OUT=REPORT/OUTPUT/eff_km_de_tesev12_seriss_s_t_x.rtf (12FEB2021 8:13)

16.2.7.1 Safety endpoints
16.2.7.1.56 Subgroup analysis by R-ISS staging
16.2.7.1.56.5 Treatment emergent severe adverse event by treatment group according to R-ISS staging - Safety population

	I or II		III		Not classified		
	Kd (N=102)	**IKd (N=155)**	**Kd (N=8)**	**IKd (N=15)**	**Kd (N=12)**	**IKd (N=7)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	71 (69.6)	120 (77.4)	5 (62.5)	12 (80.0)	5 (41.7)	2 (28.6)	0.6367
Number (%) of patients censored	31 (30.4)	35 (22.6)	3 (37.5)	3 (20.0)	7 (58.3)	5 (71.4)	
Kaplan-Meier estimates of TEAE in months							
25% quantile (95% CI)	1.8727 (0.7885 to 3.2854)	1.4127 (0.7556 to 2.4312)	0.7064 (0.0986 to 10.4805)	0.3943 (0.0657 to 0.7228)	9.6263 (0.5257 to NC)	3.7454 (0.0657 to NC)	
Median (95% CI)	5.5195 (4.0411 to 9.1992)	5.9466 (4.7967 to 7.8522)	6.2752 (0.0986 to NC)	1.3142 (0.1971 to 7.7536)	NC (6.2752 to NC)	NC (0.0657 to NC)	
75% quantile (95% CI)	NC (13.8645 to NC)	15.6057 (11.1704 to NC)	NC (0.8214 to NC)	7.7536 (0.7228 to NC)	NC (NC to NC)	NC (3.7454 to NC)	
Comparison vs. Kd							
Log-Rank test p-value[a] vs Kd		0.3544		0.3584		0.8656	
Hazard ratio (95% CI) vs Kd		1.1488 (0.8563 to 1.5412)		1.6261 (0.5703 to 4.6369)		0.8678 (0.1678 to 4.4884)	
P-value		0.3548		0.3631		0.8657	

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.56 Subgroup analysis by R-ISS staging
16.2.7.1.56.5 Treatment emergent severe adverse event by treatment group according to R-ISS staging - Safety population

	I or II		III		Not classified		
	Kd (N=102)	**IKd (N=155)**	**Kd (N=8)**	**IKd (N=15)**	**Kd (N=12)**	**IKd (N=7)**	**p-value of treatment-by-sub group interaction[c]**
probability (95% CI)[b]							
3 Months	0.6759 (0.5757 to 0.7574)	0.6581 (0.5776 to 0.7268)	0.6250 (0.2293 to 0.8607)	0.3667 (0.1357 to 0.6041)	0.9167 (0.5390 to 0.9878)	0.8571 (0.3341 to 0.9786)	
6 Months	0.4871 (0.3868 to 0.5800)	0.4903 (0.4095 to 0.5661)	0.6250 (0.2293 to 0.8607)	0.2933 (0.0917 to 0.5329)	0.9167 (0.5390 to 0.9878)	0.6857 (0.2128 to 0.9121)	
9 Months	0.4064 (0.3102 to 0.5003)	0.3935 (0.3166 to 0.4694)	0.4688 (0.1199 to 0.7629)	0.2200 (0.0539 to 0.4561)	0.7500 (0.4084 to 0.9117)	0.6857 (0.2128 to 0.9121)	
12 Months	0.3760 (0.2820 to 0.4695)	0.2903 (0.2211 to 0.3629)	0.3125 (0.0478 to 0.6408)	0.2200 (0.0539 to 0.4561)	0.6667 (0.3370 to 0.8597)	0.6857 (0.2128 to 0.9121)	
15 Months	0.3347 (0.2443 to 0.4274)	0.2550 (0.1889 to 0.3261)	0.3125 (0.0478 to 0.6408)	0.1467 (0.0239 to 0.3726)	0.5833 (0.2701 to 0.8009)	0.6857 (0.2128 to 0.9121)	
18 Months	0.3026 (0.2154 to 0.3944)	0.2252 (0.1621 to 0.2949)	0.3125 (0.0478 to 0.6408)	0.1467 (0.0239 to 0.3726)	0.5833 (0.2701 to 0.8009)	0.6857 (0.2128 to 0.9121)	
21 Months	0.3026 (0.2154 to 0.3944)	0.2177 (0.1554 to 0.2870)	0.3125 (0.0478 to 0.6408)	0.1467 (0.0239 to 0.3726)	0.5833 (0.2701 to 0.8009)	0.6857 (0.2128 to 0.9121)	
24 Months	0.2858 (0.1986 to 0.3790)	0.2177 (0.1554 to 0.2870)	0.3125 (0.0478 to 0.6408)	0.1467 (0.0239 to 0.3726)	0.5833 (0.2701 to 0.8009)	0.6857 (0.2128 to 0.9121)	
27 Months	0.2858 (0.1986 to 0.3790)	0.2177 (0.1554 to 0.2870)	0.3125 (0.0478 to 0.6408)	0.1467 (0.0239 to 0.3726)	0.5833 (0.2701 to 0.8009)	0.6857 (0.2128 to 0.9121)	

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
PGM=DEVOPS/SAR650984/EFC15246/CIR_RWE/REPORT/PGM/eff_km_sr_subgrp_sig_s_t.sas OUT=REPORT/OUTPUT/eff_km_de_tesev34_seriss_s_t_x.rtf (12FEB2021 8:13)

16.2.7.1 Safety endpoints
16.2.7.1.56 Subgroup analysis by R-ISS staging
16.2.7.1.56.5 Treatment emergent severe adverse event by treatment group according to R-ISS staging - Safety population

	I or II		III		Not classified		
	Kd (N=102)	**IKd (N=155)**	**Kd (N=8)**	**IKd (N=15)**	**Kd (N=12)**	**IKd (N=7)**	**p-value of treatment-by-sub group interaction[c]**
30 Months	0.2858 (0.1986 to 0.3790)	0.2177 (0.1554 to 0.2870)	0.3125 (0.0478 to 0.6408)	0.1467 (0.0239 to 0.3726)	0.5833 (0.2701 to 0.8009)	0.6857 (0.2128 to 0.9121)	
Number of patients at risk[b]							
3 Months	68	102	4	5	11	5	
6 Months	49	76	4	4	11	4	
9 Months	40	61	3	3	9	4	
12 Months	37	45	2	3	8	4	
15 Months	32	35	2	1	7	3	
18 Months	28	30	2	0	7	3	
21 Months	21	28	1	0	5	3	
24 Months	6	10	0	0	2	0	
27 Months	1	0	0	0	0	0	
30 Months	0	0	0	0	0	0	

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
PGM=DEVOPS/SAR650984/EFC15246/CIR_RWE/REPORT/PGM/eff_km_sr_subgrp_sig_s_t.sas OUT=REPORT/OUTPUT/eff_km_de_tesev34_seriss_s_t_x.rtf (12FEB2021 8:13)

16.2.7.1 Safety endpoints
16.2.7.1.56 Subgroup analysis by R-ISS staging
16.2.7.1.56.6 Treatment emergent severe adverse event including death by treatment group according to R-ISS staging - Safety population

	I or II		III		Not classified		
	Kd (N=102)	**IKd (N=155)**	**Kd (N=8)**	**IKd (N=15)**	**Kd (N=12)**	**IKd (N=7)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	71 (69.6)	121 (78.1)	6 (75.0)	13 (86.7)	5 (41.7)	2 (28.6)	0.7179
Number (%) of patients censored	31 (30.4)	34 (21.9)	2 (25.0)	2 (13.3)	7 (58.3)	5 (71.4)	
Kaplan-Meier estimates of TEAE in months							
25% quantile (95% CI)	1.8727 (0.7885 to 3.2854)	1.4127 (0.7556 to 2.4312)	0.7064 (0.0986 to 6.2752)	0.3943 (0.0657 to 0.7228)	9.6263 (0.5257 to NC)	3.7454 (0.0657 to NC)	
Median (95% CI)	5.5195 (4.0411 to 9.1992)	5.9466 (4.7967 to 7.8522)	3.6304 (0.0986 to NC)	0.7228 (0.1971 to 4.3368)	NC (6.2752 to NC)	NC (0.0657 to NC)	
75% quantile (95% CI)	NC (13.8645 to NC)	14.8830 (11.1704 to NC)	NC (0.8214 to NC)	7.7536 (0.7228 to NC)	NC (NC to NC)	NC (3.7454 to NC)	
Comparison vs. Kd							
Log-Rank test p-value[a] vs Kd		0.3219		0.4371		0.8656	
Hazard ratio (95% CI) vs Kd		1.1597 (0.8648 to 1.5551)		1.4663 (0.5551 to 3.8731)		0.8678 (0.1678 to 4.4884)	
P-value		0.3223		0.4399		0.8657	

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
PGM=DEVOPS/SAR650984/EFC15246/CIR_RWE/REPORT/PGM/eff_km_sr_subgrp_sig_s_t.sas OUT=REPORT/OUTPUT/eff_km_de_tesev345_seriss_s_t_x.rtf (12FEB2021 8:13)

16.2.7.1 Safety endpoints
16.2.7.1.56 Subgroup analysis by R-ISS staging
16.2.7.1.56.6 Treatment emergent severe adverse event including death by treatment group according to R-ISS staging - Safety population

	I or II		III		Not classified		
	Kd (N=102)	**IKd (N=155)**	**Kd (N=8)**	**IKd (N=15)**	**Kd (N=12)**	**IKd (N=7)**	**p-value of treatment-by-sub group interaction[c]**
probability (95% CI)[b]							
3 Months	0.6759 (0.5757 to 0.7574)	0.6581 (0.5776 to 0.7268)	0.5000 (0.1520 to 0.7749)	0.3333 (0.1215 to 0.5640)	0.9167 (0.5390 to 0.9878)	0.8571 (0.3341 to 0.9786)	
6 Months	0.4871 (0.3868 to 0.5800)	0.4903 (0.4095 to 0.5661)	0.5000 (0.1520 to 0.7749)	0.2667 (0.0826 to 0.4963)	0.9167 (0.5390 to 0.9878)	0.6857 (0.2128 to 0.9121)	
9 Months	0.4064 (0.3102 to 0.5003)	0.3935 (0.3166 to 0.4694)	0.3750 (0.0870 to 0.6744)	0.2000 (0.0489 to 0.4239)	0.7500 (0.4084 to 0.9117)	0.6857 (0.2128 to 0.9121)	
12 Months	0.3760 (0.2820 to 0.4695)	0.2903 (0.2211 to 0.3629)	0.2500 (0.0371 to 0.5581)	0.2000 (0.0489 to 0.4239)	0.6667 (0.3370 to 0.8597)	0.6857 (0.2128 to 0.9121)	
15 Months	0.3347 (0.2443 to 0.4274)	0.2491 (0.1838 to 0.3197)	0.2500 (0.0371 to 0.5581)	0.1333 (0.0219 to 0.3457)	0.5833 (0.2701 to 0.8009)	0.6857 (0.2128 to 0.9121)	
18 Months	0.3026 (0.2154 to 0.3944)	0.2200 (0.1577 to 0.2890)	0.2500 (0.0371 to 0.5581)	0.1333 (0.0219 to 0.3457)	0.5833 (0.2701 to 0.8009)	0.6857 (0.2128 to 0.9121)	
21 Months	0.3026 (0.2154 to 0.3944)	0.2127 (0.1512 to 0.2812)	0.2500 (0.0371 to 0.5581)	0.1333 (0.0219 to 0.3457)	0.5833 (0.2701 to 0.8009)	0.6857 (0.2128 to 0.9121)	
24 Months	0.2858 (0.1986 to 0.3790)	0.2127 (0.1512 to 0.2812)	0.2500 (0.0371 to 0.5581)	0.1333 (0.0219 to 0.3457)	0.5833 (0.2701 to 0.8009)	0.6857 (0.2128 to 0.9121)	
27 Months	0.2858 (0.1986 to 0.3790)	0.2127 (0.1512 to 0.2812)	0.2500 (0.0371 to 0.5581)	0.1333 (0.0219 to 0.3457)	0.5833 (0.2701 to 0.8009)	0.6857 (0.2128 to 0.9121)	

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
PGM=DEVOPS/SAR650984/EFC15246/CIR_RWE/REPORT/PGM/eff_km_sr_subgrp_sig_s_t.sas OUT=REPORT/OUTPUT/eff_km_de_tesev345_seriss_s_t_x.rtf (12FEB2021 8:13)

16.2.7.1 Safety endpoints
16.2.7.1.56 Subgroup analysis by R-ISS staging
16.2.7.1.56.6 Treatment emergent severe adverse event including death by treatment group according to R-ISS staging - Safety population

	I or II		III		Not classified		
	Kd (N=102)	**IKd (N=155)**	**Kd (N=8)**	**IKd (N=15)**	**Kd (N=12)**	**IKd (N=7)**	**p-value of treatment-by-sub group interaction[c]**
30 Months	0.2858 (0.1986 to 0.3790)	0.2127 (0.1512 to 0.2812)	0.2500 (0.0371 to 0.5581)	0.1333 (0.0219 to 0.3457)	0.5833 (0.2701 to 0.8009)	0.6857 (0.2128 to 0.9121)	
Number of patients at risk[b]							
3 Months	68	102	4	5	11	5	
6 Months	49	76	4	4	11	4	
9 Months	40	61	3	3	9	4	
12 Months	37	45	2	3	8	4	
15 Months	32	35	2	1	7	3	
18 Months	28	30	2	0	7	3	
21 Months	21	28	1	0	5	3	
24 Months	6	10	0	0	2	0	
27 Months	1	0	0	0	0	0	
30 Months	0	0	0	0	0	0	

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
PGM=DEVOPS/SAR650984/EFC15246/CIR_RWE/REPORT/PGM/eff_km_sr_subgrp_sig_s_t.sas OUT=REPORT/OUTPUT/eff_km_de_tesev345_seriss_s_t_x.rtf (12FEB2021 8:13)

16.2.7.1 Safety endpoints
16.2.7.1.57 Subgroup analysis by number of prior lines of therapy (IRT)
16.2.7.1.57.1 Treatment emergent adverse event by treatment group according to number of prior lines of therapy (IRT) - Safety population

	1		>1		
	Kd (N=54)	**IKd (N=78)**	**Kd (N=68)**	**IKd (N=99)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	51 (94.4)	74 (94.9)	66 (97.1)	98 (99.0)	0.4876
Number (%) of patients censored	3 (5.6)	4 (5.1)	2 (2.9)	1 (1.0)	
Kaplan-Meier estimates of TEAE in months					
25% quantile (95% CI)	0.1971 (0.0657 to 0.2300)	0.0657 (0.0657 to 0.0986)	0.1971 (0.0986 to 0.2628)	0.0657 (0.0657 to 0.0986)	
Median (95% CI)	0.4107 (0.2300 to 0.5914)	0.1971 (0.1314 to 0.3614)	0.4764 (0.3285 to 0.6899)	0.1643 (0.1314 to 0.2300)	
75% quantile (95% CI)	0.6571 (0.5914 to 2.2012)	0.8871 (0.3943 to 1.5113)	1.1828 (0.6899 to 1.8727)	0.6571 (0.3614 to 1.0513)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd		0.3051		0.0330	
Hazard ratio (95% CI) vs Kd		1.2056 (0.8429 to 1.7245)		1.4041 (1.0262 to 1.9212)	
P-value		0.3058		0.0339	

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
PGM=DEVOPS/SAR650984/EFC15246/CIR_RWE/REPORT/PGM/eff_km_sr_subgrp_sig_s_t.sas OUT=REPORT/OUTPUT/eff_km_de_teae_plne_s_t_x.rtf (12FEB2021 8:09)

16.2.7.1 Safety endpoints
16.2.7.1.57 Subgroup analysis by number of prior lines of therapy (IRT)
16.2.7.1.57.1 Treatment emergent adverse event by treatment group according to number of prior lines of therapy (IRT) - Safety population

	1		>1		
	Kd (N=54)	**IKd (N=78)**	**Kd (N=68)**	**IKd (N=99)**	**p-value of treatment-by-sub group interaction[c]**
Hazard ratio inverted (95% CI) vs IKd			0.7122 (0.5205 to 0.9744)		
probability (95% CI)[b]					
3 Months	0.1296 (0.0570 to 0.2330)	0.0897 (0.0395 to 0.1656)	0.0588 (0.0190 to 0.1319)	0.0606 (0.0248 to 0.1193)	
6 Months	0.0741 (0.0238 to 0.1634)	0.0641 (0.0237 to 0.1330)	0.0294 (0.0056 to 0.0912)	0.0303 (0.0082 to 0.0787)	
9 Months	0.0741 (0.0238 to 0.1634)	0.0641 (0.0237 to 0.1330)	0.0294 (0.0056 to 0.0912)	0.0101 (0.0009 to 0.0495)	
12 Months	0.0741 (0.0238 to 0.1634)	0.0513 (0.0166 to 0.1160)	0.0294 (0.0056 to 0.0912)	0.0101 (0.0009 to 0.0495)	
15 Months	0.0556 (0.0146 to 0.1387)	0.0513 (0.0166 to 0.1160)	0.0294 (0.0056 to 0.0912)	0.0101 (0.0009 to 0.0495)	
18 Months	0.0556 (0.0146 to 0.1387)	0.0513 (0.0166 to 0.1160)	0.0294 (0.0056 to 0.0912)	0.0101 (0.0009 to 0.0495)	
21 Months	0.0556 (0.0146 to 0.1387)	0.0513 (0.0166 to 0.1160)	0.0294 (0.0056 to 0.0912)	0.0101 (0.0009 to 0.0495)	
24 Months	0.0556 (0.0146 to 0.1387)	0.0513 (0.0166 to 0.1160)	0.0294 (0.0056 to 0.0912)	0.0101 (0.0009 to 0.0495)	

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
PGM=DEVOPS/SAR650984/EFC15246/CIR_RWE/REPORT/PGM/eff_km_sr_subgrp_sig_s_t.sas OUT=REPORT/OUTPUT/eff_km_de_teae_plne_s_t_x.rtf (12FEB2021 8:09)

16.2.7.1 Safety endpoints
16.2.7.1.57 Subgroup analysis by number of prior lines of therapy (IRT)
16.2.7.1.57.1 Treatment emergent adverse event by treatment group according to number of prior lines of therapy (IRT) - Safety population

	1		>1		
	Kd (N=54)	**IKd (N=78)**	**Kd (N=68)**	**IKd (N=99)**	**p-value of treatment-by-sub group interaction[c]**
27 Months	0.0556 (0.0146 to 0.1387)	0.0513 (0.0166 to 0.1160)	0.0294 (0.0056 to 0.0912)	0.0101 (0.0009 to 0.0495)	
30 Months	0.0556 (0.0146 to 0.1387)	0.0513 (0.0166 to 0.1160)	0.0294 (0.0056 to 0.0912)	0.0101 (0.0009 to 0.0495)	
Number of patients at risk[b]					
3 Months	7	7	4	6	
6 Months	4	5	2	3	
9 Months	4	5	2	1	
12 Months	4	4	2	1	
15 Months	3	4	2	1	
18 Months	3	4	2	1	
21 Months	2	4	1	1	
24 Months	0	1	1	0	
27 Months	0	0	0	0	
30 Months	0	0	0	0	

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
PGM=DEVOPS/SAR650984/EFC15246/CIR_RWE/REPORT/PGM/eff_km_sr_subgrp_sig_s_t.sas OUT=REPORT/OUTPUT/eff_km_de_teae_plne_s_t_x.rtf (12FEB2021 8:09)

16.2.7.1 Safety endpoints
16.2.7.1.57 Subgroup analysis by number of prior lines of therapy (IRT)
16.2.7.1.57.2 Treatment emergent serious adverse event by treatment group according to number of prior lines of therapy (IRT) - Safety population

	1		>1		
	Kd (N=54)	**IKd (N=78)**	**Kd (N=68)**	**IKd (N=99)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	26 (48.1)	48 (61.5)	44 (64.7)	57 (57.6)	0.0361
Number (%) of patients censored	28 (51.9)	30 (38.5)	24 (35.3)	42 (42.4)	
Kaplan-Meier estimates of TEAE in months					
25% quantile (95% CI)	7.7864 (3.8768 to 12.8131)	3.8439 (1.2813 to 5.6181)	3.3183 (1.4456 to 5.2895)	1.8727 (0.6571 to 6.5380)	
Median (95% CI)	NC (12.8131 to NC)	10.3162 (6.7680 to 17.3142)	7.6879 (5.5195 to 14.0945)	12.9446 (9.0021 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (15.4415 to NC)	NC (NC to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd		0.0531		0.3265	
Hazard ratio (95% CI) vs Kd		1.5964 (0.9895 to 2.5758)		0.8211 (0.5534 to 1.2181)	
P-value		0.0553		0.3273	
probability (95% CI)[b]					

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
PGM=DEVOPS/SAR650984/EFC15246/CIR_RWE/REPORT/PGM/eff_km_sr_subgrp_sig_s_t.sas OUT=REPORT/OUTPUT/eff_km_de_tesae_plne_s_t_x.rtf (12FEB2021 8:12)

16.2.7.1 Safety endpoints
16.2.7.1.57 Subgroup analysis by number of prior lines of therapy (IRT)
16.2.7.1.57.2 Treatment emergent serious adverse event by treatment group according to number of prior lines of therapy (IRT) - Safety population

	1		>1		
	Kd (N=54)	**IKd (N=78)**	**Kd (N=68)**	**IKd (N=99)**	**p-value of treatment-by-sub group interaction[c]**
3 Months	0.8889 (0.7693 to 0.9485)	0.7821 (0.6731 to 0.8584)	0.7642 (0.6442 to 0.8483)	0.7172 (0.6174 to 0.7952)	
6 Months	0.7778 (0.6420 to 0.8672)	0.6394 (0.5221 to 0.7351)	0.5694 (0.4427 to 0.6775)	0.6768 (0.5750 to 0.7592)	
9 Months	0.7222 (0.5822 to 0.8222)	0.5611 (0.4436 to 0.6632)	0.4940 (0.3699 to 0.6065)	0.6061 (0.5028 to 0.6944)	
12 Months	0.6667 (0.5243 to 0.7752)	0.4567 (0.3433 to 0.5631)	0.4477 (0.3262 to 0.5618)	0.5556 (0.4524 to 0.6469)	
15 Months	0.5915 (0.4486 to 0.7089)	0.4290 (0.3170 to 0.5361)	0.3682 (0.2535 to 0.4832)	0.4526 (0.3524 to 0.5474)	
18 Months	0.5533 (0.4112 to 0.6743)	0.3846 (0.2753 to 0.4927)	0.3354 (0.2243 to 0.4501)	0.4409 (0.3411 to 0.5362)	
21 Months	0.5342 (0.3928 to 0.6567)	0.3846 (0.2753 to 0.4927)	0.3354 (0.2243 to 0.4501)	0.4293 (0.3299 to 0.5249)	
24 Months	0.5046 (0.3601 to 0.6324)	0.3671 (0.2585 to 0.4761)	0.3354 (0.2243 to 0.4501)	0.4167 (0.3175 to 0.5128)	
27 Months	0.5046 (0.3601 to 0.6324)	0.3671 (0.2585 to 0.4761)	0.3354 (0.2243 to 0.4501)	0.4167 (0.3175 to 0.5128)	
30 Months	0.5046 (0.3601 to 0.6324)	0.3671 (0.2585 to 0.4761)	0.3354 (0.2243 to 0.4501)	0.4167 (0.3175 to 0.5128)	

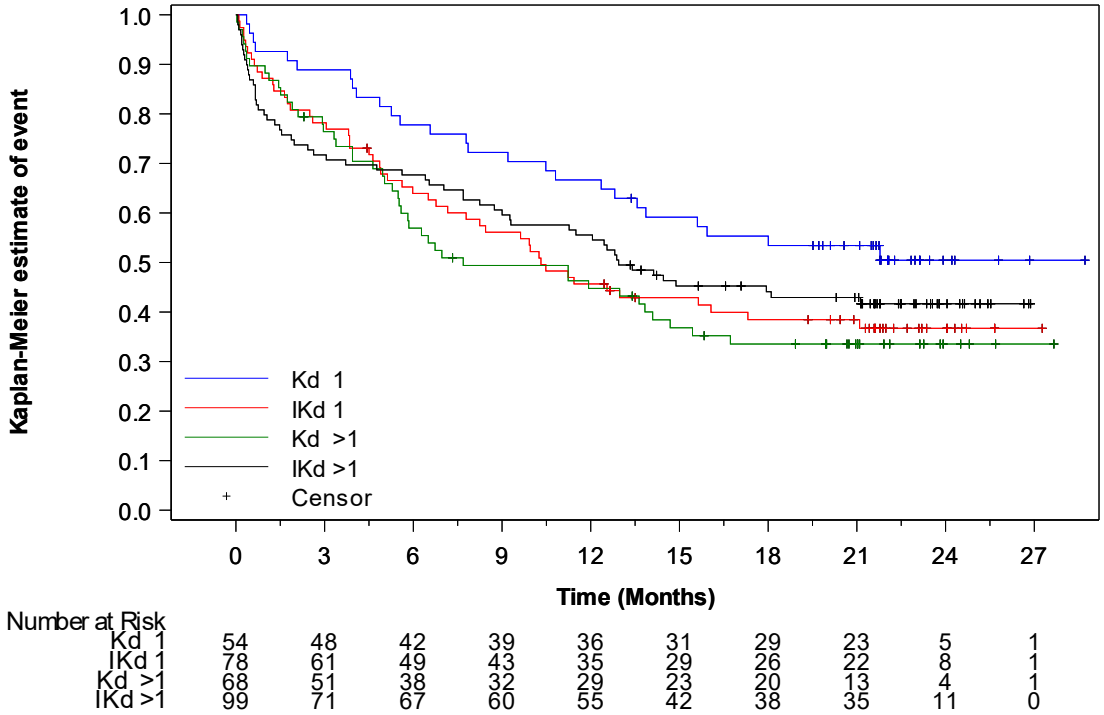
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
PGM=DEVOPS/SAR650984/EFC15246/CIR_RWE/REPORT/PGM/eff_km_sr_subgrp_sig_s_t.sas OUT=REPORT/OUTPUT/eff_km_de_tesae_plne_s_t_x.rtf (12FEB2021 8:12)

16.2.7.1 Safety endpoints
16.2.7.1.57 Subgroup analysis by number of prior lines of therapy (IRT)
16.2.7.1.57.2 Treatment emergent serious adverse event by treatment group according to number of prior lines of therapy (IRT) - Safety population

	1		>1		
	Kd (N=54)	**IKd (N=78)**	**Kd (N=68)**	**IKd (N=99)**	**p-value of treatment-by-sub group interaction[c]**
Number of patients at risk[b]					
3 Months	48	61	51	71	
6 Months	42	49	38	67	
9 Months	39	43	32	60	
12 Months	36	35	29	55	
15 Months	31	29	23	42	
18 Months	29	26	20	38	
21 Months	23	22	13	35	
24 Months	5	8	4	11	
27 Months	1	1	1	0	
30 Months	0	0	0	0	

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
PGM=DEVOPS/SAR650984/EFC15246/CIR_RWE/REPORT/PGM/eff_km_sr_subgrp_sig_s_t.sas OUT=REPORT/OUTPUT/eff_km_de_tesae_plne_s_t_x.rtf (12FEB2021 8:12)

16.2.7.1 Safety endpoints
16.2.7.1.57 Subgroup analysis by number of prior lines of therapy (IRT)
16.2.7.1.57.3 Kaplan-Meier cumulative incidence curve of treatment emergent serious adverse event by treatment group according to number of prior lines of therapy (IRT) - Safety population



Number at Risk

Kd 1	54	48	42	39	36	31	29	23	5	1
IKd 1	78	61	49	43	35	29	26	22	8	1
Kd >1	68	51	38	32	29	23	20	13	4	1
IKd >1	99	71	67	60	55	42	38	35	11	0

16.2.7.1 Safety endpoints
16.2.7.1.57 Subgroup analysis by number of prior lines of therapy (IRT)
16.2.7.1.57.4 Treatment emergent adverse event leading to discontinuation of treatment by treatment group according to number of prior lines of therapy (IRT) - Safety population

	1		>1		
	Kd (N=54)	**IKd (N=78)**	**Kd (N=68)**	**IKd (N=99)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	5 (9.3)	5 (6.4)	12 (17.6)	10 (10.1)	0.7210
Number (%) of patients censored	49 (90.7)	73 (93.6)	56 (82.4)	89 (89.9)	
Kaplan-Meier estimates of TEAE in months					
25% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (7.8522 to NC)	NC (NC to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd		0.5556		0.1254	
Hazard ratio (95% CI) vs Kd		0.6903 (0.1998 to 2.3848)		0.5246 (0.2266 to 1.2145)	
P-value		0.5579		0.1320	
probability (95% CI)[b]					
3 Months	0.9444 (0.8376 to 0.9817)	0.9744 (0.9013 to 0.9935)	0.9706 (0.8875 to 0.9926)	0.9694 (0.9081 to 0.9900)	

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
PGM=DEVOPS/SAR650984/EFC15246/CIR_RWE/REPORT/PGM/eff_km_sr_subgrp_sig_s_t.sas OUT=REPORT/OUTPUT/eff_km_de_tedisc_plne_s_t_x.rtf (12FEB2021 8:12)

16.2.7.1 Safety endpoints
16.2.7.1.57 Subgroup analysis by number of prior lines of therapy (IRT)
16.2.7.1.57.4 Treatment emergent adverse event leading to discontinuation of treatment by treatment group according to number of prior lines of therapy (IRT) - Safety population

	1		>1		
	Kd (N=54)	**IKd (N=78)**	**Kd (N=68)**	**IKd (N=99)**	**p-value of treatment-by-sub group interaction[c]**
6 Months	0.9444 (0.8376 to 0.9817)	0.9480 (0.8674 to 0.9802)	0.9238 (0.8264 to 0.9676)	0.9484 (0.8805 to 0.9782)	
9 Months	0.9259 (0.8146 to 0.9715)	0.9347 (0.8501 to 0.9723)	0.8413 (0.7246 to 0.9114)	0.9269 (0.8526 to 0.9645)	
12 Months	0.9259 (0.8146 to 0.9715)	0.9347 (0.8501 to 0.9723)	0.8413 (0.7246 to 0.9114)	0.9269 (0.8526 to 0.9645)	
15 Months	0.9259 (0.8146 to 0.9715)	0.9347 (0.8501 to 0.9723)	0.8413 (0.7246 to 0.9114)	0.9045 (0.8244 to 0.9492)	
18 Months	0.9259 (0.8146 to 0.9715)	0.9347 (0.8501 to 0.9723)	0.8047 (0.6808 to 0.8844)	0.9045 (0.8244 to 0.9492)	
21 Months	0.9058 (0.7882 to 0.9597)	0.9347 (0.8501 to 0.9723)	0.8047 (0.6808 to 0.8844)	0.8918 (0.8078 to 0.9404)	
24 Months	0.9058 (0.7882 to 0.9597)	0.9347 (0.8501 to 0.9723)	0.8047 (0.6808 to 0.8844)	0.8918 (0.8078 to 0.9404)	
27 Months	0.9058 (0.7882 to 0.9597)	0.9347 (0.8501 to 0.9723)	0.8047 (0.6808 to 0.8844)	0.8918 (0.8078 to 0.9404)	
30 Months	0.9058 (0.7882 to 0.9597)	0.9347 (0.8501 to 0.9723)	0.8047 (0.6808 to 0.8844)	0.8918 (0.8078 to 0.9404)	

Number of patients at risk[b]

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
PGM=DEVOPS/SAR650984/EFC15246/CIR_RWE/REPORT/PGM/eff_km_sr_subgrp_sig_s_t.sas OUT=REPORT/OUTPUT/eff_km_de_tedisc_plne_s_t_x.rtf (12FEB2021 8:12)

16.2.7.1 Safety endpoints
16.2.7.1.57 Subgroup analysis by number of prior lines of therapy (IRT)
16.2.7.1.57.4 Treatment emergent adverse event leading to discontinuation of treatment by treatment group according to number of prior lines of therapy (IRT) - Safety population

	1		>1		
	Kd (N=54)	**IKd (N=78)**	**Kd (N=68)**	**IKd (N=99)**	**p-value of treatment-by-sub group interaction[c]**
3 Months	51	76	64	94	
6 Months	51	71	57	90	
9 Months	49	70	50	85	
12 Months	48	69	49	83	
15 Months	46	64	46	76	
18 Months	46	62	43	71	
21 Months	38	54	35	64	
24 Months	13	18	13	22	
27 Months	2	1	2	1	
30 Months	0	0	0	0	

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
PGM=DEVOPS/SAR650984/EFC15246/CIR_RWE/REPORT/PGM/eff_km_sr_subgrp_sig_s_t.sas OUT=REPORT/OUTPUT/eff_km_de_tedisc_plne_s_t_x.rtf (12FEB2021 8:12)

16.2.7.1 Safety endpoints
16.2.7.1.57 Subgroup analysis by number of prior lines of therapy (IRT)
16.2.7.1.57.5 Treatment emergent mild adverse event by treatment group according to number of prior lines of therapy (IRT) - Safety population

	1		>1		
	Kd (N=54)	**IKd (N=78)**	**Kd (N=68)**	**IKd (N=99)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	50 (92.6)	71 (91.0)	65 (95.6)	96 (97.0)	0.4002
Number (%) of patients censored	4 (7.4)	7 (9.0)	3 (4.4)	3 (3.0)	
Kaplan-Meier estimates of TEAE in months					
25% quantile (95% CI)	0.1971 (0.0657 to 0.2628)	0.0657 (0.0657 to 0.1314)	0.1971 (0.0986 to 0.3285)	0.0657 (0.0657 to 0.0986)	
Median (95% CI)	0.5257 (0.2628 to 0.6571)	0.2136 (0.1314 to 0.3943)	0.5257 (0.3285 to 0.6899)	0.1643 (0.1314 to 0.2628)	
75% quantile (95% CI)	0.9528 (0.6571 to 4.3696)	1.4127 (0.4271 to 2.1684)	1.1828 (0.8214 to 1.9384)	0.6899 (0.3943 to 1.1828)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd		0.4206		0.0414	
Hazard ratio (95% CI) vs Kd		1.1608 (0.8073 to 1.6691)		1.3879 (1.0114 to 1.9046)	
P-value		0.4210		0.0423	

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.

16.2.7.1 Safety endpoints
16.2.7.1.57 Subgroup analysis by number of prior lines of therapy (IRT)
16.2.7.1.57.5 Treatment emergent mild adverse event by treatment group according to number of prior lines of therapy (IRT) - Safety population

	1		>1		
	Kd (N=54)	**IKd (N=78)**	**Kd (N=68)**	**IKd (N=99)**	**p-value of treatment-by-sub group interaction[c]**
Hazard ratio inverted (95% CI) vs IKd			0.7205 (0.5251 to 0.9887)		
probability (95% CI)[b]					
3 Months	0.1481 (0.0693 to 0.2551)	0.1410 (0.0750 to 0.2274)	0.0910 (0.0371 to 0.1747)	0.0836 (0.0392 to 0.1494)	
6 Months	0.0926 (0.0341 to 0.1872)	0.1154 (0.0567 to 0.1970)	0.0455 (0.0121 to 0.1152)	0.0366 (0.0103 to 0.0913)	
9 Months	0.0926 (0.0341 to 0.1872)	0.1010 (0.0465 to 0.1802)	0.0455 (0.0121 to 0.1152)	0.0122 (0.0011 to 0.0580)	
12 Months	0.0926 (0.0341 to 0.1872)	0.0865 (0.0368 to 0.1631)	0.0455 (0.0121 to 0.1152)	0.0122 (0.0011 to 0.0580)	
15 Months	0.0694 (0.0204 to 0.1608)	0.0865 (0.0368 to 0.1631)	0.0303 (0.0057 to 0.0938)	0.0122 (0.0011 to 0.0580)	
18 Months	0.0694 (0.0204 to 0.1608)	0.0865 (0.0368 to 0.1631)	0.0303 (0.0057 to 0.0938)	0.0122 (0.0011 to 0.0580)	
21 Months	0.0694 (0.0204 to 0.1608)	0.0865 (0.0368 to 0.1631)	0.0303 (0.0057 to 0.0938)	0.0122 (0.0011 to 0.0580)	
24 Months	0.0694 (0.0204 to 0.1608)	0.0865 (0.0368 to 0.1631)	0.0303 (0.0057 to 0.0938)	0.0122 (0.0011 to 0.0580)	

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.57 Subgroup analysis by number of prior lines of therapy (IRT)
16.2.7.1.57.5 Treatment emergent mild adverse event by treatment group according to number of prior lines of therapy (IRT) - Safety population

	1		>1		
	Kd (N=54)	**IKd (N=78)**	**Kd (N=68)**	**IKd (N=99)**	**p-value of treatment-by-sub group interaction[c]**
27 Months	0.0694 (0.0204 to 0.1608)	0.0865 (0.0368 to 0.1631)	0.0303 (0.0057 to 0.0938)	0.0122 (0.0011 to 0.0580)	
30 Months	0.0694 (0.0204 to 0.1608)	0.0865 (0.0368 to 0.1631)	0.0303 (0.0057 to 0.0938)	0.0122 (0.0011 to 0.0580)	
Number of patients at risk[b]					
3 Months	8	11	6	8	
6 Months	5	8	3	3	
9 Months	5	7	3	1	
12 Months	4	6	3	1	
15 Months	3	5	2	1	
18 Months	3	5	2	1	
21 Months	2	5	1	1	
24 Months	0	1	1	0	
27 Months	0	0	0	0	
30 Months	0	0	0	0	

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
PGM=DEVOPS/SAR650984/EFC15246/CIR_RWE/REPORT/PGM/eff_km_sr_subgrp_sig_s_t.sas OUT=REPORT/OUTPUT/eff_km_de_tesev12_plne_s_t_x.rtf (12FEB2021 8:12)

16.2.7.1 Safety endpoints
16.2.7.1.57 Subgroup analysis by number of prior lines of therapy (IRT)
16.2.7.1.57.6 Treatment emergent severe adverse event by treatment group according to number of prior lines of therapy (IRT) - Safety population

	1		>1		
	Kd (N=54)	**IKd (N=78)**	**Kd (N=68)**	**IKd (N=99)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	33 (61.1)	60 (76.9)	48 (70.6)	74 (74.7)	0.0854
Number (%) of patients censored	21 (38.9)	18 (23.1)	20 (29.4)	25 (25.3)	
Kaplan-Meier estimates of TEAE in months					
25% quantile (95% CI)	3.2854 (0.5914 to 6.5708)	1.2485 (0.4600 to 1.9713)	1.2156 (0.4928 to 2.9569)	1.3142 (0.6571 to 3.2854)	
Median (95% CI)	11.5483 (6.5708 to NC)	5.4867 (2.5955 to 8.4435)	5.0267 (3.2854 to 6.7351)	7.0308 (4.3696 to 8.6735)	
75% quantile (95% CI)	NC (21.7823 to NC)	17.3142 (10.4805 to NC)	NC (7.8522 to NC)	15.6057 (10.7433 to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd		0.0222		0.9964	
Hazard ratio (95% CI) vs Kd		1.6370 (1.0685 to 2.5078)		1.0008 (0.6956 to 1.4400)	
P-value		0.0235		0.9964	
Hazard ratio inverted (95% CI) vs IKd	0.6109 (0.3988 to 0.9359)				

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
PGM=DEVOPS/SAR650984/EFC15246/CIR_RWE/REPORT/PGM/eff_km_sr_subgrp_sig_s_t.sas OUT=REPORT/OUTPUT/eff_km_de_tesev34_plne_s_t_x.rtf (12FEB2021 8:13)

16.2.7.1 Safety endpoints
16.2.7.1.57 Subgroup analysis by number of prior lines of therapy (IRT)
16.2.7.1.57.6 Treatment emergent severe adverse event by treatment group according to number of prior lines of therapy (IRT) - Safety population

	1		>1		
	Kd (N=54)	**IKd (N=78)**	**Kd (N=68)**	**IKd (N=99)**	**p-value of treatment-by-sub group interaction[c]**
probability (95% CI)[b]					
3 Months	0.7593 (0.6218 to 0.8524)	0.6026 (0.4853 to 0.7012)	0.6431 (0.5162 to 0.7447)	0.6737 (0.5713 to 0.7569)	
6 Months	0.6667 (0.5243 to 0.7752)	0.4359 (0.3245 to 0.5419)	0.4287 (0.3083 to 0.5435)	0.5183 (0.4149 to 0.6120)	
9 Months	0.5556 (0.4139 to 0.6759)	0.3718 (0.2660 to 0.4775)	0.3509 (0.2382 to 0.4655)	0.4042 (0.3064 to 0.4998)	
12 Months	0.5000 (0.3612 to 0.6239)	0.2821 (0.1875 to 0.3841)	0.3190 (0.2104 to 0.4328)	0.3110 (0.2219 to 0.4041)	
15 Months	0.4444 (0.3100 to 0.5704)	0.2686 (0.1760 to 0.3699)	0.2862 (0.1822 to 0.3988)	0.2542 (0.1716 to 0.3451)	
18 Months	0.4074 (0.2767 to 0.5339)	0.2388 (0.1502 to 0.3389)	0.2683 (0.1668 to 0.3804)	0.2294 (0.1499 to 0.3191)	
21 Months	0.4074 (0.2767 to 0.5339)	0.2239 (0.1377 to 0.3231)	0.2683 (0.1668 to 0.3804)	0.2294 (0.1499 to 0.3191)	
24 Months	0.3783 (0.2472 to 0.5086)	0.2239 (0.1377 to 0.3231)	0.2683 (0.1668 to 0.3804)	0.2294 (0.1499 to 0.3191)	
27 Months	0.3783 (0.2472 to 0.5086)	0.2239 (0.1377 to 0.3231)	0.2683 (0.1668 to 0.3804)	0.2294 (0.1499 to 0.3191)	

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.57 Subgroup analysis by number of prior lines of therapy (IRT)
16.2.7.1.57.6 Treatment emergent severe adverse event by treatment group according to number of prior lines of therapy (IRT) - Safety population

	1		>1		
	Kd (N=54)	**IKd (N=78)**	**Kd (N=68)**	**IKd (N=99)**	**p-value of treatment-by-sub group interaction[c]**
30 Months	0.3783 (0.2472 to 0.5086)	0.2239 (0.1377 to 0.3231)	0.2683 (0.1668 to 0.3804)	0.2294 (0.1499 to 0.3191)	
Number of patients at risk[b]					
3 Months	41	47	42	65	
6 Months	36	34	28	50	
9 Months	30	29	22	39	
12 Months	27	22	20	30	
15 Months	24	18	17	21	
18 Months	22	16	15	17	
21 Months	18	14	9	17	
24 Months	4	4	4	6	
27 Months	0	0	1	0	
30 Months	0	0	0	0	

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
PGM=DEVOPS/SAR650984/EFC15246/CIR_RWE/REPORT/PGM/eff_km_sr_subgrp_sig_s_t.sas OUT=REPORT/OUTPUT/eff_km_de_tesev34_plne_s_t_x.rtf (12FEB2021 8:13)

16.2.7.1 Safety endpoints
16.2.7.1.57 Subgroup analysis by number of prior lines of therapy (IRT)
16.2.7.1.57.7 Treatment emergent severe adverse event including death by treatment group according to number of prior lines of therapy (IRT) - Safety population

	1		>1		
	Kd (N=54)	**IKd (N=78)**	**Kd (N=68)**	**IKd (N=99)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	33 (61.1)	60 (76.9)	49 (72.1)	76 (76.8)	0.0882
Number (%) of patients censored	21 (38.9)	18 (23.1)	19 (27.9)	23 (23.2)	
Kaplan-Meier estimates of TEAE in months					
25% quantile (95% CI)	3.2854 (0.5914 to 6.5708)	1.2485 (0.4600 to 1.9713)	1.1828 (0.4928 to 2.9240)	1.0513 (0.6571 to 2.7926)	
Median (95% CI)	11.5483 (6.5708 to NC)	5.4867 (2.5955 to 8.4435)	4.9610 (3.2854 to 6.7351)	7.0308 (4.3696 to 8.6735)	
75% quantile (95% CI)	NC (21.7823 to NC)	17.3142 (10.4805 to NC)	NC (7.4251 to NC)	14.8830 (10.7433 to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd		0.0222		0.9630	
Hazard ratio (95% CI) vs Kd		1.6370 (1.0685 to 2.5078)		1.0085 (0.7039 to 1.4450)	
P-value		0.0235		0.9630	
Hazard ratio inverted (95% CI) vs IKd	0.6109 (0.3988 to 0.9359)				

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
PGM=DEVOPS/SAR650984/EFC15246/CIR_RWE/REPORT/PGM/eff_km_sr_subgrp_sig_s_t.sas OUT=REPORT/OUTPUT/eff_km_de_tesev345_plne_s_t_x.rtf (12FEB2021 8:13)

16.2.7.1 Safety endpoints
16.2.7.1.57 Subgroup analysis by number of prior lines of therapy (IRT)
16.2.7.1.57.7 Treatment emergent severe adverse event including death by treatment group according to number of prior lines of therapy (IRT) - Safety population

	1		>1		
	Kd (N=54)	**IKd (N=78)**	**Kd (N=68)**	**IKd (N=99)**	**p-value of treatment-by-sub group interaction[c]**
probability (95% CI)[b]					
3 Months	0.7593 (0.6218 to 0.8524)	0.6026 (0.4853 to 0.7012)	0.6314 (0.5050 to 0.7338)	0.6661 (0.5638 to 0.7496)	
6 Months	0.6667 (0.5243 to 0.7752)	0.4359 (0.3245 to 0.5419)	0.4209 (0.3021 to 0.5350)	0.5124 (0.4097 to 0.6059)	
9 Months	0.5556 (0.4139 to 0.6759)	0.3718 (0.2660 to 0.4775)	0.3445 (0.2335 to 0.4580)	0.3996 (0.3027 to 0.4946)	
12 Months	0.5000 (0.3612 to 0.6239)	0.2821 (0.1875 to 0.3841)	0.3132 (0.2062 to 0.4258)	0.3074 (0.2192 to 0.3999)	
15 Months	0.4444 (0.3100 to 0.5704)	0.2686 (0.1760 to 0.3699)	0.2810 (0.1787 to 0.3923)	0.2430 (0.1628 to 0.3320)	
18 Months	0.4074 (0.2767 to 0.5339)	0.2388 (0.1502 to 0.3389)	0.2634 (0.1636 to 0.3742)	0.2192 (0.1423 to 0.3069)	
21 Months	0.4074 (0.2767 to 0.5339)	0.2239 (0.1377 to 0.3231)	0.2634 (0.1636 to 0.3742)	0.2192 (0.1423 to 0.3069)	
24 Months	0.3783 (0.2472 to 0.5086)	0.2239 (0.1377 to 0.3231)	0.2634 (0.1636 to 0.3742)	0.2192 (0.1423 to 0.3069)	
27 Months	0.3783 (0.2472 to 0.5086)	0.2239 (0.1377 to 0.3231)	0.2634 (0.1636 to 0.3742)	0.2192 (0.1423 to 0.3069)	

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.57 Subgroup analysis by number of prior lines of therapy (IRT)
16.2.7.1.57.7 Treatment emergent severe adverse event including death by treatment group according to number of prior lines of therapy (IRT) - Safety population

	1		>1		
	Kd (N=54)	**IKd (N=78)**	**Kd (N=68)**	**IKd (N=99)**	**p-value of treatment-by-sub group interaction[c]**
30 Months	0.3783 (0.2472 to 0.5086)	0.2239 (0.1377 to 0.3231)	0.2634 (0.1636 to 0.3742)	0.2192 (0.1423 to 0.3069)	
Number of patients at risk[b]					
3 Months	41	47	42	65	
6 Months	36	34	28	50	
9 Months	30	29	22	39	
12 Months	27	22	20	30	
15 Months	24	18	17	21	
18 Months	22	16	15	17	
21 Months	18	14	9	17	
24 Months	4	4	4	6	
27 Months	0	0	1	0	
30 Months	0	0	0	0	

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
PGM=DEVOPS/SAR650984/EFC15246/CIR_RWE/REPORT/PGM/eff_km_sr_subgrp_sig_s_t.sas OUT=REPORT/OUTPUT/eff_km_de_tesev345_plne_s_t_x.rtf (12FEB2021 8:13)

16.2.7.1 Safety endpoints
16.2.7.1.58 Subgroup analysis by cytogenetic abnormality (del(17p), t(4,14), t(14,16))
16.2.7.1.58.1 Treatment emergent adverse event by treatment group according to cytogenetic abnormality (del(17p), t(4,14), t(14,16)) - Safety population

	At least one		None		
	Kd (N=30)	**IKd (N=42)**	**Kd (N=77)**	**IKd (N=113)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	28 (93.3)	42 (100.0)	77 (100.0)	108 (95.6)	0.0087
Number (%) of patients censored	2 (6.7)	0 (0.0)	0 (0.0)	5 (4.4)	
Kaplan-Meier estimates of TEAE in months					
25% quantile (95% CI)	0.1643 (0.0657 to 0.2628)	0.0657 (0.0329 to 0.0986)	0.1971 (0.0986 to 0.2628)	0.0986 (0.0657 to 0.1314)	
Median (95% CI)	0.3778 (0.1971 to 0.9199)	0.1478 (0.0986 to 0.1643)	0.4928 (0.3285 to 0.6242)	0.2628 (0.1314 to 0.3943)	
75% quantile (95% CI)	1.1828 (0.5257 to 4.2053)	0.2300 (0.1643 to 0.7228)	0.6899 (0.6242 to 1.2485)	1.0185 (0.6571 to 1.5113)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd		0.0045		0.9147	
Hazard ratio (95% CI) vs Kd		2.0110 (1.2316 to 3.2837)		0.9840 (0.7323 to 1.3221)	
P-value		0.0052		0.9146	

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
PGM=DEVOPS/SAR650984/EFC15246/CIR_RWE/REPORT/PGM/eff_km_sr_subgrp_sig_s_t.sas OUT=REPORT/OUTPUT/eff_km_de_teae_cyto_s_t_x.rtf (12FEB2021 8:09)

16.2.7.1 Safety endpoints
16.2.7.1.58 Subgroup analysis by cytogenetic abnormality (del(17p), t(4,14), t(14,16))
16.2.7.1.58.1 Treatment emergent adverse event by treatment group according to cytogenetic abnormality (del(17p), t(4,14), t(14,16)) - Safety population

	At least one		None		
	Kd (N=30)	**IKd (N=42)**	**Kd (N=77)**	**IKd (N=113)**	**p-value of treatment-by-sub group interaction[c]**
Hazard ratio inverted (95% CI) vs IKd	0.4973 (0.3045 to 0.8119)				
probability (95% CI)[b]					
3 Months	0.1667 (0.0608 to 0.3178)	0.0714 (0.0185 to 0.1745)	0.0260 (0.0049 to 0.0813)	0.0885 (0.0453 to 0.1496)	
6 Months	0.0667 (0.0118 to 0.1917)	0.0238 (0.0019 to 0.1079)	0.0130 (0.0011 to 0.0624)	0.0708 (0.0331 to 0.1278)	
9 Months	0.0667 (0.0118 to 0.1917)	0.0238 (0.0019 to 0.1079)	0.0130 (0.0011 to 0.0624)	0.0531 (0.0218 to 0.1052)	
12 Months	0.0667 (0.0118 to 0.1917)	0.0238 (0.0019 to 0.1079)	0.0130 (0.0011 to 0.0624)	0.0442 (0.0165 to 0.0936)	
15 Months	0.0667 (0.0118 to 0.1917)	0.0238 (0.0019 to 0.1079)	0.0130 (0.0011 to 0.0624)	0.0442 (0.0165 to 0.0936)	
18 Months	0.0667 (0.0118 to 0.1917)	0.0238 (0.0019 to 0.1079)	0.0130 (0.0011 to 0.0624)	0.0442 (0.0165 to 0.0936)	
21 Months	0.0667 (0.0118 to 0.1917)	0.0238 (0.0019 to 0.1079)	0.0130 (0.0011 to 0.0624)	0.0442 (0.0165 to 0.0936)	
24 Months	0.0667 (0.0118 to 0.1917)	0.0238 (0.0019 to 0.1079)	0.0130 (0.0011 to 0.0624)	0.0442 (0.0165 to 0.0936)	

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
PGM=DEVOPS/SAR650984/EFC15246/CIR_RWE/REPORT/PGM/eff_km_sr_subgrp_sig_s_t.sas OUT=REPORT/OUTPUT/eff_km_de_teae_cyto_s_t_x.rtf (12FEB2021 8:09)

16.2.7.1 Safety endpoints
16.2.7.1.58 Subgroup analysis by cytogenetic abnormality (del(17p), t(4,14), t(14,16))
16.2.7.1.58.1 Treatment emergent adverse event by treatment group according to cytogenetic abnormality (del(17p), t(4,14), t(14,16)) - Safety population

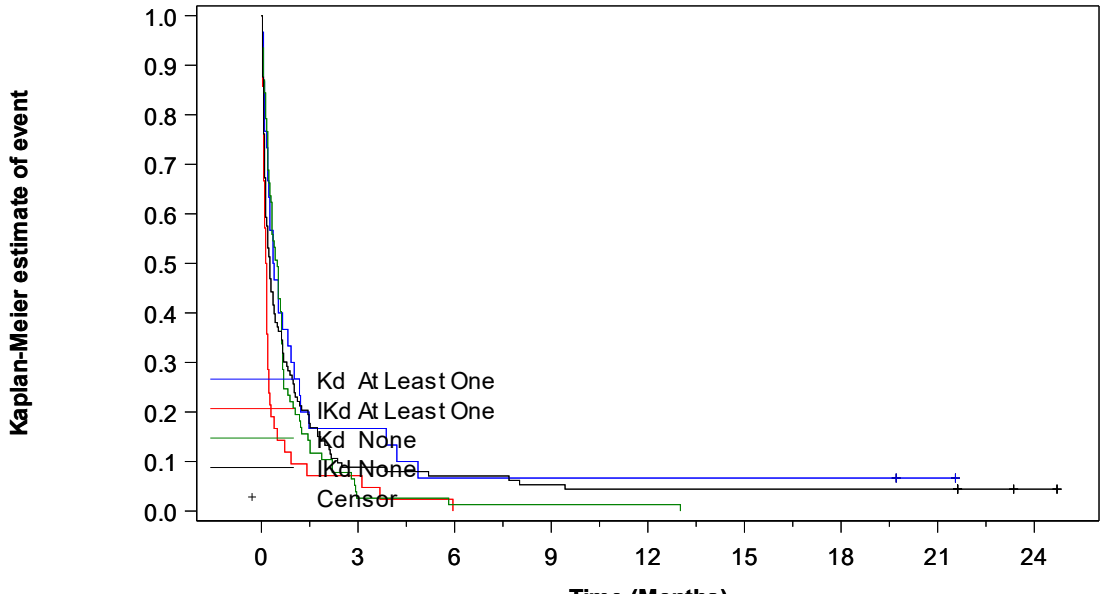
	At least one		None		
	Kd (N=30)	**IKd (N=42)**	**Kd (N=77)**	**IKd (N=113)**	**p-value of treatment-by-sub group interaction[c]**
27 Months	0.0667 (0.0118 to 0.1917)	0.0238 (0.0019 to 0.1079)	0.0130 (0.0011 to 0.0624)	0.0442 (0.0165 to 0.0936)	
30 Months	0.0667 (0.0118 to 0.1917)	0.0238 (0.0019 to 0.1079)	0.0130 (0.0011 to 0.0624)	0.0442 (0.0165 to 0.0936)	
Number of patients at risk[b]					
3 Months	5	3	2	10	
6 Months	2	0	1	8	
9 Months	2	0	1	6	
12 Months	2	0	1	5	
15 Months	2	0	0	5	
18 Months	2	0	0	5	
21 Months	1	0	0	5	
24 Months	0	0	0	1	
27 Months	0	0	0	0	
30 Months	0	0	0	0	

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
PGM=DEVOPS/SAR650984/EFC15246/CIR_RWE/REPORT/PGM/eff_km_sr_subgrp_sig_s_t.sas OUT=REPORT/OUTPUT/eff_km_de_teae_cyto_s_t_x.rtf (12FEB2021 8:09)

16.2.7.1 Safety endpoints

16.2.7.1.58 Subgroup analysis by cytogenetic abnormality (del(17p), t(4,14), t(14,16))

16.2.7.1.58.2 Kaplan-Meier cumulative incidence curve of treatment emergent adverse event by treatment group according to cytogenetic abnormality (del(17p), t(4,14), t(14,16)) - Safety population



Number at Risk									
Kd At Least One	30	5	2	2	2	2	2	1	0
IKd At Least One	42	3	0	0	0	0	0	0	0
Kd None	77	2	1	1	1	0	0	0	0
IKd None	113	10	8	6	5	5	5	5	1

16.2.7.1 Safety endpoints
16.2.7.1.58 Subgroup analysis by cytogenetic abnormality (del(17p), t(4,14), t(14,16))
16.2.7.1.58.3 Treatment emergent serious adverse event by treatment group according to cytogenetic abnormality (del(17p), t(4,14), t(14,16)) - Safety population

	At least one		None		
	Kd (N=30)	**IKd (N=42)**	**Kd (N=77)**	**IKd (N=113)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	20 (66.7)	27 (64.3)	46 (59.7)	65 (57.5)	0.9666
Number (%) of patients censored	10 (33.3)	15 (35.7)	31 (40.3)	48 (42.5)	
Kaplan-Meier estimates of TEAE in months					
25% quantile (95% CI)	3.3840 (0.4600 to 4.9610)	2.4969 (0.7228 to 4.6324)	5.2567 (2.0698 to 6.7351)	3.0554 (0.6899 to 5.9795)	
Median (95% CI)	8.5257 (4.6324 to 21.7823)	8.2464 (3.8439 to 21.0924)	13.8645 (7.7864 to NC)	12.8131 (9.2649 to NC)	
75% quantile (95% CI)	NC (12.9774 to NC)	NC (14.1273 to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd		0.9933		0.9735	
Hazard ratio (95% CI) vs Kd		0.9975 (0.5592 to 1.7795)		1.0064 (0.6898 to 1.4684)	
P-value		0.9933		0.9735	
probability (95% CI)[b]					

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
PGM=DEVOPS/SAR650984/EFC15246/CIR_RWE/REPORT/PGM/eff_km_sr_subgrp_sig_s_t.sas OUT=REPORT/OUTPUT/eff_km_de_tesae_cyto_s_t_x.rtf (12FEB2021 8:12)

16.2.7.1 Safety endpoints
16.2.7.1.58 Subgroup analysis by cytogenetic abnormality (del(17p), t(4,14), t(14,16))
16.2.7.1.58.3 Treatment emergent serious adverse event by treatment group according to cytogenetic abnormality (del(17p), t(4,14), t(14,16)) - Safety population

	At least one		None		
	Kd (N=30)	**IKd (N=42)**	**Kd (N=77)**	**IKd (N=113)**	**p-value of treatment-by-sub group interaction[c]**
3 Months	0.8000 (0.6080 to 0.9048)	0.6905 (0.5274 to 0.8070)	0.8052 (0.6978 to 0.8777)	0.7522 (0.6617 to 0.8217)	
6 Months	0.5000 (0.3130 to 0.6612)	0.5934 (0.4297 to 0.7244)	0.6883 (0.5720 to 0.7790)	0.6637 (0.5686 to 0.7426)	
9 Months	0.5000 (0.3130 to 0.6612)	0.4698 (0.3133 to 0.6116)	0.5966 (0.4783 to 0.6965)	0.6018 (0.5054 to 0.6852)	
12 Months	0.4333 (0.2556 to 0.5989)	0.4203 (0.2693 to 0.5640)	0.5436 (0.4258 to 0.6471)	0.5310 (0.4350 to 0.6179)	
15 Months	0.3636 (0.1979 to 0.5317)	0.3923 (0.2441 to 0.5375)	0.4623 (0.3475 to 0.5694)	0.4582 (0.3643 to 0.5472)	
18 Months	0.3636 (0.1979 to 0.5317)	0.3621 (0.2170 to 0.5090)	0.4070 (0.2958 to 0.5152)	0.4298 (0.3369 to 0.5192)	
21 Months	0.3636 (0.1979 to 0.5317)	0.3621 (0.2170 to 0.5090)	0.3930 (0.2829 to 0.5012)	0.4202 (0.3278 to 0.5097)	
24 Months	0.2909 (0.1242 to 0.4815)	0.3292 (0.1877 to 0.4782)	0.3930 (0.2829 to 0.5012)	0.4202 (0.3278 to 0.5097)	
27 Months	0.2909 (0.1242 to 0.4815)	0.3292 (0.1877 to 0.4782)	0.3930 (0.2829 to 0.5012)	0.4202 (0.3278 to 0.5097)	
30 Months	0.2909 (0.1242 to 0.4815)	0.3292 (0.1877 to 0.4782)	0.3930 (0.2829 to 0.5012)	0.4202 (0.3278 to 0.5097)	

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
PGM=DEVOPS/SAR650984/EFC15246/CIR_RWE/REPORT/PGM/eff_km_sr_subgrp_sig_s_t.sas OUT=REPORT/OUTPUT/eff_km_de_tesae_cyto_s_t_x.rtf (12FEB2021 8:12)

16.2.7.1 Safety endpoints
16.2.7.1.58 Subgroup analysis by cytogenetic abnormality (del(17p), t(4,14), t(14,16))
16.2.7.1.58.3 Treatment emergent serious adverse event by treatment group according to cytogenetic abnormality (del(17p), t(4,14), t(14,16)) - Safety population

	At least one		None		
	Kd (N=30)	**IKd (N=42)**	**Kd (N=77)**	**IKd (N=113)**	**p-value of treatment-by-sub group interaction[c]**
Number of patients at risk[b]					
3 Months	24	29	62	85	
6 Months	15	24	53	75	
9 Months	15	19	45	68	
12 Months	13	17	41	60	
15 Months	10	13	34	49	
18 Months	10	12	29	45	
21 Months	8	11	21	39	
24 Months	1	5	6	13	
27 Months	0	0	2	1	
30 Months	0	0	0	0	

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.58 Subgroup analysis by cytogenetic abnormality (del(17p), t(4,14), t(14,16))
16.2.7.1.58.4 Treatment emergent adverse event leading to discontinuation of treatment by treatment group according to cytogenetic abnormality (del(17p), t(4,14), t(14,16)) - Safety population

	At least one		None		
	Kd (N=30)	**IKd (N=42)**	**Kd (N=77)**	**IKd (N=113)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	3 (10.0)	2 (4.8)	14 (18.2)	11 (9.7)	0.9189
Number (%) of patients censored	27 (90.0)	40 (95.2)	63 (81.8)	102 (90.3)	
Kaplan-Meier estimates of TEAE in months					
25% quantile (95% CI)	NC (15.3758 to NC)	NC (NC to NC)	NC (8.9363 to NC)	NC (NC to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd		0.3874		0.0876	
Hazard ratio (95% CI) vs Kd		0.4630 (0.0773 to 2.7720)		0.5090 (0.2310 to 1.1213)	
P-value		0.3990		0.0938	
probability (95% CI)[b]					

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
PGM=DEVOPS/SAR650984/EFC15246/CIR_RWE/REPORT/PGM/eff_km_sr_subgrp_sig_s_t.sas OUT=REPORT/OUTPUT/eff_km_de_tedisc_cyto_s_t_x.rtf (12FEB2021 8:12)

16.2.7.1 Safety endpoints
16.2.7.1.58 Subgroup analysis by cytogenetic abnormality (del(17p), t(4,14), t(14,16))
16.2.7.1.58.4 Treatment emergent adverse event leading to discontinuation of treatment by treatment group according to cytogenetic abnormality (del(17p), t(4,14), t(14,16)) - Safety population

	At least one		None		
	Kd (N=30)	**IKd (N=42)**	**Kd (N=77)**	**IKd (N=113)**	**p-value of treatment-by-sub group interaction[c]**
3 Months	0.9667 (0.7861 to 0.9952)	0.9762 (0.8428 to 0.9966)	0.9477 (0.8666 to 0.9800)	0.9645 (0.9082 to 0.9865)	
6 Months	0.9667 (0.7861 to 0.9952)	0.9518 (0.8206 to 0.9877)	0.9076 (0.8160 to 0.9549)	0.9372 (0.8728 to 0.9696)	
9 Months	0.9309 (0.7505 to 0.9823)	0.9518 (0.8206 to 0.9877)	0.8393 (0.7342 to 0.9054)	0.9190 (0.8501 to 0.9570)	
12 Months	0.9309 (0.7505 to 0.9823)	0.9518 (0.8206 to 0.9877)	0.8393 (0.7342 to 0.9054)	0.9190 (0.8501 to 0.9570)	
15 Months	0.9309 (0.7505 to 0.9823)	0.9518 (0.8206 to 0.9877)	0.8393 (0.7342 to 0.9054)	0.9095 (0.8384 to 0.9503)	
18 Months	0.8865 (0.6848 to 0.9624)	0.9518 (0.8206 to 0.9877)	0.8248 (0.7172 to 0.8944)	0.9095 (0.8384 to 0.9503)	
21 Months	0.8865 (0.6848 to 0.9624)	0.9518 (0.8206 to 0.9877)	0.8101 (0.7001 to 0.8830)	0.8993 (0.8254 to 0.9430)	
24 Months	0.8865 (0.6848 to 0.9624)	0.9518 (0.8206 to 0.9877)	0.8101 (0.7001 to 0.8830)	0.8993 (0.8254 to 0.9430)	
27 Months	0.8865 (0.6848 to 0.9624)	0.9518 (0.8206 to 0.9877)	0.8101 (0.7001 to 0.8830)	0.8993 (0.8254 to 0.9430)	

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
PGM=DEVOPS/SAR650984/EFC15246/CIR_RWE/REPORT/PGM/eff_km_sr_subgrp_sig_s_t.sas OUT=REPORT/OUTPUT/eff_km_de_tedisc_cyto_s_t_x.rtf (12FEB2021 8:12)

16.2.7.1 Safety endpoints
16.2.7.1.58 Subgroup analysis by cytogenetic abnormality (del(17p), t(4,14), t(14,16))
16.2.7.1.58.4 Treatment emergent adverse event leading to discontinuation of treatment by treatment group according to cytogenetic abnormality (del(17p), t(4,14), t(14,16)) - Safety population

	At least one		None		
	Kd (N=30)	**IKd (N=42)**	**Kd (N=77)**	**IKd (N=113)**	**p-value of treatment-by-sub group interaction[c]**
30 Months	0.8865 (0.6848 to 0.9624)	0.9518 (0.8206 to 0.9877)	0.8101 (0.7001 to 0.8830)	0.8993 (0.8254 to 0.9430)	
Number of patients at risk[b]					
3 Months	29	41	72	108	
6 Months	27	38	67	103	
9 Months	24	36	61	101	
12 Months	23	36	61	99	
15 Months	21	33	58	93	
18 Months	20	32	56	89	
21 Months	17	28	46	78	
24 Months	5	10	17	26	
27 Months	0	0	4	2	
30 Months	0	0	0	0	

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.58 Subgroup analysis by cytogenetic abnormality (del(17p), t(4,14), t(14,16))
16.2.7.1.58.5 Treatment emergent mild adverse event by treatment group according to cytogenetic abnormality (del(17p), t(4,14), t(14,16)) - Safety population

	At least one		None		
	Kd (N=30)	**IKd (N=42)**	**Kd (N=77)**	**IKd (N=113)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	28 (93.3)	40 (95.2)	76 (98.7)	105 (92.9)	0.0592
Number (%) of patients censored	2 (6.7)	2 (4.8)	1 (1.3)	8 (7.1)	
Kaplan-Meier estimates of TEAE in months					
25% quantile (95% CI)	0.1643 (0.0657 to 0.2628)	0.0657 (0.0329 to 0.0986)	0.1971 (0.0986 to 0.2957)	0.0986 (0.0657 to 0.1314)	
Median (95% CI)	0.3778 (0.1971 to 0.9199)	0.1643 (0.0986 to 0.1971)	0.5257 (0.3285 to 0.6242)	0.2628 (0.1643 to 0.4271)	
75% quantile (95% CI)	1.1828 (0.5257 to 4.8624)	0.2628 (0.1643 to 1.6099)	0.9856 (0.6571 to 1.8727)	1.1828 (0.6571 to 1.9713)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd		0.0441		0.7660	
Hazard ratio (95% CI) vs Kd		1.6530 (1.0086 to 2.7090)		0.9554 (0.7083 to 1.2887)	
P-value		0.0462		0.7652	

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
PGM=DEVOPS/SAR650984/EFC15246/CIR_RWE/REPORT/PGM/eff_km_sr_subgrp_sig_s_t.sas OUT=REPORT/OUTPUT/eff_km_de_tesev12_cyto_s_t_x.rtf (12FEB2021 8:12)

16.2.7.1 Safety endpoints
16.2.7.1.58 Subgroup analysis by cytogenetic abnormality (del(17p), t(4,14), t(14,16))
16.2.7.1.58.5 Treatment emergent mild adverse event by treatment group according to cytogenetic abnormality (del(17p), t(4,14), t(14,16)) - Safety population

	At least one		None		
	Kd (N=30)	**IKd (N=42)**	**Kd (N=77)**	**IKd (N=113)**	**p-value of treatment-by-sub group interaction[c]**
Hazard ratio inverted (95% CI) vs IKd	0.6050 (0.3691 to 0.9915)				
probability (95% CI)[b]					
3 Months	0.1667 (0.0608 to 0.3178)	0.1190 (0.0436 to 0.2355)	0.0534 (0.0173 to 0.1203)	0.1268 (0.0731 to 0.1959)	
6 Months	0.1000 (0.0255 to 0.2358)	0.0476 (0.0087 to 0.1419)	0.0133 (0.0011 to 0.0639)	0.0982 (0.0515 to 0.1625)	
9 Months	0.1000 (0.0255 to 0.2358)	0.0476 (0.0087 to 0.1419)	0.0133 (0.0011 to 0.0639)	0.0687 (0.0309 to 0.1271)	
12 Months	0.1000 (0.0255 to 0.2358)	0.0476 (0.0087 to 0.1419)	0.0133 (0.0011 to 0.0639)	0.0589 (0.0246 to 0.1148)	
15 Months	0.0667 (0.0118 to 0.1917)	0.0476 (0.0087 to 0.1419)	0.0133 (0.0011 to 0.0639)	0.0589 (0.0246 to 0.1148)	
18 Months	0.0667 (0.0118 to 0.1917)	0.0476 (0.0087 to 0.1419)	0.0133 (0.0011 to 0.0639)	0.0589 (0.0246 to 0.1148)	
21 Months	0.0667 (0.0118 to 0.1917)	0.0476 (0.0087 to 0.1419)	0.0133 (0.0011 to 0.0639)	0.0589 (0.0246 to 0.1148)	
24 Months	0.0667 (0.0118 to 0.1917)	0.0476 (0.0087 to 0.1419)	0.0133 (0.0011 to 0.0639)	0.0589 (0.0246 to 0.1148)	

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
PGM=DEVOPS/SAR650984/EFC15246/CIR_RWE/REPORT/PGM/eff_km_sr_subgrp_sig_s_t.sas OUT=REPORT/OUTPUT/eff_km_de_tesev12_cyto_s_t_x.rtf (12FEB2021 8:12)

16.2.7.1 Safety endpoints
16.2.7.1.58 Subgroup analysis by cytogenetic abnormality (del(17p), t(4,14), t(14,16))
16.2.7.1.58.5 Treatment emergent mild adverse event by treatment group according to cytogenetic abnormality (del(17p), t(4,14), t(14,16)) - Safety population

	At least one		None		
	Kd (N=30)	**IKd (N=42)**	**Kd (N=77)**	**IKd (N=113)**	**p-value of treatment-by-sub group interaction[c]**
27 Months	0.0667 (0.0118 to 0.1917)	0.0476 (0.0087 to 0.1419)	0.0133 (0.0011 to 0.0639)	0.0589 (0.0246 to 0.1148)	
30 Months	0.0667 (0.0118 to 0.1917)	0.0476 (0.0087 to 0.1419)	0.0133 (0.0011 to 0.0639)	0.0589 (0.0246 to 0.1148)	
Number of patients at risk[b]					
3 Months	5	5	4	14	
6 Months	3	1	1	10	
9 Months	3	1	1	7	
12 Months	3	1	1	6	
15 Months	2	0	0	6	
18 Months	2	0	0	6	
21 Months	1	0	0	6	
24 Months	0	0	0	1	
27 Months	0	0	0	0	
30 Months	0	0	0	0	

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.58 Subgroup analysis by cytogenetic abnormality (del(17p), t(4,14), t(14,16))
16.2.7.1.58.6 Treatment emergent severe adverse event by treatment group according to cytogenetic abnormality (del(17p), t(4,14), t(14,16)) - Safety population

	At least one		None		
	Kd (N=30)	**IKd (N=42)**	**Kd (N=77)**	**IKd (N=113)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	19 (63.3)	36 (85.7)	58 (75.3)	85 (75.2)	0.0285
Number (%) of patients censored	11 (36.7)	6 (14.3)	19 (24.7)	28 (24.8)	
Kaplan-Meier estimates of TEAE in months					
25% quantile (95% CI)	2.3326 (0.5914 to 4.9610)	0.7556 (0.2957 to 1.9384)	1.5113 (0.4928 to 2.9240)	1.3470 (0.6571 to 3.2854)	
Median (95% CI)	10.2012 (3.9425 to NC)	4.2546 (1.8398 to 5.9466)	5.4867 (3.2854 to 7.6222)	7.1294 (5.0267 to 9.2977)	
75% quantile (95% CI)	NC (16.8542 to NC)	11.4990 (5.3552 to NC)	15.6057 (7.8522 to NC)	17.3142 (11.1047 to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd		0.0264		0.6148	
Hazard ratio (95% CI) vs Kd		1.8686 (1.0668 to 3.2729)		0.9178 (0.6570 to 1.2820)	
P-value		0.0288		0.6149	
Hazard ratio inverted (95% CI) vs IKd	0.5352 (0.3055 to 0.9373)				

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
PGM=DEVOPS/SAR650984/EFC15246/CIR_RWE/REPORT/PGM/eff_km_sr_subgrp_sig_s_t.sas OUT=REPORT/OUTPUT/eff_km_de_tesev34_cyto_s_t_x.rtf (12FEB2021 8:13)

16.2.7.1 Safety endpoints
16.2.7.1.58 Subgroup analysis by cytogenetic abnormality (del(17p), t(4,14), t(14,16))
16.2.7.1.58.6 Treatment emergent severe adverse event by treatment group according to cytogenetic abnormality (del(17p), t(4,14), t(14,16)) - Safety population

	At least one		None		
	Kd (N=30)	**IKd (N=42)**	**Kd (N=77)**	**IKd (N=113)**	**p-value of treatment-by-sub group interaction[c]**
probability (95% CI)[b]					
3 Months	0.7333 (0.5369 to 0.8567)	0.5476 (0.3865 to 0.6828)	0.6336 (0.5151 to 0.7305)	0.6720 (0.5771 to 0.7503)	
6 Months	0.5333 (0.3428 to 0.6914)	0.3333 (0.1976 to 0.4750)	0.4620 (0.3474 to 0.5689)	0.5287 (0.4324 to 0.6159)	
9 Months	0.5000 (0.3130 to 0.6612)	0.2619 (0.1413 to 0.3996)	0.3410 (0.2368 to 0.4478)	0.4211 (0.3290 to 0.5103)	
12 Months	0.5000 (0.3130 to 0.6612)	0.2381 (0.1234 to 0.3737)	0.2864 (0.1893 to 0.3909)	0.2957 (0.2142 to 0.3816)	
15 Months	0.4308 (0.2526 to 0.5972)	0.2143 (0.1061 to 0.3472)	0.2592 (0.1663 to 0.3619)	0.2553 (0.1780 to 0.3397)	
18 Months	0.3949 (0.2223 to 0.5632)	0.1339 (0.0509 to 0.2573)	0.2311 (0.1430 to 0.3318)	0.2442 (0.1680 to 0.3283)	
21 Months	0.3949 (0.2223 to 0.5632)	0.1339 (0.0509 to 0.2573)	0.2311 (0.1430 to 0.3318)	0.2331 (0.1581 to 0.3168)	
24 Months	0.3159 (0.1375 to 0.5121)	0.1339 (0.0509 to 0.2573)	0.2311 (0.1430 to 0.3318)	0.2331 (0.1581 to 0.3168)	
27 Months	0.3159 (0.1375 to 0.5121)	0.1339 (0.0509 to 0.2573)	0.2311 (0.1430 to 0.3318)	0.2331 (0.1581 to 0.3168)	

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
PGM=DEVOPS/SAR650984/EFC15246/CIR_RWE/REPORT/PGM/eff_km_sr_subgrp_sig_s_t.sas OUT=REPORT/OUTPUT/eff_km_de_tesev34_cyto_s_t_x.rtf (12FEB2021 8:13)

16.2.7.1 Safety endpoints
16.2.7.1.58 Subgroup analysis by cytogenetic abnormality (del(17p), t(4,14), t(14,16))
16.2.7.1.58.6 Treatment emergent severe adverse event by treatment group according to cytogenetic abnormality (del(17p), t(4,14), t(14,16)) - Safety population

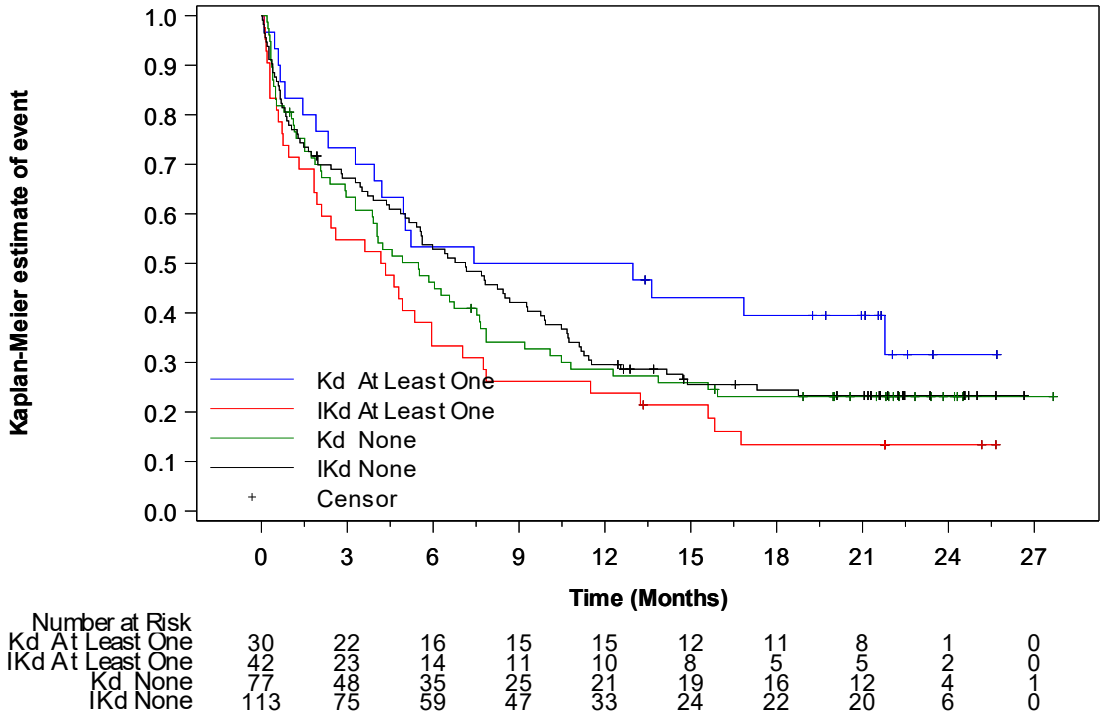
	At least one		None		
	Kd (N=30)	**IKd (N=42)**	**Kd (N=77)**	**IKd (N=113)**	**p-value of treatment-by-sub group interaction[c]**
30 Months	0.3159 (0.1375 to 0.5121)	0.1339 (0.0509 to 0.2573)	0.2311 (0.1430 to 0.3318)	0.2331 (0.1581 to 0.3168)	
Number of patients at risk[b]					
3 Months	22	23	48	75	
6 Months	16	14	35	59	
9 Months	15	11	25	47	
12 Months	15	10	21	33	
15 Months	12	8	19	24	
18 Months	11	5	16	22	
21 Months	8	5	12	20	
24 Months	1	2	4	6	
27 Months	0	0	1	0	
30 Months	0	0	0	0	

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
PGM=DEVOPS/SAR650984/EFC15246/CIR_RWE/REPORT/PGM/eff_km_sr_subgrp_sig_s_t.sas OUT=REPORT/OUTPUT/eff_km_de_tesev34_cyto_s_t_x.rtf (12FEB2021 8:13)

16.2.7.1 Safety endpoints

16.2.7.1.58 Subgroup analysis by cytogenetic abnormality (del(17p), t(4,14), t(14,16))

16.2.7.1.58.7 Kaplan-Meier cumulative incidence curve of treatment emergent severe adverse event by treatment group according to cytogenetic abnormality (del(17p), t(4,14), t(14,16)) - Safety population



Number at Risk										
Kd At Least One	30	22	16	15	15	12	11	8	1	0
IKd At Least One	42	23	14	11	10	8	5	5	2	0
Kd None	77	48	35	25	21	19	16	12	4	1
IKd None	113	75	59	47	33	24	22	20	6	0

16.2.7.1 Safety endpoints
16.2.7.1.58 Subgroup analysis by cytogenetic abnormality (del(17p), t(4,14), t(14,16))
16.2.7.1.58.8 Treatment emergent severe adverse event including death by treatment group according to cytogenetic abnormality (del(17p), t(4,14), t(14,16)) - Safety population

	At least one		None		
	Kd (N=30)	**IKd (N=42)**	**Kd (N=77)**	**IKd (N=113)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	19 (63.3)	36 (85.7)	59 (76.6)	86 (76.1)	0.0269
Number (%) of patients censored	11 (36.7)	6 (14.3)	18 (23.4)	27 (23.9)	
Kaplan-Meier estimates of TEAE in months					
25% quantile (95% CI)	2.3326 (0.5914 to 4.9610)	0.7556 (0.2957 to 1.9384)	1.2156 (0.4928 to 2.3984)	1.3470 (0.6571 to 3.2854)	
Median (95% CI)	10.2012 (3.9425 to NC)	4.2546 (1.8398 to 5.9466)	4.9281 (3.2854 to 7.5236)	7.1294 (5.0267 to 9.2977)	
75% quantile (95% CI)	NC (16.8542 to NC)	11.4990 (5.3552 to NC)	15.6057 (7.8522 to NC)	14.8830 (11.1047 to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd		0.0264		0.5950	
Hazard ratio (95% CI) vs Kd		1.8686 (1.0668 to 3.2729)		0.9140 (0.6559 to 1.2736)	
P-value		0.0288		0.5952	
Hazard ratio inverted (95% CI) vs IKd	0.5352 (0.3055 to 0.9373)				

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.58 Subgroup analysis by cytogenetic abnormality (del(17p), t(4,14), t(14,16))
16.2.7.1.58.8 Treatment emergent severe adverse event including death by treatment group according to cytogenetic abnormality (del(17p), t(4,14), t(14,16)) - Safety population

	At least one		None		
	Kd (N=30)	**IKd (N=42)**	**Kd (N=77)**	**IKd (N=113)**	**p-value of treatment-by-sub group interaction[c]**
probability (95% CI)[b]					
3 Months	0.7333 (0.5369 to 0.8567)	0.5476 (0.3865 to 0.6828)	0.6234 (0.5054 to 0.7209)	0.6720 (0.5771 to 0.7503)	
6 Months	0.5333 (0.3428 to 0.6914)	0.3333 (0.1976 to 0.4750)	0.4545 (0.3412 to 0.5610)	0.5287 (0.4324 to 0.6159)	
9 Months	0.5000 (0.3130 to 0.6612)	0.2619 (0.1413 to 0.3996)	0.3355 (0.2327 to 0.4413)	0.4211 (0.3290 to 0.5103)	
12 Months	0.5000 (0.3130 to 0.6612)	0.2381 (0.1234 to 0.3737)	0.2818 (0.1861 to 0.3853)	0.2957 (0.2142 to 0.3816)	
15 Months	0.4308 (0.2526 to 0.5972)	0.2143 (0.1061 to 0.3472)	0.2550 (0.1635 to 0.3566)	0.2468 (0.1707 to 0.3305)	
18 Months	0.3949 (0.2223 to 0.5632)	0.1339 (0.0509 to 0.2573)	0.2273 (0.1405 to 0.3269)	0.2361 (0.1612 to 0.3193)	
21 Months	0.3949 (0.2223 to 0.5632)	0.1339 (0.0509 to 0.2573)	0.2273 (0.1405 to 0.3269)	0.2254 (0.1518 to 0.3080)	
24 Months	0.3159 (0.1375 to 0.5121)	0.1339 (0.0509 to 0.2573)	0.2273 (0.1405 to 0.3269)	0.2254 (0.1518 to 0.3080)	
27 Months	0.3159 (0.1375 to 0.5121)	0.1339 (0.0509 to 0.2573)	0.2273 (0.1405 to 0.3269)	0.2254 (0.1518 to 0.3080)	

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
PGM=DEVOPS/SAR650984/EFC15246/CIR_RWE/REPORT/PGM/eff_km_sr_subgrp_sig_s_t.sas OUT=REPORT/OUTPUT/eff_km_de_tesev345_cyto_s_t_x.rtf (12FEB2021 8:13)

16.2.7.1 Safety endpoints
16.2.7.1.58 Subgroup analysis by cytogenetic abnormality (del(17p), t(4,14), t(14,16))
16.2.7.1.58.8 Treatment emergent severe adverse event including death by treatment group according to cytogenetic abnormality (del(17p), t(4,14), t(14,16)) - Safety population

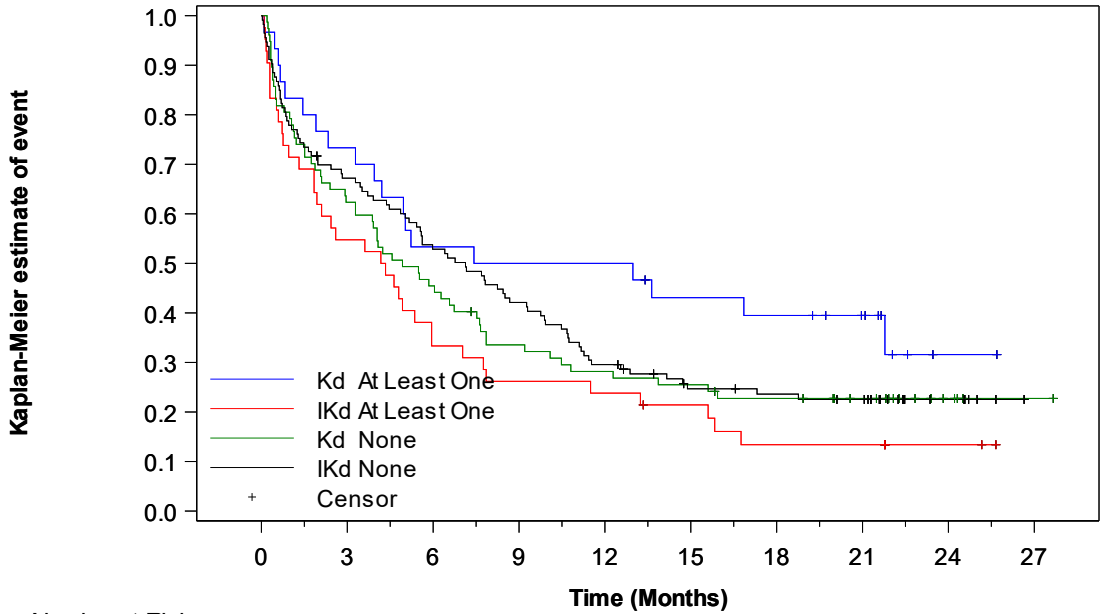
	At least one		None		
	Kd (N=30)	**IKd (N=42)**	**Kd (N=77)**	**IKd (N=113)**	**p-value of treatment-by-sub group interaction[c]**
30 Months	0.3159 (0.1375 to 0.5121)	0.1339 (0.0509 to 0.2573)	0.2273 (0.1405 to 0.3269)	0.2254 (0.1518 to 0.3080)	
Number of patients at risk[b]					
3 Months	22	23	48	75	
6 Months	16	14	35	59	
9 Months	15	11	25	47	
12 Months	15	10	21	33	
15 Months	12	8	19	24	
18 Months	11	5	16	22	
21 Months	8	5	12	20	
24 Months	1	2	4	6	
27 Months	0	0	1	0	
30 Months	0	0	0	0	

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
PGM=DEVOPS/SAR650984/EFC15246/CIR_RWE/REPORT/PGM/eff_km_sr_subgrp_sig_s_t.sas OUT=REPORT/OUTPUT/eff_km_de_tesev345_cyto_s_t_x.rtf (12FEB2021 8:13)

16.2.7.1 Safety endpoints

16.2.7.1.58 Subgroup analysis by cytogenetic abnormality (del(17p), t(4,14), t(14,16))

16.2.7.1.58.9 Kaplan-Meier cumulative incidence curve of treatment emergent severe adverse event including death by treatment group according to cytogenetic abnormality (del(17p), t(4,14), t(14,16)) - Safety population



Number at Risk										
Kd At Least One	30	22	16	15	15	12	11	8	1	0
IKd At Least One	42	23	14	11	10	8	5	5	2	0
Kd None	77	48	35	25	21	19	16	12	4	1
IKd None	113	75	59	47	33	24	22	20	6	0

16.2.7.1 Safety endpoints
16.2.7.1.59 Subgroup analysis by MM type
16.2.7.1.59.1 Treatment emergent adverse event by treatment group according to MM type - Safety population

	IgG		Non-IgG		
	Kd (N=85)	**IKd (N=124)**	**Kd (N=37)**	**IKd (N=53)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	83 (97.6)	120 (96.8)	34 (91.9)	52 (98.1)	0.1689
Number (%) of patients censored	2 (2.4)	4 (3.2)	3 (8.1)	1 (1.9)	
Kaplan-Meier estimates of TEAE in months					
25% quantile (95% CI)	0.1971 (0.0986 to 0.2300)	0.0986 (0.0657 to 0.1314)	0.1643 (0.0986 to 0.2628)	0.0657 (0.0329 to 0.0657)	
Median (95% CI)	0.5257 (0.3285 to 0.6242)	0.2300 (0.1643 to 0.3614)	0.3285 (0.2628 to 0.8214)	0.1314 (0.0657 to 0.1971)	
75% quantile (95% CI)	0.8871 (0.6571 to 1.4784)	0.8542 (0.4928 to 1.2485)	1.1828 (0.6242 to 2.9240)	0.2957 (0.1971 to 2.1355)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd		0.2376		0.0209	
Hazard ratio (95% CI) vs Kd		1.1841 (0.8943 to 1.5678)		1.6650 (1.0757 to 2.5773)	
P-value		0.2381		0.0222	

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
PGM=DEVOPS/SAR650984/EFC15246/CIR_RWE/REPORT/PGM/eff_km_sr_subgrp_sig_s_t.sas OUT=REPORT/OUTPUT/eff_km_de_teae_semm_s_t_x.rtf (12FEB2021 8:09)

16.2.7.1 Safety endpoints
16.2.7.1.59 Subgroup analysis by MM type
16.2.7.1.59.1 Treatment emergent adverse event by treatment group according to MM type - Safety population

	IgG		Non-IgG		
	Kd (N=85)	**IKd (N=124)**	**Kd (N=37)**	**IKd (N=53)**	**p-value of treatment-by-sub group interaction[c]**
Hazard ratio inverted (95% CI) vs IKd			0.6006 (0.3880 to 0.9297)		
probability (95% CI)[b]					
3 Months	0.0824 (0.0362 to 0.1527)	0.0645 (0.0302 to 0.1169)	0.1081 (0.0343 to 0.2305)	0.0943 (0.0347 to 0.1905)	
6 Months	0.0235 (0.0045 to 0.0741)	0.0484 (0.0199 to 0.0963)	0.1081 (0.0343 to 0.2305)	0.0377 (0.0070 to 0.1148)	
9 Months	0.0235 (0.0045 to 0.0741)	0.0323 (0.0106 to 0.0748)	0.1081 (0.0343 to 0.2305)	0.0377 (0.0070 to 0.1148)	
12 Months	0.0235 (0.0045 to 0.0741)	0.0323 (0.0106 to 0.0748)	0.1081 (0.0343 to 0.2305)	0.0189 (0.0015 to 0.0876)	
15 Months	0.0235 (0.0045 to 0.0741)	0.0323 (0.0106 to 0.0748)	0.0811 (0.0209 to 0.1957)	0.0189 (0.0015 to 0.0876)	
18 Months	0.0235 (0.0045 to 0.0741)	0.0323 (0.0106 to 0.0748)	0.0811 (0.0209 to 0.1957)	0.0189 (0.0015 to 0.0876)	
21 Months	0.0235 (0.0045 to 0.0741)	0.0323 (0.0106 to 0.0748)	0.0811 (0.0209 to 0.1957)	0.0189 (0.0015 to 0.0876)	
24 Months	0.0235 (0.0045 to 0.0741)	0.0323 (0.0106 to 0.0748)	0.0811 (0.0209 to 0.1957)	0.0189 (0.0015 to 0.0876)	

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
PGM=DEVOPS/SAR650984/EFC15246/CIR_RWE/REPORT/PGM/eff_km_sr_subgrp_sig_s_t.sas OUT=REPORT/OUTPUT/eff_km_de_teae_semm_s_t_x.rtf (12FEB2021 8:09)

16.2.7.1 Safety endpoints
16.2.7.1.59 Subgroup analysis by MM type
16.2.7.1.59.1 Treatment emergent adverse event by treatment group according to MM type - Safety population

	IgG		Non-IgG		
	Kd (N=85)	**IKd (N=124)**	**Kd (N=37)**	**IKd (N=53)**	**p-value of treatment-by-sub group interaction[c]**
27 Months	0.0235 (0.0045 to 0.0741)	0.0323 (0.0106 to 0.0748)	0.0811 (0.0209 to 0.1957)	0.0189 (0.0015 to 0.0876)	
30 Months	0.0235 (0.0045 to 0.0741)	0.0323 (0.0106 to 0.0748)	0.0811 (0.0209 to 0.1957)	0.0189 (0.0015 to 0.0876)	
Number of patients at risk[b]					
3 Months	7	8	4	5	
6 Months	2	6	4	2	
9 Months	2	4	4	2	
12 Months	2	4	4	1	
15 Months	2	4	3	1	
18 Months	2	4	3	1	
21 Months	2	4	1	1	
24 Months	1	1	0	0	
27 Months	0	0	0	0	
30 Months	0	0	0	0	

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
PGM=DEVOPS/SAR650984/EFC15246/CIR_RWE/REPORT/PGM/eff_km_sr_subgrp_sig_s_t.sas OUT=REPORT/OUTPUT/eff_km_de_teae_semm_s_t_x.rtf (12FEB2021 8:09)

16.2.7.1 Safety endpoints
16.2.7.1.59 Subgroup analysis by MM type
16.2.7.1.59.2 Treatment emergent serious adverse event by treatment group according to MM type - Safety population

	IgG		Non-IgG		
	Kd (N=85)	**IKd (N=124)**	**Kd (N=37)**	**IKd (N=53)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	51 (60.0)	75 (60.5)	19 (51.4)	30 (56.6)	0.8719
Number (%) of patients censored	34 (40.0)	49 (39.5)	18 (48.6)	23 (43.4)	
Kaplan-Meier estimates of TEAE in months					
25% quantile (95% CI)	4.9610 (2.9569 to 6.2752)	1.9055 (0.7228 to 5.1253)	4.6324 (1.1170 to 12.8131)	4.7639 (1.3142 to 7.6879)	
Median (95% CI)	13.6345 (6.9651 to 21.7823)	12.5010 (8.7392 to 18.1027)	13.8645 (5.8152 to NC)	12.9446 (6.7680 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd		0.7188		0.6659	
Hazard ratio (95% CI) vs Kd		1.0672 (0.7476 to 1.5233)		1.1350 (0.6386 to 2.0172)	
P-value		0.7203		0.6661	
probability (95% CI)[b]					

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
PGM=DEVOPS/SAR650984/EFC15246/CIR_RWE/REPORT/PGM/eff_km_sr_subgrp_sig_s_t.sas OUT=REPORT/OUTPUT/eff_km_de_tesae_semm_s_t_x.rtf (12FEB2021 8:12)

16.2.7.1 Safety endpoints
16.2.7.1.59 Subgroup analysis by MM type
16.2.7.1.59.2 Treatment emergent serious adverse event by treatment group according to MM type - Safety population

	IgG		Non-IgG		
	Kd (N=85)	**IKd (N=124)**	**Kd (N=37)**	**IKd (N=53)**	**p-value of treatment-by-sub group interaction[c]**
3 Months	0.8353 (0.7378 to 0.8990)	0.7177 (0.6296 to 0.7884)	0.7829 (0.6123 to 0.8850)	0.8113 (0.6777 to 0.8937)	
6 Months	0.6706 (0.5598 to 0.7594)	0.6532 (0.5624 to 0.7297)	0.6431 (0.4655 to 0.7749)	0.6773 (0.5331 to 0.7856)	
9 Months	0.5765 (0.4645 to 0.6732)	0.5887 (0.4969 to 0.6694)	0.6431 (0.4655 to 0.7749)	0.5806 (0.4357 to 0.7005)	
12 Months	0.5176 (0.4069 to 0.6175)	0.5161 (0.4249 to 0.5998)	0.6138 (0.4361 to 0.7505)	0.5031 (0.3615 to 0.6289)	
15 Months	0.4565 (0.3481 to 0.5585)	0.4331 (0.3445 to 0.5184)	0.4969 (0.3250 to 0.6472)	0.4611 (0.3216 to 0.5896)	
18 Months	0.4072 (0.3018 to 0.5098)	0.4154 (0.3275 to 0.5009)	0.4969 (0.3250 to 0.6472)	0.4150 (0.2781 to 0.5464)	
21 Months	0.4072 (0.3018 to 0.5098)	0.4064 (0.3189 to 0.4919)	0.4659 (0.2964 to 0.6189)	0.4150 (0.2781 to 0.5464)	
24 Months	0.3878 (0.2816 to 0.4926)	0.3866 (0.2996 to 0.4725)	0.4659 (0.2964 to 0.6189)	0.4150 (0.2781 to 0.5464)	
27 Months	0.3878 (0.2816 to 0.4926)	0.3866 (0.2996 to 0.4725)	0.4659 (0.2964 to 0.6189)	0.4150 (0.2781 to 0.5464)	
30 Months	0.3878 (0.2816 to 0.4926)	0.3866 (0.2996 to 0.4725)	0.4659 (0.2964 to 0.6189)	0.4150 (0.2781 to 0.5464)	

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
PGM=DEVOPS/SAR650984/EFC15246/CIR_RWE/REPORT/PGM/eff_km_sr_subgrp_sig_s_t.sas OUT=REPORT/OUTPUT/eff_km_de_tesae_semm_s_t_x.rtf (12FEB2021 8:12)

16.2.7.1 Safety endpoints
16.2.7.1.59 Subgroup analysis by MM type
16.2.7.1.59.2 Treatment emergent serious adverse event by treatment group according to MM type - Safety population

	IgG		Non-IgG		
	Kd (N=85)	**IKd (N=124)**	**Kd (N=37)**	**IKd (N=53)**	**p-value of treatment-by-sub group interaction[c]**
Number of patients at risk[b]					
3 Months	71	89	28	43	
6 Months	57	81	23	35	
9 Months	49	73	22	30	
12 Months	44	64	21	26	
15 Months	37	50	17	21	
18 Months	33	46	16	18	
21 Months	26	42	10	15	
24 Months	6	14	3	5	
27 Months	1	1	1	0	
30 Months	0	0	0	0	

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
PGM=DEVOPS/SAR650984/EFC15246/CIR_RWE/REPORT/PGM/eff_km_sr_subgrp_sig_s_t.sas OUT=REPORT/OUTPUT/eff_km_de_tesae_semm_s_t_x.rtf (12FEB2021 8:12)

16.2.7.1 Safety endpoints
16.2.7.1.59 Subgroup analysis by MM type
16.2.7.1.59.3 Treatment emergent adverse event leading to discontinuation of treatment by treatment group according to MM type - Safety population

	IgG		Non-IgG		
	Kd (N=85)	**IKd (N=124)**	**Kd (N=37)**	**IKd (N=53)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	13 (15.3)	12 (9.7)	4 (10.8)	3 (5.7)	0.8175
Number (%) of patients censored	72 (84.7)	112 (90.3)	33 (89.2)	50 (94.3)	
Kaplan-Meier estimates of TEAE in months					
25% quantile (95% CI)	NC (15.3758 to NC)	NC (NC to NC)	NC (18.2669 to NC)	NC (NC to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd		0.2142		0.3659	
Hazard ratio (95% CI) vs Kd		0.6112 (0.2789 to 1.3397)		0.5079 (0.1137 to 2.2693)	
P-value		0.2189		0.3750	
probability (95% CI)[b]					
3 Months	0.9527 (0.8787 to 0.9820)	0.9674 (0.9155 to 0.9876)	0.9730 (0.8232 to 0.9961)	0.9811 (0.8735 to 0.9973)	

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
PGM=DEVOPS/SAR650984/EFC15246/CIR_RWE/REPORT/PGM/eff_km_sr_subgrp_sig_s_t.sas OUT=REPORT/OUTPUT/eff_km_de_tedisc_semm_s_t_x.rtf (12FEB2021 8:12)

16.2.7.1 Safety endpoints
16.2.7.1.59 Subgroup analysis by MM type
16.2.7.1.59.3 Treatment emergent adverse event leading to discontinuation of treatment by treatment group according to MM type - Safety population

	IgG		Non-IgG		
	Kd (N=85)	**IKd (N=124)**	**Kd (N=37)**	**IKd (N=53)**	**p-value of treatment-by-sub group interaction[c]**
6 Months	0.9287 (0.8481 to 0.9673)	0.9508 (0.8938 to 0.9776)	0.9435 (0.7920 to 0.9856)	0.9419 (0.8303 to 0.9809)	
9 Months	0.8674 (0.7733 to 0.9243)	0.9258 (0.8622 to 0.9607)	0.9140 (0.7562 to 0.9715)	0.9419 (0.8303 to 0.9809)	
12 Months	0.8674 (0.7733 to 0.9243)	0.9258 (0.8622 to 0.9607)	0.9140 (0.7562 to 0.9715)	0.9419 (0.8303 to 0.9809)	
15 Months	0.8674 (0.7733 to 0.9243)	0.9084 (0.8406 to 0.9482)	0.9140 (0.7562 to 0.9715)	0.9419 (0.8303 to 0.9809)	
18 Months	0.8403 (0.7405 to 0.9041)	0.9084 (0.8406 to 0.9482)	0.9140 (0.7562 to 0.9715)	0.9419 (0.8303 to 0.9809)	
21 Months	0.8403 (0.7405 to 0.9041)	0.8986 (0.8282 to 0.9412)	0.8802 (0.7100 to 0.9535)	0.9419 (0.8303 to 0.9809)	
24 Months	0.8403 (0.7405 to 0.9041)	0.8986 (0.8282 to 0.9412)	0.8802 (0.7100 to 0.9535)	0.9419 (0.8303 to 0.9809)	
27 Months	0.8403 (0.7405 to 0.9041)	0.8986 (0.8282 to 0.9412)	0.8802 (0.7100 to 0.9535)	0.9419 (0.8303 to 0.9809)	
30 Months	0.8403 (0.7405 to 0.9041)	0.8986 (0.8282 to 0.9412)	0.8802 (0.7100 to 0.9535)	0.9419 (0.8303 to 0.9809)	

Number of patients at risk[b]

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
PGM=DEVOPS/SAR650984/EFC15246/CIR_RWE/REPORT/PGM/eff_km_sr_subgrp_sig_s_t.sas OUT=REPORT/OUTPUT/eff_km_de_tedisc_semm_s_t_x.rtf (12FEB2021 8:12)

16.2.7.1 Safety endpoints
16.2.7.1.59 Subgroup analysis by MM type
16.2.7.1.59.3 Treatment emergent adverse event leading to discontinuation of treatment by treatment group according to MM type - Safety population

	IgG		Non-IgG		
	Kd (N=85)	**IKd (N=124)**	**Kd (N=37)**	**IKd (N=53)**	**p-value of treatment-by-sub group interaction[c]**
3 Months	80	118	35	52	
6 Months	76	114	32	47	
9 Months	70	111	29	44	
12 Months	69	108	28	44	
15 Months	64	99	28	41	
18 Months	62	93	27	40	
21 Months	54	84	19	34	
24 Months	19	29	7	11	
27 Months	3	2	1	0	
30 Months	0	0	0	0	

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
PGM=DEVOPS/SAR650984/EFC15246/CIR_RWE/REPORT/PGM/eff_km_sr_subgrp_sig_s_t.sas OUT=REPORT/OUTPUT/eff_km_de_tedisc_semm_s_t_x.rtf (12FEB2021 8:12)

16.2.7.1 Safety endpoints
16.2.7.1.59 Subgroup analysis by MM type
16.2.7.1.59.4 Treatment emergent mild adverse event by treatment group according to MM type - Safety population

	IgG		Non-IgG		
	Kd (N=85)	**IKd (N=124)**	**Kd (N=37)**	**IKd (N=53)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	82 (96.5)	117 (94.4)	33 (89.2)	50 (94.3)	0.2397
Number (%) of patients censored	3 (3.5)	7 (5.6)	4 (10.8)	3 (5.7)	
Kaplan-Meier estimates of TEAE in months					
25% quantile (95% CI)	0.1971 (0.0986 to 0.2628)	0.0986 (0.0657 to 0.1314)	0.1643 (0.0986 to 0.2957)	0.0657 (0.0329 to 0.0657)	
Median (95% CI)	0.5257 (0.3614 to 0.6571)	0.2300 (0.1643 to 0.3614)	0.3943 (0.2628 to 0.8214)	0.1314 (0.0657 to 0.1971)	
75% quantile (95% CI)	1.0513 (0.6899 to 1.9384)	1.0185 (0.6242 to 1.4784)	1.1828 (0.6571 to 2.9240)	0.3943 (0.1971 to 2.4969)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd		0.2806		0.0475	
Hazard ratio (95% CI) vs Kd		1.1684 (0.8804 to 1.5506)		1.5619 (1.0015 to 2.4358)	
P-value		0.2811		0.0492	

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.59 Subgroup analysis by MM type
16.2.7.1.59.4 Treatment emergent mild adverse event by treatment group according to MM type - Safety population

	IgG		Non-IgG		
	Kd (N=85)	**IKd (N=124)**	**Kd (N=37)**	**IKd (N=53)**	**p-value of treatment-by-sub group interaction[c]**
Hazard ratio inverted (95% CI) vs IKd			0.6403 (0.4105 to 0.9985)		
probability (95% CI)[b]					
3 Months	0.1176 (0.0603 to 0.1959)	0.1073 (0.0604 to 0.1696)	0.1149 (0.0366 to 0.2427)	0.1132 (0.0460 to 0.2141)	
6 Months	0.0471 (0.0153 to 0.1070)	0.0743 (0.0365 to 0.1298)	0.1149 (0.0366 to 0.2427)	0.0679 (0.0191 to 0.1608)	
9 Months	0.0471 (0.0153 to 0.1070)	0.0464 (0.0180 to 0.0958)	0.1149 (0.0366 to 0.2427)	0.0679 (0.0191 to 0.1608)	
12 Months	0.0471 (0.0153 to 0.1070)	0.0464 (0.0180 to 0.0958)	0.1149 (0.0366 to 0.2427)	0.0453 (0.0088 to 0.1319)	
15 Months	0.0314 (0.0070 to 0.0894)	0.0464 (0.0180 to 0.0958)	0.0861 (0.0222 to 0.2061)	0.0453 (0.0088 to 0.1319)	
18 Months	0.0314 (0.0070 to 0.0894)	0.0464 (0.0180 to 0.0958)	0.0861 (0.0222 to 0.2061)	0.0453 (0.0088 to 0.1319)	
21 Months	0.0314 (0.0070 to 0.0894)	0.0464 (0.0180 to 0.0958)	0.0861 (0.0222 to 0.2061)	0.0453 (0.0088 to 0.1319)	
24 Months	0.0314 (0.0070 to 0.0894)	0.0464 (0.0180 to 0.0958)	0.0861 (0.0222 to 0.2061)	0.0453 (0.0088 to 0.1319)	

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
PGM=DEVOPS/SAR650984/EFC15246/CIR_RWE/REPORT/PGM/eff_km_sr_subgrp_sig_s_t.sas OUT=REPORT/OUTPUT/eff_km_de_tesev12_semm_s_t_x.rtf (12FEB2021 8:13)

16.2.7.1 Safety endpoints
16.2.7.1.59 Subgroup analysis by MM type
16.2.7.1.59.4 Treatment emergent mild adverse event by treatment group according to MM type - Safety population

	IgG		Non-IgG		
	Kd (N=85)	**IKd (N=124)**	**Kd (N=37)**	**IKd (N=53)**	**p-value of treatment-by-sub group interaction[c]**
27 Months	0.0314 (0.0070 to 0.0894)	0.0464 (0.0180 to 0.0958)	0.0861 (0.0222 to 0.2061)	0.0453 (0.0088 to 0.1319)	
30 Months	0.0314 (0.0070 to 0.0894)	0.0464 (0.0180 to 0.0958)	0.0861 (0.0222 to 0.2061)	0.0453 (0.0088 to 0.1319)	
Number of patients at risk[b]					
3 Months	10	13	4	6	
6 Months	4	8	4	3	
9 Months	4	5	4	3	
12 Months	3	5	4	2	
15 Months	2	5	3	1	
18 Months	2	5	3	1	
21 Months	2	5	1	1	
24 Months	1	1	0	0	
27 Months	0	0	0	0	
30 Months	0	0	0	0	

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
PGM=DEVOPS/SAR650984/EFC15246/CIR_RWE/REPORT/PGM/eff_km_sr_subgrp_sig_s_t.sas OUT=REPORT/OUTPUT/eff_km_de_tesev12_semm_s_t_x.rtf (12FEB2021 8:13)

16.2.7.1 Safety endpoints
16.2.7.1.59 Subgroup analysis by MM type
16.2.7.1.59.5 Treatment emergent severe adverse event by treatment group according to MM type - Safety population

	IgG		Non-IgG		
	Kd (N=85)	**IKd (N=124)**	**Kd (N=37)**	**IKd (N=53)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	59 (69.4)	95 (76.6)	22 (59.5)	39 (73.6)	0.6294
Number (%) of patients censored	26 (30.6)	29 (23.4)	15 (40.5)	14 (26.4)	
Kaplan-Meier estimates of TEAE in months					
25% quantile (95% CI)	2.3984 (0.6571 to 3.9097)	1.0513 (0.6242 to 2.0041)	1.8727 (0.3943 to 5.2238)	1.4784 (0.5914 to 3.7125)	
Median (95% CI)	6.2752 (4.2053 to 9.1992)	5.9795 (4.3368 to 8.6735)	12.2875 (2.3326 to NC)	5.6181 (3.6140 to 7.8522)	
75% quantile (95% CI)	NC (12.3532 to NC)	15.6057 (11.1047 to NC)	NC (16.8542 to NC)	NC (7.7864 to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd		0.2720		0.2353	
Hazard ratio (95% CI) vs Kd		1.1997 (0.8665 to 1.6610)		1.3716 (0.8122 to 2.3165)	
P-value		0.2727		0.2372	
probability (95% CI)[b]					

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
PGM=DEVOPS/SAR650984/EFC15246/CIR_RWE/REPORT/PGM/eff_km_sr_subgrp_sig_s_t.sas OUT=REPORT/OUTPUT/eff_km_de_tesev34_semm_s_t_x.rtf (12FEB2021 8:13)

16.2.7.1 Safety endpoints
16.2.7.1.59 Subgroup analysis by MM type
16.2.7.1.59.5 Treatment emergent severe adverse event by treatment group according to MM type - Safety population

	IgG		Non-IgG		
	Kd (N=85)	**IKd (N=124)**	**Kd (N=37)**	**IKd (N=53)**	**p-value of treatment-by-sub group interaction[c]**
3 Months	0.7161 (0.6070 to 0.7998)	0.6343 (0.5426 to 0.7125)	0.6475 (0.4714 to 0.7779)	0.6604 (0.5164 to 0.7706)	
6 Months	0.5251 (0.4135 to 0.6252)	0.4943 (0.4029 to 0.5791)	0.5631 (0.3886 to 0.7054)	0.4528 (0.3163 to 0.5797)	
9 Months	0.4058 (0.3007 to 0.5082)	0.4119 (0.3241 to 0.4974)	0.5334 (0.3602 to 0.6793)	0.3396 (0.2168 to 0.4664)	
12 Months	0.3581 (0.2573 to 0.4597)	0.2966 (0.2182 to 0.3789)	0.5038 (0.3324 to 0.6526)	0.3019 (0.1853 to 0.4270)	
15 Months	0.3338 (0.2356 to 0.4348)	0.2508 (0.1770 to 0.3313)	0.4149 (0.2530 to 0.5694)	0.2830 (0.1699 to 0.4070)	
18 Months	0.3090 (0.2137 to 0.4092)	0.2215 (0.1510 to 0.3006)	0.3830 (0.2252 to 0.5391)	0.2594 (0.1497 to 0.3834)	
21 Months	0.3090 (0.2137 to 0.4092)	0.2114 (0.1422 to 0.2900)	0.3830 (0.2252 to 0.5391)	0.2594 (0.1497 to 0.3834)	
24 Months	0.2919 (0.1973 to 0.3928)	0.2114 (0.1422 to 0.2900)	0.3830 (0.2252 to 0.5391)	0.2594 (0.1497 to 0.3834)	
27 Months	0.2919 (0.1973 to 0.3928)	0.2114 (0.1422 to 0.2900)	0.3830 (0.2252 to 0.5391)	0.2594 (0.1497 to 0.3834)	
30 Months	0.2919 (0.1973 to 0.3928)	0.2114 (0.1422 to 0.2900)	0.3830 (0.2252 to 0.5391)	0.2594 (0.1497 to 0.3834)	

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
PGM=DEVOPS/SAR650984/EFC15246/CIR_RWE/REPORT/PGM/eff_km_sr_subgrp_sig_s_t.sas OUT=REPORT/OUTPUT/eff_km_de_tesev34_semm_s_t_x.rtf (12FEB2021 8:13)

16.2.7.1 Safety endpoints
16.2.7.1.59 Subgroup analysis by MM type
16.2.7.1.59.5 Treatment emergent severe adverse event by treatment group according to MM type - Safety population

	IgG		Non-IgG		
	Kd (N=85)	**IKd (N=124)**	**Kd (N=37)**	**IKd (N=53)**	**p-value of treatment-by-sub group interaction[c]**
Number of patients at risk[b]					
3 Months	60	77	23	35	
6 Months	44	60	20	24	
9 Months	34	50	18	18	
12 Months	30	36	17	16	
15 Months	27	26	14	13	
18 Months	25	22	12	11	
21 Months	21	21	6	10	
24 Months	7	7	1	3	
27 Months	1	0	0	0	
30 Months	0	0	0	0	

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
PGM=DEVOPS/SAR650984/EFC15246/CIR_RWE/REPORT/PGM/eff_km_sr_subgrp_sig_s_t.sas OUT=REPORT/OUTPUT/eff_km_de_tesev34_semm_s_t_x.rtf (12FEB2021 8:13)

16.2.7.1 Safety endpoints
16.2.7.1.59 Subgroup analysis by MM type
16.2.7.1.59.6 Treatment emergent severe adverse event including death by treatment group according to MM type - Safety population

	IgG		Non-IgG		
	Kd (N=85)	**IKd (N=124)**	**Kd (N=37)**	**IKd (N=53)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	60 (70.6)	97 (78.2)	22 (59.5)	39 (73.6)	0.6383
Number (%) of patients censored	25 (29.4)	27 (21.8)	15 (40.5)	14 (26.4)	
Kaplan-Meier estimates of TEAE in months					
25% quantile (95% CI)	2.0698 (0.6571 to 3.8768)	1.0021 (0.6242 to 1.9713)	1.8727 (0.3943 to 5.2238)	1.4784 (0.5914 to 3.7125)	
Median (95% CI)	6.2752 (4.0739 to 9.1992)	5.9466 (4.1725 to 8.6735)	12.2875 (2.3326 to NC)	5.6181 (3.6140 to 7.8522)	
75% quantile (95% CI)	NC (12.3532 to NC)	14.8830 (11.1047 to NC)	NC (16.8542 to NC)	NC (7.7864 to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd		0.2548		0.2353	
Hazard ratio (95% CI) vs Kd		1.2057 (0.8734 to 1.6643)		1.3716 (0.8122 to 2.3165)	
P-value		0.2555		0.2372	
probability (95% CI)[b]					

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
PGM=DEVOPS/SAR650984/EFC15246/CIR_RWE/REPORT/PGM/eff_km_sr_subgrp_sig_s_t.sas OUT=REPORT/OUTPUT/eff_km_de_tesev345_semm_s_t_x.rtf (12FEB2021 8:13)

16.2.7.1 Safety endpoints
16.2.7.1.59 Subgroup analysis by MM type
16.2.7.1.59.6 Treatment emergent severe adverse event including death by treatment group according to MM type - Safety population

	IgG		Non-IgG		
	Kd (N=85)	**IKd (N=124)**	**Kd (N=37)**	**IKd (N=53)**	**p-value of treatment-by-sub group interaction[c]**
3 Months	0.7059 (0.5966 to 0.7907)	0.6284 (0.5369 to 0.7067)	0.6475 (0.4714 to 0.7779)	0.6604 (0.5164 to 0.7706)	
6 Months	0.5176 (0.4069 to 0.6175)	0.4896 (0.3988 to 0.5742)	0.5631 (0.3886 to 0.7054)	0.4528 (0.3163 to 0.5797)	
9 Months	0.4000 (0.2960 to 0.5018)	0.4080 (0.3209 to 0.4931)	0.5334 (0.3602 to 0.6793)	0.3396 (0.2168 to 0.4664)	
12 Months	0.3529 (0.2533 to 0.4539)	0.2938 (0.2160 to 0.3756)	0.5038 (0.3324 to 0.6526)	0.3019 (0.1853 to 0.4270)	
15 Months	0.3290 (0.2320 to 0.4292)	0.2409 (0.1689 to 0.3202)	0.4149 (0.2530 to 0.5694)	0.2830 (0.1699 to 0.4070)	
18 Months	0.3046 (0.2104 to 0.4039)	0.2127 (0.1442 to 0.2903)	0.3830 (0.2252 to 0.5391)	0.2594 (0.1497 to 0.3834)	
21 Months	0.3046 (0.2104 to 0.4039)	0.2031 (0.1358 to 0.2800)	0.3830 (0.2252 to 0.5391)	0.2594 (0.1497 to 0.3834)	
24 Months	0.2877 (0.1944 to 0.3877)	0.2031 (0.1358 to 0.2800)	0.3830 (0.2252 to 0.5391)	0.2594 (0.1497 to 0.3834)	
27 Months	0.2877 (0.1944 to 0.3877)	0.2031 (0.1358 to 0.2800)	0.3830 (0.2252 to 0.5391)	0.2594 (0.1497 to 0.3834)	
30 Months	0.2877 (0.1944 to 0.3877)	0.2031 (0.1358 to 0.2800)	0.3830 (0.2252 to 0.5391)	0.2594 (0.1497 to 0.3834)	

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.59 Subgroup analysis by MM type
16.2.7.1.59.6 Treatment emergent severe adverse event including death by treatment group according to MM type - Safety population

	IgG		Non-IgG		
	Kd (N=85)	**IKd (N=124)**	**Kd (N=37)**	**IKd (N=53)**	**p-value of treatment-by-sub group interaction[c]**
Number of patients at risk[b]					
3 Months	60	77	23	35	
6 Months	44	60	20	24	
9 Months	34	50	18	18	
12 Months	30	36	17	16	
15 Months	27	26	14	13	
18 Months	25	22	12	11	
21 Months	21	21	6	10	
24 Months	7	7	1	3	
27 Months	1	0	0	0	
30 Months	0	0	0	0	

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.60 Subgroup analysis by previous autologous stem-cell
16.2.7.1.60.1 Treatment emergent adverse event by treatment group according to previous autologous stem-cell - Safety population

	Yes		No		
	Kd (N=68)	**IKd (N=115)**	**Kd (N=54)**	**IKd (N=62)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	64 (94.1)	112 (97.4)	53 (98.1)	60 (96.8)	0.0320
Number (%) of patients censored	4 (5.9)	3 (2.6)	1 (1.9)	2 (3.2)	
Kaplan-Meier estimates of TEAE in months					
25% quantile (95% CI)	0.1971 (0.0986 to 0.2628)	0.0657 (NC to NC)	0.1971 (0.0657 to 0.2300)	0.1314 (0.0657 to 0.1643)	
Median (95% CI)	0.5092 (0.2957 to 0.6242)	0.1643 (0.0986 to 0.1971)	0.3614 (0.2300 to 0.5914)	0.2628 (0.1643 to 0.4928)	
75% quantile (95% CI)	1.6756 (0.6899 to 2.9240)	0.6242 (0.2957 to 0.9528)	0.6899 (0.5914 to 1.0513)	1.0185 (0.6242 to 1.4784)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd		0.0046		0.6583	
Hazard ratio (95% CI) vs Kd		1.5578 (1.1435 to 2.1221)		0.9187 (0.6317 to 1.3362)	
P-value		0.0049		0.6573	

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
PGM=DEVOPS/SAR650984/EFC15246/CIR_RWE/REPORT/PGM/eff_km_sr_subgrp_sig_s_t.sas OUT=REPORT/OUTPUT/eff_km_de_teae_auto_s_t_x.rtf (12FEB2021 8:09)

16.2.7.1 Safety endpoints
16.2.7.1.60 Subgroup analysis by previous autologous stem-cell
16.2.7.1.60.1 Treatment emergent adverse event by treatment group according to previous autologous stem-cell - Safety population

	Yes		No		
	Kd (N=68)	**IKd (N=115)**	**Kd (N=54)**	**IKd (N=62)**	**p-value of treatment-by-sub group interaction[c]**
Hazard ratio inverted (95% CI) vs IKd	0.6419 (0.4712 to 0.8745)				
probability (95% CI)[b]					
3 Months	0.1324 (0.0651 to 0.2239)	0.0783 (0.0384 to 0.1365)	0.0370 (0.0069 to 0.1129)	0.0645 (0.0208 to 0.1438)	
6 Months	0.0588 (0.0190 to 0.1319)	0.0522 (0.0214 to 0.1035)	0.0370 (0.0069 to 0.1129)	0.0323 (0.0061 to 0.0994)	
9 Months	0.0588 (0.0190 to 0.1319)	0.0348 (0.0114 to 0.0803)	0.0370 (0.0069 to 0.1129)	0.0323 (0.0061 to 0.0994)	
12 Months	0.0588 (0.0190 to 0.1319)	0.0261 (0.0071 to 0.0683)	0.0370 (0.0069 to 0.1129)	0.0323 (0.0061 to 0.0994)	
15 Months	0.0588 (0.0190 to 0.1319)	0.0261 (0.0071 to 0.0683)	0.0185 (0.0015 to 0.0862)	0.0323 (0.0061 to 0.0994)	
18 Months	0.0588 (0.0190 to 0.1319)	0.0261 (0.0071 to 0.0683)	0.0185 (0.0015 to 0.0862)	0.0323 (0.0061 to 0.0994)	
21 Months	0.0588 (0.0190 to 0.1319)	0.0261 (0.0071 to 0.0683)	0.0185 (0.0015 to 0.0862)	0.0323 (0.0061 to 0.0994)	
24 Months	0.0588 (0.0190 to 0.1319)	0.0261 (0.0071 to 0.0683)	0.0185 (0.0015 to 0.0862)	0.0323 (0.0061 to 0.0994)	

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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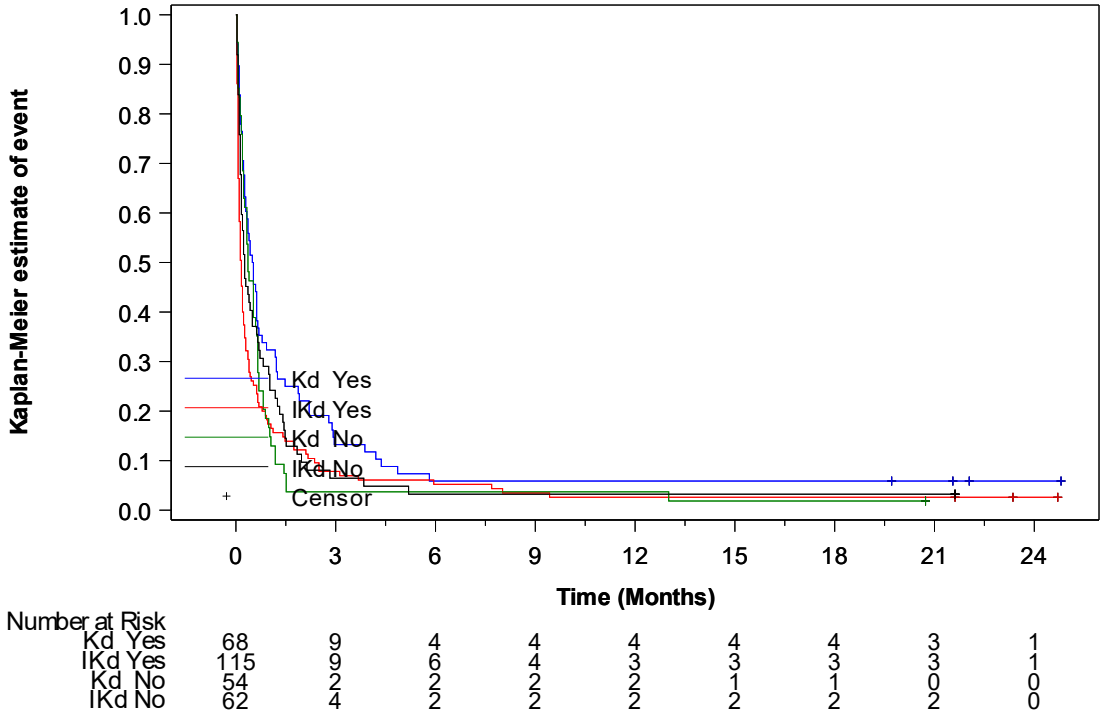
16.2.7.1 Safety endpoints
16.2.7.1.60 Subgroup analysis by previous autologous stem-cell
16.2.7.1.60.1 Treatment emergent adverse event by treatment group according to previous autologous stem-cell - Safety population

	Yes		No		
	Kd (N=68)	**IKd (N=115)**	**Kd (N=54)**	**IKd (N=62)**	**p-value of treatment-by-sub group interaction[c]**
27 Months	0.0588 (0.0190 to 0.1319)	0.0261 (0.0071 to 0.0683)	0.0185 (0.0015 to 0.0862)	0.0323 (0.0061 to 0.0994)	
30 Months	0.0588 (0.0190 to 0.1319)	0.0261 (0.0071 to 0.0683)	0.0185 (0.0015 to 0.0862)	0.0323 (0.0061 to 0.0994)	
Number of patients at risk[b]					
3 Months	9	9	2	4	
6 Months	4	6	2	2	
9 Months	4	4	2	2	
12 Months	4	3	2	2	
15 Months	4	3	1	2	
18 Months	4	3	1	2	
21 Months	3	3	0	2	
24 Months	1	1	0	0	
27 Months	0	0	0	0	
30 Months	0	0	0	0	

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
PGM=DEVOPS/SAR650984/EFC15246/CIR_RWE/REPORT/PGM/eff_km_sr_subgrp_sig_s_t.sas OUT=REPORT/OUTPUT/eff_km_de_teae_auto_s_t_x.rtf (12FEB2021 8:09)

16.2.7.1 Safety endpoints
16.2.7.1.60 Subgroup analysis by previous autologous stem-cell
16.2.7.1.60.2 Kaplan-Meier cumulative incidence curve of treatment emergent adverse event by treatment group according to previous autologous stem-cell - Safety population



Number at Risk

Kd Yes	68	9	4	4	4	4	4	3	1
IKd Yes	115	9	6	4	3	3	3	3	1
Kd No	54	2	2	2	2	1	1	0	0
IKd No	62	4	2	2	2	2	2	2	0

16.2.7.1 Safety endpoints
16.2.7.1.60 Subgroup analysis by previous autologous stem-cell
16.2.7.1.60.3 Treatment emergent serious adverse event by treatment group according to previous autologous stem-cell - Safety population

	Yes		No		
	Kd (N=68)	**IKd (N=115)**	**Kd (N=54)**	**IKd (N=62)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	35 (51.5)	61 (53.0)	35 (64.8)	44 (71.0)	0.8132
Number (%) of patients censored	33 (48.5)	54 (47.0)	19 (35.2)	18 (29.0)	
Kaplan-Meier estimates of TEAE in months					
25% quantile (95% CI)	5.5524 (3.9425 to 10.4805)	4.5010 (1.5441 to 7.6879)	2.0698 (0.6571 to 5.0267)	1.2485 (0.4600 to 3.8439)	
Median (95% CI)	15.9343 (11.2361 to NC)	14.8830 (9.9548 to NC)	9.2485 (5.0267 to 15.6057)	8.8542 (3.8439 to 12.5503)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (15.6057 to NC)	NC (12.8131 to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd		0.6556		0.4698	
Hazard ratio (95% CI) vs Kd		1.0992 (0.7253 to 1.6657)		1.1778 (0.7553 to 1.8365)	
P-value		0.6558		0.4703	
probability (95% CI)[b]					

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
PGM=DEVOPS/SAR650984/EFC15246/CIR_RWE/REPORT/PGM/eff_km_sr_subgrp_sig_s_t.sas OUT=REPORT/OUTPUT/eff_km_de_tesae_auto_s_t_x.rtf (12FEB2021 8:12)

16.2.7.1 Safety endpoints
16.2.7.1.60 Subgroup analysis by previous autologous stem-cell
16.2.7.1.60.3 Treatment emergent serious adverse event by treatment group according to previous autologous stem-cell - Safety population

	Yes		No		
	Kd (N=68)	**IKd (N=115)**	**Kd (N=54)**	**IKd (N=62)**	**p-value of treatment-by-sub group interaction[c]**
3 Months	0.8819 (0.7776 to 0.9391)	0.7826 (0.6955 to 0.8475)	0.7407 (0.6019 to 0.8375)	0.6774 (0.5459 to 0.7784)	
6 Months	0.7473 (0.6254 to 0.8347)	0.7213 (0.6296 to 0.7940)	0.5556 (0.4139 to 0.6759)	0.5484 (0.4169 to 0.6620)	
9 Months	0.6720 (0.5457 to 0.7703)	0.6334 (0.5381 to 0.7142)	0.5000 (0.3612 to 0.6239)	0.5000 (0.3706 to 0.6163)	
12 Months	0.6109 (0.4833 to 0.7160)	0.5542 (0.4584 to 0.6398)	0.4630 (0.3268 to 0.5884)	0.4355 (0.3107 to 0.5537)	
15 Months	0.5320 (0.4048 to 0.6437)	0.4974 (0.4020 to 0.5856)	0.3889 (0.2604 to 0.5154)	0.3387 (0.2247 to 0.4561)	
18 Months	0.4826 (0.3569 to 0.5973)	0.4569 (0.3621 to 0.5467)	0.3704 (0.2442 to 0.4967)	0.3387 (0.2247 to 0.4561)	
21 Months	0.4659 (0.3411 to 0.5814)	0.4569 (0.3621 to 0.5467)	0.3704 (0.2442 to 0.4967)	0.3218 (0.2100 to 0.4387)	
24 Months	0.4659 (0.3411 to 0.5814)	0.4569 (0.3621 to 0.5467)	0.3395 (0.2131 to 0.4701)	0.2860 (0.1792 to 0.4020)	
27 Months	0.4659 (0.3411 to 0.5814)	0.4569 (0.3621 to 0.5467)	0.3395 (0.2131 to 0.4701)	0.2860 (0.1792 to 0.4020)	
30 Months	0.4659 (0.3411 to 0.5814)	0.4569 (0.3621 to 0.5467)	0.3395 (0.2131 to 0.4701)	0.2860 (0.1792 to 0.4020)	

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
PGM=DEVOPS/SAR650984/EFC15246/CIR_RWE/REPORT/PGM/eff_km_sr_subgrp_sig_s_t.sas OUT=REPORT/OUTPUT/eff_km_de_tesae_auto_s_t_x.rtf (12FEB2021 8:12)

16.2.7.1 Safety endpoints
16.2.7.1.60 Subgroup analysis by previous autologous stem-cell
16.2.7.1.60.3 Treatment emergent serious adverse event by treatment group according to previous autologous stem-cell - Safety population

	Yes		No		
	Kd (N=68)	**IKd (N=115)**	**Kd (N=54)**	**IKd (N=62)**	**p-value of treatment-by-sub group interaction[c]**
Number of patients at risk[b]					
3 Months	59	90	40	42	
6 Months	50	82	30	34	
9 Months	44	72	27	31	
12 Months	40	63	25	27	
15 Months	33	51	21	20	
18 Months	29	44	20	20	
21 Months	20	39	16	18	
24 Months	6	14	3	5	
27 Months	0	1	2	0	
30 Months	0	0	0	0	

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
PGM=DEVOPS/SAR650984/EFC15246/CIR_RWE/REPORT/PGM/eff_km_sr_subgrp_sig_s_t.sas OUT=REPORT/OUTPUT/eff_km_de_tesae_auto_s_t_x.rtf (12FEB2021 8:12)

16.2.7.1 Safety endpoints
16.2.7.1.60 Subgroup analysis by previous autologous stem-cell
16.2.7.1.60.4 Treatment emergent adverse event leading to discontinuation of treatment by treatment group according to previous autologous stem-cell - Safety population

	Yes		No		
	Kd (N=68)	**IKd (N=115)**	**Kd (N=54)**	**IKd (N=62)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	6 (8.8)	10 (8.7)	11 (20.4)	5 (8.1)	0.1955
Number (%) of patients censored	62 (91.2)	105 (91.3)	43 (79.6)	57 (91.9)	
Kaplan-Meier estimates of TEAE in months					
25% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (7.3922 to NC)	NC (NC to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd		0.9607		0.0574	
Hazard ratio (95% CI) vs Kd		0.9748 (0.3543 to 2.6823)		0.3735 (0.1298 to 1.0751)	
P-value		0.9606		0.0679	
probability (95% CI)[b]					
3 Months	1.0000 (1.0000 to 1.0000)	0.9737 (0.9206 to 0.9914)	0.9067 (0.7901 to 0.9601)	0.9675 (0.8761 to 0.9918)	

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
PGM=DEVOPS/SAR650984/EFC15246/CIR_RWE/REPORT/PGM/eff_km_sr_subgrp_sig_s_t.sas OUT=REPORT/OUTPUT/eff_km_de_tedisc_auto_s_t_x.rtf (12FEB2021 8:12)

16.2.7.1 Safety endpoints
16.2.7.1.60 Subgroup analysis by previous autologous stem-cell
16.2.7.1.60.4 Treatment emergent adverse event leading to discontinuation of treatment by treatment group according to previous autologous stem-cell - Safety population

	Yes		No		
	Kd (N=68)	**IKd (N=115)**	**Kd (N=54)**	**IKd (N=62)**	**p-value of treatment-by-sub group interaction[c]**
6 Months	0.9699 (0.8850 to 0.9924)	0.9469 (0.8856 to 0.9758)	0.8870 (0.7654 to 0.9476)	0.9508 (0.8551 to 0.9839)	
9 Months	0.9235 (0.8258 to 0.9674)	0.9288 (0.8626 to 0.9637)	0.8274 (0.6941 to 0.9063)	0.9335 (0.8323 to 0.9745)	
12 Months	0.9235 (0.8258 to 0.9674)	0.9288 (0.8626 to 0.9637)	0.8274 (0.6941 to 0.9063)	0.9335 (0.8323 to 0.9745)	
15 Months	0.9235 (0.8258 to 0.9674)	0.9192 (0.8504 to 0.9571)	0.8274 (0.6941 to 0.9063)	0.9156 (0.8087 to 0.9640)	
18 Months	0.9064 (0.8031 to 0.9569)	0.9192 (0.8504 to 0.9571)	0.8056 (0.6681 to 0.8906)	0.9156 (0.8087 to 0.9640)	
21 Months	0.9064 (0.8031 to 0.9569)	0.9086 (0.8365 to 0.9499)	0.7838 (0.6428 to 0.8744)	0.9156 (0.8087 to 0.9640)	
24 Months	0.9064 (0.8031 to 0.9569)	0.9086 (0.8365 to 0.9499)	0.7838 (0.6428 to 0.8744)	0.9156 (0.8087 to 0.9640)	
27 Months	0.9064 (0.8031 to 0.9569)	0.9086 (0.8365 to 0.9499)	0.7838 (0.6428 to 0.8744)	0.9156 (0.8087 to 0.9640)	
30 Months	0.9064 (0.8031 to 0.9569)	0.9086 (0.8365 to 0.9499)	0.7838 (0.6428 to 0.8744)	0.9156 (0.8087 to 0.9640)	

Number of patients at risk[b]

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
PGM=DEVOPS/SAR650984/EFC15246/CIR_RWE/REPORT/PGM/eff_km_sr_subgrp_sig_s_t.sas OUT=REPORT/OUTPUT/eff_km_de_tedisc_auto_s_t_x.rtf (12FEB2021 8:12)

16.2.7.1 Safety endpoints
16.2.7.1.60 Subgroup analysis by previous autologous stem-cell
16.2.7.1.60.4 Treatment emergent adverse event leading to discontinuation of treatment by treatment group according to previous autologous stem-cell - Safety population

	Yes		No		
	Kd (N=68)	**IKd (N=115)**	**Kd (N=54)**	**IKd (N=62)**	**p-value of treatment-by-sub group interaction[c]**
3 Months	67	111	48	59	
6 Months	63	106	45	55	
9 Months	58	102	41	53	
12 Months	57	100	40	52	
15 Months	54	93	38	47	
18 Months	52	88	37	45	
21 Months	42	78	31	40	
24 Months	18	23	8	17	
27 Months	1	1	3	1	
30 Months	0	0	0	0	

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
PGM=DEVOPS/SAR650984/EFC15246/CIR_RWE/REPORT/PGM/eff_km_sr_subgrp_sig_s_t.sas OUT=REPORT/OUTPUT/eff_km_de_tedisc_auto_s_t_x.rtf (12FEB2021 8:12)

16.2.7.1 Safety endpoints
16.2.7.1.60 Subgroup analysis by previous autologous stem-cell
16.2.7.1.60.5 Treatment emergent mild adverse event by treatment group according to previous autologous stem-cell - Safety population

	Yes		No		
	Kd (N=68)	**IKd (N=115)**	**Kd (N=54)**	**IKd (N=62)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	64 (94.1)	110 (95.7)	51 (94.4)	57 (91.9)	0.1133
Number (%) of patients censored	4 (5.9)	5 (4.3)	3 (5.6)	5 (8.1)	
Kaplan-Meier estimates of TEAE in months					
25% quantile (95% CI)	0.1971 (0.0986 to 0.2628)	0.0657 (NC to NC)	0.1971 (0.0657 to 0.3285)	0.1314 (0.0657 to 0.1643)	
Median (95% CI)	0.5257 (0.2957 to 0.6571)	0.1643 (0.0986 to 0.1971)	0.5257 (0.3285 to 0.6571)	0.2957 (0.1643 to 0.6242)	
75% quantile (95% CI)	1.8891 (0.7885 to 2.9240)	0.6571 (0.2957 to 1.4784)	0.9856 (0.6571 to 1.4456)	1.4127 (0.6571 to 1.9713)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd		0.0201		0.9174	
Hazard ratio (95% CI) vs Kd		1.4407 (1.0570 to 1.9635)		0.9801 (0.6700 to 1.4337)	
P-value		0.0208		0.9174	

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
PGM=DEVOPS/SAR650984/EFC15246/CIR_RWE/REPORT/PGM/eff_km_sr_subgrp_sig_s_t.sas OUT=REPORT/OUTPUT/eff_km_de_tesev12_auto_s_t_x.rtf (12FEB2021 8:12)

16.2.7.1 Safety endpoints
16.2.7.1.60 Subgroup analysis by previous autologous stem-cell
16.2.7.1.60.5 Treatment emergent mild adverse event by treatment group according to previous autologous stem-cell - Safety population

	Yes		No		
	Kd (N=68)	**IKd (N=115)**	**Kd (N=54)**	**IKd (N=62)**	**p-value of treatment-by-sub group interaction[c]**
Hazard ratio inverted (95% CI) vs IKd	0.6941 (0.5093 to 0.9460)				
probability (95% CI)[b]					
3 Months	0.1471 (0.0755 to 0.2412)	0.1130 (0.0635 to 0.1784)	0.0770 (0.0248 to 0.1692)	0.1010 (0.0412 to 0.1923)	
6 Months	0.0735 (0.0272 to 0.1512)	0.0783 (0.0384 to 0.1365)	0.0578 (0.0152 to 0.1436)	0.0539 (0.0125 to 0.1426)	
9 Months	0.0735 (0.0272 to 0.1512)	0.0522 (0.0214 to 0.1035)	0.0578 (0.0152 to 0.1436)	0.0539 (0.0125 to 0.1426)	
12 Months	0.0735 (0.0272 to 0.1512)	0.0435 (0.0162 to 0.0920)	0.0578 (0.0152 to 0.1436)	0.0539 (0.0125 to 0.1426)	
15 Months	0.0588 (0.0190 to 0.1319)	0.0435 (0.0162 to 0.0920)	0.0289 (0.0029 to 0.1162)	0.0539 (0.0125 to 0.1426)	
18 Months	0.0588 (0.0190 to 0.1319)	0.0435 (0.0162 to 0.0920)	0.0289 (0.0029 to 0.1162)	0.0539 (0.0125 to 0.1426)	
21 Months	0.0588 (0.0190 to 0.1319)	0.0435 (0.0162 to 0.0920)	0.0289 (0.0029 to 0.1162)	0.0539 (0.0125 to 0.1426)	
24 Months	0.0588 (0.0190 to 0.1319)	0.0435 (0.0162 to 0.0920)	0.0289 (0.0029 to 0.1162)	0.0539 (0.0125 to 0.1426)	

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
PGM=DEVOPS/SAR650984/EFC15246/CIR_RWE/REPORT/PGM/eff_km_sr_subgrp_sig_s_t.sas OUT=REPORT/OUTPUT/eff_km_de_tesev12_auto_s_t_x.rtf (12FEB2021 8:12)

16.2.7.1 Safety endpoints
16.2.7.1.60 Subgroup analysis by previous autologous stem-cell
16.2.7.1.60.5 Treatment emergent mild adverse event by treatment group according to previous autologous stem-cell - Safety population

	Yes		No		
	Kd (N=68)	**IKd (N=115)**	**Kd (N=54)**	**IKd (N=62)**	**p-value of treatment-by-sub group interaction[c]**
27 Months	0.0588 (0.0190 to 0.1319)	0.0435 (0.0162 to 0.0920)	0.0289 (0.0029 to 0.1162)	0.0539 (0.0125 to 0.1426)	
30 Months	0.0588 (0.0190 to 0.1319)	0.0435 (0.0162 to 0.0920)	0.0289 (0.0029 to 0.1162)	0.0539 (0.0125 to 0.1426)	
Number of patients at risk[b]					
3 Months	10	13	4	6	
6 Months	5	9	3	2	
9 Months	5	6	3	2	
12 Months	5	5	2	2	
15 Months	4	4	1	2	
18 Months	4	4	1	2	
21 Months	3	4	0	2	
24 Months	1	1	0	0	
27 Months	0	0	0	0	
30 Months	0	0	0	0	

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
PGM=DEVOPS/SAR650984/EFC15246/CIR_RWE/REPORT/PGM/eff_km_sr_subgrp_sig_s_t.sas OUT=REPORT/OUTPUT/eff_km_de_tesev12_auto_s_t_x.rtf (12FEB2021 8:12)

16.2.7.1 Safety endpoints
16.2.7.1.60 Subgroup analysis by previous autologous stem-cell
16.2.7.1.60.6 Treatment emergent severe adverse event by treatment group according to previous autologous stem-cell - Safety population

	Yes		No		
	Kd (N=68)	**IKd (N=115)**	**Kd (N=54)**	**IKd (N=62)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	40 (58.8)	86 (74.8)	41 (75.9)	48 (77.4)	0.2138
Number (%) of patients censored	28 (41.2)	29 (25.2)	13 (24.1)	14 (22.6)	
Kaplan-Meier estimates of TEAE in months					
25% quantile (95% CI)	3.9425 (1.8727 to 5.4867)	1.4784 (0.7556 to 3.4497)	0.6571 (0.3285 to 1.7413)	0.7228 (0.2628 to 1.9713)	
Median (95% CI)	9.1992 (6.2752 to NC)	7.1622 (4.7967 to 9.0021)	4.0411 (1.7413 to 7.8522)	4.8624 (1.9713 to 6.5051)	
75% quantile (95% CI)	NC (NC to NC)	17.3142 (11.1704 to NC)	16.8542 (7.8522 to NC)	12.5503 (7.1294 to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd		0.0343		0.8350	
Hazard ratio (95% CI) vs Kd		1.4963 (1.0277 to 2.1786)		1.0453 (0.6887 to 1.5865)	
P-value		0.0355		0.8352	
Hazard ratio inverted (95% CI) vs IKd	0.6683 (0.4590 to 0.9730)				

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
PGM=DEVOPS/SAR650984/EFC15246/CIR_RWE/REPORT/PGM/eff_km_sr_subgrp_sig_s_t.sas OUT=REPORT/OUTPUT/eff_km_de_tesev34_auto_s_t_x.rtf (12FEB2021 8:13)

16.2.7.1 Safety endpoints
16.2.7.1.60 Subgroup analysis by previous autologous stem-cell
16.2.7.1.60.6 Treatment emergent severe adverse event by treatment group according to previous autologous stem-cell - Safety population

	Yes		No		
	Kd (N=68)	**IKd (N=115)**	**Kd (N=54)**	**IKd (N=62)**	**p-value of treatment-by-sub group interaction[c]**
probability (95% CI)[b]					
3 Months	0.7933 (0.6761 to 0.8720)	0.6849 (0.5911 to 0.7615)	0.5702 (0.4271 to 0.6900)	0.5624 (0.4300 to 0.6755)	
6 Months	0.6287 (0.5018 to 0.7317)	0.5269 (0.4314 to 0.6135)	0.4181 (0.2850 to 0.5457)	0.3970 (0.2750 to 0.5164)	
9 Months	0.5070 (0.3818 to 0.6192)	0.4127 (0.3219 to 0.5011)	0.3611 (0.2350 to 0.4885)	0.3474 (0.2313 to 0.4660)	
12 Months	0.4455 (0.3239 to 0.5599)	0.3161 (0.2332 to 0.4022)	0.3421 (0.2188 to 0.4690)	0.2647 (0.1617 to 0.3792)	
15 Months	0.4142 (0.2950 to 0.5292)	0.2662 (0.1879 to 0.3508)	0.2851 (0.1714 to 0.4094)	0.2481 (0.1484 to 0.3613)	
18 Months	0.3976 (0.2797 to 0.5130)	0.2449 (0.1687 to 0.3287)	0.2471 (0.1411 to 0.3685)	0.2100 (0.1172 to 0.3210)	
21 Months	0.3976 (0.2797 to 0.5130)	0.2337 (0.1588 to 0.3172)	0.2471 (0.1411 to 0.3685)	0.2100 (0.1172 to 0.3210)	
24 Months	0.3976 (0.2797 to 0.5130)	0.2337 (0.1588 to 0.3172)	0.2162 (0.1133 to 0.3405)	0.2100 (0.1172 to 0.3210)	
27 Months	0.3976 (0.2797 to 0.5130)	0.2337 (0.1588 to 0.3172)	0.2162 (0.1133 to 0.3405)	0.2100 (0.1172 to 0.3210)	

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
PGM=DEVOPS/SAR650984/EFC15246/CIR_RWE/REPORT/PGM/eff_km_sr_subgrp_sig_s_t.sas OUT=REPORT/OUTPUT/eff_km_de_tesev34_auto_s_t_x.rtf (12FEB2021 8:13)

16.2.7.1 Safety endpoints
16.2.7.1.60 Subgroup analysis by previous autologous stem-cell
16.2.7.1.60.6 Treatment emergent severe adverse event by treatment group according to previous autologous stem-cell - Safety population

	Yes		No		
	Kd (N=68)	**IKd (N=115)**	**Kd (N=54)**	**IKd (N=62)**	**p-value of treatment-by-sub group interaction[c]**
30 Months	0.3976 (0.2797 to 0.5130)	0.2337 (0.1588 to 0.3172)	0.2162 (0.1133 to 0.3405)	0.2100 (0.1172 to 0.3210)	
Number of patients at risk[b]					
3 Months	53	78	30	34	
6 Months	42	60	22	24	
9 Months	33	47	19	21	
12 Months	29	36	18	16	
15 Months	26	26	15	13	
18 Months	24	22	13	11	
21 Months	17	20	10	11	
24 Months	7	6	1	4	
27 Months	0	0	1	0	
30 Months	0	0	0	0	

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
PGM=DEVOPS/SAR650984/EFC15246/CIR_RWE/REPORT/PGM/eff_km_sr_subgrp_sig_s_t.sas OUT=REPORT/OUTPUT/eff_km_de_tesev34_auto_s_t_x.rtf (12FEB2021 8:13)

16.2.7.1 Safety endpoints
16.2.7.1.60 Subgroup analysis by previous autologous stem-cell
16.2.7.1.60.7 Treatment emergent severe adverse event including death by treatment group according to previous autologous stem-cell - Safety population

	Yes		No		
	Kd (N=68)	**IKd (N=115)**	**Kd (N=54)**	**IKd (N=62)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	40 (58.8)	88 (76.5)	42 (77.8)	48 (77.4)	0.1571
Number (%) of patients censored	28 (41.2)	27 (23.5)	12 (22.2)	14 (22.6)	
Kaplan-Meier estimates of TEAE in months					
25% quantile (95% CI)	3.9425 (1.8727 to 5.4867)	1.3470 (0.7228 to 3.2854)	0.6571 (0.3285 to 1.5113)	0.7228 (0.2628 to 1.9713)	
Median (95% CI)	9.1992 (6.2752 to NC)	7.0308 (4.6324 to 8.6735)	3.9589 (1.5113 to 6.2752)	4.8624 (1.9713 to 6.5051)	
75% quantile (95% CI)	NC (NC to NC)	15.6057 (11.1704 to NC)	16.8542 (6.2752 to NC)	12.5503 (7.1294 to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd		0.0243		0.9242	
Hazard ratio (95% CI) vs Kd		1.5326 (1.0540 to 2.2284)		1.0203 (0.6740 to 1.5445)	
P-value		0.0254		0.9243	
Hazard ratio inverted (95% CI) vs IKd	0.6525 (0.4488 to 0.9487)				

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
PGM=DEVOPS/SAR650984/EFC15246/CIR_RWE/REPORT/PGM/eff_km_sr_subgrp_sig_s_t.sas OUT=REPORT/OUTPUT/eff_km_de_tesev345_auto_s_t_x.rtf (12FEB2021 8:13)

16.2.7.1 Safety endpoints
16.2.7.1.60 Subgroup analysis by previous autologous stem-cell
16.2.7.1.60.7 Treatment emergent severe adverse event including death by treatment group according to previous autologous stem-cell - Safety population

	Yes		No		
	Kd (N=68)	**IKd (N=115)**	**Kd (N=54)**	**IKd (N=62)**	**p-value of treatment-by-sub group interaction[c]**
probability (95% CI)[b]					
3 Months	0.7933 (0.6761 to 0.8720)	0.6783 (0.5846 to 0.7552)	0.5556 (0.4139 to 0.6759)	0.5624 (0.4300 to 0.6755)	
6 Months	0.6287 (0.5018 to 0.7317)	0.5217 (0.4268 to 0.6083)	0.4074 (0.2767 to 0.5339)	0.3970 (0.2750 to 0.5164)	
9 Months	0.5070 (0.3818 to 0.6192)	0.4087 (0.3185 to 0.4967)	0.3519 (0.2283 to 0.4778)	0.3474 (0.2313 to 0.4660)	
12 Months	0.4455 (0.3239 to 0.5599)	0.3130 (0.2308 to 0.3986)	0.3333 (0.2125 to 0.4587)	0.2647 (0.1617 to 0.3792)	
15 Months	0.4142 (0.2950 to 0.5292)	0.2559 (0.1794 to 0.3391)	0.2778 (0.1666 to 0.4003)	0.2481 (0.1484 to 0.3613)	
18 Months	0.3976 (0.2797 to 0.5130)	0.2354 (0.1612 to 0.3177)	0.2407 (0.1372 to 0.3602)	0.2100 (0.1172 to 0.3210)	
21 Months	0.3976 (0.2797 to 0.5130)	0.2247 (0.1518 to 0.3065)	0.2407 (0.1372 to 0.3602)	0.2100 (0.1172 to 0.3210)	
24 Months	0.3976 (0.2797 to 0.5130)	0.2247 (0.1518 to 0.3065)	0.2106 (0.1103 to 0.3328)	0.2100 (0.1172 to 0.3210)	
27 Months	0.3976 (0.2797 to 0.5130)	0.2247 (0.1518 to 0.3065)	0.2106 (0.1103 to 0.3328)	0.2100 (0.1172 to 0.3210)	

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
PGM=DEVOPS/SAR650984/EFC15246/CIR_RWE/REPORT/PGM/eff_km_sr_subgrp_sig_s_t.sas OUT=REPORT/OUTPUT/eff_km_de_tesev345_auto_s_t_x.rtf (12FEB2021 8:13)

16.2.7.1 Safety endpoints
16.2.7.1.60 Subgroup analysis by previous autologous stem-cell
16.2.7.1.60.7 Treatment emergent severe adverse event including death by treatment group according to previous autologous stem-cell - Safety population

	Yes		No		
	Kd (N=68)	**IKd (N=115)**	**Kd (N=54)**	**IKd (N=62)**	**p-value of treatment-by-sub group interaction[c]**
30 Months	0.3976 (0.2797 to 0.5130)	0.2247 (0.1518 to 0.3065)	0.2106 (0.1103 to 0.3328)	0.2100 (0.1172 to 0.3210)	
Number of patients at risk[b]					
3 Months	53	78	30	34	
6 Months	42	60	22	24	
9 Months	33	47	19	21	
12 Months	29	36	18	16	
15 Months	26	26	15	13	
18 Months	24	22	13	11	
21 Months	17	20	10	11	
24 Months	7	6	1	4	
27 Months	0	0	1	0	
30 Months	0	0	0	0	

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.61 Subgroup analysis by baseline creatinine clearance (MDRD)
16.2.7.1.61.1 Treatment emergent adverse event by treatment group according to baseline creatinine clearance (MDRD) - Safety population

	>=60 mL/min/1.73m2		<60 mL/min/1.73m2		
	Kd (N=92)	**IKd (N=120)**	**Kd (N=18)**	**IKd (N=43)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	87 (94.6)	116 (96.7)	18 (100.0)	42 (97.7)	0.8698
Number (%) of patients censored	5 (5.4)	4 (3.3)	0 (0.0)	1 (2.3)	
Kaplan-Meier estimates of TEAE in months					
25% quantile (95% CI)	0.1807 (0.1314 to 0.2300)	0.0657 (0.0657 to 0.0986)	0.2628 (0.0329 to 0.5257)	0.1314 (0.0657 to 0.1643)	
Median (95% CI)	0.3778 (0.2957 to 0.5914)	0.1643 (0.1314 to 0.2300)	0.5749 (0.2628 to 0.9199)	0.2300 (0.1314 to 0.6242)	
75% quantile (95% CI)	0.8542 (0.6242 to 1.5113)	0.6407 (0.3943 to 1.1828)	1.0185 (0.6242 to 2.8912)	0.9528 (0.3943 to 1.5113)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd		0.0455		0.3478	
Hazard ratio (95% CI) vs Kd		1.3278 (1.0047 to 1.7549)		1.3035 (0.7483 to 2.2707)	
P-value		0.0463		0.3492	

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
PGM=DEVOPS/SAR650984/EFC15246/CIR_RWE/REPORT/PGM/eff_km_sr_subgrp_sig_s_t.sas OUT=REPORT/OUTPUT/eff_km_de_teae_crcl_s_t_x.rtf (12FEB2021 8:09)

16.2.7.1 Safety endpoints
16.2.7.1.61 Subgroup analysis by baseline creatinine clearance (MDRD)
16.2.7.1.61.1 Treatment emergent adverse event by treatment group according to baseline creatinine clearance (MDRD) - Safety population

	>=60 mL/min/1.73m2		<60 mL/min/1.73m2		
	Kd (N=92)	**IKd (N=120)**	**Kd (N=18)**	**IKd (N=43)**	**p-value of treatment-by-sub group interaction[c]**
Hazard ratio inverted (95% CI) vs IKd	0.7531 (0.5698 to 0.9953)				
probability (95% CI)[b]					
3 Months	0.0978 (0.0480 to 0.1686)	0.0917 (0.0486 to 0.1514)	0.0556 (0.0037 to 0.2242)	0.0465 (0.0085 to 0.1389)	
6 Months	0.0652 (0.0267 to 0.1279)	0.0583 (0.0257 to 0.1101)	0.0556 (0.0037 to 0.2242)	0.0233 (0.0018 to 0.1057)	
9 Months	0.0652 (0.0267 to 0.1279)	0.0417 (0.0156 to 0.0884)	0.0556 (0.0037 to 0.2242)	0.0233 (0.0018 to 0.1057)	
12 Months	0.0652 (0.0267 to 0.1279)	0.0333 (0.0109 to 0.0771)	0.0556 (0.0037 to 0.2242)	0.0233 (0.0018 to 0.1057)	
15 Months	0.0543 (0.0202 to 0.1138)	0.0333 (0.0109 to 0.0771)	0.0556 (0.0037 to 0.2242)	0.0233 (0.0018 to 0.1057)	
18 Months	0.0543 (0.0202 to 0.1138)	0.0333 (0.0109 to 0.0771)	0.0556 (0.0037 to 0.2242)	0.0233 (0.0018 to 0.1057)	
21 Months	0.0543 (0.0202 to 0.1138)	0.0333 (0.0109 to 0.0771)	0.0556 (0.0037 to 0.2242)	0.0233 (0.0018 to 0.1057)	
24 Months	0.0543 (0.0202 to 0.1138)	0.0333 (0.0109 to 0.0771)	0.0556 (0.0037 to 0.2242)	0.0233 (0.0018 to 0.1057)	

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
PGM=DEVOPS/SAR650984/EFC15246/CIR_RWE/REPORT/PGM/eff_km_sr_subgrp_sig_s_t.sas OUT=REPORT/OUTPUT/eff_km_de_teae_crcl_s_t_x.rtf (12FEB2021 8:09)

16.2.7.1 Safety endpoints
16.2.7.1.61 Subgroup analysis by baseline creatinine clearance (MDRD)
16.2.7.1.61.1 Treatment emergent adverse event by treatment group according to baseline creatinine clearance (MDRD) - Safety population

	>=60 mL/min/1.73m2		<60 mL/min/1.73m2		
	Kd (N=92)	**IKd (N=120)**	**Kd (N=18)**	**IKd (N=43)**	**p-value of treatment-by-sub group interaction[c]**
27 Months	0.0543 (0.0202 to 0.1138)	0.0333 (0.0109 to 0.0771)	0.0556 (0.0037 to 0.2242)	0.0233 (0.0018 to 0.1057)	
30 Months	0.0543 (0.0202 to 0.1138)	0.0333 (0.0109 to 0.0771)	0.0556 (0.0037 to 0.2242)	0.0233 (0.0018 to 0.1057)	
Number of patients at risk[b]					
3 Months	9	11	1	2	
6 Months	6	7	0	1	
9 Months	6	5	0	1	
12 Months	6	4	0	1	
15 Months	5	4	0	1	
18 Months	5	4	0	1	
21 Months	3	4	0	1	
24 Months	1	1	0	0	
27 Months	0	0	0	0	
30 Months	0	0	0	0	

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.61 Subgroup analysis by baseline creatinine clearance (MDRD)
16.2.7.1.61.2 Treatment emergent serious adverse event by treatment group according to baseline creatinine clearance (MDRD) - Safety population

	>=60 mL/min/1.73m2		<60 mL/min/1.73m2		
	Kd (N=92)	**IKd (N=120)**	**Kd (N=18)**	**IKd (N=43)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	50 (54.3)	71 (59.2)	14 (77.8)	27 (62.8)	0.1026
Number (%) of patients censored	42 (45.7)	49 (40.8)	4 (22.2)	16 (37.2)	
Kaplan-Meier estimates of TEAE in months					
25% quantile (95% CI)	5.5031 (3.3840 to 6.5708)	2.6119 (1.2485 to 6.4066)	0.9856 (0.2300 to 4.6324)	1.8727 (0.3943 to 5.6181)	
Median (95% CI)	15.4415 (11.2361 to NC)	12.8789 (9.2649 to 18.1027)	6.1273 (0.9856 to 14.6858)	11.2361 (3.8439 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	14.6858 (6.9651 to NC)	NC (21.1253 to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd		0.2837		0.2185	
Hazard ratio (95% CI) vs Kd		1.2186 (0.8485 to 1.7501)		0.6666 (0.3480 to 1.2769)	
P-value		0.2845		0.2214	
probability (95% CI)[b]					

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
PGM=DEVOPS/SAR650984/EFC15246/CIR_RWE/REPORT/PGM/eff_km_sr_subgrp_sig_s_t.sas OUT=REPORT/OUTPUT/eff_km_de_tesae_crcl_s_t_x.rtf (12FEB2021 8:12)

16.2.7.1 Safety endpoints
16.2.7.1.61 Subgroup analysis by baseline creatinine clearance (MDRD)
16.2.7.1.61.2 Treatment emergent serious adverse event by treatment group according to baseline creatinine clearance (MDRD) - Safety population

	>=60 mL/min/1.73m2		<60 mL/min/1.73m2		
	Kd (N=92)	**IKd (N=120)**	**Kd (N=18)**	**IKd (N=43)**	**p-value of treatment-by-sub group interaction[c]**
3 Months	0.8587 (0.7691 to 0.9154)	0.7417 (0.6534 to 0.8107)	0.6111 (0.3532 to 0.7921)	0.7209 (0.5612 to 0.8308)	
6 Months	0.6957 (0.5906 to 0.7788)	0.6745 (0.5827 to 0.7504)	0.5000 (0.2593 to 0.7005)	0.6047 (0.4434 to 0.7326)	
9 Months	0.6522 (0.5455 to 0.7397)	0.5986 (0.5050 to 0.6802)	0.3810 (0.1662 to 0.5951)	0.5116 (0.3548 to 0.6483)	
12 Months	0.5870 (0.4795 to 0.6796)	0.5312 (0.4378 to 0.6159)	0.3810 (0.1662 to 0.5951)	0.4419 (0.2916 to 0.5820)	
15 Months	0.5100 (0.4037 to 0.6066)	0.4433 (0.3522 to 0.5304)	0.2286 (0.0622 to 0.4564)	0.3953 (0.2511 to 0.5363)	
18 Months	0.4657 (0.3611 to 0.5636)	0.4158 (0.3258 to 0.5032)	0.2286 (0.0622 to 0.4564)	0.3953 (0.2511 to 0.5363)	
21 Months	0.4657 (0.3611 to 0.5636)	0.4065 (0.3170 to 0.4940)	0.1143 (0.0092 to 0.3664)	0.3953 (0.2511 to 0.5363)	
24 Months	0.4477 (0.3419 to 0.5480)	0.3958 (0.3065 to 0.4837)	0.1143 (0.0092 to 0.3664)	0.3649 (0.2228 to 0.5082)	
27 Months	0.4477 (0.3419 to 0.5480)	0.3958 (0.3065 to 0.4837)	0.1143 (0.0092 to 0.3664)	0.3649 (0.2228 to 0.5082)	
30 Months	0.4477 (0.3419 to 0.5480)	0.3958 (0.3065 to 0.4837)	0.1143 (0.0092 to 0.3664)	0.3649 (0.2228 to 0.5082)	

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
PGM=DEVOPS/SAR650984/EFC15246/CIR_RWE/REPORT/PGM/eff_km_sr_subgrp_sig_s_t.sas OUT=REPORT/OUTPUT/eff_km_de_tesae_crcl_s_t_x.rtf (12FEB2021 8:12)

16.2.7.1 Safety endpoints
16.2.7.1.61 Subgroup analysis by baseline creatinine clearance (MDRD)
16.2.7.1.61.2 Treatment emergent serious adverse event by treatment group according to baseline creatinine clearance (MDRD) - Safety population

	>=60 mL/min/1.73m2		<60 mL/min/1.73m2		
	Kd (N=92)	**IKd (N=120)**	**Kd (N=18)**	**IKd (N=43)**	**p-value of treatment-by-sub group interaction[c]**
Number of patients at risk[b]					
3 Months	79	89	11	31	
6 Months	64	80	9	26	
9 Months	60	71	6	22	
12 Months	54	63	6	19	
15 Months	46	49	3	15	
18 Months	42	45	2	13	
21 Months	31	39	1	13	
24 Months	7	14	1	3	
27 Months	2	0	0	1	
30 Months	0	0	0	0	

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.61 Subgroup analysis by baseline creatinine clearance (MDRD)
16.2.7.1.61.3 Treatment emergent adverse event leading to discontinuation of treatment by treatment group according to baseline creatinine clearance (MDRD) - Safety population

	>=60 mL/min/1.73m2		<60 mL/min/1.73m2		
	Kd (N=92)	**IKd (N=120)**	**Kd (N=18)**	**IKd (N=43)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	9 (9.8)	12 (10.0)	5 (27.8)	3 (7.0)	0.0392
Number (%) of patients censored	83 (90.2)	108 (90.0)	13 (72.2)	40 (93.0)	
Kaplan-Meier estimates of TEAE in months					
25% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	7.8522 (0.2300 to NC)	NC (NC to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (7.8522 to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd		0.8895		0.0138	
Hazard ratio (95% CI) vs Kd		1.0629 (0.4479 to 2.5226)		0.1976 (0.0470 to 0.8297)	
P-value		0.8900		0.0268	
probability (95% CI)[b]					
3 Months	0.9891 (0.9253 to 0.9985)	0.9663 (0.9127 to 0.9872)	0.7738 (0.5033 to 0.9087)	0.9767 (0.8462 to 0.9967)	

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.61 Subgroup analysis by baseline creatinine clearance (MDRD)
16.2.7.1.61.3 Treatment emergent adverse event leading to discontinuation of treatment by treatment group according to baseline creatinine clearance (MDRD) - Safety population

	>=60 mL/min/1.73m2		<60 mL/min/1.73m2		
	Kd (N=92)	**IKd (N=120)**	**Kd (N=18)**	**IKd (N=43)**	**p-value of treatment-by-sub group interaction[c]**
6 Months	0.9564 (0.8880 to 0.9834)	0.9318 (0.8682 to 0.9653)	0.7738 (0.5033 to 0.9087)	0.9767 (0.8462 to 0.9967)	
9 Months	0.9234 (0.8461 to 0.9627)	0.9229 (0.8571 to 0.9591)	0.7035 (0.4235 to 0.8659)	0.9291 (0.7960 to 0.9766)	
12 Months	0.9234 (0.8461 to 0.9627)	0.9229 (0.8571 to 0.9591)	0.7035 (0.4235 to 0.8659)	0.9291 (0.7960 to 0.9766)	
15 Months	0.9234 (0.8461 to 0.9627)	0.9047 (0.8345 to 0.9461)	0.7035 (0.4235 to 0.8659)	0.9291 (0.7960 to 0.9766)	
18 Months	0.9113 (0.8303 to 0.9546)	0.9047 (0.8345 to 0.9461)	0.7035 (0.4235 to 0.8659)	0.9291 (0.7960 to 0.9766)	
21 Months	0.8991 (0.8149 to 0.9463)	0.8945 (0.8213 to 0.9387)	0.7035 (0.4235 to 0.8659)	0.9291 (0.7960 to 0.9766)	
24 Months	0.8991 (0.8149 to 0.9463)	0.8945 (0.8213 to 0.9387)	0.7035 (0.4235 to 0.8659)	0.9291 (0.7960 to 0.9766)	
27 Months	0.8991 (0.8149 to 0.9463)	0.8945 (0.8213 to 0.9387)	0.7035 (0.4235 to 0.8659)	0.9291 (0.7960 to 0.9766)	
30 Months	0.8991 (0.8149 to 0.9463)	0.8945 (0.8213 to 0.9387)	0.7035 (0.4235 to 0.8659)	0.9291 (0.7960 to 0.9766)	

Number of patients at risk[b]

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
PGM=DEVOPS/SAR650984/EFC15246/CIR_RWE/REPORT/PGM/eff_km_sr_subgrp_sig_s_t.sas OUT=REPORT/OUTPUT/eff_km_de_tedisc_crcl_s_t_x.rtf (12FEB2021 8:12)

16.2.7.1 Safety endpoints
16.2.7.1.61 Subgroup analysis by baseline creatinine clearance (MDRD)
16.2.7.1.61.3 Treatment emergent adverse event leading to discontinuation of treatment by treatment group according to baseline creatinine clearance (MDRD) - Safety population

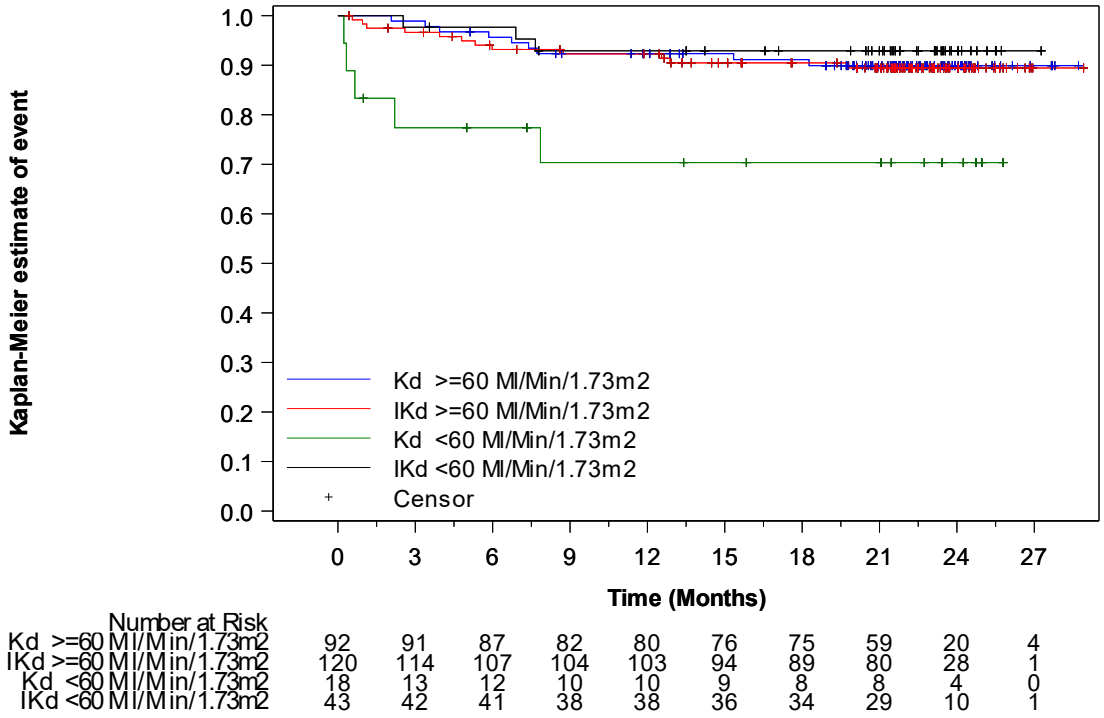
	>=60 mL/min/1.73m2		<60 mL/min/1.73m2		
	Kd (N=92)	**IKd (N=120)**	**Kd (N=18)**	**IKd (N=43)**	**p-value of treatment-by-sub group interaction[c]**
3 Months	91	114	13	42	
6 Months	87	107	12	41	
9 Months	82	104	10	38	
12 Months	80	103	10	38	
15 Months	76	94	9	36	
18 Months	75	89	8	34	
21 Months	59	80	8	29	
24 Months	20	28	4	10	
27 Months	4	1	0	1	
30 Months	0	0	0	0	

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
PGM=DEVOPS/SAR650984/EFC15246/CIR_RWE/REPORT/PGM/eff_km_sr_subgrp_sig_s_t.sas OUT=REPORT/OUTPUT/eff_km_de_tedisc_crcl_s_t_x.rtf (12FEB2021 8:12)

16.2.7.1 Safety endpoints

16.2.7.1.61 Subgroup analysis by baseline creatinine clearance (MDRD)

16.2.7.1.61.4 Kaplan-Meier cumulative incidence curve of treatment emergent adverse event leading to discontinuation of treatment by treatment group according to baseline creatinine clearance (MDRD) - Safety population



Number at Risk

Kd >=60 Ml/Min/1.73m2	92	91	87	82	80	76	75	59	20	4
IKd >=60 Ml/Min/1.73m2	120	114	107	104	103	94	89	80	28	1
Kd <60 Ml/Min/1.73m2	18	13	12	10	10	9	8	8	4	0
IKd <60 Ml/Min/1.73m2	43	42	41	38	38	36	34	29	10	1

16.2.7.1 Safety endpoints
16.2.7.1.61 Subgroup analysis by baseline creatinine clearance (MDRD)
16.2.7.1.61.5 Treatment emergent mild adverse event by treatment group according to baseline creatinine clearance (MDRD) - Safety population

	>=60 mL/min/1.73m2		<60 mL/min/1.73m2		
	Kd (N=92)	**IKd (N=120)**	**Kd (N=18)**	**IKd (N=43)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	86 (93.5)	114 (95.0)	17 (94.4)	40 (93.0)	0.7069
Number (%) of patients censored	6 (6.5)	6 (5.0)	1 (5.6)	3 (7.0)	
Kaplan-Meier estimates of TEAE in months					
25% quantile (95% CI)	0.1971 (0.1314 to 0.2300)	0.0657 (0.0657 to 0.0986)	0.2628 (0.0329 to 0.6242)	0.1314 (0.0657 to 0.1643)	
Median (95% CI)	0.4271 (0.3285 to 0.6242)	0.1807 (0.1314 to 0.2628)	0.6571 (0.2628 to 1.4456)	0.2628 (0.1314 to 0.6571)	
75% quantile (95% CI)	1.1828 (0.6571 to 1.9055)	0.6899 (0.4271 to 1.4784)	1.4456 (0.6571 to 3.8768)	1.3142 (0.6242 to 3.8439)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd		0.0395		0.6428	
Hazard ratio (95% CI) vs Kd		1.3416 (1.0132 to 1.7766)		1.1454 (0.6451 to 2.0339)	
P-value		0.0402		0.6431	

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.61 Subgroup analysis by baseline creatinine clearance (MDRD)
16.2.7.1.61.5 Treatment emergent mild adverse event by treatment group according to baseline creatinine clearance (MDRD) - Safety population

	>=60 mL/min/1.73m2		<60 mL/min/1.73m2		
	Kd (N=92)	**IKd (N=120)**	**Kd (N=18)**	**IKd (N=43)**	**p-value of treatment-by-sub group interaction[c]**
Hazard ratio inverted (95% CI) vs IKd	0.7454 (0.5629 to 0.9870)				
probability (95% CI)[b]					
3 Months	0.1196 (0.0634 to 0.1948)	0.1030 (0.0565 to 0.1658)	0.1222 (0.0205 to 0.3211)	0.1395 (0.0566 to 0.2590)	
6 Months	0.0870 (0.0406 to 0.1553)	0.0687 (0.0322 to 0.1240)	0.0611 (0.0041 to 0.2421)	0.0837 (0.0233 to 0.1946)	
9 Months	0.0870 (0.0406 to 0.1553)	0.0515 (0.0212 to 0.1021)	0.0611 (0.0041 to 0.2421)	0.0558 (0.0107 to 0.1595)	
12 Months	0.0870 (0.0406 to 0.1553)	0.0429 (0.0161 to 0.0908)	0.0611 (0.0041 to 0.2421)	0.0558 (0.0107 to 0.1595)	
15 Months	0.0621 (0.0242 to 0.1255)	0.0429 (0.0161 to 0.0908)	0.0611 (0.0041 to 0.2421)	0.0558 (0.0107 to 0.1595)	
18 Months	0.0621 (0.0242 to 0.1255)	0.0429 (0.0161 to 0.0908)	0.0611 (0.0041 to 0.2421)	0.0558 (0.0107 to 0.1595)	
21 Months	0.0621 (0.0242 to 0.1255)	0.0429 (0.0161 to 0.0908)	0.0611 (0.0041 to 0.2421)	0.0558 (0.0107 to 0.1595)	
24 Months	0.0621 (0.0242 to 0.1255)	0.0429 (0.0161 to 0.0908)	0.0611 (0.0041 to 0.2421)	0.0558 (0.0107 to 0.1595)	

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
PGM=DEVOPS/SAR650984/EFC15246/CIR_RWE/REPORT/PGM/eff_km_sr_subgrp_sig_s_t.sas OUT=REPORT/OUTPUT/eff_km_de_tesev12_crcl_s_t_x.rtf (12FEB2021 8:12)

16.2.7.1 Safety endpoints
16.2.7.1.61 Subgroup analysis by baseline creatinine clearance (MDRD)
16.2.7.1.61.5 Treatment emergent mild adverse event by treatment group according to baseline creatinine clearance (MDRD) - Safety population

	>=60 mL/min/1.73m2		<60 mL/min/1.73m2		
	Kd (N=92)	**IKd (N=120)**	**Kd (N=18)**	**IKd (N=43)**	**p-value of treatment-by-sub group interaction[c]**
27 Months	0.0621 (0.0242 to 0.1255)	0.0429 (0.0161 to 0.0908)	0.0611 (0.0041 to 0.2421)	0.0558 (0.0107 to 0.1595)	
30 Months	0.0621 (0.0242 to 0.1255)	0.0429 (0.0161 to 0.0908)	0.0611 (0.0041 to 0.2421)	0.0558 (0.0107 to 0.1595)	
Number of patients at risk[b]					
3 Months	11	12	2	6	
6 Months	8	8	0	3	
9 Months	8	6	0	2	
12 Months	7	5	0	2	
15 Months	5	4	0	2	
18 Months	5	4	0	2	
21 Months	3	4	0	2	
24 Months	1	1	0	0	
27 Months	0	0	0	0	
30 Months	0	0	0	0	

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.61 Subgroup analysis by baseline creatinine clearance (MDRD)
16.2.7.1.61.6 Treatment emergent severe adverse event by treatment group according to baseline creatinine clearance (MDRD) - Safety population

	>=60 mL/min/1.73m2		<60 mL/min/1.73m2		
	Kd (N=92)	**IKd (N=120)**	**Kd (N=18)**	**IKd (N=43)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	60 (65.2)	91 (75.8)	13 (72.2)	34 (79.1)	0.3032
Number (%) of patients censored	32 (34.8)	29 (24.2)	5 (27.8)	9 (20.9)	
Kaplan-Meier estimates of TEAE in months					
25% quantile (95% CI)	2.9405 (1.2156 to 4.0411)	1.3142 (0.7228 to 2.4312)	0.6571 (0.2300 to 1.8727)	0.7556 (0.3943 to 3.4497)	
Median (95% CI)	7.4743 (4.9610 to 13.8645)	5.9795 (4.7967 to 8.6735)	1.9055 (0.6571 to 13.6345)	4.3696 (2.0041 to 7.7536)	
75% quantile (95% CI)	NC (21.7823 to NC)	15.8357 (11.1704 to NC)	13.6345 (1.9055 to NC)	11.5318 (7.6879 to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd		0.0608		0.8182	
Hazard ratio (95% CI) vs Kd		1.3653 (0.9847 to 1.8932)		0.9277 (0.4889 to 1.7601)	
P-value		0.0619		0.8182	
probability (95% CI)[b]					

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.61 Subgroup analysis by baseline creatinine clearance (MDRD)
16.2.7.1.61.6 Treatment emergent severe adverse event by treatment group according to baseline creatinine clearance (MDRD) - Safety population

	>=60 mL/min/1.73m2		<60 mL/min/1.73m2		
	Kd (N=92)	**IKd (N=120)**	**Kd (N=18)**	**IKd (N=43)**	**p-value of treatment-by-sub group interaction[c]**
3 Months	0.7391 (0.6366 to 0.8168)	0.6472 (0.5542 to 0.7257)	0.4848 (0.2418 to 0.6913)	0.6279 (0.4663 to 0.7529)	
6 Months	0.5543 (0.4472 to 0.6489)	0.4939 (0.4011 to 0.5801)	0.4848 (0.2418 to 0.6913)	0.4186 (0.2712 to 0.5593)	
9 Months	0.4891 (0.3838 to 0.5862)	0.4088 (0.3197 to 0.4956)	0.2828 (0.0941 to 0.5092)	0.3023 (0.1740 to 0.4411)	
12 Months	0.4348 (0.3323 to 0.5328)	0.3151 (0.2336 to 0.3997)	0.2828 (0.0941 to 0.5092)	0.2326 (0.1205 to 0.3660)	
15 Months	0.3913 (0.2920 to 0.4891)	0.2680 (0.1909 to 0.3510)	0.1886 (0.0378 to 0.4275)	0.2093 (0.1036 to 0.3400)	
18 Months	0.3587 (0.2623 to 0.4559)	0.2271 (0.1544 to 0.3084)	0.1886 (0.0378 to 0.4275)	0.2093 (0.1036 to 0.3400)	
21 Months	0.3587 (0.2623 to 0.4559)	0.2168 (0.1454 to 0.2975)	0.1886 (0.0378 to 0.4275)	0.2093 (0.1036 to 0.3400)	
24 Months	0.3408 (0.2439 to 0.4398)	0.2168 (0.1454 to 0.2975)	0.1886 (0.0378 to 0.4275)	0.2093 (0.1036 to 0.3400)	
27 Months	0.3408 (0.2439 to 0.4398)	0.2168 (0.1454 to 0.2975)	0.1886 (0.0378 to 0.4275)	0.2093 (0.1036 to 0.3400)	
30 Months	0.3408 (0.2439 to 0.4398)	0.2168 (0.1454 to 0.2975)	0.1886 (0.0378 to 0.4275)	0.2093 (0.1036 to 0.3400)	

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.61 Subgroup analysis by baseline creatinine clearance (MDRD)
16.2.7.1.61.6 Treatment emergent severe adverse event by treatment group according to baseline creatinine clearance (MDRD) - Safety population

	>=60 mL/min/1.73m2		<60 mL/min/1.73m2		
	Kd (N=92)	**IKd (N=120)**	**Kd (N=18)**	**IKd (N=43)**	**p-value of treatment-by-sub group interaction[c]**
Number of patients at risk[b]					
3 Months	68	76	8	27	
6 Months	51	58	8	18	
9 Months	45	48	4	13	
12 Months	40	37	4	10	
15 Months	36	27	2	8	
18 Months	33	22	1	7	
21 Months	23	20	1	7	
24 Months	6	5	1	3	
27 Months	1	0	0	0	
30 Months	0	0	0	0	

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.61 Subgroup analysis by baseline creatinine clearance (MDRD)
16.2.7.1.61.7 Treatment emergent severe adverse event including death by treatment group according to baseline creatinine clearance (MDRD) - Safety population

	>=60 mL/min/1.73m2		<60 mL/min/1.73m2		
	Kd (N=92)	**IKd (N=120)**	**Kd (N=18)**	**IKd (N=43)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	60 (65.2)	93 (77.5)	14 (77.8)	34 (79.1)	0.1876
Number (%) of patients censored	32 (34.8)	27 (22.5)	4 (22.2)	9 (20.9)	
Kaplan-Meier estimates of TEAE in months					
25% quantile (95% CI)	2.9405 (1.2156 to 4.0411)	1.2977 (0.6571 to 2.4312)	0.6571 (0.2300 to 1.5113)	0.7556 (0.3943 to 3.4497)	
Median (95% CI)	7.4743 (4.9610 to 13.8645)	5.9466 (4.7639 to 8.4435)	1.8891 (0.6571 to 7.8522)	4.3696 (2.0041 to 7.7536)	
75% quantile (95% CI)	NC (21.7823 to NC)	15.6057 (11.1704 to NC)	13.6345 (1.9055 to NC)	11.5318 (7.6879 to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd		0.0436		0.6408	
Hazard ratio (95% CI) vs Kd		1.3959 (1.0081 to 1.9329)		0.8621 (0.4621 to 1.6086)	
P-value		0.0446		0.6411	
Hazard ratio inverted (95% CI) vs IKd	0.7164 (0.5174 to 0.9919)				

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.61 Subgroup analysis by baseline creatinine clearance (MDRD)
16.2.7.1.61.7 Treatment emergent severe adverse event including death by treatment group according to baseline creatinine clearance (MDRD) - Safety population

	>=60 mL/min/1.73m2		<60 mL/min/1.73m2		
	Kd (N=92)	**IKd (N=120)**	**Kd (N=18)**	**IKd (N=43)**	**p-value of treatment-by-sub group interaction[c]**
probability (95% CI)[b]					
3 Months	0.7391 (0.6366 to 0.8168)	0.6411 (0.5482 to 0.7197)	0.4444 (0.2158 to 0.6512)	0.6279 (0.4663 to 0.7529)	
6 Months	0.5543 (0.4472 to 0.6489)	0.4892 (0.3969 to 0.5752)	0.4444 (0.2158 to 0.6512)	0.4186 (0.2712 to 0.5593)	
9 Months	0.4891 (0.3838 to 0.5862)	0.4049 (0.3165 to 0.4914)	0.2593 (0.0855 to 0.4766)	0.3023 (0.1740 to 0.4411)	
12 Months	0.4348 (0.3323 to 0.5328)	0.3121 (0.2312 to 0.3962)	0.2593 (0.0855 to 0.4766)	0.2326 (0.1205 to 0.3660)	
15 Months	0.3913 (0.2920 to 0.4891)	0.2581 (0.1827 to 0.3398)	0.1728 (0.0348 to 0.3994)	0.2093 (0.1036 to 0.3400)	
18 Months	0.3587 (0.2623 to 0.4559)	0.2187 (0.1479 to 0.2984)	0.1728 (0.0348 to 0.3994)	0.2093 (0.1036 to 0.3400)	
21 Months	0.3587 (0.2623 to 0.4559)	0.2088 (0.1393 to 0.2879)	0.1728 (0.0348 to 0.3994)	0.2093 (0.1036 to 0.3400)	
24 Months	0.3408 (0.2439 to 0.4398)	0.2088 (0.1393 to 0.2879)	0.1728 (0.0348 to 0.3994)	0.2093 (0.1036 to 0.3400)	
27 Months	0.3408 (0.2439 to 0.4398)	0.2088 (0.1393 to 0.2879)	0.1728 (0.0348 to 0.3994)	0.2093 (0.1036 to 0.3400)	

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.61 Subgroup analysis by baseline creatinine clearance (MDRD)
16.2.7.1.61.7 Treatment emergent severe adverse event including death by treatment group according to baseline creatinine clearance (MDRD) - Safety population

	>=60 mL/min/1.73m2		<60 mL/min/1.73m2		
	Kd (N=92)	**IKd (N=120)**	**Kd (N=18)**	**IKd (N=43)**	**p-value of treatment-by-sub group interaction[c]**
30 Months	0.3408 (0.2439 to 0.4398)	0.2088 (0.1393 to 0.2879)	0.1728 (0.0348 to 0.3994)	0.2093 (0.1036 to 0.3400)	
Number of patients at risk[b]					
3 Months	68	76	8	27	
6 Months	51	58	8	18	
9 Months	45	48	4	13	
12 Months	40	37	4	10	
15 Months	36	27	2	8	
18 Months	33	22	1	7	
21 Months	23	20	1	7	
24 Months	6	5	1	3	
27 Months	1	0	0	0	
30 Months	0	0	0	0	

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
PGM=DEVOPS/SAR650984/EFC15246/CIR_RWE/REPORT/PGM/eff_km_sr_subgrp_sig_s_t.sas OUT=REPORT/OUTPUT/eff_km_de_tesev345_crcl_s_t_x.rtf (12FEB2021 8:13)

16.2.7.1 Safety endpoints
16.2.7.1.62 Subgroup analysis by previous treatment with PI
16.2.7.1.62.1 Treatment emergent adverse event by treatment group according to previous treatment with PI - Safety population

	Yes		No		
	Kd (N=47)	**IKd (N=79)**	**Kd (N=75)**	**IKd (N=98)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	43 (91.5)	76 (96.2)	74 (98.7)	96 (98.0)	0.7414
Number (%) of patients censored	4 (8.5)	3 (3.8)	1 (1.3)	2 (2.0)	
Kaplan-Meier estimates of TEAE in months					
25% quantile (95% CI)	0.2300 (0.1314 to 0.3614)	0.0657 (0.0657 to 0.1314)	0.1314 (0.0657 to 0.1971)	0.0657 (0.0657 to 0.0986)	
Median (95% CI)	0.6242 (0.3285 to 0.8214)	0.1971 (0.1314 to 0.4928)	0.3614 (0.2628 to 0.5257)	0.1643 (0.0986 to 0.2300)	
75% quantile (95% CI)	1.5113 (0.6899 to 4.3696)	1.4127 (0.6899 to 1.9713)	0.7885 (0.5914 to 1.1828)	0.4271 (0.2628 to 0.7885)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd		0.0743		0.0777	
Hazard ratio (95% CI) vs Kd		1.4054 (0.9654 to 2.0461)		1.3152 (0.9691 to 1.7849)	
P-value		0.0757		0.0786	

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
PGM=DEVOPS/SAR650984/EFC15246/CIR_RWE/REPORT/PGM/eff_km_sr_subgrp_sig_s_t.sas OUT=REPORT/OUTPUT/eff_km_de_teae_pi_s_t_x.rtf (12FEB2021 8:09)

16.2.7.1 Safety endpoints
16.2.7.1.62 Subgroup analysis by previous treatment with PI
16.2.7.1.62.1 Treatment emergent adverse event by treatment group according to previous treatment with PI - Safety population

	Yes		No		
	Kd (N=47)	**IKd (N=79)**	**Kd (N=75)**	**IKd (N=98)**	**p-value of treatment-by-sub group interaction[c]**
probability (95% CI)[b]					
3 Months	0.1702 (0.0797 to 0.2895)	0.1013 (0.0473 to 0.1793)	0.0400 (0.0106 to 0.1022)	0.0510 (0.0190 to 0.1072)	
6 Months	0.1064 (0.0390 to 0.2127)	0.0633 (0.0234 to 0.1314)	0.0133 (0.0011 to 0.0639)	0.0306 (0.0082 to 0.0794)	
9 Months	0.1064 (0.0390 to 0.2127)	0.0506 (0.0164 to 0.1146)	0.0133 (0.0011 to 0.0639)	0.0204 (0.0039 to 0.0648)	
12 Months	0.1064 (0.0390 to 0.2127)	0.0380 (0.0101 to 0.0973)	0.0133 (0.0011 to 0.0639)	0.0204 (0.0039 to 0.0648)	
15 Months	0.0851 (0.0272 to 0.1856)	0.0380 (0.0101 to 0.0973)	0.0133 (0.0011 to 0.0639)	0.0204 (0.0039 to 0.0648)	
18 Months	0.0851 (0.0272 to 0.1856)	0.0380 (0.0101 to 0.0973)	0.0133 (0.0011 to 0.0639)	0.0204 (0.0039 to 0.0648)	
21 Months	0.0851 (0.0272 to 0.1856)	0.0380 (0.0101 to 0.0973)	0.0133 (0.0011 to 0.0639)	0.0204 (0.0039 to 0.0648)	
24 Months	0.0851 (0.0272 to 0.1856)	0.0380 (0.0101 to 0.0973)	0.0133 (0.0011 to 0.0639)	0.0204 (0.0039 to 0.0648)	
27 Months	0.0851 (0.0272 to 0.1856)	0.0380 (0.0101 to 0.0973)	0.0133 (0.0011 to 0.0639)	0.0204 (0.0039 to 0.0648)	

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.62 Subgroup analysis by previous treatment with PI
16.2.7.1.62.1 Treatment emergent adverse event by treatment group according to previous treatment with PI - Safety population

	Yes		No		
	Kd (N=47)	**IKd (N=79)**	**Kd (N=75)**	**IKd (N=98)**	**p-value of treatment-by-sub group interaction[c]**
30 Months	0.0851 (0.0272 to 0.1856)	0.0380 (0.0101 to 0.0973)	0.0133 (0.0011 to 0.0639)	0.0204 (0.0039 to 0.0648)	
Number of patients at risk[b]					
3 Months	8	8	3	5	
6 Months	5	5	1	3	
9 Months	5	4	1	2	
12 Months	5	3	1	2	
15 Months	4	3	1	2	
18 Months	4	3	1	2	
21 Months	2	3	1	2	
24 Months	1	1	0	0	
27 Months	0	0	0	0	
30 Months	0	0	0	0	

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.62 Subgroup analysis by previous treatment with PI
16.2.7.1.62.2 Treatment emergent serious adverse event by treatment group according to previous treatment with PI - Safety population

	Yes		No		
	Kd (N=47)	**IKd (N=79)**	**Kd (N=75)**	**IKd (N=98)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	31 (66.0)	52 (65.8)	39 (52.0)	53 (54.1)	0.8336
Number (%) of patients censored	16 (34.0)	27 (34.2)	36 (48.0)	45 (45.9)	
Kaplan-Meier estimates of TEAE in months					
25% quantile (95% CI)	3.3840 (1.7413 to 6.2752)	1.6427 (0.6571 to 4.7639)	4.8624 (3.3183 to 6.5708)	3.8439 (1.4784 to 9.2977)	
Median (95% CI)	11.2361 (5.5852 to 16.7228)	8.2464 (5.1253 to 12.5503)	15.4415 (9.1992 to NC)	17.3142 (11.4990 to NC)	
75% quantile (95% CI)	NC (15.9343 to NC)	NC (14.8830 to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd		0.6365		0.8350	
Hazard ratio (95% CI) vs Kd		1.1132 (0.7134 to 1.7368)		1.0448 (0.6908 to 1.5802)	
P-value		0.6367		0.8355	
probability (95% CI)[b]					

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.62 Subgroup analysis by previous treatment with PI
16.2.7.1.62.2 Treatment emergent serious adverse event by treatment group according to previous treatment with PI - Safety population

	Yes		No		
	Kd (N=47)	**IKd (N=79)**	**Kd (N=75)**	**IKd (N=98)**	**p-value of treatment-by-sub group interaction[c]**
3 Months	0.7660 (0.6174 to 0.8629)	0.6835 (0.5687 to 0.7738)	0.8531 (0.7505 to 0.9158)	0.7959 (0.7018 to 0.8632)	
6 Months	0.6383 (0.4843 to 0.7573)	0.5823 (0.4659 to 0.6819)	0.6771 (0.5580 to 0.7706)	0.7242 (0.6242 to 0.8018)	
9 Months	0.5516 (0.3990 to 0.6803)	0.4684 (0.3556 to 0.5732)	0.6229 (0.5025 to 0.7221)	0.6828 (0.5806 to 0.7651)	
12 Months	0.4854 (0.3365 to 0.6190)	0.4051 (0.2968 to 0.5105)	0.5823 (0.4619 to 0.6848)	0.6001 (0.4958 to 0.6895)	
15 Months	0.3939 (0.2536 to 0.5311)	0.3518 (0.2482 to 0.4569)	0.5136 (0.3946 to 0.6203)	0.5139 (0.4099 to 0.6084)	
18 Months	0.3475 (0.2137 to 0.4849)	0.3377 (0.2354 to 0.4427)	0.4858 (0.3679 to 0.5938)	0.4799 (0.3765 to 0.5758)	
21 Months	0.3475 (0.2137 to 0.4849)	0.3377 (0.2354 to 0.4427)	0.4715 (0.3543 to 0.5800)	0.4684 (0.3654 to 0.5648)	
24 Months	0.3089 (0.1754 to 0.4526)	0.3377 (0.2354 to 0.4427)	0.4715 (0.3543 to 0.5800)	0.4424 (0.3397 to 0.5402)	
27 Months	0.3089 (0.1754 to 0.4526)	0.3377 (0.2354 to 0.4427)	0.4715 (0.3543 to 0.5800)	0.4424 (0.3397 to 0.5402)	
30 Months	0.3089 (0.1754 to 0.4526)	0.3377 (0.2354 to 0.4427)	0.4715 (0.3543 to 0.5800)	0.4424 (0.3397 to 0.5402)	

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.62 Subgroup analysis by previous treatment with PI
16.2.7.1.62.2 Treatment emergent serious adverse event by treatment group according to previous treatment with PI - Safety population

	Yes		No		
	Kd (N=47)	**IKd (N=79)**	**Kd (N=75)**	**IKd (N=98)**	**p-value of treatment-by-sub group interaction[c]**
Number of patients at risk[b]					
3 Months	36	54	63	78	
6 Months	30	46	50	70	
9 Months	25	37	46	66	
12 Months	22	32	43	58	
15 Months	17	25	37	46	
18 Months	15	22	34	42	
21 Months	12	20	24	37	
24 Months	4	6	5	13	
27 Months	2	0	0	1	
30 Months	0	0	0	0	

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.62 Subgroup analysis by previous treatment with PI
16.2.7.1.62.3 Treatment emergent adverse event leading to discontinuation of treatment by treatment group according to previous treatment with PI - Safety population

	Yes		No		
	Kd (N=47)	**IKd (N=79)**	**Kd (N=75)**	**IKd (N=98)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	8 (17.0)	8 (10.1)	9 (12.0)	7 (7.1)	0.9552
Number (%) of patients censored	39 (83.0)	71 (89.9)	66 (88.0)	91 (92.9)	
Kaplan-Meier estimates of TEAE in months					
25% quantile (95% CI)	NC (7.8522 to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd		0.2769		0.2506	
Hazard ratio (95% CI) vs Kd		0.5843 (0.2193 to 1.5571)		0.5648 (0.2103 to 1.5167)	
P-value		0.2826		0.2570	
probability (95% CI)[b]					
3 Months	0.9149 (0.7889 to 0.9672)	0.9615 (0.8855 to 0.9874)	0.9865 (0.9079 to 0.9981)	0.9795 (0.9205 to 0.9948)	

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.62 Subgroup analysis by previous treatment with PI
16.2.7.1.62.3 Treatment emergent adverse event leading to discontinuation of treatment by treatment group according to previous treatment with PI - Safety population

	Yes		No		
	Kd (N=47)	**IKd (N=79)**	**Kd (N=75)**	**IKd (N=98)**	**p-value of treatment-by-sub group interaction[c]**
6 Months	0.9149 (0.7889 to 0.9672)	0.9485 (0.8687 to 0.9804)	0.9444 (0.8584 to 0.9788)	0.9479 (0.8793 to 0.9780)	
9 Months	0.8713 (0.7357 to 0.9401)	0.9216 (0.8338 to 0.9640)	0.8860 (0.7848 to 0.9413)	0.9374 (0.8658 to 0.9714)	
12 Months	0.8713 (0.7357 to 0.9401)	0.9216 (0.8338 to 0.9640)	0.8860 (0.7848 to 0.9413)	0.9374 (0.8658 to 0.9714)	
15 Months	0.8713 (0.7357 to 0.9401)	0.9072 (0.8150 to 0.9547)	0.8860 (0.7848 to 0.9413)	0.9263 (0.8516 to 0.9642)	
18 Months	0.8464 (0.7040 to 0.9239)	0.9072 (0.8150 to 0.9547)	0.8705 (0.7655 to 0.9305)	0.9263 (0.8516 to 0.9642)	
21 Months	0.8215 (0.6736 to 0.9068)	0.8904 (0.7919 to 0.9439)	0.8705 (0.7655 to 0.9305)	0.9263 (0.8516 to 0.9642)	
24 Months	0.8215 (0.6736 to 0.9068)	0.8904 (0.7919 to 0.9439)	0.8705 (0.7655 to 0.9305)	0.9263 (0.8516 to 0.9642)	
27 Months	0.8215 (0.6736 to 0.9068)	0.8904 (0.7919 to 0.9439)	0.8705 (0.7655 to 0.9305)	0.9263 (0.8516 to 0.9642)	
30 Months	0.8215 (0.6736 to 0.9068)	0.8904 (0.7919 to 0.9439)	0.8705 (0.7655 to 0.9305)	0.9263 (0.8516 to 0.9642)	

Number of patients at risk[b]

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.62 Subgroup analysis by previous treatment with PI
16.2.7.1.62.3 Treatment emergent adverse event leading to discontinuation of treatment by treatment group according to previous treatment with PI - Safety population

	Yes		No		
	Kd (N=47)	**IKd (N=79)**	**Kd (N=75)**	**IKd (N=98)**	**p-value of treatment-by-sub group interaction[c]**
3 Months	43	75	72	95	
6 Months	43	71	65	90	
9 Months	39	68	60	87	
12 Months	38	65	59	87	
15 Months	35	59	57	81	
18 Months	34	55	55	78	
21 Months	27	47	46	71	
24 Months	10	13	16	27	
27 Months	2	0	2	2	
30 Months	0	0	0	0	

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.62 Subgroup analysis by previous treatment with PI
16.2.7.1.62.4 Treatment emergent mild adverse event by treatment group according to previous treatment with PI - Safety population

	Yes		No		
	Kd (N=47)	**IKd (N=79)**	**Kd (N=75)**	**IKd (N=98)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	41 (87.2)	74 (93.7)	74 (98.7)	93 (94.9)	0.4469
Number (%) of patients censored	6 (12.8)	5 (6.3)	1 (1.3)	5 (5.1)	
Kaplan-Meier estimates of TEAE in months					
25% quantile (95% CI)	0.2300 (0.1643 to 0.3614)	0.0657 (0.0657 to 0.1314)	0.1314 (0.0657 to 0.2300)	0.0657 (0.0657 to 0.0986)	
Median (95% CI)	0.6571 (0.3614 to 1.4456)	0.2300 (0.1314 to 0.4928)	0.3943 (0.2628 to 0.5914)	0.1643 (0.1314 to 0.2300)	
75% quantile (95% CI)	2.2012 (1.0185 to 5.8152)	1.4784 (0.9528 to 2.3655)	0.8871 (0.6242 to 1.2156)	0.5257 (0.2957 to 1.0185)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd		0.0544		0.2071	
Hazard ratio (95% CI) vs Kd		1.4535 (0.9909 to 2.1323)		1.2184 (0.8959 to 1.6570)	
P-value		0.0558		0.2078	

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CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.62 Subgroup analysis by previous treatment with PI
16.2.7.1.62.4 Treatment emergent mild adverse event by treatment group according to previous treatment with PI - Safety population

	Yes		No		
	Kd (N=47)	**IKd (N=79)**	**Kd (N=75)**	**IKd (N=98)**	**p-value of treatment-by-sub group interaction[c]**
probability (95% CI)[b]					
3 Months	0.1989 (0.0986 to 0.3243)	0.1392 (0.0740 to 0.2247)	0.0667 (0.0247 to 0.1380)	0.0852 (0.0400 to 0.1518)	
6 Months	0.1326 (0.0540 to 0.2470)	0.0820 (0.0335 to 0.1586)	0.0267 (0.0051 to 0.0833)	0.0639 (0.0262 to 0.1251)	
9 Months	0.1326 (0.0540 to 0.2470)	0.0656 (0.0232 to 0.1394)	0.0267 (0.0051 to 0.0833)	0.0426 (0.0139 to 0.0972)	
12 Months	0.1326 (0.0540 to 0.2470)	0.0492 (0.0141 to 0.1193)	0.0267 (0.0051 to 0.0833)	0.0426 (0.0139 to 0.0972)	
15 Months	0.1061 (0.0370 to 0.2171)	0.0492 (0.0141 to 0.1193)	0.0133 (0.0011 to 0.0639)	0.0426 (0.0139 to 0.0972)	
18 Months	0.1061 (0.0370 to 0.2171)	0.0492 (0.0141 to 0.1193)	0.0133 (0.0011 to 0.0639)	0.0426 (0.0139 to 0.0972)	
21 Months	0.1061 (0.0370 to 0.2171)	0.0492 (0.0141 to 0.1193)	0.0133 (0.0011 to 0.0639)	0.0426 (0.0139 to 0.0972)	
24 Months	0.1061 (0.0370 to 0.2171)	0.0492 (0.0141 to 0.1193)	0.0133 (0.0011 to 0.0639)	0.0426 (0.0139 to 0.0972)	
27 Months	0.1061 (0.0370 to 0.2171)	0.0492 (0.0141 to 0.1193)	0.0133 (0.0011 to 0.0639)	0.0426 (0.0139 to 0.0972)	

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
PGM=DEVOPS/SAR650984/EFC15246/CIR_RWE/REPORT/PGM/eff_km_sr_subgrp_sig_s_t.sas OUT=REPORT/OUTPUT/eff_km_de_tesev12_pi_s_t_x.rtf (12FEB2021 8:12)

16.2.7.1 Safety endpoints
16.2.7.1.62 Subgroup analysis by previous treatment with PI
16.2.7.1.62.4 Treatment emergent mild adverse event by treatment group according to previous treatment with PI - Safety population

	Yes		No		
	Kd (N=47)	**IKd (N=79)**	**Kd (N=75)**	**IKd (N=98)**	**p-value of treatment-by-sub group interaction[c]**
30 Months	0.1061 (0.0370 to 0.2171)	0.0492 (0.0141 to 0.1193)	0.0133 (0.0011 to 0.0639)	0.0426 (0.0139 to 0.0972)	
Number of patients at risk[b]					
3 Months	9	11	5	8	
6 Months	6	5	2	6	
9 Months	6	4	2	4	
12 Months	5	3	2	4	
15 Months	4	3	1	3	
18 Months	4	3	1	3	
21 Months	2	3	1	3	
24 Months	1	1	0	0	
27 Months	0	0	0	0	
30 Months	0	0	0	0	

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.62 Subgroup analysis by previous treatment with PI
16.2.7.1.62.5 Treatment emergent severe adverse event by treatment group according to previous treatment with PI - Safety population

	Yes		No		
	Kd (N=47)	**IKd (N=79)**	**Kd (N=75)**	**IKd (N=98)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	33 (70.2)	59 (74.7)	48 (64.0)	75 (76.5)	0.5128
Number (%) of patients censored	14 (29.8)	20 (25.3)	27 (36.0)	23 (23.5)	
Kaplan-Meier estimates of TEAE in months					
25% quantile (95% CI)	1.9055 (0.6571 to 4.0411)	1.2485 (0.6242 to 2.5955)	1.8727 (0.5257 to 3.9097)	1.2813 (0.5257 to 1.9713)	
Median (95% CI)	6.2752 (4.0411 to 12.3532)	7.6550 (4.3368 to 9.9220)	6.7351 (4.2382 to 12.9774)	5.4209 (3.6140 to 7.1622)	
75% quantile (95% CI)	NC (12.2875 to NC)	18.7598 (11.4333 to NC)	NC (16.8542 to NC)	15.8357 (9.7577 to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd		0.5668		0.1065	
Hazard ratio (95% CI) vs Kd		1.1326 (0.7395 to 1.7348)		1.3470 (0.9369 to 1.9365)	
P-value		0.5670		0.1078	
probability (95% CI)[b]					

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.62 Subgroup analysis by previous treatment with PI
16.2.7.1.62.5 Treatment emergent severe adverse event by treatment group according to previous treatment with PI - Safety population

	Yes		No		
	Kd (N=47)	**IKd (N=79)**	**Kd (N=75)**	**IKd (N=98)**	**p-value of treatment-by-sub group interaction[c]**
3 Months	0.7021 (0.5495 to 0.8115)	0.6549 (0.5385 to 0.7487)	0.6905 (0.5718 to 0.7824)	0.6319 (0.5282 to 0.7188)	
6 Months	0.5106 (0.3609 to 0.6420)	0.5265 (0.4104 to 0.6300)	0.5524 (0.4318 to 0.6574)	0.4454 (0.3450 to 0.5408)	
9 Months	0.4226 (0.2802 to 0.5582)	0.4109 (0.3015 to 0.5171)	0.4557 (0.3393 to 0.5648)	0.3729 (0.2776 to 0.4680)	
12 Months	0.4004 (0.2605 to 0.5364)	0.3339 (0.2322 to 0.4386)	0.4005 (0.2883 to 0.5101)	0.2693 (0.1855 to 0.3601)	
15 Months	0.3322 (0.2018 to 0.4682)	0.2651 (0.1722 to 0.3672)	0.3729 (0.2634 to 0.4822)	0.2571 (0.1746 to 0.3475)	
18 Months	0.3084 (0.1819 to 0.4440)	0.2504 (0.1595 to 0.3518)	0.3447 (0.2383 to 0.4535)	0.2191 (0.1412 to 0.3080)	
21 Months	0.3084 (0.1819 to 0.4440)	0.2347 (0.1461 to 0.3355)	0.3447 (0.2383 to 0.4535)	0.2191 (0.1412 to 0.3080)	
24 Months	0.2644 (0.1377 to 0.4095)	0.2347 (0.1461 to 0.3355)	0.3447 (0.2383 to 0.4535)	0.2191 (0.1412 to 0.3080)	
27 Months	0.2644 (0.1377 to 0.4095)	0.2347 (0.1461 to 0.3355)	0.3447 (0.2383 to 0.4535)	0.2191 (0.1412 to 0.3080)	
30 Months	0.2644 (0.1377 to 0.4095)	0.2347 (0.1461 to 0.3355)	0.3447 (0.2383 to 0.4535)	0.2191 (0.1412 to 0.3080)	

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.62 Subgroup analysis by previous treatment with PI
16.2.7.1.62.5 Treatment emergent severe adverse event by treatment group according to previous treatment with PI - Safety population

	Yes		No		
	Kd (N=47)	**IKd (N=79)**	**Kd (N=75)**	**IKd (N=98)**	**p-value of treatment-by-sub group interaction[c]**
Number of patients at risk[b]					
3 Months	33	51	50	61	
6 Months	24	41	40	43	
9 Months	19	32	33	36	
12 Months	18	26	29	26	
15 Months	14	18	27	21	
18 Months	13	16	24	17	
21 Months	9	14	18	17	
24 Months	2	3	6	7	
27 Months	1	0	0	0	
30 Months	0	0	0	0	

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.62 Subgroup analysis by previous treatment with PI
16.2.7.1.62.6 Treatment emergent severe adverse event including death by treatment group according to previous treatment with PI - Safety population

	Yes		No		
	Kd (N=47)	**IKd (N=79)**	**Kd (N=75)**	**IKd (N=98)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	33 (70.2)	60 (75.9)	49 (65.3)	76 (77.6)	0.5663
Number (%) of patients censored	14 (29.8)	19 (24.1)	26 (34.7)	22 (22.4)	
Kaplan-Meier estimates of TEAE in months					
25% quantile (95% CI)	1.9055 (0.6571 to 4.0411)	1.0513 (0.5914 to 2.5955)	1.4456 (0.5257 to 3.8768)	1.2813 (0.5257 to 1.9713)	
Median (95% CI)	6.2752 (4.0411 to 12.3532)	6.5051 (4.3368 to 9.0021)	6.7351 (4.2053 to 12.9774)	5.4209 (3.6140 to 7.1622)	
75% quantile (95% CI)	NC (12.2875 to NC)	15.6057 (11.4333 to NC)	NC (15.6057 to NC)	14.1602 (9.7577 to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd		0.5159		0.1100	
Hazard ratio (95% CI) vs Kd		1.1512 (0.7525 to 1.7610)		1.3396 (0.9348 to 1.9199)	
P-value		0.5163		0.1112	
probability (95% CI)[b]					

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.62 Subgroup analysis by previous treatment with PI
16.2.7.1.62.6 Treatment emergent severe adverse event including death by treatment group according to previous treatment with PI - Safety population

	Yes		No		
	Kd (N=47)	**IKd (N=79)**	**Kd (N=75)**	**IKd (N=98)**	**p-value of treatment-by-sub group interaction[c]**
3 Months	0.7021 (0.5495 to 0.8115)	0.6456 (0.5296 to 0.7399)	0.6790 (0.5604 to 0.7720)	0.6319 (0.5282 to 0.7188)	
6 Months	0.5106 (0.3609 to 0.6420)	0.5190 (0.4039 to 0.6222)	0.5432 (0.4236 to 0.6482)	0.4454 (0.3450 to 0.5408)	
9 Months	0.4226 (0.2802 to 0.5582)	0.4051 (0.2968 to 0.5105)	0.4481 (0.3330 to 0.5567)	0.3729 (0.2776 to 0.4680)	
12 Months	0.4004 (0.2605 to 0.5364)	0.3291 (0.2287 to 0.4329)	0.3938 (0.2830 to 0.5026)	0.2693 (0.1855 to 0.3601)	
15 Months	0.3322 (0.2018 to 0.4682)	0.2613 (0.1696 to 0.3624)	0.3667 (0.2586 to 0.4751)	0.2468 (0.1659 to 0.3363)	
18 Months	0.3084 (0.1819 to 0.4440)	0.2468 (0.1572 to 0.3472)	0.3390 (0.2340 to 0.4468)	0.2103 (0.1343 to 0.2979)	
21 Months	0.3084 (0.1819 to 0.4440)	0.2314 (0.1439 to 0.3311)	0.3390 (0.2340 to 0.4468)	0.2103 (0.1343 to 0.2979)	
24 Months	0.2644 (0.1377 to 0.4095)	0.2314 (0.1439 to 0.3311)	0.3390 (0.2340 to 0.4468)	0.2103 (0.1343 to 0.2979)	
27 Months	0.2644 (0.1377 to 0.4095)	0.2314 (0.1439 to 0.3311)	0.3390 (0.2340 to 0.4468)	0.2103 (0.1343 to 0.2979)	
30 Months	0.2644 (0.1377 to 0.4095)	0.2314 (0.1439 to 0.3311)	0.3390 (0.2340 to 0.4468)	0.2103 (0.1343 to 0.2979)	

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.62 Subgroup analysis by previous treatment with PI
16.2.7.1.62.6 Treatment emergent severe adverse event including death by treatment group according to previous treatment with PI - Safety population

	Yes		No		
	Kd (N=47)	**IKd (N=79)**	**Kd (N=75)**	**IKd (N=98)**	**p-value of treatment-by-sub group interaction[c]**
Number of patients at risk[b]					
3 Months	33	51	50	61	
6 Months	24	41	40	43	
9 Months	19	32	33	36	
12 Months	18	26	29	26	
15 Months	14	18	27	21	
18 Months	13	16	24	17	
21 Months	9	14	18	17	
24 Months	2	3	6	7	
27 Months	1	0	0	0	
30 Months	0	0	0	0	

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.63 Subgroup analysis by previous treatment with IMID
16.2.7.1.63.1 Treatment emergent adverse event by treatment group according to previous treatment with IMID - Safety population

	Yes		No		
	Kd (N=62)	**IKd (N=80)**	**Kd (N=60)**	**IKd (N=97)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	60 (96.8)	79 (98.8)	57 (95.0)	93 (95.9)	0.4181
Number (%) of patients censored	2 (3.2)	1 (1.3)	3 (5.0)	4 (4.1)	
Kaplan-Meier estimates of TEAE in months					
25% quantile (95% CI)	0.2300 (0.0986 to 0.3614)	0.0657 (0.0329 to 0.0986)	0.1478 (0.0986 to 0.1971)	0.0657 (0.0657 to 0.1314)	
Median (95% CI)	0.5585 (0.3614 to 0.8214)	0.1807 (0.0986 to 0.2628)	0.3285 (0.1971 to 0.5257)	0.1971 (0.1314 to 0.2628)	
75% quantile (95% CI)	1.1828 (0.8871 to 1.5113)	0.6899 (0.2957 to 1.4784)	0.6571 (0.5257 to 2.2012)	0.6899 (0.3943 to 1.3142)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd		0.0456		0.2843	
Hazard ratio (95% CI) vs Kd		1.4088 (1.0052 to 1.9746)		1.1977 (0.8605 to 1.6670)	
P-value		0.0466		0.2850	

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.63 Subgroup analysis by previous treatment with IMID
16.2.7.1.63.1 Treatment emergent adverse event by treatment group according to previous treatment with IMID - Safety population

	Yes		No		
	Kd (N=62)	**IKd (N=80)**	**Kd (N=60)**	**IKd (N=97)**	**p-value of treatment-by-sub group interaction[c]**
Hazard ratio inverted (95% CI) vs IKd	0.7098 (0.5064 to 0.9948)				
probability (95% CI)[b]					
3 Months	0.0806 (0.0297 to 0.1648)	0.0625 (0.0232 to 0.1298)	0.1000 (0.0407 to 0.1909)	0.0825 (0.0386 to 0.1477)	
6 Months	0.0323 (0.0061 to 0.0994)	0.0250 (0.0048 to 0.0784)	0.0667 (0.0215 to 0.1482)	0.0619 (0.0253 to 0.1217)	
9 Months	0.0323 (0.0061 to 0.0994)	0.0250 (0.0048 to 0.0784)	0.0667 (0.0215 to 0.1482)	0.0412 (0.0135 to 0.0944)	
12 Months	0.0323 (0.0061 to 0.0994)	0.0125 (0.0011 to 0.0602)	0.0667 (0.0215 to 0.1482)	0.0412 (0.0135 to 0.0944)	
15 Months	0.0323 (0.0061 to 0.0994)	0.0125 (0.0011 to 0.0602)	0.0500 (0.0132 to 0.1258)	0.0412 (0.0135 to 0.0944)	
18 Months	0.0323 (0.0061 to 0.0994)	0.0125 (0.0011 to 0.0602)	0.0500 (0.0132 to 0.1258)	0.0412 (0.0135 to 0.0944)	
21 Months	0.0323 (0.0061 to 0.0994)	0.0125 (0.0011 to 0.0602)	0.0500 (0.0132 to 0.1258)	0.0412 (0.0135 to 0.0944)	
24 Months	0.0323 (0.0061 to 0.0994)	0.0125 (0.0011 to 0.0602)	0.0500 (0.0132 to 0.1258)	0.0412 (0.0135 to 0.0944)	

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.63 Subgroup analysis by previous treatment with IMID
16.2.7.1.63.1 Treatment emergent adverse event by treatment group according to previous treatment with IMID - Safety population

	Yes		No		
	Kd (N=62)	**IKd (N=80)**	**Kd (N=60)**	**IKd (N=97)**	**p-value of treatment-by-sub group interaction[c]**
27 Months	0.0323 (0.0061 to 0.0994)	0.0125 (0.0011 to 0.0602)	0.0500 (0.0132 to 0.1258)	0.0412 (0.0135 to 0.0944)	
30 Months	0.0323 (0.0061 to 0.0994)	0.0125 (0.0011 to 0.0602)	0.0500 (0.0132 to 0.1258)	0.0412 (0.0135 to 0.0944)	
Number of patients at risk[b]					
3 Months	5	5	6	8	
6 Months	2	2	4	6	
9 Months	2	2	4	4	
12 Months	2	1	4	4	
15 Months	2	1	3	4	
18 Months	2	1	3	4	
21 Months	1	1	2	4	
24 Months	0	0	1	1	
27 Months	0	0	0	0	
30 Months	0	0	0	0	

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.63 Subgroup analysis by previous treatment with IMID
16.2.7.1.63.2 Treatment emergent serious adverse event by treatment group according to previous treatment with IMID - Safety population

	Yes		No		
	Kd (N=62)	**IKd (N=80)**	**Kd (N=60)**	**IKd (N=97)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	35 (56.5)	46 (57.5)	35 (58.3)	59 (60.8)	0.5521
Number (%) of patients censored	27 (43.5)	34 (42.5)	25 (41.7)	38 (39.2)	
Kaplan-Meier estimates of TEAE in months					
25% quantile (95% CI)	3.9425 (1.5113 to 5.5524)	3.4497 (0.9528 to 7.1622)	5.3881 (2.1027 to 10.4805)	2.4312 (0.6899 to 4.8953)	
Median (95% CI)	13.8316 (5.8152 to NC)	13.4045 (9.2977 to NC)	13.5688 (10.4805 to NC)	10.3162 (7.6879 to 16.0657)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd		0.9622		0.4077	
Hazard ratio (95% CI) vs Kd		0.9894 (0.6372 to 1.5363)		1.1930 (0.7852 to 1.8127)	
P-value		0.9622		0.4083	
probability (95% CI)[b]					

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
PGM=DEVOPS/SAR650984/EFC15246/CIR_RWE/REPORT/PGM/eff_km_sr_subgrp_sig_s_t.sas OUT=REPORT/OUTPUT/eff_km_de_tesae_imid_s_t_x.rtf (12FEB2021 8:12)

16.2.7.1 Safety endpoints
16.2.7.1.63 Subgroup analysis by previous treatment with IMID
16.2.7.1.63.2 Treatment emergent serious adverse event by treatment group according to previous treatment with IMID - Safety population

	Yes		No		
	Kd (N=62)	**IKd (N=80)**	**Kd (N=60)**	**IKd (N=97)**	**p-value of treatment-by-sub group interaction[c]**
3 Months	0.8061 (0.6839 to 0.8849)	0.7750 (0.6669 to 0.8518)	0.8333 (0.7124 to 0.9066)	0.7216 (0.6210 to 0.7998)	
6 Months	0.6252 (0.4917 to 0.7328)	0.6875 (0.5736 to 0.7768)	0.7000 (0.5669 to 0.7992)	0.6384 (0.5342 to 0.7252)	
9 Months	0.5265 (0.3947 to 0.6422)	0.6375 (0.5221 to 0.7321)	0.6667 (0.5324 to 0.7704)	0.5442 (0.4397 to 0.6373)	
12 Months	0.5265 (0.3947 to 0.6422)	0.5625 (0.4471 to 0.6628)	0.5641 (0.4292 to 0.6787)	0.4709 (0.3687 to 0.5665)	
15 Months	0.4771 (0.3481 to 0.5952)	0.4844 (0.3708 to 0.5888)	0.4579 (0.3273 to 0.5791)	0.4050 (0.3060 to 0.5016)	
18 Months	0.4271 (0.3019 to 0.5465)	0.4571 (0.3446 to 0.5625)	0.4396 (0.3102 to 0.5615)	0.3808 (0.2831 to 0.4778)	
21 Months	0.4271 (0.3019 to 0.5465)	0.4432 (0.3313 to 0.5491)	0.4212 (0.2933 to 0.5437)	0.3808 (0.2831 to 0.4778)	
24 Months	0.4271 (0.3019 to 0.5465)	0.4104 (0.2991 to 0.5183)	0.3965 (0.2687 to 0.5214)	0.3808 (0.2831 to 0.4778)	
27 Months	0.4271 (0.3019 to 0.5465)	0.4104 (0.2991 to 0.5183)	0.3965 (0.2687 to 0.5214)	0.3808 (0.2831 to 0.4778)	
30 Months	0.4271 (0.3019 to 0.5465)	0.4104 (0.2991 to 0.5183)	0.3965 (0.2687 to 0.5214)	0.3808 (0.2831 to 0.4778)	

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
PGM=DEVOPS/SAR650984/EFC15246/CIR_RWE/REPORT/PGM/eff_km_sr_subgrp_sig_s_t.sas OUT=REPORT/OUTPUT/eff_km_de_tesae_imid_s_t_x.rtf (12FEB2021 8:12)

16.2.7.1 Safety endpoints
16.2.7.1.63 Subgroup analysis by previous treatment with IMID
16.2.7.1.63.2 Treatment emergent serious adverse event by treatment group according to previous treatment with IMID - Safety population

	Yes		No		
	Kd (N=62)	**IKd (N=80)**	**Kd (N=60)**	**IKd (N=97)**	**p-value of treatment-by-sub group interaction[c]**
Number of patients at risk[b]					
3 Months	49	62	50	70	
6 Months	38	55	42	61	
9 Months	32	51	39	52	
12 Months	32	45	33	45	
15 Months	29	36	25	35	
18 Months	25	33	24	31	
21 Months	18	27	18	30	
24 Months	3	7	6	12	
27 Months	1	0	1	1	
30 Months	0	0	0	0	

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.63 Subgroup analysis by previous treatment with IMID
16.2.7.1.63.3 Treatment emergent adverse event leading to discontinuation of treatment by treatment group according to previous treatment with IMID - Safety population

	Yes		No		
	Kd (N=62)	**IKd (N=80)**	**Kd (N=60)**	**IKd (N=97)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	9 (14.5)	4 (5.0)	8 (13.3)	11 (11.3)	0.2042
Number (%) of patients censored	53 (85.5)	76 (95.0)	52 (86.7)	86 (88.7)	
Kaplan-Meier estimates of TEAE in months					
25% quantile (95% CI)	NC (15.3429 to NC)	NC (NC to NC)	NC (18.2669 to NC)	NC (NC to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd		0.0489		0.7230	
Hazard ratio (95% CI) vs Kd		0.3250 (0.1001 to 1.0556)		0.8483 (0.3412 to 2.1092)	
P-value		0.0615		0.7233	
probability (95% CI)[b]					
3 Months	0.9511 (0.8559 to 0.9840)	0.9875 (0.9146 to 0.9982)	0.9667 (0.8732 to 0.9916)	0.9583 (0.8928 to 0.9842)	

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.63 Subgroup analysis by previous treatment with IMID
16.2.7.1.63.3 Treatment emergent adverse event leading to discontinuation of treatment by treatment group according to previous treatment with IMID - Safety population

	Yes		No		
	Kd (N=62)	**IKd (N=80)**	**Kd (N=60)**	**IKd (N=97)**	**p-value of treatment-by-sub group interaction[c]**
6 Months	0.9344 (0.8345 to 0.9749)	0.9745 (0.9019 to 0.9936)	0.9330 (0.8313 to 0.9743)	0.9265 (0.8520 to 0.9643)	
9 Months	0.8815 (0.7671 to 0.9417)	0.9615 (0.8854 to 0.9874)	0.8815 (0.7673 to 0.9417)	0.9048 (0.8250 to 0.9493)	
12 Months	0.8815 (0.7671 to 0.9417)	0.9615 (0.8854 to 0.9874)	0.8815 (0.7673 to 0.9417)	0.9048 (0.8250 to 0.9493)	
15 Months	0.8815 (0.7671 to 0.9417)	0.9476 (0.8662 to 0.9800)	0.8815 (0.7673 to 0.9417)	0.8935 (0.8110 to 0.9413)	
18 Months	0.8448 (0.7224 to 0.9162)	0.9476 (0.8662 to 0.9800)	0.8815 (0.7673 to 0.9417)	0.8935 (0.8110 to 0.9413)	
21 Months	0.8448 (0.7224 to 0.9162)	0.9476 (0.8662 to 0.9800)	0.8615 (0.7414 to 0.9284)	0.8806 (0.7943 to 0.9322)	
24 Months	0.8448 (0.7224 to 0.9162)	0.9476 (0.8662 to 0.9800)	0.8615 (0.7414 to 0.9284)	0.8806 (0.7943 to 0.9322)	
27 Months	0.8448 (0.7224 to 0.9162)	0.9476 (0.8662 to 0.9800)	0.8615 (0.7414 to 0.9284)	0.8806 (0.7943 to 0.9322)	
30 Months	0.8448 (0.7224 to 0.9162)	0.9476 (0.8662 to 0.9800)	0.8615 (0.7414 to 0.9284)	0.8806 (0.7943 to 0.9322)	

Number of patients at risk[b]

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
PGM=DEVOPS/SAR650984/EFC15246/CIR_RWE/REPORT/PGM/eff_km_sr_subgrp_sig_s_t.sas OUT=REPORT/OUTPUT/eff_km_de_tedisc_imid_s_t_x.rtf (12FEB2021 8:12)

16.2.7.1 Safety endpoints
16.2.7.1.63 Subgroup analysis by previous treatment with IMID
16.2.7.1.63.3 Treatment emergent adverse event leading to discontinuation of treatment by treatment group according to previous treatment with IMID - Safety population

	Yes		No		
	Kd (N=62)	**IKd (N=80)**	**Kd (N=60)**	**IKd (N=97)**	**p-value of treatment-by-sub group interaction[c]**
3 Months	57	78	58	92	
6 Months	53	75	55	86	
9 Months	50	72	49	83	
12 Months	49	71	48	81	
15 Months	48	65	44	75	
18 Months	45	63	44	70	
21 Months	38	55	35	63	
24 Months	14	23	12	17	
27 Months	3	1	1	1	
30 Months	0	0	0	0	

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.63 Subgroup analysis by previous treatment with IMID
16.2.7.1.63.4 Treatment emergent mild adverse event by treatment group according to previous treatment with IMID - Safety population

	Yes		No		
	Kd (N=62)	**IKd (N=80)**	**Kd (N=60)**	**IKd (N=97)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	59 (95.2)	77 (96.3)	56 (93.3)	90 (92.8)	0.2832
Number (%) of patients censored	3 (4.8)	3 (3.8)	4 (6.7)	7 (7.2)	
Kaplan-Meier estimates of TEAE in months					
25% quantile (95% CI)	0.2628 (0.0986 to 0.4271)	0.0657 (0.0329 to 0.0986)	0.1643 (0.0986 to 0.2300)	0.0657 (0.0657 to 0.1314)	
Median (95% CI)	0.6571 (0.4271 to 0.9528)	0.1971 (0.1314 to 0.2957)	0.3450 (0.2300 to 0.5257)	0.1971 (0.1314 to 0.2628)	
75% quantile (95% CI)	1.2156 (0.9528 to 1.9384)	0.7392 (0.3614 to 1.5113)	0.6735 (0.5257 to 2.7926)	1.1828 (0.4600 to 2.1355)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd		0.0361		0.4213	
Hazard ratio (95% CI) vs Kd		1.4380 (1.0221 to 2.0232)		1.1469 (0.8210 to 1.6023)	
P-value		0.0371		0.4216	

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
PGM=DEVOPS/SAR650984/EFC15246/CIR_RWE/REPORT/PGM/eff_km_sr_subgrp_sig_s_t.sas OUT=REPORT/OUTPUT/eff_km_de_tesev12_imid_s_t_x.rtf (12FEB2021 8:12)

16.2.7.1 Safety endpoints
16.2.7.1.63 Subgroup analysis by previous treatment with IMID
16.2.7.1.63.4 Treatment emergent mild adverse event by treatment group according to previous treatment with IMID - Safety population

	Yes		No		
	Kd (N=62)	**IKd (N=80)**	**Kd (N=60)**	**IKd (N=97)**	**p-value of treatment-by-sub group interaction[c]**
Hazard ratio inverted (95% CI) vs IKd	0.6954 (0.4943 to 0.9784)				
probability (95% CI)[b]					
3 Months	0.0995 (0.0406 to 0.1900)	0.0750 (0.0306 to 0.1459)	0.1333 (0.0623 to 0.2316)	0.1385 (0.0782 to 0.2157)	
6 Months	0.0498 (0.0131 to 0.1252)	0.0469 (0.0140 to 0.1116)	0.0833 (0.0307 to 0.1699)	0.0937 (0.0453 to 0.1635)	
9 Months	0.0498 (0.0131 to 0.1252)	0.0469 (0.0140 to 0.1116)	0.0833 (0.0307 to 0.1699)	0.0586 (0.0223 to 0.1204)	
12 Months	0.0498 (0.0131 to 0.1252)	0.0313 (0.0065 to 0.0922)	0.0833 (0.0307 to 0.1699)	0.0586 (0.0223 to 0.1204)	
15 Months	0.0332 (0.0062 to 0.1020)	0.0313 (0.0065 to 0.0922)	0.0625 (0.0184 to 0.1459)	0.0586 (0.0223 to 0.1204)	
18 Months	0.0332 (0.0062 to 0.1020)	0.0313 (0.0065 to 0.0922)	0.0625 (0.0184 to 0.1459)	0.0586 (0.0223 to 0.1204)	
21 Months	0.0332 (0.0062 to 0.1020)	0.0313 (0.0065 to 0.0922)	0.0625 (0.0184 to 0.1459)	0.0586 (0.0223 to 0.1204)	
24 Months	0.0332 (0.0062 to 0.1020)	0.0313 (0.0065 to 0.0922)	0.0625 (0.0184 to 0.1459)	0.0586 (0.0223 to 0.1204)	

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.63 Subgroup analysis by previous treatment with IMID
16.2.7.1.63.4 Treatment emergent mild adverse event by treatment group according to previous treatment with IMID - Safety population

	Yes		No		
	Kd (N=62)	**IKd (N=80)**	**Kd (N=60)**	**IKd (N=97)**	**p-value of treatment-by-sub group interaction[c]**
27 Months	0.0332 (0.0062 to 0.1020)	0.0313 (0.0065 to 0.0922)	0.0625 (0.0184 to 0.1459)	0.0586 (0.0223 to 0.1204)	
30 Months	0.0332 (0.0062 to 0.1020)	0.0313 (0.0065 to 0.0922)	0.0625 (0.0184 to 0.1459)	0.0586 (0.0223 to 0.1204)	
Number of patients at risk[b]					
3 Months	6	6	8	13	
6 Months	3	3	5	8	
9 Months	3	3	5	5	
12 Months	3	2	4	5	
15 Months	2	1	3	5	
18 Months	2	1	3	5	
21 Months	1	1	2	5	
24 Months	0	0	1	1	
27 Months	0	0	0	0	
30 Months	0	0	0	0	

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
PGM=DEVOPS/SAR650984/EFC15246/CIR_RWE/REPORT/PGM/eff_km_sr_subgrp_sig_s_t.sas OUT=REPORT/OUTPUT/eff_km_de_tesev12_imid_s_t_x.rtf (12FEB2021 8:12)

16.2.7.1 Safety endpoints
16.2.7.1.63 Subgroup analysis by previous treatment with IMID
16.2.7.1.63.5 Treatment emergent severe adverse event by treatment group according to previous treatment with IMID - Safety population

	Yes		No		
	Kd (N=62)	**IKd (N=80)**	**Kd (N=60)**	**IKd (N=97)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	43 (69.4)	60 (75.0)	38 (63.3)	74 (76.3)	0.3131
Number (%) of patients censored	19 (30.6)	20 (25.0)	22 (36.7)	23 (23.7)	
Kaplan-Meier estimates of TEAE in months					
25% quantile (95% CI)	1.2156 (0.4928 to 2.3326)	1.3142 (0.7228 to 2.8255)	3.2854 (1.1170 to 5.2238)	1.2485 (0.4600 to 2.1027)	
Median (95% CI)	5.0267 (2.3984 to 7.8522)	5.6181 (3.5154 to 7.7864)	9.1992 (5.2238 to 13.8645)	5.9466 (4.1725 to 9.0021)	
75% quantile (95% CI)	NC (10.0862 to NC)	16.7556 (9.2977 to NC)	NC (21.7823 to NC)	15.8357 (11.4333 to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd		0.7350		0.0626	
Hazard ratio (95% CI) vs Kd		1.0697 (0.7226 to 1.5836)		1.4478 (0.9785 to 2.1421)	
P-value		0.7363		0.0641	
probability (95% CI)[b]					

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.63 Subgroup analysis by previous treatment with IMID
16.2.7.1.63.5 Treatment emergent severe adverse event by treatment group according to previous treatment with IMID - Safety population

	Yes		No		
	Kd (N=62)	**IKd (N=80)**	**Kd (N=60)**	**IKd (N=97)**	**p-value of treatment-by-sub group interaction[c]**
3 Months	0.6248 (0.4912 to 0.7326)	0.6491 (0.5337 to 0.7427)	0.7667 (0.6381 to 0.8546)	0.6366 (0.5321 to 0.7238)	
6 Months	0.4728 (0.3432 to 0.5918)	0.4709 (0.3581 to 0.5756)	0.6000 (0.4651 to 0.7111)	0.4905 (0.3874 to 0.5857)	
9 Months	0.3715 (0.2513 to 0.4917)	0.3691 (0.2642 to 0.4741)	0.5152 (0.3824 to 0.6328)	0.4070 (0.3085 to 0.5030)	
12 Months	0.3546 (0.2365 to 0.4745)	0.2673 (0.1754 to 0.3678)	0.4465 (0.3179 to 0.5670)	0.3235 (0.2326 to 0.4176)	
15 Months	0.3377 (0.2219 to 0.4572)	0.2524 (0.1624 to 0.3525)	0.3770 (0.2551 to 0.4983)	0.2679 (0.1832 to 0.3597)	
18 Months	0.2852 (0.1772 to 0.4027)	0.2366 (0.1487 to 0.3363)	0.3770 (0.2551 to 0.4983)	0.2312 (0.1511 to 0.3214)	
21 Months	0.2852 (0.1772 to 0.4027)	0.2366 (0.1487 to 0.3363)	0.3770 (0.2551 to 0.4983)	0.2183 (0.1400 to 0.3079)	
24 Months	0.2852 (0.1772 to 0.4027)	0.2366 (0.1487 to 0.3363)	0.3519 (0.2305 to 0.4755)	0.2183 (0.1400 to 0.3079)	
27 Months	0.2852 (0.1772 to 0.4027)	0.2366 (0.1487 to 0.3363)	0.3519 (0.2305 to 0.4755)	0.2183 (0.1400 to 0.3079)	
30 Months	0.2852 (0.1772 to 0.4027)	0.2366 (0.1487 to 0.3363)	0.3519 (0.2305 to 0.4755)	0.2183 (0.1400 to 0.3079)	

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.63 Subgroup analysis by previous treatment with IMID
16.2.7.1.63.5 Treatment emergent severe adverse event by treatment group according to previous treatment with IMID - Safety population

	Yes		No		
	Kd (N=62)	**IKd (N=80)**	**Kd (N=60)**	**IKd (N=97)**	**p-value of treatment-by-sub group interaction[c]**
Number of patients at risk[b]					
3 Months	37	51	46	61	
6 Months	28	37	36	47	
9 Months	22	29	30	39	
12 Months	21	21	26	31	
15 Months	20	16	21	23	
18 Months	16	15	21	18	
21 Months	11	14	16	17	
24 Months	2	4	6	6	
27 Months	0	0	1	0	
30 Months	0	0	0	0	

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
PGM=DEVOPS/SAR650984/EFC15246/CIR_RWE/REPORT/PGM/eff_km_sr_subgrp_sig_s_t.sas OUT=REPORT/OUTPUT/eff_km_de_tesev34_imid_s_t_x.rtf (12FEB2021 8:13)

16.2.7.1 Safety endpoints
16.2.7.1.63 Subgroup analysis by previous treatment with IMID
16.2.7.1.63.6 Treatment emergent severe adverse event including death by treatment group according to previous treatment with IMID - Safety population

	Yes		No		
	Kd (N=62)	**IKd (N=80)**	**Kd (N=60)**	**IKd (N=97)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	44 (71.0)	61 (76.3)	38 (63.3)	75 (77.3)	0.2800
Number (%) of patients censored	18 (29.0)	19 (23.8)	22 (36.7)	22 (22.7)	
Kaplan-Meier estimates of TEAE in months					
25% quantile (95% CI)	1.1499 (0.4928 to 2.3326)	1.3142 (0.7228 to 2.8255)	3.2854 (1.1170 to 5.2238)	1.0513 (0.4271 to 2.0041)	
Median (95% CI)	4.9281 (2.3326 to 7.8522)	5.6181 (3.5154 to 7.7864)	9.1992 (5.2238 to 13.8645)	5.6181 (3.9097 to 8.4435)	
75% quantile (95% CI)	NC (7.8522 to NC)	14.1602 (9.2977 to NC)	NC (21.7823 to NC)	15.8357 (11.2690 to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd		0.7438		0.0537	
Hazard ratio (95% CI) vs Kd		1.0666 (0.7233 to 1.5727)		1.4658 (0.9916 to 2.1669)	
P-value		0.7450		0.0552	
probability (95% CI)[b]					

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.

16.2.7.1 Safety endpoints
16.2.7.1.63 Subgroup analysis by previous treatment with IMID
16.2.7.1.63.6 Treatment emergent severe adverse event including death by treatment group according to previous treatment with IMID - Safety population

	Yes		No		
	Kd (N=62)	**IKd (N=80)**	**Kd (N=60)**	**IKd (N=97)**	**p-value of treatment-by-sub group interaction[c]**
3 Months	0.6121 (0.4792 to 0.7206)	0.6491 (0.5337 to 0.7427)	0.7667 (0.6381 to 0.8546)	0.6289 (0.5247 to 0.7163)	
6 Months	0.4632 (0.3353 to 0.5816)	0.4709 (0.3581 to 0.5756)	0.6000 (0.4651 to 0.7111)	0.4845 (0.3822 to 0.5794)	
9 Months	0.3639 (0.2457 to 0.4830)	0.3691 (0.2642 to 0.4741)	0.5152 (0.3824 to 0.6328)	0.4021 (0.3045 to 0.4975)	
12 Months	0.3474 (0.2313 to 0.4660)	0.2673 (0.1754 to 0.3678)	0.4465 (0.3179 to 0.5670)	0.3196 (0.2296 to 0.4130)	
15 Months	0.3309 (0.2170 to 0.4490)	0.2398 (0.1521 to 0.3387)	0.3770 (0.2551 to 0.4983)	0.2646 (0.1809 to 0.3557)	
18 Months	0.2794 (0.1733 to 0.3954)	0.2248 (0.1393 to 0.3230)	0.3770 (0.2551 to 0.4983)	0.2284 (0.1492 to 0.3178)	
21 Months	0.2794 (0.1733 to 0.3954)	0.2248 (0.1393 to 0.3230)	0.3770 (0.2551 to 0.4983)	0.2157 (0.1383 to 0.3045)	
24 Months	0.2794 (0.1733 to 0.3954)	0.2248 (0.1393 to 0.3230)	0.3519 (0.2305 to 0.4755)	0.2157 (0.1383 to 0.3045)	
27 Months	0.2794 (0.1733 to 0.3954)	0.2248 (0.1393 to 0.3230)	0.3519 (0.2305 to 0.4755)	0.2157 (0.1383 to 0.3045)	
30 Months	0.2794 (0.1733 to 0.3954)	0.2248 (0.1393 to 0.3230)	0.3519 (0.2305 to 0.4755)	0.2157 (0.1383 to 0.3045)	

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.63 Subgroup analysis by previous treatment with IMID
16.2.7.1.63.6 Treatment emergent severe adverse event including death by treatment group according to previous treatment with IMID - Safety population

	Yes		No		
	Kd (N=62)	**IKd (N=80)**	**Kd (N=60)**	**IKd (N=97)**	**p-value of treatment-by-sub group interaction[c]**
Number of patients at risk[b]					
3 Months	37	51	46	61	
6 Months	28	37	36	47	
9 Months	22	29	30	39	
12 Months	21	21	26	31	
15 Months	20	16	21	23	
18 Months	16	15	21	18	
21 Months	11	14	16	17	
24 Months	2	4	6	6	
27 Months	0	0	1	0	
30 Months	0	0	0	0	

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.64 Subgroup analysis by previous treatment with PI and IMiD
16.2.7.1.64.1 Treatment emergent adverse event by treatment group according to previous treatment with PI and IMiD - Safety population

	Yes		No		
	Kd (N=17)	**IKd (N=22)**	**Kd (N=105)**	**IKd (N=155)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	15 (88.2)	21 (95.5)	102 (97.1)	151 (97.4)	0.6742
Number (%) of patients censored	2 (11.8)	1 (4.5)	3 (2.9)	4 (2.6)	
Kaplan-Meier estimates of TEAE in months					
25% quantile (95% CI)	0.6242 (0.0329 to 1.0185)	0.0657 (0.0329 to 0.2957)	0.1643 (0.0986 to 0.1971)	0.0657 (0.0657 to 0.0986)	
Median (95% CI)	1.2156 (0.3614 to 2.9240)	0.4600 (0.0657 to 1.5113)	0.3614 (0.2628 to 0.5257)	0.1643 (0.1314 to 0.2300)	
75% quantile (95% CI)	2.9240 (1.2156 to NC)	1.7413 (0.6242 to 9.4292)	0.6899 (0.6242 to 1.1828)	0.6571 (0.3943 to 0.9856)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd		0.3159		0.0584	
Hazard ratio (95% CI) vs Kd		1.4035 (0.7214 to 2.7305)		1.2748 (0.9908 to 1.6401)	
P-value		0.3181		0.0590	

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.64 Subgroup analysis by previous treatment with PI and IMiD
16.2.7.1.64.1 Treatment emergent adverse event by treatment group according to previous treatment with PI and IMiD - Safety population

	Yes		No		
	Kd (N=17)	**IKd (N=22)**	**Kd (N=105)**	**IKd (N=155)**	**p-value of treatment-by-sub group interaction[c]**
probability (95% CI)[b]					
3 Months	0.2353 (0.0731 to 0.4492)	0.1364 (0.0341 to 0.3087)	0.0667 (0.0294 to 0.1250)	0.0645 (0.0330 to 0.1105)	
6 Months	0.1176 (0.0196 to 0.3120)	0.0909 (0.0156 to 0.2511)	0.0381 (0.0125 to 0.0876)	0.0387 (0.0159 to 0.0777)	
9 Months	0.1176 (0.0196 to 0.3120)	0.0909 (0.0156 to 0.2511)	0.0381 (0.0125 to 0.0876)	0.0258 (0.0085 to 0.0604)	
12 Months	0.1176 (0.0196 to 0.3120)	0.0455 (0.0032 to 0.1894)	0.0381 (0.0125 to 0.0876)	0.0258 (0.0085 to 0.0604)	
15 Months	0.1176 (0.0196 to 0.3120)	0.0455 (0.0032 to 0.1894)	0.0286 (0.0077 to 0.0744)	0.0258 (0.0085 to 0.0604)	
18 Months	0.1176 (0.0196 to 0.3120)	0.0455 (0.0032 to 0.1894)	0.0286 (0.0077 to 0.0744)	0.0258 (0.0085 to 0.0604)	
21 Months	0.1176 (0.0196 to 0.3120)	0.0455 (0.0032 to 0.1894)	0.0286 (0.0077 to 0.0744)	0.0258 (0.0085 to 0.0604)	
24 Months	0.1176 (0.0196 to 0.3120)	0.0455 (0.0032 to 0.1894)	0.0286 (0.0077 to 0.0744)	0.0258 (0.0085 to 0.0604)	
27 Months	0.1176 (0.0196 to 0.3120)	0.0455 (0.0032 to 0.1894)	0.0286 (0.0077 to 0.0744)	0.0258 (0.0085 to 0.0604)	

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.64 Subgroup analysis by previous treatment with PI and IMiD
16.2.7.1.64.1 Treatment emergent adverse event by treatment group according to previous treatment with PI and IMiD - Safety population

	Yes		No		
	Kd (N=17)	**IKd (N=22)**	**Kd (N=105)**	**IKd (N=155)**	**p-value of treatment-by-sub group interaction[c]**
30 Months	0.1176 (0.0196 to 0.3120)	0.0455 (0.0032 to 0.1894)	0.0286 (0.0077 to 0.0744)	0.0258 (0.0085 to 0.0604)	
Number of patients at risk[b]					
3 Months	4	3	7	10	
6 Months	2	2	4	6	
9 Months	2	2	4	4	
12 Months	2	1	4	4	
15 Months	2	1	3	4	
18 Months	2	1	3	4	
21 Months	1	1	2	4	
24 Months	0	0	1	1	
27 Months	0	0	0	0	
30 Months	0	0	0	0	

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.64 Subgroup analysis by previous treatment with PI and IMiD
16.2.7.1.64.2 Treatment emergent serious adverse event by treatment group according to previous treatment with PI and IMiD - Safety population

	Yes		No		
	Kd (N=17)	**IKd (N=22)**	**Kd (N=105)**	**IKd (N=155)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	10 (58.8)	13 (59.1)	60 (57.1)	92 (59.4)	0.9287
Number (%) of patients censored	7 (41.2)	9 (40.9)	45 (42.9)	63 (40.6)	
Kaplan-Meier estimates of TEAE in months					
25% quantile (95% CI)	5.0267 (0.2300 to 7.8522)	1.9713 (0.3285 to 6.4066)	4.8624 (2.9569 to 5.8152)	3.0554 (1.2813 to 5.6181)	
Median (95% CI)	13.8316 (2.9240 to NC)	8.2300 (1.9713 to NC)	13.6345 (9.1992 to NC)	12.5503 (9.2977 to 17.9384)	
75% quantile (95% CI)	NC (13.8316 to NC)	NC (9.9220 to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd		0.7568		0.6292	
Hazard ratio (95% CI) vs Kd		1.1392 (0.4991 to 2.6002)		1.0834 (0.7825 to 1.5000)	
P-value		0.7570		0.6293	
probability (95% CI)[b]					

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.64 Subgroup analysis by previous treatment with PI and IMiD
16.2.7.1.64.2 Treatment emergent serious adverse event by treatment group according to previous treatment with PI and IMiD - Safety population

	Yes		No		
	Kd (N=17)	**IKd (N=22)**	**Kd (N=105)**	**IKd (N=155)**	**p-value of treatment-by-sub group interaction[c]**
3 Months	0.7647 (0.4883 to 0.9045)	0.6818 (0.4462 to 0.8338)	0.8285 (0.7416 to 0.8883)	0.7548 (0.6791 to 0.8151)	
6 Months	0.7059 (0.4315 to 0.8656)	0.5909 (0.3610 to 0.7621)	0.6551 (0.5554 to 0.7376)	0.6706 (0.5905 to 0.7385)	
9 Months	0.5294 (0.2762 to 0.7303)	0.5000 (0.2818 to 0.6843)	0.6067 (0.5062 to 0.6931)	0.5989 (0.5172 to 0.6713)	
12 Months	0.5294 (0.2762 to 0.7303)	0.4545 (0.2444 to 0.6433)	0.5480 (0.4474 to 0.6378)	0.5208 (0.4392 to 0.5962)	
15 Months	0.4706 (0.2296 to 0.6797)	0.4545 (0.2444 to 0.6433)	0.4678 (0.3690 to 0.5605)	0.4391 (0.3592 to 0.5161)	
18 Months	0.4118 (0.1858 to 0.6264)	0.4091 (0.2085 to 0.6007)	0.4371 (0.3396 to 0.5304)	0.4169 (0.3376 to 0.4942)	
21 Months	0.4118 (0.1858 to 0.6264)	0.4091 (0.2085 to 0.6007)	0.4267 (0.3296 to 0.5201)	0.4095 (0.3304 to 0.4869)	
24 Months	0.4118 (0.1858 to 0.6264)	0.4091 (0.2085 to 0.6007)	0.4096 (0.3114 to 0.5052)	0.3928 (0.3139 to 0.4706)	
27 Months	0.4118 (0.1858 to 0.6264)	0.4091 (0.2085 to 0.6007)	0.4096 (0.3114 to 0.5052)	0.3928 (0.3139 to 0.4706)	
30 Months	0.4118 (0.1858 to 0.6264)	0.4091 (0.2085 to 0.6007)	0.4096 (0.3114 to 0.5052)	0.3928 (0.3139 to 0.4706)	

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.64 Subgroup analysis by previous treatment with PI and IMiD
16.2.7.1.64.2 Treatment emergent serious adverse event by treatment group according to previous treatment with PI and IMiD - Safety population

	Yes		No		
	Kd (N=17)	**IKd (N=22)**	**Kd (N=105)**	**IKd (N=155)**	**p-value of treatment-by-sub group interaction[c]**
Number of patients at risk[b]					
3 Months	13	15	86	117	
6 Months	12	13	68	103	
9 Months	9	11	62	92	
12 Months	9	10	56	80	
15 Months	8	10	46	61	
18 Months	7	8	42	56	
21 Months	6	7	30	50	
24 Months	2	1	7	18	
27 Months	1	0	1	1	
30 Months	0	0	0	0	

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.64 Subgroup analysis by previous treatment with PI and IMiD
16.2.7.1.64.3 Treatment emergent adverse event leading to discontinuation of treatment by treatment group according to previous treatment with PI and IMiD - Safety population

	Yes		No		
	Kd (N=17)	**IKd (N=22)**	**Kd (N=105)**	**IKd (N=155)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	4 (23.5)	1 (4.5)	13 (12.4)	14 (9.0)	0.2584
Number (%) of patients censored	13 (76.5)	21 (95.5)	92 (87.6)	141 (91.0)	
Kaplan-Meier estimates of TEAE in months					
25% quantile (95% CI)	NC (0.2300 to NC)	NC (0.9528 to NC)	NC (NC to NC)	NC (NC to NC)	
Median (95% CI)	NC (15.3758 to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd		0.0957		0.3602	
Hazard ratio (95% CI) vs Kd		0.1894 (0.0212 to 1.6947)		0.7042 (0.3310 to 1.4983)	
P-value		0.1367		0.3627	
probability (95% CI)[b]					
3 Months	0.8824 (0.6060 to 0.9692)	0.9545 (0.7187 to 0.9935)	0.9713 (0.9138 to 0.9907)	0.9739 (0.9321 to 0.9901)	

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.64 Subgroup analysis by previous treatment with PI and IMiD
16.2.7.1.64.3 Treatment emergent adverse event leading to discontinuation of treatment by treatment group according to previous treatment with PI and IMiD - Safety population

	Yes		No		
	Kd (N=17)	**IKd (N=22)**	**Kd (N=105)**	**IKd (N=155)**	**p-value of treatment-by-sub group interaction[c]**
6 Months	0.8824 (0.6060 to 0.9692)	0.9545 (0.7187 to 0.9935)	0.9417 (0.8747 to 0.9734)	0.9473 (0.8973 to 0.9733)	
9 Months	0.8235 (0.5471 to 0.9394)	0.9545 (0.7187 to 0.9935)	0.8905 (0.8108 to 0.9379)	0.9269 (0.8719 to 0.9589)	
12 Months	0.8235 (0.5471 to 0.9394)	0.9545 (0.7187 to 0.9935)	0.8905 (0.8108 to 0.9379)	0.9269 (0.8719 to 0.9589)	
15 Months	0.8235 (0.5471 to 0.9394)	0.9545 (0.7187 to 0.9935)	0.8905 (0.8108 to 0.9379)	0.9128 (0.8544 to 0.9484)	
18 Months	0.7647 (0.4883 to 0.9045)	0.9545 (0.7187 to 0.9935)	0.8791 (0.7966 to 0.9296)	0.9128 (0.8544 to 0.9484)	
21 Months	0.7647 (0.4883 to 0.9045)	0.9545 (0.7187 to 0.9935)	0.8675 (0.7823 to 0.9210)	0.9048 (0.8444 to 0.9426)	
24 Months	0.7647 (0.4883 to 0.9045)	0.9545 (0.7187 to 0.9935)	0.8675 (0.7823 to 0.9210)	0.9048 (0.8444 to 0.9426)	
27 Months	0.7647 (0.4883 to 0.9045)	0.9545 (0.7187 to 0.9935)	0.8675 (0.7823 to 0.9210)	0.9048 (0.8444 to 0.9426)	
30 Months	0.7647 (0.4883 to 0.9045)	0.9545 (0.7187 to 0.9935)	0.8675 (0.7823 to 0.9210)	0.9048 (0.8444 to 0.9426)	

Number of patients at risk[b]

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.64 Subgroup analysis by previous treatment with PI and IMiD
16.2.7.1.64.3 Treatment emergent adverse event leading to discontinuation of treatment by treatment group according to previous treatment with PI and IMiD - Safety population

	Yes		No		
	Kd (N=17)	**IKd (N=22)**	**Kd (N=105)**	**IKd (N=155)**	**p-value of treatment-by-sub group interaction[c]**
3 Months	15	21	100	149	
6 Months	15	20	93	141	
9 Months	14	20	85	135	
12 Months	14	19	83	133	
15 Months	14	18	78	122	
18 Months	13	17	76	116	
21 Months	11	16	62	102	
24 Months	5	6	21	34	
27 Months	1	0	3	2	
30 Months	0	0	0	0	

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.64 Subgroup analysis by previous treatment with PI and IMiD
16.2.7.1.64.4 Treatment emergent mild adverse event by treatment group according to previous treatment with PI and IMiD - Safety population

	Yes		No		
	Kd (N=17)	**IKd (N=22)**	**Kd (N=105)**	**IKd (N=155)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	14 (82.4)	20 (90.9)	101 (96.2)	147 (94.8)	0.6724
Number (%) of patients censored	3 (17.6)	2 (9.1)	4 (3.8)	8 (5.2)	
Kaplan-Meier estimates of TEAE in months					
25% quantile (95% CI)	0.6571 (0.0329 to 1.4456)	0.0657 (0.0329 to 0.2957)	0.1971 (0.0986 to 0.2300)	0.0657 (0.0657 to 0.0986)	
Median (95% CI)	1.4784 (0.6242 to 2.9240)	0.5092 (0.0657 to 1.7413)	0.3943 (0.2957 to 0.5914)	0.1643 (0.1314 to 0.2300)	
75% quantile (95% CI)	4.3696 (1.4784 to NC)	1.9713 (0.6242 to 9.4292)	0.8871 (0.6571 to 1.2485)	0.6899 (0.4271 to 1.1828)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd		0.3488		0.0967	
Hazard ratio (95% CI) vs Kd		1.3855 (0.6983 to 2.7489)		1.2398 (0.9616 to 1.5986)	
P-value		0.3509		0.0974	

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.64 Subgroup analysis by previous treatment with PI and IMiD
16.2.7.1.64.4 Treatment emergent mild adverse event by treatment group according to previous treatment with PI and IMiD - Safety population

	Yes		No		
	Kd (N=17)	**IKd (N=22)**	**Kd (N=105)**	**IKd (N=155)**	**p-value of treatment-by-sub group interaction[c]**
probability (95% CI)[b]					
3 Months	0.2534 (0.0789 to 0.4761)	0.1818 (0.0568 to 0.3629)	0.0952 (0.0487 to 0.1604)	0.0990 (0.0582 to 0.1526)	
6 Months	0.1267 (0.0210 to 0.3314)	0.1212 (0.0243 to 0.3017)	0.0571 (0.0234 to 0.1128)	0.0644 (0.0324 to 0.1115)	
9 Months	0.1267 (0.0210 to 0.3314)	0.1212 (0.0243 to 0.3017)	0.0571 (0.0234 to 0.1128)	0.0429 (0.0180 to 0.0848)	
12 Months	0.1267 (0.0210 to 0.3314)	0.0606 (0.0046 to 0.2323)	0.0571 (0.0234 to 0.1128)	0.0429 (0.0180 to 0.0848)	
15 Months	0.1267 (0.0210 to 0.3314)	0.0606 (0.0046 to 0.2323)	0.0343 (0.0099 to 0.0849)	0.0429 (0.0180 to 0.0848)	
18 Months	0.1267 (0.0210 to 0.3314)	0.0606 (0.0046 to 0.2323)	0.0343 (0.0099 to 0.0849)	0.0429 (0.0180 to 0.0848)	
21 Months	0.1267 (0.0210 to 0.3314)	0.0606 (0.0046 to 0.2323)	0.0343 (0.0099 to 0.0849)	0.0429 (0.0180 to 0.0848)	
24 Months	0.1267 (0.0210 to 0.3314)	0.0606 (0.0046 to 0.2323)	0.0343 (0.0099 to 0.0849)	0.0429 (0.0180 to 0.0848)	
27 Months	0.1267 (0.0210 to 0.3314)	0.0606 (0.0046 to 0.2323)	0.0343 (0.0099 to 0.0849)	0.0429 (0.0180 to 0.0848)	

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.64 Subgroup analysis by previous treatment with PI and IMiD
16.2.7.1.64.4 Treatment emergent mild adverse event by treatment group according to previous treatment with PI and IMiD - Safety population

	Yes		No		
	Kd (N=17)	**IKd (N=22)**	**Kd (N=105)**	**IKd (N=155)**	**p-value of treatment-by-sub group interaction[c]**
30 Months	0.1267 (0.0210 to 0.3314)	0.0606 (0.0046 to 0.2323)	0.0343 (0.0099 to 0.0849)	0.0429 (0.0180 to 0.0848)	
Number of patients at risk[b]					
3 Months	4	4	10	15	
6 Months	2	2	6	9	
9 Months	2	2	6	6	
12 Months	2	1	5	6	
15 Months	2	1	3	5	
18 Months	2	1	3	5	
21 Months	1	1	2	5	
24 Months	0	0	1	1	
27 Months	0	0	0	0	
30 Months	0	0	0	0	

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.64 Subgroup analysis by previous treatment with PI and IMiD
16.2.7.1.64.5 Treatment emergent severe adverse event by treatment group according to previous treatment with PI and IMiD - Safety population

	Yes		No		
	Kd (N=17)	**IKd (N=22)**	**Kd (N=105)**	**IKd (N=155)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	12 (70.6)	14 (63.6)	69 (65.7)	120 (77.4)	0.4063
Number (%) of patients censored	5 (29.4)	8 (36.4)	36 (34.3)	35 (22.6)	
Kaplan-Meier estimates of TEAE in months					
25% quantile (95% CI)	1.9055 (0.2300 to 5.0267)	0.7228 (0.1643 to 5.0267)	2.0698 (0.6571 to 3.8768)	1.3142 (0.6899 to 1.9713)	
Median (95% CI)	7.6550 (1.5113 to NC)	7.4579 (0.7228 to NC)	6.5708 (4.5667 to 12.2875)	5.6181 (4.3696 to 7.7536)	
75% quantile (95% CI)	NC (7.6550 to NC)	NC (8.5092 to NC)	NC (16.8542 to NC)	14.8830 (10.7433 to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd		0.8724		0.0695	
Hazard ratio (95% CI) vs Kd		0.9384 (0.4331 to 2.0332)		1.3152 (0.9775 to 1.7695)	
P-value		0.8720		0.0703	
probability (95% CI)[b]					

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.64 Subgroup analysis by previous treatment with PI and IMiD
16.2.7.1.64.5 Treatment emergent severe adverse event by treatment group according to previous treatment with PI and IMiD - Safety population

	Yes		No		
	Kd (N=17)	**IKd (N=22)**	**Kd (N=105)**	**IKd (N=155)**	**p-value of treatment-by-sub group interaction[c]**
3 Months	0.7059 (0.4315 to 0.8656)	0.6818 (0.4462 to 0.8338)	0.6934 (0.5951 to 0.7723)	0.6364 (0.5551 to 0.7068)	
6 Months	0.5294 (0.2762 to 0.7303)	0.5455 (0.3207 to 0.7239)	0.5371 (0.4365 to 0.6275)	0.4724 (0.3916 to 0.5488)	
9 Months	0.3529 (0.1448 to 0.5704)	0.4545 (0.2444 to 0.6433)	0.4584 (0.3602 to 0.5511)	0.3805 (0.3039 to 0.4567)	
12 Months	0.3529 (0.1448 to 0.5704)	0.3636 (0.1743 to 0.5567)	0.4086 (0.3131 to 0.5016)	0.2887 (0.2191 to 0.3617)	
15 Months	0.3529 (0.1448 to 0.5704)	0.3636 (0.1743 to 0.5567)	0.3582 (0.2664 to 0.4507)	0.2449 (0.1792 to 0.3162)	
18 Months	0.2941 (0.1071 to 0.5115)	0.3636 (0.1743 to 0.5567)	0.3374 (0.2474 to 0.4295)	0.2130 (0.1504 to 0.2828)	
21 Months	0.2941 (0.1071 to 0.5115)	0.3636 (0.1743 to 0.5567)	0.3374 (0.2474 to 0.4295)	0.2048 (0.1431 to 0.2742)	
24 Months	0.2941 (0.1071 to 0.5115)	0.3636 (0.1743 to 0.5567)	0.3214 (0.2312 to 0.4148)	0.2048 (0.1431 to 0.2742)	
27 Months	0.2941 (0.1071 to 0.5115)	0.3636 (0.1743 to 0.5567)	0.3214 (0.2312 to 0.4148)	0.2048 (0.1431 to 0.2742)	
30 Months	0.2941 (0.1071 to 0.5115)	0.3636 (0.1743 to 0.5567)	0.3214 (0.2312 to 0.4148)	0.2048 (0.1431 to 0.2742)	

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.64 Subgroup analysis by previous treatment with PI and IMiD
16.2.7.1.64.5 Treatment emergent severe adverse event by treatment group according to previous treatment with PI and IMiD - Safety population

	Yes		No		
	Kd (N=17)	**IKd (N=22)**	**Kd (N=105)**	**IKd (N=155)**	**p-value of treatment-by-sub group interaction[c]**
Number of patients at risk[b]					
3 Months	12	15	71	97	
6 Months	9	12	55	72	
9 Months	6	10	46	58	
12 Months	6	8	41	44	
15 Months	6	7	35	32	
18 Months	5	7	32	26	
21 Months	3	6	24	25	
24 Months	0	1	8	9	
27 Months	0	0	1	0	
30 Months	0	0	0	0	

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.64 Subgroup analysis by previous treatment with PI and IMiD
16.2.7.1.64.6 Treatment emergent severe adverse event including death by treatment group according to previous treatment with PI and IMiD - Safety population

	Yes		No		
	Kd (N=17)	**IKd (N=22)**	**Kd (N=105)**	**IKd (N=155)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	12 (70.6)	14 (63.6)	70 (66.7)	122 (78.7)	0.4041
Number (%) of patients censored	5 (29.4)	8 (36.4)	35 (33.3)	33 (21.3)	
Kaplan-Meier estimates of TEAE in months					
25% quantile (95% CI)	1.9055 (0.2300 to 5.0267)	0.7228 (0.1643 to 5.0267)	1.8727 (0.6571 to 3.2854)	1.2813 (0.6571 to 1.9713)	
Median (95% CI)	7.6550 (1.5113 to NC)	7.4579 (0.7228 to NC)	6.5708 (4.2382 to 11.4004)	5.6181 (4.3368 to 7.6879)	
75% quantile (95% CI)	NC (7.6550 to NC)	NC (8.5092 to NC)	NC (16.8542 to NC)	14.7187 (10.7433 to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd		0.8724		0.0648	
Hazard ratio (95% CI) vs Kd		0.9384 (0.4331 to 2.0332)		1.3186 (0.9823 to 1.7702)	
P-value		0.8720		0.0656	
probability (95% CI)[b]					

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.64 Subgroup analysis by previous treatment with PI and IMiD
16.2.7.1.64.6 Treatment emergent severe adverse event including death by treatment group according to previous treatment with PI and IMiD - Safety population

	Yes		No		
	Kd (N=17)	**IKd (N=22)**	**Kd (N=105)**	**IKd (N=155)**	**p-value of treatment-by-sub group interaction[c]**
3 Months	0.7059 (0.4315 to 0.8656)	0.6818 (0.4462 to 0.8338)	0.6852 (0.5869 to 0.7648)	0.6317 (0.5505 to 0.7023)	
6 Months	0.5294 (0.2762 to 0.7303)	0.5455 (0.3207 to 0.7239)	0.5308 (0.4307 to 0.6211)	0.4689 (0.3885 to 0.5452)	
9 Months	0.3529 (0.1448 to 0.5704)	0.4545 (0.2444 to 0.6433)	0.4530 (0.3555 to 0.5453)	0.3777 (0.3015 to 0.4536)	
12 Months	0.3529 (0.1448 to 0.5704)	0.3636 (0.1743 to 0.5567)	0.4038 (0.3091 to 0.4963)	0.2865 (0.2174 to 0.3592)	
15 Months	0.3529 (0.1448 to 0.5704)	0.3636 (0.1743 to 0.5567)	0.3540 (0.2631 to 0.4459)	0.2372 (0.1728 to 0.3075)	
18 Months	0.2941 (0.1071 to 0.5115)	0.3636 (0.1743 to 0.5567)	0.3335 (0.2443 to 0.4250)	0.2062 (0.1451 to 0.2750)	
21 Months	0.2941 (0.1071 to 0.5115)	0.3636 (0.1743 to 0.5567)	0.3335 (0.2443 to 0.4250)	0.1983 (0.1381 to 0.2666)	
24 Months	0.2941 (0.1071 to 0.5115)	0.3636 (0.1743 to 0.5567)	0.3176 (0.2283 to 0.4104)	0.1983 (0.1381 to 0.2666)	
27 Months	0.2941 (0.1071 to 0.5115)	0.3636 (0.1743 to 0.5567)	0.3176 (0.2283 to 0.4104)	0.1983 (0.1381 to 0.2666)	
30 Months	0.2941 (0.1071 to 0.5115)	0.3636 (0.1743 to 0.5567)	0.3176 (0.2283 to 0.4104)	0.1983 (0.1381 to 0.2666)	

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.64 Subgroup analysis by previous treatment with PI and IMiD
16.2.7.1.64.6 Treatment emergent severe adverse event including death by treatment group according to previous treatment with PI and IMiD - Safety population

	Yes		No		
	Kd (N=17)	**IKd (N=22)**	**Kd (N=105)**	**IKd (N=155)**	**p-value of treatment-by-sub group interaction[c]**
Number of patients at risk[b]					
3 Months	12	15	71	97	
6 Months	9	12	55	72	
9 Months	6	10	46	58	
12 Months	6	8	41	44	
15 Months	6	7	35	32	
18 Months	5	7	32	26	
21 Months	3	6	24	25	
24 Months	0	1	8	9	
27 Months	0	0	1	0	
30 Months	0	0	0	0	

CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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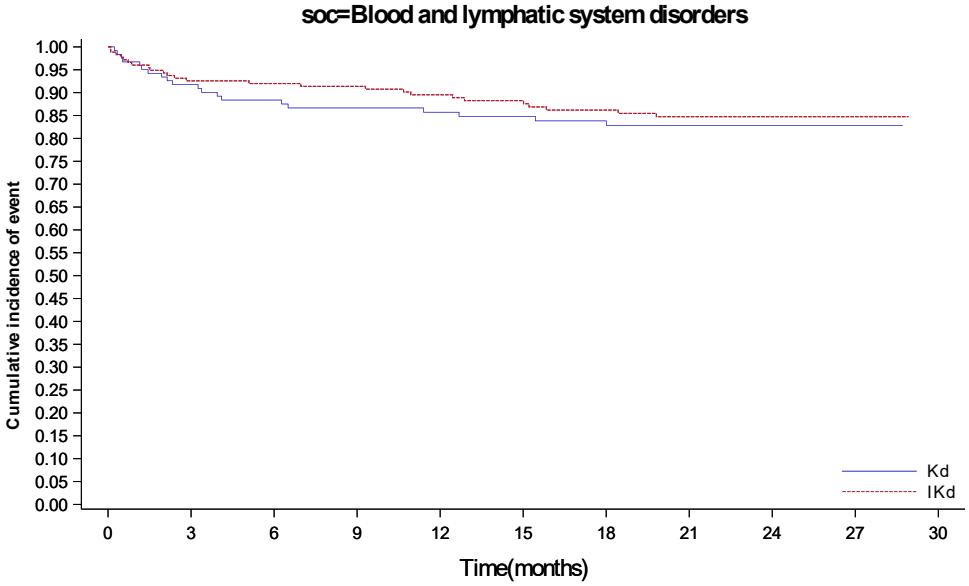
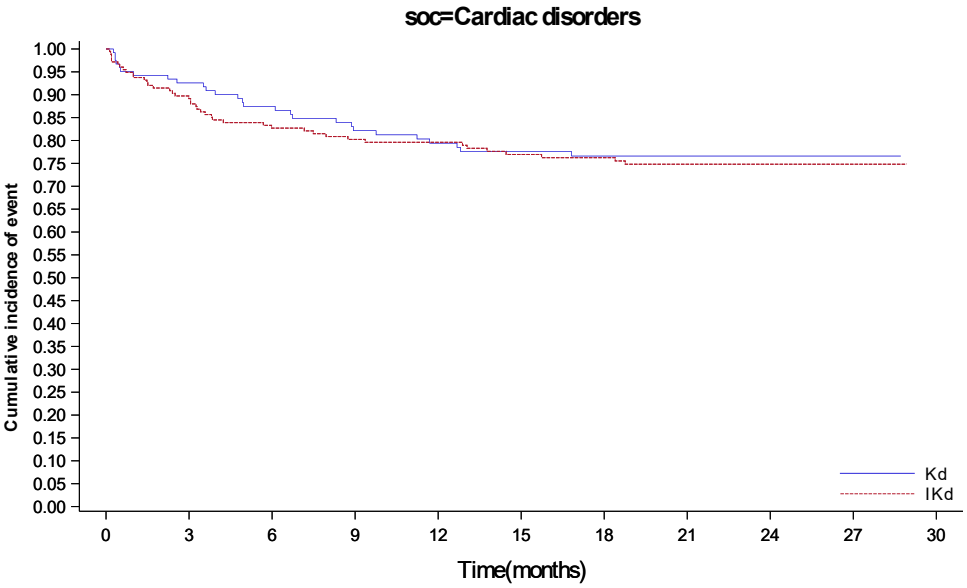
16.2.7.1 Safety endpoints
16.2.7.1.65 Analysis according to SOC/PT
16.2.7.1.65.2 Kaplan-Meier cumulative incidence curve of treatment emergent adverse event according to SOC by treatment group - Safety population



Number at Risk

Kd	122	110	102	94	92	87	84	64	21	2	0
IKd	177	160	153	148	142	129	120	104	34	1	0

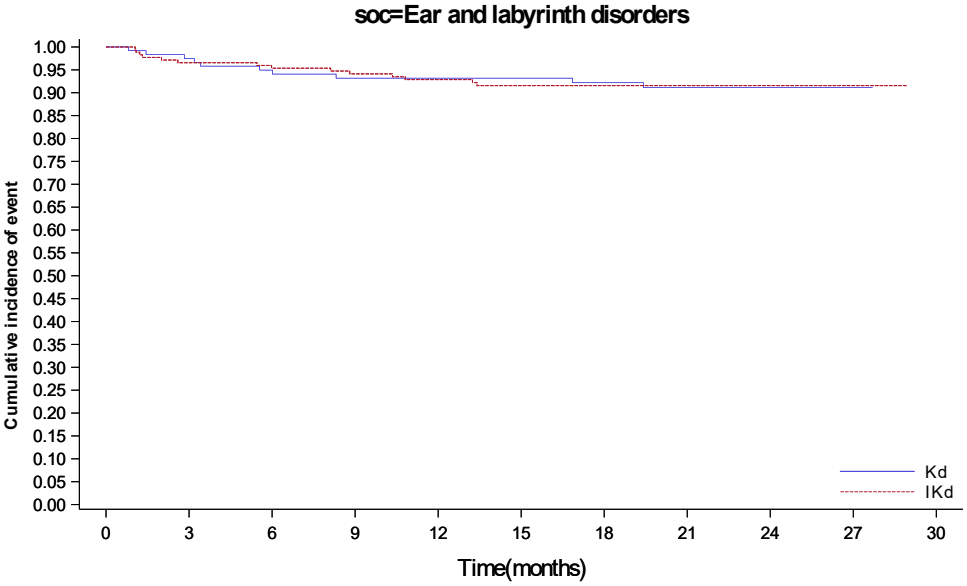
16.2.7.1 Safety endpoints
16.2.7.1.65 Analysis according to SOC/PT
16.2.7.1.65.2 Kaplan-Meier cumulative incidence curve of treatment emergent adverse event according to SOC by treatment group - Safety population



Number at Risk

Kd	122	110	100	91	86	81	79	62	25	4	0
IKd	177	154	137	128	125	112	107	94	30	1	0

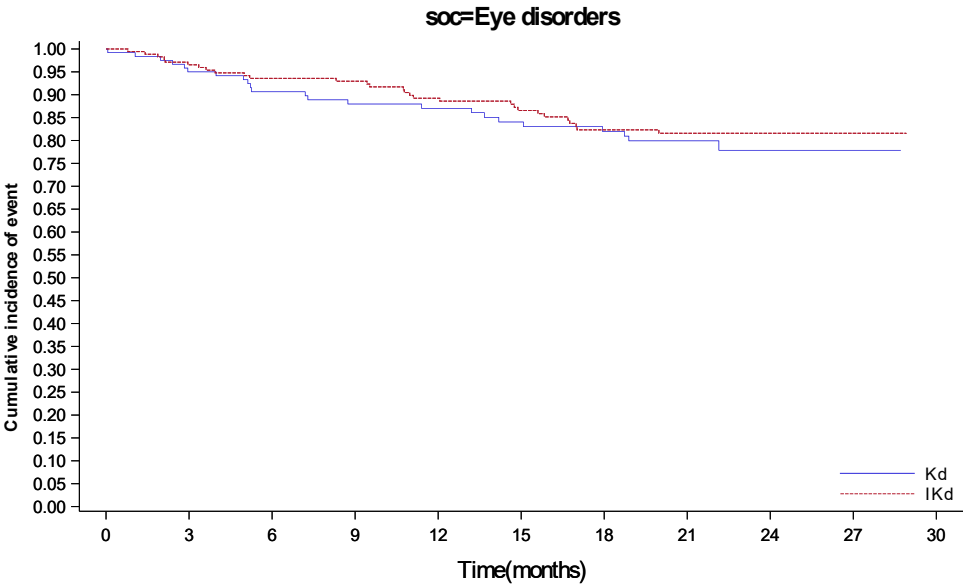
16.2.7.1 Safety endpoints
16.2.7.1.65 Analysis according to SOC/PT
16.2.7.1.65.2 Kaplan-Meier cumulative incidence curve of treatment emergent adverse event according to SOC by treatment group - Safety population



Number at Risk

Kd	122	116	109	101	99	93	91	71	25	2	0
IKd	177	167	158	151	147	134	127	113	34	1	0

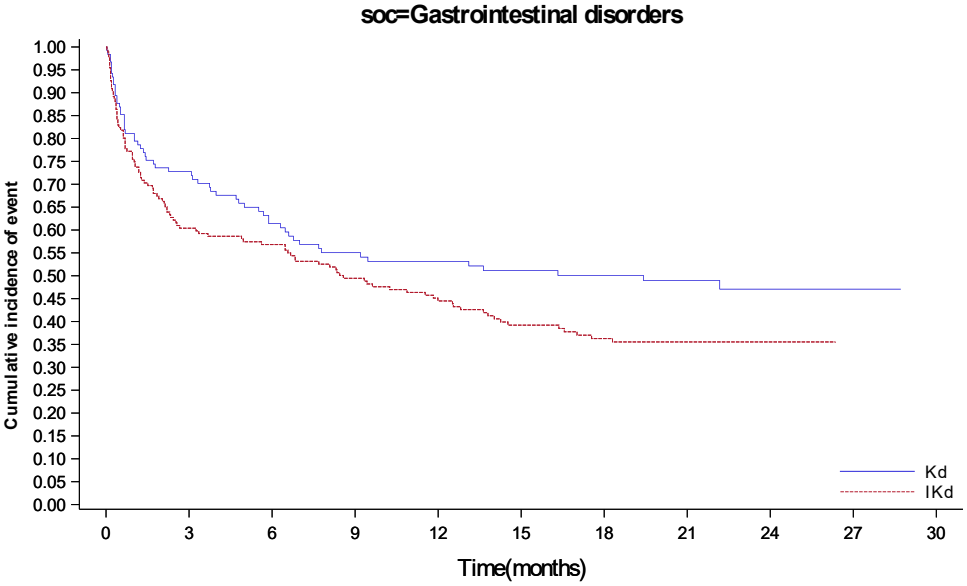
16.2.7.1 Safety endpoints
16.2.7.1.65 Analysis according to SOC/PT
16.2.7.1.65.2 Kaplan-Meier cumulative incidence curve of treatment emergent adverse event according to SOC by treatment group - Safety population



Number at Risk

Kd	122	113	103	95	92	83	79	60	21	3	0
IKd	176	166	155	150	141	126	113	101	32	2	0

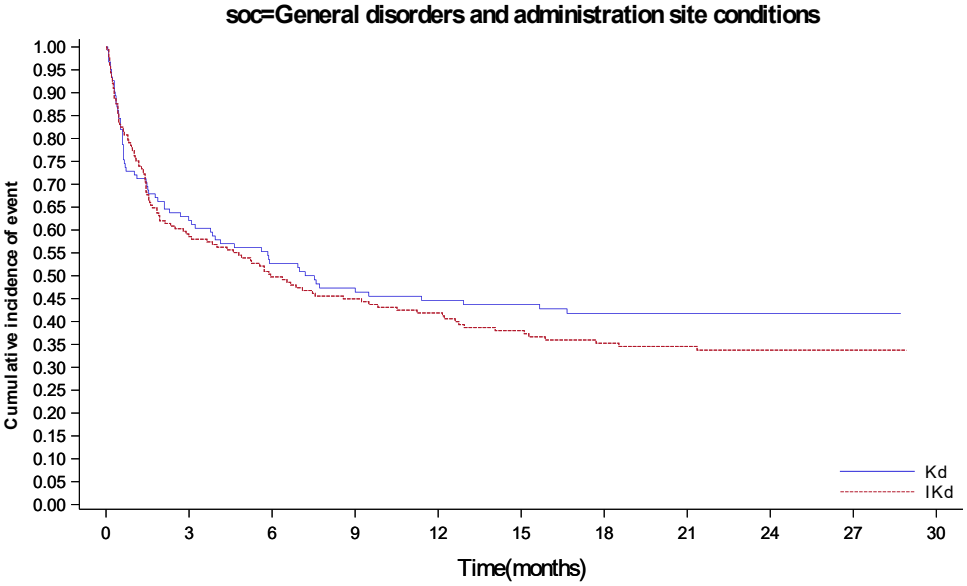
16.2.7.1 Safety endpoints
16.2.7.1.65 Analysis according to SOC/PT
16.2.7.1.65.2 Kaplan-Meier cumulative incidence curve of treatment emergent adverse event according to SOC by treatment group - Safety population



Number at Risk

Kd	122	86	68	58	54	50	48	33	14	2	0
IKd	176	103	93	80	71	56	49	43	15	0	

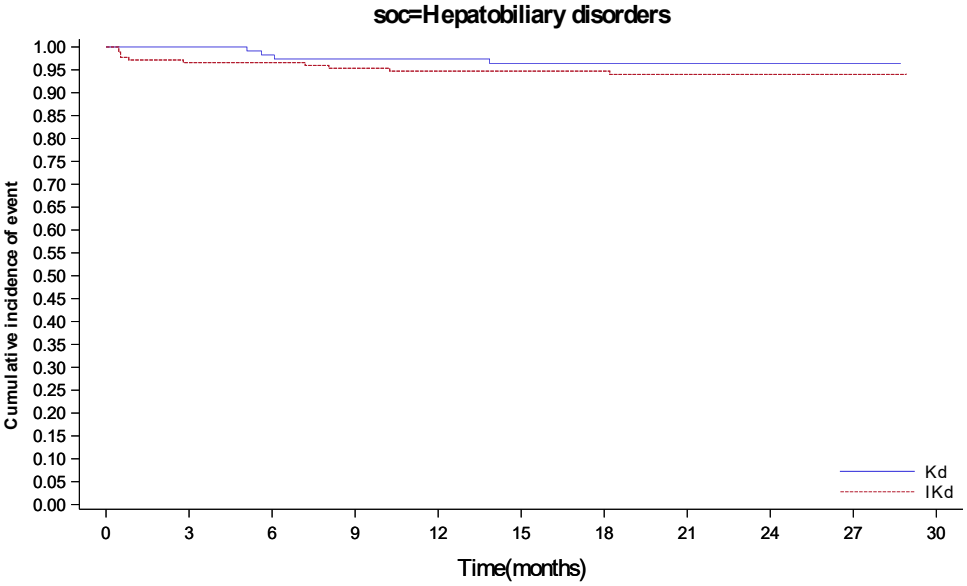
16.2.7.1 Safety endpoints
16.2.7.1.65 Analysis according to SOC/PT
16.2.7.1.65.2 Kaplan-Meier cumulative incidence curve of treatment emergent adverse event according to SOC by treatment group - Safety population



Number at Risk

Kd	122	74	60	53	49	46	43	32	13	1	0
IKd	177	102	84	73	66	56	50	47	16	1	0

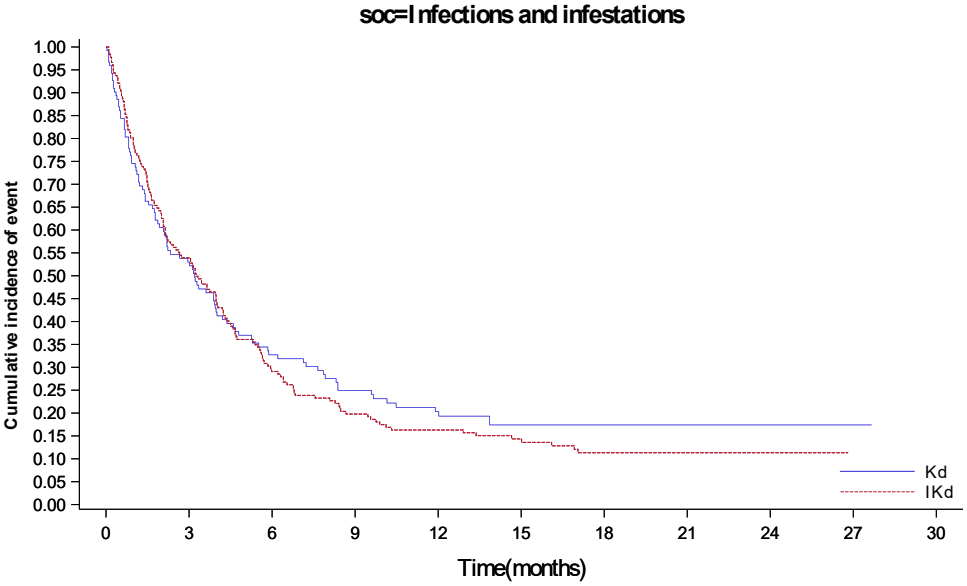
16.2.7.1 Safety endpoints
16.2.7.1.65 Analysis according to SOC/PT
16.2.7.1.65.2 Kaplan-Meier cumulative incidence curve of treatment emergent adverse event according to SOC by treatment group - Safety population



Number at Risk

Kd	122	119	112	105	103	96	94	74	27	4	0
IKd	177	167	160	153	149	138	131	116	36	1	0

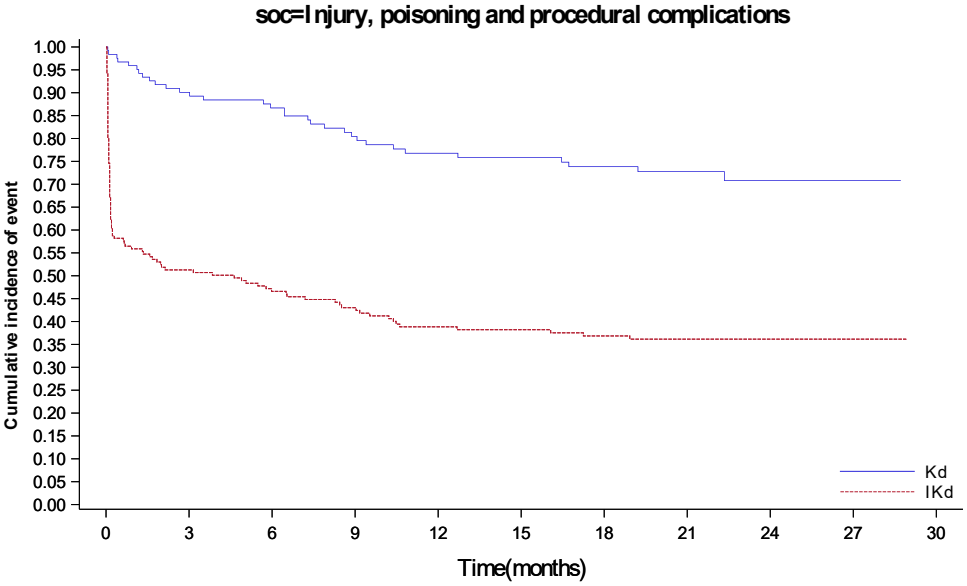
16.2.7.1 Safety endpoints
16.2.7.1.65 Analysis according to SOC/PT
16.2.7.1.65.2 Kaplan-Meier cumulative incidence curve of treatment emergent adverse event according to SOC by treatment group - Safety population



Number at Risk

Kd	122	63	38	27	21	18	17	11	4	1	0
IKd	177	94	50	34	28	19	15	11	4	0	

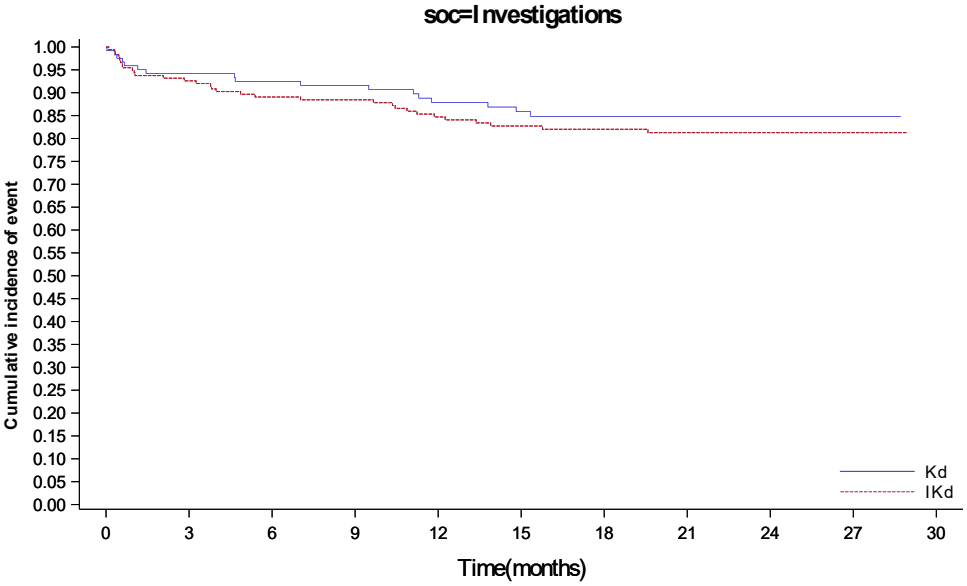
16.2.7.1 Safety endpoints
16.2.7.1.65 Analysis according to SOC/PT
16.2.7.1.65.2 Kaplan-Meier cumulative incidence curve of treatment emergent adverse event according to SOC by treatment group - Safety population



Number at Risk

Kd	122	108	99	88	82	76	72	55	20	3	0
IKd	177	89	79	72	64	58	53	46	14	1	0

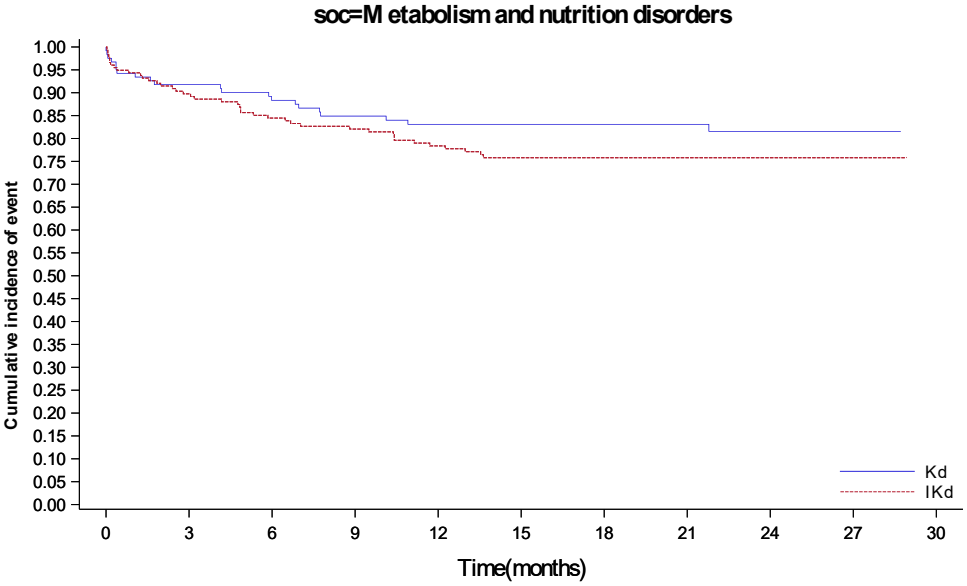
16.2.7.1 Safety endpoints
16.2.7.1.65 Analysis according to SOC/PT
16.2.7.1.65.2 Kaplan-Meier cumulative incidence curve of treatment emergent adverse event according to SOC by treatment group - Safety population



Number at Risk

Kd	122	112	105	98	93	85	82	65	23	4	0
IKd	177	160	147	142	133	119	113	102	33	2	0

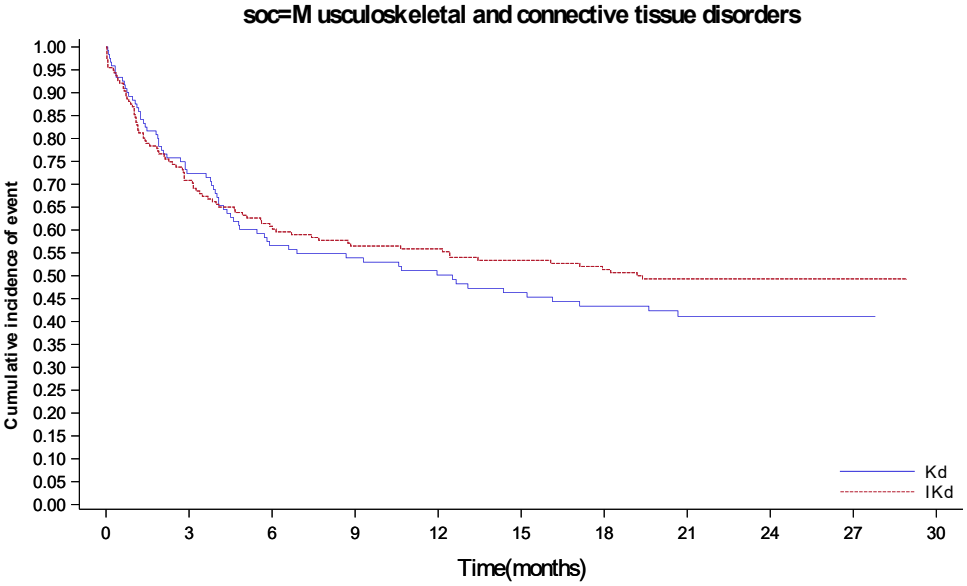
16.2.7.1 Safety endpoints
16.2.7.1.65 Analysis according to SOC/PT
16.2.7.1.65.2 Kaplan-Meier cumulative incidence curve of treatment emergent adverse event according to SOC by treatment group - Safety population



Number at Risk

Kd	122	109	103	95	91	87	85	67	24	3	0
IKd	177	156	142	134	126	112	107	95	29	1	0

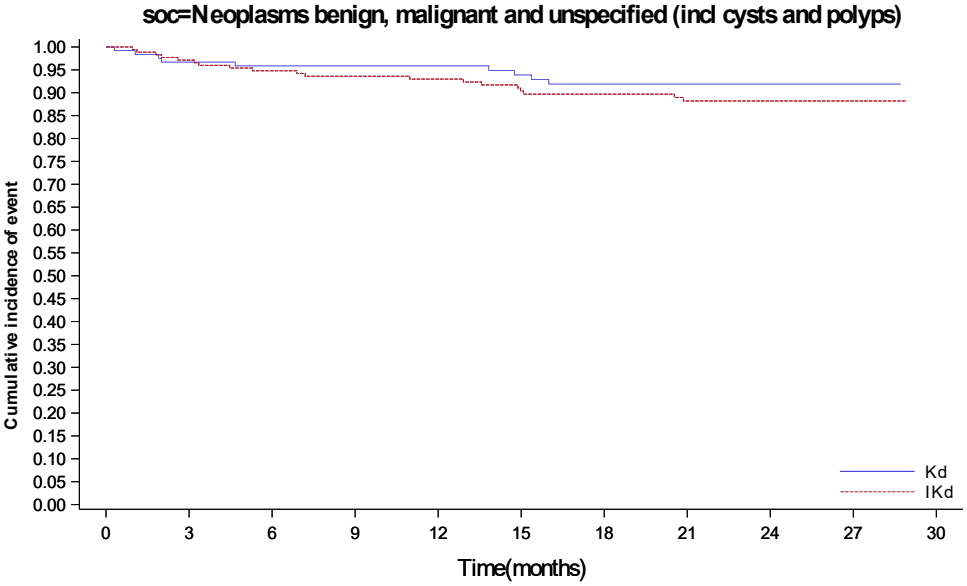
16.2.7.1 Safety endpoints
16.2.7.1.65 Analysis according to SOC/PT
16.2.7.1.65.2 Kaplan-Meier cumulative incidence curve of treatment emergent adverse event according to SOC by treatment group - Safety population



Number at Risk

Kd	121	85	64	58	52	48	44	31	8	2	0
IKd	177	122	100	91	90	80	76	63	21	2	0

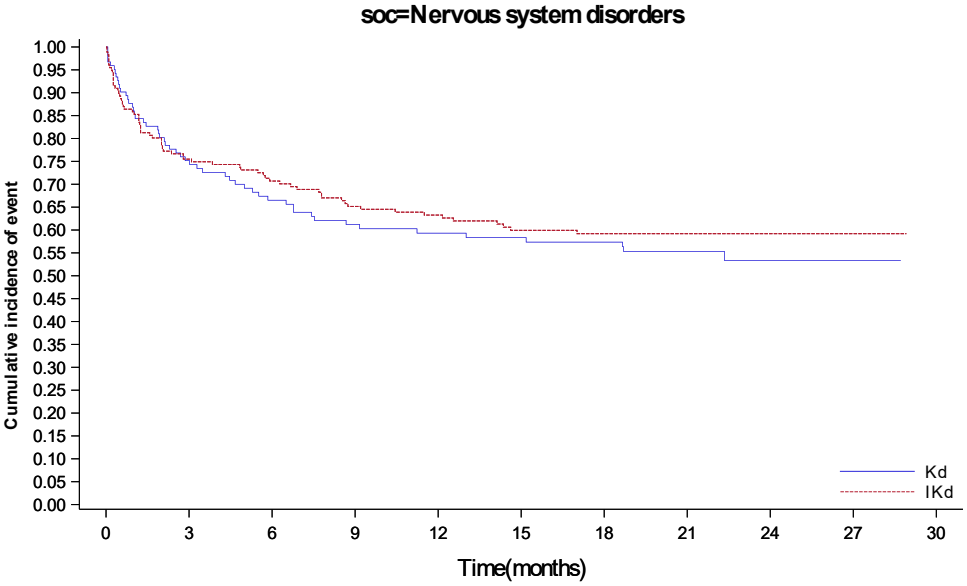
16.2.7.1 Safety endpoints
16.2.7.1.65 Analysis according to SOC/PT
16.2.7.1.65.2 Kaplan-Meier cumulative incidence curve of treatment emergent adverse event according to SOC by treatment group - Safety population



Number at Risk

Kd	122	116	111	105	103	95	91	72	27	4	0
IKd	177	169	158	152	149	135	129	113	37	2	0

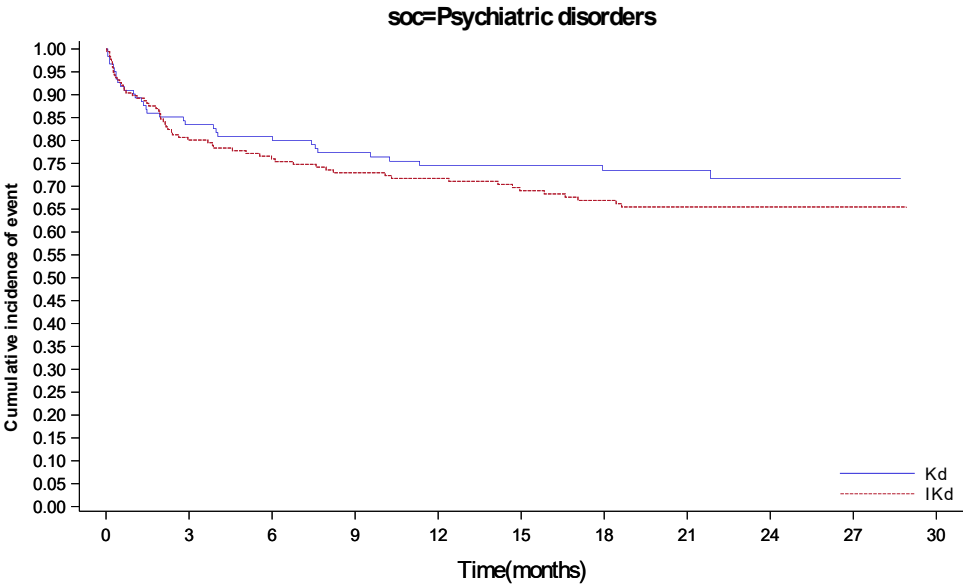
16.2.7.1 Safety endpoints
16.2.7.1.65 Analysis according to SOC/PT
16.2.7.1.65.2 Kaplan-Meier cumulative incidence curve of treatment emergent adverse event according to SOC by treatment group - Safety population



Number at Risk

Kd	122	89	76	65	61	59	57	42	14	3	0
IKd	177	130	116	104	99	86	79	72	21	2	0

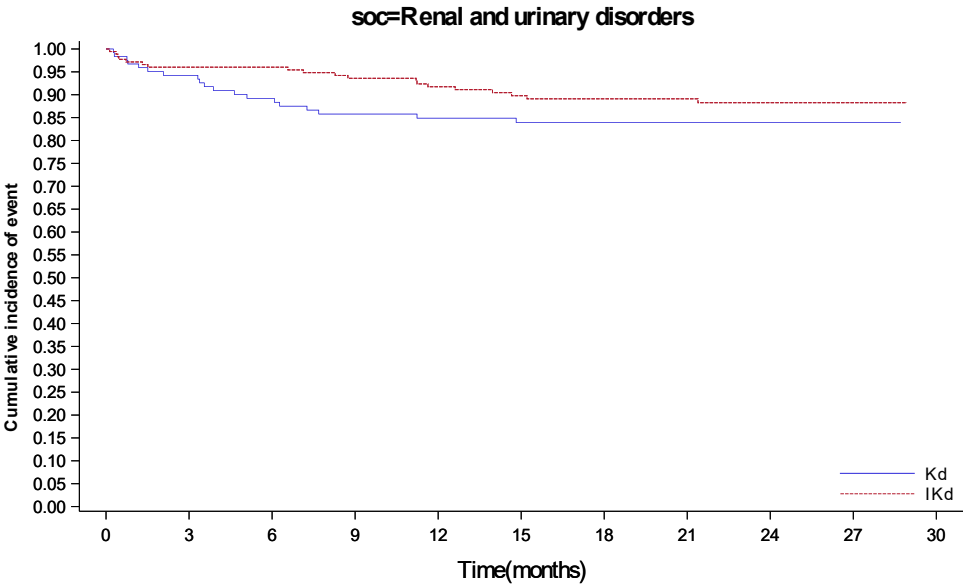
16.2.7.1 Safety endpoints
16.2.7.1.65 Analysis according to SOC/PT
16.2.7.1.65.2 Kaplan-Meier cumulative incidence curve of treatment emergent adverse event according to SOC by treatment group - Safety population



Number at Risk

Kd	122	99	92	83	78	73	70	54	18	2	0
IKd	177	139	127	118	113	100	94	82	27	2	0

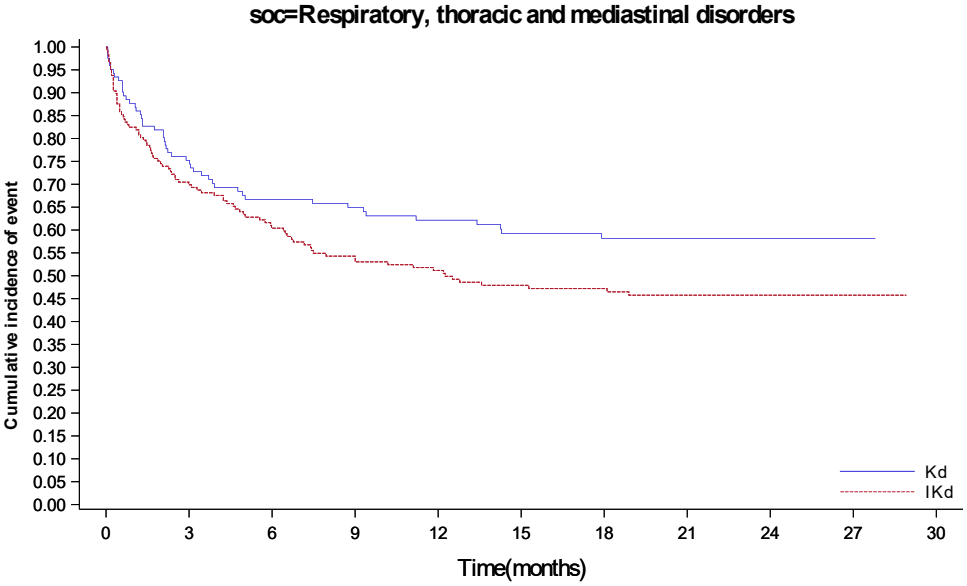
16.2.7.1 Safety endpoints
16.2.7.1.65 Analysis according to SOC/PT
16.2.7.1.65.2 Kaplan-Meier cumulative incidence curve of treatment emergent adverse event according to SOC by treatment group - Safety population



Number at Risk

Kd	122	114	104	96	93	88	87	68	24	4	0
IKd	177	166	161	152	147	133	125	113	34	2	0

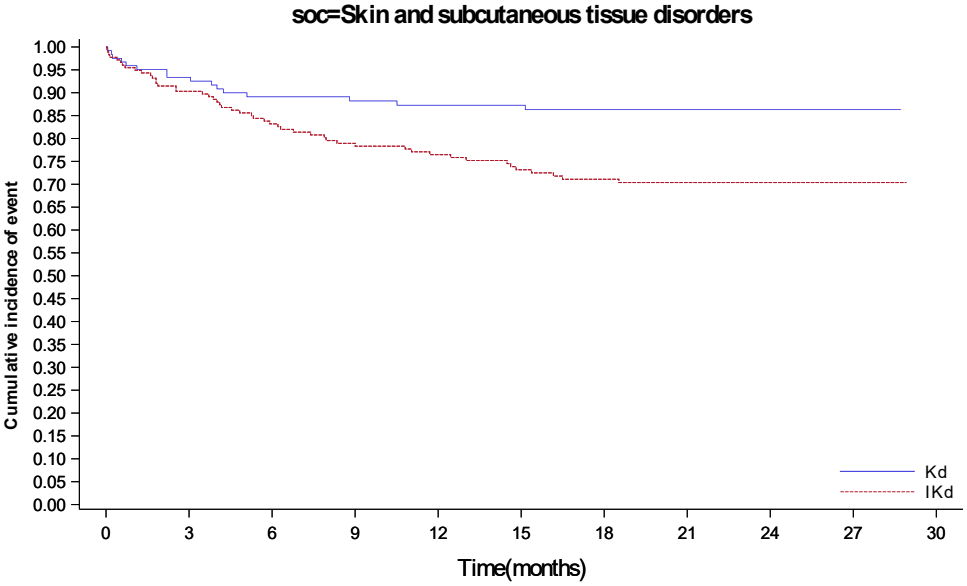
16.2.7.1 Safety endpoints
16.2.7.1.65 Analysis according to SOC/PT
16.2.7.1.65.2 Kaplan-Meier cumulative incidence curve of treatment emergent adverse event according to SOC by treatment group - Safety population



Number at Risk

Kd	122	90	77	70	65	60	57	45	16	3	0
IKd	177	121	100	87	80	68	65	58	19	1	0

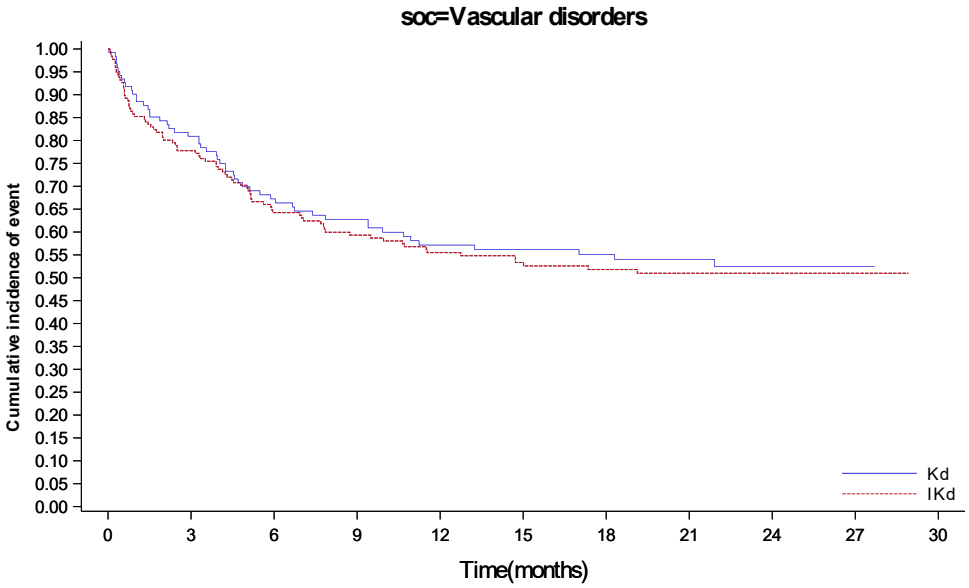
16.2.7.1 Safety endpoints
16.2.7.1.65 Analysis according to SOC/PT
16.2.7.1.65.2 Kaplan-Meier cumulative incidence curve of treatment emergent adverse event according to SOC by treatment group - Safety population



Number at Risk

Kd	122	111	101	96	93	87	84	68	24	3	0
IKd	177	156	138	128	122	108	99	86	24	1	0

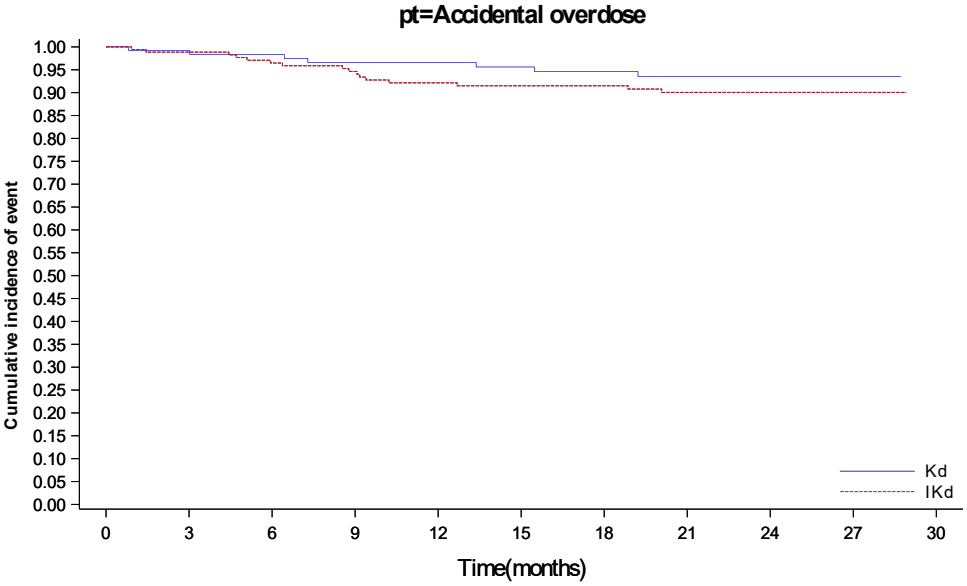
16.2.7.1 Safety endpoints
16.2.7.1.65 Analysis according to SOC/PT
16.2.7.1.65.2 Kaplan-Meier cumulative incidence curve of treatment emergent adverse event according to SOC by treatment group - Safety population



Number at Risk

Kd	122	96	76	67	59	53	52	41	18	2	0
IKd	177	135	107	94	85	71	64	56	17	2	0

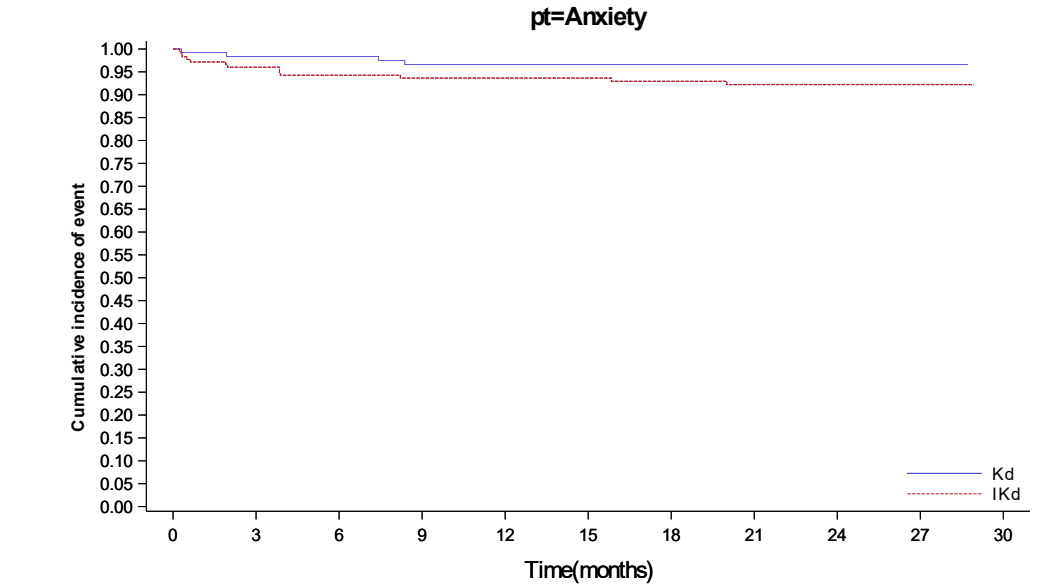
16.2.7.1 Safety endpoints
16.2.7.1.65 Analysis according to SOC/PT
16.2.7.1.65.4 Kaplan-Meier cumulative incidence curve of treatment emergent adverse event according to PT by treatment group - Safety population



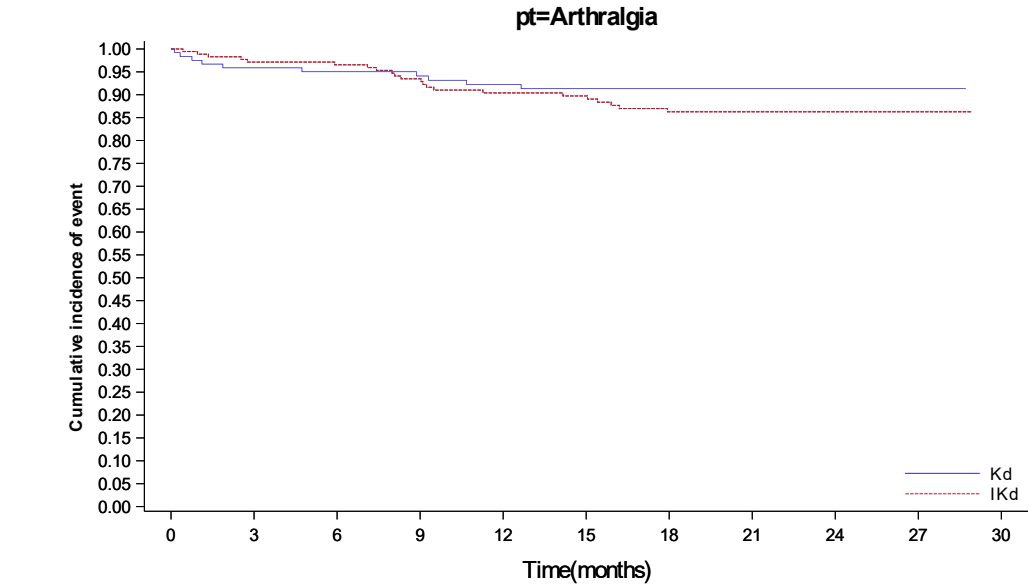
Number at Risk

Kd	122	118	112	105	103	96	93	72	26	4	0
IKd	177	171	160	152	146	135	128	112	34	2	0

16.2.7.1 Safety endpoints
16.2.7.1.65 Analysis according to SOC/PT
16.2.7.1.65.4 Kaplan-Meier cumulative incidence curve of treatment emergent adverse event according to PT by treatment group - Safety population



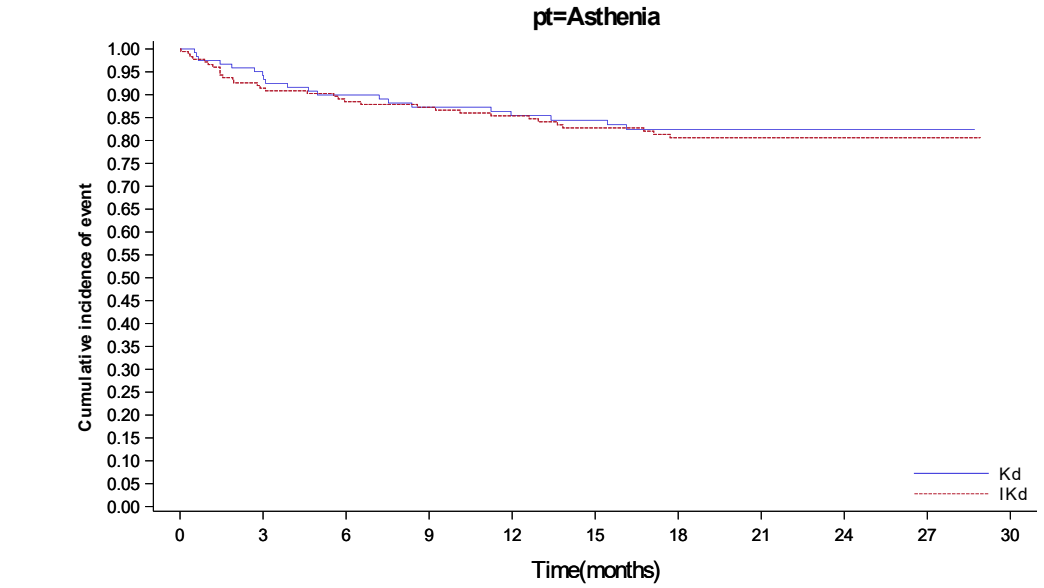
16.2.7.1 Safety endpoints
16.2.7.1.65 Analysis according to SOC/PT
16.2.7.1.65.4 Kaplan-Meier cumulative incidence curve of treatment emergent adverse event according to PT by treatment group - Safety population



Number at Risk

Kd	122	114	109	102	98	91	89	72	28	4	0
IKd	177	168	161	152	144	132	121	111	36	2	0

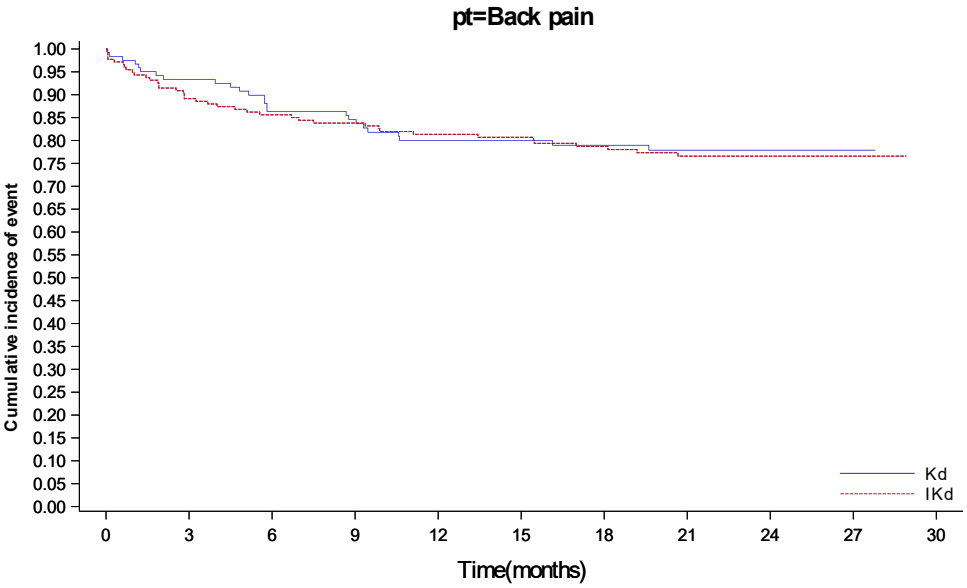
16.2.7.1 Safety endpoints
16.2.7.1.65 Analysis according to SOC/PT
16.2.7.1.65.4 Kaplan-Meier cumulative incidence curve of treatment emergent adverse event according to PT by treatment group - Safety population



Number at Risk

Kd	122	112	103	94	90	84	81	63	27	4	0
IKd	177	158	147	140	134	120	111	100	33	2	0

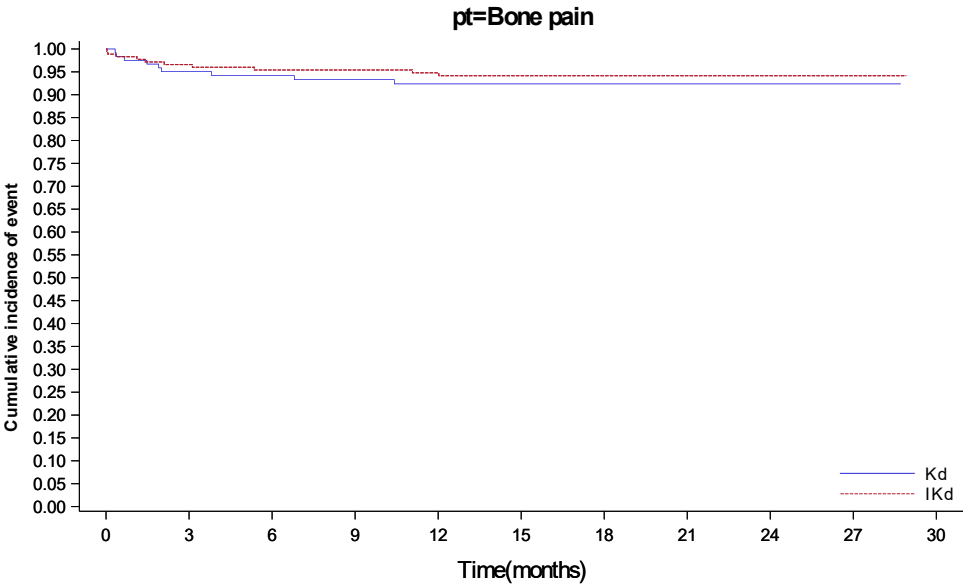
16.2.7.1 Safety endpoints
16.2.7.1.65 Analysis according to SOC/PT
16.2.7.1.65.4 Kaplan-Meier cumulative incidence curve of treatment emergent adverse event according to PT by treatment group - Safety population



Number at Risk

Kd	122	111	98	92	85	81	78	58	21	3	0
IKd	177	154	143	136	131	122	114	100	28	2	0

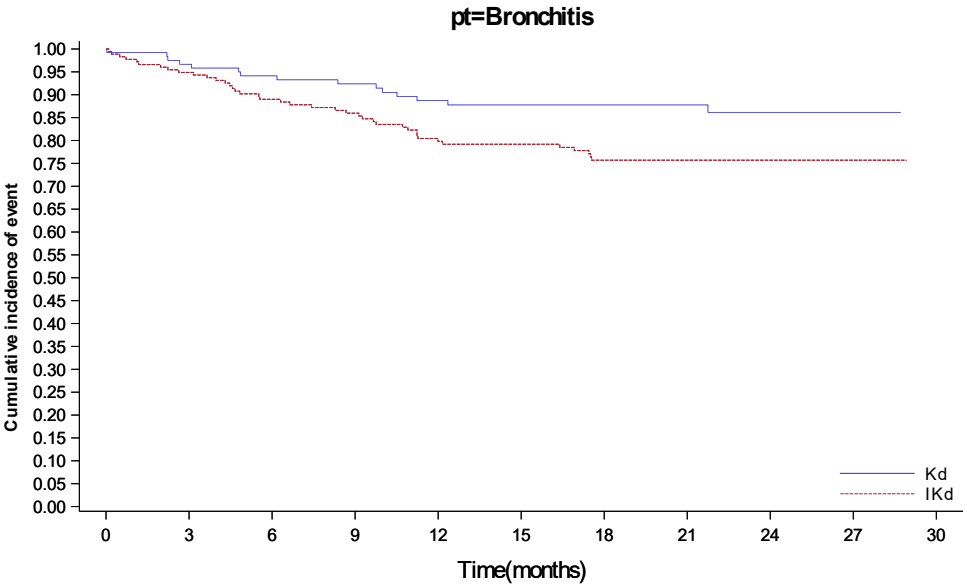
16.2.7.1 Safety endpoints
16.2.7.1.65 Analysis according to SOC/PT
16.2.7.1.65.4 Kaplan-Meier cumulative incidence curve of treatment emergent adverse event according to PT by treatment group - Safety population



Number at Risk

Kd	122	113	107	100	97	92	90	71	27	4	0
IKd	177	167	158	153	149	137	131	117	38	2	0

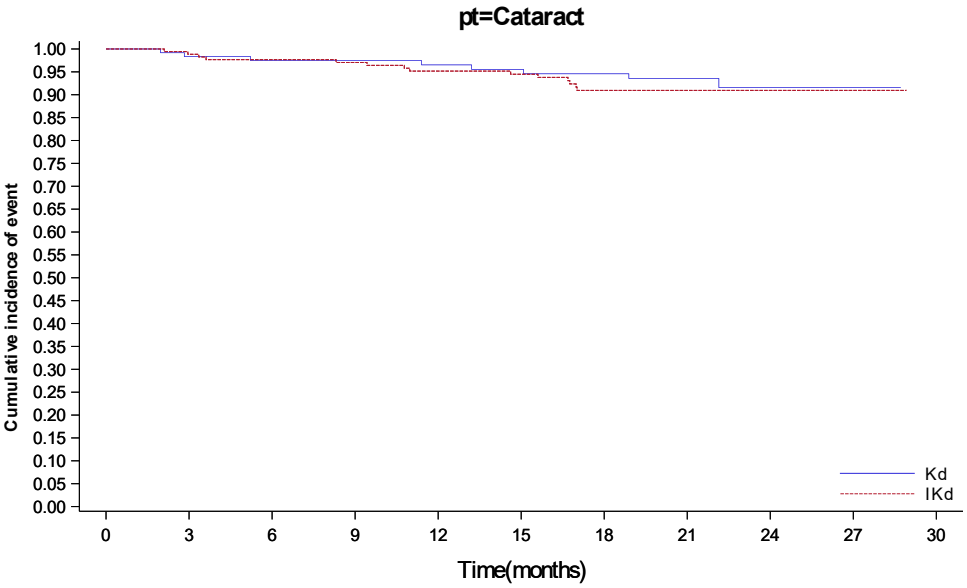
16.2.7.1 Safety endpoints
16.2.7.1.65 Analysis according to SOC/PT
16.2.7.1.65.4 Kaplan-Meier cumulative incidence curve of treatment emergent adverse event according to PT by treatment group - Safety population



Number at Risk

Kd	122	115	108	101	95	88	86	67	24	4	0
IKd	177	165	148	140	127	117	106	92	30	1	0

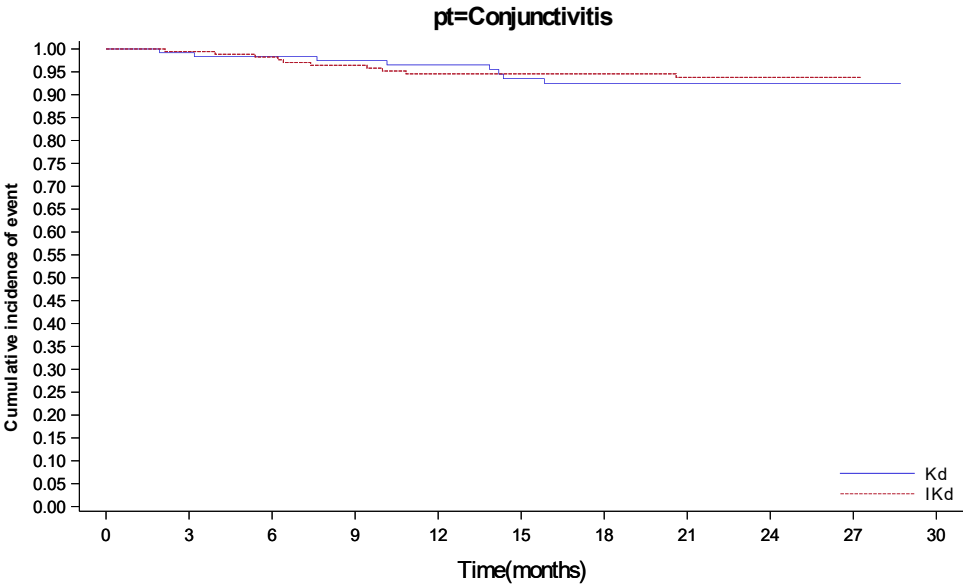
16.2.7.1 Safety endpoints
16.2.7.1.65 Analysis according to SOC/PT
16.2.7.1.65.4 Kaplan-Meier cumulative incidence curve of treatment emergent adverse event according to PT by treatment group - Safety population



Number at Risk

Kd	122	117	111	106	103	96	93	72	26	4	0
IKd	176	170	161	155	149	137	125	111	33	2	0

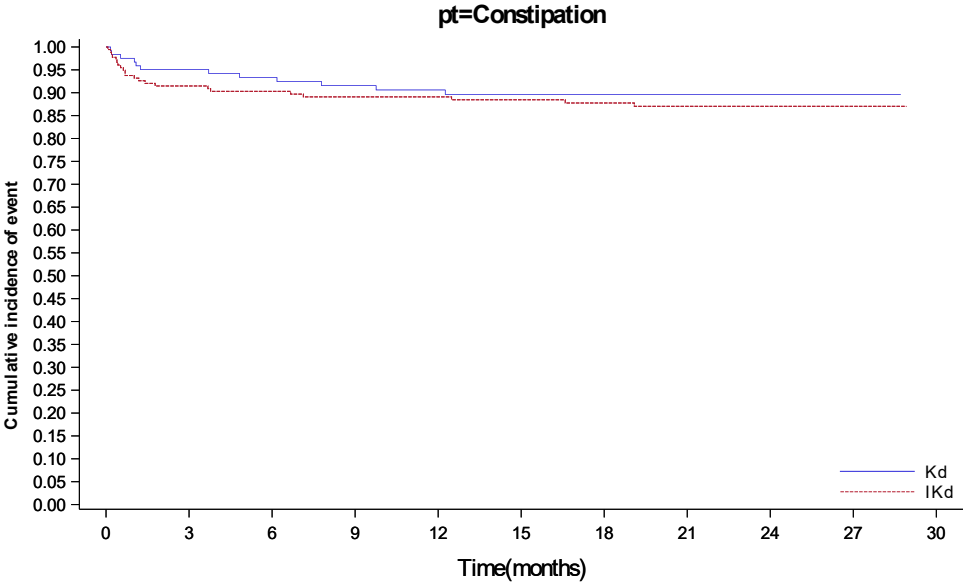
16.2.7.1 Safety endpoints
16.2.7.1.65 Analysis according to SOC/PT
16.2.7.1.65.4 Kaplan-Meier cumulative incidence curve of treatment emergent adverse event according to PT by treatment group - Safety population



Number at Risk

Kd	122	118	112	105	102	93	90	72	25	4	0
IKd	177	172	163	155	149	138	131	115	36	1	0

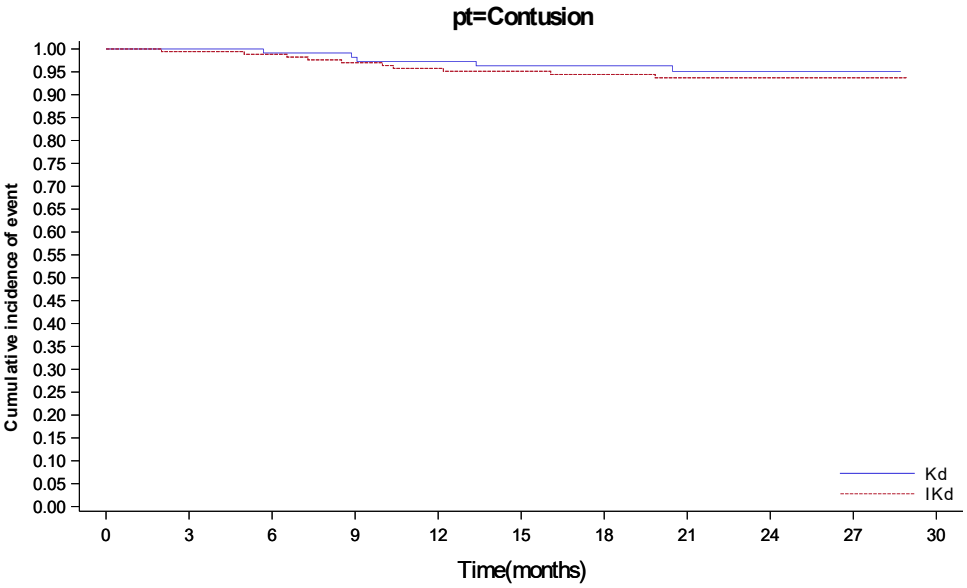
16.2.7.1 Safety endpoints
16.2.7.1.65 Analysis according to SOC/PT
16.2.7.1.65.4 Kaplan-Meier cumulative incidence curve of treatment emergent adverse event according to PT by treatment group - Safety population



Number at Risk

Kd	122	113	106	98	95	88	87	70	23	4	0
IKd	177	158	150	145	142	130	122	109	35	2	0

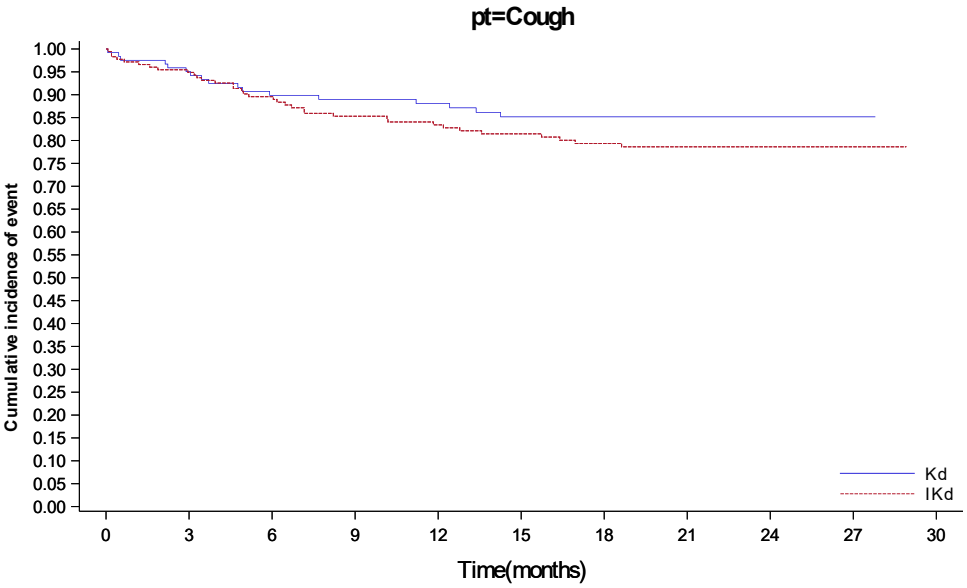
16.2.7.1 Safety endpoints
16.2.7.1.65 Analysis according to SOC/PT
16.2.7.1.65.4 Kaplan-Meier cumulative incidence curve of treatment emergent adverse event according to PT by treatment group - Safety population



Number at Risk

Kd	122	119	113	106	103	96	94	74	28	3	0
IKd	177	172	164	156	151	140	132	117	37	2	0

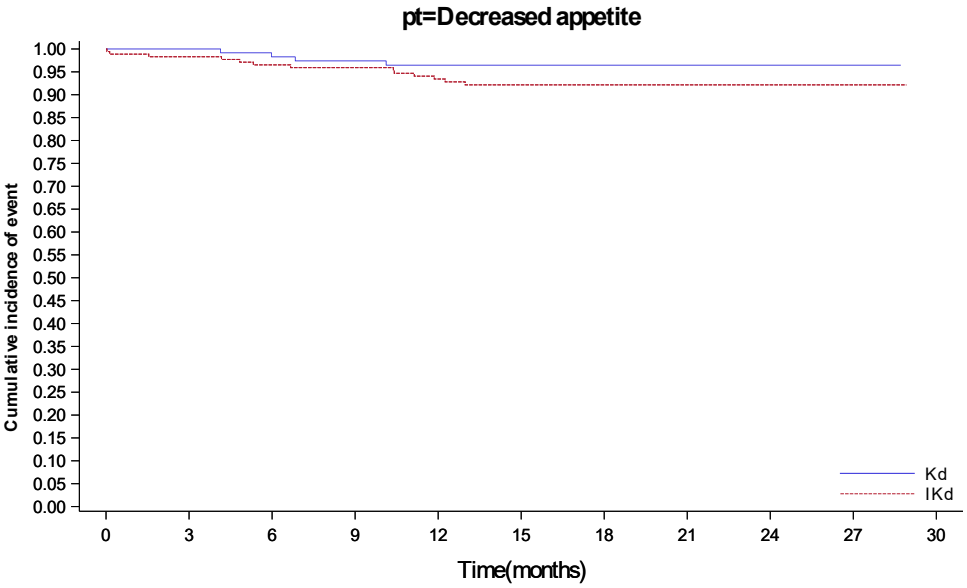
16.2.7.1 Safety endpoints
16.2.7.1.65 Analysis according to SOC/PT
16.2.7.1.65.4 Kaplan-Meier cumulative incidence curve of treatment emergent adverse event according to PT by treatment group - Safety population



Number at Risk

Kd	122	113	103	96	93	85	83	64	26	3	0
IKd	177	164	148	136	130	118	110	98	32	2	0

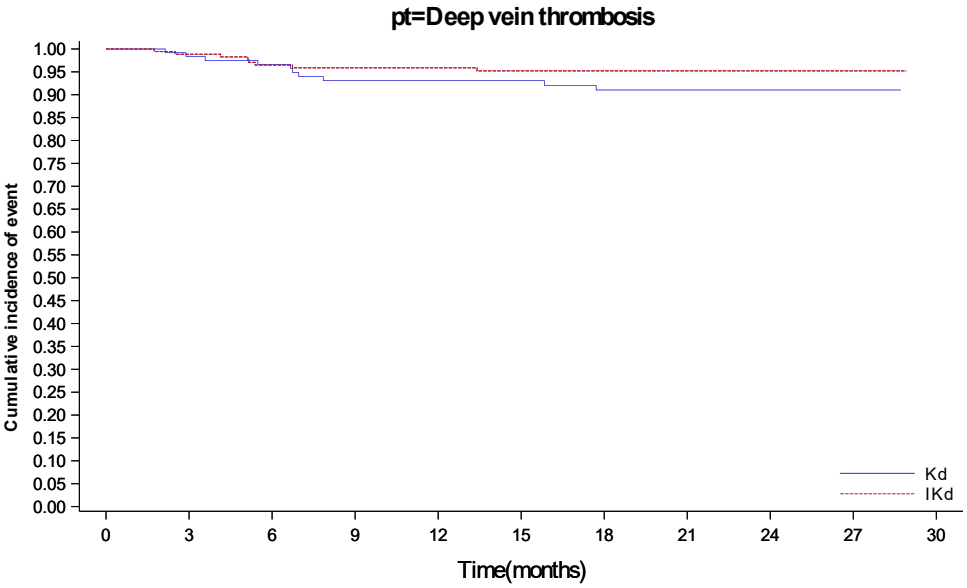
16.2.7.1 Safety endpoints
16.2.7.1.65 Analysis according to SOC/PT
16.2.7.1.65.4 Kaplan-Meier cumulative incidence curve of treatment emergent adverse event according to PT by treatment group - Safety population



Number at Risk

Kd	122	119	112	106	103	97	95	75	27	4	0
IKd	177	170	161	155	148	136	130	117	37	2	0

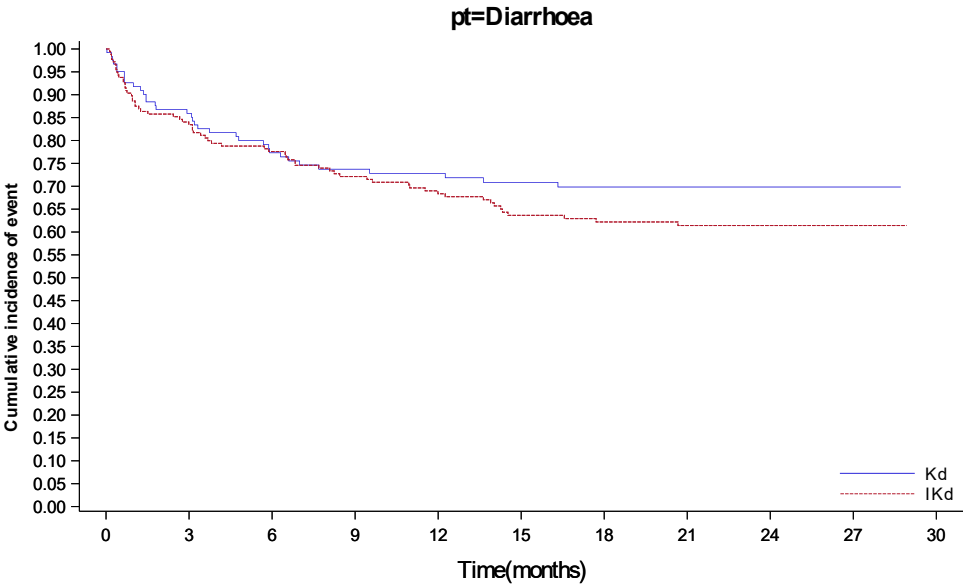
16.2.7.1 Safety endpoints
16.2.7.1.65 Analysis according to SOC/PT
16.2.7.1.65.4 Kaplan-Meier cumulative incidence curve of treatment emergent adverse event according to PT by treatment group - Safety population



Number at Risk

Kd	122	117	110	100	98	92	89	71	26	4	0
IKd	177	171	160	154	151	139	132	118	38	2	0

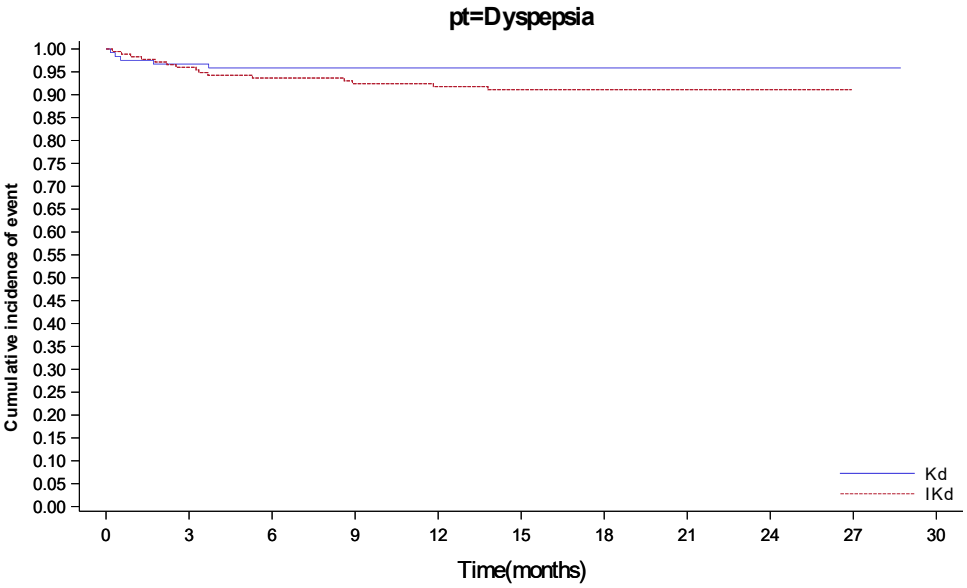
16.2.7.1 Safety endpoints
16.2.7.1.65 Analysis according to SOC/PT
16.2.7.1.65.4 Kaplan-Meier cumulative incidence curve of treatment emergent adverse event according to PT by treatment group - Safety population



Number at Risk

Kd	122	102	87	79	76	71	68	52	23	4	0
IKd	177	144	129	116	107	92	85	76	26	1	0

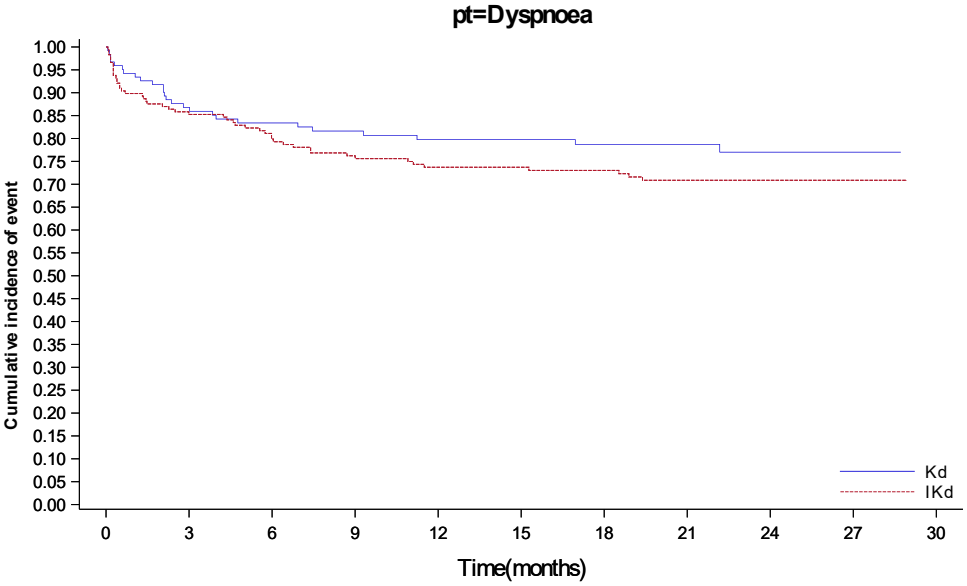
16.2.7.1 Safety endpoints
16.2.7.1.65 Analysis according to SOC/PT
16.2.7.1.65.4 Kaplan-Meier cumulative incidence curve of treatment emergent adverse event according to PT by treatment group - Safety population



Number at Risk

Kd	122	115	109	103	101	96	94	75	27	4	0
IKd	177	166	155	148	144	133	127	113	34	0	

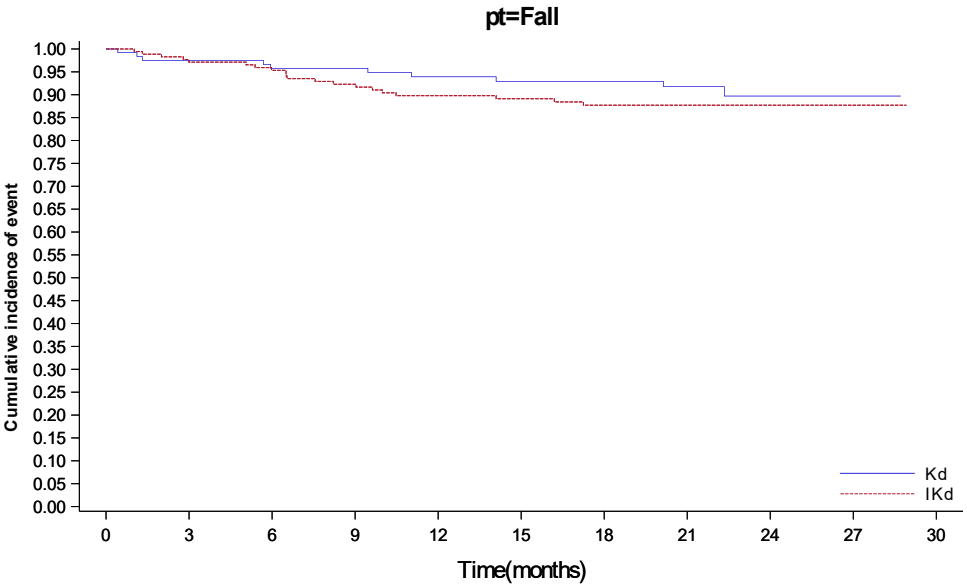
16.2.7.1 Safety endpoints
16.2.7.1.65 Analysis according to SOC/PT
16.2.7.1.65.4 Kaplan-Meier cumulative incidence curve of treatment emergent adverse event according to PT by treatment group - Safety population



Number at Risk

Kd	122	104	95	87	83	79	76	61	23	4	0
IKd	177	148	132	122	116	107	102	90	28	1	0

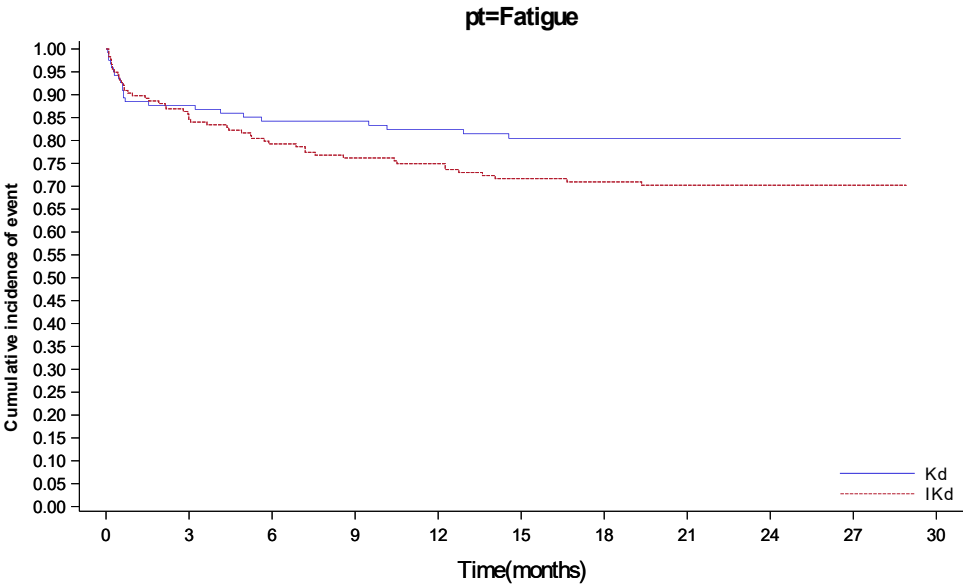
16.2.7.1 Safety endpoints
16.2.7.1.65 Analysis according to SOC/PT
16.2.7.1.65.4 Kaplan-Meier cumulative incidence curve of treatment emergent adverse event according to PT by treatment group - Safety population



Number at Risk

Kd	122	116	109	104	100	93	91	71	25	3	0
IKd	177	168	158	148	141	130	122	109	36	2	0

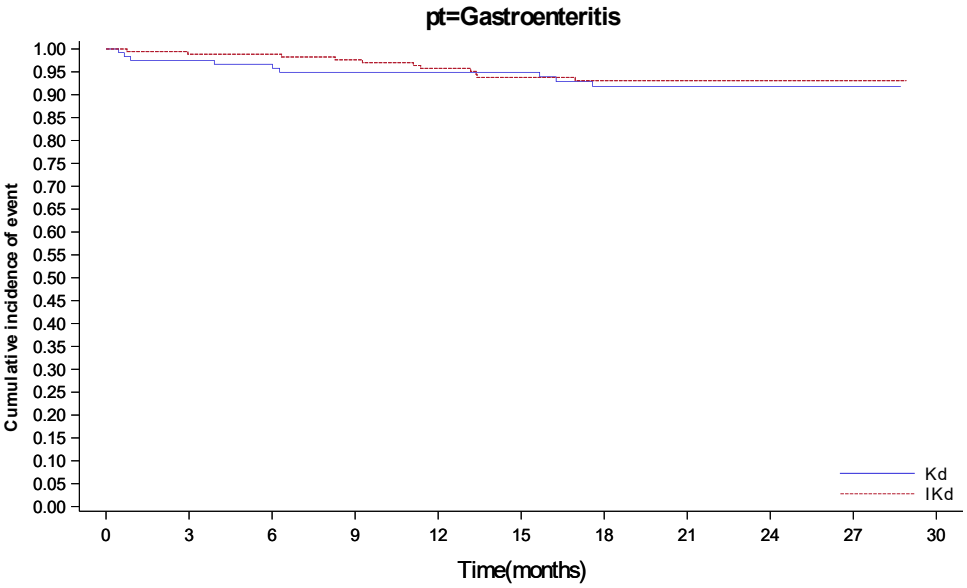
16.2.7.1 Safety endpoints
16.2.7.1.65 Analysis according to SOC/PT
16.2.7.1.65.4 Kaplan-Meier cumulative incidence curve of treatment emergent adverse event according to PT by treatment group - Safety population



Number at Risk

Kd	122	105	96	92	89	82	81	63	26	4	0
IKd	177	146	131	122	117	104	98	88	27	1	0

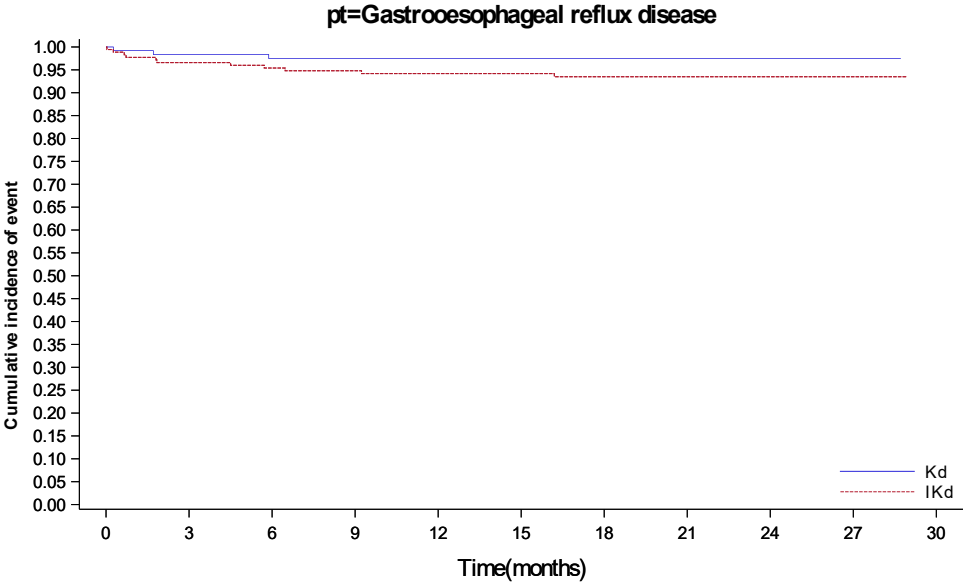
16.2.7.1 Safety endpoints
16.2.7.1.65 Analysis according to SOC/PT
16.2.7.1.65.4 Kaplan-Meier cumulative incidence curve of treatment emergent adverse event according to PT by treatment group - Safety population



Number at Risk

Kd	122	116	110	102	100	94	89	70	26	4	0
IKd	177	171	164	157	151	137	129	115	36	2	0

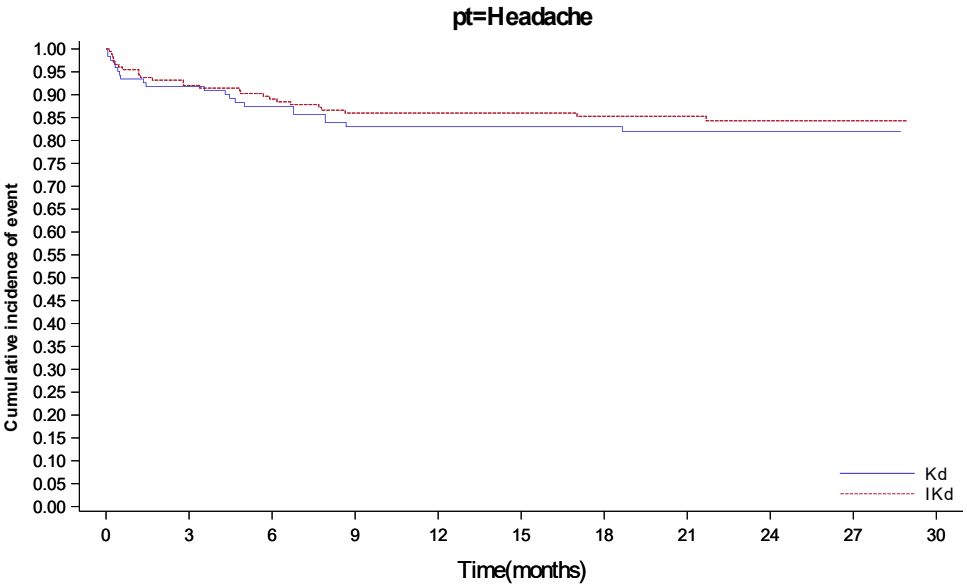
16.2.7.1 Safety endpoints
16.2.7.1.65 Analysis according to SOC/PT
16.2.7.1.65.4 Kaplan-Meier cumulative incidence curve of treatment emergent adverse event according to PT by treatment group - Safety population



Number at Risk

Kd	122	117	111	105	103	97	95	75	28	4	0
IKd	177	167	159	153	149	139	132	118	38	2	0

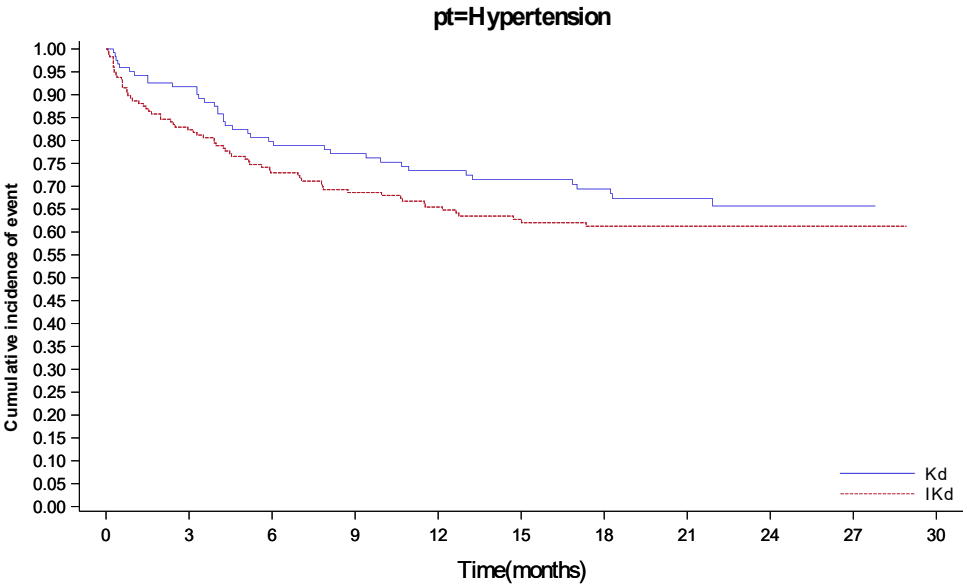
16.2.7.1 Safety endpoints
16.2.7.1.65 Analysis according to SOC/PT
16.2.7.1.65.4 Kaplan-Meier cumulative incidence curve of treatment emergent adverse event according to PT by treatment group - Safety population



Number at Risk

Kd	122	109	99	88	86	81	79	62	19	4	0
IKd	177	159	147	138	135	126	118	106	32	2	0

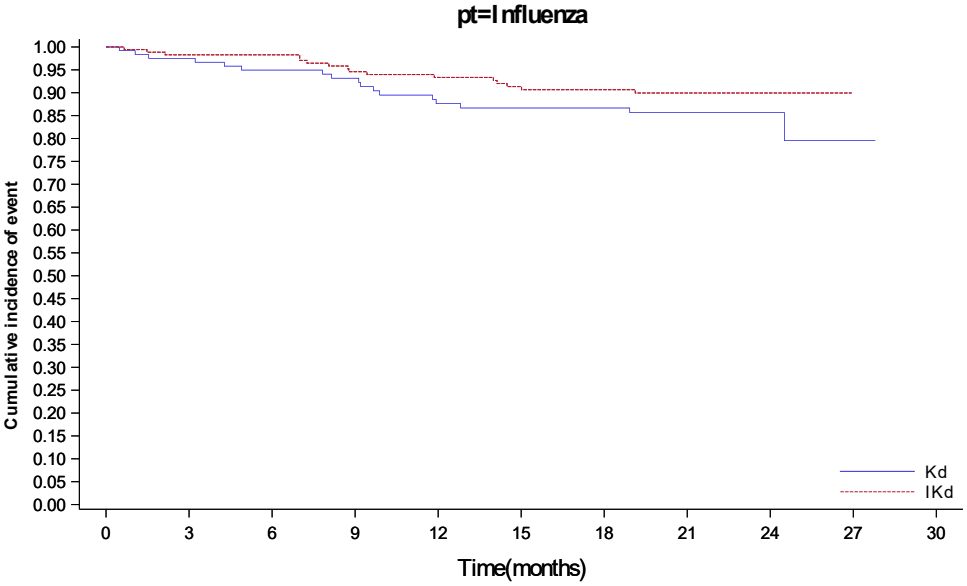
16.2.7.1 Safety endpoints
16.2.7.1.65 Analysis according to SOC/PT
16.2.7.1.65.4 Kaplan-Meier cumulative incidence curve of treatment emergent adverse event according to PT by treatment group - Safety population



Number at Risk

Kd	122	109	91	83	77	70	67	53	21	3	0
IKd	177	143	121	109	101	86	78	71	22	2	0

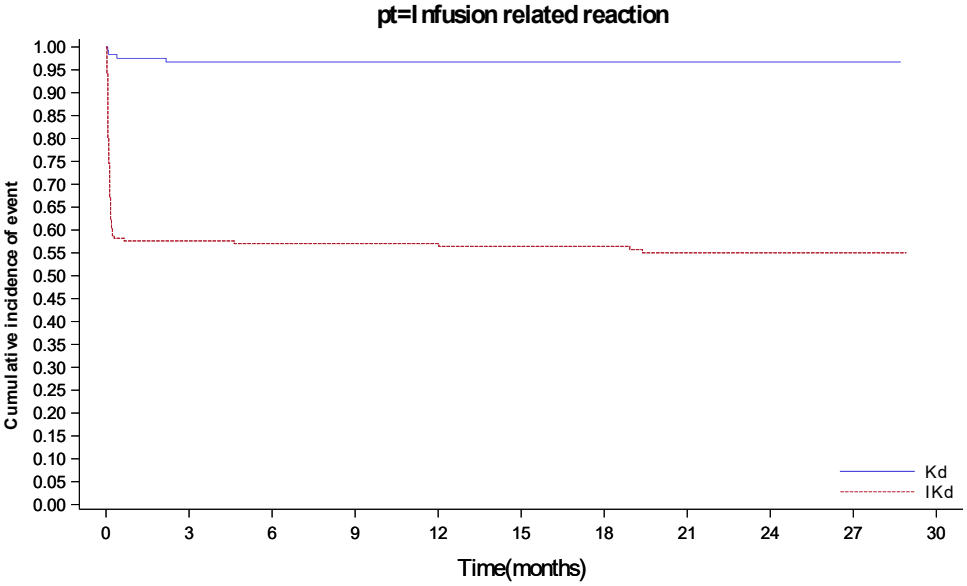
16.2.7.1 Safety endpoints
16.2.7.1.65 Analysis according to SOC/PT
16.2.7.1.65.4 Kaplan-Meier cumulative incidence curve of treatment emergent adverse event according to PT by treatment group - Safety population



Number at Risk

Kd	122	116	108	101	93	88	86	67	23	2	0
IKd	177	170	163	152	148	134	126	111	37	0	

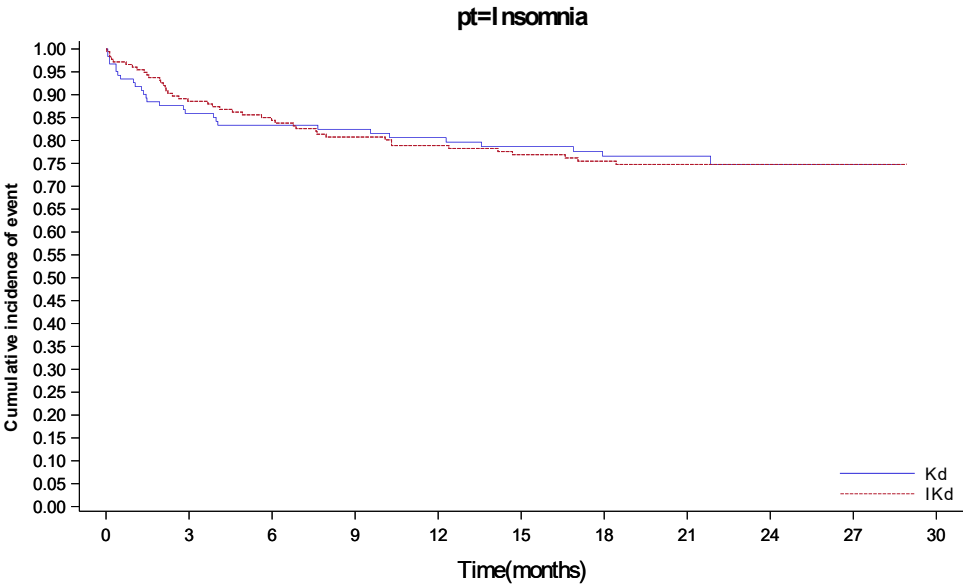
16.2.7.1 Safety endpoints
16.2.7.1.65 Analysis according to SOC/PT
16.2.7.1.65.4 Kaplan-Meier cumulative incidence curve of treatment emergent adverse event according to PT by treatment group - Safety population



Number at Risk

Kd	122	116	111	105	103	97	95	75	28	4	0
IKd	177	100	97	96	94	85	80	68	23	1	0

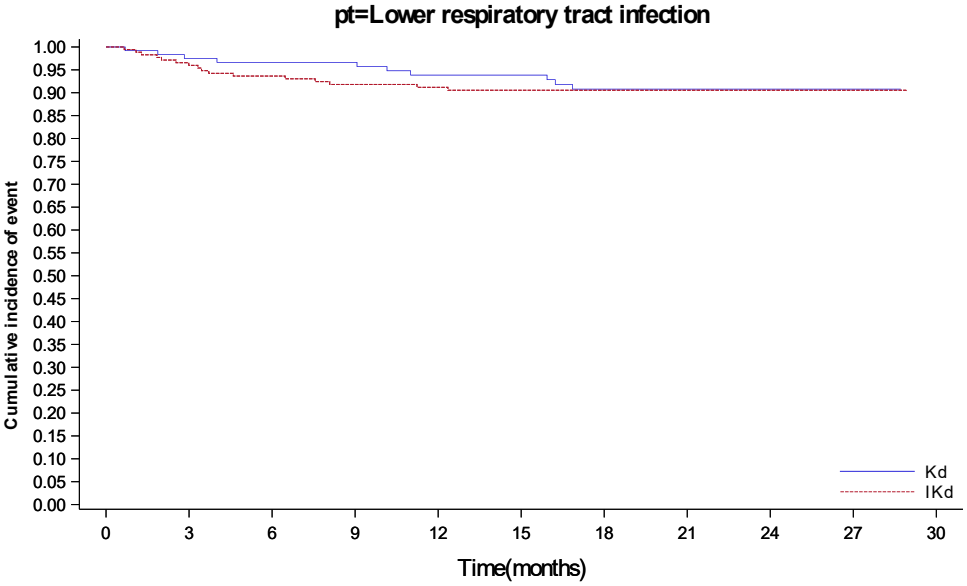
16.2.7.1 Safety endpoints
16.2.7.1.65 Analysis according to SOC/PT
16.2.7.1.65.4 Kaplan-Meier cumulative incidence curve of treatment emergent adverse event according to PT by treatment group - Safety population



Number at Risk

Kd	122	102	95	89	85	78	74	58	19	2	0
IKd	177	153	140	130	124	112	106	94	31	2	0

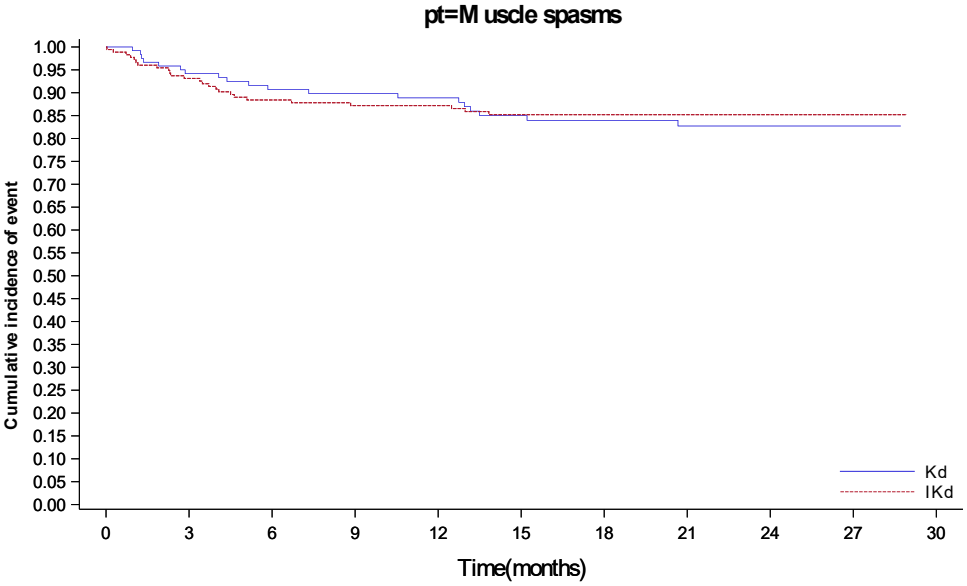
16.2.7.1 Safety endpoints
16.2.7.1.65 Analysis according to SOC/PT
16.2.7.1.65.4 Kaplan-Meier cumulative incidence curve of treatment emergent adverse event according to PT by treatment group - Safety population



Number at Risk

Kd	122	116	110	104	99	93	88	68	25	4	0
IKd	177	166	155	147	143	131	124	109	35	2	0

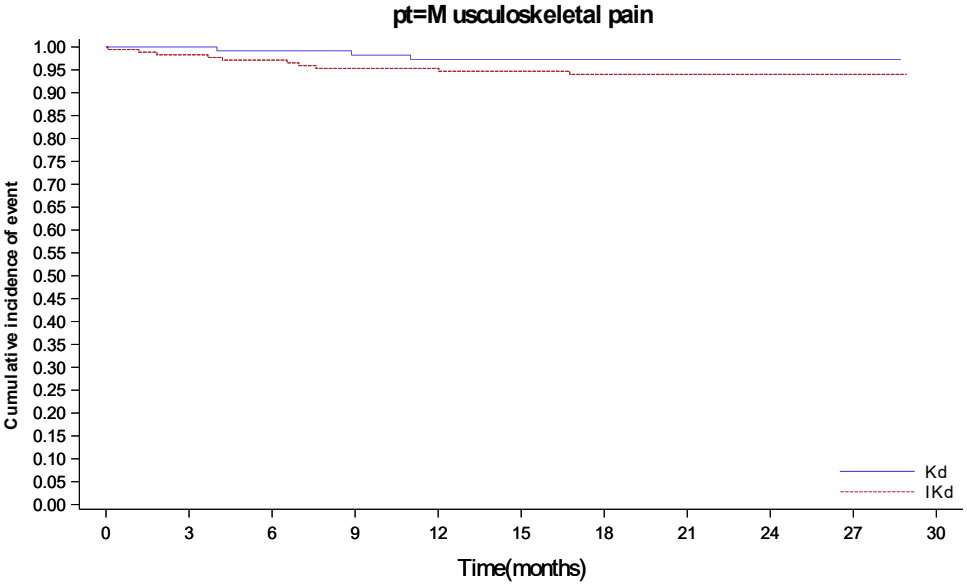
16.2.7.1 Safety endpoints
16.2.7.1.65 Analysis according to SOC/PT
16.2.7.1.65.4 Kaplan-Meier cumulative incidence curve of treatment emergent adverse event according to PT by treatment group - Safety population



Number at Risk

Kd	122	112	103	96	93	85	82	62	22	3	0
IKd	177	161	146	139	136	124	120	107	34	2	0

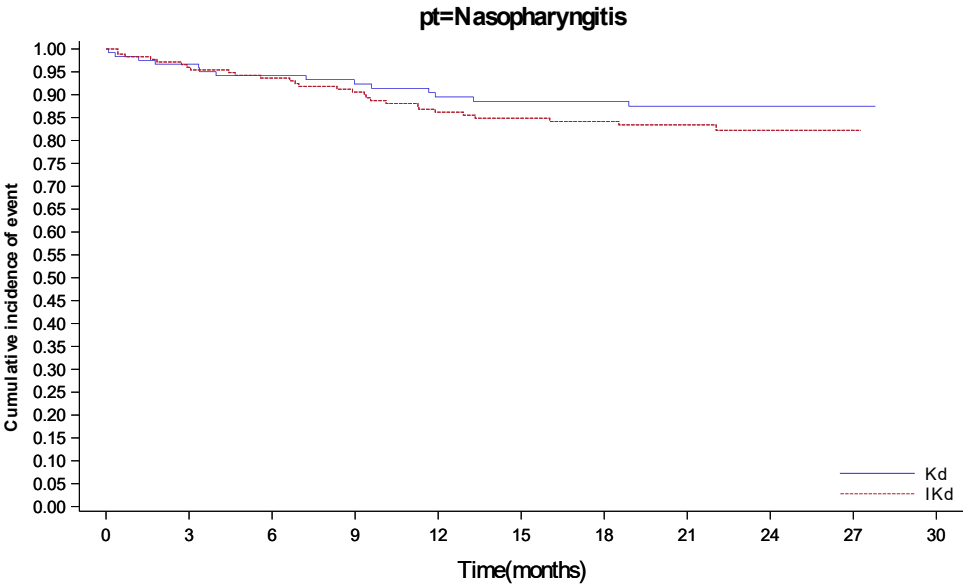
16.2.7.1 Safety endpoints
16.2.7.1.65 Analysis according to SOC/PT
16.2.7.1.65.4 Kaplan-Meier cumulative incidence curve of treatment emergent adverse event according to PT by treatment group - Safety population



Number at Risk

Kd	122	119	113	106	103	97	95	76	29	4	0
IKd	177	170	162	155	153	141	135	121	39	2	0

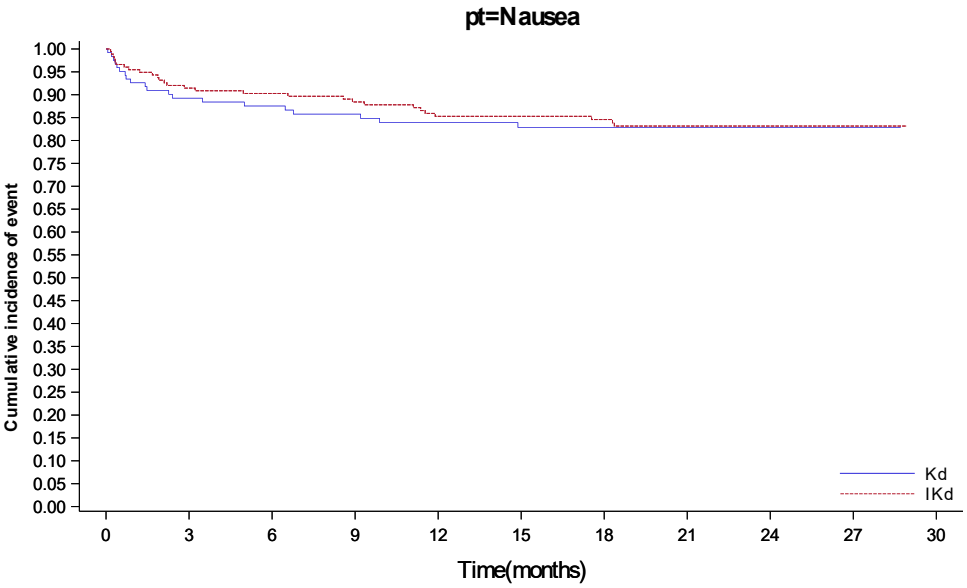
16.2.7.1 Safety endpoints
16.2.7.1.65 Analysis according to SOC/PT
16.2.7.1.65.4 Kaplan-Meier cumulative incidence curve of treatment emergent adverse event according to PT by treatment group - Safety population



Number at Risk

Kd	122	115	107	99	94	88	86	67	22	2	0
IKd	177	166	155	145	135	122	114	103	28	1	0

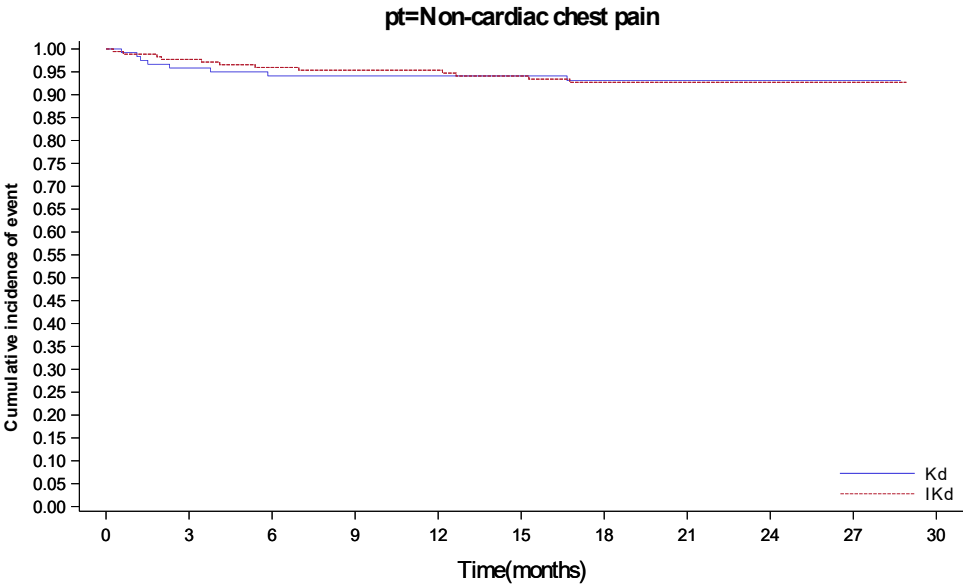
16.2.7.1 Safety endpoints
16.2.7.1.65 Analysis according to SOC/PT
16.2.7.1.65.4 Kaplan-Meier cumulative incidence curve of treatment emergent adverse event according to PT by treatment group - Safety population



Number at Risk

Kd	122	106	99	91	87	81	80	62	24	4	0
IKd	177	158	149	142	134	126	119	105	35	2	0

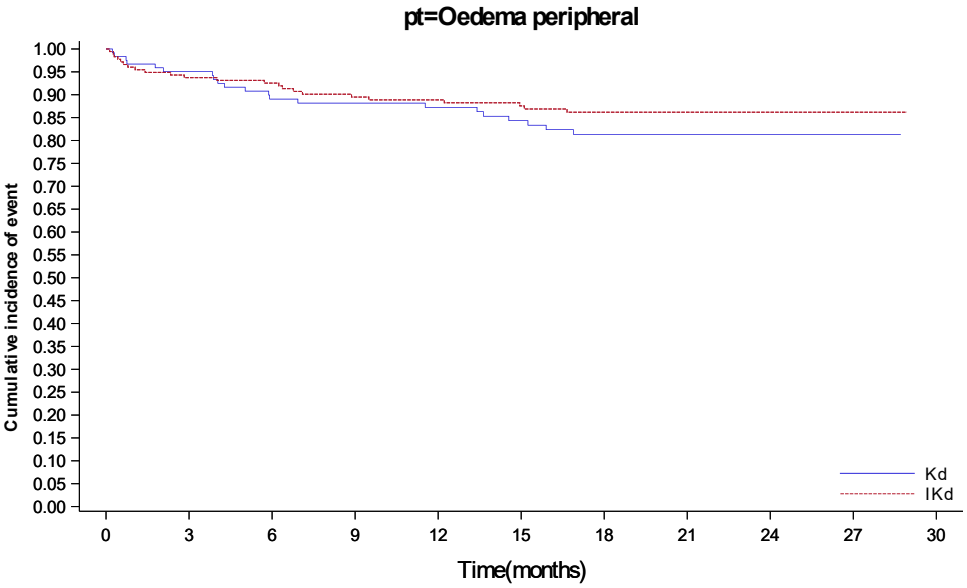
16.2.7.1 Safety endpoints
16.2.7.1.65 Analysis according to SOC/PT
16.2.7.1.65.4 Kaplan-Meier cumulative incidence curve of treatment emergent adverse event according to PT by treatment group - Safety population



Number at Risk

Kd	122	114	107	101	99	94	91	72	28	4	0
IKd	177	169	160	154	151	139	131	117	39	2	0

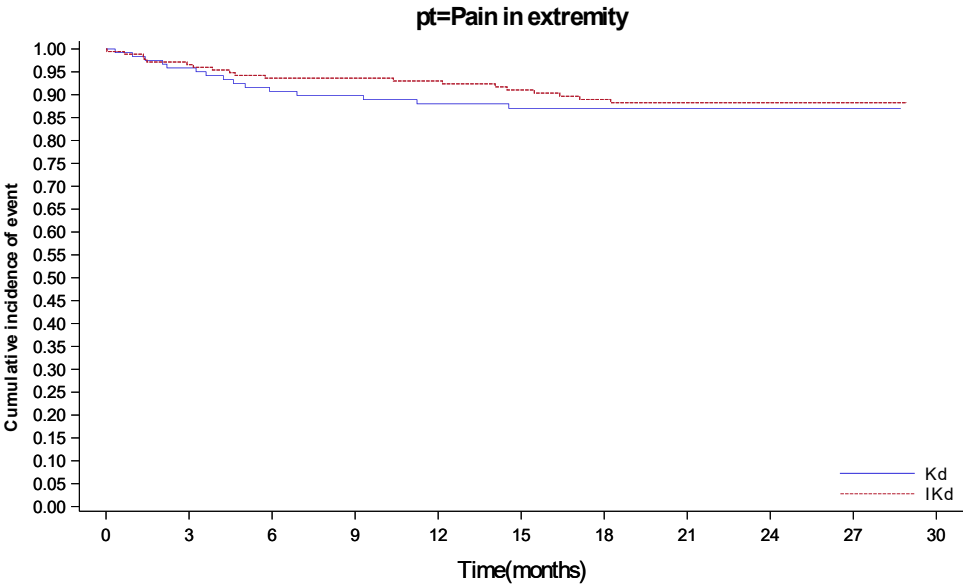
16.2.7.1 Safety endpoints
16.2.7.1.65 Analysis according to SOC/PT
16.2.7.1.65.4 Kaplan-Meier cumulative incidence curve of treatment emergent adverse event according to PT by treatment group - Safety population



Number at Risk

Kd	122	114	102	96	93	86	82	65	24	3	0
IKd	177	162	153	144	141	129	120	109	35	2	0

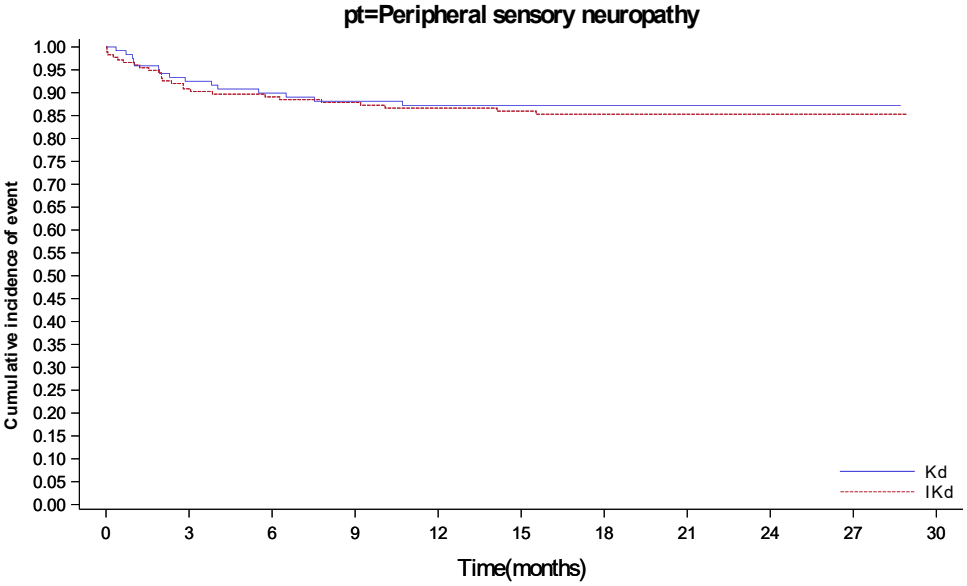
16.2.7.1 Safety endpoints
16.2.7.1.65 Analysis according to SOC/PT
16.2.7.1.65.4 Kaplan-Meier cumulative incidence curve of treatment emergent adverse event according to PT by treatment group - Safety population



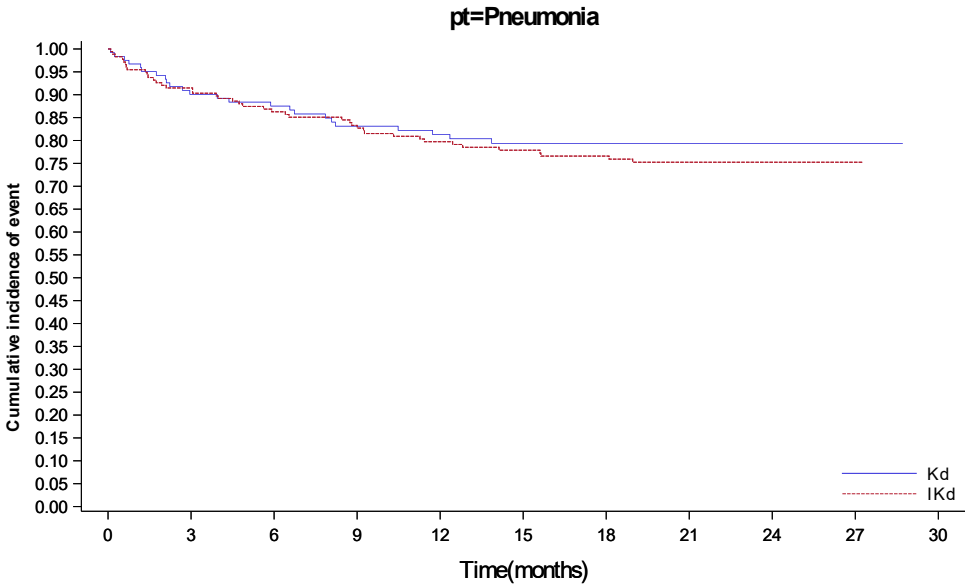
Number at Risk

Kd	122	114	104	98	94	87	85	67	27	4	0
IKd	177	167	155	151	148	134	125	111	35	2	0

16.2.7.1 Safety endpoints
16.2.7.1.65 Analysis according to SOC/PT
16.2.7.1.65.4 Kaplan-Meier cumulative incidence curve of treatment emergent adverse event according to PT by treatment group - Safety population



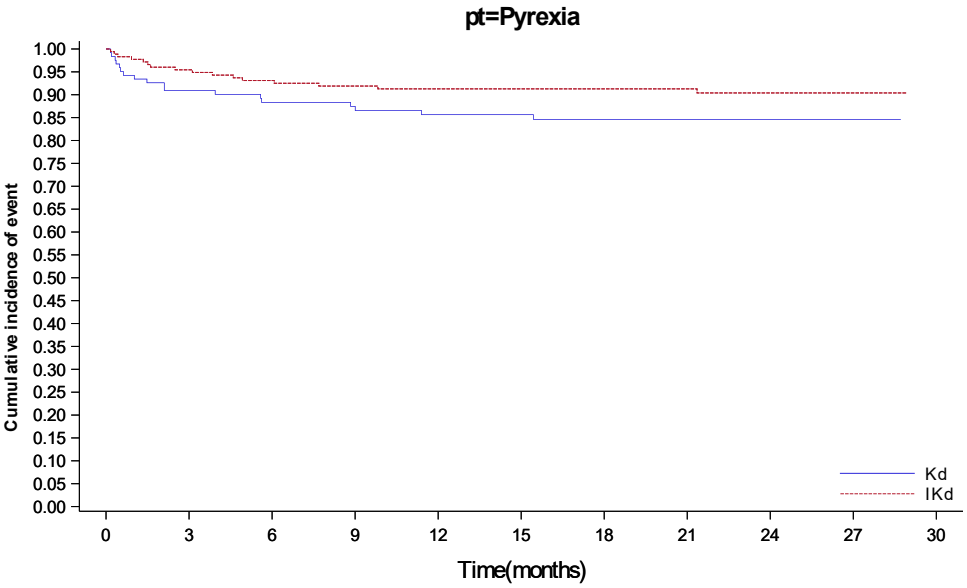
16.2.7.1 Safety endpoints
16.2.7.1.65 Analysis according to SOC/PT
16.2.7.1.65.4 Kaplan-Meier cumulative incidence curve of treatment emergent adverse event according to PT by treatment group - Safety population



Number at Risk

Kd	122	108	101	91	88	80	78	60	25	3	0
IKd	177	159	146	140	133	121	114	101	33	1	0

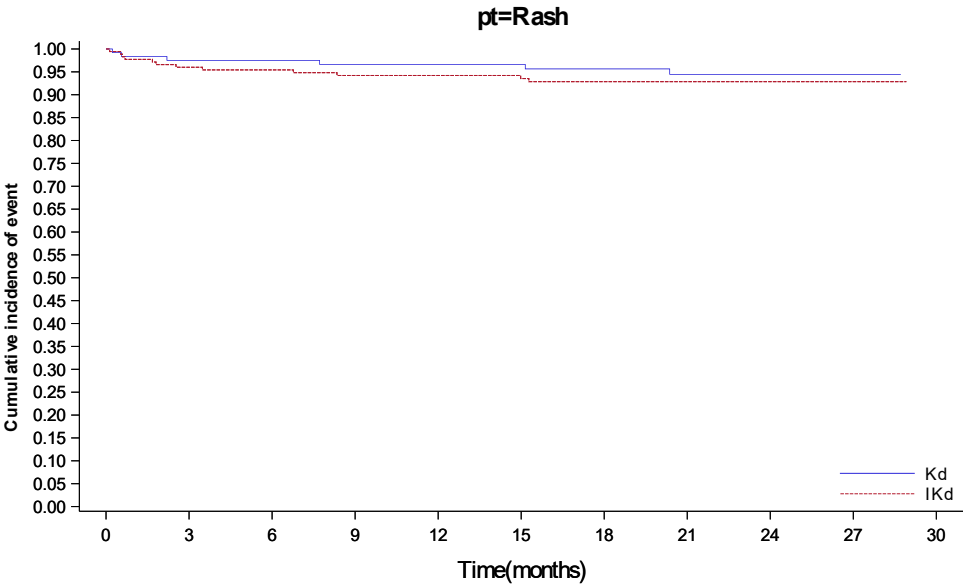
16.2.7.1 Safety endpoints
16.2.7.1.65 Analysis according to SOC/PT
16.2.7.1.65.4 Kaplan-Meier cumulative incidence curve of treatment emergent adverse event according to PT by treatment group - Safety population



Number at Risk

Kd	122	109	101	96	92	86	83	64	24	3	0
IKd	177	166	155	148	144	133	126	112	36	2	0

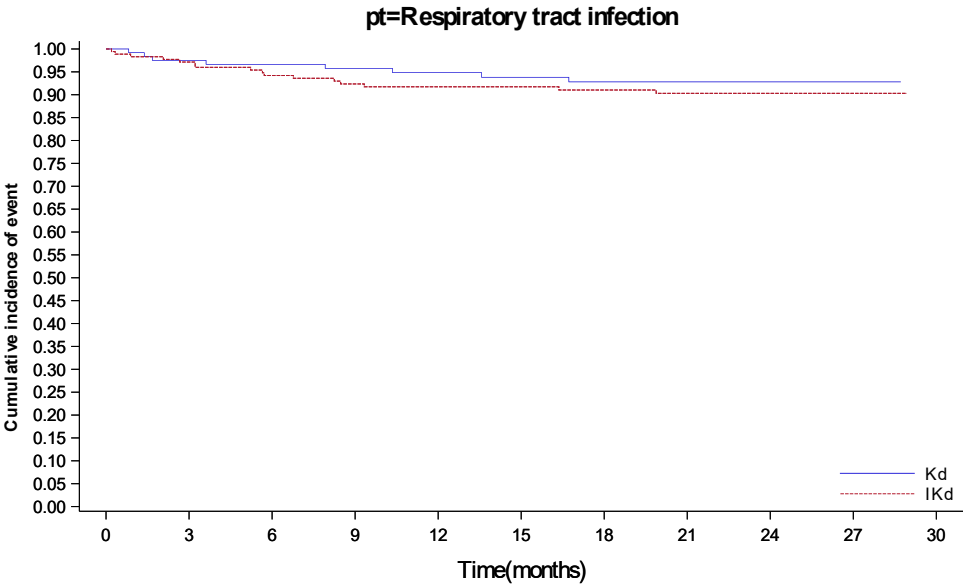
16.2.7.1 Safety endpoints
16.2.7.1.65 Analysis according to SOC/PT
16.2.7.1.65.4 Kaplan-Meier cumulative incidence curve of treatment emergent adverse event according to PT by treatment group - Safety population



Number at Risk

Kd	122	116	111	105	103	97	94	74	26	3	0
IKd	177	166	158	152	150	139	131	117	36	2	0

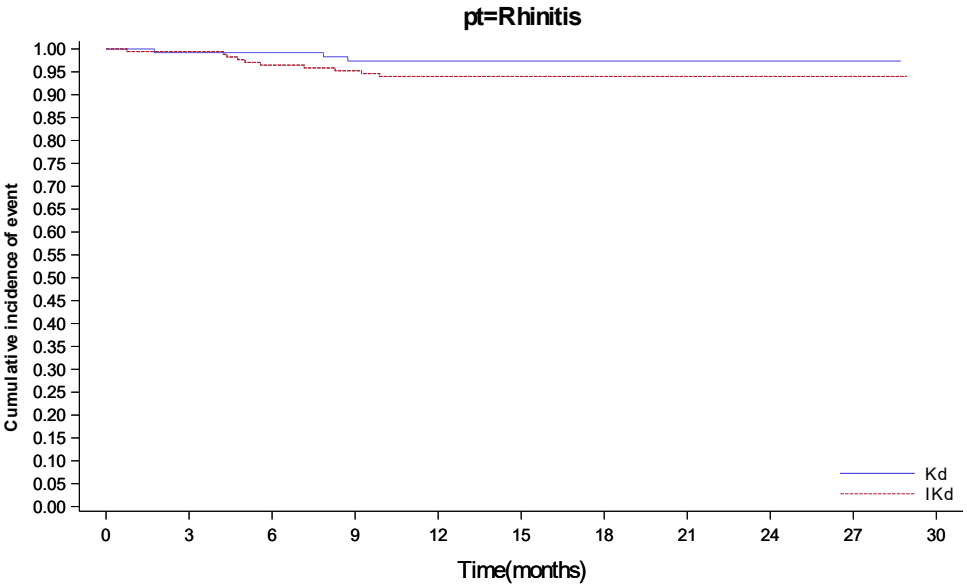
16.2.7.1 Safety endpoints
16.2.7.1.65 Analysis according to SOC/PT
16.2.7.1.65.4 Kaplan-Meier cumulative incidence curve of treatment emergent adverse event according to PT by treatment group - Safety population



Number at Risk

Kd	122	116	110	103	100	93	90	71	26	4	0
IKd	177	168	156	148	144	133	127	113	35	1	0

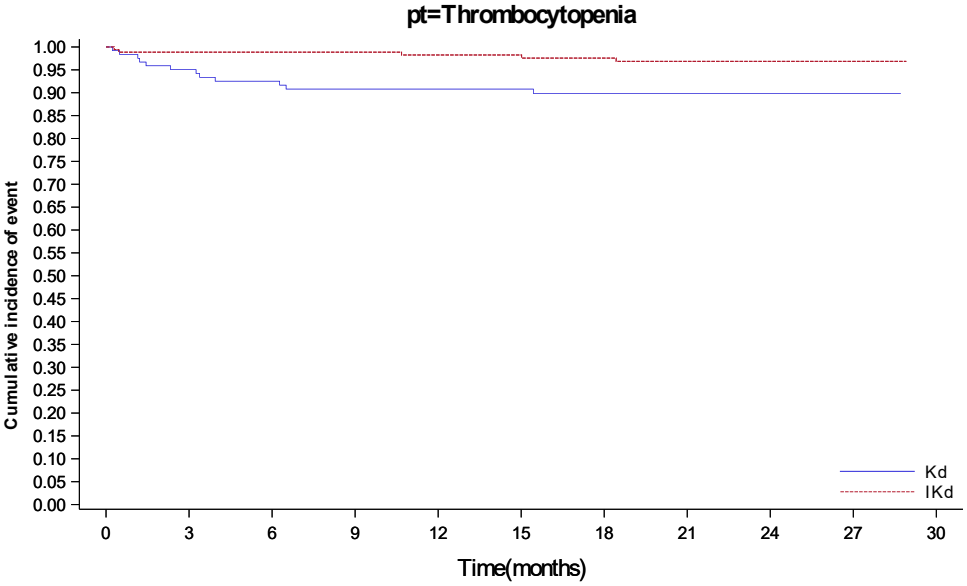
16.2.7.1 Safety endpoints
16.2.7.1.65 Analysis according to SOC/PT
16.2.7.1.65.4 Kaplan-Meier cumulative incidence curve of treatment emergent adverse event according to PT by treatment group - Safety population



Number at Risk

Kd	122	118	113	105	103	98	96	76	28	4	0
IKd	177	172	160	153	149	139	132	118	36	1	0

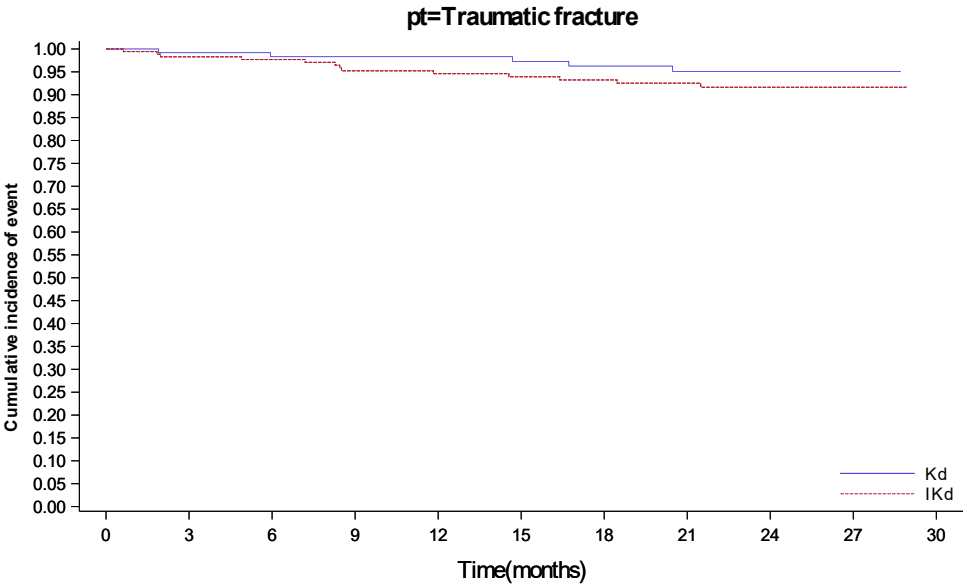
16.2.7.1 Safety endpoints
16.2.7.1.65 Analysis according to SOC/PT
16.2.7.1.65.4 Kaplan-Meier cumulative incidence curve of treatment emergent adverse event according to PT by treatment group - Safety population



Number at Risk

Kd	122	114	107	99	98	93	90	71	27	4	0
IKd	177	171	165	160	156	145	137	121	39	2	0

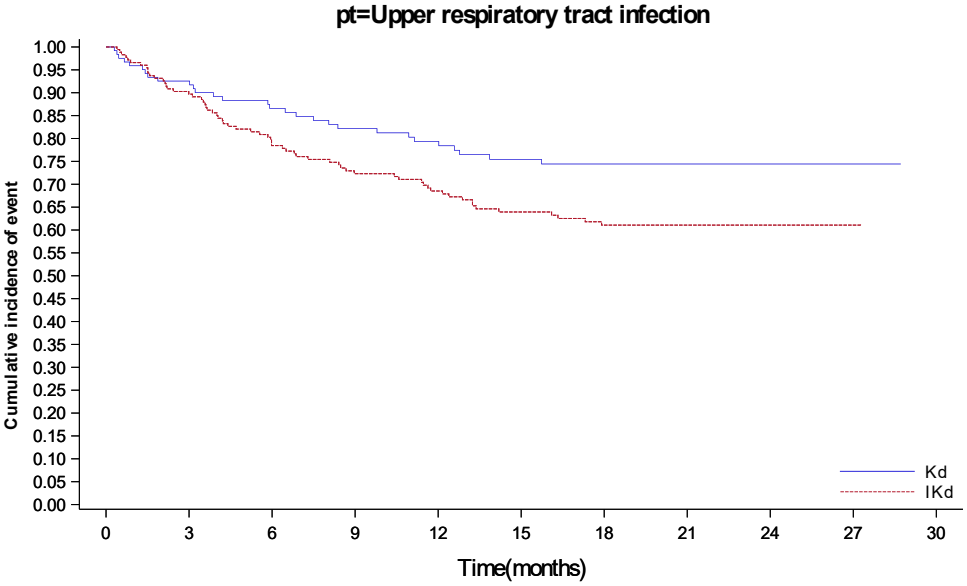
16.2.7.1 Safety endpoints
16.2.7.1.65 Analysis according to SOC/PT
16.2.7.1.65.4 Kaplan-Meier cumulative incidence curve of treatment emergent adverse event according to PT by treatment group - Safety population



Number at Risk

Kd	122	118	112	106	104	97	94	75	27	3	0
IKd	177	170	162	153	150	139	132	116	34	1	0

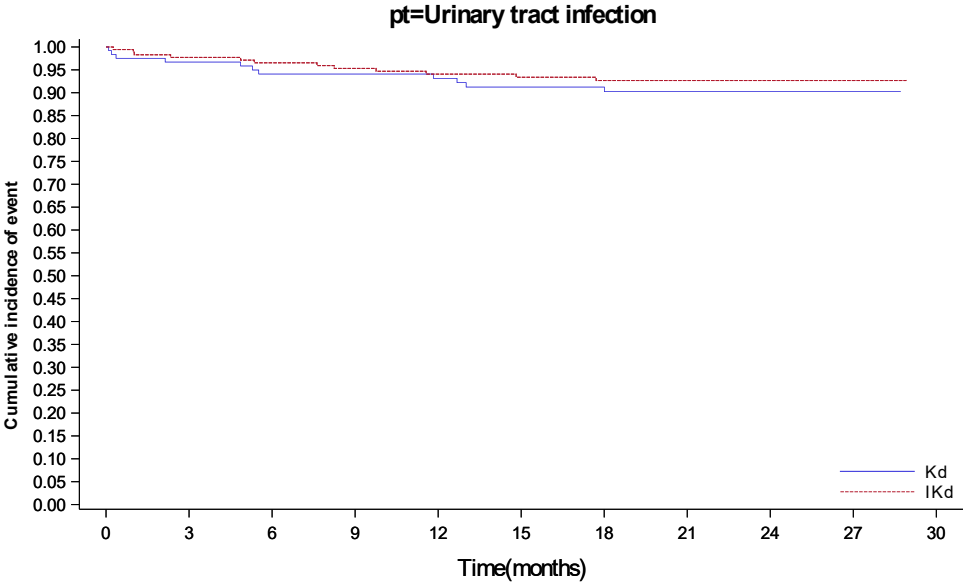
16.2.7.1 Safety endpoints
16.2.7.1.65 Analysis according to SOC/PT
16.2.7.1.65.4 Kaplan-Meier cumulative incidence curve of treatment emergent adverse event according to PT by treatment group - Safety population



Number at Risk

Kd	122	110	99	88	83	74	72	57	21	3	0
IKd	177	155	130	116	108	92	84	75	22	1	0

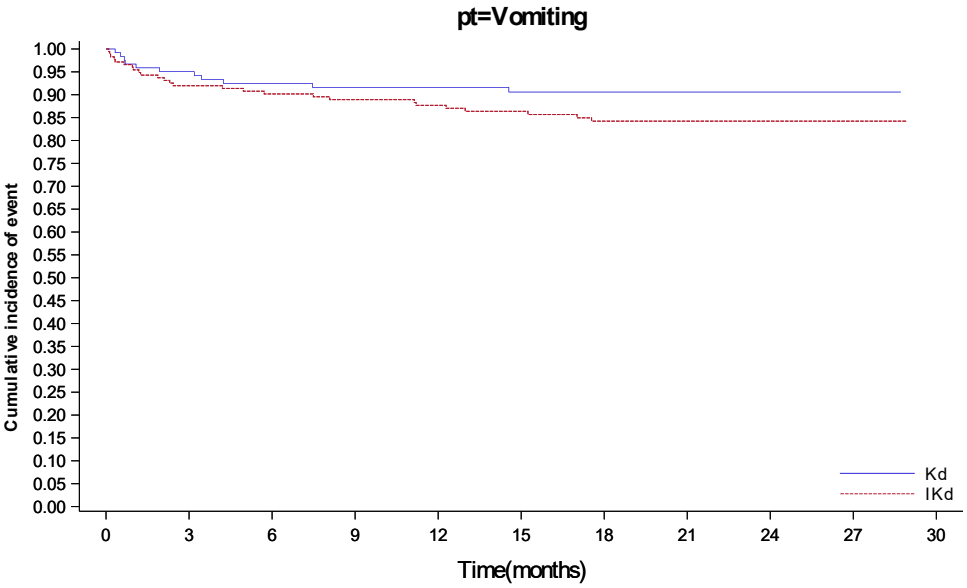
16.2.7.1 Safety endpoints
16.2.7.1.65 Analysis according to SOC/PT
16.2.7.1.65.4 Kaplan-Meier cumulative incidence curve of treatment emergent adverse event according to PT by treatment group - Safety population



Number at Risk

Kd	122	115	107	102	99	91	90	69	25	4	0
IKd	177	170	161	154	149	137	129	114	37	2	0

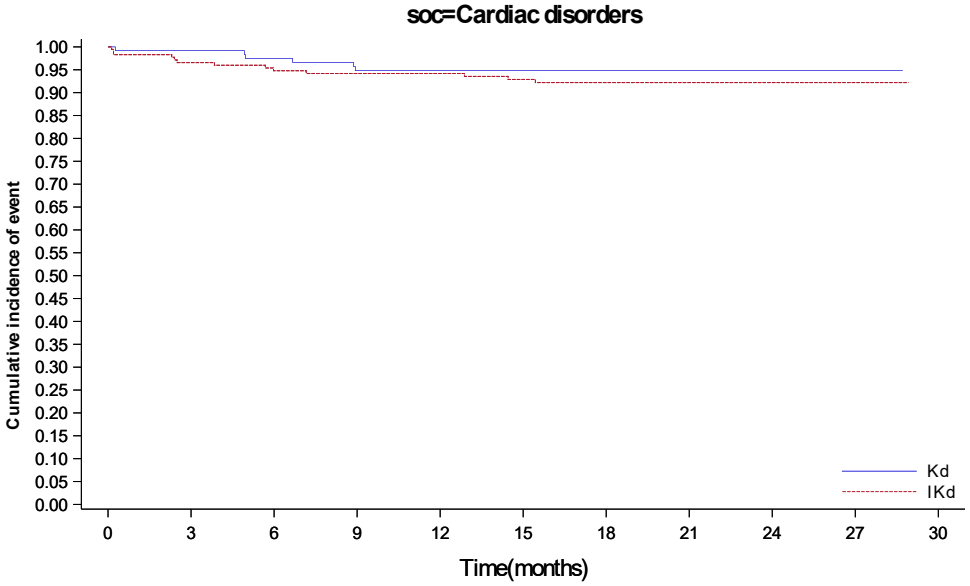
16.2.7.1 Safety endpoints
16.2.7.1.65 Analysis according to SOC/PT
16.2.7.1.65.4 Kaplan-Meier cumulative incidence curve of treatment emergent adverse event according to PT by treatment group - Safety population



Number at Risk

Kd	122	113	105	98	96	89	88	69	24	4	0
IKd	176	158	148	142	137	124	114	101	35	2	0

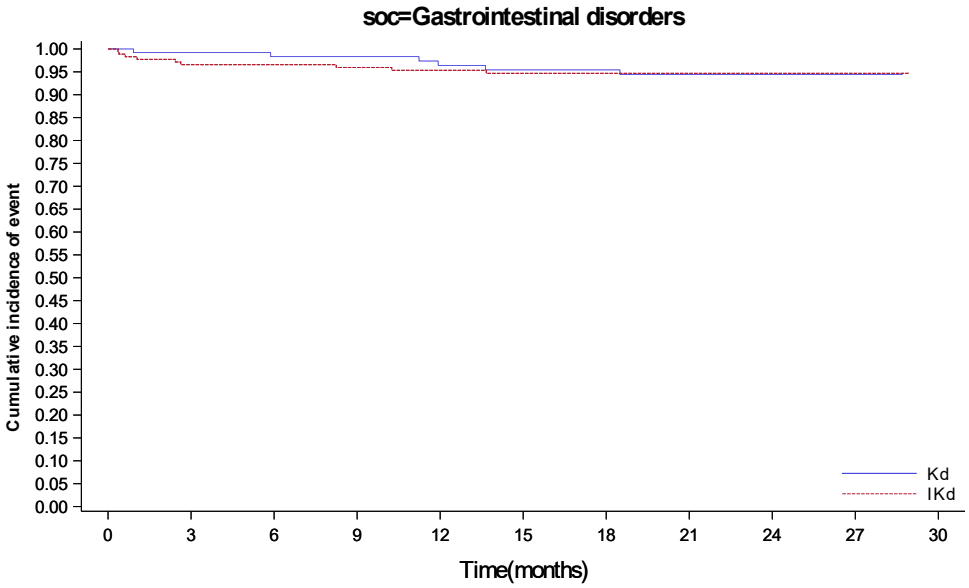
16.2.7.1 Safety endpoints
16.2.7.1.65 Analysis according to SOC/PT
16.2.7.1.65.6 Kaplan-Meier cumulative incidence curve of treatment emergent serious adverse event according to SOC by treatment group - Safety population



Number at Risk

Kd	122	118	112	105	103	98	96	76	29	4	0
IKd	177	167	158	152	150	138	131	118	38	2	0

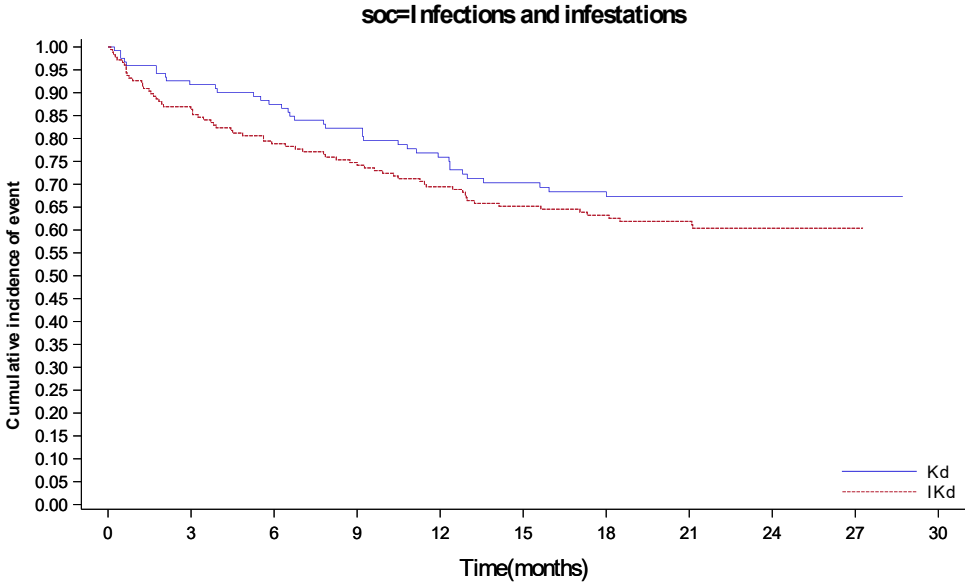
16.2.7.1 Safety endpoints
16.2.7.1.65 Analysis according to SOC/PT
16.2.7.1.65.6 Kaplan-Meier cumulative incidence curve of treatment emergent serious adverse event according to SOC by treatment group - Safety population



Number at Risk

Kd	122	118	112	106	102	95	93	73	27	4	0
IKd	177	167	160	155	152	140	133	119	39	2	0

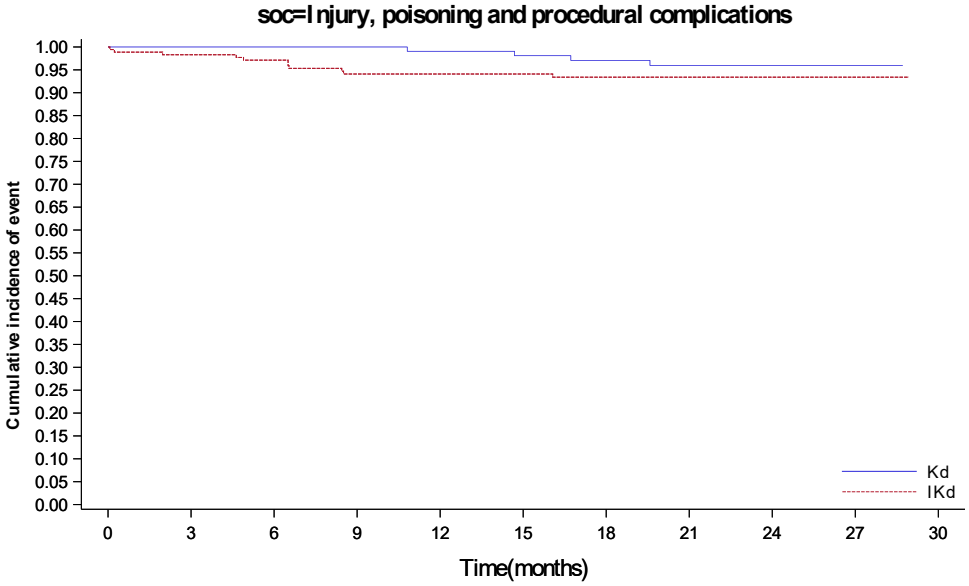
16.2.7.1 Safety endpoints
16.2.7.1.65 Analysis according to SOC/PT
16.2.7.1.65.6 Kaplan-Meier cumulative incidence curve of treatment emergent serious adverse event according to SOC by treatment group - Safety population



Number at Risk

Kd	122	110	101	91	83	72	68	52	16	2	0
IKd	177	150	135	127	118	102	95	83	26	1	0

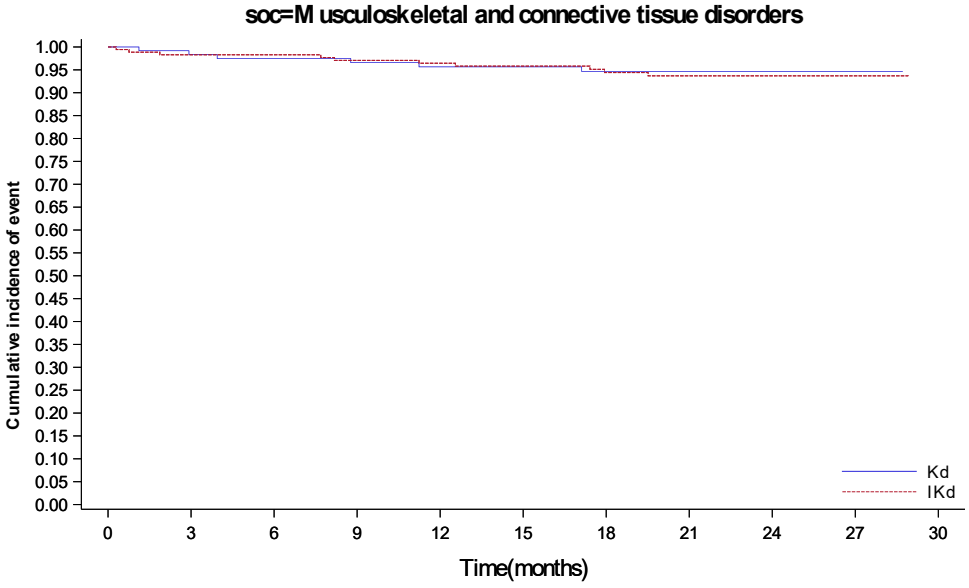
16.2.7.1 Safety endpoints
16.2.7.1.65 Analysis according to SOC/PT
16.2.7.1.65.6 Kaplan-Meier cumulative incidence curve of treatment emergent serious adverse event according to SOC by treatment group - Safety population



Number at Risk

Kd	122	119	114	108	105	98	95	75	28	3	0
IKd	177	171	162	152	149	139	131	116	37	2	0

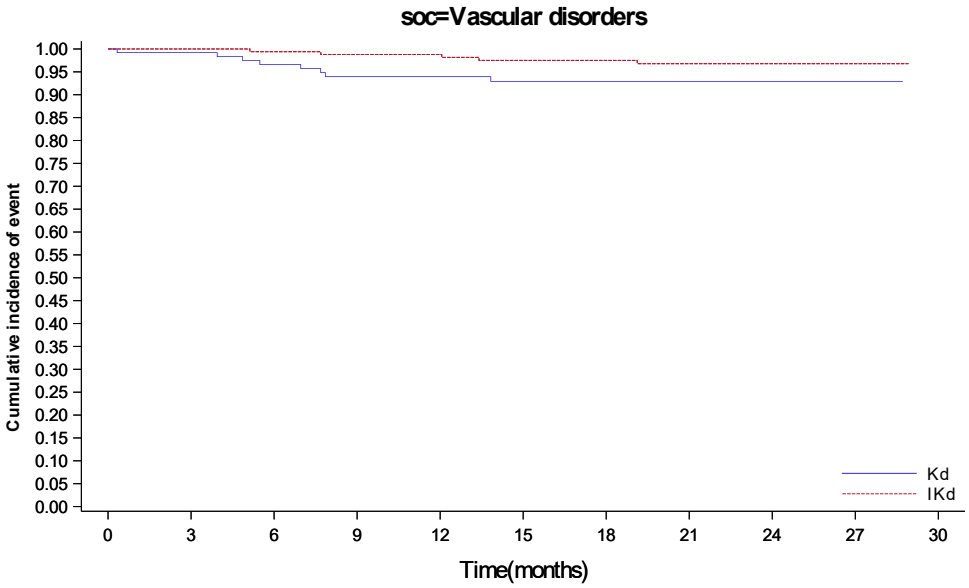
16.2.7.1 Safety endpoints
16.2.7.1.65 Analysis according to SOC/PT
16.2.7.1.65.6 Kaplan-Meier cumulative incidence curve of treatment emergent serious adverse event according to SOC by treatment group - Safety population



Number at Risk

Kd	122	117	111	105	102	96	93	74	27	4	0
IKd	177	170	163	157	154	142	133	118	37	2	0

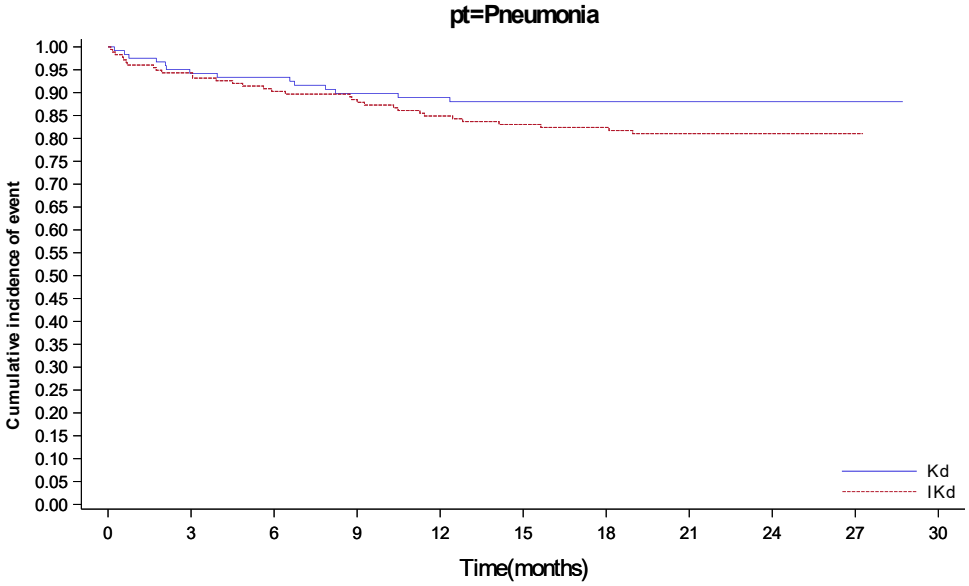
16.2.7.1 Safety endpoints
16.2.7.1.65 Analysis according to SOC/PT
16.2.7.1.65.6 Kaplan-Meier cumulative incidence curve of treatment emergent serious adverse event according to SOC by treatment group - Safety population



Number at Risk

Kd	122	118	110	102	100	93	92	73	28	4	0
IKd	177	173	165	159	156	143	136	120	39	2	0

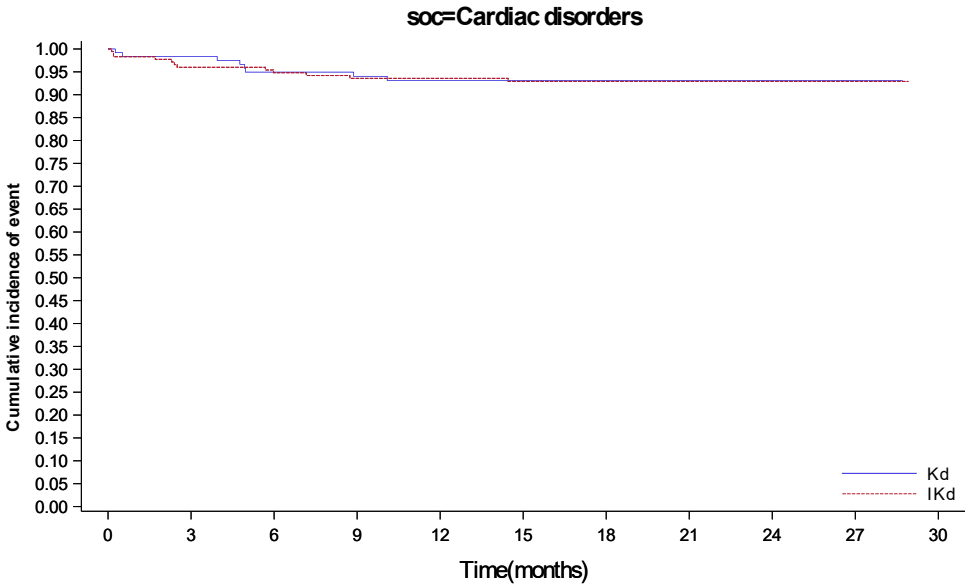
16.2.7.1 Safety endpoints
16.2.7.1.65 Analysis according to SOC/PT
16.2.7.1.65.8 Kaplan-Meier cumulative incidence curve of treatment emergent serious adverse event according to PT by treatment group - Safety population



Number at Risk

Kd	122	113	107	98	96	89	87	69	27	3	0
IKd	177	164	153	148	141	129	122	109	35	1	0

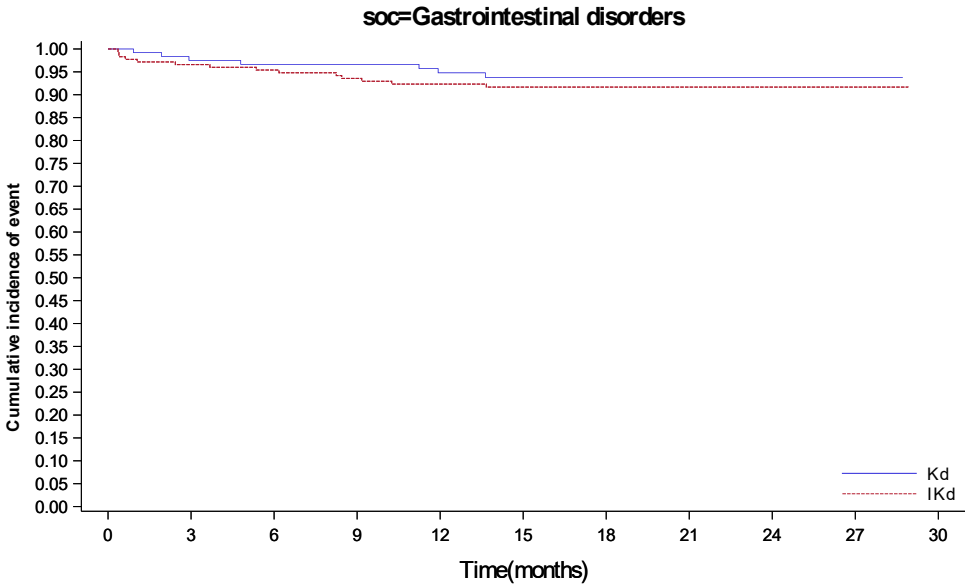
16.2.7.1 Safety endpoints
16.2.7.1.65 Analysis according to SOC/PT
16.2.7.1.65.18 Kaplan-Meier cumulative incidence curve of treatment emergent severe adverse event according to SOC by treatment group - Safety population



Number at Risk

Kd	122	117	109	103	100	95	94	74	29	4	0
IKd	177	166	158	151	149	137	131	118	38	2	0

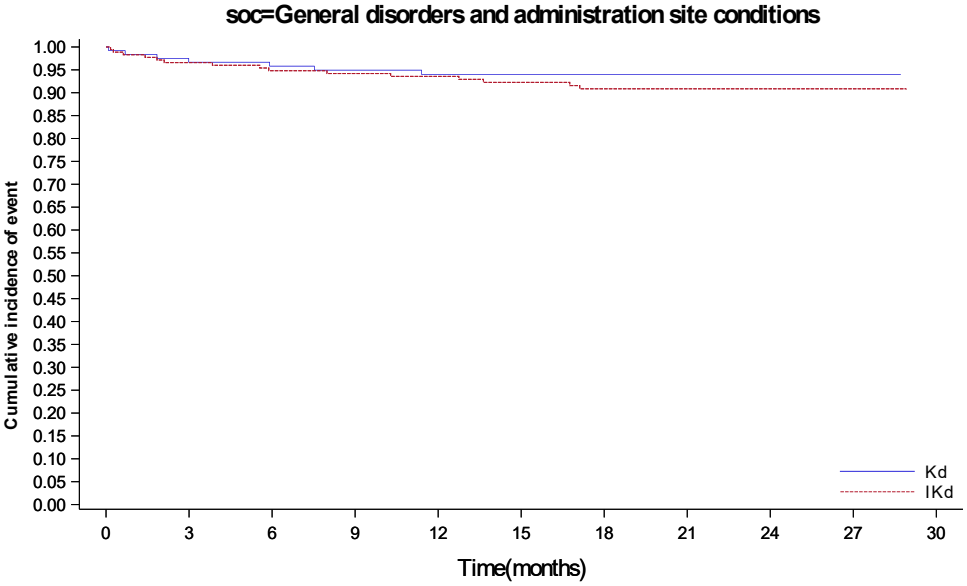
16.2.7.1 Safety endpoints
16.2.7.1.65 Analysis according to SOC/PT
16.2.7.1.65.18 Kaplan-Meier cumulative incidence curve of treatment emergent severe adverse event according to SOC by treatment group - Safety population



Number at Risk

Kd	122	116	110	105	101	94	92	74	28	4	0
IKd	177	167	158	151	147	136	129	115	38	2	0

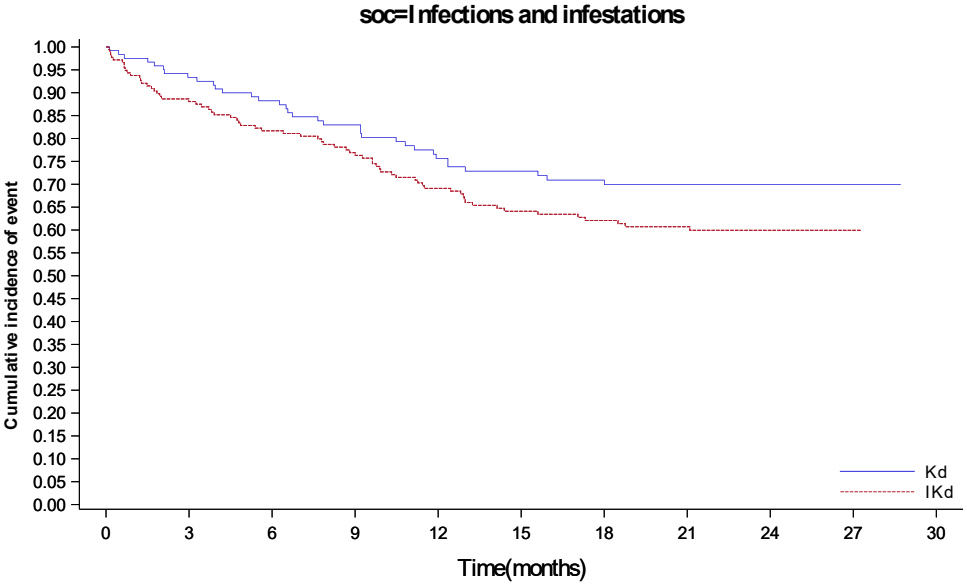
16.2.7.1 Safety endpoints
16.2.7.1.65 Analysis according to SOC/PT
16.2.7.1.65.18 Kaplan-Meier cumulative incidence curve of treatment emergent severe adverse event according to SOC by treatment group - Safety population



Number at Risk

Kd	122	115	111	105	102	97	96	76	28	4	0
IKd	177	167	158	152	148	135	127	112	33	2	0

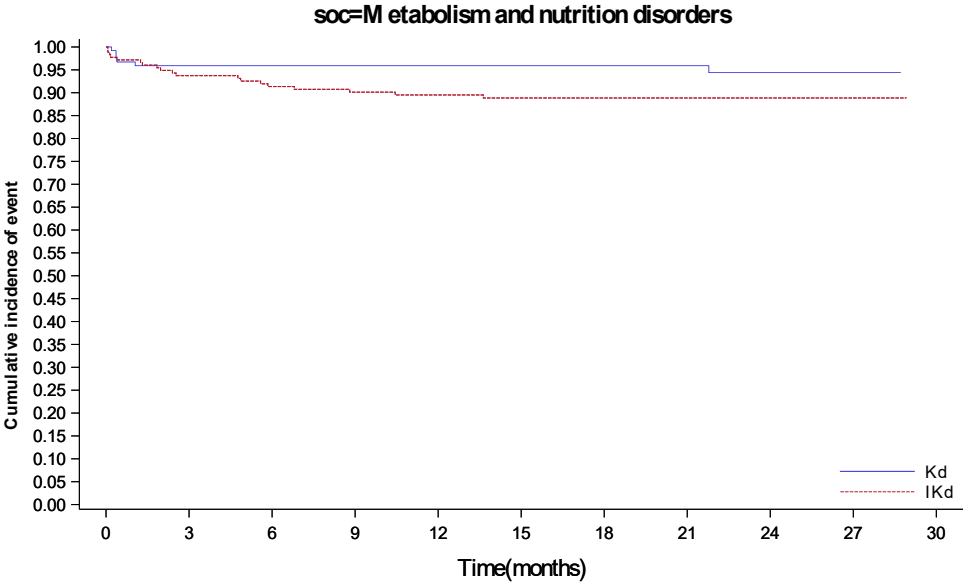
16.2.7.1 Safety endpoints
16.2.7.1.65 Analysis according to SOC/PT
16.2.7.1.65.18 Kaplan-Meier cumulative incidence curve of treatment emergent severe adverse event according to SOC by treatment group - Safety population



Number at Risk

Kd	122	111	101	91	82	75	71	54	18	2	0
IKd	177	153	139	128	115	98	91	79	26	1	0

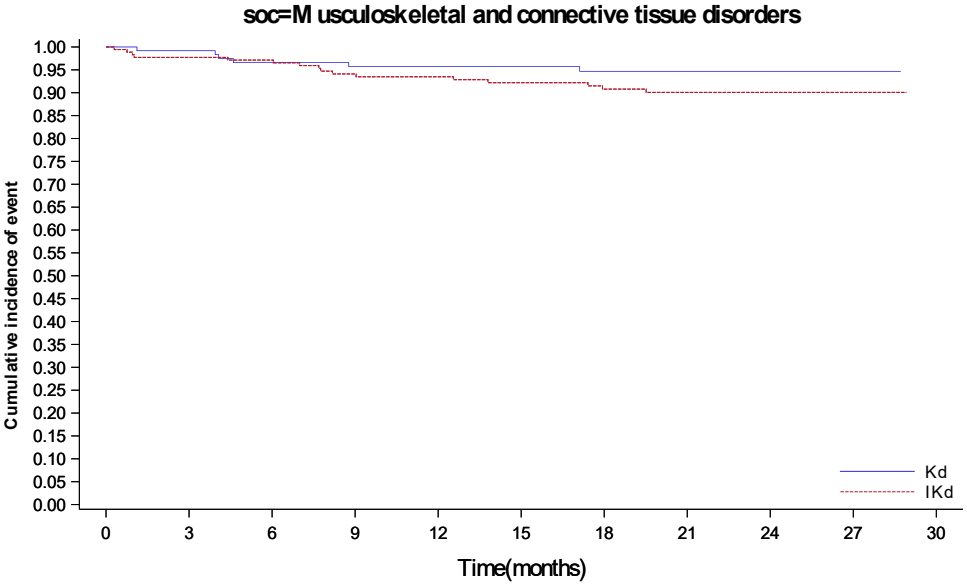
16.2.7.1 Safety endpoints
16.2.7.1.65 Analysis according to SOC/PT
16.2.7.1.65.18 Kaplan-Meier cumulative incidence curve of treatment emergent severe adverse event according to SOC by treatment group - Safety population



Number at Risk

Kd	122	114	110	105	103	98	96	77	29	4	0
IKd	177	162	152	146	143	131	124	110	37	2	0

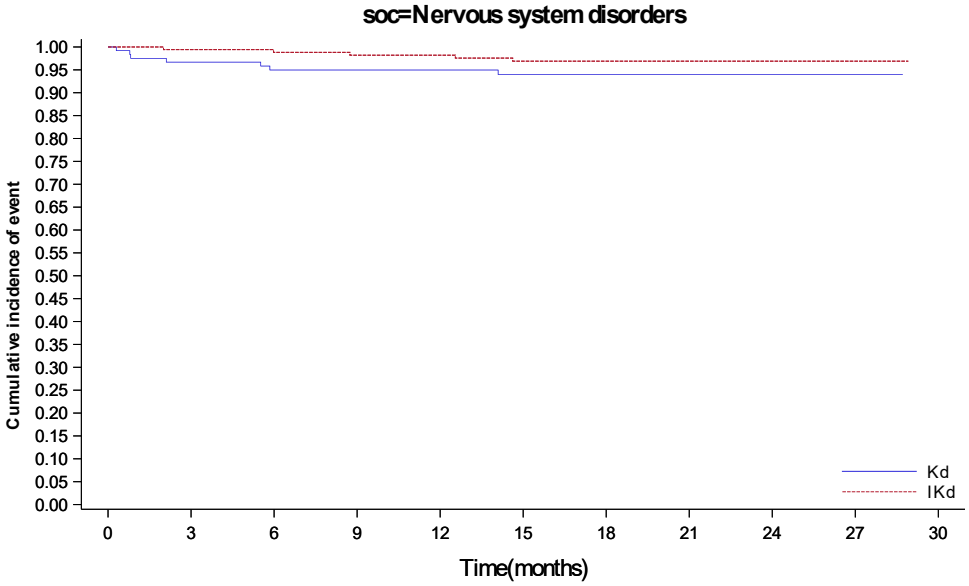
16.2.7.1 Safety endpoints
16.2.7.1.65 Analysis according to SOC/PT
16.2.7.1.65.18 Kaplan-Meier cumulative incidence curve of treatment emergent severe adverse event according to SOC by treatment group - Safety population



Number at Risk

Kd	122	118	110	104	102	97	94	75	27	4	0
IKd	177	169	162	152	149	137	129	115	35	2	0

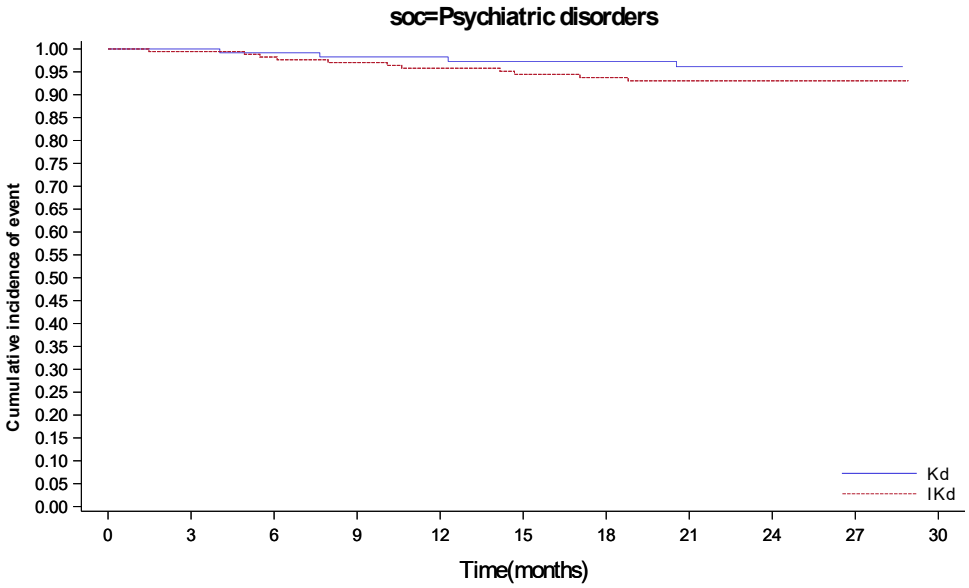
16.2.7.1 Safety endpoints
16.2.7.1.65 Analysis according to SOC/PT
16.2.7.1.65.18 Kaplan-Meier cumulative incidence curve of treatment emergent severe adverse event according to SOC by treatment group - Safety population



Number at Risk

Kd	122	115	110	104	102	96	94	75	28	4	0
IKd	177	172	164	159	156	143	136	121	40	2	0

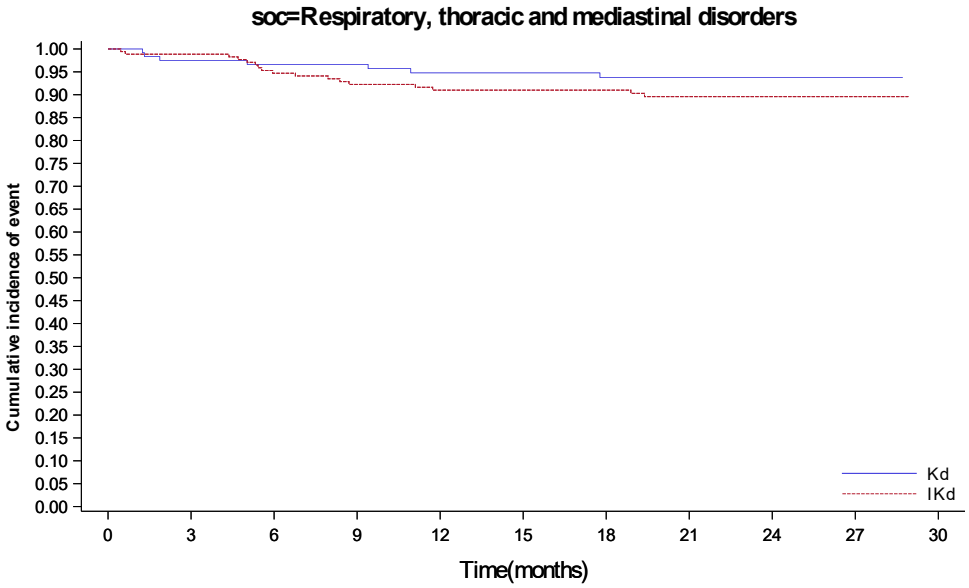
16.2.7.1 Safety endpoints
16.2.7.1.65 Analysis according to SOC/PT
16.2.7.1.65.18 Kaplan-Meier cumulative incidence curve of treatment emergent severe adverse event according to SOC by treatment group - Safety population



Number at Risk

Kd	122	119	113	106	104	97	95	74	26	4	0
IKd	177	172	163	157	152	139	132	117	39	2	0

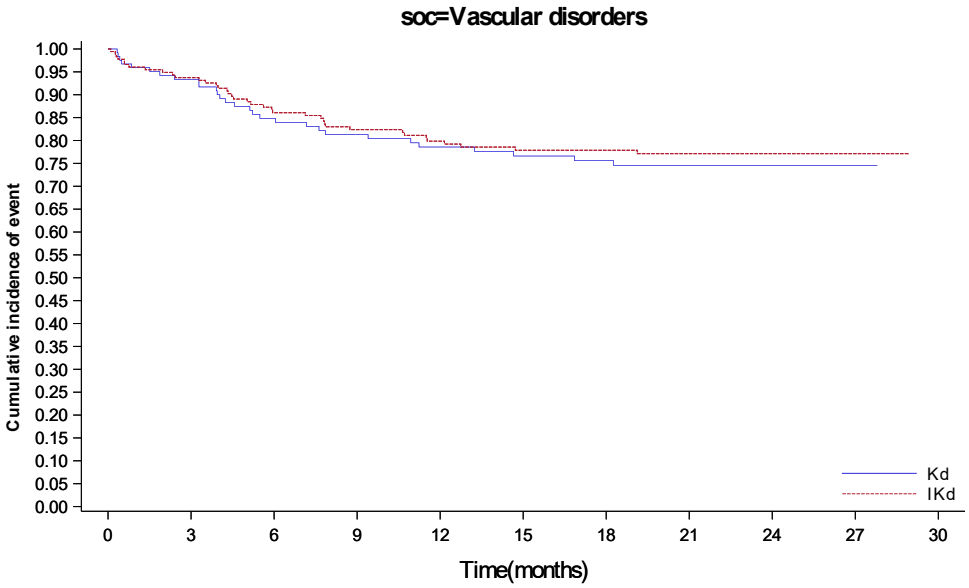
16.2.7.1 Safety endpoints
16.2.7.1.65 Analysis according to SOC/PT
16.2.7.1.65.18 Kaplan-Meier cumulative incidence curve of treatment emergent severe adverse event according to SOC by treatment group - Safety population



Number at Risk

Kd	122	116	110	104	100	94	91	72	28	4	0
IKd	177	171	158	149	144	135	129	112	33	2	0

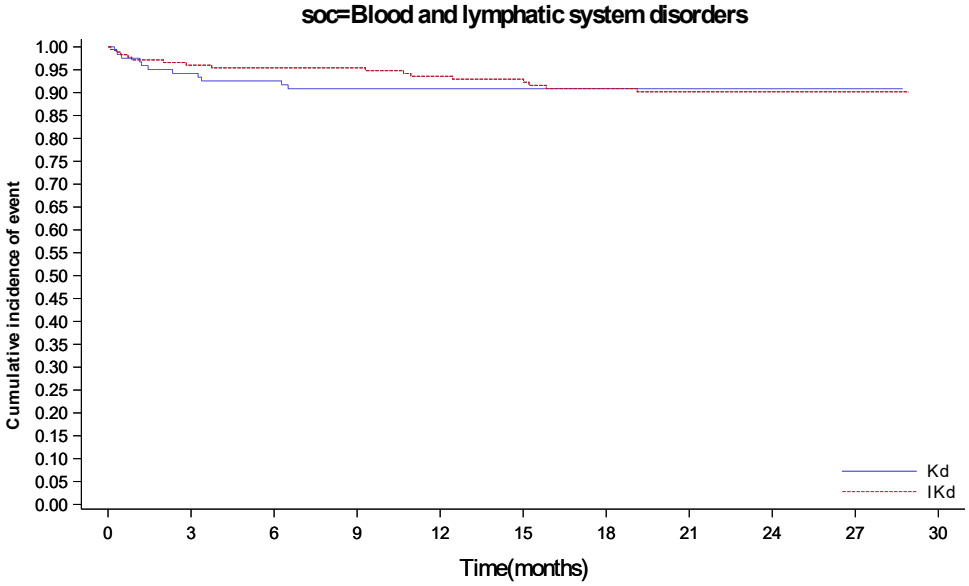
16.2.7.1 Safety endpoints
16.2.7.1.65 Analysis according to SOC/PT
16.2.7.1.65.18 Kaplan-Meier cumulative incidence curve of treatment emergent severe adverse event according to SOC by treatment group - Safety population



Number at Risk

Kd	122	111	97	89	84	76	74	58	23	3	0
IKd	177	162	143	132	125	111	104	95	33	2	0

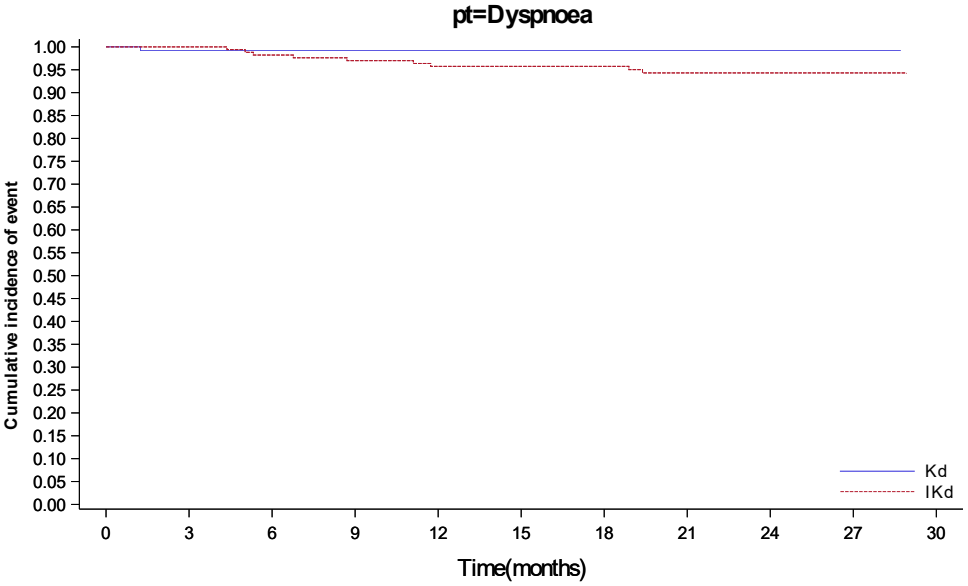
16.2.7.1 Safety endpoints
16.2.7.1.65 Analysis according to SOC/PT
16.2.7.1.65.18 Kaplan-Meier cumulative incidence curve of treatment emergent severe adverse event according to SOC by treatment group - Safety population



Number at Risk

Kd	122	113	107	99	98	93	91	72	28	4	0
IKd	177	166	159	155	149	137	128	113	38	2	0

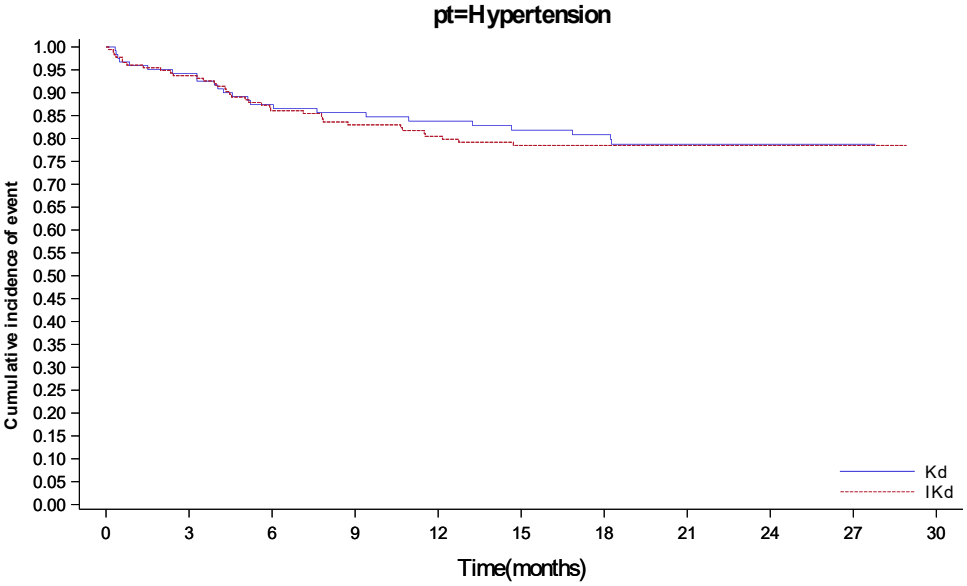
16.2.7.1 Safety endpoints
16.2.7.1.65 Analysis according to SOC/PT
16.2.7.1.65.20 Kaplan-Meier cumulative incidence curve of treatment emergent severe adverse event according to PT by treatment group - Safety population



Number at Risk

Kd	122	118	113	107	105	99	97	77	29	4	0
IKd	177	173	163	156	151	140	134	117	35	2	0

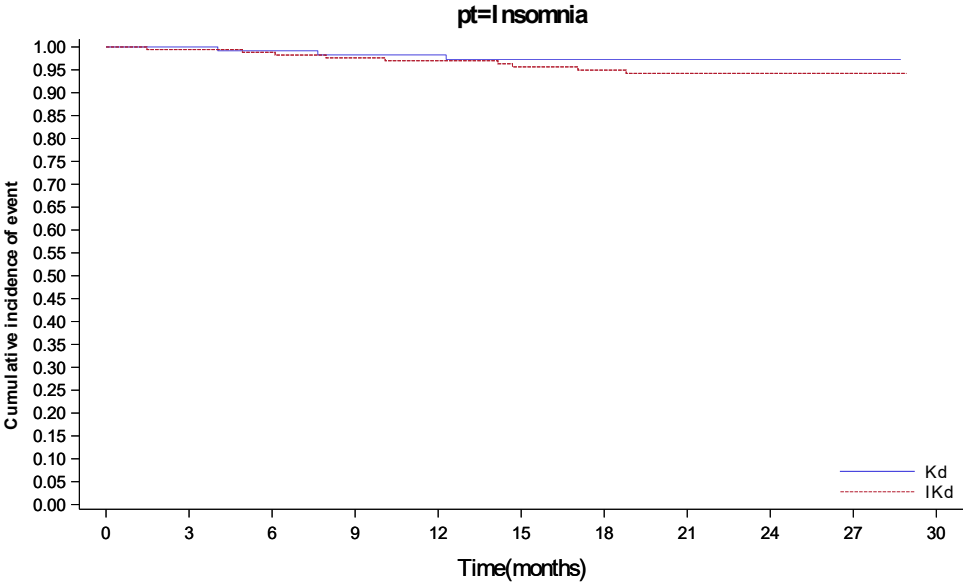
16.2.7.1 Safety endpoints
16.2.7.1.65 Analysis according to SOC/PT
16.2.7.1.65.20 Kaplan-Meier cumulative incidence curve of treatment emergent severe adverse event according to PT by treatment group - Safety population



Number at Risk

Kd	122	112	100	93	89	81	79	62	24	3	0
IKd	177	162	143	133	126	112	105	97	33	2	0

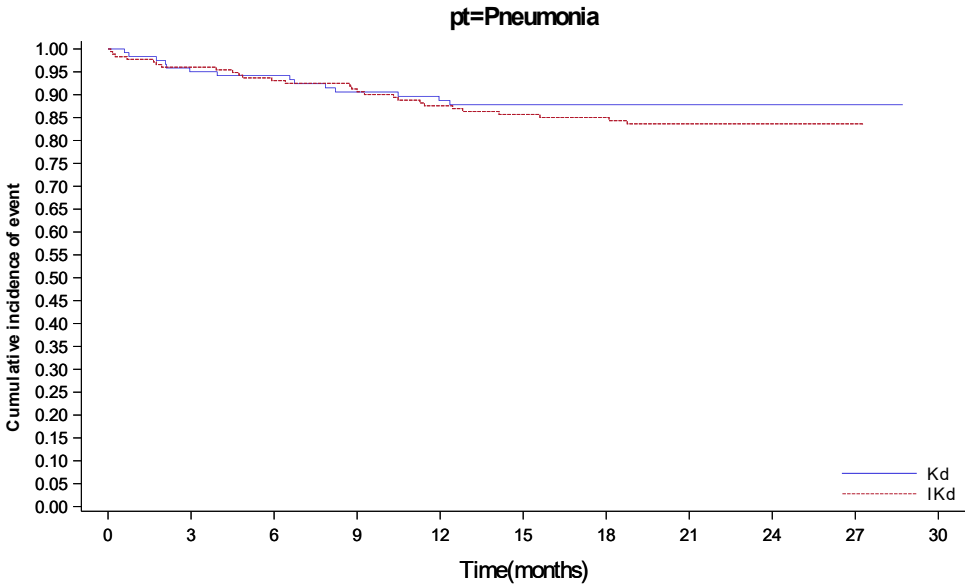
16.2.7.1 Safety endpoints
16.2.7.1.65 Analysis according to SOC/PT
16.2.7.1.65.20 Kaplan-Meier cumulative incidence curve of treatment emergent severe adverse event according to PT by treatment group - Safety population



Number at Risk

Kd	122	119	113	106	104	97	95	75	27	4	0
IKd	177	172	164	157	153	140	133	118	40	2	0

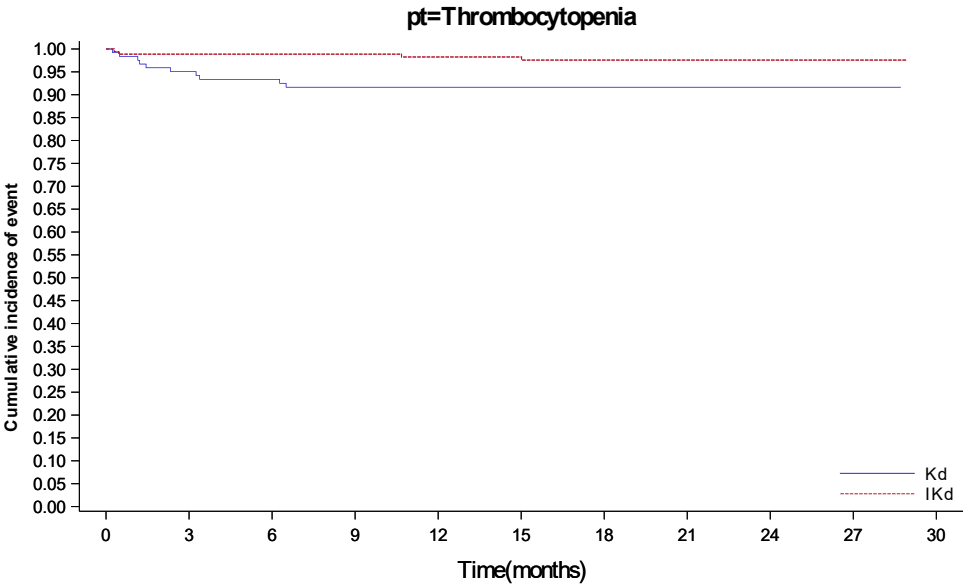
16.2.7.1 Safety endpoints
16.2.7.1.65 Analysis according to SOC/PT
16.2.7.1.65.20 Kaplan-Meier cumulative incidence curve of treatment emergent severe adverse event according to PT by treatment group - Safety population



Number at Risk

Kd	122	113	107	98	95	88	86	68	27	3	0
IKd	177	166	156	149	142	130	123	109	35	1	0

16.2.7.1 Safety endpoints
16.2.7.1.65 Analysis according to SOC/PT
16.2.7.1.65.20 Kaplan-Meier cumulative incidence curve of treatment emergent severe adverse event according to PT by treatment group - Safety population



Number at Risk

Kd	122	114	108	100	99	94	92	73	28	4	0
IKd	177	171	165	160	156	145	137	122	39	2	0

16.2.7.1 Safety endpoints
16.2.7.1.67 Subgroup analysis by age
16.2.7.1.67.1 Treatment emergent adverse event per SOC by treatment group according to age - Safety population

	<65 years		>=65 years		
	Kd (N=65)	**IKd (N=87)**	**Kd (N=57)**	**IKd (N=90)**	**p-value of treatment-by-sub group interaction[c]**
27 Months	0	0	1	0	
30 Months	0	0	0	0	
Injury, poisoning and procedural complications (days)					
Number (%) of events	15 (23.1)	55 (63.2)	17 (29.8)	56 (62.2)	0.3419
Number (%) of patients censored	50 (76.9)	32 (36.8)	40 (70.2)	34 (37.8)	
Kaplan-Meier estimates of event in months					
25% quantile (95% CI)	NC (6.4394 to NC)	0.0986 (0.0657 to 0.1314)	10.8090 (3.5154 to NC)	0.1314 (0.0986 to 0.6571)	
Median (95% CI)	NC (NC to NC)	0.2300 (0.1643 to 10.6119)	NC (22.3409 to NC)	5.7823 (1.6756 to 9.5277)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	<.0001		<.0001	
Hazard ratio (95% CI) vs Kd	-	4.10 (2.31 to 7.27)		3.02 (1.75 to 5.20)	

SOC are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.

16.2.7.1 Safety endpoints
16.2.7.1.67 Subgroup analysis by age
16.2.7.1.67.1 Treatment emergent adverse event per SOC by treatment group according to age - Safety population

	<65 years		>=65 years		
	Kd (N=65)	**IKd (N=87)**	**Kd (N=57)**	**IKd (N=90)**	**p-value of treatment-by-sub group interaction[c]**
P-value	-	<.0001		<.0001	
Hazard ratio inverted (95% CI) vs IKd	0.24 (0.14 to 0.43)		0.33 (0.19 to 0.57)		
Events probability (95% CI)[b]					
3 Months	0.9228 (0.8244 to 0.9671)	0.4598 (0.3529 to 0.5601)	0.8756 (0.7566 to 0.9387)	0.5629 (0.4536 to 0.6585)	
6 Months	0.8907 (0.7842 to 0.9464)	0.4483 (0.3420 to 0.5488)	0.8387 (0.7128 to 0.9127)	0.4800 (0.3723 to 0.5796)	
9 Months	0.8237 (0.7039 to 0.8984)	0.4253 (0.3205 to 0.5260)	0.7823 (0.6483 to 0.8702)	0.4313 (0.3258 to 0.5323)	
12 Months	0.7887 (0.6634 to 0.8717)	0.3908 (0.2888 to 0.4913)	0.7442 (0.6061 to 0.8400)	0.3820 (0.2798 to 0.4833)	
15 Months	0.7703 (0.6424 to 0.8574)	0.3908 (0.2888 to 0.4913)	0.7442 (0.6061 to 0.8400)	0.3693 (0.2681 to 0.4706)	
18 Months	0.7506 (0.6195 to 0.8421)	0.3768 (0.2754 to 0.4778)	0.7235 (0.5831 to 0.8235)	0.3561 (0.2559 to 0.4574)	
21 Months	0.7506 (0.6195 to 0.8421)	0.3629 (0.2623 to 0.4641)	0.7002 (0.5564 to 0.8052)	0.3561 (0.2559 to 0.4574)	

SOC are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.

16.2.7.1 Safety endpoints
16.2.7.1.67 Subgroup analysis by age
16.2.7.1.67.1 Treatment emergent adverse event per SOC by treatment group according to age - Safety population

	<65 years		>=65 years		
	Kd (N=65)	**IKd (N=87)**	**Kd (N=57)**	**IKd (N=90)**	**p-value of treatment-by-sub group interaction[c]**
24 Months	0.7506 (0.6195 to 0.8421)	0.3629 (0.2623 to 0.4641)	0.6564 (0.4935 to 0.7781)	0.3561 (0.2559 to 0.4574)	
27 Months	0.7506 (0.6195 to 0.8421)	0.3629 (0.2623 to 0.4641)	0.6564 (0.4935 to 0.7781)	0.3561 (0.2559 to 0.4574)	
30 Months	0.7506 (0.6195 to 0.8421)	0.3629 (0.2623 to 0.4641)	0.6564 (0.4935 to 0.7781)	0.3561 (0.2559 to 0.4574)	
Number of patients at risk[b]					
3 Months	59	40	49	49	
6 Months	54	39	45	40	
9 Months	47	37	41	35	
12 Months	44	34	38	30	
15 Months	40	30	36	28	
18 Months	38	27	34	26	
21 Months	28	25	27	21	
24 Months	13	8	7	6	
27 Months	1	0	2	1	
30 Months	0	0	0	0	

SOC are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
PGM=DEVOPS/SAR650984/EFC15246/CIR_RWE/REPORT/PGM/ae_km_socpt_subgp_sr_s_t.sas OUT=REPORT/OUTPUT/ae_km_teaesoc_age_s_t_x.rtf (12FEB2021 8:25)

16.2.7.1 Safety endpoints
16.2.7.1.67 Subgroup analysis by age
16.2.7.1.67.1 Treatment emergent adverse event per SOC by treatment group according to age - Safety population

	<65 years		>=65 years		
	Kd (N=65)	**IKd (N=87)**	**Kd (N=57)**	**IKd (N=90)**	**p-value of treatment-by-sub group interaction[c]**
27 Months	0	0	3	1	
30 Months	0	0	0	0	
Skin and subcutaneous tissue disorders (days)					
Number (%) of events	9 (13.8)	21 (24.1)	7 (12.3)	28 (31.1)	0.4831
Number (%) of patients censored	56 (86.2)	66 (75.9)	50 (87.7)	62 (68.9)	
Kaplan-Meier estimates of event in months					
25% quantile (95% CI)	NC (15.1458 to NC)	16.1643 (4.5339 to NC)	NC (10.5133 to NC)	9.0021 (5.7166 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.1340		0.0123	
Hazard ratio (95% CI) vs Kd	-	1.80 (0.82 to 3.93)		2.76 (1.20 to 6.31)	
P-value	-	0.1398		0.0165	
Hazard ratio inverted (95% CI) vs IKd			0.36 (0.16 to 0.83)		

SOC are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
PGM=DEVOPS/SAR650984/EFC15246/CIR_RWE/REPORT/PGM/ae_km_socpt_subgp_sr_s_t.sas OUT=REPORT/OUTPUT/ae_km_teaesoc_age_s_t_x.rtf (12FEB2021 8:25)

16.2.7.1 Safety endpoints
16.2.7.1.67 Subgroup analysis by age
16.2.7.1.67.1 Treatment emergent adverse event per SOC by treatment group according to age - Safety population

	<65 years		>=65 years		
	Kd (N=65)	**IKd (N=87)**	**Kd (N=57)**	**IKd (N=90)**	**p-value of treatment-by-sub group interaction[c]**
Events probability (95% CI)[b]					
3 Months	0.9231 (0.8250 to 0.9672)	0.8966 (0.8106 to 0.9448)	0.9464 (0.8429 to 0.9824)	0.9098 (0.8277 to 0.9538)	
6 Months	0.8756 (0.7665 to 0.9358)	0.8374 (0.7409 to 0.9003)	0.9089 (0.7947 to 0.9611)	0.8264 (0.7285 to 0.8916)	
9 Months	0.8756 (0.7665 to 0.9358)	0.8251 (0.7266 to 0.8907)	0.8896 (0.7703 to 0.9489)	0.7540 (0.6478 to 0.8323)	
12 Months	0.8756 (0.7665 to 0.9358)	0.8005 (0.6986 to 0.8710)	0.8693 (0.7449 to 0.9356)	0.7293 (0.6210 to 0.8113)	
15 Months	0.8756 (0.7665 to 0.9358)	0.7752 (0.6702 to 0.8505)	0.8693 (0.7449 to 0.9356)	0.6893 (0.5774 to 0.7771)	
18 Months	0.8570 (0.7425 to 0.9231)	0.7470 (0.6380 to 0.8275)	0.8693 (0.7449 to 0.9356)	0.6758 (0.5629 to 0.7654)	
21 Months	0.8570 (0.7425 to 0.9231)	0.7470 (0.6380 to 0.8275)	0.8693 (0.7449 to 0.9356)	0.6617 (0.5478 to 0.7532)	
24 Months	0.8570 (0.7425 to 0.9231)	0.7470 (0.6380 to 0.8275)	0.8693 (0.7449 to 0.9356)	0.6617 (0.5478 to 0.7532)	

SOC are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
PGM=DEVOPS/SAR650984/EFC15246/CIR_RWE/REPORT/PGM/ae_km_socpt_subgp_sr_s_t.sas OUT=REPORT/OUTPUT/ae_km_teaesoc_age_s_t_x.rtf (12FEB2021 8:25)

16.2.7.1 Safety endpoints
16.2.7.1.67 Subgroup analysis by age
16.2.7.1.67.1 Treatment emergent adverse event per SOC by treatment group according to age - Safety population

	<65 years		>=65 years		
	Kd (N=65)	**IKd (N=87)**	**Kd (N=57)**	**IKd (N=90)**	**p-value of treatment-by-sub group interaction[c]**
27 Months	0.8570 (0.7425 to 0.9231)	0.7470 (0.6380 to 0.8275)	0.8693 (0.7449 to 0.9356)	0.6617 (0.5478 to 0.7532)	
30 Months	0.8570 (0.7425 to 0.9231)	0.7470 (0.6380 to 0.8275)	0.8693 (0.7449 to 0.9356)	0.6617 (0.5478 to 0.7532)	
Number of patients at risk[b]					
3 Months	59	76	52	80	
6 Months	53	69	48	69	
9 Months	52	67	44	61	
12 Months	51	65	42	57	
15 Months	47	57	40	51	
18 Months	45	51	39	48	
21 Months	35	47	33	39	
24 Months	15	15	9	9	
27 Months	1	0	2	1	
30 Months	0	0	0	0	
Vascular disorders (days)					

SOC are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
PGM=DEVOPS/SAR650984/EFC15246/CIR_RWE/REPORT/PGM/ae_km_socpt_subgp_sr_s_t.sas OUT=REPORT/OUTPUT/ae_km_teaesoc_age_s_t_x.rtf (12FEB2021 8:25)

16.2.7.1 Safety endpoints
16.2.7.1.68 Subgroup analysis by gender
16.2.7.1.68.1 Treatment emergent adverse event per SOC by treatment group according to gender - Safety population

	Male		Female		
	Kd (N=68)	**IKd (N=99)**	**Kd (N=54)**	**IKd (N=78)**	**p-value of treatment-by-sub group interaction[c]**
24 Months	0.7379 (0.6067 to 0.8312)	0.3093 (0.2189 to 0.4039)	0.6678 (0.5002 to 0.7903)	0.4268 (0.3144 to 0.5344)	
27 Months	0.7379 (0.6067 to 0.8312)	0.3093 (0.2189 to 0.4039)	0.6678 (0.5002 to 0.7903)	0.4268 (0.3144 to 0.5344)	
30 Months	0.7379 (0.6067 to 0.8312)	0.3093 (0.2189 to 0.4039)	0.6678 (0.5002 to 0.7903)	0.4268 (0.3144 to 0.5344)	
Number of patients at risk[b]					
3 Months	61	42	47	47	
6 Months	55	36	44	43	
9 Months	50	35	38	37	
12 Months	46	31	36	33	
15 Months	44	28	32	30	
18 Months	41	24	31	29	
21 Months	30	21	25	25	
24 Months	11	8	9	6	
27 Months	1	1	2	0	
30 Months	0	0	0	0	

SOC are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
PGM=DEVOPS/SAR650984/EFC15246/CIR_RWE/REPORT/PGM/ae_km_socpt_subgp_sr_s_t.sas OUT=REPORT/OUTPUT/ae_km_teaesoc_sex_s_t_x.rtf (12FEB2021 8:26)

16.2.7.1 Safety endpoints
16.2.7.1.68 Subgroup analysis by gender
16.2.7.1.68.1 Treatment emergent adverse event per SOC by treatment group according to gender - Safety population

	Male		Female		
	Kd (N=68)	**IKd (N=99)**	**Kd (N=54)**	**IKd (N=78)**	**p-value of treatment-by-sub group interaction[c]**
27 Months	1	1	2	0	
30 Months	0	0	0	0	
Skin and subcutaneous tissue disorders (days)					
Number (%) of events	7 (10.3)	27 (27.3)	9 (16.7)	22 (28.2)	0.4260
Number (%) of patients censored	61 (89.7)	72 (72.7)	45 (83.3)	56 (71.8)	
Kaplan-Meier estimates of event in months					
25% quantile (95% CI)	NC (NC to NC)	14.6201 (4.1068 to NC)	NC (5.0924 to NC)	13.0103 (5.9138 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.0115		0.1368	
Hazard ratio (95% CI) vs Kd	-	2.79 (1.22 to 6.41)		1.79 (0.82 to 3.88)	
P-value	-	0.0155		0.1426	
Hazard ratio inverted (95% CI) vs IKd	0.36 (0.16 to 0.82)				

SOC are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
PGM=DEVOPS/SAR650984/EFC15246/CIR_RWE/REPORT/PGM/ae_km_socpt_subgp_sr_s_t.sas OUT=REPORT/OUTPUT/ae_km_teaesoc_sex_s_t_x.rtf (12FEB2021 8:26)

16.2.7.1 Safety endpoints
16.2.7.1.68 Subgroup analysis by gender
16.2.7.1.68.1 Treatment emergent adverse event per SOC by treatment group according to gender - Safety population

	Male		Female		
	Kd (N=68)	**IKd (N=99)**	**Kd (N=54)**	**IKd (N=78)**	**p-value of treatment-by-sub group interaction[c]**
Events probability (95% CI)[b]					
3 Months	0.9251 (0.8293 to 0.9681)	0.8674 (0.7826 to 0.9208)	0.9444 (0.8376 to 0.9817)	0.9482 (0.8679 to 0.9802)	
6 Months	0.9092 (0.8088 to 0.9582)	0.8246 (0.7329 to 0.8872)	0.8704 (0.7472 to 0.9360)	0.8430 (0.7401 to 0.9077)	
9 Months	0.8920 (0.7864 to 0.9471)	0.7800 (0.6825 to 0.8508)	0.8704 (0.7472 to 0.9360)	0.8026 (0.6940 to 0.8760)	
12 Months	0.8920 (0.7864 to 0.9471)	0.7574 (0.6574 to 0.8319)	0.8514 (0.7248 to 0.9228)	0.7752 (0.6633 to 0.8539)	
15 Months	0.8920 (0.7864 to 0.9471)	0.7330 (0.6302 to 0.8114)	0.8514 (0.7248 to 0.9228)	0.7315 (0.6149 to 0.8180)	
18 Months	0.8920 (0.7864 to 0.9471)	0.7206 (0.6165 to 0.8009)	0.8302 (0.6986 to 0.9079)	0.7011 (0.5815 to 0.7924)	
21 Months	0.8920 (0.7864 to 0.9471)	0.7074 (0.6019 to 0.7898)	0.8302 (0.6986 to 0.9079)	0.7011 (0.5815 to 0.7924)	
24 Months	0.8920 (0.7864 to 0.9471)	0.7074 (0.6019 to 0.7898)	0.8302 (0.6986 to 0.9079)	0.7011 (0.5815 to 0.7924)	

SOC are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.68 Subgroup analysis by gender
16.2.7.1.68.1 Treatment emergent adverse event per SOC by treatment group according to gender - Safety population

	Male		Female		
	Kd (N=68)	**IKd (N=99)**	**Kd (N=54)**	**IKd (N=78)**	**p-value of treatment-by-sub group interaction[c]**
27 Months	0.8920 (0.7864 to 0.9471)	0.7074 (0.6019 to 0.7898)	0.8302 (0.6986 to 0.9079)	0.7011 (0.5815 to 0.7924)	
30 Months	0.8920 (0.7864 to 0.9471)	0.7074 (0.6019 to 0.7898)	0.8302 (0.6986 to 0.9079)	0.7011 (0.5815 to 0.7924)	
Number of patients at risk[b]					
3 Months	60	83	51	73	
6 Months	54	74	47	64	
9 Months	50	69	46	59	
12 Months	49	67	44	55	
15 Months	47	60	40	48	
18 Months	46	55	38	44	
21 Months	35	49	33	37	
24 Months	14	15	10	9	
27 Months	1	1	2	0	
30 Months	0	0	0	0	
Vascular disorders (days)					

SOC are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
PGM=DEVOPS/SAR650984/EFC15246/CIR_RWE/REPORT/PGM/ae_km_socpt_subgp_sr_s_t.sas OUT=REPORT/OUTPUT/ae_km_teaesoc_sex_s_t_x.rtf (12FEB2021 8:26)

16.2.7.1 Safety endpoints
16.2.7.1.69 Subgroup analysis by ethnic origin
16.2.7.1.69.1 Treatment emergent adverse event per SOC by treatment group according to ethnic origin - Safety population

	White		Other		
	Kd (N=83)	**IKd (N=130)**	**Kd (N=27)**	**IKd (N=33)**	**p-value of treatment-by-sub group interaction[c]**
27 Months	0	0	1	0	
30 Months	0	0	0	0	
Injury, poisoning and procedural complications (days)					
Number (%) of events	25 (30.1)	79 (60.8)	5 (18.5)	21 (63.6)	0.2762
Number (%) of patients censored	58 (69.9)	51 (39.2)	22 (81.5)	12 (36.4)	
Kaplan-Meier estimates of event in months					
25% quantile (95% CI)	12.7146 (6.4394 to NC)	0.0986 (0.0657 to 0.1314)	NC (2.1684 to NC)	0.0986 (0.0657 to 0.1314)	
Median (95% CI)	NC (NC to NC)	3.8439 (0.6571 to 10.6119)	NC (NC to NC)	0.9199 (0.1314 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (10.2177 to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	<.0001		0.0003	
Hazard ratio (95% CI) vs Kd	-	2.92 (1.86 to 4.58)		5.02 (1.88 to 13.36)	

SOC are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.69 Subgroup analysis by ethnic origin
16.2.7.1.69.1 Treatment emergent adverse event per SOC by treatment group according to ethnic origin - Safety population

	White		Other		
	Kd (N=83)	**IKd (N=130)**	**Kd (N=27)**	**IKd (N=33)**	**p-value of treatment-by-sub group interaction[c]**
P-value	-	<.0001		0.0012	
Hazard ratio inverted (95% CI) vs IKd	0.34 (0.22 to 0.54)		0.20 (0.07 to 0.53)		
Events probability (95% CI)[b]					
3 Months	0.8908 (0.8006 to 0.9416)	0.5132 (0.4239 to 0.5954)	0.9259 (0.7350 to 0.9809)	0.4848 (0.3083 to 0.6406)	
6 Months	0.8538 (0.7569 to 0.9142)	0.4652 (0.3771 to 0.5485)	0.8873 (0.6899 to 0.9622)	0.4848 (0.3083 to 0.6406)	
9 Months	0.7905 (0.6846 to 0.8642)	0.4328 (0.3459 to 0.5165)	0.8451 (0.6372 to 0.9391)	0.4545 (0.2818 to 0.6121)	
12 Months	0.7516 (0.6416 to 0.8321)	0.4083 (0.3226 to 0.4921)	0.8028 (0.5880 to 0.9132)	0.3939 (0.2306 to 0.5535)	
15 Months	0.7382 (0.6269 to 0.8209)	0.4000 (0.3146 to 0.4837)	0.8028 (0.5880 to 0.9132)	0.3939 (0.2306 to 0.5535)	
18 Months	0.7098 (0.5956 to 0.7971)	0.3909 (0.3059 to 0.4748)	0.8028 (0.5880 to 0.9132)	0.3581 (0.1996 to 0.5197)	
21 Months	0.6944 (0.5785 to 0.7842)	0.3816 (0.2969 to 0.4656)	0.8028 (0.5880 to 0.9132)	0.3581 (0.1996 to 0.5197)	

SOC are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.69 Subgroup analysis by ethnic origin
16.2.7.1.69.1 Treatment emergent adverse event per SOC by treatment group according to ethnic origin - Safety population

	White		Other		
	Kd (N=83)	**IKd (N=130)**	**Kd (N=27)**	**IKd (N=33)**	**p-value of treatment-by-sub group interaction[c]**
24 Months	0.6596 (0.5275 to 0.7629)	0.3816 (0.2969 to 0.4656)	0.8028 (0.5880 to 0.9132)	0.3581 (0.1996 to 0.5197)	
27 Months	0.6596 (0.5275 to 0.7629)	0.3816 (0.2969 to 0.4656)	0.8028 (0.5880 to 0.9132)	0.3581 (0.1996 to 0.5197)	
30 Months	0.6596 (0.5275 to 0.7629)	0.3816 (0.2969 to 0.4656)	0.8028 (0.5880 to 0.9132)	0.3581 (0.1996 to 0.5197)	
Number of patients at risk[b]					
3 Months	73	65	25	16	
6 Months	68	58	23	16	
9 Months	61	53	20	15	
12 Months	56	50	19	12	
15 Months	53	46	16	11	
18 Months	49	42	16	10	
21 Months	34	35	15	10	
24 Months	10	10	7	3	
27 Months	0	0	3	1	
30 Months	0	0	0	0	

SOC are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.69 Subgroup analysis by ethnic origin
16.2.7.1.69.1 Treatment emergent adverse event per SOC by treatment group according to ethnic origin - Safety population

	White		Other		
	Kd (N=83)	**IKd (N=130)**	**Kd (N=27)**	**IKd (N=33)**	**p-value of treatment-by-sub group interaction[c]**
Skin and subcutaneous tissue disorders (days)					
Number (%) of events	12 (14.5)	37 (28.5)	3 (11.1)	8 (24.2)	0.7864
Number (%) of patients censored	71 (85.5)	93 (71.5)	24 (88.9)	25 (75.8)	
Kaplan-Meier estimates of event in months					
25% quantile (95% CI)	NC (15.1458 to NC)	12.4517 (6.2094 to NC)	NC (0.2300 to NC)	15.3758 (0.1314 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.0253		0.1810	
Hazard ratio (95% CI) vs Kd	-	2.07 (1.08 to 3.97)		2.41 (0.64 to 9.08)	
P-value	-	0.0286		0.1950	
Hazard ratio inverted (95% CI) vs IKd	0.48 (0.25 to 0.93)				
Events probability (95% CI)[b]					

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CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.69 Subgroup analysis by ethnic origin
16.2.7.1.69.1 Treatment emergent adverse event per SOC by treatment group according to ethnic origin - Safety population

	White		Other		
	Kd (N=83)	**IKd (N=130)**	**Kd (N=27)**	**IKd (N=33)**	**p-value of treatment-by-sub group interaction[c]**
3 Months	0.9265 (0.8437 to 0.9663)	0.9220 (0.8598 to 0.9572)	0.9259 (0.7350 to 0.9809)	0.8182 (0.6394 to 0.9139)	
6 Months	0.8769 (0.7833 to 0.9318)	0.8327 (0.7549 to 0.8876)	0.9259 (0.7350 to 0.9809)	0.8182 (0.6394 to 0.9139)	
9 Months	0.8638 (0.7675 to 0.9222)	0.7830 (0.6996 to 0.8458)	0.9259 (0.7350 to 0.9809)	0.7855 (0.6016 to 0.8916)	
12 Months	0.8638 (0.7675 to 0.9222)	0.7580 (0.6724 to 0.8242)	0.8873 (0.6899 to 0.9622)	0.7855 (0.6016 to 0.8916)	
15 Months	0.8638 (0.7675 to 0.9222)	0.7232 (0.6346 to 0.7938)	0.8873 (0.6899 to 0.9622)	0.7855 (0.6016 to 0.8916)	
18 Months	0.8494 (0.7497 to 0.9117)	0.7047 (0.6145 to 0.7776)	0.8873 (0.6899 to 0.9622)	0.7441 (0.5496 to 0.8642)	
21 Months	0.8494 (0.7497 to 0.9117)	0.6952 (0.6042 to 0.7692)	0.8873 (0.6899 to 0.9622)	0.7441 (0.5496 to 0.8642)	
24 Months	0.8494 (0.7497 to 0.9117)	0.6952 (0.6042 to 0.7692)	0.8873 (0.6899 to 0.9622)	0.7441 (0.5496 to 0.8642)	
27 Months	0.8494 (0.7497 to 0.9117)	0.6952 (0.6042 to 0.7692)	0.8873 (0.6899 to 0.9622)	0.7441 (0.5496 to 0.8642)	

SOC are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.69 Subgroup analysis by ethnic origin
16.2.7.1.69.1 Treatment emergent adverse event per SOC by treatment group according to ethnic origin - Safety population

	White		Other		
	Kd (N=83)	**IKd (N=130)**	**Kd (N=27)**	**IKd (N=33)**	**p-value of treatment-by-sub group interaction[c]**
30 Months	0.8494 (0.7497 to 0.9117)	0.6952 (0.6042 to 0.7692)	0.8873 (0.6899 to 0.9622)	0.7441 (0.5496 to 0.8642)	
Number of patients at risk[b]					
3 Months	75	117	25	26	
6 Months	69	102	24	25	
9 Months	65	94	24	23	
12 Months	63	91	23	22	
15 Months	60	81	20	19	
18 Months	57	74	20	17	
21 Months	42	62	19	17	
24 Months	13	16	8	6	
27 Months	0	0	3	1	
30 Months	0	0	0	0	
Vascular disorders (days)					
Number (%) of events	42 (50.6)	66 (50.8)	7 (25.9)	13 (39.4)	0.3677
Number (%) of patients censored	41 (49.4)	64 (49.2)	20 (74.1)	20 (60.6)	

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CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.70 Subgroup analysis by geographical region
16.2.7.1.70.1 Treatment emergent adverse event per SOC by treatment group according to geographical region - Safety population

	Europe		America		Asia		Other countries		
	Pd (N=60)	**IPd (N=85)**	**Pd (N=20)**	**IPd (N=23)**	**Pd (N=20)**	**IPd (N=24)**	**Pd (N=22)**	**IPd (N=45)**	**p-value of treatment-by-subgroup interaction[c]**
24 Months	2	1	1	0	1	1	0	2	
27 Months	0	0	0	0	1	0	0	0	
30 Months	0	0	0	0	0	0	0	0	
Injury, poisoning and procedural complications (days)									
Number (%) of events	13 (21.7)	45 (52.9)	9 (45.0)	14 (60.9)	2 (10.0)	15 (62.5)	8 (36.4)	37 (82.2)	0.2352
Number (%) of patients censored	47 (78.3)	40 (47.1)	11 (55.0)	9 (39.1)	18 (90.0)	9 (37.5)	14 (63.6)	8 (17.8)	
Kaplan-Meier estimates of event in months									
25% quantile (95% CI)	22.3409 (5.9466 to NC)	0.0986 (0.0657 to 0.2300)	8.9692 (1.1828 to 16.7228)	0.1314 (0.0657 to 0.6899)	NC (2.1684 to NC)	0.1314 (0.0329 to 0.1643)	7.3922 (0.3943 to NC)	0.0657 (0.0657 to 0.1314)	

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CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.70 Subgroup analysis by geographical region
16.2.7.1.70.1 Treatment emergent adverse event per SOC by treatment group according to geographical region - Safety population

	Europe		America		Asia		Other countries		
	Pd (N=60)	**IPd (N=85)**	**Pd (N=20)**	**IPd (N=23)**	**Pd (N=20)**	**IPd (N=24)**	**Pd (N=22)**	**IPd (N=45)**	**p-value of treatment-by-subgroup interaction[c]**
Median (95% CI)	NC (NC to NC)	9.5277 (2.1355 to NC)	NC (8.8706 to NC)	2.0041 (0.2300 to NC)	NC (NC to NC)	8.7392 (0.1314 to NC)	NC (7.3922 to NC)	0.1643 (0.1314 to 1.5770)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (10.6119 to NC)	NC (NC to NC)	NC (10.2177 to NC)	NC (NC to NC)	5.7823 (1.3142 to NC)	
Comparison vs. Pd									
Log-Rank test p-value[a] vs Kd	-	<.0001		0.1150		0.0006		<.0001	
Hazard ratio (95% CI) vs Kd	-	3.20 (1.73 to 5.95)		1.94 (0.84 to 4.51)		8.71 (1.99 to 38.22)		4.43 (2.04 to 9.62)	
P-value	-	0.0002		0.1216		0.0041		0.0002	
Hazard ratio inverted (95% CI) vs IKd	0.31 (0.17 to 0.58)				0.11 (0.03 to 0.50)		0.23 (0.10 to 0.49)		

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CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.70 Subgroup analysis by geographical region
16.2.7.1.70.1 Treatment emergent adverse event per SOC by treatment group according to geographical region - Safety population

	Europe		America		Asia		Other countries		
	Pd (N=60)	**IPd (N=85)**	**Pd (N=20)**	**IPd (N=23)**	**Pd (N=20)**	**IPd (N=24)**	**Pd (N=22)**	**IPd (N=45)**	**p-value of treatment-by-subgroup interaction[c]**
Events probability (95% CI)[b]									
3 Months	0.9158 (0.8094 to 0.9641)	0.6104 (0.4981 to 0.7050)	0.9000 (0.6560 to 0.9740)	0.4783 (0.2683 to 0.6613)	0.9500 (0.6947 to 0.9928)	0.5417 (0.3271 to 0.7143)	0.8182 (0.5853 to 0.9276)	0.3333 (0.2018 to 0.4704)	
6 Months	0.8625 (0.7435 to 0.9288)	0.5728 (0.4600 to 0.6704)	0.9000 (0.6560 to 0.9740)	0.4783 (0.2683 to 0.6613)	0.8972 (0.6475 to 0.9733)	0.5417 (0.3271 to 0.7143)	0.8182 (0.5853 to 0.9276)	0.2222 (0.1150 to 0.3514)	
9 Months	0.8433 (0.7200 to 0.9154)	0.5219 (0.4094 to 0.6227)	0.7500 (0.4999 to 0.8875)	0.4783 (0.2683 to 0.6613)	0.8972 (0.6475 to 0.9733)	0.5000 (0.2910 to 0.6776)	0.6818 (0.4462 to 0.8338)	0.2000 (0.0989 to 0.3265)	
12 Months	0.8241 (0.6971 to 0.9015)	0.4837 (0.3724 to 0.5863)	0.6500 (0.4030 to 0.8153)	0.4348 (0.2329 to 0.6212)	0.8972 (0.6475 to 0.9733)	0.4167 (0.2224 to 0.6006)	0.6331 (0.3981 to 0.7971)	0.1750 (0.0807 to 0.2991)	

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CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.70 Subgroup analysis by geographical region
16.2.7.1.70.1 Treatment emergent adverse event per SOC by treatment group according to geographical region - Safety population

	Europe		America		Asia		Other countries		
	Pd (N=60)	IPd (N=85)	Pd (N=20)	IPd (N=23)	Pd (N=20)	IPd (N=24)	Pd (N=22)	IPd (N=45)	p-value of treatment-by-subgroup interaction[c]
15 Months	0.8241 (0.6971 to 0.9015)	0.4706 (0.3597 to 0.5737)	0.6000 (0.3573 to 0.7760)	0.4348 (0.2329 to 0.6212)	0.8972 (0.6475 to 0.9733)	0.4167 (0.2224 to 0.6006)	0.6331 (0.3981 to 0.7971)	0.1750 (0.0807 to 0.2991)	
18 Months	0.8030 (0.6714 to 0.8862)	0.4706 (0.3597 to 0.5737)	0.5455 (0.3073 to 0.7324)	0.3865 (0.1934 to 0.5769)	0.8972 (0.6475 to 0.9733)	0.3646 (0.1782 to 0.5542)	0.6331 (0.3981 to 0.7971)	0.1750 (0.0807 to 0.2991)	
21 Months	0.7807 (0.6444 to 0.8698)	0.4559 (0.3452 to 0.5598)	0.5455 (0.3073 to 0.7324)	0.3865 (0.1934 to 0.5769)	0.8972 (0.6475 to 0.9733)	0.3646 (0.1782 to 0.5542)	0.6331 (0.3981 to 0.7971)	0.1750 (0.0807 to 0.2991)	
24 Months	0.7319 (0.5632 to 0.8440)	0.4559 (0.3452 to 0.5598)	0.5455 (0.3073 to 0.7324)	0.3865 (0.1934 to 0.5769)	0.8972 (0.6475 to 0.9733)	0.3646 (0.1782 to 0.5542)	0.6331 (0.3981 to 0.7971)	0.1750 (0.0807 to 0.2991)	
27 Months	0.7319 (0.5632 to 0.8440)	0.4559 (0.3452 to 0.5598)	0.5455 (0.3073 to 0.7324)	0.3865 (0.1934 to 0.5769)	0.8972 (0.6475 to 0.9733)	0.3646 (0.1782 to 0.5542)	0.6331 (0.3981 to 0.7971)	0.1750 (0.0807 to 0.2991)	

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CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.70 Subgroup analysis by geographical region
16.2.7.1.70.1 Treatment emergent adverse event per SOC by treatment group according to geographical region - Safety population

	Europe		America		Asia		Other countries		
	Pd (N=60)	**IPd (N=85)**	**Pd (N=20)**	**IPd (N=23)**	**Pd (N=20)**	**IPd (N=24)**	**Pd (N=22)**	**IPd (N=45)**	**p-value of treatment-by-subgroup interaction[c]**
30 Months	0.7319 (0.5632 to 0.8440)	0.4559 (0.3452 to 0.5598)	0.5455 (0.3073 to 0.7324)	0.3865 (0.1934 to 0.5769)	0.8972 (0.6475 to 0.9733)	0.3646 (0.1782 to 0.5542)	0.6331 (0.3981 to 0.7971)	0.1750 (0.0807 to 0.2991)	
Number of patients at risk[b]									
3 Months	53	50	18	11	19	13	18	15	
6 Months	46	45	18	11	17	13	18	10	
9 Months	44	41	15	11	15	12	14	8	
12 Months	41	38	13	10	15	9	13	7	
15 Months	39	34	12	9	12	8	13	7	
18 Months	38	32	9	8	12	7	13	6	
21 Months	28	27	6	7	11	7	10	5	
24 Months	11	9	1	1	6	3	2	1	
27 Months	0	0	0	0	3	1	0	0	
30 Months	0	0	0	0	0	0	0	0	

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CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
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16.2.7.1 Safety endpoints
16.2.7.1.70 Subgroup analysis by geographical region
16.2.7.1.70.1 Treatment emergent adverse event per SOC by treatment group according to geographical region - Safety population

	Europe		America		Asia		Other countries		
	Pd (N=60)	IPd (N=85)	Pd (N=20)	IPd (N=23)	Pd (N=20)	IPd (N=24)	Pd (N=22)	IPd (N=45)	p-value of treatment-by-subgroup interaction[c]
24 Months	8	12	1	0	4	5	3	2	
27 Months	0	0	0	0	2	1	1	0	
30 Months	0	0	0	0	0	0	0	0	
Skin and subcutaneous tissue disorders (days)									
Number (%) of events	5 (8.3)	20 (23.5)	4 (20.0)	12 (52.2)	2 (10.0)	5 (20.8)	5 (22.7)	12 (26.7)	0.5526
Number (%) of patients censored	55 (91.7)	65 (76.5)	16 (80.0)	11 (47.8)	18 (90.0)	19 (79.2)	17 (77.3)	33 (73.3)	
Kaplan-Meier estimates of event in months									
25% quantile (95% CI)	NC (NC to NC)	18.5298 (7.8850 to NC)	NC (2.2012 to NC)	4.1068 (0.1314 to 7.3922)	NC (0.1971 to NC)	NC (0.0329 to NC)	NC (0.5585 to NC)	12.4517 (1.8727 to NC)	

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CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.70 Subgroup analysis by geographical region
16.2.7.1.70.1 Treatment emergent adverse event per SOC by treatment group according to geographical region - Safety population

	Europe		America		Asia		Other countries		
	Pd (N=60)	**IPd (N=85)**	**Pd (N=20)**	**IPd (N=23)**	**Pd (N=20)**	**IPd (N=24)**	**Pd (N=22)**	**IPd (N=45)**	**p-value of treatment-by-subgroup interaction[c]**
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	13.0103 (4.1068 to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (13.0103 to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd									
Log-Rank test p-value[a] vs Kd	-	0.0259		0.0256		0.3536		0.7368	
Hazard ratio (95% CI) vs Kd	-	2.90 (1.09 to 7.72)		3.37 (1.09 to 10.48)		2.13 (0.41 to 11.01)		1.20 (0.42 to 3.39)	
P-value	-	0.0335		0.0356		0.3650		0.7371	
Hazard ratio inverted (95% CI) vs IKd	0.35 (0.13 to 0.92)		0.30 (0.10 to 0.92)						

SOC are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.70 Subgroup analysis by geographical region
16.2.7.1.70.1 Treatment emergent adverse event per SOC by treatment group according to geographical region - Safety population

	Europe		America		Asia		Other countries		
	Pd (N=60)	**IPd (N=85)**	**Pd (N=20)**	**IPd (N=23)**	**Pd (N=20)**	**IPd (N=24)**	**Pd (N=22)**	**IPd (N=45)**	**p-value of treatment-by-subgroup interaction[c]**
Events probability (95% CI)[b]									
3 Months	0.9664 (0.8722 to 0.9915)	0.9759 (0.9071 to 0.9939)	0.9500 (0.6947 to 0.9928)	0.8238 (0.5958 to 0.9300)	0.9000 (0.6560 to 0.9740)	0.8333 (0.6148 to 0.9339)	0.8636 (0.6344 to 0.9539)	0.8444 (0.7012 to 0.9226)	
6 Months	0.9309 (0.8261 to 0.9735)	0.8749 (0.7797 to 0.9307)	0.8500 (0.6038 to 0.9490)	0.6865 (0.4520 to 0.8368)	0.9000 (0.6560 to 0.9740)	0.8333 (0.6148 to 0.9339)	0.8182 (0.5853 to 0.9276)	0.8216 (0.6748 to 0.9065)	
9 Months	0.9309 (0.8261 to 0.9735)	0.8363 (0.7346 to 0.9015)	0.8500 (0.6038 to 0.9490)	0.5492 (0.3242 to 0.7270)	0.9000 (0.6560 to 0.9740)	0.8333 (0.6148 to 0.9339)	0.7701 (0.5325 to 0.8973)	0.7975 (0.6466 to 0.8892)	
12 Months	0.9309 (0.8261 to 0.9735)	0.8103 (0.7050 to 0.8811)	0.7969 (0.5448 to 0.9186)	0.5034 (0.2848 to 0.6873)	0.9000 (0.6560 to 0.9740)	0.8333 (0.6148 to 0.9339)	0.7701 (0.5325 to 0.8973)	0.7733 (0.6191 to 0.8712)	
15 Months	0.9309 (0.8261 to 0.9735)	0.7829 (0.6738 to 0.8592)	0.7969 (0.5448 to 0.9186)	0.4531 (0.2413 to 0.6435)	0.9000 (0.6560 to 0.9740)	0.8333 (0.6148 to 0.9339)	0.7701 (0.5325 to 0.8973)	0.7233 (0.5635 to 0.8328)	

SOC are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.70 Subgroup analysis by geographical region
16.2.7.1.70.1 Treatment emergent adverse event per SOC by treatment group according to geographical region - Safety population

	Europe		America		Asia		Other countries		
	Pd (N=60)	IPd (N=85)	Pd (N=20)	IPd (N=23)	Pd (N=20)	IPd (N=24)	Pd (N=22)	IPd (N=45)	p-value of treatment-by-subgroup interaction[c]
18 Months	0.9097 (0.7957 to 0.9616)	0.7539 (0.6410 to 0.8357)	0.7969 (0.5448 to 0.9186)	0.4531 (0.2413 to 0.6435)	0.9000 (0.6560 to 0.9740)	0.7738 (0.5326 to 0.9009)	0.7701 (0.5325 to 0.8973)	0.7233 (0.5635 to 0.8328)	
21 Months	0.9097 (0.7957 to 0.9616)	0.7394 (0.6249 to 0.8237)	0.7969 (0.5448 to 0.9186)	0.4531 (0.2413 to 0.6435)	0.9000 (0.6560 to 0.9740)	0.7738 (0.5326 to 0.9009)	0.7701 (0.5325 to 0.8973)	0.7233 (0.5635 to 0.8328)	
24 Months	0.9097 (0.7957 to 0.9616)	0.7394 (0.6249 to 0.8237)	0.7969 (0.5448 to 0.9186)	0.4531 (0.2413 to 0.6435)	0.9000 (0.6560 to 0.9740)	0.7738 (0.5326 to 0.9009)	0.7701 (0.5325 to 0.8973)	0.7233 (0.5635 to 0.8328)	
27 Months	0.9097 (0.7957 to 0.9616)	0.7394 (0.6249 to 0.8237)	0.7969 (0.5448 to 0.9186)	0.4531 (0.2413 to 0.6435)	0.9000 (0.6560 to 0.9740)	0.7738 (0.5326 to 0.9009)	0.7701 (0.5325 to 0.8973)	0.7233 (0.5635 to 0.8328)	
30 Months	0.9097 (0.7957 to 0.9616)	0.7394 (0.6249 to 0.8237)	0.7969 (0.5448 to 0.9186)	0.4531 (0.2413 to 0.6435)	0.9000 (0.6560 to 0.9740)	0.7738 (0.5326 to 0.9009)	0.7701 (0.5325 to 0.8973)	0.7233 (0.5635 to 0.8328)	

SOC are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.70 Subgroup analysis by geographical region
16.2.7.1.70.1 Treatment emergent adverse event per SOC by treatment group according to geographical region - Safety population

	Europe		America		Asia		Other countries		
	Pd (N=60)	IPd (N=85)	Pd (N=20)	IPd (N=23)	Pd (N=20)	IPd (N=24)	Pd (N=22)	IPd (N=45)	p-value of treatment-by-subgroup interaction[c]
Number of patients at risk[b]									
3 Months	55	80	19	18	18	20	19	38	
6 Months	49	68	17	15	17	19	18	36	
9 Months	48	65	16	12	17	18	15	33	
12 Months	46	62	15	11	17	17	15	32	
15 Months	44	57	14	9	14	14	15	28	
18 Months	43	52	12	8	14	12	15	27	
21 Months	35	44	8	7	13	12	12	23	
24 Months	12	12	2	0	7	6	3	6	
27 Months	0	0	0	0	3	1	0	0	
30 Months	0	0	0	0	0	0	0	0	
Vascular disorders (days)									
Number (%) of events	21 (35.0)	38 (44.7)	17 (85.0)	11 (47.8)	4 (20.0)	9 (37.5)	12 (54.5)	24 (53.3)	0.0333

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CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.71 Subgroup analysis by regulatory region
16.2.7.1.71.1 Treatment emergent adverse event per SOC by treatment group according to regulatory region - Safety population

	Western countries		Other countries		
	Kd (N=55)	**IKd (N=97)**	**Kd (N=67)**	**IKd (N=80)**	**p-value of treatment-by-sub group interaction[c]**
27 Months	0	0	1	0	
30 Months	0	0	0	0	
Injury, poisoning and procedural complications (days)					
Number (%) of events	17 (30.9)	68 (70.1)	15 (22.4)	43 (53.8)	0.9003
Number (%) of patients censored	38 (69.1)	29 (29.9)	52 (77.6)	37 (46.3)	
Kaplan-Meier estimates of event in months					
25% quantile (95% CI)	10.3819 (1.7741 to NC)	0.0986 (0.0657 to 0.1314)	NC (7.2936 to NC)	0.1314 (0.0657 to 0.1643)	
Median (95% CI)	NC (22.3409 to NC)	1.3470 (0.1971 to 5.4867)	NC (NC to NC)	10.2177 (0.9199 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (9.5277 to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	<.0001		<.0001	
Hazard ratio (95% CI) vs Kd	-	3.53 (2.07 to 6.03)		3.29 (1.82 to 5.93)	

SOC are presented if at least 10 events in a arm
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CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.71 Subgroup analysis by regulatory region
16.2.7.1.71.1 Treatment emergent adverse event per SOC by treatment group according to regulatory region - Safety population

	Western countries		Other countries		
	Kd (N=55)	**IKd (N=97)**	**Kd (N=67)**	**IKd (N=80)**	**p-value of treatment-by-sub group interaction[c]**
P-value	-	<.0001		<.0001	
Hazard ratio inverted (95% CI) vs IKd	0.28 (0.17 to 0.48)		0.30 (0.17 to 0.55)		
Events probability (95% CI)[b]					
3 Months	0.8716 (0.7494 to 0.9367)	0.4518 (0.3507 to 0.5475)	0.9254 (0.8300 to 0.9682)	0.5867 (0.4709 to 0.6856)	
6 Months	0.8527 (0.7268 to 0.9235)	0.3774 (0.2812 to 0.4732)	0.8796 (0.7735 to 0.9379)	0.5737 (0.4578 to 0.6736)	
9 Months	0.7512 (0.6096 to 0.8476)	0.3559 (0.2614 to 0.4513)	0.8487 (0.7370 to 0.9156)	0.5209 (0.4056 to 0.6241)	
12 Months	0.7106 (0.5656 to 0.8147)	0.3127 (0.2226 to 0.4068)	0.8154 (0.6975 to 0.8909)	0.4808 (0.3668 to 0.5859)	
15 Months	0.7106 (0.5656 to 0.8147)	0.3012 (0.2122 to 0.3949)	0.7977 (0.6766 to 0.8774)	0.4808 (0.3668 to 0.5859)	
18 Months	0.7106 (0.5656 to 0.8147)	0.3012 (0.2122 to 0.3949)	0.7597 (0.6319 to 0.8483)	0.4508 (0.3374 to 0.5575)	
21 Months	0.6884 (0.5414 to 0.7967)	0.2881 (0.2002 to 0.3818)	0.7597 (0.6319 to 0.8483)	0.4508 (0.3374 to 0.5575)	

SOC are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.71 Subgroup analysis by regulatory region
16.2.7.1.71.1 Treatment emergent adverse event per SOC by treatment group according to regulatory region - Safety population

	Western countries		Other countries		
	Kd (N=55)	**IKd (N=97)**	**Kd (N=67)**	**IKd (N=80)**	**p-value of treatment-by-sub group interaction[c]**
24 Months	0.6479 (0.4863 to 0.7700)	0.2881 (0.2002 to 0.3818)	0.7597 (0.6319 to 0.8483)	0.4508 (0.3374 to 0.5575)	
27 Months	0.6479 (0.4863 to 0.7700)	0.2881 (0.2002 to 0.3818)	0.7597 (0.6319 to 0.8483)	0.4508 (0.3374 to 0.5575)	
30 Months	0.6479 (0.4863 to 0.7700)	0.2881 (0.2002 to 0.3818)	0.7597 (0.6319 to 0.8483)	0.4508 (0.3374 to 0.5575)	
Number of patients at risk[b]					
3 Months	46	43	62	46	
6 Months	42	35	57	44	
9 Months	37	33	51	39	
12 Months	35	29	47	35	
15 Months	33	25	43	33	
18 Months	33	23	39	30	
21 Months	25	19	30	27	
24 Months	8	6	12	8	
27 Months	0	0	3	1	
30 Months	0	0	0	0	

SOC are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.71 Subgroup analysis by regulatory region
16.2.7.1.71.1 Treatment emergent adverse event per SOC by treatment group according to regulatory region - Safety population

	Western countries		Other countries		
	Kd (N=55)	**IKd (N=97)**	**Kd (N=67)**	**IKd (N=80)**	**p-value of treatment-by-sub group interaction[c]**
Skin and subcutaneous tissue disorders (days)					
Number (%) of events	9 (16.4)	28 (28.9)	7 (10.4)	21 (26.3)	0.4703
Number (%) of patients censored	46 (83.6)	69 (71.1)	60 (89.6)	59 (73.8)	
Kaplan-Meier estimates of event in months					
25% quantile (95% CI)	NC (3.8111 to NC)	10.8090 (4.8296 to NC)	NC (NC to NC)	16.1643 (6.2094 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.1336		0.0159	
Hazard ratio (95% CI) vs Kd	-	1.76 (0.83 to 3.74)		2.74 (1.17 to 6.46)	
P-value	-	0.1388		0.0208	
Hazard ratio inverted (95% CI) vs IKd			0.36 (0.15 to 0.86)		
Events probability (95% CI)[b]					

SOC are presented if at least 10 events in a arm
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CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.71 Subgroup analysis by regulatory region
16.2.7.1.71.1 Treatment emergent adverse event per SOC by treatment group according to regulatory region - Safety population

	Western countries		Other countries		
	Kd (N=55)	**IKd (N=97)**	**Kd (N=67)**	**IKd (N=80)**	**p-value of treatment-by-sub group interaction[c]**
3 Months	0.9070 (0.7908 to 0.9602)	0.8856 (0.8029 to 0.9349)	0.9552 (0.8676 to 0.9853)	0.9245 (0.8396 to 0.9654)	
6 Months	0.8482 (0.7191 to 0.9211)	0.8096 (0.7148 to 0.8756)	0.9247 (0.8284 to 0.9679)	0.8594 (0.7604 to 0.9196)	
9 Months	0.8482 (0.7191 to 0.9211)	0.7653 (0.6655 to 0.8388)	0.9090 (0.8085 to 0.9581)	0.8193 (0.7138 to 0.8888)	
12 Months	0.8270 (0.6934 to 0.9062)	0.7318 (0.6292 to 0.8103)	0.9090 (0.8085 to 0.9581)	0.8054 (0.6979 to 0.8779)	
15 Months	0.8270 (0.6934 to 0.9062)	0.6958 (0.5901 to 0.7793)	0.9090 (0.8085 to 0.9581)	0.7769 (0.6654 to 0.8552)	
18 Months	0.8270 (0.6934 to 0.9062)	0.6958 (0.5901 to 0.7793)	0.8908 (0.7839 to 0.9466)	0.7296 (0.6116 to 0.8170)	
21 Months	0.8270 (0.6934 to 0.9062)	0.6958 (0.5901 to 0.7793)	0.8908 (0.7839 to 0.9466)	0.7131 (0.5930 to 0.8034)	
24 Months	0.8270 (0.6934 to 0.9062)	0.6958 (0.5901 to 0.7793)	0.8908 (0.7839 to 0.9466)	0.7131 (0.5930 to 0.8034)	
27 Months	0.8270 (0.6934 to 0.9062)	0.6958 (0.5901 to 0.7793)	0.8908 (0.7839 to 0.9466)	0.7131 (0.5930 to 0.8034)	

SOC are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.71 Subgroup analysis by regulatory region
16.2.7.1.71.1 Treatment emergent adverse event per SOC by treatment group according to regulatory region - Safety population

	Western countries		Other countries		
	Kd (N=55)	**IKd (N=97)**	**Kd (N=67)**	**IKd (N=80)**	**p-value of treatment-by-sub group interaction[c]**
30 Months	0.8270 (0.6934 to 0.9062)	0.6958 (0.5901 to 0.7793)	0.8908 (0.7839 to 0.9466)	0.7131 (0.5930 to 0.8034)	
Number of patients at risk[b]					
3 Months	47	84	64	72	
6 Months	41	73	60	65	
9 Months	40	69	56	59	
12 Months	39	65	54	57	
15 Months	37	58	50	50	
18 Months	37	55	47	44	
21 Months	31	47	37	39	
24 Months	8	13	16	11	
27 Months	0	0	3	1	
30 Months	0	0	0	0	
Vascular disorders (days)					
Number (%) of events	22 (40.0)	40 (41.2)	32 (47.8)	42 (52.5)	0.6944
Number (%) of patients censored	33 (60.0)	57 (58.8)	35 (52.2)	38 (47.5)	

SOC are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.72 Subgroup analysis by baseline ECOG PS
16.2.7.1.72.1 Treatment emergent adverse event per SOC by treatment group according to baseline ECOG PS - Safety population

	0 or 1		>1		
	Kd (N=117)	**IKd (N=167)**	**Kd (N=5)**	**IKd (N=10)**	**p-value of treatment-by-sub group interaction[c]**
27 Months	1	0	0	0	
30 Months	0	0	0	0	
Injury, poisoning and procedural complications (days)					
Number (%) of events	30 (25.6)	102 (61.1)	2 (40.0)	9 (90.0)	0.8016
Number (%) of patients censored	87 (74.4)	65 (38.9)	3 (60.0)	1 (10.0)	
Kaplan-Meier estimates of event in months					
25% quantile (95% CI)	16.7228 (8.6078 to NC)	0.0986 (0.0657 to 0.1314)	2.6612 (1.1828 to NC)	0.0657 (0.0329 to 0.2957)	
Median (95% CI)	NC (NC to NC)	5.4867 (0.6899 to 10.2177)	NC (1.1828 to NC)	0.2136 (0.0329 to 5.0595)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (1.1828 to NC)	5.0595 (0.1314 to 17.2485)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	<.0001		0.0384	

SOC are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
PGM=DEVOPS/SAR650984/EFC15246/CIR_RWE/REPORT/PGM/ae_km_socpt_subgp_sr_s_t.sas OUT=REPORT/OUTPUT/ae_km_teaesoc_ecog_s_t_x.rtf (12FEB2021 8:25)

16.2.7.1 Safety endpoints
16.2.7.1.72 Subgroup analysis by baseline ECOG PS
16.2.7.1.72.1 Treatment emergent adverse event per SOC by treatment group according to baseline ECOG PS - Safety population

	0 or 1		>1		
	Kd (N=117)	**IKd (N=167)**	**Kd (N=5)**	**IKd (N=10)**	**p-value of treatment-by-sub group interaction[c]**
Hazard ratio (95% CI) vs Kd	-	3.45 (2.30 to 5.20)		4.54 (0.96 to 21.53)	
P-value	-	<.0001		0.0568	
Hazard ratio inverted (95% CI) vs IKd	0.29 (0.19 to 0.44)				
Events probability (95% CI)[b]					
3 Months	0.9141 (0.8462 to 0.9528)	0.5263 (0.4478 to 0.5988)	0.6000 (0.1257 to 0.8818)	0.2667 (0.0476 to 0.5634)	
6 Months	0.8785 (0.8034 to 0.9262)	0.4833 (0.4054 to 0.5567)	0.6000 (0.1257 to 0.8818)	0.1333 (0.0078 to 0.4332)	
9 Months	0.8141 (0.7290 to 0.8747)	0.4458 (0.3689 to 0.5197)	0.6000 (0.1257 to 0.8818)	0.1333 (0.0078 to 0.4332)	
12 Months	0.7762 (0.6867 to 0.8430)	0.4018 (0.3266 to 0.4757)	0.6000 (0.1257 to 0.8818)	0.1333 (0.0078 to 0.4332)	
15 Months	0.7664 (0.6758 to 0.8347)	0.3952 (0.3203 to 0.4691)	0.6000 (0.1257 to 0.8818)	0.1333 (0.0078 to 0.4332)	
18 Months	0.7457 (0.6527 to 0.8172)	0.3880 (0.3133 to 0.4620)	0.6000 (0.1257 to 0.8818)	0.1333 (0.0078 to 0.4332)	
21 Months	0.7347 (0.6404 to 0.8079)	0.3807 (0.3062 to 0.4548)	0.6000 (0.1257 to 0.8818)	0.1333 (0.0078 to 0.4332)	

SOC are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.72 Subgroup analysis by baseline ECOG PS
16.2.7.1.72.1 Treatment emergent adverse event per SOC by treatment group according to baseline ECOG PS - Safety population

	0 or 1		>1		
	Kd (N=117)	**IKd (N=167)**	**Kd (N=5)**	**IKd (N=10)**	**p-value of treatment-by-sub group interaction[c]**
24 Months	0.7143 (0.6128 to 0.7936)	0.3807 (0.3062 to 0.4548)	0.6000 (0.1257 to 0.8818)	0.1333 (0.0078 to 0.4332)	
27 Months	0.7143 (0.6128 to 0.7936)	0.3807 (0.3062 to 0.4548)	0.6000 (0.1257 to 0.8818)	0.1333 (0.0078 to 0.4332)	
30 Months	0.7143 (0.6128 to 0.7936)	0.3807 (0.3062 to 0.4548)	0.6000 (0.1257 to 0.8818)	0.1333 (0.0078 to 0.4332)	
Number of patients at risk[b]					
3 Months	105	87	3	2	
6 Months	97	78	2	1	
9 Months	86	71	2	1	
12 Months	80	63	2	1	
15 Months	75	57	1	1	
18 Months	71	53	1	0	
21 Months	54	46	1	0	
24 Months	19	14	1	0	
27 Months	3	1	0	0	
30 Months	0	0	0	0	

SOC are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.72 Subgroup analysis by baseline ECOG PS
16.2.7.1.72.1 Treatment emergent adverse event per SOC by treatment group according to baseline ECOG PS - Safety population

	0 or 1		>1		
	Kd (N=117)	**IKd (N=167)**	**Kd (N=5)**	**IKd (N=10)**	**p-value of treatment-by-sub group interaction[c]**
27 Months	3	1	0	0	
30 Months	0	0	0	0	
Skin and subcutaneous tissue disorders (days)					
Number (%) of events	16 (13.7)	47 (28.1)	0 (0.0)	2 (20.0)	0.9850
Number (%) of patients censored	101 (86.3)	120 (71.9)	5 (100.0)	8 (80.0)	
Kaplan-Meier estimates of event in months					
25% quantile (95% CI)	NC (NC to NC)	14.4887 (6.7680 to NC)	NC (NC to NC)	NC (2.5298 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (2.5298 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.0060		0.3043	
Hazard ratio (95% CI) vs Kd	-	2.17 (1.23 to 3.83)		NC	
P-value	-	0.0074		0.9979	
Hazard ratio inverted (95% CI) vs IKd	0.46 (0.26 to 0.81)				

SOC are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.72 Subgroup analysis by baseline ECOG PS
16.2.7.1.72.1 Treatment emergent adverse event per SOC by treatment group according to baseline ECOG PS - Safety population

	0 or 1		>1		
	Kd (N=117)	**IKd (N=167)**	**Kd (N=5)**	**IKd (N=10)**	**p-value of treatment-by-sub group interaction[c]**
Events probability (95% CI)[b]					
3 Months	0.9310 (0.8668 to 0.9649)	0.9038 (0.8477 to 0.9399)	1.0000 (1.0000 to 1.0000)	0.8889 (0.4330 to 0.9836)	
6 Months	0.8862 (0.8121 to 0.9323)	0.8350 (0.7685 to 0.8838)	1.0000 (1.0000 to 1.0000)	0.7778 (0.3648 to 0.9393)	
9 Months	0.8769 (0.8009 to 0.9252)	0.7899 (0.7185 to 0.8452)	1.0000 (1.0000 to 1.0000)	0.7778 (0.3648 to 0.9393)	
12 Months	0.8674 (0.7895 to 0.9179)	0.7638 (0.6901 to 0.8223)	1.0000 (1.0000 to 1.0000)	0.7778 (0.3648 to 0.9393)	
15 Months	0.8674 (0.7895 to 0.9179)	0.7291 (0.6523 to 0.7917)	1.0000 (1.0000 to 1.0000)	0.7778 (0.3648 to 0.9393)	
18 Months	0.8572 (0.7772 to 0.9101)	0.7072 (0.6286 to 0.7722)	1.0000 (1.0000 to 1.0000)	0.7778 (0.3648 to 0.9393)	
21 Months	0.8572 (0.7772 to 0.9101)	0.6996 (0.6204 to 0.7655)	1.0000 (1.0000 to 1.0000)	0.7778 (0.3648 to 0.9393)	
24 Months	0.8572 (0.7772 to 0.9101)	0.6996 (0.6204 to 0.7655)	1.0000 (1.0000 to 1.0000)	0.7778 (0.3648 to 0.9393)	

SOC are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.72 Subgroup analysis by baseline ECOG PS
16.2.7.1.72.1 Treatment emergent adverse event per SOC by treatment group according to baseline ECOG PS - Safety population

	0 or 1		>1		
	Kd (N=117)	**IKd (N=167)**	**Kd (N=5)**	**IKd (N=10)**	**p-value of treatment-by-sub group interaction[c]**
27 Months	0.8572 (0.7772 to 0.9101)	0.6996 (0.6204 to 0.7655)	1.0000 (1.0000 to 1.0000)	0.7778 (0.3648 to 0.9393)	
30 Months	0.8572 (0.7772 to 0.9101)	0.6996 (0.6204 to 0.7655)	1.0000 (1.0000 to 1.0000)	0.7778 (0.3648 to 0.9393)	
Number of patients at risk[b]					
3 Months	106	148	5	8	
6 Months	97	131	4	7	
9 Months	92	121	4	7	
12 Months	89	116	4	6	
15 Months	85	102	2	6	
18 Months	82	94	2	5	
21 Months	66	81	2	5	
24 Months	23	24	1	0	
27 Months	3	1	0	0	
30 Months	0	0	0	0	
Vascular disorders (days)					

SOC are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.73 Subgroup analysis by ISS staging at study entry
16.2.7.1.73.1 Treatment emergent adverse event per SOC by treatment group according to ISS staging at study entry - Safety population

	I		II		III		
	Kd (N=70)	**IKd (N=89)**	**Kd (N=31)**	**IKd (N=63)**	**Kd (N=20)**	**IKd (N=24)**	**p-value of treatment-by-sub group interaction[c]**
30 Months	0.1981 (0.1142 to 0.2988)	0.1439 (0.0793 to 0.2271)	0.0817 (0.0152 to 0.2236)	0.0933 (0.0358 to 0.1846)	0.2204 (0.0605 to 0.4426)	0.0880 (0.0152 to 0.2440)	
Number of patients at risk[b]							
3 Months	34	54	16	31	12	8	
6 Months	20	30	11	16	6	4	
9 Months	17	19	5	12	5	3	
12 Months	14	16	4	10	3	2	
15 Months	13	11	2	8	3	0	
18 Months	13	10	2	5	2	0	
21 Months	8	7	1	4	2	0	
24 Months	3	3	1	1	0	0	
27 Months	1	0	0	0	0	0	
30 Months	0	0	0	0	0	0	
Injury, poisoning and procedural complications (days)							
Number (%) of events	16 (22.9)	51 (57.3)	10 (32.3)	44 (69.8)	6 (30.0)	15 (62.5)	0.9483

SOC are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.73 Subgroup analysis by ISS staging at study entry
16.2.7.1.73.1 Treatment emergent adverse event per SOC by treatment group according to ISS staging at study entry - Safety population

	I		II		III		
	Kd (N=70)	**IKd (N=89)**	**Kd (N=31)**	**IKd (N=63)**	**Kd (N=20)**	**IKd (N=24)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of patients censored	54 (77.1)	38 (42.7)	21 (67.7)	19 (30.2)	14 (70.0)	9 (37.5)	
Kaplan-Meier estimates of event in months							
25% quantile (95% CI)	22.3409 (8.8706 to NC)	0.1314 (0.0657 to 0.1643)	7.8850 (1.1170 to NC)	0.0986 (0.0657 to 0.1314)	16.4600 (0.0986 to NC)	0.1314 (0.0657 to 0.1643)	
Median (95% CI)	NC (NC to NC)	8.4435 (0.6242 to NC)	NC (8.6078 to NC)	1.9713 (0.1314 to 8.5092)	NC (16.4600 to NC)	0.6078 (0.1314 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (9.5277 to NC)	NC (NC to NC)	NC (0.9199 to NC)	
Comparison vs. Kd							
Log-Rank test p-value[a] vs Kd	-	<.0001		0.0008		0.0071	
Hazard ratio (95% CI) vs Kd	-	3.59 (2.04 to 6.31)		3.08 (1.55 to 6.13)		3.50 (1.33 to 9.18)	
P-value	-	<.0001		0.0014		0.0110	
Hazard ratio inverted (95% CI) vs IKd	0.28 (0.16 to 0.49)		0.32 (0.16 to 0.65)		0.29 (0.11 to 0.75)		
Events probability (95% CI)[b]							

SOC are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.73 Subgroup analysis by ISS staging at study entry
16.2.7.1.73.1 Treatment emergent adverse event per SOC by treatment group according to ISS staging at study entry - Safety population

	I		II		III		
	Kd (N=70)	**IKd (N=89)**	**Kd (N=31)**	**IKd (N=63)**	**Kd (N=20)**	**IKd (N=24)**	**p-value of treatment-by-sub group interaction[c]**
3 Months	0.9571 (0.8730 to 0.9860)	0.5730 (0.4638 to 0.6680)	0.8052 (0.6167 to 0.9074)	0.4762 (0.3493 to 0.5925)	0.8444 (0.5911 to 0.9471)	0.4000 (0.2036 to 0.5901)	
6 Months	0.8996 (0.8008 to 0.9508)	0.5393 (0.4306 to 0.6361)	0.8052 (0.6167 to 0.9074)	0.4127 (0.2910 to 0.5302)	0.8444 (0.5911 to 0.9471)	0.3429 (0.1562 to 0.5395)	
9 Months	0.8553 (0.7476 to 0.9194)	0.4936 (0.3862 to 0.5923)	0.6968 (0.4966 to 0.8299)	0.3810 (0.2626 to 0.4983)	0.7795 (0.5099 to 0.9120)	0.3429 (0.1562 to 0.5395)	
12 Months	0.8094 (0.6943 to 0.8847)	0.4477 (0.3424 to 0.5475)	0.6601 (0.4587 to 0.8014)	0.3333 (0.2210 to 0.4496)	0.7795 (0.5099 to 0.9120)	0.3429 (0.1562 to 0.5395)	
15 Months	0.7936 (0.6761 to 0.8723)	0.4477 (0.3424 to 0.5475)	0.6601 (0.4587 to 0.8014)	0.3175 (0.2074 to 0.4331)	0.7795 (0.5099 to 0.9120)	0.3429 (0.1562 to 0.5395)	
18 Months	0.7936 (0.6761 to 0.8723)	0.4342 (0.3291 to 0.5345)	0.6601 (0.4587 to 0.8014)	0.3016 (0.1940 to 0.4164)	0.6063 (0.3080 to 0.8084)	0.3429 (0.1562 to 0.5395)	
21 Months	0.7767 (0.6566 to 0.8592)	0.4206 (0.3160 to 0.5215)	0.6601 (0.4587 to 0.8014)	0.3016 (0.1940 to 0.4164)	0.6063 (0.3080 to 0.8084)	0.3429 (0.1562 to 0.5395)	
24 Months	0.7479 (0.6161 to 0.8402)	0.4206 (0.3160 to 0.5215)	0.6601 (0.4587 to 0.8014)	0.3016 (0.1940 to 0.4164)	0.6063 (0.3080 to 0.8084)	0.3429 (0.1562 to 0.5395)	
27 Months	0.7479 (0.6161 to 0.8402)	0.4206 (0.3160 to 0.5215)	0.6601 (0.4587 to 0.8014)	0.3016 (0.1940 to 0.4164)	0.6063 (0.3080 to 0.8084)	0.3429 (0.1562 to 0.5395)	

SOC are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.73 Subgroup analysis by ISS staging at study entry
16.2.7.1.73.1 Treatment emergent adverse event per SOC by treatment group according to ISS staging at study entry - Safety population

	I		II		III		
	Kd (N=70)	**IKd (N=89)**	**Kd (N=31)**	**IKd (N=63)**	**Kd (N=20)**	**IKd (N=24)**	**p-value of treatment-by-sub group interaction[c]**
30 Months	0.7479 (0.6161 to 0.8402)	0.4206 (0.3160 to 0.5215)	0.6601 (0.4587 to 0.8014)	0.3016 (0.1940 to 0.4164)	0.6063 (0.3080 to 0.8084)	0.3429 (0.1562 to 0.5395)	
Number of patients at risk[b]							
3 Months	67	51	24	30	16	8	
6 Months	62	48	23	26	13	5	
9 Months	56	43	19	24	12	5	
12 Months	52	38	17	21	12	5	
15 Months	50	35	15	20	10	3	
18 Months	50	32	15	19	6	2	
21 Months	38	27	11	17	5	2	
24 Months	14	9	5	4	1	1	
27 Months	2	1	1	0	0	0	
30 Months	0	0	0	0	0	0	
Investigations (days)							
Number (%) of events	12 (17.1)	14 (15.7)	4 (12.9)	11 (17.5)	1 (5.0)	6 (25.0)	0.2677
Number (%) of patients censored	58 (82.9)	75 (84.3)	27 (87.1)	52 (82.5)	19 (95.0)	18 (75.0)	

SOC are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
PGM=DEVOPS/SAR650984/EFC15246/CIR_RWE/REPORT/PGM/ae_km_socpt_subgp_sr_s_t.sas OUT=REPORT/OUTPUT/ae_km_teaesoc_seiss_s_t_x.rtf (12FEB2021 8:26)

16.2.7.1 Safety endpoints
16.2.7.1.73 Subgroup analysis by ISS staging at study entry
16.2.7.1.73.1 Treatment emergent adverse event per SOC by treatment group according to ISS staging at study entry - Safety population

	I		II		III		
	Kd (N=70)	**IKd (N=89)**	**Kd (N=31)**	**IKd (N=63)**	**Kd (N=20)**	**IKd (N=24)**	**p-value of treatment-by-sub group interaction[c]**
Skin and subcutaneous tissue disorders (days)							
Number (%) of events	13 (18.6)	22 (24.7)	3 (9.7)	18 (28.6)	0 (0.0)	8 (33.3)	0.5541
Number (%) of patients censored	57 (81.4)	67 (75.3)	28 (90.3)	45 (71.4)	20 (100.0)	16 (66.7)	
Kaplan-Meier estimates of event in months							
25% quantile (95% CI)	NC (8.8049 to NC)	16.1643 (4.5339 to NC)	NC (3.0554 to NC)	13.0103 (5.7166 to NC)	NC (NC to NC)	14.6201 (0.1314 to 18.5298)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (14.6201 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (18.5298 to NC)	
Comparison vs. Kd							
Log-Rank test p-value[a] vs Kd	-	0.3535		0.0592		0.0039	
Hazard ratio (95% CI) vs Kd	-	1.38 (0.70 to 2.74)		3.06 (0.90 to 10.38)		NC	
P-value	-	0.3556		0.0732		0.9954	

SOC are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.73 Subgroup analysis by ISS staging at study entry
16.2.7.1.73.1 Treatment emergent adverse event per SOC by treatment group according to ISS staging at study entry - Safety population

	I		II		III		
	Kd (N=70)	**IKd (N=89)**	**Kd (N=31)**	**IKd (N=63)**	**Kd (N=20)**	**IKd (N=24)**	**p-value of treatment-by-sub group interaction[c]**
Events probability (95% CI)[b]							
3 Months	0.9143 (0.8191 to 0.9606)	0.9100 (0.8280 to 0.9539)	0.9355 (0.7659 to 0.9835)	0.9048 (0.8002 to 0.9560)	1.0000 (1.0000 to 1.0000)	0.8671 (0.6416 to 0.9552)	
6 Months	0.8569 (0.7504 to 0.9203)	0.8190 (0.7216 to 0.8849)	0.9021 (0.7262 to 0.9673)	0.8368 (0.7176 to 0.9088)	1.0000 (1.0000 to 1.0000)	0.8671 (0.6416 to 0.9552)	
9 Months	0.8424 (0.7335 to 0.9095)	0.7842 (0.6827 to 0.8566)	0.9021 (0.7262 to 0.9673)	0.7855 (0.6591 to 0.8696)	1.0000 (1.0000 to 1.0000)	0.8129 (0.5720 to 0.9260)	
12 Months	0.8276 (0.7164 to 0.8982)	0.7842 (0.6827 to 0.8566)	0.9021 (0.7262 to 0.9673)	0.7514 (0.6215 to 0.8422)	1.0000 (1.0000 to 1.0000)	0.7587 (0.5102 to 0.8929)	
15 Months	0.8276 (0.7164 to 0.8982)	0.7593 (0.6548 to 0.8360)	0.9021 (0.7262 to 0.9673)	0.7160 (0.5830 to 0.8132)	1.0000 (1.0000 to 1.0000)	0.6828 (0.4125 to 0.8484)	
18 Months	0.8123 (0.6986 to 0.8864)	0.7459 (0.6398 to 0.8250)	0.9021 (0.7262 to 0.9673)	0.6977 (0.5631 to 0.7979)	1.0000 (1.0000 to 1.0000)	0.6069 (0.3319 to 0.7977)	
21 Months	0.8123 (0.6986 to 0.8864)	0.7459 (0.6398 to 0.8250)	0.9021 (0.7262 to 0.9673)	0.6977 (0.5631 to 0.7979)	1.0000 (1.0000 to 1.0000)	0.5202 (0.2465 to 0.7371)	
24 Months	0.8123 (0.6986 to 0.8864)	0.7459 (0.6398 to 0.8250)	0.9021 (0.7262 to 0.9673)	0.6977 (0.5631 to 0.7979)	1.0000 (1.0000 to 1.0000)	0.5202 (0.2465 to 0.7371)	
27 Months	0.8123 (0.6986 to 0.8864)	0.7459 (0.6398 to 0.8250)	0.9021 (0.7262 to 0.9673)	0.6977 (0.5631 to 0.7979)	1.0000 (1.0000 to 1.0000)	0.5202 (0.2465 to 0.7371)	

SOC are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.73 Subgroup analysis by ISS staging at study entry
16.2.7.1.73.1 Treatment emergent adverse event per SOC by treatment group according to ISS staging at study entry - Safety population

	I		II		III		
	Kd (N=70)	**IKd (N=89)**	**Kd (N=31)**	**IKd (N=63)**	**Kd (N=20)**	**IKd (N=24)**	**p-value of treatment-by-sub group interaction[c]**
30 Months	0.8123 (0.6986 to 0.8864)	0.7459 (0.6398 to 0.8250)	0.9021 (0.7262 to 0.9673)	0.6977 (0.5631 to 0.7979)	1.0000 (1.0000 to 1.0000)	0.5202 (0.2465 to 0.7371)	
Number of patients at risk[b]							
3 Months	64	80	28	56	18	19	
6 Months	59	71	26	49	15	17	
9 Months	57	66	24	46	14	15	
12 Months	55	65	23	44	14	13	
15 Months	54	59	20	40	12	9	
18 Months	53	54	20	38	10	7	
21 Months	42	47	17	34	8	5	
24 Months	15	15	7	9	2	0	
27 Months	2	1	1	0	0	0	
30 Months	0	0	0	0	0	0	
Vascular disorders (days)							
Number (%) of events	36 (51.4)	42 (47.2)	10 (32.3)	34 (54.0)	7 (35.0)	6 (25.0)	0.1447
Number (%) of patients censored	34 (48.6)	47 (52.8)	21 (67.7)	29 (46.0)	13 (65.0)	18 (75.0)	

SOC are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.74 Subgroup analysis by R-ISS staging
16.2.7.1.74.1 Treatment emergent adverse event per SOC by treatment group according to R-ISS staging - Safety population

	I or II		III		Not classified		
	Kd (N=102)	**IKd (N=155)**	**Kd (N=8)**	**IKd (N=15)**	**Kd (N=12)**	**IKd (N=7)**	**p-value of treatment-by-sub group interaction[c]**
30 Months	0.1505 (0.0874 to 0.2296)	0.1130 (0.0683 to 0.1701)	0.1944 (0.0093 to 0.5634)	0.1455 (0.0237 to 0.3704)	0.3333 (0.1027 to 0.5884)	0.1714 (0.0079 to 0.5256)	
Number of patients at risk[b]							
3 Months	51	84	6	6	6	4	
6 Months	30	47	2	2	6	1	
9 Months	21	31	2	2	4	1	
12 Months	16	25	1	2	4	1	
15 Months	13	19	1	0	4	0	
18 Months	12	15	1	0	4	0	
21 Months	7	11	1	0	3	0	
24 Months	4	4	0	0	0	0	
27 Months	1	0	0	0	0	0	
30 Months	0	0	0	0	0	0	
Injury, poisoning and procedural complications (days)							
Number (%) of events	29 (28.4)	96 (61.9)	2 (25.0)	10 (66.7)	1 (8.3)	5 (71.4)	0.2631

SOC are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.74 Subgroup analysis by R-ISS staging
16.2.7.1.74.1 Treatment emergent adverse event per SOC by treatment group according to R-ISS staging - Safety population

	I or II		III		Not classified		
	Kd (N=102)	**IKd (N=155)**	**Kd (N=8)**	**IKd (N=15)**	**Kd (N=12)**	**IKd (N=7)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of patients censored	73 (71.6)	59 (38.1)	6 (75.0)	5 (33.3)	11 (91.7)	2 (28.6)	
Kaplan-Meier estimates of event in months							
25% quantile (95% CI)	10.8090 (7.2936 to NC)	0.0986 (0.0657 to 0.1314)	NC (0.0986 to NC)	0.0657 (0.0657 to 0.2957)	NC (12.7146 to NC)	0.0657 (0.0657 to 0.2300)	
Median (95% CI)	NC (NC to NC)	5.7823 (0.6899 to 10.3819)	NC (0.0986 to NC)	0.9199 (0.0657 to NC)	NC (NC to NC)	0.2300 (0.0657 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (0.9199 to NC)	NC (NC to NC)	NC (0.1643 to NC)	
Comparison vs. Kd							
Log-Rank test p-value[a] vs Kd	-	<.0001		0.0496		0.0021	
Hazard ratio (95% CI) vs Kd	-	3.09 (2.03 to 4.68)		4.15 (0.89 to 19.27)		14.30 (1.62 to 126.41)	
P-value	-	<.0001		0.0691		0.0167	
Hazard ratio inverted (95% CI) vs IKd	0.32 (0.21 to 0.49)				0.07 (0.01 to 0.62)		

SOC are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.74 Subgroup analysis by R-ISS staging
16.2.7.1.74.1 Treatment emergent adverse event per SOC by treatment group according to R-ISS staging - Safety population

	I or II		III		Not classified		
	Kd (N=102)	**IKd (N=155)**	**Kd (N=8)**	**IKd (N=15)**	**Kd (N=12)**	**IKd (N=7)**	**p-value of treatment-by-sub group interaction[c]**
Events probability (95% CI)[b]							
3 Months	0.9012 (0.8241 to 0.9456)	0.5355 (0.4539 to 0.6102)	0.7500 (0.3148 to 0.9309)	0.3556 (0.1212 to 0.6025)	1.0000 (1.0000 to 1.0000)	0.2857 (0.0411 to 0.6115)	
6 Months	0.8603 (0.7754 to 0.9148)	0.4898 (0.4090 to 0.5657)	0.7500 (0.3148 to 0.9309)	0.2667 (0.0692 to 0.5199)	1.0000 (1.0000 to 1.0000)	0.2857 (0.0411 to 0.6115)	
9 Months	0.7864 (0.6911 to 0.8553)	0.4503 (0.3706 to 0.5266)	0.7500 (0.3148 to 0.9309)	0.2667 (0.0692 to 0.5199)	1.0000 (1.0000 to 1.0000)	0.2857 (0.0411 to 0.6115)	
12 Months	0.7427 (0.6430 to 0.8184)	0.4039 (0.3262 to 0.4803)	0.7500 (0.3148 to 0.9309)	0.2667 (0.0692 to 0.5199)	1.0000 (1.0000 to 1.0000)	0.2857 (0.0411 to 0.6115)	
15 Months	0.7427 (0.6430 to 0.8184)	0.3970 (0.3195 to 0.4733)	0.7500 (0.3148 to 0.9309)	0.2667 (0.0692 to 0.5199)	0.9167 (0.5390 to 0.9878)	0.2857 (0.0411 to 0.6115)	
18 Months	0.7179 (0.6154 to 0.7976)	0.3823 (0.3053 to 0.4586)	0.7500 (0.3148 to 0.9309)	0.2667 (0.0692 to 0.5199)	0.9167 (0.5390 to 0.9878)	0.2857 (0.0411 to 0.6115)	
21 Months	0.7049 (0.6008 to 0.7866)	0.3749 (0.2983 to 0.4513)	0.7500 (0.3148 to 0.9309)	0.2667 (0.0692 to 0.5199)	0.9167 (0.5390 to 0.9878)	0.2857 (0.0411 to 0.6115)	
24 Months	0.6806 (0.5678 to 0.7698)	0.3749 (0.2983 to 0.4513)	0.7500 (0.3148 to 0.9309)	0.2667 (0.0692 to 0.5199)	0.9167 (0.5390 to 0.9878)	0.2857 (0.0411 to 0.6115)	
27 Months	0.6806 (0.5678 to 0.7698)	0.3749 (0.2983 to 0.4513)	0.7500 (0.3148 to 0.9309)	0.2667 (0.0692 to 0.5199)	0.9167 (0.5390 to 0.9878)	0.2857 (0.0411 to 0.6115)	

SOC are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.74 Subgroup analysis by R-ISS staging
16.2.7.1.74.1 Treatment emergent adverse event per SOC by treatment group according to R-ISS staging - Safety population

	I or II		III		Not classified		
	Kd (N=102)	**IKd (N=155)**	**Kd (N=8)**	**IKd (N=15)**	**Kd (N=12)**	**IKd (N=7)**	**p-value of treatment-by-sub group interaction[c]**
30 Months	0.6806 (0.5678 to 0.7698)	0.3749 (0.2983 to 0.4513)	0.7500 (0.3148 to 0.9309)	0.2667 (0.0692 to 0.5199)	0.9167 (0.5390 to 0.9878)	0.2857 (0.0411 to 0.6115)	
Number of patients at risk[b]							
3 Months	90	83	6	4	12	2	
6 Months	83	75	4	2	12	2	
9 Months	72	68	4	2	12	2	
12 Months	66	60	4	2	12	2	
15 Months	61	56	4	1	11	1	
18 Months	57	52	4	0	11	1	
21 Months	43	45	3	0	9	1	
24 Months	16	14	1	0	3	0	
27 Months	3	1	0	0	0	0	
30 Months	0	0	0	0	0	0	
Investigations (days)							
Number (%) of events	16 (15.7)	26 (16.8)	1 (12.5)	5 (33.3)	0 (0.0)	0 (0.0)	0.6252
Number (%) of patients censored	86 (84.3)	129 (83.2)	7 (87.5)	10 (66.7)	12 (100.0)	7 (100.0)	

SOC are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.74 Subgroup analysis by R-ISS staging
16.2.7.1.74.1 Treatment emergent adverse event per SOC by treatment group according to R-ISS staging - Safety population

	I or II		III		Not classified		
	Kd (N=102)	**IKd (N=155)**	**Kd (N=8)**	**IKd (N=15)**	**Kd (N=12)**	**IKd (N=7)**	**p-value of treatment-by-sub group interaction[c]**
30 Months	0.5779 (0.4721 to 0.6699)	0.4294 (0.3488 to 0.5074)	0.6250 (0.2293 to 0.8607)	0.6500 (0.3513 to 0.8375)	0.5833 (0.2701 to 0.8009)	0.8571 (0.3341 to 0.9786)	
Number of patients at risk[b]							
3 Months	76	107	6	9	8	5	
6 Months	64	87	5	8	8	5	
9 Months	57	76	5	7	8	4	
12 Months	52	70	5	6	8	4	
15 Months	47	61	5	4	8	3	
18 Months	45	59	5	3	7	3	
21 Months	35	53	4	2	6	3	
24 Months	15	19	1	0	0	0	
27 Months	3	1	0	0	0	0	
30 Months	0	0	0	0	0	0	
Skin and subcutaneous tissue disorders (days)							
Number (%) of events	16 (15.7)	43 (27.7)	0 (0.0)	4 (26.7)	0 (0.0)	2 (28.6)	0.9999

SOC are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.74 Subgroup analysis by R-ISS staging
16.2.7.1.74.1 Treatment emergent adverse event per SOC by treatment group according to R-ISS staging - Safety population

	I or II		III		Not classified		
	Kd (N=102)	**IKd (N=155)**	**Kd (N=8)**	**IKd (N=15)**	**Kd (N=12)**	**IKd (N=7)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of patients censored	86 (84.3)	112 (72.3)	8 (100.0)	11 (73.3)	12 (100.0)	5 (71.4)	
Kaplan-Meier estimates of event in months							
25% quantile (95% CI)	NC (15.1458 to NC)	14.4887 (6.3080 to NC)	NC (NC to NC)	14.6201 (1.8070 to NC)	NC (NC to NC)	11.6961 (3.8768 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (7.9507 to NC)	NC (NC to NC)	NC (3.8768 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (11.6961 to NC)	
Comparison vs. Kd							
Log-Rank test p-value[a] vs Kd	-	0.0405		0.1184		0.0269	
Hazard ratio (95% CI) vs Kd	-	1.81 (1.02 to 3.21)		NC		NC	
P-value	-	0.0436		0.9970		0.9980	
Hazard ratio inverted (95% CI) vs IKd	0.55 (0.31 to 0.98)						
Events probability (95% CI)[b]							

SOC are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.74 Subgroup analysis by R-ISS staging
16.2.7.1.74.1 Treatment emergent adverse event per SOC by treatment group according to R-ISS staging - Safety population

	I or II		III		Not classified		
	Kd (N=102)	**IKd (N=155)**	**Kd (N=8)**	**IKd (N=15)**	**Kd (N=12)**	**IKd (N=7)**	**p-value of treatment-by-sub group interaction[c]**
3 Months	0.9211 (0.8484 to 0.9597)	0.9032 (0.8445 to 0.9405)	1.0000 (1.0000 to 1.0000)	0.8462 (0.5122 to 0.9591)	1.0000 (1.0000 to 1.0000)	1.0000 (1.0000 to 1.0000)	
6 Months	0.8700 (0.7866 to 0.9224)	0.8299 (0.7603 to 0.8809)	1.0000 (1.0000 to 1.0000)	0.8462 (0.5122 to 0.9591)	1.0000 (1.0000 to 1.0000)	0.8333 (0.2731 to 0.9747)	
9 Months	0.8594 (0.7740 to 0.9143)	0.7892 (0.7152 to 0.8461)	1.0000 (1.0000 to 1.0000)	0.7615 (0.4267 to 0.9165)	1.0000 (1.0000 to 1.0000)	0.8333 (0.2731 to 0.9747)	
12 Months	0.8485 (0.7612 to 0.9058)	0.7687 (0.6928 to 0.8281)	1.0000 (1.0000 to 1.0000)	0.7615 (0.4267 to 0.9165)	1.0000 (1.0000 to 1.0000)	0.6250 (0.1419 to 0.8931)	
15 Months	0.8485 (0.7612 to 0.9058)	0.7400 (0.6616 to 0.8029)	1.0000 (1.0000 to 1.0000)	0.6346 (0.2756 to 0.8518)	1.0000 (1.0000 to 1.0000)	0.6250 (0.1419 to 0.8931)	
18 Months	0.8364 (0.7465 to 0.8966)	0.7175 (0.6372 to 0.7830)	1.0000 (1.0000 to 1.0000)	0.6346 (0.2756 to 0.8518)	1.0000 (1.0000 to 1.0000)	0.6250 (0.1419 to 0.8931)	
21 Months	0.8364 (0.7465 to 0.8966)	0.7097 (0.6289 to 0.7761)	1.0000 (1.0000 to 1.0000)	0.6346 (0.2756 to 0.8518)	1.0000 (1.0000 to 1.0000)	0.6250 (0.1419 to 0.8931)	
24 Months	0.8364 (0.7465 to 0.8966)	0.7097 (0.6289 to 0.7761)	1.0000 (1.0000 to 1.0000)	0.6346 (0.2756 to 0.8518)	1.0000 (1.0000 to 1.0000)	0.6250 (0.1419 to 0.8931)	
27 Months	0.8364 (0.7465 to 0.8966)	0.7097 (0.6289 to 0.7761)	1.0000 (1.0000 to 1.0000)	0.6346 (0.2756 to 0.8518)	1.0000 (1.0000 to 1.0000)	0.6250 (0.1419 to 0.8931)	

SOC are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
PGM=DEVOPS/SAR650984/EFC15246/CIR_RWE/REPORT/PGM/ae_km_socpt_subgp_sr_s_t.sas OUT=REPORT/OUTPUT/ae_km_teaesoc_seriss_s_t_x.rtf (12FEB2021 8:26)

16.2.7.1 Safety endpoints
16.2.7.1.74 Subgroup analysis by R-ISS staging
16.2.7.1.74.1 Treatment emergent adverse event per SOC by treatment group according to R-ISS staging - Safety population

	I or II		III		Not classified		
	Kd (N=102)	**IKd (N=155)**	**Kd (N=8)**	**IKd (N=15)**	**Kd (N=12)**	**IKd (N=7)**	**p-value of treatment-by-sub group interaction[c]**
30 Months	0.8364 (0.7465 to 0.8966)	0.7097 (0.6289 to 0.7761)	1.0000 (1.0000 to 1.0000)	0.6346 (0.2756 to 0.8518)	1.0000 (1.0000 to 1.0000)	0.6250 (0.1419 to 0.8931)	
Number of patients at risk[b]							
3 Months	92	139	7	11	12	6	
6 Months	84	123	5	10	12	5	
9 Months	79	115	5	9	12	4	
12 Months	76	111	5	8	12	3	
15 Months	70	101	5	5	12	2	
18 Months	67	93	5	4	12	2	
21 Months	54	81	4	3	10	2	
24 Months	20	24	1	0	3	0	
27 Months	3	1	0	0	0	0	
30 Months	0	0	0	0	0	0	
Vascular disorders (days)							
Number (%) of events	48 (47.1)	78 (50.3)	1 (12.5)	3 (20.0)	5 (41.7)	1 (14.3)	0.5278
Number (%) of patients censored	54 (52.9)	77 (49.7)	7 (87.5)	12 (80.0)	7 (58.3)	6 (85.7)	

SOC are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.75 Subgroup analysis by number of prior lines of therapy (IRT)
16.2.7.1.75.1 Treatment emergent adverse event per SOC by treatment group according to number of prior lines of therapy (IRT) - Safety population

	1		>1		
	Kd (N=54)	**IKd (N=78)**	**Kd (N=68)**	**IKd (N=99)**	**p-value of treatment-by-sub group interaction[c]**
24 Months	0.7155 (0.5591 to 0.8247)	0.3616 (0.2547 to 0.4693)	0.7035 (0.5690 to 0.8030)	0.3616 (0.2664 to 0.4574)	
27 Months	0.7155 (0.5591 to 0.8247)	0.3616 (0.2547 to 0.4693)	0.7035 (0.5690 to 0.8030)	0.3616 (0.2664 to 0.4574)	
30 Months	0.7155 (0.5591 to 0.8247)	0.3616 (0.2547 to 0.4693)	0.7035 (0.5690 to 0.8030)	0.3616 (0.2664 to 0.4574)	
Number of patients at risk[b]					
3 Months	48	43	60	46	
6 Months	46	37	53	42	
9 Months	42	33	46	39	
12 Months	39	30	43	34	
15 Months	37	26	39	32	
18 Months	36	24	36	29	
21 Months	28	19	27	27	
24 Months	10	8	10	6	
27 Months	1	0	2	1	
30 Months	0	0	0	0	

SOC are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
PGM=DEVOPS/SAR650984/EFC15246/CIR_RWE/REPORT/PGM/ae_km_socpt_subgp_sr_s_t.sas OUT=REPORT/OUTPUT/ae_km_teaesoc_plne_s_t_x.rtf (12FEB2021 8:25)

16.2.7.1 Safety endpoints
16.2.7.1.75 Subgroup analysis by number of prior lines of therapy (IRT)
16.2.7.1.75.1 Treatment emergent adverse event per SOC by treatment group according to number of prior lines of therapy (IRT) - Safety population

	1		>1		
	Kd (N=54)	**IKd (N=78)**	**Kd (N=68)**	**IKd (N=99)**	**p-value of treatment-by-sub group interaction[c]**
Skin and subcutaneous tissue disorders (days)					
Number (%) of events	8 (14.8)	20 (25.6)	8 (11.8)	29 (29.3)	0.5096
Number (%) of patients censored	46 (85.2)	58 (74.4)	60 (88.2)	70 (70.7)	
Kaplan-Meier estimates of event in months					
25% quantile (95% CI)	NC (4.0082 to NC)	16.4928 (5.3224 to NC)	NC (NC to NC)	11.0390 (5.7166 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.1532		0.0113	
Hazard ratio (95% CI) vs Kd	-	1.80 (0.79 to 4.09)		2.65 (1.21 to 5.79)	
P-value	-	0.1594		0.0148	
Hazard ratio inverted (95% CI) vs IKd			0.38 (0.17 to 0.83)		
Events probability (95% CI)[b]					

SOC are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.75 Subgroup analysis by number of prior lines of therapy (IRT)
16.2.7.1.75.1 Treatment emergent adverse event per SOC by treatment group according to number of prior lines of therapy (IRT) - Safety population

	1		>1		
	Kd (N=54)	**IKd (N=78)**	**Kd (N=68)**	**IKd (N=99)**	**p-value of treatment-by-sub group interaction[c]**
3 Months	0.9074 (0.7917 to 0.9604)	0.9103 (0.8210 to 0.9562)	0.9554 (0.8681 to 0.9854)	0.8973 (0.8176 to 0.9434)	
6 Months	0.8696 (0.7458 to 0.9356)	0.8435 (0.7407 to 0.9080)	0.9081 (0.8067 to 0.9577)	0.8225 (0.7300 to 0.8858)	
9 Months	0.8696 (0.7458 to 0.9356)	0.8027 (0.6939 to 0.8761)	0.8910 (0.7845 to 0.9466)	0.7789 (0.6812 to 0.8500)	
12 Months	0.8507 (0.7235 to 0.9224)	0.8027 (0.6939 to 0.8761)	0.8910 (0.7845 to 0.9466)	0.7336 (0.6314 to 0.8117)	
15 Months	0.8507 (0.7235 to 0.9224)	0.7735 (0.6607 to 0.8528)	0.8910 (0.7845 to 0.9466)	0.6976 (0.5922 to 0.7808)	
18 Months	0.8507 (0.7235 to 0.9224)	0.7437 (0.6274 to 0.8286)	0.8712 (0.7577 to 0.9338)	0.6847 (0.5781 to 0.7697)	
21 Months	0.8507 (0.7235 to 0.9224)	0.7285 (0.6106 to 0.8160)	0.8712 (0.7577 to 0.9338)	0.6847 (0.5781 to 0.7697)	
24 Months	0.8507 (0.7235 to 0.9224)	0.7285 (0.6106 to 0.8160)	0.8712 (0.7577 to 0.9338)	0.6847 (0.5781 to 0.7697)	
27 Months	0.8507 (0.7235 to 0.9224)	0.7285 (0.6106 to 0.8160)	0.8712 (0.7577 to 0.9338)	0.6847 (0.5781 to 0.7697)	

SOC are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.75 Subgroup analysis by number of prior lines of therapy (IRT)
16.2.7.1.75.1 Treatment emergent adverse event per SOC by treatment group according to number of prior lines of therapy (IRT) - Safety population

	1		>1		
	Kd (N=54)	**IKd (N=78)**	**Kd (N=68)**	**IKd (N=99)**	**p-value of treatment-by-sub group interaction[c]**
30 Months	0.8507 (0.7235 to 0.9224)	0.7285 (0.6106 to 0.8160)	0.8712 (0.7577 to 0.9338)	0.6847 (0.5781 to 0.7697)	
Number of patients at risk[b]					
3 Months	49	71	62	85	
6 Months	46	62	55	76	
9 Months	46	59	50	69	
12 Months	44	58	49	64	
15 Months	42	53	45	55	
18 Months	42	49	42	50	
21 Months	35	41	33	45	
24 Months	12	9	12	15	
27 Months	1	0	2	1	
30 Months	0	0	0	0	
Vascular disorders (days)					
Number (%) of events	27 (50.0)	40 (51.3)	27 (39.7)	42 (42.4)	0.8518
Number (%) of patients censored	27 (50.0)	38 (48.7)	41 (60.3)	57 (57.6)	

SOC are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.76 Subgroup analysis by cytogenetic abnormality (del(17p), t(4,14), t(14,16))
16.2.7.1.76.1 Treatment emergent adverse event per SOC by treatment group according to cytogenetic abnormality (del(17p), t(4,14), t(14,16)) - Safety population

	At least one		None		
	Kd (N=30)	**IKd (N=42)**	**Kd (N=77)**	**IKd (N=113)**	**p-value of treatment-by-sub group interaction[c]**
24 Months	0.6938 (0.4291 to 0.8539)	0.2483 (0.1278 to 0.3894)	0.6679 (0.5455 to 0.7643)	0.4242 (0.3308 to 0.5144)	
27 Months	0.6938 (0.4291 to 0.8539)	0.2483 (0.1278 to 0.3894)	0.6679 (0.5455 to 0.7643)	0.4242 (0.3308 to 0.5144)	
30 Months	0.6938 (0.4291 to 0.8539)	0.2483 (0.1278 to 0.3894)	0.6679 (0.5455 to 0.7643)	0.4242 (0.3308 to 0.5144)	
Number of patients at risk[b]					
3 Months	28	19	66	64	
6 Months	24	15	61	58	
9 Months	23	14	51	53	
12 Months	21	11	48	48	
15 Months	19	9	45	45	
18 Months	19	8	41	41	
21 Months	14	6	32	36	
24 Months	5	2	11	11	
27 Months	0	0	3	1	
30 Months	0	0	0	0	

SOC are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.76 Subgroup analysis by cytogenetic abnormality (del(17p), t(4,14), t(14,16))
16.2.7.1.76.1 Treatment emergent adverse event per SOC by treatment group according to cytogenetic abnormality (del(17p), t(4,14), t(14,16)) - Safety population

	At least one		None		
	Kd (N=30)	**IKd (N=42)**	**Kd (N=77)**	**IKd (N=113)**	**p-value of treatment-by-sub group interaction[c]**
27 Months	0	0	3	1	
30 Months	0	0	0	0	
Skin and subcutaneous tissue disorders (days)					
Number (%) of events	4 (13.3)	9 (21.4)	12 (15.6)	34 (30.1)	0.7887
Number (%) of patients censored	26 (86.7)	33 (78.6)	65 (84.4)	79 (69.9)	
Kaplan-Meier estimates of event in months					
25% quantile (95% CI)	NC (5.0924 to NC)	NC (4.0082 to NC)	NC (8.8049 to NC)	13.0103 (5.9138 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.4056		0.0352	
Hazard ratio (95% CI) vs Kd	-	1.64 (0.50 to 5.33)		2.00 (1.04 to 3.86)	
P-value	-	0.4105		0.0390	
Hazard ratio inverted (95% CI) vs IKd			0.50 (0.26 to 0.97)		

SOC are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.76 Subgroup analysis by cytogenetic abnormality (del(17p), t(4,14), t(14,16))
16.2.7.1.76.1 Treatment emergent adverse event per SOC by treatment group according to cytogenetic abnormality (del(17p), t(4,14), t(14,16)) - Safety population

	At least one		None		
	Kd (N=30)	**IKd (N=42)**	**Kd (N=77)**	**IKd (N=113)**	**p-value of treatment-by-sub group interaction[c]**
Events probability (95% CI)[b]					
3 Months	0.9333 (0.7589 to 0.9829)	0.9048 (0.7658 to 0.9631)	0.9207 (0.8319 to 0.9636)	0.9017 (0.8296 to 0.9443)	
6 Months	0.8988 (0.7180 to 0.9662)	0.8571 (0.7094 to 0.9331)	0.8661 (0.7653 to 0.9256)	0.8267 (0.7417 to 0.8858)	
9 Months	0.8988 (0.7180 to 0.9662)	0.8571 (0.7094 to 0.9331)	0.8519 (0.7483 to 0.9152)	0.7605 (0.6683 to 0.8302)	
12 Months	0.8988 (0.7180 to 0.9662)	0.8304 (0.6763 to 0.9154)	0.8372 (0.7309 to 0.9042)	0.7510 (0.6580 to 0.8220)	
15 Months	0.8988 (0.7180 to 0.9662)	0.7738 (0.6086 to 0.8760)	0.8372 (0.7309 to 0.9042)	0.7205 (0.6248 to 0.7957)	
18 Months	0.8560 (0.6577 to 0.9439)	0.7738 (0.6086 to 0.8760)	0.8372 (0.7309 to 0.9042)	0.6889 (0.5906 to 0.7681)	
21 Months	0.8560 (0.6577 to 0.9439)	0.7738 (0.6086 to 0.8760)	0.8372 (0.7309 to 0.9042)	0.6781 (0.5791 to 0.7586)	
24 Months	0.8560 (0.6577 to 0.9439)	0.7738 (0.6086 to 0.8760)	0.8372 (0.7309 to 0.9042)	0.6781 (0.5791 to 0.7586)	

SOC are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.76 Subgroup analysis by cytogenetic abnormality (del(17p), t(4,14), t(14,16))
16.2.7.1.76.1 Treatment emergent adverse event per SOC by treatment group according to cytogenetic abnormality (del(17p), t(4,14), t(14,16)) - Safety population

	At least one		None		
	Kd (N=30)	**IKd (N=42)**	**Kd (N=77)**	**IKd (N=113)**	**p-value of treatment-by-sub group interaction[c]**
27 Months	0.8560 (0.6577 to 0.9439)	0.7738 (0.6086 to 0.8760)	0.8372 (0.7309 to 0.9042)	0.6781 (0.5791 to 0.7586)	
30 Months	0.8560 (0.6577 to 0.9439)	0.7738 (0.6086 to 0.8760)	0.8372 (0.7309 to 0.9042)	0.6781 (0.5791 to 0.7586)	
Number of patients at risk[b]					
3 Months	28	38	69	99	
6 Months	25	33	62	88	
9 Months	24	32	58	80	
12 Months	23	31	57	77	
15 Months	21	26	53	70	
18 Months	20	25	51	64	
21 Months	16	20	42	56	
24 Months	5	7	15	14	
27 Months	0	0	3	1	
30 Months	0	0	0	0	
Vascular disorders (days)					

SOC are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.77 Subgroup analysis by MM type
16.2.7.1.77.1 Treatment emergent adverse event per SOC by treatment group according to MM type - Safety population

	IgG		Non-IgG		
	Kd (N=85)	**IKd (N=124)**	**Kd (N=37)**	**IKd (N=53)**	**p-value of treatment-by-sub group interaction[c]**
27 Months	1	0	0	0	
30 Months	0	0	0	0	
Injury, poisoning and procedural complications (days)					
Number (%) of events	22 (25.9)	74 (59.7)	10 (27.0)	37 (69.8)	0.5426
Number (%) of patients censored	63 (74.1)	50 (40.3)	27 (73.0)	16 (30.2)	
Kaplan-Meier estimates of event in months					
25% quantile (95% CI)	16.7228 (7.8850 to NC)	0.1314 (0.0986 to 0.1643)	16.4600 (1.3142 to NC)	0.0657 (0.0329 to 0.0986)	
Median (95% CI)	NC (NC to NC)	5.7823 (1.3470 to 12.6817)	NC (NC to NC)	0.1971 (0.0986 to 9.5277)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (9.1663 to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	<.0001		<.0001	
Hazard ratio (95% CI) vs Kd	-	3.36 (2.08 to 5.42)		4.02 (1.99 to 8.12)	

SOC are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
PGM=DEVOPS/SAR650984/EFC15246/CIR_RWE/REPORT/PGM/ae_km_socpt_subgp_sr_s_t.sas OUT=REPORT/OUTPUT/ae_km_teaesoc_semm_s_t_x.rtf (12FEB2021 8:26)

16.2.7.1 Safety endpoints
16.2.7.1.77 Subgroup analysis by MM type
16.2.7.1.77.1 Treatment emergent adverse event per SOC by treatment group according to MM type - Safety population

	IgG		Non-IgG		
	Kd (N=85)	**IKd (N=124)**	**Kd (N=37)**	**IKd (N=53)**	**p-value of treatment-by-sub group interaction[c]**
P-value	-	<.0001		0.0001	
Hazard ratio inverted (95% CI) vs IKd	0.30 (0.18 to 0.48)		0.25 (0.12 to 0.50)		
Events probability (95% CI)[b]					
3 Months	0.9294 (0.8496 to 0.9677)	0.5461 (0.4540 to 0.6291)	0.8331 (0.6654 to 0.9214)	0.4340 (0.2992 to 0.5612)	
6 Months	0.9050 (0.8189 to 0.9513)	0.4876 (0.3966 to 0.5725)	0.7756 (0.6007 to 0.8810)	0.4142 (0.2814 to 0.5420)	
9 Months	0.8183 (0.7166 to 0.8863)	0.4451 (0.3555 to 0.5308)	0.7756 (0.6007 to 0.8810)	0.3945 (0.2637 to 0.5225)	
12 Months	0.7671 (0.6592 to 0.8448)	0.4195 (0.3309 to 0.5053)	0.7756 (0.6007 to 0.8810)	0.3156 (0.1957 to 0.4425)	
15 Months	0.7539 (0.6445 to 0.8338)	0.4105 (0.3224 to 0.4965)	0.7756 (0.6007 to 0.8810)	0.3156 (0.1957 to 0.4425)	
18 Months	0.7397 (0.6286 to 0.8221)	0.4008 (0.3129 to 0.4869)	0.7403 (0.5584 to 0.8563)	0.2931 (0.1762 to 0.4199)	
21 Months	0.7397 (0.6286 to 0.8221)	0.3907 (0.3032 to 0.4771)	0.7033 (0.5153 to 0.8296)	0.2931 (0.1762 to 0.4199)	

SOC are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.77 Subgroup analysis by MM type
16.2.7.1.77.1 Treatment emergent adverse event per SOC by treatment group according to MM type - Safety population

	IgG		Non-IgG		
	Kd (N=85)	**IKd (N=124)**	**Kd (N=37)**	**IKd (N=53)**	**p-value of treatment-by-sub group interaction[c]**
24 Months	0.7165 (0.5982 to 0.8056)	0.3907 (0.3032 to 0.4771)	0.7033 (0.5153 to 0.8296)	0.2931 (0.1762 to 0.4199)	
27 Months	0.7165 (0.5982 to 0.8056)	0.3907 (0.3032 to 0.4771)	0.7033 (0.5153 to 0.8296)	0.2931 (0.1762 to 0.4199)	
30 Months	0.7165 (0.5982 to 0.8056)	0.3907 (0.3032 to 0.4771)	0.7033 (0.5153 to 0.8296)	0.2931 (0.1762 to 0.4199)	
Number of patients at risk[b]					
3 Months	79	66	29	23	
6 Months	74	58	25	21	
9 Months	64	52	24	20	
12 Months	59	48	23	16	
15 Months	53	44	23	14	
18 Months	51	40	21	13	
21 Months	42	37	13	9	
24 Months	17	14	3	0	
27 Months	2	1	1	0	
30 Months	0	0	0	0	

SOC are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.77 Subgroup analysis by MM type
16.2.7.1.77.1 Treatment emergent adverse event per SOC by treatment group according to MM type - Safety population

	IgG		Non-IgG		
	Kd (N=85)	**IKd (N=124)**	**Kd (N=37)**	**IKd (N=53)**	**p-value of treatment-by-sub group interaction[c]**
Skin and subcutaneous tissue disorders (days)					
Number (%) of events	14 (16.5)	32 (25.8)	2 (5.4)	17 (32.1)	0.0832
Number (%) of patients censored	71 (83.5)	92 (74.2)	35 (94.6)	36 (67.9)	
Kaplan-Meier estimates of event in months					
25% quantile (95% CI)	NC (10.5133 to NC)	15.3758 (6.3080 to NC)	NC (NC to NC)	11.0390 (1.8070 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.1296		0.0039	
Hazard ratio (95% CI) vs Kd	-	1.62 (0.86 to 3.03)		6.52 (1.51 to 28.23)	
P-value	-	0.1334		0.0122	
Hazard ratio inverted (95% CI) vs IKd			0.15 (0.04 to 0.66)		
Events probability (95% CI)[b]					

SOC are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.77 Subgroup analysis by MM type
16.2.7.1.77.1 Treatment emergent adverse event per SOC by treatment group according to MM type - Safety population

	IgG		Non-IgG		
	Kd (N=85)	**IKd (N=124)**	**Kd (N=37)**	**IKd (N=53)**	**p-value of treatment-by-sub group interaction[c]**
3 Months	0.9291 (0.8490 to 0.9675)	0.9262 (0.8629 to 0.9609)	0.9452 (0.7980 to 0.9860)	0.8491 (0.7208 to 0.9215)	
6 Months	0.8681 (0.7744 to 0.9247)	0.8332 (0.7533 to 0.8890)	0.9452 (0.7980 to 0.9860)	0.8298 (0.6983 to 0.9076)	
9 Months	0.8557 (0.7598 to 0.9154)	0.7898 (0.7049 to 0.8529)	0.9452 (0.7980 to 0.9860)	0.7893 (0.6516 to 0.8775)	
12 Months	0.8429 (0.7448 to 0.9057)	0.7812 (0.6954 to 0.8455)	0.9452 (0.7980 to 0.9860)	0.7253 (0.5797 to 0.8276)	
15 Months	0.8429 (0.7448 to 0.9057)	0.7530 (0.6641 to 0.8215)	0.9452 (0.7980 to 0.9860)	0.6805 (0.5309 to 0.7914)	
18 Months	0.8289 (0.7278 to 0.8951)	0.7336 (0.6427 to 0.8048)	0.9452 (0.7980 to 0.9860)	0.6562 (0.5044 to 0.7716)	
21 Months	0.8289 (0.7278 to 0.8951)	0.7234 (0.6315 to 0.7961)	0.9452 (0.7980 to 0.9860)	0.6562 (0.5044 to 0.7716)	
24 Months	0.8289 (0.7278 to 0.8951)	0.7234 (0.6315 to 0.7961)	0.9452 (0.7980 to 0.9860)	0.6562 (0.5044 to 0.7716)	
27 Months	0.8289 (0.7278 to 0.8951)	0.7234 (0.6315 to 0.7961)	0.9452 (0.7980 to 0.9860)	0.6562 (0.5044 to 0.7716)	

SOC are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.77 Subgroup analysis by MM type
16.2.7.1.77.1 Treatment emergent adverse event per SOC by treatment group according to MM type - Safety population

	IgG		Non-IgG		
	Kd (N=85)	**IKd (N=124)**	**Kd (N=37)**	**IKd (N=53)**	**p-value of treatment-by-sub group interaction[c]**
30 Months	0.8289 (0.7278 to 0.8951)	0.7234 (0.6315 to 0.7961)	0.9452 (0.7980 to 0.9860)	0.6562 (0.5044 to 0.7716)	
Number of patients at risk[b]					
3 Months	78	111	33	45	
6 Months	70	97	31	41	
9 Months	67	91	29	37	
12 Months	65	88	28	34	
15 Months	60	79	27	29	
18 Months	58	72	26	27	
21 Months	49	65	19	21	
24 Months	17	16	7	8	
27 Months	2	1	1	0	
30 Months	0	0	0	0	
Vascular disorders (days)					
Number (%) of events	44 (51.8)	61 (49.2)	10 (27.0)	21 (39.6)	0.2384
Number (%) of patients censored	41 (48.2)	63 (50.8)	27 (73.0)	32 (60.4)	

SOC are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.78 Subgroup analysis by previous autologous stem-cell
16.2.7.1.78.1 Treatment emergent adverse event per SOC by treatment group according to previous autologous stem-cell - Safety population

	Yes		No		
	Kd (N=68)	**IKd (N=115)**	**Kd (N=54)**	**IKd (N=62)**	**p-value of treatment-by-sub group interaction[c]**
27 Months	0	0	1	0	
30 Months	0	0	0	0	
Injury, poisoning and procedural complications (days)					
Number (%) of events	13 (19.1)	77 (67.0)	19 (35.2)	34 (54.8)	0.0058
Number (%) of patients censored	55 (80.9)	38 (33.0)	35 (64.8)	28 (45.2)	
Kaplan-Meier estimates of event in months					
25% quantile (95% CI)	NC (9.0678 to NC)	0.0657 (0.0657 to 0.1314)	7.3922 (1.7741 to 22.3409)	0.2300 (0.0986 to 2.0041)	
Median (95% CI)	NC (NC to NC)	0.2957 (0.1643 to 7.1951)	NC (22.3409 to NC)	8.5092 (2.1355 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (16.0657 to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	<.0001		0.0168	
Hazard ratio (95% CI) vs Kd	-	5.56 (3.08 to 10.05)		1.96 (1.12 to 3.44)	

SOC are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.78 Subgroup analysis by previous autologous stem-cell
16.2.7.1.78.1 Treatment emergent adverse event per SOC by treatment group according to previous autologous stem-cell - Safety population

	Yes		No		
	Kd (N=68)	**IKd (N=115)**	**Kd (N=54)**	**IKd (N=62)**	**p-value of treatment-by-sub group interaction[c]**
P-value	-	<.0001		0.0189	
Hazard ratio inverted (95% CI) vs IKd	0.18 (0.10 to 0.32)		0.51 (0.29 to 0.89)		
Events probability (95% CI)[b]					
3 Months	0.9559 (0.8694 to 0.9856)	0.4514 (0.3588 to 0.5395)	0.8308 (0.7000 to 0.9082)	0.6265 (0.4933 to 0.7339)	
6 Months	0.9255 (0.8302 to 0.9683)	0.4248 (0.3335 to 0.5131)	0.7912 (0.6545 to 0.8786)	0.5412 (0.4083 to 0.6565)	
9 Months	0.8776 (0.7697 to 0.9369)	0.3979 (0.3081 to 0.4861)	0.7100 (0.5652 to 0.8142)	0.4889 (0.3578 to 0.6075)	
12 Months	0.8610 (0.7495 to 0.9253)	0.3527 (0.2661 to 0.4402)	0.6492 (0.5017 to 0.7629)	0.4539 (0.3250 to 0.5741)	
15 Months	0.8441 (0.7291 to 0.9131)	0.3432 (0.2573 to 0.4305)	0.6492 (0.5017 to 0.7629)	0.4539 (0.3250 to 0.5741)	
18 Months	0.8074 (0.6847 to 0.8862)	0.3217 (0.2371 to 0.4091)	0.6492 (0.5017 to 0.7629)	0.4539 (0.3250 to 0.5741)	
21 Months	0.7887 (0.6626 to 0.8720)	0.3217 (0.2371 to 0.4091)	0.6492 (0.5017 to 0.7629)	0.4342 (0.3061 to 0.5555)	

SOC are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.78 Subgroup analysis by previous autologous stem-cell
16.2.7.1.78.1 Treatment emergent adverse event per SOC by treatment group according to previous autologous stem-cell - Safety population

	Yes		No		
	Kd (N=68)	**IKd (N=115)**	**Kd (N=54)**	**IKd (N=62)**	**p-value of treatment-by-sub group interaction[c]**
24 Months	0.7887 (0.6626 to 0.8720)	0.3217 (0.2371 to 0.4091)	0.5992 (0.4300 to 0.7329)	0.4342 (0.3061 to 0.5555)	
27 Months	0.7887 (0.6626 to 0.8720)	0.3217 (0.2371 to 0.4091)	0.5992 (0.4300 to 0.7329)	0.4342 (0.3061 to 0.5555)	
30 Months	0.7887 (0.6626 to 0.8720)	0.3217 (0.2371 to 0.4091)	0.5992 (0.4300 to 0.7329)	0.4342 (0.3061 to 0.5555)	
Number of patients at risk[b]					
3 Months	64	51	44	38	
6 Months	60	48	39	31	
9 Months	53	44	35	28	
12 Months	51	39	31	25	
15 Months	47	34	29	24	
18 Months	44	30	28	23	
21 Months	33	27	22	19	
24 Months	13	6	7	8	
27 Months	1	0	2	1	
30 Months	0	0	0	0	

SOC are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.78 Subgroup analysis by previous autologous stem-cell
16.2.7.1.78.1 Treatment emergent adverse event per SOC by treatment group according to previous autologous stem-cell - Safety population

	Yes		No		
	Kd (N=68)	**IKd (N=115)**	**Kd (N=54)**	**IKd (N=62)**	**p-value of treatment-by-sub group interaction[c]**
27 Months	1	0	2	1	
30 Months	0	0	0	0	
Skin and subcutaneous tissue disorders (days)					
Number (%) of events	12 (17.6)	27 (23.5)	4 (7.4)	22 (35.5)	0.0316
Number (%) of patients censored	56 (82.4)	88 (76.5)	50 (92.6)	40 (64.5)	
Kaplan-Meier estimates of event in months					
25% quantile (95% CI)	NC (5.0924 to NC)	NC (7.3922 to NC)	NC (NC to NC)	7.9507 (4.8296 to 14.8172)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (14.8172 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.3901		0.0004	
Hazard ratio (95% CI) vs Kd	-	1.35 (0.68 to 2.66)		5.50 (1.89 to 15.98)	
P-value	-	0.3919		0.0017	

SOC are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.78 Subgroup analysis by previous autologous stem-cell
16.2.7.1.78.1 Treatment emergent adverse event per SOC by treatment group according to previous autologous stem-cell - Safety population

	Yes		No		
	Kd (N=68)	**IKd (N=115)**	**Kd (N=54)**	**IKd (N=62)**	**p-value of treatment-by-sub group interaction[c]**
Hazard ratio inverted (95% CI) vs IKd			0.18 (0.06 to 0.53)		
Events probability (95% CI)[b]					
3 Months	0.9118 (0.8141 to 0.9594)	0.9036 (0.8328 to 0.9455)	0.9615 (0.8548 to 0.9902)	0.9018 (0.7943 to 0.9547)	
6 Months	0.8509 (0.7406 to 0.9169)	0.8499 (0.7696 to 0.9039)	0.9419 (0.8306 to 0.9809)	0.7967 (0.6694 to 0.8792)	
9 Months	0.8509 (0.7406 to 0.9169)	0.8221 (0.7378 to 0.8814)	0.9210 (0.8028 to 0.9696)	0.7259 (0.5915 to 0.8224)	
12 Months	0.8349 (0.7215 to 0.9051)	0.7939 (0.7062 to 0.8581)	0.9210 (0.8028 to 0.9696)	0.7077 (0.5720 to 0.8073)	
15 Months	0.8349 (0.7215 to 0.9051)	0.7845 (0.6957 to 0.8501)	0.9210 (0.8028 to 0.9696)	0.6289 (0.4881 to 0.7410)	
18 Months	0.8175 (0.7005 to 0.8922)	0.7635 (0.6720 to 0.8327)	0.9210 (0.8028 to 0.9696)	0.6087 (0.4671 to 0.7234)	
21 Months	0.8175 (0.7005 to 0.8922)	0.7526 (0.6597 to 0.8235)	0.9210 (0.8028 to 0.9696)	0.6087 (0.4671 to 0.7234)	
24 Months	0.8175 (0.7005 to 0.8922)	0.7526 (0.6597 to 0.8235)	0.9210 (0.8028 to 0.9696)	0.6087 (0.4671 to 0.7234)	

SOC are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
PGM=DEVOPS/SAR650984/EFC15246/CIR_RWE/REPORT/PGM/ae_km_socpt_subgp_sr_s_t.sas OUT=REPORT/OUTPUT/ae_km_teaesoc_auto_s_t_x.rtf (12FEB2021 8:25)

16.2.7.1 Safety endpoints
16.2.7.1.78 Subgroup analysis by previous autologous stem-cell
16.2.7.1.78.1 Treatment emergent adverse event per SOC by treatment group according to previous autologous stem-cell - Safety population

	Yes		No		
	Kd (N=68)	**IKd (N=115)**	**Kd (N=54)**	**IKd (N=62)**	**p-value of treatment-by-sub group interaction[c]**
27 Months	0.8175 (0.7005 to 0.8922)	0.7526 (0.6597 to 0.8235)	0.9210 (0.8028 to 0.9696)	0.6087 (0.4671 to 0.7234)	
30 Months	0.8175 (0.7005 to 0.8922)	0.7526 (0.6597 to 0.8235)	0.9210 (0.8028 to 0.9696)	0.6087 (0.4671 to 0.7234)	
Number of patients at risk[b]					
3 Months	61	102	50	54	
6 Months	55	93	46	45	
9 Months	53	88	43	40	
12 Months	51	84	42	38	
15 Months	48	77	39	31	
18 Months	46	70	38	29	
21 Months	36	61	32	25	
24 Months	14	17	10	7	
27 Months	1	0	2	1	
30 Months	0	0	0	0	
Vascular disorders (days)					

SOC are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.79 Subgroup analysis by baseline creatinine clearance (MDRD)
16.2.7.1.79.1 Treatment emergent adverse event per SOC by treatment group according to baseline creatinine clearance (MDRD) - Safety population

	>=60 mL/min/1.73m2		<60 mL/min/1.73m2		
	Kd (N=92)	**IKd (N=120)**	**Kd (N=18)**	**IKd (N=43)**	**p-value of treatment-by-sub group interaction[c]**
27 Months	1	0	0	0	
30 Months	0	0	0	0	
Injury, poisoning and procedural complications (days)					
Number (%) of events	26 (28.3)	72 (60.0)	4 (22.2)	28 (65.1)	0.8067
Number (%) of patients censored	66 (71.7)	48 (40.0)	14 (77.8)	15 (34.9)	
Kaplan-Meier estimates of event in months					
25% quantile (95% CI)	12.7146 (7.3922 to NC)	0.0986 (0.0657 to 0.1314)	16.4600 (0.0986 to NC)	0.1314 (0.0657 to 0.6899)	
Median (95% CI)	NC (NC to NC)	2.1355 (0.1643 to 12.6817)	NC (16.4600 to NC)	5.9795 (0.2300 to 17.2485)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (10.4805 to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	<.0001		0.0074	
Hazard ratio (95% CI) vs Kd	-	3.16 (2.01 to 4.96)		3.79 (1.33 to 10.82)	

SOC are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.79 Subgroup analysis by baseline creatinine clearance (MDRD)
16.2.7.1.79.1 Treatment emergent adverse event per SOC by treatment group according to baseline creatinine clearance (MDRD) - Safety population

	>=60 mL/min/1.73m2		<60 mL/min/1.73m2		
	Kd (N=92)	**IKd (N=120)**	**Kd (N=18)**	**IKd (N=43)**	**p-value of treatment-by-sub group interaction[c]**
P-value	-	<.0001		0.0127	
Hazard ratio inverted (95% CI) vs IKd	0.32 (0.20 to 0.50)		0.26 (0.09 to 0.75)		
Events probability (95% CI)[b]					
3 Months	0.9022 (0.8204 to 0.9479)	0.4982 (0.4056 to 0.5839)	0.8854 (0.6139 to 0.9701)	0.5349 (0.3765 to 0.6698)	
6 Months	0.8584 (0.7687 to 0.9152)	0.4638 (0.3723 to 0.5503)	0.8854 (0.6139 to 0.9701)	0.4863 (0.3309 to 0.6250)	
9 Months	0.8025 (0.7049 to 0.8707)	0.4377 (0.3473 to 0.5245)	0.8173 (0.5311 to 0.9377)	0.4376 (0.2868 to 0.5788)	
12 Months	0.7566 (0.6541 to 0.8326)	0.4202 (0.3306 to 0.5071)	0.8173 (0.5311 to 0.9377)	0.3647 (0.2236 to 0.5070)	
15 Months	0.7446 (0.6409 to 0.8225)	0.4111 (0.3219 to 0.4981)	0.8173 (0.5311 to 0.9377)	0.3647 (0.2236 to 0.5070)	
18 Months	0.7320 (0.6269 to 0.8118)	0.4011 (0.3122 to 0.4883)	0.7265 (0.4117 to 0.8913)	0.3386 (0.2014 to 0.4812)	
21 Months	0.7189 (0.6124 to 0.8008)	0.3908 (0.3022 to 0.4782)	0.7265 (0.4117 to 0.8913)	0.3386 (0.2014 to 0.4812)	

SOC are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.79 Subgroup analysis by baseline creatinine clearance (MDRD)
16.2.7.1.79.1 Treatment emergent adverse event per SOC by treatment group according to baseline creatinine clearance (MDRD) - Safety population

	>=60 mL/min/1.73m2		<60 mL/min/1.73m2		
	Kd (N=92)	**IKd (N=120)**	**Kd (N=18)**	**IKd (N=43)**	**p-value of treatment-by-sub group interaction[c]**
24 Months	0.6941 (0.5786 to 0.7838)	0.3908 (0.3022 to 0.4782)	0.7265 (0.4117 to 0.8913)	0.3386 (0.2014 to 0.4812)	
27 Months	0.6941 (0.5786 to 0.7838)	0.3908 (0.3022 to 0.4782)	0.7265 (0.4117 to 0.8913)	0.3386 (0.2014 to 0.4812)	
30 Months	0.6941 (0.5786 to 0.7838)	0.3908 (0.3022 to 0.4782)	0.7265 (0.4117 to 0.8913)	0.3386 (0.2014 to 0.4812)	
Number of patients at risk[b]					
3 Months	83	58	15	23	
6 Months	78	54	13	20	
9 Months	70	50	11	18	
12 Months	64	47	11	15	
15 Months	59	43	10	14	
18 Months	58	39	7	13	
21 Months	43	32	6	13	
24 Months	15	10	2	3	
27 Months	3	1	0	0	
30 Months	0	0	0	0	

SOC are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.79 Subgroup analysis by baseline creatinine clearance (MDRD)
16.2.7.1.79.1 Treatment emergent adverse event per SOC by treatment group according to baseline creatinine clearance (MDRD) - Safety population

	>=60 mL/min/1.73m2		<60 mL/min/1.73m2		
	Kd (N=92)	**IKd (N=120)**	**Kd (N=18)**	**IKd (N=43)**	**p-value of treatment-by-sub group interaction[c]**
Skin and subcutaneous tissue disorders (days)					
Number (%) of events	15 (16.3)	30 (25.0)	0 (0.0)	15 (34.9)	0.9808
Number (%) of patients censored	77 (83.7)	90 (75.0)	18 (100.0)	28 (65.1)	
Kaplan-Meier estimates of event in months					
25% quantile (95% CI)	NC (15.1458 to NC)	14.8172 (7.8850 to NC)	NC (NC to NC)	5.7166 (1.8070 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (18.5298 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.1093		0.0123	
Hazard ratio (95% CI) vs Kd	-	1.65 (0.89 to 3.07)		NC	
P-value	-	0.1131		0.9917	
Events probability (95% CI)[b]					

SOC are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.79 Subgroup analysis by baseline creatinine clearance (MDRD)
16.2.7.1.79.1 Treatment emergent adverse event per SOC by treatment group according to baseline creatinine clearance (MDRD) - Safety population

	>=60 mL/min/1.73m2		<60 mL/min/1.73m2		
	Kd (N=92)	**IKd (N=120)**	**Kd (N=18)**	**IKd (N=43)**	**p-value of treatment-by-sub group interaction[c]**
3 Months	0.9130 (0.8336 to 0.9555)	0.9157 (0.8490 to 0.9537)	1.0000 (1.0000 to 1.0000)	0.8605 (0.7155 to 0.9348)	
6 Months	0.8696 (0.7818 to 0.9237)	0.8628 (0.7857 to 0.9136)	1.0000 (1.0000 to 1.0000)	0.7410 (0.5810 to 0.8474)	
9 Months	0.8584 (0.7687 to 0.9152)	0.8081 (0.7230 to 0.8693)	1.0000 (1.0000 to 1.0000)	0.7171 (0.5557 to 0.8284)	
12 Months	0.8471 (0.7555 to 0.9065)	0.7895 (0.7023 to 0.8538)	1.0000 (1.0000 to 1.0000)	0.6932 (0.5307 to 0.8090)	
15 Months	0.8471 (0.7555 to 0.9065)	0.7498 (0.6580 to 0.8203)	1.0000 (1.0000 to 1.0000)	0.6932 (0.5307 to 0.8090)	
18 Months	0.8347 (0.7406 to 0.8969)	0.7287 (0.6345 to 0.8023)	1.0000 (1.0000 to 1.0000)	0.6675 (0.5036 to 0.7880)	
21 Months	0.8347 (0.7406 to 0.8969)	0.7287 (0.6345 to 0.8023)	1.0000 (1.0000 to 1.0000)	0.6397 (0.4739 to 0.7654)	
24 Months	0.8347 (0.7406 to 0.8969)	0.7287 (0.6345 to 0.8023)	1.0000 (1.0000 to 1.0000)	0.6397 (0.4739 to 0.7654)	
27 Months	0.8347 (0.7406 to 0.8969)	0.7287 (0.6345 to 0.8023)	1.0000 (1.0000 to 1.0000)	0.6397 (0.4739 to 0.7654)	

SOC are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.79 Subgroup analysis by baseline creatinine clearance (MDRD)
16.2.7.1.79.1 Treatment emergent adverse event per SOC by treatment group according to baseline creatinine clearance (MDRD) - Safety population

	>=60 mL/min/1.73m2		<60 mL/min/1.73m2		
	Kd (N=92)	**IKd (N=120)**	**Kd (N=18)**	**IKd (N=43)**	**p-value of treatment-by-sub group interaction[c]**
30 Months	0.8347 (0.7406 to 0.8969)	0.7287 (0.6345 to 0.8023)	1.0000 (1.0000 to 1.0000)	0.6397 (0.4739 to 0.7654)	
Number of patients at risk[b]					
3 Months	84	106	16	37	
6 Months	79	96	14	31	
9 Months	76	87	13	30	
12 Months	73	84	13	29	
15 Months	68	73	12	27	
18 Months	67	67	10	24	
21 Months	52	58	9	21	
24 Months	17	17	4	5	
27 Months	3	1	0	0	
30 Months	0	0	0	0	
Vascular disorders (days)					
Number (%) of events	41 (44.6)	59 (49.2)	8 (44.4)	20 (46.5)	0.2840
Number (%) of patients censored	51 (55.4)	61 (50.8)	10 (55.6)	23 (53.5)	

SOC are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.80 Subgroup analysis by previous treament with PI
16.2.7.1.80.1 Treatment emergent adverse event per SOC by treatment group according to previous treament with PI - Safety population

	Yes		No		
	Kd (N=47)	**IKd (N=79)**	**Kd (N=75)**	**IKd (N=98)**	**p-value of treatment-by-sub group interaction[c]**
27 Months	1	0	0	0	
30 Months	0	0	0	0	
Injury, poisoning and procedural complications (days)					
Number (%) of events	9 (19.1)	48 (60.8)	23 (30.7)	63 (64.3)	0.4196
Number (%) of patients censored	38 (80.9)	31 (39.2)	52 (69.3)	35 (35.7)	
Kaplan-Meier estimates of event in months					
25% quantile (95% CI)	NC (6.4394 to NC)	0.1314 (0.0657 to 0.6242)	9.0678 (5.9466 to NC)	0.0986 (0.0657 to 0.1314)	
Median (95% CI)	NC (NC to NC)	6.5051 (1.6756 to 12.6817)	NC (NC to NC)	0.6899 (0.1643 to 10.2177)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	<.0001		<.0001	
Hazard ratio (95% CI) vs Kd	-	4.63 (2.26 to 9.45)		3.11 (1.92 to 5.02)	

SOC are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.80 Subgroup analysis by previous treament with PI
16.2.7.1.80.1 Treatment emergent adverse event per SOC by treatment group according to previous treament with PI - Safety population

	Yes		No		
	Kd (N=47)	**IKd (N=79)**	**Kd (N=75)**	**IKd (N=98)**	**p-value of treatment-by-sub group interaction[c]**
P-value	-	<.0001		<.0001	
Hazard ratio inverted (95% CI) vs IKd	0.22 (0.11 to 0.44)		0.32 (0.20 to 0.52)		
Events probability (95% CI)[b]					
3 Months	0.9130 (0.7847 to 0.9664)	0.5550 (0.4385 to 0.6567)	0.8931 (0.7976 to 0.9451)	0.4788 (0.3770 to 0.5734)	
6 Months	0.8913 (0.7584 to 0.9533)	0.5014 (0.3861 to 0.6061)	0.8508 (0.7465 to 0.9145)	0.4371 (0.3374 to 0.5325)	
9 Months	0.8690 (0.7314 to 0.9389)	0.4325 (0.3202 to 0.5396)	0.7634 (0.6468 to 0.8460)	0.4267 (0.3276 to 0.5221)	
12 Months	0.8455 (0.7028 to 0.9233)	0.4046 (0.2942 to 0.5121)	0.7185 (0.5977 to 0.8087)	0.3747 (0.2793 to 0.4697)	
15 Months	0.8455 (0.7028 to 0.9233)	0.3901 (0.2807 to 0.4979)	0.7032 (0.5813 to 0.7958)	0.3747 (0.2793 to 0.4697)	
18 Months	0.8191 (0.6696 to 0.9055)	0.3901 (0.2807 to 0.4979)	0.6869 (0.5634 to 0.7820)	0.3497 (0.2557 to 0.4451)	
21 Months	0.8191 (0.6696 to 0.9055)	0.3745 (0.2661 to 0.4826)	0.6701 (0.5453 to 0.7678)	0.3497 (0.2557 to 0.4451)	

SOC are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.80 Subgroup analysis by previous treament with PI
16.2.7.1.80.1 Treatment emergent adverse event per SOC by treatment group according to previous treament with PI - Safety population

	Yes		No		
	Kd (N=47)	**IKd (N=79)**	**Kd (N=75)**	**IKd (N=98)**	**p-value of treatment-by-sub group interaction[c]**
24 Months	0.7606 (0.5650 to 0.8771)	0.3745 (0.2661 to 0.4826)	0.6701 (0.5453 to 0.7678)	0.3497 (0.2557 to 0.4451)	
27 Months	0.7606 (0.5650 to 0.8771)	0.3745 (0.2661 to 0.4826)	0.6701 (0.5453 to 0.7678)	0.3497 (0.2557 to 0.4451)	
30 Months	0.7606 (0.5650 to 0.8771)	0.3745 (0.2661 to 0.4826)	0.6701 (0.5453 to 0.7678)	0.3497 (0.2557 to 0.4451)	
Number of patients at risk[b]					
3 Months	42	43	66	46	
6 Months	40	37	59	42	
9 Months	37	31	51	41	
12 Months	35	28	47	36	
15 Months	32	26	44	32	
18 Months	30	25	42	28	
21 Months	24	20	31	26	
24 Months	8	6	12	8	
27 Months	2	0	1	1	
30 Months	0	0	0	0	

SOC are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.80 Subgroup analysis by previous treament with PI
16.2.7.1.80.1 Treatment emergent adverse event per SOC by treatment group according to previous treament with PI - Safety population

	Yes		No		
	Kd (N=47)	**IKd (N=79)**	**Kd (N=75)**	**IKd (N=98)**	**p-value of treatment-by-sub group interaction[c]**
27 Months	1	0	2	1	
30 Months	0	0	0	0	
Skin and subcutaneous tissue disorders (days)					
Number (%) of events	5 (10.6)	20 (25.3)	11 (14.7)	29 (29.6)	0.7560
Number (%) of patients censored	42 (89.4)	59 (74.7)	64 (85.3)	69 (70.4)	
Kaplan-Meier estimates of event in months					
25% quantile (95% CI)	NC (NC to NC)	14.6201 (5.9138 to NC)	NC (15.1458 to NC)	13.0103 (4.5339 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.0541		0.0311	
Hazard ratio (95% CI) vs Kd	-	2.53 (0.95 to 6.75)		2.11 (1.05 to 4.22)	
P-value	-	0.0631		0.0351	
Hazard ratio inverted (95% CI) vs IKd			0.47 (0.24 to 0.95)		

SOC are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.80 Subgroup analysis by previous treament with PI
16.2.7.1.80.1 Treatment emergent adverse event per SOC by treatment group according to previous treament with PI - Safety population

	Yes		No		
	Kd (N=47)	**IKd (N=79)**	**Kd (N=75)**	**IKd (N=98)**	**p-value of treatment-by-sub group interaction[c]**
Events probability (95% CI)[b]					
3 Months	0.9352 (0.8124 to 0.9786)	0.9234 (0.8373 to 0.9648)	0.9330 (0.8464 to 0.9715)	0.8869 (0.8050 to 0.9357)	
6 Months	0.8907 (0.7570 to 0.9530)	0.8428 (0.7396 to 0.9076)	0.8914 (0.7944 to 0.9442)	0.8233 (0.7311 to 0.8862)	
9 Months	0.8907 (0.7570 to 0.9530)	0.7734 (0.6607 to 0.8528)	0.8768 (0.7764 to 0.9340)	0.8016 (0.7066 to 0.8686)	
12 Months	0.8907 (0.7570 to 0.9530)	0.7594 (0.6452 to 0.8412)	0.8617 (0.7578 to 0.9232)	0.7686 (0.6700 to 0.8412)	
15 Months	0.8907 (0.7570 to 0.9530)	0.7439 (0.6276 to 0.8286)	0.8617 (0.7578 to 0.9232)	0.7225 (0.6193 to 0.8021)	
18 Months	0.8907 (0.7570 to 0.9530)	0.7277 (0.6094 to 0.8155)	0.8454 (0.7376 to 0.9115)	0.6982 (0.5929 to 0.7812)	
21 Months	0.8907 (0.7570 to 0.9530)	0.7277 (0.6094 to 0.8155)	0.8454 (0.7376 to 0.9115)	0.6857 (0.5794 to 0.7704)	
24 Months	0.8907 (0.7570 to 0.9530)	0.7277 (0.6094 to 0.8155)	0.8454 (0.7376 to 0.9115)	0.6857 (0.5794 to 0.7704)	

SOC are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.80 Subgroup analysis by previous treament with PI
16.2.7.1.80.1 Treatment emergent adverse event per SOC by treatment group according to previous treament with PI - Safety population

	Yes		No		
	Kd (N=47)	**IKd (N=79)**	**Kd (N=75)**	**IKd (N=98)**	**p-value of treatment-by-sub group interaction[c]**
27 Months	0.8907 (0.7570 to 0.9530)	0.7277 (0.6094 to 0.8155)	0.8454 (0.7376 to 0.9115)	0.6857 (0.5794 to 0.7704)	
30 Months	0.8907 (0.7570 to 0.9530)	0.7277 (0.6094 to 0.8155)	0.8454 (0.7376 to 0.9115)	0.6857 (0.5794 to 0.7704)	
Number of patients at risk[b]					
3 Months	43	71	68	85	
6 Months	40	62	61	76	
9 Months	38	55	58	73	
12 Months	37	52	56	70	
15 Months	34	47	53	61	
18 Months	33	43	51	56	
21 Months	26	37	42	49	
24 Months	10	9	14	15	
27 Months	2	0	1	1	
30 Months	0	0	0	0	
Vascular disorders (days)					

SOC are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.81 Subgroup analysis by previous treatment with IMiD
16.2.7.1.81.1 Treatment emergent adverse event per SOC by treatment group according to previous treatment with IMiD - Safety population

	Yes		No		
	Kd (N=62)	**IKd (N=80)**	**Kd (N=60)**	**IKd (N=97)**	**p-value of treatment-by-sub group interaction[c]**
27 Months	0	0	1	0	
30 Months	0	0	0	0	
Injury, poisoning and procedural complications (days)					
Number (%) of events	15 (24.2)	56 (70.0)	17 (28.3)	55 (56.7)	0.2634
Number (%) of patients censored	47 (75.8)	24 (30.0)	43 (71.7)	42 (43.3)	
Kaplan-Meier estimates of event in months					
25% quantile (95% CI)	10.8090 (6.4394 to NC)	0.0986 (0.0657 to 0.1643)	16.7228 (5.9466 to NC)	0.1314 (0.0657 to 0.1643)	
Median (95% CI)	NC (NC to NC)	1.6591 (0.1643 to 6.5380)	NC (NC to NC)	8.2793 (0.9199 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (9.5277 to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	<.0001		0.0001	
Hazard ratio (95% CI) vs Kd	-	4.47 (2.52 to 7.93)		2.80 (1.62 to 4.83)	

SOC are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.81 Subgroup analysis by previous treatment with IMiD
16.2.7.1.81.1 Treatment emergent adverse event per SOC by treatment group according to previous treatment with IMiD - Safety population

	Yes		No		
	Kd (N=62)	**IKd (N=80)**	**Kd (N=60)**	**IKd (N=97)**	**p-value of treatment-by-sub group interaction[c]**
P-value	-	<.0001		0.0002	
Hazard ratio inverted (95% CI) vs IKd	0.22 (0.13 to 0.40)		0.36 (0.21 to 0.62)		
Events probability (95% CI)[b]					
3 Months	0.9185 (0.8153 to 0.9653)	0.4750 (0.3626 to 0.5791)	0.8833 (0.7708 to 0.9426)	0.5442 (0.4397 to 0.6373)	
6 Months	0.8835 (0.7708 to 0.9428)	0.3989 (0.2916 to 0.5039)	0.8497 (0.7310 to 0.9188)	0.5225 (0.4182 to 0.6167)	
9 Months	0.7749 (0.6434 to 0.8629)	0.3732 (0.2682 to 0.4779)	0.8320 (0.7101 to 0.9059)	0.4782 (0.3750 to 0.5742)	
12 Months	0.7380 (0.6027 to 0.8333)	0.3088 (0.2110 to 0.4117)	0.7958 (0.6682 to 0.8786)	0.4560 (0.3536 to 0.5525)	
15 Months	0.7380 (0.6027 to 0.8333)	0.2948 (0.1986 to 0.3973)	0.7769 (0.6464 to 0.8641)	0.4560 (0.3536 to 0.5525)	
18 Months	0.7380 (0.6027 to 0.8333)	0.2948 (0.1986 to 0.3973)	0.7360 (0.5994 to 0.8323)	0.4320 (0.3304 to 0.5293)	
21 Months	0.7380 (0.6027 to 0.8333)	0.2948 (0.1986 to 0.3973)	0.7137 (0.5737 to 0.8148)	0.4196 (0.3185 to 0.5173)	

SOC are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.81 Subgroup analysis by previous treatment with IMiD
16.2.7.1.81.1 Treatment emergent adverse event per SOC by treatment group according to previous treatment with IMiD - Safety population

	Yes		No		
	Kd (N=62)	**IKd (N=80)**	**Kd (N=60)**	**IKd (N=97)**	**p-value of treatment-by-sub group interaction[c]**
24 Months	0.7380 (0.6027 to 0.8333)	0.2948 (0.1986 to 0.3973)	0.6691 (0.5073 to 0.7882)	0.4196 (0.3185 to 0.5173)	
27 Months	0.7380 (0.6027 to 0.8333)	0.2948 (0.1986 to 0.3973)	0.6691 (0.5073 to 0.7882)	0.4196 (0.3185 to 0.5173)	
30 Months	0.7380 (0.6027 to 0.8333)	0.2948 (0.1986 to 0.3973)	0.6691 (0.5073 to 0.7882)	0.4196 (0.3185 to 0.5173)	
Number of patients at risk[b]					
3 Months	55	38	53	51	
6 Months	49	31	50	48	
9 Months	42	29	46	43	
12 Months	39	24	43	40	
15 Months	38	19	38	39	
18 Months	37	18	35	35	
21 Months	30	15	25	31	
24 Months	11	8	9	6	
27 Months	2	1	1	0	
30 Months	0	0	0	0	

SOC are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.81 Subgroup analysis by previous treatment with IMiD
16.2.7.1.81.1 Treatment emergent adverse event per SOC by treatment group according to previous treatment with IMiD - Safety population

	Yes		No		
	Kd (N=62)	**IKd (N=80)**	**Kd (N=60)**	**IKd (N=97)**	**p-value of treatment-by-sub group interaction[c]**
27 Months	2	1	1	0	
30 Months	0	0	0	0	
Skin and subcutaneous tissue disorders (days)					
Number (%) of events	7 (11.3)	23 (28.8)	9 (15.0)	26 (26.8)	0.5661
Number (%) of patients censored	55 (88.7)	57 (71.3)	51 (85.0)	71 (73.2)	
Kaplan-Meier estimates of event in months					
25% quantile (95% CI)	NC (NC to NC)	13.0103 (4.8296 to NC)	NC (5.0924 to NC)	16.1643 (6.2094 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.0190		0.0910	
Hazard ratio (95% CI) vs Kd	-	2.65 (1.14 to 6.17)		1.90 (0.89 to 4.06)	
P-value	-	0.0241		0.0966	
Hazard ratio inverted (95% CI) vs IKd	0.38 (0.16 to 0.88)				

SOC are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.81 Subgroup analysis by previous treatment with IMiD
16.2.7.1.81.1 Treatment emergent adverse event per SOC by treatment group according to previous treatment with IMiD - Safety population

	Yes		No		
	Kd (N=62)	**IKd (N=80)**	**Kd (N=60)**	**IKd (N=97)**	**p-value of treatment-by-sub group interaction[c]**
Events probability (95% CI)[b]					
3 Months	0.9669 (0.8742 to 0.9916)	0.9122 (0.8245 to 0.9571)	0.9000 (0.7909 to 0.9538)	0.8956 (0.8145 to 0.9424)	
6 Months	0.9154 (0.8086 to 0.9639)	0.8205 (0.7157 to 0.8896)	0.8660 (0.7499 to 0.9307)	0.8416 (0.7509 to 0.9013)	
9 Months	0.8971 (0.7850 to 0.9525)	0.7808 (0.6711 to 0.8577)	0.8660 (0.7499 to 0.9307)	0.7966 (0.6997 to 0.8653)	
12 Months	0.8780 (0.7606 to 0.9400)	0.7671 (0.6559 to 0.8465)	0.8660 (0.7499 to 0.9307)	0.7625 (0.6617 to 0.8369)	
15 Months	0.8780 (0.7606 to 0.9400)	0.7091 (0.5917 to 0.7983)	0.8660 (0.7499 to 0.9307)	0.7502 (0.6480 to 0.8267)	
18 Months	0.8780 (0.7606 to 0.9400)	0.6937 (0.5749 to 0.7853)	0.8459 (0.7241 to 0.9169)	0.7248 (0.6196 to 0.8053)	
21 Months	0.8780 (0.7606 to 0.9400)	0.6937 (0.5749 to 0.7853)	0.8459 (0.7241 to 0.9169)	0.7116 (0.6050 to 0.7942)	
24 Months	0.8780 (0.7606 to 0.9400)	0.6937 (0.5749 to 0.7853)	0.8459 (0.7241 to 0.9169)	0.7116 (0.6050 to 0.7942)	

SOC are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.81 Subgroup analysis by previous treatment with IMiD
16.2.7.1.81.1 Treatment emergent adverse event per SOC by treatment group according to previous treatment with IMiD - Safety population

	Yes		No		
	Kd (N=62)	**IKd (N=80)**	**Kd (N=60)**	**IKd (N=97)**	**p-value of treatment-by-sub group interaction[c]**
27 Months	0.8780 (0.7606 to 0.9400)	0.6937 (0.5749 to 0.7853)	0.8459 (0.7241 to 0.9169)	0.7116 (0.6050 to 0.7942)	
30 Months	0.8780 (0.7606 to 0.9400)	0.6937 (0.5749 to 0.7853)	0.8459 (0.7241 to 0.9169)	0.7116 (0.6050 to 0.7942)	
Number of patients at risk[b]					
3 Months	57	71	54	85	
6 Months	50	62	51	76	
9 Months	47	58	49	70	
12 Months	45	56	48	66	
15 Months	44	47	43	61	
18 Months	43	44	41	55	
21 Months	36	37	32	49	
24 Months	12	13	12	11	
27 Months	2	1	1	0	
30 Months	0	0	0	0	
Vascular disorders (days)					

SOC are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.82 Subgroup analysis by previous treatment with PI and IMiD
16.2.7.1.82.1 Treatment emergent adverse event per SOC by treatment group according to previous treatment with PI and IMiD - Safety population

	Yes		No		
	Kd (N=17)	**IKd (N=22)**	**Kd (N=105)**	**IKd (N=155)**	**p-value of treatment-by-sub group interaction[c]**
27 Months	0	0	1	0	
30 Months	0	0	0	0	
Injury, poisoning and procedural complications (days)					
Number (%) of events	2 (11.8)	15 (68.2)	30 (28.6)	96 (61.9)	0.2314
Number (%) of patients censored	15 (88.2)	7 (31.8)	75 (71.4)	59 (38.1)	
Kaplan-Meier estimates of event in months					
25% quantile (95% CI)	NC (2.1684 to NC)	0.2957 (0.0329 to 4.6324)	12.7146 (7.2936 to NC)	0.0986 (0.0657 to 0.1314)	
Median (95% CI)	NC (NC to NC)	5.0595 (0.2957 to 12.6817)	NC (NC to NC)	3.1540 (0.1971 to 9.1663)	
75% quantile (95% CI)	NC (NC to NC)	NC (6.5380 to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.0007		<.0001	
Hazard ratio (95% CI) vs Kd	-	8.58 (1.95 to 37.70)		3.18 (2.10 to 4.79)	

SOC are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.82 Subgroup analysis by previous treatment with PI and IMiD
16.2.7.1.82.1 Treatment emergent adverse event per SOC by treatment group according to previous treatment with PI and IMiD - Safety population

	Yes		No		
	Kd (N=17)	**IKd (N=22)**	**Kd (N=105)**	**IKd (N=155)**	**p-value of treatment-by-sub group interaction[c]**
P-value	-	0.0044		<.0001	
Hazard ratio inverted (95% CI) vs IKd	0.12 (0.03 to 0.51)		0.31 (0.21 to 0.48)		
Events probability (95% CI)[b]					
3 Months	0.9375 (0.6323 to 0.9910)	0.5909 (0.3610 to 0.7621)	0.8951 (0.8186 to 0.9405)	0.5019 (0.4206 to 0.5776)	
6 Months	0.9375 (0.6323 to 0.9910)	0.4959 (0.2766 to 0.6819)	0.8558 (0.7721 to 0.9104)	0.4618 (0.3815 to 0.5382)	
9 Months	0.8705 (0.5733 to 0.9660)	0.3967 (0.1954 to 0.5924)	0.7941 (0.7016 to 0.8607)	0.4347 (0.3553 to 0.5114)	
12 Months	0.8705 (0.5733 to 0.9660)	0.3471 (0.1583 to 0.5448)	0.7517 (0.6546 to 0.8251)	0.3940 (0.3163 to 0.4706)	
15 Months	0.8705 (0.5733 to 0.9660)	0.2975 (0.1236 to 0.4951)	0.7407 (0.6425 to 0.8157)	0.3940 (0.3163 to 0.4706)	
18 Months	0.8705 (0.5733 to 0.9660)	0.2975 (0.1236 to 0.4951)	0.7168 (0.6159 to 0.7955)	0.3782 (0.3010 to 0.4550)	
21 Months	0.8705 (0.5733 to 0.9660)	0.2975 (0.1236 to 0.4951)	0.7040 (0.6016 to 0.7847)	0.3702 (0.2932 to 0.4471)	

SOC are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.

16.2.7.1 Safety endpoints
16.2.7.1.82 Subgroup analysis by previous treatment with PI and IMiD
16.2.7.1.82.1 Treatment emergent adverse event per SOC by treatment group according to previous treatment with PI and IMiD - Safety population

	Yes		No		
	Kd (N=17)	**IKd (N=22)**	**Kd (N=105)**	**IKd (N=155)**	**p-value of treatment-by-sub group interaction[c]**
24 Months	0.8705 (0.5733 to 0.9660)	0.2975 (0.1236 to 0.4951)	0.6813 (0.5713 to 0.7687)	0.3702 (0.2932 to 0.4471)	
27 Months	0.8705 (0.5733 to 0.9660)	0.2975 (0.1236 to 0.4951)	0.6813 (0.5713 to 0.7687)	0.3702 (0.2932 to 0.4471)	
30 Months	0.8705 (0.5733 to 0.9660)	0.2975 (0.1236 to 0.4951)	0.6813 (0.5713 to 0.7687)	0.3702 (0.2932 to 0.4471)	
Number of patients at risk[b]					
3 Months	15	13	93	76	
6 Months	14	10	85	69	
9 Months	13	8	75	64	
12 Months	13	7	69	57	
15 Months	13	6	63	52	
18 Months	13	6	59	47	
21 Months	11	5	44	41	
24 Months	4	2	16	12	
27 Months	1	0	2	1	
30 Months	0	0	0	0	

SOC are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.82 Subgroup analysis by previous treatment with PI and IMiD
16.2.7.1.82.1 Treatment emergent adverse event per SOC by treatment group according to previous treatment with PI and IMiD - Safety population

	Yes		No		
	Kd (N=17)	**IKd (N=22)**	**Kd (N=105)**	**IKd (N=155)**	**p-value of treatment-by-sub group interaction[c]**
Skin and subcutaneous tissue disorders (days)					
Number (%) of events	2 (11.8)	6 (27.3)	14 (13.3)	43 (27.7)	0.9382
Number (%) of patients censored	15 (88.2)	16 (72.7)	91 (86.7)	112 (72.3)	
Kaplan-Meier estimates of event in months					
25% quantile (95% CI)	NC (0.5585 to NC)	8.3450 (4.0082 to NC)	NC (NC to NC)	14.6201 (6.7680 to NC)	
Median (95% CI)	NC (NC to NC)	NC (8.3450 to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.3188		0.0083	
Hazard ratio (95% CI) vs Kd	-	2.21 (0.45 to 10.97)		2.21 (1.21 to 4.03)	
P-value	-	0.3314		0.0101	
Hazard ratio inverted (95% CI) vs IKd			0.45 (0.25 to 0.83)		
Events probability (95% CI)[b]					

SOC are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.82 Subgroup analysis by previous treatment with PI and IMiD
16.2.7.1.82.1 Treatment emergent adverse event per SOC by treatment group according to previous treatment with PI and IMiD - Safety population

	Yes		No		
	Kd (N=17)	**IKd (N=22)**	**Kd (N=105)**	**IKd (N=155)**	**p-value of treatment-by-sub group interaction[c]**
3 Months	0.9375 (0.6323 to 0.9910)	1.0000 (1.0000 to 1.0000)	0.9330 (0.8647 to 0.9675)	0.8893 (0.8279 to 0.9297)	
6 Months	0.8705 (0.5733 to 0.9660)	0.8042 (0.5584 to 0.9218)	0.8936 (0.8161 to 0.9397)	0.8353 (0.7661 to 0.8856)	
9 Months	0.8705 (0.5733 to 0.9660)	0.7037 (0.4553 to 0.8548)	0.8833 (0.8035 to 0.9320)	0.8009 (0.7276 to 0.8564)	
12 Months	0.8705 (0.5733 to 0.9660)	0.7037 (0.4553 to 0.8548)	0.8726 (0.7906 to 0.9240)	0.7728 (0.6967 to 0.8321)	
15 Months	0.8705 (0.5733 to 0.9660)	0.7037 (0.4553 to 0.8548)	0.8726 (0.7906 to 0.9240)	0.7353 (0.6557 to 0.7994)	
18 Months	0.8705 (0.5733 to 0.9660)	0.7037 (0.4553 to 0.8548)	0.8608 (0.7759 to 0.9153)	0.7118 (0.6301 to 0.7786)	
21 Months	0.8705 (0.5733 to 0.9660)	0.7037 (0.4553 to 0.8548)	0.8608 (0.7759 to 0.9153)	0.7037 (0.6214 to 0.7714)	
24 Months	0.8705 (0.5733 to 0.9660)	0.7037 (0.4553 to 0.8548)	0.8608 (0.7759 to 0.9153)	0.7037 (0.6214 to 0.7714)	
27 Months	0.8705 (0.5733 to 0.9660)	0.7037 (0.4553 to 0.8548)	0.8608 (0.7759 to 0.9153)	0.7037 (0.6214 to 0.7714)	

SOC are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.82 Subgroup analysis by previous treatment with PI and IMiD
16.2.7.1.82.1 Treatment emergent adverse event per SOC by treatment group according to previous treatment with PI and IMiD - Safety population

	Yes		No		
	Kd (N=17)	**IKd (N=22)**	**Kd (N=105)**	**IKd (N=155)**	**p-value of treatment-by-sub group interaction[c]**
30 Months	0.8705 (0.5733 to 0.9660)	0.7037 (0.4553 to 0.8548)	0.8608 (0.7759 to 0.9153)	0.7037 (0.6214 to 0.7714)	
Number of patients at risk[b]					
3 Months	15	21	96	135	
6 Months	13	16	88	122	
9 Months	13	14	83	114	
12 Months	13	13	80	109	
15 Months	13	12	74	96	
18 Months	13	11	71	88	
21 Months	11	10	57	76	
24 Months	4	2	20	22	
27 Months	1	0	2	1	
30 Months	0	0	0	0	
Vascular disorders (days)					
Number (%) of events	5 (29.4)	10 (45.5)	49 (46.7)	72 (46.5)	0.3847
Number (%) of patients censored	12 (70.6)	12 (54.5)	56 (53.3)	83 (53.5)	

SOC are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.67 Subgroup analysis by age
16.2.7.1.67.3 Treatment emergent adverse event per PT by treatment group according to age - Safety population

	<65 years		>=65 years		
	Kd (N=65)	**IKd (N=87)**	**Kd (N=57)**	**IKd (N=90)**	**p-value of treatment-by-sub group interaction[c]**
6 Months	57	78	50	80	
9 Months	54	75	46	78	
12 Months	53	74	44	75	
15 Months	49	65	43	72	
18 Months	48	62	42	69	
21 Months	34	57	37	60	
24 Months	17	19	10	19	
27 Months	1	0	3	2	
30 Months	0	0	0	0	
Bronchitis (days)					
Number (%) of events	12 (18.5)	18 (20.7)	3 (5.3)	22 (24.4)	0.0355
Number (%) of patients censored	53 (81.5)	69 (79.3)	54 (94.7)	68 (75.6)	
Kaplan-Meier estimates of event in months					
25% quantile (95% CI)	NC (9.7577 to NC)	NC (10.7105 to NC)	NC (NC to NC)	16.9199 (9.1335 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	

PT are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.67 Subgroup analysis by age
16.2.7.1.67.3 Treatment emergent adverse event per PT by treatment group according to age - Safety population

	<65 years		>=65 years		
	Kd (N=65)	**IKd (N=87)**	**Kd (N=57)**	**IKd (N=90)**	**p-value of treatment-by-sub group interaction[c]**
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.7569		0.0031	
Hazard ratio (95% CI) vs Kd	-	1.12 (0.54 to 2.33)		5.12 (1.53 to 17.11)	
P-value	-	0.7571		0.0080	
Hazard ratio inverted (95% CI) vs IKd			0.20 (0.06 to 0.65)		
Events probability (95% CI)[b]					
3 Months	0.9536 (0.8630 to 0.9848)	0.9537 (0.8814 to 0.9824)	0.9818 (0.8779 to 0.9974)	0.9439 (0.8705 to 0.9763)	
6 Months	0.9062 (0.8030 to 0.9567)	0.8946 (0.8071 to 0.9437)	0.9818 (0.8779 to 0.9974)	0.8857 (0.7978 to 0.9368)	
9 Months	0.8735 (0.7628 to 0.9347)	0.8700 (0.7775 to 0.9259)	0.9818 (0.8779 to 0.9974)	0.8496 (0.7549 to 0.9098)	
12 Months	0.8231 (0.7030 to 0.8980)	0.8203 (0.7195 to 0.8877)	0.9618 (0.8554 to 0.9903)	0.7764 (0.6718 to 0.8513)	

PT are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.67 Subgroup analysis by age
16.2.7.1.67.3 Treatment emergent adverse event per PT by treatment group according to age - Safety population

	<65 years		>=65 years		
	Kd (N=65)	**IKd (N=87)**	**Kd (N=57)**	**IKd (N=90)**	**p-value of treatment-by-sub group interaction[c]**
15 Months	0.8231 (0.7030 to 0.8980)	0.8203 (0.7195 to 0.8877)	0.9413 (0.8286 to 0.9807)	0.7639 (0.6579 to 0.8409)	
18 Months	0.8231 (0.7030 to 0.8980)	0.7764 (0.6677 to 0.8533)	0.9413 (0.8286 to 0.9807)	0.7375 (0.6287 to 0.8190)	
21 Months	0.8231 (0.7030 to 0.8980)	0.7764 (0.6677 to 0.8533)	0.9413 (0.8286 to 0.9807)	0.7375 (0.6287 to 0.8190)	
24 Months	0.7937 (0.6599 to 0.8795)	0.7764 (0.6677 to 0.8533)	0.9413 (0.8286 to 0.9807)	0.7375 (0.6287 to 0.8190)	
27 Months	0.7937 (0.6599 to 0.8795)	0.7764 (0.6677 to 0.8533)	0.9413 (0.8286 to 0.9807)	0.7375 (0.6287 to 0.8190)	
30 Months	0.7937 (0.6599 to 0.8795)	0.7764 (0.6677 to 0.8533)	0.9413 (0.8286 to 0.9807)	0.7375 (0.6287 to 0.8190)	
Number of patients at risk[b]					
3 Months	61	81	54	84	
6 Months	56	74	52	74	
9 Months	52	70	49	70	
12 Months	48	65	47	62	
15 Months	44	59	44	58	

PT are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.67 Subgroup analysis by age
16.2.7.1.67.3 Treatment emergent adverse event per PT by treatment group according to age - Safety population

	<65 years		>=65 years		
	Kd (N=65)	**IKd (N=87)**	**Kd (N=57)**	**IKd (N=90)**	**p-value of treatment-by-sub group interaction[c]**
18 Months	43	53	43	53	
21 Months	30	48	37	44	
24 Months	15	15	9	15	
27 Months	1	0	3	1	
30 Months	0	0	0	0	
Cataract (days)					
Number (%) of events	5 (7.7)	4 (4.6)	3 (5.3)	11 (12.2)	0.1621
Number (%) of patients censored	60 (92.3)	83 (95.4)	54 (94.7)	79 (87.8)	
Kaplan-Meier estimates of event in months					
25% quantile (95% CI)	NC (22.1437 to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.4123		0.2218	

PT are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.67 Subgroup analysis by age
16.2.7.1.67.3 Treatment emergent adverse event per PT by treatment group according to age - Safety population

	<65 years		>=65 years		
	Kd (N=65)	**IKd (N=87)**	**Kd (N=57)**	**IKd (N=90)**	**p-value of treatment-by-sub group interaction[c]**
30 Months	0.7121 (0.4143 to 0.8774)	0.8821 (0.7850 to 0.9370)	0.8865 (0.7642 to 0.9475)	0.9155 (0.8306 to 0.9588)	
Number of patients at risk[b]					
3 Months	63	84	53	86	
6 Months	58	82	50	81	
9 Months	55	76	46	76	
12 Months	50	75	43	73	
15 Months	46	65	42	69	
18 Months	45	60	41	66	
21 Months	32	54	35	57	
24 Months	14	19	9	18	
27 Months	0	0	2	0	
30 Months	0	0	0	0	
Infusion related reaction (days)					
Number (%) of events	2 (3.1)	48 (55.2)	2 (3.5)	31 (34.4)	0.4670
Number (%) of patients censored	63 (96.9)	39 (44.8)	55 (96.5)	59 (65.6)	

PT are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.67 Subgroup analysis by age
16.2.7.1.67.3 Treatment emergent adverse event per PT by treatment group according to age - Safety population

	<65 years		>=65 years		
	Kd (N=65)	**IKd (N=87)**	**Kd (N=57)**	**IKd (N=90)**	**p-value of treatment-by-sub group interaction[c]**
Kaplan-Meier estimates of event in months					
25% quantile (95% CI)	NC (NC to NC)	0.0986 (0.0657 to 0.1314)	NC (NC to NC)	0.1314 (0.0986 to 19.3840)	
Median (95% CI)	NC (NC to NC)	0.2300 (0.1643 to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	<.0001		<.0001	
Hazard ratio (95% CI) vs Kd	-	24.77 (6.01 to 102.09)		11.35 (2.72 to 47.46)	
P-value	-	<.0001		0.0009	
Hazard ratio inverted (95% CI) vs IKd	0.04 (0.01 to 0.17)		0.09 (0.02 to 0.37)		
Events probability (95% CI)[b]					
3 Months	0.9692 (0.8825 to 0.9922)	0.4828 (0.3747 to 0.5826)	0.9649 (0.8669 to 0.9911)	0.6663 (0.5587 to 0.7534)	

PT are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.67 Subgroup analysis by age
16.2.7.1.67.3 Treatment emergent adverse event per PT by treatment group according to age - Safety population

	<65 years		>=65 years		
	Kd (N=65)	**IKd (N=87)**	**Kd (N=57)**	**IKd (N=90)**	**p-value of treatment-by-sub group interaction[c]**
6 Months	0.9692 (0.8825 to 0.9922)	0.4713 (0.3637 to 0.5714)	0.9649 (0.8669 to 0.9911)	0.6663 (0.5587 to 0.7534)	
9 Months	0.9692 (0.8825 to 0.9922)	0.4713 (0.3637 to 0.5714)	0.9649 (0.8669 to 0.9911)	0.6663 (0.5587 to 0.7534)	
12 Months	0.9692 (0.8825 to 0.9922)	0.4713 (0.3637 to 0.5714)	0.9649 (0.8669 to 0.9911)	0.6663 (0.5587 to 0.7534)	
15 Months	0.9692 (0.8825 to 0.9922)	0.4595 (0.3525 to 0.5599)	0.9649 (0.8669 to 0.9911)	0.6663 (0.5587 to 0.7534)	
18 Months	0.9692 (0.8825 to 0.9922)	0.4595 (0.3525 to 0.5599)	0.9649 (0.8669 to 0.9911)	0.6663 (0.5587 to 0.7534)	
21 Months	0.9692 (0.8825 to 0.9922)	0.4451 (0.3383 to 0.5464)	0.9649 (0.8669 to 0.9911)	0.6524 (0.5435 to 0.7414)	
24 Months	0.9692 (0.8825 to 0.9922)	0.4451 (0.3383 to 0.5464)	0.9649 (0.8669 to 0.9911)	0.6524 (0.5435 to 0.7414)	
27 Months	0.9692 (0.8825 to 0.9922)	0.4451 (0.3383 to 0.5464)	0.9649 (0.8669 to 0.9911)	0.6524 (0.5435 to 0.7414)	
30 Months	0.9692 (0.8825 to 0.9922)	0.4451 (0.3383 to 0.5464)	0.9649 (0.8669 to 0.9911)	0.6524 (0.5435 to 0.7414)	

PT are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.67 Subgroup analysis by age
16.2.7.1.67.3 Treatment emergent adverse event per PT by treatment group according to age - Safety population

	<65 years		>=65 years		
	Kd (N=65)	**IKd (N=87)**	**Kd (N=57)**	**IKd (N=90)**	**p-value of treatment-by-sub group interaction[c]**
Number of patients at risk[b]					
3 Months	62	42	54	58	
6 Months	59	41	52	56	
9 Months	56	41	49	55	
12 Months	55	40	48	54	
15 Months	51	34	46	51	
18 Months	50	32	45	48	
21 Months	36	29	39	39	
24 Months	17	10	11	13	
27 Months	1	0	3	1	
30 Months	0	0	0	0	
Insomnia (days)					
Number (%) of events	13 (20.0)	20 (23.0)	15 (26.3)	22 (24.4)	0.5682
Number (%) of patients censored	52 (80.0)	67 (77.0)	42 (73.7)	68 (75.6)	
Kaplan-Meier estimates of event in months					
25% quantile (95% CI)	NC (3.9754 to NC)	NC (4.9281 to NC)	12.2875 (1.4456 to NC)	17.0513 (10.0862 to NC)	

PT are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.67 Subgroup analysis by age
16.2.7.1.67.3 Treatment emergent adverse event per PT by treatment group according to age - Safety population

	<65 years		>=65 years		
	Kd (N=65)	**IKd (N=87)**	**Kd (N=57)**	**IKd (N=90)**	**p-value of treatment-by-sub group interaction[c]**
18 Months	51	64	45	68	
21 Months	37	59	39	59	
24 Months	17	18	11	18	
27 Months	1	0	3	1	
30 Months	0	0	0	0	
Thrombocytopenia (days)					
Number (%) of events	8 (12.3)	3 (3.4)	4 (7.0)	2 (2.2)	0.8780
Number (%) of patients censored	57 (87.7)	84 (96.6)	53 (93.0)	88 (97.8)	
Kaplan-Meier estimates of event in months					
25% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.0358		0.1556	

PT are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.67 Subgroup analysis by age
16.2.7.1.67.3 Treatment emergent adverse event per PT by treatment group according to age - Safety population

	<65 years		>=65 years		
	Kd (N=65)	**IKd (N=87)**	**Kd (N=57)**	**IKd (N=90)**	**p-value of treatment-by-sub group interaction[c]**
Hazard ratio (95% CI) vs Kd	-	0.27 (0.07 to 1.00)		0.31 (0.06 to 1.71)	
P-value	-	0.0507		0.1793	
Events probability (95% CI)[b]					
3 Months	0.9228 (0.8244 to 0.9671)	0.9885 (0.9212 to 0.9984)	0.9825 (0.8819 to 0.9975)	0.9888 (0.9229 to 0.9984)	
6 Months	0.8756 (0.7666 to 0.9358)	0.9885 (0.9212 to 0.9984)	0.9825 (0.8819 to 0.9975)	0.9888 (0.9229 to 0.9984)	
9 Months	0.8756 (0.7666 to 0.9358)	0.9885 (0.9212 to 0.9984)	0.9454 (0.8400 to 0.9821)	0.9888 (0.9229 to 0.9984)	
12 Months	0.8756 (0.7666 to 0.9358)	0.9761 (0.9079 to 0.9940)	0.9454 (0.8400 to 0.9821)	0.9888 (0.9229 to 0.9984)	
15 Months	0.8756 (0.7666 to 0.9358)	0.9761 (0.9079 to 0.9940)	0.9454 (0.8400 to 0.9821)	0.9888 (0.9229 to 0.9984)	
18 Months	0.8756 (0.7666 to 0.9358)	0.9761 (0.9079 to 0.9940)	0.9244 (0.8103 to 0.9710)	0.9756 (0.9054 to 0.9939)	
21 Months	0.8756 (0.7666 to 0.9358)	0.9614 (0.8841 to 0.9875)	0.9244 (0.8103 to 0.9710)	0.9756 (0.9054 to 0.9939)	

PT are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.67 Subgroup analysis by age
16.2.7.1.67.3 Treatment emergent adverse event per PT by treatment group according to age - Safety population

	<65 years		>=65 years		
	Kd (N=65)	**IKd (N=87)**	**Kd (N=57)**	**IKd (N=90)**	**p-value of treatment-by-sub group interaction[c]**
24 Months	0.8756 (0.7666 to 0.9358)	0.9614 (0.8841 to 0.9875)	0.9244 (0.8103 to 0.9710)	0.9756 (0.9054 to 0.9939)	
27 Months	0.8756 (0.7666 to 0.9358)	0.9614 (0.8841 to 0.9875)	0.9244 (0.8103 to 0.9710)	0.9756 (0.9054 to 0.9939)	
30 Months	0.8756 (0.7666 to 0.9358)	0.9614 (0.8841 to 0.9875)	0.9244 (0.8103 to 0.9710)	0.9756 (0.9054 to 0.9939)	
Number of patients at risk[b]					
3 Months	59	84	55	87	
6 Months	54	83	53	82	
9 Months	51	80	48	80	
12 Months	51	78	47	78	
15 Months	48	70	45	75	
18 Months	47	66	43	71	
21 Months	34	60	37	61	
24 Months	16	20	11	19	
27 Months	1	0	3	2	
30 Months	0	0	0	0	

PT are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.67 Subgroup analysis by age
16.2.7.1.67.3 Treatment emergent adverse event per PT by treatment group according to age - Safety population

	<65 years		>=65 years		
	Kd (N=65)	**IKd (N=87)**	**Kd (N=57)**	**IKd (N=90)**	**p-value of treatment-by-sub group interaction[c]**
30 Months	0.9488 (0.8487 to 0.9833)	0.9572 (0.8706 to 0.9863)	0.9549 (0.8308 to 0.9886)	0.8774 (0.7836 to 0.9322)	
Number of patients at risk[b]					
3 Months	63	85	55	85	
6 Months	59	83	53	79	
9 Months	56	78	50	75	
12 Months	55	78	49	72	
15 Months	51	70	46	69	
18 Months	49	66	45	66	
21 Months	37	61	38	55	
24 Months	17	18	10	16	
27 Months	1	0	2	1	
30 Months	0	0	0	0	
Upper respiratory tract infection (days)					
Number (%) of events	14 (21.5)	28 (32.2)	15 (26.3)	36 (40.0)	0.9312
Number (%) of patients censored	51 (78.5)	59 (67.8)	42 (73.7)	54 (60.0)	

PT are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.67 Subgroup analysis by age
16.2.7.1.67.3 Treatment emergent adverse event per PT by treatment group according to age - Safety population

	<65 years		>=65 years		
	Kd (N=65)	**IKd (N=87)**	**Kd (N=57)**	**IKd (N=90)**	**p-value of treatment-by-sub group interaction[c]**
Kaplan-Meier estimates of event in months					
25% quantile (95% CI)	NC (8.3778 to NC)	11.6304 (6.3737 to 17.3142)	11.1376 (3.8768 to NC)	5.5524 (3.6140 to 10.5791)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (13.2402 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.1611		0.1111	
Hazard ratio (95% CI) vs Kd	-	1.58 (0.83 to 2.99)		1.62 (0.89 to 2.97)	
P-value	-	0.1648		0.1147	
Events probability (95% CI)[b]					
3 Months	0.9538 (0.8637 to 0.9849)	0.9078 (0.8240 to 0.9528)	0.8924 (0.7760 to 0.9502)	0.8867 (0.7996 to 0.9374)	
6 Months	0.8902 (0.7833 to 0.9461)	0.8483 (0.7531 to 0.9090)	0.8374 (0.7106 to 0.9119)	0.7216 (0.6138 to 0.8041)	

PT are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.67 Subgroup analysis by age
16.2.7.1.67.3 Treatment emergent adverse event per PT by treatment group according to age - Safety population

	<65 years		>=65 years		
	Kd (N=65)	**IKd (N=87)**	**Kd (N=57)**	**IKd (N=90)**	**p-value of treatment-by-sub group interaction[c]**
9 Months	0.8559 (0.7411 to 0.9224)	0.7745 (0.6692 to 0.8499)	0.7815 (0.6473 to 0.8697)	0.6727 (0.5620 to 0.7613)	
12 Months	0.8385 (0.7201 to 0.9098)	0.7357 (0.6264 to 0.8176)	0.7415 (0.6022 to 0.8382)	0.6358 (0.5236 to 0.7283)	
15 Months	0.7650 (0.6345 to 0.8541)	0.6816 (0.5677 to 0.7714)	0.7415 (0.6022 to 0.8382)	0.5979 (0.4848 to 0.6939)	
18 Months	0.7650 (0.6345 to 0.8541)	0.6510 (0.5342 to 0.7453)	0.7197 (0.5776 to 0.8210)	0.5710 (0.4573 to 0.6694)	
21 Months	0.7650 (0.6345 to 0.8541)	0.6510 (0.5342 to 0.7453)	0.7197 (0.5776 to 0.8210)	0.5710 (0.4573 to 0.6694)	
24 Months	0.7650 (0.6345 to 0.8541)	0.6510 (0.5342 to 0.7453)	0.7197 (0.5776 to 0.8210)	0.5710 (0.4573 to 0.6694)	
27 Months	0.7650 (0.6345 to 0.8541)	0.6510 (0.5342 to 0.7453)	0.7197 (0.5776 to 0.8210)	0.5710 (0.4573 to 0.6694)	
30 Months	0.7650 (0.6345 to 0.8541)	0.6510 (0.5342 to 0.7453)	0.7197 (0.5776 to 0.8210)	0.5710 (0.4573 to 0.6694)	
Number of patients at risk[b]					
3 Months	61	77	49	78	

PT are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.67 Subgroup analysis by age
16.2.7.1.67.3 Treatment emergent adverse event per PT by treatment group according to age - Safety population

	<65 years		>=65 years		
	Kd (N=65)	**IKd (N=87)**	**Kd (N=57)**	**IKd (N=90)**	**p-value of treatment-by-sub group interaction[c]**
6 Months	54	70	45	60	
9 Months	49	61	39	55	
12 Months	47	57	36	51	
15 Months	40	47	34	45	
18 Months	39	42	33	42	
21 Months	29	38	28	37	
24 Months	13	14	8	8	
27 Months	1	0	2	1	
30 Months	0	0	0	0	
Urinary tract infection (days)					
Number (%) of events	4 (6.2)	7 (8.0)	7 (12.3)	5 (5.6)	0.2011
Number (%) of patients censored	61 (93.8)	80 (92.0)	50 (87.7)	85 (94.4)	
Kaplan-Meier estimates of event in months					
25% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (18.0041 to NC)	NC (NC to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	

PT are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.68 Subgroup analysis by gender
16.2.7.1.68.2 Treatment emergent adverse event per PT by treatment group according to gender - Safety population

	Male		Female		
	Kd (N=68)	**IKd (N=99)**	**Kd (N=54)**	**IKd (N=78)**	**p-value of treatment-by-sub group interaction[c]**
18 Months	50	68	40	63	
21 Months	37	61	34	56	
24 Months	14	19	13	19	
27 Months	1	1	3	1	
30 Months	0	0	0	0	
Bronchitis (days)					
Number (%) of events	6 (8.8)	20 (20.2)	9 (16.7)	20 (25.6)	0.5278
Number (%) of patients censored	62 (91.2)	79 (79.8)	45 (83.3)	58 (74.4)	
Kaplan-Meier estimates of event in months					
25% quantile (95% CI)	NC (NC to NC)	NC (11.2361 to NC)	NC (9.7577 to NC)	17.5113 (9.1335 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.0546		0.2201	

PT are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.68 Subgroup analysis by gender
16.2.7.1.68.2 Treatment emergent adverse event per PT by treatment group according to gender - Safety population

	Male		Female		
	Kd (N=68)	**IKd (N=99)**	**Kd (N=54)**	**IKd (N=78)**	**p-value of treatment-by-sub group interaction[c]**
Hazard ratio (95% CI) vs Kd	-	2.38 (0.96 to 5.93)		1.63 (0.74 to 3.58)	
P-value	-	0.0624		0.2248	
Events probability (95% CI)[b]					
3 Months	0.9853 (0.9002 to 0.9979)	0.9492 (0.8822 to 0.9785)	0.9444 (0.8376 to 0.9817)	0.9482 (0.8679 to 0.9802)	
6 Months	0.9699 (0.8849 to 0.9924)	0.8963 (0.8157 to 0.9428)	0.9074 (0.7917 to 0.9604)	0.8824 (0.7861 to 0.9370)	
9 Months	0.9535 (0.8624 to 0.9848)	0.8625 (0.7748 to 0.9179)	0.8885 (0.7685 to 0.9483)	0.8558 (0.7547 to 0.9175)	
12 Months	0.9188 (0.8153 to 0.9655)	0.8055 (0.7087 to 0.8729)	0.8499 (0.7220 to 0.9220)	0.7890 (0.6787 to 0.8650)	
15 Months	0.9011 (0.7925 to 0.9545)	0.8055 (0.7087 to 0.8729)	0.8499 (0.7220 to 0.9220)	0.7751 (0.6633 to 0.8538)	
18 Months	0.9011 (0.7925 to 0.9545)	0.7799 (0.6791 to 0.8524)	0.8499 (0.7220 to 0.9220)	0.7295 (0.6120 to 0.8166)	
21 Months	0.9011 (0.7925 to 0.9545)	0.7799 (0.6791 to 0.8524)	0.8499 (0.7220 to 0.9220)	0.7295 (0.6120 to 0.8166)	

PT are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
PGM=DEVOPS/SAR650984/EFC15246/CIR_RWE/REPORT/PGM/ae_km_socpt_subgp_sr_s_t.sas OUT=REPORT/OUTPUT/ae_km_teaept_sex_s_t_x.rtf (12FEB2021 8:25)

16.2.7.1 Safety endpoints
16.2.7.1.68 Subgroup analysis by gender
16.2.7.1.68.2 Treatment emergent adverse event per PT by treatment group according to gender - Safety population

	Male		Female		
	Kd (N=68)	**IKd (N=99)**	**Kd (N=54)**	**IKd (N=78)**	**p-value of treatment-by-sub group interaction[c]**
24 Months	0.9011 (0.7925 to 0.9545)	0.7799 (0.6791 to 0.8524)	0.8172 (0.6722 to 0.9025)	0.7295 (0.6120 to 0.8166)	
27 Months	0.9011 (0.7925 to 0.9545)	0.7799 (0.6791 to 0.8524)	0.8172 (0.6722 to 0.9025)	0.7295 (0.6120 to 0.8166)	
30 Months	0.9011 (0.7925 to 0.9545)	0.7799 (0.6791 to 0.8524)	0.8172 (0.6722 to 0.9025)	0.7295 (0.6120 to 0.8166)	
Number of patients at risk[b]					
3 Months	64	92	51	73	
6 Months	59	81	49	67	
9 Months	55	76	46	64	
12 Months	52	70	43	57	
15 Months	49	65	39	52	
18 Months	48	59	38	47	
21 Months	35	51	32	41	
24 Months	13	17	11	13	
27 Months	1	1	3	0	
30 Months	0	0	0	0	

PT are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.68 Subgroup analysis by gender
16.2.7.1.68.2 Treatment emergent adverse event per PT by treatment group according to gender - Safety population

	Male		Female		
	Kd (N=68)	**IKd (N=99)**	**Kd (N=54)**	**IKd (N=78)**	**p-value of treatment-by-sub group interaction[c]**
21 Months	34	56	33	55	
24 Months	12	19	11	18	
27 Months	1	0	1	0	
30 Months	0	0	0	0	
Infusion related reaction (days)					
Number (%) of events	3 (4.4)	51 (51.5)	1 (1.9)	28 (35.9)	0.7327
Number (%) of patients censored	65 (95.6)	48 (48.5)	53 (98.1)	50 (64.1)	
Kaplan-Meier estimates of event in months					
25% quantile (95% CI)	NC (NC to NC)	0.0986 (0.0657 to 0.1314)	NC (NC to NC)	0.1314 (0.0657 to 0.2957)	
Median (95% CI)	NC (NC to NC)	18.9240 (0.1643 to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	<.0001		<.0001	

PT are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.68 Subgroup analysis by gender
16.2.7.1.68.2 Treatment emergent adverse event per PT by treatment group according to gender - Safety population

	Male		Female		
	Kd (N=68)	**IKd (N=99)**	**Kd (N=54)**	**IKd (N=78)**	**p-value of treatment-by-sub group interaction[c]**
Hazard ratio (95% CI) vs Kd	-	15.26 (4.76 to 48.94)		23.32 (3.17 to 171.49)	
P-value	-	<.0001		0.0020	
Hazard ratio inverted (95% CI) vs IKd	0.07 (0.02 to 0.21)		0.04 (0.01 to 0.32)		
Events probability (95% CI)[b]					
3 Months	0.9557 (0.8688 to 0.9855)	0.5150 (0.4126 to 0.6080)	0.9815 (0.8757 to 0.9974)	0.6538 (0.5372 to 0.7479)	
6 Months	0.9557 (0.8688 to 0.9855)	0.5150 (0.4126 to 0.6080)	0.9815 (0.8757 to 0.9974)	0.6408 (0.5238 to 0.7361)	
9 Months	0.9557 (0.8688 to 0.9855)	0.5150 (0.4126 to 0.6080)	0.9815 (0.8757 to 0.9974)	0.6408 (0.5238 to 0.7361)	
12 Months	0.9557 (0.8688 to 0.9855)	0.5150 (0.4126 to 0.6080)	0.9815 (0.8757 to 0.9974)	0.6408 (0.5238 to 0.7361)	
15 Months	0.9557 (0.8688 to 0.9855)	0.5040 (0.4018 to 0.5976)	0.9815 (0.8757 to 0.9974)	0.6408 (0.5238 to 0.7361)	
18 Months	0.9557 (0.8688 to 0.9855)	0.5040 (0.4018 to 0.5976)	0.9815 (0.8757 to 0.9974)	0.6408 (0.5238 to 0.7361)	
21 Months	0.9557 (0.8688 to 0.9855)	0.4768 (0.3738 to 0.5726)	0.9815 (0.8757 to 0.9974)	0.6408 (0.5238 to 0.7361)	

PT are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.68 Subgroup analysis by gender
16.2.7.1.68.2 Treatment emergent adverse event per PT by treatment group according to gender - Safety population

	Male		Female		
	Kd (N=68)	**IKd (N=99)**	**Kd (N=54)**	**IKd (N=78)**	**p-value of treatment-by-sub group interaction[c]**
24 Months	0.9557 (0.8688 to 0.9855)	0.4768 (0.3738 to 0.5726)	0.9815 (0.8757 to 0.9974)	0.6408 (0.5238 to 0.7361)	
27 Months	0.9557 (0.8688 to 0.9855)	0.4768 (0.3738 to 0.5726)	0.9815 (0.8757 to 0.9974)	0.6408 (0.5238 to 0.7361)	
30 Months	0.9557 (0.8688 to 0.9855)	0.4768 (0.3738 to 0.5726)	0.9815 (0.8757 to 0.9974)	0.6408 (0.5238 to 0.7361)	
Number of patients at risk[b]					
3 Months	63	50	53	50	
6 Months	58	48	53	49	
9 Months	55	48	50	48	
12 Months	54	47	49	47	
15 Months	52	41	45	44	
18 Months	51	37	44	43	
21 Months	38	30	37	38	
24 Months	15	11	13	12	
27 Months	1	1	3	0	
30 Months	0	0	0	0	

PT are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.68 Subgroup analysis by gender
16.2.7.1.68.2 Treatment emergent adverse event per PT by treatment group according to gender - Safety population

	Male		Female		
	Kd (N=68)	**IKd (N=99)**	**Kd (N=54)**	**IKd (N=78)**	**p-value of treatment-by-sub group interaction[c]**
6 Months	58	90	49	75	
9 Months	54	87	45	73	
12 Months	54	85	44	71	
15 Months	52	78	41	67	
18 Months	50	72	40	65	
21 Months	37	63	34	58	
24 Months	15	21	12	18	
27 Months	1	1	3	1	
30 Months	0	0	0	0	
Traumatic fracture (days)					
Number (%) of events	1 (1.5)	5 (5.1)	4 (7.4)	8 (10.3)	0.4664
Number (%) of patients censored	67 (98.5)	94 (94.9)	50 (92.6)	70 (89.7)	
Kaplan-Meier estimates of event in months					
25% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	

PT are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.68 Subgroup analysis by gender
16.2.7.1.68.2 Treatment emergent adverse event per PT by treatment group according to gender - Safety population

	Male		Female		
	Kd (N=68)	**IKd (N=99)**	**Kd (N=54)**	**IKd (N=78)**	**p-value of treatment-by-sub group interaction[c]**
21 Months	40	63	35	53	
24 Months	16	20	11	14	
27 Months	1	1	2	0	
30 Months	0	0	0	0	
Upper respiratory tract infection (days)					
Number (%) of events	19 (27.9)	36 (36.4)	10 (18.5)	28 (35.9)	0.2744
Number (%) of patients censored	49 (72.1)	63 (63.6)	44 (81.5)	50 (64.1)	
Kaplan-Meier estimates of event in months					
25% quantile (95% CI)	12.5832 (5.8480 to NC)	8.6735 (4.2382 to 12.8789)	NC (7.4908 to NC)	6.8008 (4.0082 to 13.3717)	
Median (95% CI)	NC (NC to NC)	NC (16.3285 to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.3221		0.0300	

PT are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.68 Subgroup analysis by gender
16.2.7.1.68.2 Treatment emergent adverse event per PT by treatment group according to gender - Safety population

	Male		Female		
	Kd (N=68)	**IKd (N=99)**	**Kd (N=54)**	**IKd (N=78)**	**p-value of treatment-by-sub group interaction[c]**
Hazard ratio (95% CI) vs Kd	-	1.32 (0.76 to 2.31)		2.18 (1.06 to 4.49)	
P-value	-	0.3237		0.0343	
Hazard ratio inverted (95% CI) vs IKd			0.46 (0.22 to 0.94)		
Events probability (95% CI)[b]					
3 Months	0.9099 (0.8104 to 0.9585)	0.8871 (0.8054 to 0.9359)	0.9444 (0.8376 to 0.9817)	0.9092 (0.8190 to 0.9557)	
6 Months	0.8299 (0.7136 to 0.9022)	0.8009 (0.7056 to 0.8682)	0.9074 (0.7917 to 0.9604)	0.7650 (0.6531 to 0.8449)	
9 Months	0.7801 (0.6566 to 0.8637)	0.7440 (0.6423 to 0.8207)	0.8700 (0.7465 to 0.9358)	0.6980 (0.5813 to 0.7880)	
12 Months	0.7801 (0.6566 to 0.8637)	0.6977 (0.5923 to 0.7807)	0.8107 (0.6763 to 0.8934)	0.6704 (0.5521 to 0.7639)	
15 Months	0.7066 (0.5739 to 0.8048)	0.6375 (0.5288 to 0.7276)	0.8107 (0.6763 to 0.8934)	0.6418 (0.5223 to 0.7388)	
18 Months	0.6875 (0.5530 to 0.7890)	0.5969 (0.4858 to 0.6915)	0.8107 (0.6763 to 0.8934)	0.6266 (0.5062 to 0.7254)	
21 Months	0.6875 (0.5530 to 0.7890)	0.5969 (0.4858 to 0.6915)	0.8107 (0.6763 to 0.8934)	0.6266 (0.5062 to 0.7254)	

PT are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.68 Subgroup analysis by gender
16.2.7.1.68.2 Treatment emergent adverse event per PT by treatment group according to gender - Safety population

	Male		Female		
	Kd (N=68)	**IKd (N=99)**	**Kd (N=54)**	**IKd (N=78)**	**p-value of treatment-by-sub group interaction[c]**
24 Months	0.6875 (0.5530 to 0.7890)	0.5969 (0.4858 to 0.6915)	0.8107 (0.6763 to 0.8934)	0.6266 (0.5062 to 0.7254)	
27 Months	0.6875 (0.5530 to 0.7890)	0.5969 (0.4858 to 0.6915)	0.8107 (0.6763 to 0.8934)	0.6266 (0.5062 to 0.7254)	
30 Months	0.6875 (0.5530 to 0.7890)	0.5969 (0.4858 to 0.6915)	0.8107 (0.6763 to 0.8934)	0.6266 (0.5062 to 0.7254)	
Number of patients at risk[b]					
3 Months	59	85	51	70	
6 Months	50	72	49	58	
9 Months	44	65	44	51	
12 Months	43	60	40	48	
15 Months	37	49	37	43	
18 Months	35	43	37	41	
21 Months	26	37	31	38	
24 Months	10	11	11	11	
27 Months	1	0	2	1	
30 Months	0	0	0	0	

PT are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.69 Subgroup analysis by ethnic origin
16.2.7.1.69.2 Treatment emergent adverse event per PT by treatment group according to ethnic origin - Safety population

	White		Other		
	Kd (N=83)	**IKd (N=130)**	**Kd (N=27)**	**IKd (N=33)**	**p-value of treatment-by-sub group interaction[c]**
18 Months	61	99	21	24	
21 Months	44	86	20	24	
24 Months	16	28	8	8	
27 Months	1	1	3	1	
30 Months	0	0	0	0	
Bronchitis (days)					
Number (%) of events	10 (12.0)	29 (22.3)	1 (3.7)	3 (9.1)	0.8374
Number (%) of patients censored	73 (88.0)	101 (77.7)	26 (96.3)	30 (90.9)	
Kaplan-Meier estimates of event in months					
25% quantile (95% CI)	NC (NC to NC)	NC (9.7577 to NC)	NC (NC to NC)	NC (6.3080 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.0573		0.3942	

PT are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.69 Subgroup analysis by ethnic origin
16.2.7.1.69.2 Treatment emergent adverse event per PT by treatment group according to ethnic origin - Safety population

	White		Other		
	Kd (N=83)	**IKd (N=130)**	**Kd (N=27)**	**IKd (N=33)**	**p-value of treatment-by-sub group interaction[c]**
Hazard ratio (95% CI) vs Kd	-	1.98 (0.97 to 4.07)		2.58 (0.27 to 24.81)	
P-value	-	0.0622		0.4117	
Events probability (95% CI)[b]					
3 Months	0.9630 (0.8896 to 0.9879)	0.9458 (0.8896 to 0.9738)	1.0000 (1.0000 to 1.0000)	0.9688 (0.7982 to 0.9955)	
6 Months	0.9383 (0.8580 to 0.9738)	0.8736 (0.8019 to 0.9206)	1.0000 (1.0000 to 1.0000)	0.9375 (0.7725 to 0.9840)	
9 Months	0.9256 (0.8418 to 0.9659)	0.8488 (0.7731 to 0.9008)	0.9615 (0.7569 to 0.9945)	0.9052 (0.7340 to 0.9684)	
12 Months	0.8995 (0.8090 to 0.9485)	0.7900 (0.7069 to 0.8520)	0.9615 (0.7569 to 0.9945)	0.9052 (0.7340 to 0.9684)	
15 Months	0.8861 (0.7924 to 0.9391)	0.7816 (0.6976 to 0.8448)	0.9615 (0.7569 to 0.9945)	0.9052 (0.7340 to 0.9684)	
18 Months	0.8861 (0.7924 to 0.9391)	0.7631 (0.6769 to 0.8291)	0.9615 (0.7569 to 0.9945)	0.9052 (0.7340 to 0.9684)	
21 Months	0.8861 (0.7924 to 0.9391)	0.7631 (0.6769 to 0.8291)	0.9615 (0.7569 to 0.9945)	0.9052 (0.7340 to 0.9684)	

PT are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.69 Subgroup analysis by ethnic origin
16.2.7.1.69.2 Treatment emergent adverse event per PT by treatment group according to ethnic origin - Safety population

	White		Other		
	Kd (N=83)	**IKd (N=130)**	**Kd (N=27)**	**IKd (N=33)**	**p-value of treatment-by-sub group interaction[c]**
24 Months	0.8615 (0.7521 to 0.9249)	0.7631 (0.6769 to 0.8291)	0.9615 (0.7569 to 0.9945)	0.9052 (0.7340 to 0.9684)	
27 Months	0.8615 (0.7521 to 0.9249)	0.7631 (0.6769 to 0.8291)	0.9615 (0.7569 to 0.9945)	0.9052 (0.7340 to 0.9684)	
30 Months	0.8615 (0.7521 to 0.9249)	0.7631 (0.6769 to 0.8291)	0.9615 (0.7569 to 0.9945)	0.9052 (0.7340 to 0.9684)	
Number of patients at risk[b]					
3 Months	78	121	27	31	
6 Months	74	107	26	29	
9 Months	71	101	23	28	
12 Months	67	94	23	27	
15 Months	63	88	20	23	
18 Months	61	81	20	22	
21 Months	43	68	19	22	
24 Months	15	22	8	8	
27 Months	1	0	3	1	
30 Months	0	0	0	0	

PT are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.69 Subgroup analysis by ethnic origin
16.2.7.1.69.2 Treatment emergent adverse event per PT by treatment group according to ethnic origin - Safety population

	White		Other		
	Kd (N=83)	**IKd (N=130)**	**Kd (N=27)**	**IKd (N=33)**	**p-value of treatment-by-sub group interaction[c]**
18 Months	60	98	18	18	
21 Months	43	85	17	17	
24 Months	14	29	6	6	
27 Months	1	0	1	0	
30 Months	0	0	0	0	
Infusion related reaction (days)					
Number (%) of events	3 (3.6)	55 (42.3)	1 (3.7)	16 (48.5)	0.8771
Number (%) of patients censored	80 (96.4)	75 (57.7)	26 (96.3)	17 (51.5)	
Kaplan-Meier estimates of event in months					
25% quantile (95% CI)	NC (NC to NC)	0.0986 (0.0657 to 0.1314)	NC (NC to NC)	0.0986 (0.0657 to 0.1314)	
Median (95% CI)	NC (NC to NC)	NC (18.9240 to NC)	NC (NC to NC)	NC (0.1314 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	<.0001		0.0002	

PT are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.69 Subgroup analysis by ethnic origin
16.2.7.1.69.2 Treatment emergent adverse event per PT by treatment group according to ethnic origin - Safety population

	White		Other		
	Kd (N=83)	**IKd (N=130)**	**Kd (N=27)**	**IKd (N=33)**	**p-value of treatment-by-sub group interaction[c]**
Hazard ratio (95% CI) vs Kd	-	14.34 (4.48 to 45.87)		17.10 (2.26 to 129.22)	
P-value	-	<.0001		0.0059	
Hazard ratio inverted (95% CI) vs IKd	0.07 (0.02 to 0.22)		0.06 (0.01 to 0.44)		
Events probability (95% CI)[b]					
3 Months	0.9639 (0.8921 to 0.9882)	0.5921 (0.5025 to 0.6709)	0.9630 (0.7649 to 0.9947)	0.5152 (0.3354 to 0.6685)	
6 Months	0.9639 (0.8921 to 0.9882)	0.5921 (0.5025 to 0.6709)	0.9630 (0.7649 to 0.9947)	0.5152 (0.3354 to 0.6685)	
9 Months	0.9639 (0.8921 to 0.9882)	0.5921 (0.5025 to 0.6709)	0.9630 (0.7649 to 0.9947)	0.5152 (0.3354 to 0.6685)	
12 Months	0.9639 (0.8921 to 0.9882)	0.5921 (0.5025 to 0.6709)	0.9630 (0.7649 to 0.9947)	0.5152 (0.3354 to 0.6685)	
15 Months	0.9639 (0.8921 to 0.9882)	0.5921 (0.5025 to 0.6709)	0.9630 (0.7649 to 0.9947)	0.5152 (0.3354 to 0.6685)	
18 Months	0.9639 (0.8921 to 0.9882)	0.5921 (0.5025 to 0.6709)	0.9630 (0.7649 to 0.9947)	0.5152 (0.3354 to 0.6685)	

PT are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.69 Subgroup analysis by ethnic origin
16.2.7.1.69.2 Treatment emergent adverse event per PT by treatment group according to ethnic origin - Safety population

	White		Other		
	Kd (N=83)	**IKd (N=130)**	**Kd (N=27)**	**IKd (N=33)**	**p-value of treatment-by-sub group interaction[c]**
21 Months	0.9639 (0.8921 to 0.9882)	0.5736 (0.4833 to 0.6539)	0.9630 (0.7649 to 0.9947)	0.5152 (0.3354 to 0.6685)	
24 Months	0.9639 (0.8921 to 0.9882)	0.5736 (0.4833 to 0.6539)	0.9630 (0.7649 to 0.9947)	0.5152 (0.3354 to 0.6685)	
27 Months	0.9639 (0.8921 to 0.9882)	0.5736 (0.4833 to 0.6539)	0.9630 (0.7649 to 0.9947)	0.5152 (0.3354 to 0.6685)	
30 Months	0.9639 (0.8921 to 0.9882)	0.5736 (0.4833 to 0.6539)	0.9630 (0.7649 to 0.9947)	0.5152 (0.3354 to 0.6685)	
Number of patients at risk[b]					
3 Months	79	75	26	17	
6 Months	77	74	25	17	
9 Months	74	73	23	17	
12 Months	72	73	23	16	
15 Months	69	68	20	14	
18 Months	67	64	20	13	
21 Months	49	53	19	13	
24 Months	18	18	7	4	

PT are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.69 Subgroup analysis by ethnic origin
16.2.7.1.69.2 Treatment emergent adverse event per PT by treatment group according to ethnic origin - Safety population

	White		Other		
	Kd (N=83)	**IKd (N=130)**	**Kd (N=27)**	**IKd (N=33)**	**p-value of treatment-by-sub group interaction[c]**
27 Months	1	0	3	1	
30 Months	0	0	0	0	
Insomnia (days)					
Number (%) of events	18 (21.7)	26 (20.0)	8 (29.6)	11 (33.3)	0.6013
Number (%) of patients censored	65 (78.3)	104 (80.0)	19 (70.4)	22 (66.7)	
Kaplan-Meier estimates of event in months					
25% quantile (95% CI)	NC (2.8583 to NC)	NC (10.3162 to NC)	9.5606 (0.3614 to NC)	7.5893 (1.1170 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (13.5688 to NC)	NC (12.3860 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.6791		0.7396	
Hazard ratio (95% CI) vs Kd	-	0.88 (0.48 to 1.61)		1.17 (0.47 to 2.90)	
P-value	-	0.6793		0.7398	

PT are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.69 Subgroup analysis by ethnic origin
16.2.7.1.69.2 Treatment emergent adverse event per PT by treatment group according to ethnic origin - Safety population

	White		Other		
	Kd (N=83)	**IKd (N=130)**	**Kd (N=27)**	**IKd (N=33)**	**p-value of treatment-by-sub group interaction[c]**
30 Months	0.9618 (0.8863 to 0.9875)	0.9597 (0.9059 to 0.9830)	1.0000 (1.0000 to 1.0000)	1.0000 (1.0000 to 1.0000)	
Number of patients at risk[b]					
3 Months	80	126	27	32	
6 Months	78	117	26	31	
9 Months	73	113	24	30	
12 Months	71	113	24	29	
15 Months	69	108	21	25	
18 Months	67	102	21	24	
21 Months	49	88	20	24	
24 Months	17	28	8	8	
27 Months	1	0	3	1	
30 Months	0	0	0	0	
Thrombocytopenia (days)					
Number (%) of events	9 (10.8)	3 (2.3)	2 (7.4)	0 (0.0)	0.9932
Number (%) of patients censored	74 (89.2)	127 (97.7)	25 (92.6)	33 (100.0)	

PT are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.69 Subgroup analysis by ethnic origin
16.2.7.1.69.2 Treatment emergent adverse event per PT by treatment group according to ethnic origin - Safety population

	White		Other		
	Kd (N=83)	**IKd (N=130)**	**Kd (N=27)**	**IKd (N=33)**	**p-value of treatment-by-sub group interaction[c]**
Kaplan-Meier estimates of event in months					
25% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (6.5051 to NC)	NC (NC to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.0092		0.1194	
Hazard ratio (95% CI) vs Kd	-	0.21 (0.06 to 0.77)		NC	
P-value	-	0.0185		0.9977	
Events probability (95% CI)[b]					
3 Months	0.9393 (0.8603 to 0.9743)	0.9846 (0.9397 to 0.9961)	1.0000 (1.0000 to 1.0000)	1.0000 (1.0000 to 1.0000)	
6 Months	0.9149 (0.8298 to 0.9585)	0.9846 (0.9397 to 0.9961)	0.9630 (0.7649 to 0.9947)	1.0000 (1.0000 to 1.0000)	

PT are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.69 Subgroup analysis by ethnic origin
16.2.7.1.69.2 Treatment emergent adverse event per PT by treatment group according to ethnic origin - Safety population

	White		Other		
	Kd (N=83)	**IKd (N=130)**	**Kd (N=27)**	**IKd (N=33)**	**p-value of treatment-by-sub group interaction[c]**
9 Months	0.9025 (0.8145 to 0.9500)	0.9846 (0.9397 to 0.9961)	0.9244 (0.7302 to 0.9806)	1.0000 (1.0000 to 1.0000)	
12 Months	0.9025 (0.8145 to 0.9500)	0.9761 (0.9278 to 0.9923)	0.9244 (0.7302 to 0.9806)	1.0000 (1.0000 to 1.0000)	
15 Months	0.9025 (0.8145 to 0.9500)	0.9761 (0.9278 to 0.9923)	0.9244 (0.7302 to 0.9806)	1.0000 (1.0000 to 1.0000)	
18 Months	0.8889 (0.7971 to 0.9406)	0.9761 (0.9278 to 0.9923)	0.9244 (0.7302 to 0.9806)	1.0000 (1.0000 to 1.0000)	
21 Months	0.8889 (0.7971 to 0.9406)	0.9761 (0.9278 to 0.9923)	0.9244 (0.7302 to 0.9806)	1.0000 (1.0000 to 1.0000)	
24 Months	0.8889 (0.7971 to 0.9406)	0.9761 (0.9278 to 0.9923)	0.9244 (0.7302 to 0.9806)	1.0000 (1.0000 to 1.0000)	
27 Months	0.8889 (0.7971 to 0.9406)	0.9761 (0.9278 to 0.9923)	0.9244 (0.7302 to 0.9806)	1.0000 (1.0000 to 1.0000)	
30 Months	0.8889 (0.7971 to 0.9406)	0.9761 (0.9278 to 0.9923)	0.9244 (0.7302 to 0.9806)	1.0000 (1.0000 to 1.0000)	
Number of patients at risk[b]					
3 Months	77	125	27	32	

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CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.69 Subgroup analysis by ethnic origin
16.2.7.1.69.2 Treatment emergent adverse event per PT by treatment group according to ethnic origin - Safety population

	White		Other		
	Kd (N=83)	**IKd (N=130)**	**Kd (N=27)**	**IKd (N=33)**	**p-value of treatment-by-sub group interaction[c]**
6 Months	74	121	25	31	
9 Months	70	117	22	30	
12 Months	69	116	22	29	
15 Months	66	110	20	25	
18 Months	63	104	20	24	
21 Months	45	90	19	24	
24 Months	16	29	8	8	
27 Months	1	1	3	1	
30 Months	0	0	0	0	
Traumatic fracture (days)					
Number (%) of events	5 (6.0)	9 (6.9)	0 (0.0)	2 (6.1)	0.9919
Number (%) of patients censored	78 (94.0)	121 (93.1)	27 (100.0)	31 (93.9)	
Kaplan-Meier estimates of event in months					
25% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (21.4867 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	

PT are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.69 Subgroup analysis by ethnic origin
16.2.7.1.69.2 Treatment emergent adverse event per PT by treatment group according to ethnic origin - Safety population

	White		Other		
	Kd (N=83)	**IKd (N=130)**	**Kd (N=27)**	**IKd (N=33)**	**p-value of treatment-by-sub group interaction[c]**
21 Months	48	85	20	23	
24 Months	16	25	8	7	
27 Months	0	0	3	1	
30 Months	0	0	0	0	
Upper respiratory tract infection (days)					
Number (%) of events	22 (26.5)	49 (37.7)	7 (25.9)	15 (45.5)	0.5508
Number (%) of patients censored	61 (73.5)	81 (62.3)	20 (74.1)	18 (54.5)	
Kaplan-Meier estimates of event in months					
25% quantile (95% CI)	11.1376 (5.8480 to NC)	6.8008 (4.0411 to 11.6304)	15.7372 (4.2053 to NC)	6.5051 (2.1684 to 13.3717)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (15.7372 to NC)	NC (8.4764 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.1189		0.1011	

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CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.69 Subgroup analysis by ethnic origin
16.2.7.1.69.2 Treatment emergent adverse event per PT by treatment group according to ethnic origin - Safety population

	White		Other		
	Kd (N=83)	**IKd (N=130)**	**Kd (N=27)**	**IKd (N=33)**	**p-value of treatment-by-sub group interaction[c]**
Hazard ratio (95% CI) vs Kd	-	1.49 (0.90 to 2.46)		2.08 (0.85 to 5.12)	
P-value	-	0.1214		0.1089	
Events probability (95% CI)[b]					
3 Months	0.9024 (0.8142 to 0.9499)	0.8907 (0.8224 to 0.9338)	0.9630 (0.7649 to 0.9947)	0.8759 (0.7022 to 0.9515)	
6 Months	0.8275 (0.7260 to 0.8940)	0.7612 (0.6764 to 0.8266)	0.9259 (0.7350 to 0.9809)	0.7820 (0.5964 to 0.8896)	
9 Months	0.7761 (0.6683 to 0.8527)	0.7111 (0.6226 to 0.7825)	0.8873 (0.6899 to 0.9622)	0.6517 (0.4593 to 0.7900)	
12 Months	0.7494 (0.6386 to 0.8306)	0.6597 (0.5684 to 0.7362)	0.8470 (0.6415 to 0.9398)	0.6517 (0.4593 to 0.7900)	
15 Months	0.7216 (0.6081 to 0.8074)	0.6159 (0.5230 to 0.6960)	0.7573 (0.5348 to 0.8839)	0.5865 (0.3959 to 0.7355)	
18 Months	0.7216 (0.6081 to 0.8074)	0.5967 (0.5030 to 0.6784)	0.7100 (0.4825 to 0.8513)	0.5083 (0.3186 to 0.6701)	
21 Months	0.7216 (0.6081 to 0.8074)	0.5967 (0.5030 to 0.6784)	0.7100 (0.4825 to 0.8513)	0.5083 (0.3186 to 0.6701)	

PT are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.69 Subgroup analysis by ethnic origin
16.2.7.1.69.2 Treatment emergent adverse event per PT by treatment group according to ethnic origin - Safety population

	White		Other		
	Kd (N=83)	**IKd (N=130)**	**Kd (N=27)**	**IKd (N=33)**	**p-value of treatment-by-sub group interaction[c]**
24 Months	0.7216 (0.6081 to 0.8074)	0.5967 (0.5030 to 0.6784)	0.7100 (0.4825 to 0.8513)	0.5083 (0.3186 to 0.6701)	
27 Months	0.7216 (0.6081 to 0.8074)	0.5967 (0.5030 to 0.6784)	0.7100 (0.4825 to 0.8513)	0.5083 (0.3186 to 0.6701)	
30 Months	0.7216 (0.6081 to 0.8074)	0.5967 (0.5030 to 0.6784)	0.7100 (0.4825 to 0.8513)	0.5083 (0.3186 to 0.6701)	
Number of patients at risk[b]					
3 Months	73	113	26	28	
6 Months	65	93	25	24	
9 Months	58	83	22	20	
12 Months	54	77	21	20	
15 Months	50	67	16	15	
18 Months	49	61	15	13	
21 Months	36	53	14	13	
24 Months	13	16	5	4	
27 Months	0	1	3	0	
30 Months	0	0	0	0	

PT are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
PGM=DEVOPS/SAR650984/EFC15246/CIR_RWE/REPORT/PGM/ae_km_socpt_subgp_sr_s_t.sas OUT=REPORT/OUTPUT/ae_km_teaept_race_s_t_x.rtf (12FEB2021 8:25)

16.2.7.1 Safety endpoints
16.2.7.1.70 Subgroup analysis by geographical region
16.2.7.1.70.3 Treatment emergent adverse event per PT by treatment group according to geographical region - Safety population

	Europe		America		Asia		Other countries		
	Pd (N=60)	IPd (N=85)	Pd (N=20)	IPd (N=23)	Pd (N=20)	IPd (N=24)	Pd (N=22)	IPd (N=45)	p-value of treatment-by-subgroup interaction[c]
9 Months	45	72	18	21	17	22	20	38	
12 Months	42	70	18	20	17	21	20	38	
15 Months	41	66	17	17	14	18	20	36	
18 Months	41	64	15	16	14	17	20	34	
21 Months	33	57	10	13	13	17	15	30	
24 Months	13	18	2	1	7	8	5	11	
27 Months	0	1	0	0	3	1	1	0	
30 Months	0	0	0	0	0	0	0	0	
Bronchitis (days)									
Number (%) of events	14 (23.3)	29 (34.1)	0 (0.0)	2 (8.7)	1 (5.0)	2 (8.3)	0 (0.0)	7 (15.6)	0.9999
Number (%) of patients censored	46 (76.7)	56 (65.9)	20 (100.0)	21 (91.3)	19 (95.0)	22 (91.7)	22 (100.0)	38 (84.4)	

PT are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.70 Subgroup analysis by geographical region
16.2.7.1.70.3 Treatment emergent adverse event per PT by treatment group according to geographical region - Safety population

	Europe		America		Asia		Other countries		
	Pd (N=60)	**IPd (N=85)**	**Pd (N=20)**	**IPd (N=23)**	**Pd (N=20)**	**IPd (N=24)**	**Pd (N=22)**	**IPd (N=45)**	**p-value of treatment-by-subgroup interaction[c]**
Kaplan-Meier estimates of event in months									
25% quantile (95% CI)	21.7495 (8.3778 to NC)	11.2361 (6.6366 to 17.5113)	NC (NC to NC)	NC (2.6283 to NC)	NC (6.1766 to NC)	NC (1.9713 to NC)	NC (NC to NC)	NC (10.7105 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd									
Log-Rank test p-value[a] vs Kd	-	0.2018		0.1728		0.6581		0.0520	
Hazard ratio (95% CI) vs Kd	-	1.51 (0.80 to 2.86)		NC		1.71 (0.15 to 18.85)		NC	

PT are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.70 Subgroup analysis by geographical region
16.2.7.1.70.3 Treatment emergent adverse event per PT by treatment group according to geographical region - Safety population

	Europe		America		Asia		Other countries		
	Pd (N=60)	**IPd (N=85)**	**Pd (N=20)**	**IPd (N=23)**	**Pd (N=20)**	**IPd (N=24)**	**Pd (N=22)**	**IPd (N=45)**	**p-value of treatment-by-subgroup interaction[c]**
P-value	-	0.2051		0.9977		0.6620		0.9939	
Events probability (95% CI)[b]									
3 Months	0.9313 (0.8271 to 0.9736)	0.9286 (0.8478 to 0.9673)	1.0000 (1.0000 to 1.0000)	0.9545 (0.7187 to 0.9935)	1.0000 (1.0000 to 1.0000)	0.9583 (0.7392 to 0.9940)	1.0000 (1.0000 to 1.0000)	0.9778 (0.8525 to 0.9968)	
6 Months	0.8779 (0.7606 to 0.9399)	0.8661 (0.7711 to 0.9236)	1.0000 (1.0000 to 1.0000)	0.9545 (0.7187 to 0.9935)	1.0000 (1.0000 to 1.0000)	0.9167 (0.7061 to 0.9785)	1.0000 (1.0000 to 1.0000)	0.8873 (0.7501 to 0.9515)	
9 Months	0.8592 (0.7378 to 0.9270)	0.8024 (0.6976 to 0.8741)	1.0000 (1.0000 to 1.0000)	0.9545 (0.7187 to 0.9935)	0.9474 (0.6812 to 0.9924)	0.9167 (0.7061 to 0.9785)	1.0000 (1.0000 to 1.0000)	0.8873 (0.7501 to 0.9515)	
12 Months	0.7845 (0.6513 to 0.8716)	0.6998 (0.5861 to 0.7879)	1.0000 (1.0000 to 1.0000)	0.9068 (0.6758 to 0.9759)	0.9474 (0.6812 to 0.9924)	0.9167 (0.7061 to 0.9785)	1.0000 (1.0000 to 1.0000)	0.8627 (0.7192 to 0.9359)	

PT are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.

16.2.7.1 Safety endpoints
16.2.7.1.70 Subgroup analysis by geographical region
16.2.7.1.70.3 Treatment emergent adverse event per PT by treatment group according to geographical region - Safety population

	Europe		America		Asia		Other countries		
	Pd (N=60)	IPd (N=85)	Pd (N=20)	IPd (N=23)	Pd (N=20)	IPd (N=24)	Pd (N=22)	IPd (N=45)	p-value of treatment-by-subgroup interaction[c]
15 Months	0.7649 (0.6291 to 0.8564)	0.6866 (0.5721 to 0.7764)	1.0000 (1.0000 to 1.0000)	0.9068 (0.6758 to 0.9759)	0.9474 (0.6812 to 0.9924)	0.9167 (0.7061 to 0.9785)	1.0000 (1.0000 to 1.0000)	0.8627 (0.7192 to 0.9359)	
18 Months	0.7649 (0.6291 to 0.8564)	0.6294 (0.5114 to 0.7264)	1.0000 (1.0000 to 1.0000)	0.9068 (0.6758 to 0.9759)	0.9474 (0.6812 to 0.9924)	0.9167 (0.7061 to 0.9785)	1.0000 (1.0000 to 1.0000)	0.8357 (0.6849 to 0.9184)	
21 Months	0.7649 (0.6291 to 0.8564)	0.6294 (0.5114 to 0.7264)	1.0000 (1.0000 to 1.0000)	0.9068 (0.6758 to 0.9759)	0.9474 (0.6812 to 0.9924)	0.9167 (0.7061 to 0.9785)	1.0000 (1.0000 to 1.0000)	0.8357 (0.6849 to 0.9184)	
24 Months	0.7301 (0.5799 to 0.8339)	0.6294 (0.5114 to 0.7264)	1.0000 (1.0000 to 1.0000)	0.9068 (0.6758 to 0.9759)	0.9474 (0.6812 to 0.9924)	0.9167 (0.7061 to 0.9785)	1.0000 (1.0000 to 1.0000)	0.8357 (0.6849 to 0.9184)	
27 Months	0.7301 (0.5799 to 0.8339)	0.6294 (0.5114 to 0.7264)	1.0000 (1.0000 to 1.0000)	0.9068 (0.6758 to 0.9759)	0.9474 (0.6812 to 0.9924)	0.9167 (0.7061 to 0.9785)	1.0000 (1.0000 to 1.0000)	0.8357 (0.6849 to 0.9184)	

PT are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.70 Subgroup analysis by geographical region
16.2.7.1.70.3 Treatment emergent adverse event per PT by treatment group according to geographical region - Safety population

	Europe		America		Asia		Other countries		
	Pd (N=60)	**IPd (N=85)**	**Pd (N=20)**	**IPd (N=23)**	**Pd (N=20)**	**IPd (N=24)**	**Pd (N=22)**	**IPd (N=45)**	**p-value of treatment-by-subgroup interaction[c]**
30 Months	0.7301 (0.5799 to 0.8339)	0.6294 (0.5114 to 0.7264)	1.0000 (1.0000 to 1.0000)	0.9068 (0.6758 to 0.9759)	0.9474 (0.6812 to 0.9924)	0.9167 (0.7061 to 0.9785)	1.0000 (1.0000 to 1.0000)	0.8357 (0.6849 to 0.9184)	
Number of patients at risk[b]									
3 Months	53	77	20	21	20	23	22	44	
6 Months	47	68	20	21	19	21	22	38	
9 Months	46	63	19	20	16	21	20	36	
12 Months	40	53	19	19	16	20	20	35	
15 Months	37	50	18	17	13	17	20	33	
18 Months	37	44	16	16	13	16	20	30	
21 Months	29	38	11	12	12	16	15	26	
24 Months	10	12	2	1	7	8	5	9	
27 Months	0	0	0	0	3	1	1	0	
30 Months	0	0	0	0	0	0	0	0	

PT are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.70 Subgroup analysis by geographical region
16.2.7.1.70.3 Treatment emergent adverse event per PT by treatment group according to geographical region - Safety population

	Europe		America		Asia		Other countries		
	Pd (N=60)	IPd (N=85)	Pd (N=20)	IPd (N=23)	Pd (N=20)	IPd (N=24)	Pd (N=22)	IPd (N=45)	p-value of treatment-by-subgroup interaction[c]
9 Months	50	72	18	20	16	21	17	39	
12 Months	46	70	16	19	15	20	16	39	
15 Months	45	67	15	15	13	16	15	36	
18 Months	45	64	13	14	13	14	15	34	
21 Months	35	58	9	10	12	13	11	30	
24 Months	12	19	2	1	6	6	3	11	
27 Months	0	0	0	0	1	0	1	0	
30 Months	0	0	0	0	0	0	0	0	
Infusion related reaction (days)									
Number (%) of events	2 (3.3)	34 (40.0)	0 (0.0)	8 (34.8)	1 (5.0)	10 (41.7)	1 (4.5)	27 (60.0)	0.9817
Number (%) of patients censored	58 (96.7)	51 (60.0)	20 (100.0)	15 (65.2)	19 (95.0)	14 (58.3)	21 (95.5)	18 (40.0)	

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CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.70 Subgroup analysis by geographical region
16.2.7.1.70.3 Treatment emergent adverse event per PT by treatment group according to geographical region - Safety population

	Europe		America		Asia		Other countries		
	Pd (N=60)	IPd (N=85)	Pd (N=20)	IPd (N=23)	Pd (N=20)	IPd (N=24)	Pd (N=22)	IPd (N=45)	p-value of treatment-by-subgroup interaction[c]
Kaplan-Meier estimates of event in months									
25% quantile (95% CI)	NC (NC to NC)	0.0986 (0.0657 to 0.2300)	NC (NC to NC)	0.1314 (0.0657 to NC)	NC (2.1684 to NC)	0.1314 (0.0329 to 0.1643)	NC (0.3943 to NC)	0.0657 (0.0657 to 0.1314)	
Median (95% CI)	NC (NC to NC)	NC (18.9240 to NC)	NC (NC to NC)	NC (0.2300 to NC)	NC (NC to NC)	NC (0.1314 to NC)	NC (NC to NC)	0.1643 (0.1314 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd									
Log-Rank test p-value[a] vs Kd	-	<.0001		0.0047		0.0054		<.0001	

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CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.70 Subgroup analysis by geographical region
16.2.7.1.70.3 Treatment emergent adverse event per PT by treatment group according to geographical region - Safety population

	Europe		America		Asia		Other countries		
	Pd (N=60)	**IPd (N=85)**	**Pd (N=20)**	**IPd (N=23)**	**Pd (N=20)**	**IPd (N=24)**	**Pd (N=22)**	**IPd (N=45)**	**p-value of treatment-by-subgroup interaction[c]**
Hazard ratio (95% CI) vs Kd	-	14.31 (3.44 to 59.59)		NC		10.49 (1.34 to 82.16)		19.04 (2.58 to 140.48)	
P-value	-	0.0003		0.9954		0.0252		0.0039	
Hazard ratio inverted (95% CI) vs IKd	0.07 (0.02 to 0.29)				0.10 (0.01 to 0.75)		0.05 (0.01 to 0.39)		
Events probability (95% CI)[b]									
3 Months	0.9667 (0.8732 to 0.9916)	0.6471 (0.5356 to 0.7382)	1.0000 (1.0000 to 1.0000)	0.6522 (0.4235 to 0.8084)	0.9500 (0.6947 to 0.9928)	0.5833 (0.3645 to 0.7499)	0.9545 (0.7187 to 0.9935)	0.4000 (0.2582 to 0.5379)	
6 Months	0.9667 (0.8732 to 0.9916)	0.6346 (0.5227 to 0.7270)	1.0000 (1.0000 to 1.0000)	0.6522 (0.4235 to 0.8084)	0.9500 (0.6947 to 0.9928)	0.5833 (0.3645 to 0.7499)	0.9545 (0.7187 to 0.9935)	0.4000 (0.2582 to 0.5379)	
9 Months	0.9667 (0.8732 to 0.9916)	0.6346 (0.5227 to 0.7270)	1.0000 (1.0000 to 1.0000)	0.6522 (0.4235 to 0.8084)	0.9500 (0.6947 to 0.9928)	0.5833 (0.3645 to 0.7499)	0.9545 (0.7187 to 0.9935)	0.4000 (0.2582 to 0.5379)	

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[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.70 Subgroup analysis by geographical region
16.2.7.1.70.3 Treatment emergent adverse event per PT by treatment group according to geographical region - Safety population

	Europe		America		Asia		Other countries		
	Pd (N=60)	IPd (N=85)	Pd (N=20)	IPd (N=23)	Pd (N=20)	IPd (N=24)	Pd (N=22)	IPd (N=45)	p-value of treatment-by-subgroup interaction[c]
12 Months	0.9667 (0.8732 to 0.9916)	0.6346 (0.5227 to 0.7270)	1.0000 (1.0000 to 1.0000)	0.6522 (0.4235 to 0.8084)	0.9500 (0.6947 to 0.9928)	0.5833 (0.3645 to 0.7499)	0.9545 (0.7187 to 0.9935)	0.4000 (0.2582 to 0.5379)	
15 Months	0.9667 (0.8732 to 0.9916)	0.6217 (0.5093 to 0.7154)	1.0000 (1.0000 to 1.0000)	0.6522 (0.4235 to 0.8084)	0.9500 (0.6947 to 0.9928)	0.5833 (0.3645 to 0.7499)	0.9545 (0.7187 to 0.9935)	0.4000 (0.2582 to 0.5379)	
18 Months	0.9667 (0.8732 to 0.9916)	0.6217 (0.5093 to 0.7154)	1.0000 (1.0000 to 1.0000)	0.6522 (0.4235 to 0.8084)	0.9500 (0.6947 to 0.9928)	0.5833 (0.3645 to 0.7499)	0.9545 (0.7187 to 0.9935)	0.4000 (0.2582 to 0.5379)	
21 Months	0.9667 (0.8732 to 0.9916)	0.5927 (0.4787 to 0.6898)	1.0000 (1.0000 to 1.0000)	0.6522 (0.4235 to 0.8084)	0.9500 (0.6947 to 0.9928)	0.5833 (0.3645 to 0.7499)	0.9545 (0.7187 to 0.9935)	0.4000 (0.2582 to 0.5379)	
24 Months	0.9667 (0.8732 to 0.9916)	0.5927 (0.4787 to 0.6898)	1.0000 (1.0000 to 1.0000)	0.6522 (0.4235 to 0.8084)	0.9500 (0.6947 to 0.9928)	0.5833 (0.3645 to 0.7499)	0.9545 (0.7187 to 0.9935)	0.4000 (0.2582 to 0.5379)	

PT are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.70 Subgroup analysis by geographical region
16.2.7.1.70.3 Treatment emergent adverse event per PT by treatment group according to geographical region - Safety population

	Europe		America		Asia		Other countries		
	Pd (N=60)	**IPd (N=85)**	**Pd (N=20)**	**IPd (N=23)**	**Pd (N=20)**	**IPd (N=24)**	**Pd (N=22)**	**IPd (N=45)**	**p-value of treatment-by-subgroup interaction[c]**
27 Months	0.9667 (0.8732 to 0.9916)	0.5927 (0.4787 to 0.6898)	1.0000 (1.0000 to 1.0000)	0.6522 (0.4235 to 0.8084)	0.9500 (0.6947 to 0.9928)	0.5833 (0.3645 to 0.7499)	0.9545 (0.7187 to 0.9935)	0.4000 (0.2582 to 0.5379)	
30 Months	0.9667 (0.8732 to 0.9916)	0.5927 (0.4787 to 0.6898)	1.0000 (1.0000 to 1.0000)	0.6522 (0.4235 to 0.8084)	0.9500 (0.6947 to 0.9928)	0.5833 (0.3645 to 0.7499)	0.9545 (0.7187 to 0.9935)	0.4000 (0.2582 to 0.5379)	
Number of patients at risk[b]									
3 Months	56	53	20	15	19	14	21	18	
6 Months	52	50	20	15	18	14	21	18	
9 Months	51	50	19	15	16	14	19	17	
12 Months	49	49	19	15	16	13	19	17	
15 Months	47	45	18	13	13	11	19	16	
18 Months	47	43	16	12	13	10	19	15	
21 Months	38	36	11	9	12	10	14	13	

PT are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.70 Subgroup analysis by geographical region
16.2.7.1.70.3 Treatment emergent adverse event per PT by treatment group according to geographical region - Safety population

	Europe		America		Asia		Other countries		
	Pd (N=60)	IPd (N=85)	Pd (N=20)	IPd (N=23)	Pd (N=20)	IPd (N=24)	Pd (N=22)	IPd (N=45)	p-value of treatment-by-subgroup interaction[c]
24 Months	15	12	2	1	6	4	5	6	
27 Months	0	0	0	0	3	1	1	0	
30 Months	0	0	0	0	0	0	0	0	
Insomnia (days)									
Number (%) of events	13 (21.7)	14 (16.5)	5 (25.0)	6 (26.1)	5 (25.0)	7 (29.2)	5 (22.7)	15 (33.3)	0.6774
Number (%) of patients censored	47 (78.3)	71 (83.5)	15 (75.0)	17 (73.9)	15 (75.0)	17 (70.8)	17 (77.3)	30 (66.7)	
Kaplan-Meier estimates of event in months									
25% quantile (95% CI)	21.8480 (2.8583 to NC)	NC (10.3162 to NC)	13.5688 (0.1314 to NC)	4.5667 (0.1314 to NC)	7.6550 (0.3614 to NC)	9.9877 (0.1971 to NC)	NC (0.0657 to NC)	10.0862 (2.0698 to NC)	

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CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.70 Subgroup analysis by geographical region
16.2.7.1.70.3 Treatment emergent adverse event per PT by treatment group according to geographical region - Safety population

	Europe		America		Asia		Other countries		
	Pd (N=60)	IPd (N=85)	Pd (N=20)	IPd (N=23)	Pd (N=20)	IPd (N=24)	Pd (N=22)	IPd (N=45)	p-value of treatment-by-subgroup interaction[c]
15 Months	47	65	17	18	14	18	20	38	
18 Months	47	62	15	17	14	17	20	36	
21 Months	38	56	10	13	13	17	15	32	
24 Months	14	16	2	1	7	8	5	11	
27 Months	0	0	0	0	3	1	1	0	
30 Months	0	0	0	0	0	0	0	0	
Thrombocytopenia (days)									
Number (%) of events	9 (15.0)	4 (4.7)	0 (0.0)	0 (0.0)	2 (10.0)	0 (0.0)	1 (4.5)	1 (2.2)	0.9886
Number (%) of patients censored	51 (85.0)	81 (95.3)	20 (100.0)	23 (100.0)	18 (90.0)	24 (100.0)	21 (95.5)	44 (97.8)	
Kaplan-Meier estimates of event in months									

PT are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.70 Subgroup analysis by geographical region
16.2.7.1.70.3 Treatment emergent adverse event per PT by treatment group according to geographical region - Safety population

	Europe		America		Asia		Other countries		
	Pd (N=60)	**IPd (N=85)**	**Pd (N=20)**	**IPd (N=23)**	**Pd (N=20)**	**IPd (N=24)**	**Pd (N=22)**	**IPd (N=45)**	**p-value of treatment-by-subgroup interaction[c]**
25% quantile (95% CI)	NC (6.2752 to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (3.3840 to NC)	NC (NC to NC)	NC (2.3326 to NC)	NC (NC to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd									
Log-Rank test p-value[a] vs Kd	-	0.0280				0.1155		0.6112	
Hazard ratio (95% CI) vs Kd	-	0.29 (0.09 to 0.94)		NC		NC		0.49 (0.03 to 7.91)	
P-value	-	0.0391				0.9977		0.6185	

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CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.70 Subgroup analysis by geographical region
16.2.7.1.70.3 Treatment emergent adverse event per PT by treatment group according to geographical region - Safety population

	Europe		America		Asia		Other countries		
	Pd (N=60)	**IPd (N=85)**	**Pd (N=20)**	**IPd (N=23)**	**Pd (N=20)**	**IPd (N=24)**	**Pd (N=22)**	**IPd (N=45)**	**p-value of treatment-by-subgroup interaction[c]**
Events probability (95% CI)[b]									
3 Months	0.9158 (0.8094 to 0.9641)	0.9882 (0.9194 to 0.9983)	1.0000 (1.0000 to 1.0000)	1.0000 (1.0000 to 1.0000)	1.0000 (1.0000 to 1.0000)	1.0000 (1.0000 to 1.0000)	0.9545 (0.7187 to 0.9935)	0.9778 (0.8525 to 0.9968)	
6 Months	0.8809 (0.7662 to 0.9414)	0.9882 (0.9194 to 0.9983)	1.0000 (1.0000 to 1.0000)	1.0000 (1.0000 to 1.0000)	0.9500 (0.6947 to 0.9928)	1.0000 (1.0000 to 1.0000)	0.9545 (0.7187 to 0.9935)	0.9778 (0.8525 to 0.9968)	
9 Months	0.8625 (0.7436 to 0.9288)	0.9882 (0.9194 to 0.9983)	1.0000 (1.0000 to 1.0000)	1.0000 (1.0000 to 1.0000)	0.8972 (0.6475 to 0.9733)	1.0000 (1.0000 to 1.0000)	0.9545 (0.7187 to 0.9935)	0.9778 (0.8525 to 0.9968)	
12 Months	0.8625 (0.7436 to 0.9288)	0.9756 (0.9057 to 0.9938)	1.0000 (1.0000 to 1.0000)	1.0000 (1.0000 to 1.0000)	0.8972 (0.6475 to 0.9733)	1.0000 (1.0000 to 1.0000)	0.9545 (0.7187 to 0.9935)	0.9778 (0.8525 to 0.9968)	
15 Months	0.8625 (0.7436 to 0.9288)	0.9756 (0.9057 to 0.9938)	1.0000 (1.0000 to 1.0000)	1.0000 (1.0000 to 1.0000)	0.8972 (0.6475 to 0.9733)	1.0000 (1.0000 to 1.0000)	0.9545 (0.7187 to 0.9935)	0.9778 (0.8525 to 0.9968)	

PT are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.70 Subgroup analysis by geographical region
16.2.7.1.70.3 Treatment emergent adverse event per PT by treatment group according to geographical region - Safety population

	Europe		America		Asia		Other countries		
	Pd (N=60)	**IPd (N=85)**	**Pd (N=20)**	**IPd (N=23)**	**Pd (N=20)**	**IPd (N=24)**	**Pd (N=22)**	**IPd (N=45)**	**p-value of treatment-by-subgroup interaction[c]**
18 Months	0.8425 (0.7185 to 0.9150)	0.9620 (0.8866 to 0.9876)	1.0000 (1.0000 to 1.0000)	1.0000 (1.0000 to 1.0000)	0.8972 (0.6475 to 0.9733)	1.0000 (1.0000 to 1.0000)	0.9545 (0.7187 to 0.9935)	0.9778 (0.8525 to 0.9968)	
21 Months	0.8425 (0.7185 to 0.9150)	0.9479 (0.8666 to 0.9802)	1.0000 (1.0000 to 1.0000)	1.0000 (1.0000 to 1.0000)	0.8972 (0.6475 to 0.9733)	1.0000 (1.0000 to 1.0000)	0.9545 (0.7187 to 0.9935)	0.9778 (0.8525 to 0.9968)	
24 Months	0.8425 (0.7185 to 0.9150)	0.9479 (0.8666 to 0.9802)	1.0000 (1.0000 to 1.0000)	1.0000 (1.0000 to 1.0000)	0.8972 (0.6475 to 0.9733)	1.0000 (1.0000 to 1.0000)	0.9545 (0.7187 to 0.9935)	0.9778 (0.8525 to 0.9968)	
27 Months	0.8425 (0.7185 to 0.9150)	0.9479 (0.8666 to 0.9802)	1.0000 (1.0000 to 1.0000)	1.0000 (1.0000 to 1.0000)	0.8972 (0.6475 to 0.9733)	1.0000 (1.0000 to 1.0000)	0.9545 (0.7187 to 0.9935)	0.9778 (0.8525 to 0.9968)	
30 Months	0.8425 (0.7185 to 0.9150)	0.9479 (0.8666 to 0.9802)	1.0000 (1.0000 to 1.0000)	1.0000 (1.0000 to 1.0000)	0.8972 (0.6475 to 0.9733)	1.0000 (1.0000 to 1.0000)	0.9545 (0.7187 to 0.9935)	0.9778 (0.8525 to 0.9968)	

PT are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.70 Subgroup analysis by geographical region
16.2.7.1.70.3 Treatment emergent adverse event per PT by treatment group according to geographical region - Safety population

	Europe		America		Asia		Other countries		
	Pd (N=60)	IPd (N=85)	Pd (N=20)	IPd (N=23)	Pd (N=20)	IPd (N=24)	Pd (N=22)	IPd (N=45)	p-value of treatment-by-subgroup interaction[c]
Number of patients at risk[b]									
3 Months	53	81	20	22	20	24	21	44	
6 Months	48	78	20	22	18	23	21	42	
9 Months	46	78	19	21	15	22	19	39	
12 Months	45	75	19	21	15	21	19	39	
15 Months	43	72	18	18	13	18	19	37	
18 Months	42	68	16	17	13	17	19	35	
21 Months	34	60	11	13	12	17	14	31	
24 Months	13	20	2	1	7	8	5	10	
27 Months	0	1	0	0	3	1	1	0	
30 Months	0	0	0	0	0	0	0	0	
Traumatic fracture (days)									
Number (%) of events	2 (3.3)	5 (5.9)	1 (5.0)	1 (4.3)	0 (0.0)	2 (8.3)	2 (9.1)	5 (11.1)	0.9875

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[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.70 Subgroup analysis by geographical region
16.2.7.1.70.3 Treatment emergent adverse event per PT by treatment group according to geographical region - Safety population

	Europe		America		Asia		Other countries		
	Pd (N=60)	IPd (N=85)	Pd (N=20)	IPd (N=23)	Pd (N=20)	IPd (N=24)	Pd (N=22)	IPd (N=45)	p-value of treatment-by-subgroup interaction[c]
24 Months	14	17	2	1	7	7	4	9	
27 Months	0	0	0	0	3	1	0	0	
30 Months	0	0	0	0	0	0	0	0	
Upper respiratory tract infection (days)									
Number (%) of events	8 (13.3)	21 (24.7)	11 (55.0)	13 (56.5)	4 (20.0)	11 (45.8)	6 (27.3)	19 (42.2)	0.5960
Number (%) of patients censored	52 (86.7)	64 (75.3)	9 (45.0)	10 (43.5)	16 (80.0)	13 (54.2)	16 (72.7)	26 (57.8)	
Kaplan-Meier estimates of event in months									
25% quantile (95% CI)	NC (9.7906 to NC)	12.3860 (7.2936 to NC)	2.5133 (0.3943 to 10.9405)	2.2012 (0.4928 to 6.8665)	NC (1.5113 to NC)	6.5051 (2.0698 to 13.3717)	12.5832 (0.2957 to NC)	5.5524 (2.4312 to 12.1561)	

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CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.70 Subgroup analysis by geographical region
16.2.7.1.70.3 Treatment emergent adverse event per PT by treatment group according to geographical region - Safety population

	Europe		America		Asia		Other countries		
	Pd (N=60)	**IPd (N=85)**	**Pd (N=20)**	**IPd (N=23)**	**Pd (N=20)**	**IPd (N=24)**	**Pd (N=22)**	**IPd (N=45)**	**p-value of treatment-by-subgroup interaction[c]**
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	11.1376 (1.8727 to NC)	12.8789 (3.5811 to NC)	NC (13.8645 to NC)	NC (8.0821 to NC)	NC (12.5832 to NC)	NC (11.4004 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (15.7372 to NC)	NC (14.1930 to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Pd									
Log-Rank test p-value[a] vs Kd	-	0.1143		0.8984		0.0822		0.2594	
Hazard ratio (95% CI) vs Kd	-	1.91 (0.84 to 4.30)		1.05 (0.47 to 2.36)		2.66 (0.84 to 8.35)		1.69 (0.67 to 4.23)	
P-value	-	0.1206		0.8986		0.0947		0.2648	
Events probability (95% CI)[b]									

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[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1.70 Subgroup analysis by geographical region
16.2.7.1.70.3 Treatment emergent adverse event per PT by treatment group according to geographical region - Safety population

	Europe		America		Asia		Other countries		
	Pd (N=60)	IPd (N=85)	Pd (N=20)	IPd (N=23)	Pd (N=20)	IPd (N=24)	Pd (N=22)	IPd (N=45)	p-value of treatment-by-subgroup interaction[c]
3 Months	1.0000 (1.0000 to 1.0000)	0.9641 (0.8929 to 0.9883)	0.7500 (0.4999 to 0.8875)	0.7343 (0.5011 to 0.8711)	0.9500 (0.6947 to 0.9928)	0.8750 (0.6608 to 0.9579)	0.8636 (0.6344 to 0.9539)	0.8667 (0.7271 to 0.9378)	
6 Months	0.9457 (0.8408 to 0.9822)	0.8754 (0.7806 to 0.9310)	0.6000 (0.3573 to 0.7760)	0.5966 (0.3671 to 0.7663)	0.9500 (0.6947 to 0.9928)	0.7917 (0.5698 to 0.9075)	0.8182 (0.5853 to 0.9276)	0.7070 (0.5493 to 0.8182)	
9 Months	0.8885 (0.7683 to 0.9484)	0.8110 (0.7060 to 0.8816)	0.6000 (0.3573 to 0.7760)	0.5507 (0.3257 to 0.7281)	0.8972 (0.6475 to 0.9733)	0.6597 (0.4327 to 0.8134)	0.7727 (0.5374 to 0.8985)	0.6818 (0.5220 to 0.7979)	
12 Months	0.8692 (0.7449 to 0.9355)	0.7587 (0.6478 to 0.8388)	0.4909 (0.2603 to 0.6865)	0.5507 (0.3257 to 0.7281)	0.8972 (0.6475 to 0.9733)	0.6597 (0.4327 to 0.8134)	0.7727 (0.5374 to 0.8985)	0.6313 (0.4692 to 0.7560)	
15 Months	0.8490 (0.7202 to 0.9216)	0.7453 (0.6333 to 0.8277)	0.4909 (0.2603 to 0.6865)	0.4337 (0.2175 to 0.6329)	0.7676 (0.4870 to 0.9074)	0.5718 (0.3499 to 0.7426)	0.7212 (0.4805 to 0.8644)	0.5808 (0.4185 to 0.7125)	

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CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.70 Subgroup analysis by geographical region
16.2.7.1.70.3 Treatment emergent adverse event per PT by treatment group according to geographical region - Safety population

	Europe		America		Asia		Other countries		
	Pd (N=60)	**IPd (N=85)**	**Pd (N=20)**	**IPd (N=23)**	**Pd (N=20)**	**IPd (N=24)**	**Pd (N=22)**	**IPd (N=45)**	**p-value of treatment-by-subgroup interaction[c]**
18 Months	0.8490 (0.7202 to 0.9216)	0.7307 (0.6170 to 0.8156)	0.4364 (0.2161 to 0.6383)	0.3717 (0.1668 to 0.5788)	0.7676 (0.4870 to 0.9074)	0.5146 (0.2927 to 0.6982)	0.7212 (0.4805 to 0.8644)	0.5544 (0.3923 to 0.6894)	
21 Months	0.8490 (0.7202 to 0.9216)	0.7307 (0.6170 to 0.8156)	0.4364 (0.2161 to 0.6383)	0.3717 (0.1668 to 0.5788)	0.7676 (0.4870 to 0.9074)	0.5146 (0.2927 to 0.6982)	0.7212 (0.4805 to 0.8644)	0.5544 (0.3923 to 0.6894)	
24 Months	0.8490 (0.7202 to 0.9216)	0.7307 (0.6170 to 0.8156)	0.4364 (0.2161 to 0.6383)	0.3717 (0.1668 to 0.5788)	0.7676 (0.4870 to 0.9074)	0.5146 (0.2927 to 0.6982)	0.7212 (0.4805 to 0.8644)	0.5544 (0.3923 to 0.6894)	
27 Months	0.8490 (0.7202 to 0.9216)	0.7307 (0.6170 to 0.8156)	0.4364 (0.2161 to 0.6383)	0.3717 (0.1668 to 0.5788)	0.7676 (0.4870 to 0.9074)	0.5146 (0.2927 to 0.6982)	0.7212 (0.4805 to 0.8644)	0.5544 (0.3923 to 0.6894)	
30 Months	0.8490 (0.7202 to 0.9216)	0.7307 (0.6170 to 0.8156)	0.4364 (0.2161 to 0.6383)	0.3717 (0.1668 to 0.5788)	0.7676 (0.4870 to 0.9074)	0.5146 (0.2927 to 0.6982)	0.7212 (0.4805 to 0.8644)	0.5544 (0.3923 to 0.6894)	

PT are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.70 Subgroup analysis by geographical region
16.2.7.1.70.3 Treatment emergent adverse event per PT by treatment group according to geographical region - Safety population

	Europe		America		Asia		Other countries		
	Pd (N=60)	**IPd (N=85)**	**Pd (N=20)**	**IPd (N=23)**	**Pd (N=20)**	**IPd (N=24)**	**Pd (N=22)**	**IPd (N=45)**	**p-value of treatment-by-subgroup interaction[c]**
Number of patients at risk[b]									
3 Months	57	79	15	16	19	21	19	39	
6 Months	50	68	12	13	19	18	18	31	
9 Months	46	63	11	11	16	15	15	27	
12 Months	43	57	9	11	16	15	15	25	
15 Months	40	53	9	7	11	10	14	22	
18 Months	40	50	7	6	11	9	14	19	
21 Months	32	45	5	4	10	9	10	17	
24 Months	12	12	2	0	4	4	3	6	
27 Months	0	1	0	0	3	0	0	0	
30 Months	0	0	0	0	0	0	0	0	
Urinary tract infection (days)									
Number (%) of events	3 (5.0)	6 (7.1)	3 (15.0)	3 (13.0)	1 (5.0)	1 (4.2)	4 (18.2)	2 (4.4)	0.4544

PT are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.71 Subgroup analysis by regulatory region
16.2.7.1.71.3 Treatment emergent adverse event per PT by treatment group according to regulatory region - Safety population

	Western countries		Other countries		
	Kd (N=55)	**IKd (N=97)**	**Kd (N=67)**	**IKd (N=80)**	**p-value of treatment-by-sub group interaction[c]**
18 Months	43	68	47	63	
21 Months	34	59	37	58	
24 Months	12	18	15	20	
27 Months	1	0	3	2	
30 Months	0	0	0	0	
Bronchitis (days)					
Number (%) of events	9 (16.4)	23 (23.7)	6 (9.0)	17 (21.3)	0.4000
Number (%) of patients censored	46 (83.6)	74 (76.3)	61 (91.0)	63 (78.8)	
Kaplan-Meier estimates of event in months					
25% quantile (95% CI)	NC (10.5133 to NC)	17.5441 (8.6735 to NC)	NC (NC to NC)	NC (9.7577 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.3003		0.0449	

PT are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.71 Subgroup analysis by regulatory region
16.2.7.1.71.3 Treatment emergent adverse event per PT by treatment group according to regulatory region - Safety population

	Western countries		Other countries		
	Kd (N=55)	**IKd (N=97)**	**Kd (N=67)**	**IKd (N=80)**	**p-value of treatment-by-sub group interaction[c]**
Hazard ratio (95% CI) vs Kd	-	1.50 (0.69 to 3.24)		2.51 (0.99 to 6.36)	
P-value	-	0.3038		0.0528	
Events probability (95% CI)[b]					
3 Months	0.9437 (0.8354 to 0.9815)	0.9582 (0.8925 to 0.9841)	0.9851 (0.8987 to 0.9979)	0.9373 (0.8560 to 0.9734)	
6 Months	0.9240 (0.8099 to 0.9708)	0.8934 (0.8109 to 0.9412)	0.9550 (0.8669 to 0.9853)	0.8860 (0.7923 to 0.9390)	
9 Months	0.9039 (0.7842 to 0.9589)	0.8373 (0.7445 to 0.8986)	0.9396 (0.8470 to 0.9769)	0.8860 (0.7923 to 0.9390)	
12 Months	0.8423 (0.7088 to 0.9180)	0.7802 (0.6801 to 0.8524)	0.9231 (0.8249 to 0.9673)	0.8189 (0.7131 to 0.8886)	
15 Months	0.8423 (0.7088 to 0.9180)	0.7802 (0.6801 to 0.8524)	0.9057 (0.8016 to 0.9566)	0.8052 (0.6976 to 0.8778)	
18 Months	0.8423 (0.7088 to 0.9180)	0.7414 (0.6362 to 0.8205)	0.9057 (0.8016 to 0.9566)	0.7748 (0.6622 to 0.8539)	
21 Months	0.8423 (0.7088 to 0.9180)	0.7414 (0.6362 to 0.8205)	0.9057 (0.8016 to 0.9566)	0.7748 (0.6622 to 0.8539)	

PT are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.71 Subgroup analysis by regulatory region
16.2.7.1.71.3 Treatment emergent adverse event per PT by treatment group according to regulatory region - Safety population

	Western countries		Other countries		
	Kd (N=55)	**IKd (N=97)**	**Kd (N=67)**	**IKd (N=80)**	**p-value of treatment-by-sub group interaction[c]**
24 Months	0.8111 (0.6640 to 0.8985)	0.7414 (0.6362 to 0.8205)	0.9057 (0.8016 to 0.9566)	0.7748 (0.6622 to 0.8539)	
27 Months	0.8111 (0.6640 to 0.8985)	0.7414 (0.6362 to 0.8205)	0.9057 (0.8016 to 0.9566)	0.7748 (0.6622 to 0.8539)	
30 Months	0.8111 (0.6640 to 0.8985)	0.7414 (0.6362 to 0.8205)	0.9057 (0.8016 to 0.9566)	0.7748 (0.6622 to 0.8539)	
Number of patients at risk[b]					
3 Months	49	91	66	74	
6 Months	46	80	62	68	
9 Months	44	74	57	66	
12 Months	41	67	54	60	
15 Months	39	62	49	55	
18 Months	39	56	47	50	
21 Months	31	47	36	45	
24 Months	9	16	15	14	
27 Months	1	0	3	1	
30 Months	0	0	0	0	

PT are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.71 Subgroup analysis by regulatory region
16.2.7.1.71.3 Treatment emergent adverse event per PT by treatment group according to regulatory region - Safety population

	Western countries		Other countries		
	Kd (N=55)	**IKd (N=97)**	**Kd (N=67)**	**IKd (N=80)**	**p-value of treatment-by-sub group interaction[c]**
18 Months	41	73	45	53	
21 Months	32	63	35	48	
24 Months	9	20	14	17	
27 Months	1	0	1	0	
30 Months	0	0	0	0	
Infusion related reaction (days)					
Number (%) of events	3 (5.5)	49 (50.5)	1 (1.5)	30 (37.5)	0.4073
Number (%) of patients censored	52 (94.5)	48 (49.5)	66 (98.5)	50 (62.5)	
Kaplan-Meier estimates of event in months					
25% quantile (95% CI)	NC (NC to NC)	0.0986 (0.0657 to 0.1314)	NC (NC to NC)	0.1314 (0.0657 to 0.1643)	
Median (95% CI)	NC (NC to NC)	19.3840 (0.1971 to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	<.0001		<.0001	

PT are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.71 Subgroup analysis by regulatory region
16.2.7.1.71.3 Treatment emergent adverse event per PT by treatment group according to regulatory region - Safety population

	Western countries		Other countries		
	Kd (N=55)	**IKd (N=97)**	**Kd (N=67)**	**IKd (N=80)**	**p-value of treatment-by-sub group interaction[c]**
Hazard ratio (95% CI) vs Kd	-	12.02 (3.74 to 38.59)		30.14 (4.11 to 221.15)	
P-value	-	<.0001		0.0008	
Hazard ratio inverted (95% CI) vs IKd	0.08 (0.03 to 0.27)		0.03 (0.00 to 0.24)		
Events probability (95% CI)[b]					
3 Months	0.9455 (0.8404 to 0.9821)	0.5359 (0.4319 to 0.6291)	0.9851 (0.8987 to 0.9979)	0.6250 (0.5094 to 0.7207)	
6 Months	0.9455 (0.8404 to 0.9821)	0.5254 (0.4216 to 0.6190)	0.9851 (0.8987 to 0.9979)	0.6250 (0.5094 to 0.7207)	
9 Months	0.9455 (0.8404 to 0.9821)	0.5254 (0.4216 to 0.6190)	0.9851 (0.8987 to 0.9979)	0.6250 (0.5094 to 0.7207)	
12 Months	0.9455 (0.8404 to 0.9821)	0.5254 (0.4216 to 0.6190)	0.9851 (0.8987 to 0.9979)	0.6250 (0.5094 to 0.7207)	
15 Months	0.9455 (0.8404 to 0.9821)	0.5144 (0.4108 to 0.6086)	0.9851 (0.8987 to 0.9979)	0.6250 (0.5094 to 0.7207)	
18 Months	0.9455 (0.8404 to 0.9821)	0.5144 (0.4108 to 0.6086)	0.9851 (0.8987 to 0.9979)	0.6250 (0.5094 to 0.7207)	

PT are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.71 Subgroup analysis by regulatory region
16.2.7.1.71.3 Treatment emergent adverse event per PT by treatment group according to regulatory region - Safety population

	Western countries		Other countries		
	Kd (N=55)	**IKd (N=97)**	**Kd (N=67)**	**IKd (N=80)**	**p-value of treatment-by-sub group interaction[c]**
21 Months	0.9455 (0.8404 to 0.9821)	0.4887 (0.3847 to 0.5847)	0.9851 (0.8987 to 0.9979)	0.6250 (0.5094 to 0.7207)	
24 Months	0.9455 (0.8404 to 0.9821)	0.4887 (0.3847 to 0.5847)	0.9851 (0.8987 to 0.9979)	0.6250 (0.5094 to 0.7207)	
27 Months	0.9455 (0.8404 to 0.9821)	0.4887 (0.3847 to 0.5847)	0.9851 (0.8987 to 0.9979)	0.6250 (0.5094 to 0.7207)	
30 Months	0.9455 (0.8404 to 0.9821)	0.4887 (0.3847 to 0.5847)	0.9851 (0.8987 to 0.9979)	0.6250 (0.5094 to 0.7207)	
Number of patients at risk[b]					
3 Months	50	51	66	49	
6 Months	47	49	64	48	
9 Months	46	49	59	47	
12 Months	46	48	57	46	
15 Months	44	43	53	42	
18 Months	44	40	51	40	
21 Months	35	31	40	37	
24 Months	12	11	16	12	

PT are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.71 Subgroup analysis by regulatory region
16.2.7.1.71.3 Treatment emergent adverse event per PT by treatment group according to regulatory region - Safety population

	Western countries		Other countries		
	Kd (N=55)	**IKd (N=97)**	**Kd (N=67)**	**IKd (N=80)**	**p-value of treatment-by-sub group interaction[c]**
30 Months	0.9792 (0.8612 to 0.9970)	0.9122 (0.8319 to 0.9551)	0.9692 (0.8823 to 0.9922)	0.9740 (0.9001 to 0.9934)	
Number of patients at risk[b]					
3 Months	52	94	66	78	
6 Months	49	86	64	74	
9 Months	47	83	58	70	
12 Months	47	80	56	69	
15 Months	46	74	52	65	
18 Months	46	70	50	62	
21 Months	37	61	39	57	
24 Months	12	17	16	19	
27 Months	1	0	3	1	
30 Months	0	0	0	0	
Thrombocytopenia (days)					
Number (%) of events	5 (9.1)	5 (5.2)	7 (10.4)	0 (0.0)	0.9918
Number (%) of patients censored	50 (90.9)	92 (94.8)	60 (89.6)	80 (100.0)	

PT are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.71 Subgroup analysis by regulatory region
16.2.7.1.71.3 Treatment emergent adverse event per PT by treatment group according to regulatory region - Safety population

	Western countries		Other countries		
	Kd (N=55)	**IKd (N=97)**	**Kd (N=67)**	**IKd (N=80)**	**p-value of treatment-by-sub group interaction[c]**
Kaplan-Meier estimates of event in months					
25% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.3376		0.0033	
Hazard ratio (95% CI) vs Kd	-	0.55 (0.16 to 1.90)		NC	
P-value	-	0.3448		0.9933	
Events probability (95% CI)[b]					
3 Months	0.9448 (0.8384 to 0.9818)	0.9793 (0.9197 to 0.9948)	0.9552 (0.8676 to 0.9853)	1.0000 (1.0000 to 1.0000)	
6 Months	0.9066 (0.7899 to 0.9600)	0.9793 (0.9197 to 0.9948)	0.9403 (0.8487 to 0.9772)	1.0000 (1.0000 to 1.0000)	

PT are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.71 Subgroup analysis by regulatory region
16.2.7.1.71.3 Treatment emergent adverse event per PT by treatment group according to regulatory region - Safety population

	Western countries		Other countries		
	Kd (N=55)	**IKd (N=97)**	**Kd (N=67)**	**IKd (N=80)**	**p-value of treatment-by-sub group interaction[c]**
9 Months	0.9066 (0.7899 to 0.9600)	0.9793 (0.9197 to 0.9948)	0.9095 (0.8095 to 0.9583)	1.0000 (1.0000 to 1.0000)	
12 Months	0.9066 (0.7899 to 0.9600)	0.9681 (0.9044 to 0.9896)	0.9095 (0.8095 to 0.9583)	1.0000 (1.0000 to 1.0000)	
15 Months	0.9066 (0.7899 to 0.9600)	0.9681 (0.9044 to 0.9896)	0.9095 (0.8095 to 0.9583)	1.0000 (1.0000 to 1.0000)	
18 Months	0.9066 (0.7899 to 0.9600)	0.9559 (0.8864 to 0.9833)	0.8913 (0.7848 to 0.9468)	1.0000 (1.0000 to 1.0000)	
21 Months	0.9066 (0.7899 to 0.9600)	0.9430 (0.8678 to 0.9760)	0.8913 (0.7848 to 0.9468)	1.0000 (1.0000 to 1.0000)	
24 Months	0.9066 (0.7899 to 0.9600)	0.9430 (0.8678 to 0.9760)	0.8913 (0.7848 to 0.9468)	1.0000 (1.0000 to 1.0000)	
27 Months	0.9066 (0.7899 to 0.9600)	0.9430 (0.8678 to 0.9760)	0.8913 (0.7848 to 0.9468)	1.0000 (1.0000 to 1.0000)	
30 Months	0.9066 (0.7899 to 0.9600)	0.9430 (0.8678 to 0.9760)	0.8913 (0.7848 to 0.9468)	1.0000 (1.0000 to 1.0000)	
Number of patients at risk[b]					
3 Months	50	93	64	78	

PT are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.71 Subgroup analysis by regulatory region
16.2.7.1.71.3 Treatment emergent adverse event per PT by treatment group according to regulatory region - Safety population

	Western countries		Other countries		
	Kd (N=55)	**IKd (N=97)**	**Kd (N=67)**	**IKd (N=80)**	**p-value of treatment-by-sub group interaction[c]**
6 Months	46	89	61	76	
9 Months	45	88	54	72	
12 Months	45	85	53	71	
15 Months	43	79	50	66	
18 Months	43	74	47	63	
21 Months	35	63	36	58	
24 Months	10	19	17	20	
27 Months	1	0	3	2	
30 Months	0	0	0	0	
Traumatic fracture (days)					
Number (%) of events	2 (3.6)	7 (7.2)	3 (4.5)	6 (7.5)	0.8610
Number (%) of patients censored	53 (96.4)	90 (92.8)	64 (95.5)	74 (92.5)	
Kaplan-Meier estimates of event in months					
25% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	

PT are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.71 Subgroup analysis by regulatory region
16.2.7.1.71.3 Treatment emergent adverse event per PT by treatment group according to regulatory region - Safety population

	Western countries		Other countries		
	Kd (N=55)	**IKd (N=97)**	**Kd (N=67)**	**IKd (N=80)**	**p-value of treatment-by-sub group interaction[c]**
21 Months	36	62	39	54	
24 Months	11	18	16	16	
27 Months	0	0	3	1	
30 Months	0	0	0	0	
Upper respiratory tract infection (days)					
Number (%) of events	8 (14.5)	34 (35.1)	21 (31.3)	30 (37.5)	0.1148
Number (%) of patients censored	47 (85.5)	63 (64.9)	46 (68.7)	50 (62.5)	
Kaplan-Meier estimates of event in months					
25% quantile (95% CI)	NC (10.9405 to NC)	8.4764 (4.6982 to 12.3860)	11.1376 (3.8768 to NC)	8.0821 (3.5811 to 13.3717)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (16.3285 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.0098		0.4629	

PT are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.71 Subgroup analysis by regulatory region
16.2.7.1.71.3 Treatment emergent adverse event per PT by treatment group according to regulatory region - Safety population

	Western countries		Other countries		
	Kd (N=55)	**IKd (N=97)**	**Kd (N=67)**	**IKd (N=80)**	**p-value of treatment-by-sub group interaction[c]**
Hazard ratio (95% CI) vs Kd	-	2.66 (1.23 to 5.74)		1.23 (0.71 to 2.15)	
P-value	-	0.0130		0.4637	
Hazard ratio inverted (95% CI) vs IKd	0.38 (0.17 to 0.81)				
Events probability (95% CI)[b]					
3 Months	0.9633 (0.8611 to 0.9907)	0.9165 (0.8401 to 0.9574)	0.8955 (0.7933 to 0.9488)	0.8733 (0.7773 to 0.9298)	
6 Months	0.9440 (0.8363 to 0.9816)	0.7752 (0.6762 to 0.8473)	0.8054 (0.6886 to 0.8821)	0.7951 (0.6874 to 0.8691)	
9 Months	0.8825 (0.7565 to 0.9455)	0.7306 (0.6277 to 0.8094)	0.7744 (0.6539 to 0.8574)	0.7134 (0.5976 to 0.8012)	
12 Months	0.8614 (0.7306 to 0.9316)	0.6846 (0.5785 to 0.7692)	0.7408 (0.6160 to 0.8304)	0.6854 (0.5678 to 0.7772)	
15 Months	0.8404 (0.7055 to 0.9170)	0.6491 (0.5412 to 0.7378)	0.6856 (0.5545 to 0.7853)	0.6279 (0.5075 to 0.7266)	
18 Months	0.8404 (0.7055 to 0.9170)	0.6229 (0.5133 to 0.7146)	0.6665 (0.5337 to 0.7694)	0.5961 (0.4741 to 0.6986)	
21 Months	0.8404 (0.7055 to 0.9170)	0.6229 (0.5133 to 0.7146)	0.6665 (0.5337 to 0.7694)	0.5961 (0.4741 to 0.6986)	

PT are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.71 Subgroup analysis by regulatory region
16.2.7.1.71.3 Treatment emergent adverse event per PT by treatment group according to regulatory region - Safety population

	Western countries		Other countries		
	Kd (N=55)	**IKd (N=97)**	**Kd (N=67)**	**IKd (N=80)**	**p-value of treatment-by-sub group interaction[c]**
24 Months	0.8404 (0.7055 to 0.9170)	0.6229 (0.5133 to 0.7146)	0.6665 (0.5337 to 0.7694)	0.5961 (0.4741 to 0.6986)	
27 Months	0.8404 (0.7055 to 0.9170)	0.6229 (0.5133 to 0.7146)	0.6665 (0.5337 to 0.7694)	0.5961 (0.4741 to 0.6986)	
30 Months	0.8404 (0.7055 to 0.9170)	0.6229 (0.5133 to 0.7146)	0.6665 (0.5337 to 0.7694)	0.5961 (0.4741 to 0.6986)	
Number of patients at risk[b]					
3 Months	50	87	60	68	
6 Months	46	70	53	60	
9 Months	42	65	46	51	
12 Months	41	59	42	49	
15 Months	38	52	36	40	
18 Months	38	47	34	37	
21 Months	31	41	26	34	
24 Months	10	10	11	12	
27 Months	0	0	3	1	
30 Months	0	0	0	0	

PT are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.72 Subgroup analysis by baseline ECOG PS
16.2.7.1.72.2 Treatment emergent adverse event per PT by treatment group according to baseline ECOG PS - Safety population

	0 or 1		>1		
	Kd (N=117)	**IKd (N=167)**	**Kd (N=5)**	**IKd (N=10)**	**p-value of treatment-by-sub group interaction[c]**
18 Months	88	126	2	5	
21 Months	69	112	2	5	
24 Months	26	38	1	0	
27 Months	4	2	0	0	
30 Months	0	0	0	0	
Bronchitis (days)					
Number (%) of events	14 (12.0)	39 (23.4)	1 (20.0)	1 (10.0)	0.3160
Number (%) of patients censored	103 (88.0)	128 (76.6)	4 (80.0)	9 (90.0)	
Kaplan-Meier estimates of event in months					
25% quantile (95% CI)	NC (NC to NC)	17.5441 (11.2361 to NC)	NC (11.2361 to NC)	NC (4.4682 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (11.2361 to NC)	NC (4.4682 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (11.2361 to NC)	NC (NC to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.0182		0.6452	

PT are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.72 Subgroup analysis by baseline ECOG PS
16.2.7.1.72.2 Treatment emergent adverse event per PT by treatment group according to baseline ECOG PS - Safety population

	0 or 1		>1		
	Kd (N=117)	**IKd (N=167)**	**Kd (N=5)**	**IKd (N=10)**	**p-value of treatment-by-sub group interaction[c]**
Hazard ratio (95% CI) vs Kd	-	2.05 (1.12 to 3.78)		0.53 (0.03 to 8.43)	
P-value	-	0.0209		0.6508	
Hazard ratio inverted (95% CI) vs IKd	0.49 (0.26 to 0.90)				
Events probability (95% CI)[b]					
3 Months	0.9653 (0.9101 to 0.9868)	0.9459 (0.8986 to 0.9715)	1.0000 (1.0000 to 1.0000)	1.0000 (1.0000 to 1.0000)	
6 Months	0.9386 (0.8756 to 0.9703)	0.8902 (0.8313 to 0.9294)	1.0000 (1.0000 to 1.0000)	0.8889 (0.4330 to 0.9836)	
9 Months	0.9205 (0.8527 to 0.9578)	0.8580 (0.7940 to 0.9034)	1.0000 (1.0000 to 1.0000)	0.8889 (0.4330 to 0.9836)	
12 Months	0.8920 (0.8175 to 0.9372)	0.7929 (0.7211 to 0.8481)	0.7500 (0.1279 to 0.9605)	0.8889 (0.4330 to 0.9836)	
15 Months	0.8822 (0.8056 to 0.9299)	0.7863 (0.7138 to 0.8424)	0.7500 (0.1279 to 0.9605)	0.8889 (0.4330 to 0.9836)	
18 Months	0.8822 (0.8056 to 0.9299)	0.7497 (0.6732 to 0.8107)	0.7500 (0.1279 to 0.9605)	0.8889 (0.4330 to 0.9836)	
21 Months	0.8822 (0.8056 to 0.9299)	0.7497 (0.6732 to 0.8107)	0.7500 (0.1279 to 0.9605)	0.8889 (0.4330 to 0.9836)	

PT are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.72 Subgroup analysis by baseline ECOG PS
16.2.7.1.72.2 Treatment emergent adverse event per PT by treatment group according to baseline ECOG PS - Safety population

	0 or 1		>1		
	Kd (N=117)	**IKd (N=167)**	**Kd (N=5)**	**IKd (N=10)**	**p-value of treatment-by-sub group interaction[c]**
24 Months	0.8659 (0.7814 to 0.9194)	0.7497 (0.6732 to 0.8107)	0.7500 (0.1279 to 0.9605)	0.8889 (0.4330 to 0.9836)	
27 Months	0.8659 (0.7814 to 0.9194)	0.7497 (0.6732 to 0.8107)	0.7500 (0.1279 to 0.9605)	0.8889 (0.4330 to 0.9836)	
30 Months	0.8659 (0.7814 to 0.9194)	0.7497 (0.6732 to 0.8107)	0.7500 (0.1279 to 0.9605)	0.8889 (0.4330 to 0.9836)	
Number of patients at risk[b]					
3 Months	110	156	5	9	
6 Months	104	140	4	8	
9 Months	97	132	4	8	
12 Months	92	120	3	7	
15 Months	87	110	1	7	
18 Months	85	100	1	6	
21 Months	66	87	1	5	
24 Months	24	30	0	0	
27 Months	4	1	0	0	
30 Months	0	0	0	0	

PT are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.72 Subgroup analysis by baseline ECOG PS
16.2.7.1.72.2 Treatment emergent adverse event per PT by treatment group according to baseline ECOG PS - Safety population

	0 or 1		>1		
	Kd (N=117)	**IKd (N=167)**	**Kd (N=5)**	**IKd (N=10)**	**p-value of treatment-by-sub group interaction[c]**
21 Months	65	105	2	6	
24 Months	22	37	1	0	
27 Months	2	0	0	0	
30 Months	0	0	0	0	
Infusion related reaction (days)					
Number (%) of events	4 (3.4)	73 (43.7)	0 (0.0)	6 (60.0)	0.9855
Number (%) of patients censored	113 (96.6)	94 (56.3)	5 (100.0)	4 (40.0)	
Kaplan-Meier estimates of event in months					
25% quantile (95% CI)	NC (NC to NC)	0.0986 (0.0657 to 0.1314)	NC (NC to NC)	0.0657 (0.0329 to 0.2957)	
Median (95% CI)	NC (NC to NC)	NC (12.0246 to NC)	NC (NC to NC)	0.2136 (0.0329 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (0.1314 to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	<.0001		0.0455	

PT are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.72 Subgroup analysis by baseline ECOG PS
16.2.7.1.72.2 Treatment emergent adverse event per PT by treatment group according to baseline ECOG PS - Safety population

	0 or 1		>1		
	Kd (N=117)	**IKd (N=167)**	**Kd (N=5)**	**IKd (N=10)**	**p-value of treatment-by-sub group interaction[c]**
Hazard ratio (95% CI) vs Kd	-	15.97 (5.83 to 43.72)		NC	
P-value	-	<.0001		0.9962	
Hazard ratio inverted (95% CI) vs IKd	0.06 (0.02 to 0.17)				
Events probability (95% CI)[b]					
3 Months	0.9657 (0.9113 to 0.9870)	0.5868 (0.5082 to 0.6571)	1.0000 (1.0000 to 1.0000)	0.4000 (0.1227 to 0.6702)	
6 Months	0.9657 (0.9113 to 0.9870)	0.5807 (0.5020 to 0.6513)	1.0000 (1.0000 to 1.0000)	0.4000 (0.1227 to 0.6702)	
9 Months	0.9657 (0.9113 to 0.9870)	0.5807 (0.5020 to 0.6513)	1.0000 (1.0000 to 1.0000)	0.4000 (0.1227 to 0.6702)	
12 Months	0.9657 (0.9113 to 0.9870)	0.5807 (0.5020 to 0.6513)	1.0000 (1.0000 to 1.0000)	0.4000 (0.1227 to 0.6702)	
15 Months	0.9657 (0.9113 to 0.9870)	0.5743 (0.4955 to 0.6452)	1.0000 (1.0000 to 1.0000)	0.4000 (0.1227 to 0.6702)	
18 Months	0.9657 (0.9113 to 0.9870)	0.5743 (0.4955 to 0.6452)	1.0000 (1.0000 to 1.0000)	0.4000 (0.1227 to 0.6702)	
21 Months	0.9657 (0.9113 to 0.9870)	0.5594 (0.4800 to 0.6313)	1.0000 (1.0000 to 1.0000)	0.4000 (0.1227 to 0.6702)	

PT are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.72 Subgroup analysis by baseline ECOG PS
16.2.7.1.72.2 Treatment emergent adverse event per PT by treatment group according to baseline ECOG PS - Safety population

	0 or 1		>1		
	Kd (N=117)	**IKd (N=167)**	**Kd (N=5)**	**IKd (N=10)**	**p-value of treatment-by-sub group interaction[c]**
24 Months	0.9657 (0.9113 to 0.9870)	0.5594 (0.4800 to 0.6313)	1.0000 (1.0000 to 1.0000)	0.4000 (0.1227 to 0.6702)	
27 Months	0.9657 (0.9113 to 0.9870)	0.5594 (0.4800 to 0.6313)	1.0000 (1.0000 to 1.0000)	0.4000 (0.1227 to 0.6702)	
30 Months	0.9657 (0.9113 to 0.9870)	0.5594 (0.4800 to 0.6313)	1.0000 (1.0000 to 1.0000)	0.4000 (0.1227 to 0.6702)	
Number of patients at risk[b]					
3 Months	111	97	5	3	
6 Months	107	94	4	3	
9 Months	101	93	4	3	
12 Months	99	91	4	3	
15 Months	95	82	2	3	
18 Months	93	77	2	3	
21 Months	73	66	2	2	
24 Months	27	23	1	0	
27 Months	4	1	0	0	
30 Months	0	0	0	0	

PT are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.72 Subgroup analysis by baseline ECOG PS
16.2.7.1.72.2 Treatment emergent adverse event per PT by treatment group according to baseline ECOG PS - Safety population

	0 or 1		>1		
	Kd (N=117)	**IKd (N=167)**	**Kd (N=5)**	**IKd (N=10)**	**p-value of treatment-by-sub group interaction[c]**
30 Months	0.9820 (0.9300 to 0.9955)	0.9365 (0.8852 to 0.9653)	0.7500 (0.1279 to 0.9605)	1.0000 (1.0000 to 1.0000)	
Number of patients at risk[b]					
3 Months	113	163	5	9	
6 Months	109	151	4	9	
9 Months	102	144	3	9	
12 Months	100	141	3	8	
15 Months	96	131	2	8	
18 Months	94	125	2	7	
21 Months	74	112	2	6	
24 Months	27	36	1	0	
27 Months	4	1	0	0	
30 Months	0	0	0	0	
Thrombocytopenia (days)					
Number (%) of events	11 (9.4)	4 (2.4)	1 (20.0)	1 (10.0)	0.6819
Number (%) of patients censored	106 (90.6)	163 (97.6)	4 (80.0)	9 (90.0)	

PT are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
PGM=DEVOPS/SAR650984/EFC15246/CIR_RWE/REPORT/PGM/ae_km_socpt_subgp_sr_s_t.sas OUT=REPORT/OUTPUT/ae_km_teaept_ecog_s_t_x.rtf (12FEB2021 8:25)

16.2.7.1 Safety endpoints
16.2.7.1.72 Subgroup analysis by baseline ECOG PS
16.2.7.1.72.2 Treatment emergent adverse event per PT by treatment group according to baseline ECOG PS - Safety population

	0 or 1		>1		
	Kd (N=117)	**IKd (N=167)**	**Kd (N=5)**	**IKd (N=10)**	**p-value of treatment-by-sub group interaction[c]**
Kaplan-Meier estimates of event in months					
25% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (3.2526 to NC)	NC (18.4312 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (3.2526 to NC)	NC (18.4312 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (3.2526 to NC)	NC (NC to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.0093		0.5073	
Hazard ratio (95% CI) vs Kd	-	0.25 (0.08 to 0.77)		0.40 (0.02 to 6.62)	
P-value	-	0.0164		0.5211	
Events probability (95% CI)[b]					
3 Months	0.9483 (0.8886 to 0.9765)	0.9880 (0.9530 to 0.9970)	1.0000 (1.0000 to 1.0000)	1.0000 (1.0000 to 1.0000)	
6 Months	0.9308 (0.8663 to 0.9648)	0.9880 (0.9530 to 0.9970)	0.8000 (0.2038 to 0.9692)	1.0000 (1.0000 to 1.0000)	

PT are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.72 Subgroup analysis by baseline ECOG PS
16.2.7.1.72.2 Treatment emergent adverse event per PT by treatment group according to baseline ECOG PS - Safety population

	0 or 1		>1		
	Kd (N=117)	**IKd (N=167)**	**Kd (N=5)**	**IKd (N=10)**	**p-value of treatment-by-sub group interaction[c]**
9 Months	0.9127 (0.8438 to 0.9521)	0.9880 (0.9530 to 0.9970)	0.8000 (0.2038 to 0.9692)	1.0000 (1.0000 to 1.0000)	
12 Months	0.9127 (0.8438 to 0.9521)	0.9815 (0.9436 to 0.9940)	0.8000 (0.2038 to 0.9692)	1.0000 (1.0000 to 1.0000)	
15 Months	0.9127 (0.8438 to 0.9521)	0.9815 (0.9436 to 0.9940)	0.8000 (0.2038 to 0.9692)	1.0000 (1.0000 to 1.0000)	
18 Months	0.9027 (0.8309 to 0.9450)	0.9743 (0.9328 to 0.9903)	0.8000 (0.2038 to 0.9692)	1.0000 (1.0000 to 1.0000)	
21 Months	0.9027 (0.8309 to 0.9450)	0.9743 (0.9328 to 0.9903)	0.8000 (0.2038 to 0.9692)	0.8571 (0.3341 to 0.9786)	
24 Months	0.9027 (0.8309 to 0.9450)	0.9743 (0.9328 to 0.9903)	0.8000 (0.2038 to 0.9692)	0.8571 (0.3341 to 0.9786)	
27 Months	0.9027 (0.8309 to 0.9450)	0.9743 (0.9328 to 0.9903)	0.8000 (0.2038 to 0.9692)	0.8571 (0.3341 to 0.9786)	
30 Months	0.9027 (0.8309 to 0.9450)	0.9743 (0.9328 to 0.9903)	0.8000 (0.2038 to 0.9692)	0.8571 (0.3341 to 0.9786)	
Number of patients at risk[b]					
3 Months	109	162	5	9	

PT are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.72 Subgroup analysis by baseline ECOG PS
16.2.7.1.72.2 Treatment emergent adverse event per PT by treatment group according to baseline ECOG PS - Safety population

	0 or 1		>1		
	Kd (N=117)	**IKd (N=167)**	**Kd (N=5)**	**IKd (N=10)**	**p-value of treatment-by-sub group interaction[c]**
6 Months	103	156	4	9	
9 Months	95	151	4	9	
12 Months	94	148	4	8	
15 Months	91	137	2	8	
18 Months	88	130	2	7	
21 Months	69	116	2	5	
24 Months	26	39	1	0	
27 Months	4	2	0	0	
30 Months	0	0	0	0	
Traumatic fracture (days)					
Number (%) of events	5 (4.3)	13 (7.8)	0 (0.0)	0 (0.0)	0.9998
Number (%) of patients censored	112 (95.7)	154 (92.2)	5 (100.0)	10 (100.0)	
Kaplan-Meier estimates of event in months					
25% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	

PT are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.72 Subgroup analysis by baseline ECOG PS
16.2.7.1.72.2 Treatment emergent adverse event per PT by treatment group according to baseline ECOG PS - Safety population

	0 or 1		>1		
	Kd (N=117)	**IKd (N=167)**	**Kd (N=5)**	**IKd (N=10)**	**p-value of treatment-by-sub group interaction[c]**
21 Months	73	110	2	6	
24 Months	26	34	1	0	
27 Months	3	1	0	0	
30 Months	0	0	0	0	
Upper respiratory tract infection (days)					
Number (%) of events	27 (23.1)	62 (37.1)	2 (40.0)	2 (20.0)	0.1987
Number (%) of patients censored	90 (76.9)	105 (62.9)	3 (60.0)	8 (80.0)	
Kaplan-Meier estimates of event in months					
25% quantile (95% CI)	NC (8.0493 to NC)	8.0821 (4.6982 to 11.7290)	15.7372 (3.2197 to NC)	NC (3.5811 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	15.7372 (3.2197 to NC)	NC (3.5811 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (3.2197 to NC)	NC (NC to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.0170		0.3721	

PT are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.72 Subgroup analysis by baseline ECOG PS
16.2.7.1.72.2 Treatment emergent adverse event per PT by treatment group according to baseline ECOG PS - Safety population

	0 or 1		>1		
	Kd (N=117)	**IKd (N=167)**	**Kd (N=5)**	**IKd (N=10)**	**p-value of treatment-by-sub group interaction[c]**
Hazard ratio (95% CI) vs Kd	-	1.72 (1.10 to 2.71)		0.42 (0.06 to 3.00)	
P-value	-	0.0185		0.3867	
Hazard ratio inverted (95% CI) vs IKd	0.58 (0.37 to 0.91)				
Events probability (95% CI)[b]					
3 Months	0.9223 (0.8560 to 0.9588)	0.8913 (0.8330 to 0.9301)	1.0000 (1.0000 to 1.0000)	1.0000 (1.0000 to 1.0000)	
6 Months	0.8689 (0.7919 to 0.9188)	0.7787 (0.7067 to 0.8351)	0.8000 (0.2038 to 0.9692)	0.8889 (0.4330 to 0.9836)	
9 Months	0.8232 (0.7393 to 0.8822)	0.7201 (0.6435 to 0.7830)	0.8000 (0.2038 to 0.9692)	0.7778 (0.3648 to 0.9393)	
12 Months	0.7941 (0.7063 to 0.8583)	0.6802 (0.6013 to 0.7467)	0.8000 (0.2038 to 0.9692)	0.7778 (0.3648 to 0.9393)	
15 Months	0.7536 (0.6610 to 0.8242)	0.6319 (0.5509 to 0.7023)	0.8000 (0.2038 to 0.9692)	0.7778 (0.3648 to 0.9393)	
18 Months	0.7536 (0.6610 to 0.8242)	0.6017 (0.5194 to 0.6745)	0.4000 (0.0114 to 0.8290)	0.7778 (0.3648 to 0.9393)	
21 Months	0.7536 (0.6610 to 0.8242)	0.6017 (0.5194 to 0.6745)	0.4000 (0.0114 to 0.8290)	0.7778 (0.3648 to 0.9393)	

PT are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.72 Subgroup analysis by baseline ECOG PS
16.2.7.1.72.2 Treatment emergent adverse event per PT by treatment group according to baseline ECOG PS - Safety population

	0 or 1		>1		
	Kd (N=117)	**IKd (N=167)**	**Kd (N=5)**	**IKd (N=10)**	**p-value of treatment-by-sub group interaction[c]**
24 Months	0.7536 (0.6610 to 0.8242)	0.6017 (0.5194 to 0.6745)	0.4000 (0.0114 to 0.8290)	0.7778 (0.3648 to 0.9393)	
27 Months	0.7536 (0.6610 to 0.8242)	0.6017 (0.5194 to 0.6745)	0.4000 (0.0114 to 0.8290)	0.7778 (0.3648 to 0.9393)	
30 Months	0.7536 (0.6610 to 0.8242)	0.6017 (0.5194 to 0.6745)	0.4000 (0.0114 to 0.8290)	0.7778 (0.3648 to 0.9393)	
Number of patients at risk[b]					
3 Months	105	146	5	9	
6 Months	96	122	3	8	
9 Months	85	109	3	7	
12 Months	80	102	3	6	
15 Months	72	86	2	6	
18 Months	71	79	1	5	
21 Months	56	71	1	4	
24 Months	20	22	1	0	
27 Months	3	1	0	0	
30 Months	0	0	0	0	

PT are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.73 Subgroup analysis by ISS staging at study entry
16.2.7.1.73.2 Treatment emergent adverse event per PT by treatment group according to ISS staging at study entry - Safety population

	I		II		III		
	Kd (N=70)	**IKd (N=89)**	**Kd (N=31)**	**IKd (N=63)**	**Kd (N=20)**	**IKd (N=24)**	**p-value of treatment-by-sub group interaction[c]**
6 Months	63	85	28	52	15	20	
9 Months	59	82	26	52	14	18	
12 Months	58	80	25	52	13	16	
15 Months	57	74	22	50	12	12	
18 Months	57	71	22	49	10	10	
21 Months	44	64	18	43	8	9	
24 Months	17	22	8	15	2	1	
27 Months	3	2	1	0	0	0	
30 Months	0	0	0	0	0	0	
Bronchitis (days)							
Number (%) of events	8 (11.4)	21 (23.6)	6 (19.4)	14 (22.2)	1 (5.0)	4 (16.7)	0.4670
Number (%) of patients censored	62 (88.6)	68 (76.4)	25 (80.6)	49 (77.8)	19 (95.0)	20 (83.3)	
Kaplan-Meier estimates of event in months							
25% quantile (95% CI)	NC (NC to NC)	NC (8.2793 to NC)	NC (4.8624 to NC)	NC (9.7577 to NC)	NC (0.0329 to NC)	NC (0.0986 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	

PT are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.73 Subgroup analysis by ISS staging at study entry
16.2.7.1.73.2 Treatment emergent adverse event per PT by treatment group according to ISS staging at study entry - Safety population

	I		II		III		
	Kd (N=70)	**IKd (N=89)**	**Kd (N=31)**	**IKd (N=63)**	**Kd (N=20)**	**IKd (N=24)**	**p-value of treatment-by-sub group interaction[c]**
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Kd							
Log-Rank test p-value[a] vs Kd	-	0.0453		0.7970		0.2565	
Hazard ratio (95% CI) vs Kd	-	2.25 (1.00 to 5.07)		1.13 (0.44 to 2.95)		3.31 (0.37 to 29.60)	
P-value	-	0.0514		0.7972		0.2847	
Events probability (95% CI)[b]							
3 Months	0.9714 (0.8906 to 0.9928)	0.9548 (0.8840 to 0.9828)	0.9677 (0.7923 to 0.9954)	0.9680 (0.8780 to 0.9919)	0.9500 (0.6947 to 0.9928)	0.8730 (0.6558 to 0.9572)	
6 Months	0.9571 (0.8730 to 0.9860)	0.8866 (0.7995 to 0.9373)	0.8986 (0.7174 to 0.9662)	0.9017 (0.7941 to 0.9546)	0.9500 (0.6947 to 0.9928)	0.8730 (0.6558 to 0.9572)	
9 Months	0.9279 (0.8354 to 0.9694)	0.8401 (0.7449 to 0.9020)	0.8986 (0.7174 to 0.9662)	0.8844 (0.7725 to 0.9432)	0.9500 (0.6947 to 0.9928)	0.8730 (0.6558 to 0.9572)	
12 Months	0.9127 (0.8159 to 0.9598)	0.7926 (0.6910 to 0.8640)	0.7908 (0.5918 to 0.9003)	0.8150 (0.6906 to 0.8932)	0.9500 (0.6947 to 0.9928)	0.8185 (0.5818 to 0.9286)	

PT are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.73 Subgroup analysis by ISS staging at study entry
16.2.7.1.73.2 Treatment emergent adverse event per PT by treatment group according to ISS staging at study entry - Safety population

	I		II		III		
	Kd (N=70)	**IKd (N=89)**	**Kd (N=31)**	**IKd (N=63)**	**Kd (N=20)**	**IKd (N=24)**	**p-value of treatment-by-sub group interaction[c]**
15 Months	0.8970 (0.7958 to 0.9496)	0.7926 (0.6910 to 0.8640)	0.7908 (0.5918 to 0.9003)	0.7977 (0.6710 to 0.8798)	0.9500 (0.6947 to 0.9928)	0.8185 (0.5818 to 0.9286)	
18 Months	0.8970 (0.7958 to 0.9496)	0.7525 (0.6454 to 0.8314)	0.7908 (0.5918 to 0.9003)	0.7606 (0.6288 to 0.8509)	0.9500 (0.6947 to 0.9928)	0.8185 (0.5818 to 0.9286)	
21 Months	0.8970 (0.7958 to 0.9496)	0.7525 (0.6454 to 0.8314)	0.7908 (0.5918 to 0.9003)	0.7606 (0.6288 to 0.8509)	0.9500 (0.6947 to 0.9928)	0.8185 (0.5818 to 0.9286)	
24 Months	0.8720 (0.7560 to 0.9352)	0.7525 (0.6454 to 0.8314)	0.7908 (0.5918 to 0.9003)	0.7606 (0.6288 to 0.8509)	0.9500 (0.6947 to 0.9928)	0.8185 (0.5818 to 0.9286)	
27 Months	0.8720 (0.7560 to 0.9352)	0.7525 (0.6454 to 0.8314)	0.7908 (0.5918 to 0.9003)	0.7606 (0.6288 to 0.8509)	0.9500 (0.6947 to 0.9928)	0.8185 (0.5818 to 0.9286)	
30 Months	0.8720 (0.7560 to 0.9352)	0.7525 (0.6454 to 0.8314)	0.7908 (0.5918 to 0.9003)	0.7606 (0.6288 to 0.8509)	0.9500 (0.6947 to 0.9928)	0.8185 (0.5818 to 0.9286)	
Number of patients at risk[b]							
3 Months	68	84	29	60	17	20	
6 Months	66	77	26	52	15	18	
9 Months	61	71	25	51	14	17	
12 Months	59	65	21	47	14	15	
15 Months	57	61	18	44	12	12	

PT are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.73 Subgroup analysis by ISS staging at study entry
16.2.7.1.73.2 Treatment emergent adverse event per PT by treatment group according to ISS staging at study entry - Safety population

	I		II		III		
	Kd (N=70)	**IKd (N=89)**	**Kd (N=31)**	**IKd (N=63)**	**Kd (N=20)**	**IKd (N=24)**	**p-value of treatment-by-sub group interaction[c]**
18 Months	57	55	18	41	10	10	
21 Months	43	49	15	35	8	8	
24 Months	16	16	6	13	2	1	
27 Months	3	1	1	0	0	0	
30 Months	0	0	0	0	0	0	
Cataract (days)							
Number (%) of events	7 (10.0)	8 (9.0)	1 (3.2)	5 (7.9)	0 (0.0)	2 (8.3)	0.7502
Number (%) of patients censored	63 (90.0)	81 (91.0)	30 (96.8)	58 (92.1)	20 (100.0)	22 (91.7)	
Kaplan-Meier estimates of event in months							
25% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (2.1027 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Kd							
Log-Rank test p-value[a] vs Kd	-	0.8919		0.4172		0.3545	

PT are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.73 Subgroup analysis by ISS staging at study entry
16.2.7.1.73.2 Treatment emergent adverse event per PT by treatment group according to ISS staging at study entry - Safety population

	I		II		III		
	Kd (N=70)	**IKd (N=89)**	**Kd (N=31)**	**IKd (N=63)**	**Kd (N=20)**	**IKd (N=24)**	**p-value of treatment-by-sub group interaction[c]**
Number of patients at risk[b]							
3 Months	67	86	30	62	18	21	
6 Months	64	85	28	58	15	19	
9 Months	61	79	25	55	14	17	
12 Months	56	77	22	55	14	15	
15 Months	54	70	21	52	12	11	
18 Months	54	65	21	51	10	9	
21 Months	41	59	17	45	8	6	
24 Months	14	19	7	17	2	1	
27 Months	2	0	0	0	0	0	
30 Months	0	0	0	0	0	0	
Infusion related reaction (days)							
Number (%) of events	1 (1.4)	37 (41.6)	2 (6.5)	29 (46.0)	1 (5.0)	12 (50.0)	0.5412
Number (%) of patients censored	69 (98.6)	52 (58.4)	29 (93.5)	34 (54.0)	19 (95.0)	12 (50.0)	
Kaplan-Meier estimates of event in months							

PT are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.73 Subgroup analysis by ISS staging at study entry
16.2.7.1.73.2 Treatment emergent adverse event per PT by treatment group according to ISS staging at study entry - Safety population

	I		II		III		
	Kd (N=70)	**IKd (N=89)**	**Kd (N=31)**	**IKd (N=63)**	**Kd (N=20)**	**IKd (N=24)**	**p-value of treatment-by-sub group interaction[c]**
25% quantile (95% CI)	NC (NC to NC)	0.1314 (0.0657 to 0.1643)	NC (NC to NC)	0.0986 (0.0657 to 0.1314)	NC (0.0986 to NC)	0.1314 (0.0657 to 0.1643)	
Median (95% CI)	NC (NC to NC)	NC (0.6571 to NC)	NC (NC to NC)	NC (0.1314 to NC)	NC (NC to NC)	NC (0.1314 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Kd							
Log-Rank test p-value[a] vs Kd	-	<.0001		0.0003		0.0022	
Hazard ratio (95% CI) vs Kd	-	36.37 (4.99 to 265.20)		8.81 (2.10 to 36.95)		12.16 (1.58 to 93.77)	
P-value	-	0.0004		0.0029		0.0165	
Hazard ratio inverted (95% CI) vs IKd	0.03 (0.00 to 0.20)		0.11 (0.03 to 0.48)		0.08 (0.01 to 0.63)		
Events probability (95% CI)[b]							
3 Months	0.9857 (0.9029 to 0.9980)	0.6067 (0.4974 to 0.6994)	0.9355 (0.7659 to 0.9835)	0.5714 (0.4404 to 0.6826)	0.9500 (0.6947 to 0.9928)	0.5000 (0.2910 to 0.6776)	
6 Months	0.9857 (0.9029 to 0.9980)	0.6067 (0.4974 to 0.6994)	0.9355 (0.7659 to 0.9835)	0.5556 (0.4249 to 0.6679)	0.9500 (0.6947 to 0.9928)	0.5000 (0.2910 to 0.6776)	

PT are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.73 Subgroup analysis by ISS staging at study entry
16.2.7.1.73.2 Treatment emergent adverse event per PT by treatment group according to ISS staging at study entry - Safety population

	I		II		III		
	Kd (N=70)	**IKd (N=89)**	**Kd (N=31)**	**IKd (N=63)**	**Kd (N=20)**	**IKd (N=24)**	**p-value of treatment-by-sub group interaction[c]**
9 Months	0.9857 (0.9029 to 0.9980)	0.6067 (0.4974 to 0.6994)	0.9355 (0.7659 to 0.9835)	0.5556 (0.4249 to 0.6679)	0.9500 (0.6947 to 0.9928)	0.5000 (0.2910 to 0.6776)	
12 Months	0.9857 (0.9029 to 0.9980)	0.6067 (0.4974 to 0.6994)	0.9355 (0.7659 to 0.9835)	0.5556 (0.4249 to 0.6679)	0.9500 (0.6947 to 0.9928)	0.5000 (0.2910 to 0.6776)	
15 Months	0.9857 (0.9029 to 0.9980)	0.5948 (0.4853 to 0.6885)	0.9355 (0.7659 to 0.9835)	0.5556 (0.4249 to 0.6679)	0.9500 (0.6947 to 0.9928)	0.5000 (0.2910 to 0.6776)	
18 Months	0.9857 (0.9029 to 0.9980)	0.5948 (0.4853 to 0.6885)	0.9355 (0.7659 to 0.9835)	0.5556 (0.4249 to 0.6679)	0.9500 (0.6947 to 0.9928)	0.5000 (0.2910 to 0.6776)	
21 Months	0.9857 (0.9029 to 0.9980)	0.5810 (0.4708 to 0.6761)	0.9355 (0.7659 to 0.9835)	0.5387 (0.4084 to 0.6523)	0.9500 (0.6947 to 0.9928)	0.5000 (0.2910 to 0.6776)	
24 Months	0.9857 (0.9029 to 0.9980)	0.5810 (0.4708 to 0.6761)	0.9355 (0.7659 to 0.9835)	0.5387 (0.4084 to 0.6523)	0.9500 (0.6947 to 0.9928)	0.5000 (0.2910 to 0.6776)	
27 Months	0.9857 (0.9029 to 0.9980)	0.5810 (0.4708 to 0.6761)	0.9355 (0.7659 to 0.9835)	0.5387 (0.4084 to 0.6523)	0.9500 (0.6947 to 0.9928)	0.5000 (0.2910 to 0.6776)	
30 Months	0.9857 (0.9029 to 0.9980)	0.5810 (0.4708 to 0.6761)	0.9355 (0.7659 to 0.9835)	0.5387 (0.4084 to 0.6523)	0.9500 (0.6947 to 0.9928)	0.5000 (0.2910 to 0.6776)	
Number of patients at risk[b]							
3 Months	69	54	28	36	18	10	

PT are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.73 Subgroup analysis by ISS staging at study entry
16.2.7.1.73.2 Treatment emergent adverse event per PT by treatment group according to ISS staging at study entry - Safety population

	I		II		III		
	Kd (N=70)	**IKd (N=89)**	**Kd (N=31)**	**IKd (N=63)**	**Kd (N=20)**	**IKd (N=24)**	**p-value of treatment-by-sub group interaction[c]**
6 Months	68	54	27	35	15	8	
9 Months	65	53	25	35	14	8	
12 Months	64	51	24	35	14	8	
15 Months	63	47	21	33	12	5	
18 Months	63	43	21	33	10	4	
21 Months	49	37	17	28	8	3	
24 Months	19	14	7	8	2	1	
27 Months	3	1	1	0	0	0	
30 Months	0	0	0	0	0	0	
Insomnia (days)							
Number (%) of events	16 (22.9)	22 (24.7)	7 (22.6)	14 (22.2)	5 (25.0)	5 (20.8)	0.8677
Number (%) of patients censored	54 (77.1)	67 (75.3)	24 (77.4)	49 (77.8)	15 (75.0)	19 (79.2)	
Kaplan-Meier estimates of event in months							
25% quantile (95% CI)	NC (9.5606 to NC)	17.0513 (6.7680 to NC)	NC (0.9856 to NC)	NC (2.9569 to NC)	3.8768 (0.1314 to NC)	NC (0.1314 to NC)	

PT are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.73 Subgroup analysis by ISS staging at study entry
16.2.7.1.73.2 Treatment emergent adverse event per PT by treatment group according to ISS staging at study entry - Safety population

	I		II		III		
	Kd (N=70)	**IKd (N=89)**	**Kd (N=31)**	**IKd (N=63)**	**Kd (N=20)**	**IKd (N=24)**	**p-value of treatment-by-sub group interaction[c]**
27 Months	0.9710 (0.8890 to 0.9927)	0.9074 (0.8232 to 0.9526)	1.0000 (1.0000 to 1.0000)	0.9831 (0.8857 to 0.9976)	0.9333 (0.6126 to 0.9903)	0.9500 (0.6947 to 0.9928)	
30 Months	0.9710 (0.8890 to 0.9927)	0.9074 (0.8232 to 0.9526)	1.0000 (1.0000 to 1.0000)	0.9831 (0.8857 to 0.9976)	0.9333 (0.6126 to 0.9903)	0.9500 (0.6947 to 0.9928)	
Number of patients at risk[b]							
3 Months	69	87	30	62	18	22	
6 Months	68	83	29	57	15	19	
9 Months	64	78	27	57	13	17	
12 Months	63	75	26	57	13	16	
15 Months	62	70	23	55	12	13	
18 Months	62	66	23	54	10	11	
21 Months	48	60	19	48	8	9	
24 Months	18	18	8	17	2	1	
27 Months	3	1	1	0	0	0	
30 Months	0	0	0	0	0	0	
Thrombocytopenia (days)							

PT are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.73 Subgroup analysis by ISS staging at study entry
16.2.7.1.73.2 Treatment emergent adverse event per PT by treatment group according to ISS staging at study entry - Safety population

	I		II		III		
	Kd (N=70)	**IKd (N=89)**	**Kd (N=31)**	**IKd (N=63)**	**Kd (N=20)**	**IKd (N=24)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	6 (8.6)	2 (2.2)	3 (9.7)	2 (3.2)	3 (15.0)	1 (4.2)	0.9938
Number (%) of patients censored	64 (91.4)	87 (97.8)	28 (90.3)	61 (96.8)	17 (85.0)	23 (95.8)	
Kaplan-Meier estimates of event in months							
25% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (6.5051 to NC)	NC (NC to NC)	NC (0.2300 to NC)	NC (15.0144 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Kd							
Log-Rank test p-value[a] vs Kd	-	0.0752		0.1689		0.2242	
Hazard ratio (95% CI) vs Kd	-	0.26 (0.05 to 1.29)		0.30 (0.05 to 1.83)		0.27 (0.03 to 2.60)	
P-value	-	0.0986		0.1940		0.2572	
Events probability (95% CI)[b]							
3 Months	0.9571 (0.8730 to 0.9860)	0.9888 (0.9229 to 0.9984)	0.9355 (0.7659 to 0.9835)	0.9841 (0.8926 to 0.9977)	0.9500 (0.6947 to 0.9928)	1.0000 (1.0000 to 1.0000)	

PT are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.73 Subgroup analysis by ISS staging at study entry
16.2.7.1.73.2 Treatment emergent adverse event per PT by treatment group according to ISS staging at study entry - Safety population

	I		II		III		
	Kd (N=70)	**IKd (N=89)**	**Kd (N=31)**	**IKd (N=63)**	**Kd (N=20)**	**IKd (N=24)**	**p-value of treatment-by-sub group interaction[c]**
6 Months	0.9286 (0.8369 to 0.9696)	0.9888 (0.9229 to 0.9984)	0.9355 (0.7659 to 0.9835)	0.9841 (0.8926 to 0.9977)	0.8972 (0.6475 to 0.9733)	1.0000 (1.0000 to 1.0000)	
9 Months	0.9286 (0.8369 to 0.9696)	0.9888 (0.9229 to 0.9984)	0.9008 (0.7229 to 0.9669)	0.9841 (0.8926 to 0.9977)	0.8374 (0.5740 to 0.9449)	1.0000 (1.0000 to 1.0000)	
12 Months	0.9286 (0.8369 to 0.9696)	0.9769 (0.9105 to 0.9942)	0.9008 (0.7229 to 0.9669)	0.9841 (0.8926 to 0.9977)	0.8374 (0.5740 to 0.9449)	1.0000 (1.0000 to 1.0000)	
15 Months	0.9286 (0.8369 to 0.9696)	0.9769 (0.9105 to 0.9942)	0.9008 (0.7229 to 0.9669)	0.9841 (0.8926 to 0.9977)	0.8374 (0.5740 to 0.9449)	1.0000 (1.0000 to 1.0000)	
18 Months	0.9133 (0.8172 to 0.9601)	0.9769 (0.9105 to 0.9942)	0.9008 (0.7229 to 0.9669)	0.9841 (0.8926 to 0.9977)	0.8374 (0.5740 to 0.9449)	0.9231 (0.5664 to 0.9888)	
21 Months	0.9133 (0.8172 to 0.9601)	0.9769 (0.9105 to 0.9942)	0.9008 (0.7229 to 0.9669)	0.9662 (0.8713 to 0.9915)	0.8374 (0.5740 to 0.9449)	0.9231 (0.5664 to 0.9888)	
24 Months	0.9133 (0.8172 to 0.9601)	0.9769 (0.9105 to 0.9942)	0.9008 (0.7229 to 0.9669)	0.9662 (0.8713 to 0.9915)	0.8374 (0.5740 to 0.9449)	0.9231 (0.5664 to 0.9888)	
27 Months	0.9133 (0.8172 to 0.9601)	0.9769 (0.9105 to 0.9942)	0.9008 (0.7229 to 0.9669)	0.9662 (0.8713 to 0.9915)	0.8374 (0.5740 to 0.9449)	0.9231 (0.5664 to 0.9888)	
30 Months	0.9133 (0.8172 to 0.9601)	0.9769 (0.9105 to 0.9942)	0.9008 (0.7229 to 0.9669)	0.9662 (0.8713 to 0.9915)	0.8374 (0.5740 to 0.9449)	0.9231 (0.5664 to 0.9888)	

PT are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.73 Subgroup analysis by ISS staging at study entry
16.2.7.1.73.2 Treatment emergent adverse event per PT by treatment group according to ISS staging at study entry - Safety population

	I		II		III		
	Kd (N=70)	**IKd (N=89)**	**Kd (N=31)**	**IKd (N=63)**	**Kd (N=20)**	**IKd (N=24)**	**p-value of treatment-by-sub group interaction[c]**
Number of patients at risk[b]							
3 Months	67	87	28	61	18	22	
6 Months	64	86	27	58	15	20	
9 Months	61	83	24	58	13	18	
12 Months	61	80	23	58	13	17	
15 Months	61	75	20	56	11	13	
18 Months	60	71	20	55	9	10	
21 Months	46	64	17	48	7	8	
24 Months	17	21	8	17	2	1	
27 Months	3	2	1	0	0	0	
30 Months	0	0	0	0	0	0	
Traumatic fracture (days)							
Number (%) of events	3 (4.3)	8 (9.0)	0 (0.0)	4 (6.3)	2 (10.0)	1 (4.2)	0.5043
Number (%) of patients censored	67 (95.7)	81 (91.0)	31 (100.0)	59 (93.7)	18 (90.0)	23 (95.8)	
Kaplan-Meier estimates of event in months							

PT are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.73 Subgroup analysis by ISS staging at study entry
16.2.7.1.73.2 Treatment emergent adverse event per PT by treatment group according to ISS staging at study entry - Safety population

	I		II		III		
	Kd (N=70)	**IKd (N=89)**	**Kd (N=31)**	**IKd (N=63)**	**Kd (N=20)**	**IKd (N=24)**	**p-value of treatment-by-sub group interaction[c]**
12 Months	63	77	26	56	14	16	
15 Months	62	72	23	54	11	12	
18 Months	62	69	23	52	8	10	
21 Months	48	61	19	46	7	8	
24 Months	17	18	8	15	2	1	
27 Months	2	1	1	0	0	0	
30 Months	0	0	0	0	0	0	
Upper respiratory tract infection (days)							
Number (%) of events	20 (28.6)	34 (38.2)	5 (16.1)	24 (38.1)	4 (20.0)	6 (25.0)	0.4475
Number (%) of patients censored	50 (71.4)	55 (61.8)	26 (83.9)	39 (61.9)	16 (80.0)	18 (75.0)	
Kaplan-Meier estimates of event in months							
25% quantile (95% CI)	12.0246 (5.9138 to NC)	8.0821 (4.2382 to 13.2402)	NC (4.2053 to NC)	6.8665 (3.5154 to 11.6304)	15.7372 (1.4127 to NC)	16.3285 (0.4928 to NC)	
Median (95% CI)	NC (NC to NC)	NC (17.9055 to NC)	NC (NC to NC)	NC (11.6304 to NC)	NC (15.7372 to NC)	NC (8.4107 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	

PT are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
PGM=DEVOPS/SAR650984/EFC15246/CIR_RWE/REPORT/PGM/ae_km_socpt_subgp_sr_s_t.sas OUT=REPORT/OUTPUT/ae_km_teaept_seiss_s_t_x.rtf (12FEB2021 8:25)

16.2.7.1 Safety endpoints
16.2.7.1.73 Subgroup analysis by ISS staging at study entry
16.2.7.1.73.2 Treatment emergent adverse event per PT by treatment group according to ISS staging at study entry - Safety population

	I		II		III		
	Kd (N=70)	**IKd (N=89)**	**Kd (N=31)**	**IKd (N=63)**	**Kd (N=20)**	**IKd (N=24)**	**p-value of treatment-by-sub group interaction[c]**
Comparison vs. Kd							
Log-Rank test p-value[a] vs Kd	-	0.2460		0.0335		0.7508	
Hazard ratio (95% CI) vs Kd	-	1.38 (0.80 to 2.41)		2.73 (1.04 to 7.15)		1.23 (0.35 to 4.36)	
P-value	-	0.2481		0.0414		0.7512	
Hazard ratio inverted (95% CI) vs IKd			0.37 (0.14 to 0.96)				
Events probability (95% CI)[b]							
3 Months	0.9143 (0.8191 to 0.9606)	0.8985 (0.8139 to 0.9458)	0.9677 (0.7923 to 0.9954)	0.8883 (0.7799 to 0.9451)	0.8889 (0.6242 to 0.9710)	0.9110 (0.6884 to 0.9770)	
6 Months	0.8424 (0.7335 to 0.9095)	0.7730 (0.6706 to 0.8472)	0.9010 (0.7236 to 0.9670)	0.7547 (0.6261 to 0.8443)	0.8889 (0.6242 to 0.9710)	0.9110 (0.6884 to 0.9770)	
9 Months	0.7838 (0.6671 to 0.8636)	0.7377 (0.6321 to 0.8173)	0.9010 (0.7236 to 0.9670)	0.6860 (0.5525 to 0.7872)	0.8205 (0.5371 to 0.9390)	0.7519 (0.4991 to 0.8896)	
12 Months	0.7530 (0.6329 to 0.8387)	0.7137 (0.6062 to 0.7967)	0.8650 (0.6786 to 0.9472)	0.6174 (0.4820 to 0.7272)	0.8205 (0.5371 to 0.9390)	0.7519 (0.4991 to 0.8896)	

PT are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.73 Subgroup analysis by ISS staging at study entry
16.2.7.1.73.2 Treatment emergent adverse event per PT by treatment group according to ISS staging at study entry - Safety population

	I		II		III		
	Kd (N=70)	**IKd (N=89)**	**Kd (N=31)**	**IKd (N=63)**	**Kd (N=20)**	**IKd (N=24)**	**p-value of treatment-by-sub group interaction[c]**
15 Months	0.7053 (0.5807 to 0.7991)	0.6263 (0.5141 to 0.7196)	0.8238 (0.6249 to 0.9232)	0.6174 (0.4820 to 0.7272)	0.8205 (0.5371 to 0.9390)	0.7519 (0.4991 to 0.8896)	
18 Months	0.7053 (0.5807 to 0.7991)	0.5997 (0.4865 to 0.6956)	0.8238 (0.6249 to 0.9232)	0.5987 (0.4628 to 0.7107)	0.7293 (0.4149 to 0.8929)	0.6684 (0.3888 to 0.8421)	
21 Months	0.7053 (0.5807 to 0.7991)	0.5997 (0.4865 to 0.6956)	0.8238 (0.6249 to 0.9232)	0.5987 (0.4628 to 0.7107)	0.7293 (0.4149 to 0.8929)	0.6684 (0.3888 to 0.8421)	
24 Months	0.7053 (0.5807 to 0.7991)	0.5997 (0.4865 to 0.6956)	0.8238 (0.6249 to 0.9232)	0.5987 (0.4628 to 0.7107)	0.7293 (0.4149 to 0.8929)	0.6684 (0.3888 to 0.8421)	
27 Months	0.7053 (0.5807 to 0.7991)	0.5997 (0.4865 to 0.6956)	0.8238 (0.6249 to 0.9232)	0.5987 (0.4628 to 0.7107)	0.7293 (0.4149 to 0.8929)	0.6684 (0.3888 to 0.8421)	
30 Months	0.7053 (0.5807 to 0.7991)	0.5997 (0.4865 to 0.6956)	0.8238 (0.6249 to 0.9232)	0.5987 (0.4628 to 0.7107)	0.7293 (0.4149 to 0.8929)	0.6684 (0.3888 to 0.8421)	
Number of patients at risk[b]							
3 Months	64	79	29	55	16	20	
6 Months	58	67	27	44	13	18	
9 Months	51	62	25	40	11	13	
12 Months	48	59	23	36	11	12	
15 Months	44	48	20	34	9	9	

PT are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.73 Subgroup analysis by ISS staging at study entry
16.2.7.1.73.2 Treatment emergent adverse event per PT by treatment group according to ISS staging at study entry - Safety population

	I		II		III		
	Kd (N=70)	**IKd (N=89)**	**Kd (N=31)**	**IKd (N=63)**	**Kd (N=20)**	**IKd (N=24)**	**p-value of treatment-by-sub group interaction[c]**
18 Months	44	45	20	32	7	6	
21 Months	34	40	16	30	6	4	
24 Months	13	12	7	10	1	0	
27 Months	2	1	1	0	0	0	
30 Months	0	0	0	0	0	0	
Urinary tract infection (days)							
Number (%) of events	6 (8.6)	6 (6.7)	3 (9.7)	6 (9.5)	2 (10.0)	0 (0.0)	0.9850
Number (%) of patients censored	64 (91.4)	83 (93.3)	28 (90.3)	57 (90.5)	18 (90.0)	24 (100.0)	
Kaplan-Meier estimates of event in months							
25% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (18.0041 to NC)	NC (NC to NC)	NC (4.8624 to NC)	NC (NC to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Kd							
Log-Rank test p-value[a] vs Kd	-	0.6944		0.9176		0.1029	

PT are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.74 Subgroup analysis by R-ISS staging
16.2.7.1.74.2 Treatment emergent adverse event per PT by treatment group according to R-ISS staging - Safety population

	I or II		III		Not classified		
	Kd (N=102)	**IKd (N=155)**	**Kd (N=8)**	**IKd (N=15)**	**Kd (N=12)**	**IKd (N=7)**	**p-value of treatment-by-sub group interaction[c]**
Number of patients at risk[b]							
3 Months	96	148	7	13	10	6	
6 Months	92	140	5	12	10	6	
9 Months	85	137	5	11	10	5	
12 Months	82	135	5	9	10	5	
15 Months	77	127	5	7	10	3	
18 Months	75	123	5	5	10	3	
21 Months	58	110	4	4	9	3	
24 Months	24	38	1	0	2	0	
27 Months	4	2	0	0	0	0	
30 Months	0	0	0	0	0	0	
Bronchitis (days)							
Number (%) of events	14 (13.7)	35 (22.6)	0 (0.0)	2 (13.3)	1 (8.3)	3 (42.9)	0.3905
Number (%) of patients censored	88 (86.3)	120 (77.4)	8 (100.0)	13 (86.7)	11 (91.7)	4 (57.1)	
Kaplan-Meier estimates of event in months							

PT are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.74 Subgroup analysis by R-ISS staging
16.2.7.1.74.2 Treatment emergent adverse event per PT by treatment group according to R-ISS staging - Safety population

	I or II		III		Not classified		
	Kd (N=102)	**IKd (N=155)**	**Kd (N=8)**	**IKd (N=15)**	**Kd (N=12)**	**IKd (N=7)**	**p-value of treatment-by-sub group interaction[c]**
25% quantile (95% CI)	NC (NC to NC)	NC (11.2361 to NC)	NC (NC to NC)	NC (0.1971 to NC)	NC (12.3532 to NC)	7.4251 (0.0986 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (11.9918 to NC)	NC (NC to NC)	NC (0.0986 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (7.4251 to NC)	
Comparison vs. Kd							
Log-Rank test p-value[a] vs Kd	-	0.0970		0.3094		0.0335	
Hazard ratio (95% CI) vs Kd	-	1.68 (0.90 to 3.12)		NC		8.14 (0.83 to 79.85)	
P-value	-	0.1009		0.9979		0.0718	
Events probability (95% CI)[b]							
3 Months	0.9604 (0.8979 to 0.9849)	0.9548 (0.9074 to 0.9782)	1.0000 (1.0000 to 1.0000)	0.9333 (0.6126 to 0.9903)	1.0000 (1.0000 to 1.0000)	0.8571 (0.3341 to 0.9786)	
6 Months	0.9299 (0.8586 to 0.9660)	0.8884 (0.8265 to 0.9291)	1.0000 (1.0000 to 1.0000)	0.9333 (0.6126 to 0.9903)	1.0000 (1.0000 to 1.0000)	0.8571 (0.3341 to 0.9786)	
9 Months	0.9094 (0.8331 to 0.9518)	0.8610 (0.7948 to 0.9071)	1.0000 (1.0000 to 1.0000)	0.9333 (0.6126 to 0.9903)	1.0000 (1.0000 to 1.0000)	0.6857 (0.2128 to 0.9121)	

PT are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.74 Subgroup analysis by R-ISS staging
16.2.7.1.74.2 Treatment emergent adverse event per PT by treatment group according to R-ISS staging - Safety population

	I or II		III		Not classified		
	Kd (N=102)	**IKd (N=155)**	**Kd (N=8)**	**IKd (N=15)**	**Kd (N=12)**	**IKd (N=7)**	**p-value of treatment-by-sub group interaction[c]**
12 Months	0.8661 (0.7804 to 0.9200)	0.8059 (0.7327 to 0.8609)	1.0000 (1.0000 to 1.0000)	0.8400 (0.4874 to 0.9586)	1.0000 (1.0000 to 1.0000)	0.5143 (0.1178 to 0.8132)	
15 Months	0.8661 (0.7804 to 0.9200)	0.7989 (0.7250 to 0.8549)	1.0000 (1.0000 to 1.0000)	0.8400 (0.4874 to 0.9586)	0.9167 (0.5390 to 0.9878)	0.5143 (0.1178 to 0.8132)	
18 Months	0.8661 (0.7804 to 0.9200)	0.7610 (0.6828 to 0.8223)	1.0000 (1.0000 to 1.0000)	0.8400 (0.4874 to 0.9586)	0.9167 (0.5390 to 0.9878)	0.5143 (0.1178 to 0.8132)	
21 Months	0.8661 (0.7804 to 0.9200)	0.7610 (0.6828 to 0.8223)	1.0000 (1.0000 to 1.0000)	0.8400 (0.4874 to 0.9586)	0.9167 (0.5390 to 0.9878)	0.5143 (0.1178 to 0.8132)	
24 Months	0.8473 (0.7525 to 0.9079)	0.7610 (0.6828 to 0.8223)	1.0000 (1.0000 to 1.0000)	0.8400 (0.4874 to 0.9586)	0.9167 (0.5390 to 0.9878)	0.5143 (0.1178 to 0.8132)	
27 Months	0.8473 (0.7525 to 0.9079)	0.7610 (0.6828 to 0.8223)	1.0000 (1.0000 to 1.0000)	0.8400 (0.4874 to 0.9586)	0.9167 (0.5390 to 0.9878)	0.5143 (0.1178 to 0.8132)	
30 Months	0.8473 (0.7525 to 0.9079)	0.7610 (0.6828 to 0.8223)	1.0000 (1.0000 to 1.0000)	0.8400 (0.4874 to 0.9586)	0.9167 (0.5390 to 0.9878)	0.5143 (0.1178 to 0.8132)	
Number of patients at risk[b]							
3 Months	96	147	7	13	12	5	
6 Months	91	131	5	12	12	5	
9 Months	84	125	5	11	12	4	

PT are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.74 Subgroup analysis by R-ISS staging
16.2.7.1.74.2 Treatment emergent adverse event per PT by treatment group according to R-ISS staging - Safety population

	I or II		III		Not classified		
	Kd (N=102)	**IKd (N=155)**	**Kd (N=8)**	**IKd (N=15)**	**Kd (N=12)**	**IKd (N=7)**	**p-value of treatment-by-sub group interaction[c]**
12 Months	78	115	5	9	12	3	
15 Months	72	108	5	7	11	2	
18 Months	70	99	5	5	11	2	
21 Months	54	87	4	3	9	2	
24 Months	21	30	1	0	2	0	
27 Months	4	1	0	0	0	0	
30 Months	0	0	0	0	0	0	
Cataract (days)							
Number (%) of events	8 (7.8)	14 (9.0)	0 (0.0)	1 (6.7)	0 (0.0)	0 (0.0)	1.0000
Number (%) of patients censored	94 (92.2)	141 (91.0)	8 (100.0)	14 (93.3)	12 (100.0)	7 (100.0)	
Kaplan-Meier estimates of event in months							
25% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	

PT are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.74 Subgroup analysis by R-ISS staging
16.2.7.1.74.2 Treatment emergent adverse event per PT by treatment group according to R-ISS staging - Safety population

	I or II		III		Not classified		
	Kd (N=102)	**IKd (N=155)**	**Kd (N=8)**	**IKd (N=15)**	**Kd (N=12)**	**IKd (N=7)**	**p-value of treatment-by-sub group interaction[c]**
6 Months	92	145	5	12	11	6	
9 Months	85	136	5	11	11	5	
12 Months	77	134	5	9	11	5	
15 Months	72	123	5	7	11	4	
18 Months	70	117	5	5	11	4	
21 Months	54	104	4	3	9	4	
24 Months	19	37	1	0	3	0	
27 Months	2	0	0	0	0	0	
30 Months	0	0	0	0	0	0	
Infusion related reaction (days)							
Number (%) of events	3 (2.9)	67 (43.2)	1 (12.5)	7 (46.7)	0 (0.0)	5 (71.4)	0.5255
Number (%) of patients censored	99 (97.1)	88 (56.8)	7 (87.5)	8 (53.3)	12 (100.0)	2 (28.6)	
Kaplan-Meier estimates of event in months							
25% quantile (95% CI)	NC (NC to NC)	0.0986 (0.0657 to 0.1314)	NC (0.0986 to NC)	0.0657 (0.0657 to 0.2957)	NC (NC to NC)	0.0657 (0.0657 to 0.2300)	

PT are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.74 Subgroup analysis by R-ISS staging
16.2.7.1.74.2 Treatment emergent adverse event per PT by treatment group according to R-ISS staging - Safety population

	I or II		III		Not classified		
	Kd (N=102)	**IKd (N=155)**	**Kd (N=8)**	**IKd (N=15)**	**Kd (N=12)**	**IKd (N=7)**	**p-value of treatment-by-sub group interaction[c]**
Median (95% CI)	NC (NC to NC)	NC (12.0246 to NC)	NC (0.0986 to NC)	NC (0.0657 to NC)	NC (NC to NC)	0.2300 (0.0657 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (0.1643 to NC)	
Comparison vs. Kd							
Log-Rank test p-value[a] vs Kd	-	<.0001		0.1345		0.0007	
Hazard ratio (95% CI) vs Kd	-	18.28 (5.75 to 58.16)		4.34 (0.53 to 35.37)		NC	
P-value	-	<.0001		0.1703		0.9968	
Hazard ratio inverted (95% CI) vs IKd	0.05 (0.02 to 0.17)						
Events probability (95% CI)[b]							
3 Months	0.9705 (0.9113 to 0.9904)	0.5935 (0.5119 to 0.6661)	0.8750 (0.3870 to 0.9814)	0.5333 (0.2632 to 0.7438)	1.0000 (1.0000 to 1.0000)	0.2857 (0.0411 to 0.6115)	
6 Months	0.9705 (0.9113 to 0.9904)	0.5870 (0.5053 to 0.6599)	0.8750 (0.3870 to 0.9814)	0.5333 (0.2632 to 0.7438)	1.0000 (1.0000 to 1.0000)	0.2857 (0.0411 to 0.6115)	
9 Months	0.9705 (0.9113 to 0.9904)	0.5870 (0.5053 to 0.6599)	0.8750 (0.3870 to 0.9814)	0.5333 (0.2632 to 0.7438)	1.0000 (1.0000 to 1.0000)	0.2857 (0.0411 to 0.6115)	

PT are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
PGM=DEVOPS/SAR650984/EFC15246/CIR_RWE/REPORT/PGM/ae_km_socpt_subgp_sr_s_t.sas OUT=REPORT/OUTPUT/ae_km_teaept_seriss_s_t_x.rtf (12FEB2021 8:25)

16.2.7.1 Safety endpoints
16.2.7.1.74 Subgroup analysis by R-ISS staging
16.2.7.1.74.2 Treatment emergent adverse event per PT by treatment group according to R-ISS staging - Safety population

	I or II		III		Not classified		
	Kd (N=102)	**IKd (N=155)**	**Kd (N=8)**	**IKd (N=15)**	**Kd (N=12)**	**IKd (N=7)**	**p-value of treatment-by-sub group interaction[c]**
12 Months	0.9705 (0.9113 to 0.9904)	0.5870 (0.5053 to 0.6599)	0.8750 (0.3870 to 0.9814)	0.5333 (0.2632 to 0.7438)	1.0000 (1.0000 to 1.0000)	0.2857 (0.0411 to 0.6115)	
15 Months	0.9705 (0.9113 to 0.9904)	0.5803 (0.4985 to 0.6535)	0.8750 (0.3870 to 0.9814)	0.5333 (0.2632 to 0.7438)	1.0000 (1.0000 to 1.0000)	0.2857 (0.0411 to 0.6115)	
18 Months	0.9705 (0.9113 to 0.9904)	0.5803 (0.4985 to 0.6535)	0.8750 (0.3870 to 0.9814)	0.5333 (0.2632 to 0.7438)	1.0000 (1.0000 to 1.0000)	0.2857 (0.0411 to 0.6115)	
21 Months	0.9705 (0.9113 to 0.9904)	0.5652 (0.4830 to 0.6393)	0.8750 (0.3870 to 0.9814)	0.5333 (0.2632 to 0.7438)	1.0000 (1.0000 to 1.0000)	0.2857 (0.0411 to 0.6115)	
24 Months	0.9705 (0.9113 to 0.9904)	0.5652 (0.4830 to 0.6393)	0.8750 (0.3870 to 0.9814)	0.5333 (0.2632 to 0.7438)	1.0000 (1.0000 to 1.0000)	0.2857 (0.0411 to 0.6115)	
27 Months	0.9705 (0.9113 to 0.9904)	0.5652 (0.4830 to 0.6393)	0.8750 (0.3870 to 0.9814)	0.5333 (0.2632 to 0.7438)	1.0000 (1.0000 to 1.0000)	0.2857 (0.0411 to 0.6115)	
30 Months	0.9705 (0.9113 to 0.9904)	0.5652 (0.4830 to 0.6393)	0.8750 (0.3870 to 0.9814)	0.5333 (0.2632 to 0.7438)	1.0000 (1.0000 to 1.0000)	0.2857 (0.0411 to 0.6115)	
Number of patients at risk[b]							
3 Months	97	92	7	6	12	2	
6 Months	94	90	5	5	12	2	
9 Months	88	89	5	5	12	2	

PT are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
PGM=DEVOPS/SAR650984/EFC15246/CIR_RWE/REPORT/PGM/ae_km_socpt_subgp_sr_s_t.sas OUT=REPORT/OUTPUT/ae_km_teaept_seriss_s_t_x.rtf (12FEB2021 8:25)

16.2.7.1 Safety endpoints
16.2.7.1.74 Subgroup analysis by R-ISS staging
16.2.7.1.74.2 Treatment emergent adverse event per PT by treatment group according to R-ISS staging - Safety population

	I or II		III		Not classified		
	Kd (N=102)	**IKd (N=155)**	**Kd (N=8)**	**IKd (N=15)**	**Kd (N=12)**	**IKd (N=7)**	**p-value of treatment-by-sub group interaction[c]**
12 Months	86	87	5	5	12	2	
15 Months	80	81	5	3	12	1	
18 Months	78	77	5	2	12	1	
21 Months	61	66	4	1	10	1	
24 Months	24	23	1	0	3	0	
27 Months	4	1	0	0	0	0	
30 Months	0	0	0	0	0	0	
Insomnia (days)							
Number (%) of events	24 (23.5)	38 (24.5)	3 (37.5)	3 (20.0)	1 (8.3)	1 (14.3)	0.5424
Number (%) of patients censored	78 (76.5)	117 (75.5)	5 (62.5)	12 (80.0)	11 (91.7)	6 (85.7)	
Kaplan-Meier estimates of event in months							
25% quantile (95% CI)	21.8480 (4.0411 to NC)	18.4312 (7.5893 to NC)	1.4456 (0.3614 to NC)	NC (0.1314 to NC)	NC (16.8871 to NC)	NC (5.9795 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (0.3614 to NC)	NC (10.0862 to NC)	NC (NC to NC)	NC (5.9795 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (3.8768 to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	

PT are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.74 Subgroup analysis by R-ISS staging
16.2.7.1.74.2 Treatment emergent adverse event per PT by treatment group according to R-ISS staging - Safety population

	I or II		III		Not classified		
	Kd (N=102)	**IKd (N=155)**	**Kd (N=8)**	**IKd (N=15)**	**Kd (N=12)**	**IKd (N=7)**	**p-value of treatment-by-sub group interaction[c]**
27 Months	0.9688 (0.9063 to 0.9898)	0.9328 (0.8787 to 0.9633)	1.0000 (1.0000 to 1.0000)	1.0000 (1.0000 to 1.0000)	1.0000 (1.0000 to 1.0000)	1.0000 (1.0000 to 1.0000)	
30 Months	0.9688 (0.9063 to 0.9898)	0.9328 (0.8787 to 0.9633)	1.0000 (1.0000 to 1.0000)	1.0000 (1.0000 to 1.0000)	1.0000 (1.0000 to 1.0000)	1.0000 (1.0000 to 1.0000)	
Number of patients at risk[b]							
3 Months	99	153	7	13	12	6	
6 Months	96	142	5	12	12	6	
9 Months	88	137	5	11	12	5	
12 Months	86	134	5	10	12	5	
15 Months	81	127	5	8	12	4	
18 Months	79	122	5	6	12	4	
21 Months	62	110	4	4	10	4	
24 Months	24	36	1	0	3	0	
27 Months	4	1	0	0	0	0	
30 Months	0	0	0	0	0	0	
Thrombocytopenia (days)							

PT are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.74 Subgroup analysis by R-ISS staging
16.2.7.1.74.2 Treatment emergent adverse event per PT by treatment group according to R-ISS staging - Safety population

	I or II		III		Not classified		
	Kd (N=102)	**IKd (N=155)**	**Kd (N=8)**	**IKd (N=15)**	**Kd (N=12)**	**IKd (N=7)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	10 (9.8)	4 (2.6)	2 (25.0)	1 (6.7)	0 (0.0)	0 (0.0)	0.9999
Number (%) of patients censored	92 (90.2)	151 (97.4)	6 (75.0)	14 (93.3)	12 (100.0)	7 (100.0)	
Kaplan-Meier estimates of event in months							
25% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	6.2752 (3.2526 to NC)	NC (15.0144 to NC)	NC (NC to NC)	NC (NC to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (3.2526 to NC)	NC (15.0144 to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (6.2752 to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Kd							
Log-Rank test p-value[a] vs Kd	-	0.0115		0.2072			
Hazard ratio (95% CI) vs Kd	-	0.25 (0.08 to 0.80)		0.24 (0.02 to 2.66)		NC	
P-value	-	0.0194		0.2455			
Events probability (95% CI)[b]							

PT are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.74 Subgroup analysis by R-ISS staging
16.2.7.1.74.2 Treatment emergent adverse event per PT by treatment group according to R-ISS staging - Safety population

	I or II		III		Not classified		
	Kd (N=102)	**IKd (N=155)**	**Kd (N=8)**	**IKd (N=15)**	**Kd (N=12)**	**IKd (N=7)**	**p-value of treatment-by-sub group interaction[c]**
3 Months	0.9411 (0.8735 to 0.9731)	0.9871 (0.9494 to 0.9968)	1.0000 (1.0000 to 1.0000)	1.0000 (1.0000 to 1.0000)	1.0000 (1.0000 to 1.0000)	1.0000 (1.0000 to 1.0000)	
6 Months	0.9210 (0.8483 to 0.9597)	0.9871 (0.9494 to 0.9968)	0.8571 (0.3341 to 0.9786)	1.0000 (1.0000 to 1.0000)	1.0000 (1.0000 to 1.0000)	1.0000 (1.0000 to 1.0000)	
9 Months	0.9108 (0.8356 to 0.9526)	0.9871 (0.9494 to 0.9968)	0.6857 (0.2128 to 0.9121)	1.0000 (1.0000 to 1.0000)	1.0000 (1.0000 to 1.0000)	1.0000 (1.0000 to 1.0000)	
12 Months	0.9108 (0.8356 to 0.9526)	0.9802 (0.9400 to 0.9936)	0.6857 (0.2128 to 0.9121)	1.0000 (1.0000 to 1.0000)	1.0000 (1.0000 to 1.0000)	1.0000 (1.0000 to 1.0000)	
15 Months	0.9108 (0.8356 to 0.9526)	0.9802 (0.9400 to 0.9936)	0.6857 (0.2128 to 0.9121)	1.0000 (1.0000 to 1.0000)	1.0000 (1.0000 to 1.0000)	1.0000 (1.0000 to 1.0000)	
18 Months	0.8990 (0.8201 to 0.9444)	0.9802 (0.9400 to 0.9936)	0.6857 (0.2128 to 0.9121)	0.8750 (0.3870 to 0.9814)	1.0000 (1.0000 to 1.0000)	1.0000 (1.0000 to 1.0000)	
21 Months	0.8990 (0.8201 to 0.9444)	0.9726 (0.9284 to 0.9897)	0.6857 (0.2128 to 0.9121)	0.8750 (0.3870 to 0.9814)	1.0000 (1.0000 to 1.0000)	1.0000 (1.0000 to 1.0000)	
24 Months	0.8990 (0.8201 to 0.9444)	0.9726 (0.9284 to 0.9897)	0.6857 (0.2128 to 0.9121)	0.8750 (0.3870 to 0.9814)	1.0000 (1.0000 to 1.0000)	1.0000 (1.0000 to 1.0000)	
27 Months	0.8990 (0.8201 to 0.9444)	0.9726 (0.9284 to 0.9897)	0.6857 (0.2128 to 0.9121)	0.8750 (0.3870 to 0.9814)	1.0000 (1.0000 to 1.0000)	1.0000 (1.0000 to 1.0000)	

PT are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.74 Subgroup analysis by R-ISS staging
16.2.7.1.74.2 Treatment emergent adverse event per PT by treatment group according to R-ISS staging - Safety population

	I or II		III		Not classified		
	Kd (N=102)	**IKd (N=155)**	**Kd (N=8)**	**IKd (N=15)**	**Kd (N=12)**	**IKd (N=7)**	**p-value of treatment-by-sub group interaction[c]**
30 Months	0.8990 (0.8201 to 0.9444)	0.9726 (0.9284 to 0.9897)	0.6857 (0.2128 to 0.9121)	0.8750 (0.3870 to 0.9814)	1.0000 (1.0000 to 1.0000)	1.0000 (1.0000 to 1.0000)	
Number of patients at risk[b]							
3 Months	95	152	7	13	12	6	
6 Months	90	147	5	12	12	6	
9 Months	83	144	4	11	12	5	
12 Months	82	141	4	10	12	5	
15 Months	77	133	4	8	12	4	
18 Months	74	128	4	5	12	4	
21 Months	58	114	3	3	10	4	
24 Months	23	39	1	0	3	0	
27 Months	4	2	0	0	0	0	
30 Months	0	0	0	0	0	0	
Traumatic fracture (days)							
Number (%) of events	4 (3.9)	12 (7.7)	1 (12.5)	1 (6.7)	0 (0.0)	0 (0.0)	0.7363
Number (%) of patients censored	98 (96.1)	143 (92.3)	7 (87.5)	14 (93.3)	12 (100.0)	7 (100.0)	

PT are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.74 Subgroup analysis by R-ISS staging
16.2.7.1.74.2 Treatment emergent adverse event per PT by treatment group according to R-ISS staging - Safety population

	I or II		III		Not classified		
	Kd (N=102)	**IKd (N=155)**	**Kd (N=8)**	**IKd (N=15)**	**Kd (N=12)**	**IKd (N=7)**	**p-value of treatment-by-sub group interaction[c]**
6 Months	95	145	5	11	12	6	
9 Months	89	138	5	10	12	5	
12 Months	87	136	5	9	12	5	
15 Months	81	128	4	7	12	4	
18 Months	78	123	4	5	12	4	
21 Months	62	109	3	3	10	4	
24 Months	23	34	1	0	3	0	
27 Months	3	1	0	0	0	0	
30 Months	0	0	0	0	0	0	
Upper respiratory tract infection (days)							
Number (%) of events	26 (25.5)	60 (38.7)	0 (0.0)	2 (13.3)	3 (25.0)	2 (28.6)	0.9995
Number (%) of patients censored	76 (74.5)	95 (61.3)	8 (100.0)	13 (86.7)	9 (75.0)	5 (71.4)	
Kaplan-Meier estimates of event in months							
25% quantile (95% CI)	13.8645 (6.8665 to NC)	7.2936 (4.2053 to 11.4661)	NC (NC to NC)	NC (6.3737 to NC)	NC (0.2957 to NC)	5.9466 (4.2382 to NC)	

PT are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.74 Subgroup analysis by R-ISS staging
16.2.7.1.74.2 Treatment emergent adverse event per PT by treatment group according to R-ISS staging - Safety population

	I or II		III		Not classified		
	Kd (N=102)	**IKd (N=155)**	**Kd (N=8)**	**IKd (N=15)**	**Kd (N=12)**	**IKd (N=7)**	**p-value of treatment-by-sub group interaction[c]**
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (16.3285 to NC)	NC (8.3778 to NC)	NC (4.2382 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (5.9466 to NC)	
Comparison vs. Kd							
Log-Rank test p-value[a] vs Kd	-	0.0455		0.2897		0.6062	
Hazard ratio (95% CI) vs Kd	-	1.59 (1.01 to 2.52)		NC		1.60 (0.26 to 9.79)	
P-value	-	0.0475		0.9979		0.6092	
Hazard ratio inverted (95% CI) vs IKd	0.63 (0.40 to 0.99)						
Events probability (95% CI)[b]							
3 Months	0.9210 (0.8482 to 0.9597)	0.8837 (0.8218 to 0.9251)	1.0000 (1.0000 to 1.0000)	1.0000 (1.0000 to 1.0000)	0.9167 (0.5390 to 0.9878)	1.0000 (1.0000 to 1.0000)	
6 Months	0.8502 (0.7638 to 0.9069)	0.7708 (0.6956 to 0.8297)	1.0000 (1.0000 to 1.0000)	1.0000 (1.0000 to 1.0000)	0.9167 (0.5390 to 0.9878)	0.6667 (0.1946 to 0.9044)	
9 Months	0.8088 (0.7167 to 0.8736)	0.7093 (0.6296 to 0.7749)	1.0000 (1.0000 to 1.0000)	0.9167 (0.5390 to 0.9878)	0.8333 (0.4817 to 0.9555)	0.6667 (0.1946 to 0.9044)	

PT are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.74 Subgroup analysis by R-ISS staging
16.2.7.1.74.2 Treatment emergent adverse event per PT by treatment group according to R-ISS staging - Safety population

	I or II		III		Not classified		
	Kd (N=102)	**IKd (N=155)**	**Kd (N=8)**	**IKd (N=15)**	**Kd (N=12)**	**IKd (N=7)**	**p-value of treatment-by-sub group interaction[c]**
12 Months	0.7756 (0.6791 to 0.8463)	0.6677 (0.5860 to 0.7369)	1.0000 (1.0000 to 1.0000)	0.9167 (0.5390 to 0.9878)	0.8333 (0.4817 to 0.9555)	0.6667 (0.1946 to 0.9044)	
15 Months	0.7403 (0.6396 to 0.8168)	0.6175 (0.5340 to 0.6905)	1.0000 (1.0000 to 1.0000)	0.9167 (0.5390 to 0.9878)	0.7500 (0.4084 to 0.9117)	0.6667 (0.1946 to 0.9044)	
18 Months	0.7279 (0.6258 to 0.8064)	0.5947 (0.5103 to 0.6692)	1.0000 (1.0000 to 1.0000)	0.7857 (0.3614 to 0.9445)	0.7500 (0.4084 to 0.9117)	0.6667 (0.1946 to 0.9044)	
21 Months	0.7279 (0.6258 to 0.8064)	0.5947 (0.5103 to 0.6692)	1.0000 (1.0000 to 1.0000)	0.7857 (0.3614 to 0.9445)	0.7500 (0.4084 to 0.9117)	0.6667 (0.1946 to 0.9044)	
24 Months	0.7279 (0.6258 to 0.8064)	0.5947 (0.5103 to 0.6692)	1.0000 (1.0000 to 1.0000)	0.7857 (0.3614 to 0.9445)	0.7500 (0.4084 to 0.9117)	0.6667 (0.1946 to 0.9044)	
27 Months	0.7279 (0.6258 to 0.8064)	0.5947 (0.5103 to 0.6692)	1.0000 (1.0000 to 1.0000)	0.7857 (0.3614 to 0.9445)	0.7500 (0.4084 to 0.9117)	0.6667 (0.1946 to 0.9044)	
30 Months	0.7279 (0.6258 to 0.8064)	0.5947 (0.5103 to 0.6692)	1.0000 (1.0000 to 1.0000)	0.7857 (0.3614 to 0.9445)	0.7500 (0.4084 to 0.9117)	0.6667 (0.1946 to 0.9044)	
Number of patients at risk[b]							
3 Months	92	136	7	13	11	6	
6 Months	83	114	5	12	11	4	
9 Months	73	103	5	10	10	3	

PT are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
PGM=DEVOPS/SAR650984/EFC15246/CIR_RWE/REPORT/PGM/ae_km_socpt_subgp_sr_s_t.sas OUT=REPORT/OUTPUT/ae_km_teaept_seriss_s_t_x.rtf (12FEB2021 8:25)

16.2.7.1 Safety endpoints
16.2.7.1.74 Subgroup analysis by R-ISS staging
16.2.7.1.74.2 Treatment emergent adverse event per PT by treatment group according to R-ISS staging - Safety population

	I or II		III		Not classified		
	Kd (N=102)	**IKd (N=155)**	**Kd (N=8)**	**IKd (N=15)**	**Kd (N=12)**	**IKd (N=7)**	**p-value of treatment-by-sub group interaction[c]**
12 Months	68	96	5	9	10	3	
15 Months	60	83	5	7	9	2	
18 Months	58	78	5	4	9	2	
21 Months	46	71	4	2	7	2	
24 Months	19	22	1	0	1	0	
27 Months	3	1	0	0	0	0	
30 Months	0	0	0	0	0	0	
Urinary tract infection (days)							
Number (%) of events	9 (8.8)	11 (7.1)	1 (12.5)	0 (0.0)	1 (8.3)	1 (14.3)	0.7950
Number (%) of patients censored	93 (91.2)	144 (92.9)	7 (87.5)	15 (100.0)	11 (91.7)	6 (85.7)	
Kaplan-Meier estimates of event in months							
25% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (5.2895 to NC)	NC (NC to NC)	NC (2.1355 to NC)	NC (11.5647 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (5.2895 to NC)	NC (NC to NC)	NC (NC to NC)	NC (11.5647 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (5.2895 to NC)	NC (NC to NC)	NC (NC to NC)	NC (11.5647 to NC)	

PT are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.75 Subgroup analysis by number of prior lines of therapy (IRT)
16.2.7.1.75.3 Treatment emergent adverse event per PT by treatment group according to number of prior lines of therapy (IRT) - Safety population

	1		>1		
	Kd (N=54)	**IKd (N=78)**	**Kd (N=68)**	**IKd (N=99)**	**p-value of treatment-by-sub group interaction[c]**
18 Months	45	61	45	70	
21 Months	35	53	36	64	
24 Months	13	18	14	20	
27 Months	2	1	2	1	
30 Months	0	0	0	0	
Bronchitis (days)					
Number (%) of events	5 (9.3)	18 (23.1)	10 (14.7)	22 (22.2)	0.3285
Number (%) of patients censored	49 (90.7)	60 (76.9)	58 (85.3)	77 (77.8)	
Kaplan-Meier estimates of event in months					
25% quantile (95% CI)	NC (NC to NC)	NC (9.6591 to NC)	NC (11.2361 to NC)	NC (10.9076 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.0328		0.2870	

PT are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.75 Subgroup analysis by number of prior lines of therapy (IRT)
16.2.7.1.75.3 Treatment emergent adverse event per PT by treatment group according to number of prior lines of therapy (IRT) - Safety population

	1		>1		
	Kd (N=54)	**IKd (N=78)**	**Kd (N=68)**	**IKd (N=99)**	**p-value of treatment-by-sub group interaction[c]**
Hazard ratio (95% CI) vs Kd	-	2.81 (1.04 to 7.57)		1.50 (0.71 to 3.16)	
P-value	-	0.0411		0.2904	
Hazard ratio inverted (95% CI) vs IKd	0.36 (0.13 to 0.96)				
Events probability (95% CI)[b]					
3 Months	1.0000 (1.0000 to 1.0000)	0.9487 (0.8691 to 0.9804)	0.9396 (0.8469 to 0.9769)	0.9489 (0.8815 to 0.9784)	
6 Months	0.9811 (0.8735 to 0.9973)	0.9093 (0.8192 to 0.9557)	0.9085 (0.8075 to 0.9578)	0.8751 (0.7904 to 0.9271)	
9 Months	0.9623 (0.8574 to 0.9904)	0.8686 (0.7694 to 0.9271)	0.8923 (0.7871 to 0.9472)	0.8529 (0.7641 to 0.9102)	
12 Months	0.9238 (0.8095 to 0.9707)	0.8005 (0.6909 to 0.8747)	0.8573 (0.7431 to 0.9233)	0.7966 (0.6995 to 0.8653)	
15 Months	0.9041 (0.7848 to 0.9589)	0.7867 (0.6754 to 0.8636)	0.8573 (0.7431 to 0.9233)	0.7966 (0.6995 to 0.8653)	
18 Months	0.9041 (0.7848 to 0.9589)	0.7565 (0.6411 to 0.8393)	0.8573 (0.7431 to 0.9233)	0.7581 (0.6552 to 0.8340)	
21 Months	0.9041 (0.7848 to 0.9589)	0.7565 (0.6411 to 0.8393)	0.8573 (0.7431 to 0.9233)	0.7581 (0.6552 to 0.8340)	

PT are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.75 Subgroup analysis by number of prior lines of therapy (IRT)
16.2.7.1.75.3 Treatment emergent adverse event per PT by treatment group according to number of prior lines of therapy (IRT) - Safety population

	1		>1		
	Kd (N=54)	**IKd (N=78)**	**Kd (N=68)**	**IKd (N=99)**	**p-value of treatment-by-sub group interaction[c]**
24 Months	0.9041 (0.7848 to 0.9589)	0.7565 (0.6411 to 0.8393)	0.8230 (0.6855 to 0.9044)	0.7581 (0.6552 to 0.8340)	
27 Months	0.9041 (0.7848 to 0.9589)	0.7565 (0.6411 to 0.8393)	0.8230 (0.6855 to 0.9044)	0.7581 (0.6552 to 0.8340)	
30 Months	0.9041 (0.7848 to 0.9589)	0.7565 (0.6411 to 0.8393)	0.8230 (0.6855 to 0.9044)	0.7581 (0.6552 to 0.8340)	
Number of patients at risk[b]					
3 Months	54	74	61	91	
6 Months	52	67	56	81	
9 Months	50	64	51	76	
12 Months	47	58	48	69	
15 Months	44	53	44	64	
18 Months	44	49	42	57	
21 Months	34	41	33	51	
24 Months	12	12	12	18	
27 Months	2	0	2	1	
30 Months	0	0	0	0	

PT are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.75 Subgroup analysis by number of prior lines of therapy (IRT)
16.2.7.1.75.3 Treatment emergent adverse event per PT by treatment group according to number of prior lines of therapy (IRT) - Safety population

	1		>1		
	Kd (N=54)	**IKd (N=78)**	**Kd (N=68)**	**IKd (N=99)**	**p-value of treatment-by-sub group interaction[c]**
6 Months	51	73	57	90	
9 Months	49	71	52	81	
12 Months	46	69	47	79	
15 Months	44	64	44	70	
18 Months	44	61	42	65	
21 Months	36	53	31	58	
24 Months	12	17	11	20	
27 Months	1	0	1	0	
30 Months	0	0	0	0	
Infusion related reaction (days)					
Number (%) of events	3 (5.6)	32 (41.0)	1 (1.5)	47 (47.5)	0.1980
Number (%) of patients censored	51 (94.4)	46 (59.0)	67 (98.5)	52 (52.5)	
Kaplan-Meier estimates of event in months					
25% quantile (95% CI)	NC (NC to NC)	0.1314 (0.0657 to 0.1971)	NC (NC to NC)	0.0986 (0.0657 to 0.1314)	
Median (95% CI)	NC (NC to NC)	NC (0.6571 to NC)	NC (NC to NC)	NC (0.1643 to NC)	

PT are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.75 Subgroup analysis by number of prior lines of therapy (IRT)
16.2.7.1.75.3 Treatment emergent adverse event per PT by treatment group according to number of prior lines of therapy (IRT) - Safety population

	1		>1		
	Kd (N=54)	**IKd (N=78)**	**Kd (N=68)**	**IKd (N=99)**	**p-value of treatment-by-sub group interaction[c]**
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	<.0001		<.0001	
Hazard ratio (95% CI) vs Kd	-	9.10 (2.78 to 29.76)		40.95 (5.65 to 296.74)	
P-value	-	0.0003		0.0002	
Hazard ratio inverted (95% CI) vs IKd	0.11 (0.03 to 0.36)		0.02 (0.00 to 0.18)		
Events probability (95% CI)[b]					
3 Months	0.9444 (0.8376 to 0.9817)	0.6154 (0.4982 to 0.7130)	0.9853 (0.9002 to 0.9979)	0.5455 (0.4424 to 0.6373)	
6 Months	0.9444 (0.8376 to 0.9817)	0.6026 (0.4853 to 0.7012)	0.9853 (0.9002 to 0.9979)	0.5455 (0.4424 to 0.6373)	
9 Months	0.9444 (0.8376 to 0.9817)	0.6026 (0.4853 to 0.7012)	0.9853 (0.9002 to 0.9979)	0.5455 (0.4424 to 0.6373)	
12 Months	0.9444 (0.8376 to 0.9817)	0.6026 (0.4853 to 0.7012)	0.9853 (0.9002 to 0.9979)	0.5455 (0.4424 to 0.6373)	

PT are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.75 Subgroup analysis by number of prior lines of therapy (IRT)
16.2.7.1.75.3 Treatment emergent adverse event per PT by treatment group according to number of prior lines of therapy (IRT) - Safety population

	1		>1		
	Kd (N=54)	**IKd (N=78)**	**Kd (N=68)**	**IKd (N=99)**	**p-value of treatment-by-sub group interaction[c]**
15 Months	0.9444 (0.8376 to 0.9817)	0.6026 (0.4853 to 0.7012)	0.9853 (0.9002 to 0.9979)	0.5343 (0.4313 to 0.6268)	
18 Months	0.9444 (0.8376 to 0.9817)	0.6026 (0.4853 to 0.7012)	0.9853 (0.9002 to 0.9979)	0.5343 (0.4313 to 0.6268)	
21 Months	0.9444 (0.8376 to 0.9817)	0.5875 (0.4696 to 0.6878)	0.9853 (0.9002 to 0.9979)	0.5210 (0.4174 to 0.6147)	
24 Months	0.9444 (0.8376 to 0.9817)	0.5875 (0.4696 to 0.6878)	0.9853 (0.9002 to 0.9979)	0.5210 (0.4174 to 0.6147)	
27 Months	0.9444 (0.8376 to 0.9817)	0.5875 (0.4696 to 0.6878)	0.9853 (0.9002 to 0.9979)	0.5210 (0.4174 to 0.6147)	
30 Months	0.9444 (0.8376 to 0.9817)	0.5875 (0.4696 to 0.6878)	0.9853 (0.9002 to 0.9979)	0.5210 (0.4174 to 0.6147)	
Number of patients at risk[b]					
3 Months	51	48	65	52	
6 Months	50	46	61	51	
9 Months	49	46	56	50	
12 Months	48	45	55	49	
15 Months	46	42	51	43	

PT are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.75 Subgroup analysis by number of prior lines of therapy (IRT)
16.2.7.1.75.3 Treatment emergent adverse event per PT by treatment group according to number of prior lines of therapy (IRT) - Safety population

	1		>1		
	Kd (N=54)	**IKd (N=78)**	**Kd (N=68)**	**IKd (N=99)**	**p-value of treatment-by-sub group interaction[c]**
18 Months	46	40	49	40	
21 Months	36	33	39	35	
24 Months	13	14	15	9	
27 Months	2	0	2	1	
30 Months	0	0	0	0	
Insomnia (days)					
Number (%) of events	12 (22.2)	19 (24.4)	16 (23.5)	23 (23.2)	0.7384
Number (%) of patients censored	42 (77.8)	59 (75.6)	52 (76.5)	76 (76.8)	
Kaplan-Meier estimates of event in months					
25% quantile (95% CI)	NC (1.3470 to NC)	16.5914 (6.1109 to NC)	21.8480 (2.8583 to NC)	18.4312 (5.9795 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.7950		0.8263	

PT are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.75 Subgroup analysis by number of prior lines of therapy (IRT)
16.2.7.1.75.3 Treatment emergent adverse event per PT by treatment group according to number of prior lines of therapy (IRT) - Safety population

	1		>1		
	Kd (N=54)	**IKd (N=78)**	**Kd (N=68)**	**IKd (N=99)**	**p-value of treatment-by-sub group interaction[c]**
Thrombocytopenia (days)					
Number (%) of events	1 (1.9)	4 (5.1)	11 (16.2)	1 (1.0)	0.0106
Number (%) of patients censored	53 (98.1)	74 (94.9)	57 (83.8)	98 (99.0)	
Kaplan-Meier estimates of event in months					
25% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (6.2752 to NC)	NC (NC to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.3193		0.0002	
Hazard ratio (95% CI) vs Kd	-	2.89 (0.32 to 25.90)		0.06 (0.01 to 0.45)	
P-value	-	0.3419		0.0066	
Events probability (95% CI)[b]					

PT are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.75 Subgroup analysis by number of prior lines of therapy (IRT)
16.2.7.1.75.3 Treatment emergent adverse event per PT by treatment group according to number of prior lines of therapy (IRT) - Safety population

	1		>1		
	Kd (N=54)	**IKd (N=78)**	**Kd (N=68)**	**IKd (N=99)**	**p-value of treatment-by-sub group interaction[c]**
3 Months	1.0000 (1.0000 to 1.0000)	0.9872 (0.9125 to 0.9982)	0.9106 (0.8118 to 0.9588)	0.9898 (0.9298 to 0.9986)	
6 Months	1.0000 (1.0000 to 1.0000)	0.9872 (0.9125 to 0.9982)	0.8648 (0.7562 to 0.9273)	0.9898 (0.9298 to 0.9986)	
9 Months	1.0000 (1.0000 to 1.0000)	0.9872 (0.9125 to 0.9982)	0.8328 (0.7182 to 0.9038)	0.9898 (0.9298 to 0.9986)	
12 Months	1.0000 (1.0000 to 1.0000)	0.9738 (0.8994 to 0.9934)	0.8328 (0.7182 to 0.9038)	0.9898 (0.9298 to 0.9986)	
15 Months	1.0000 (1.0000 to 1.0000)	0.9738 (0.8994 to 0.9934)	0.8328 (0.7182 to 0.9038)	0.9898 (0.9298 to 0.9986)	
18 Months	0.9796 (0.8638 to 0.9971)	0.9593 (0.8789 to 0.9867)	0.8328 (0.7182 to 0.9038)	0.9898 (0.9298 to 0.9986)	
21 Months	0.9796 (0.8638 to 0.9971)	0.9443 (0.8580 to 0.9788)	0.8328 (0.7182 to 0.9038)	0.9898 (0.9298 to 0.9986)	
24 Months	0.9796 (0.8638 to 0.9971)	0.9443 (0.8580 to 0.9788)	0.8328 (0.7182 to 0.9038)	0.9898 (0.9298 to 0.9986)	
27 Months	0.9796 (0.8638 to 0.9971)	0.9443 (0.8580 to 0.9788)	0.8328 (0.7182 to 0.9038)	0.9898 (0.9298 to 0.9986)	

PT are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
PGM=DEVOPS/SAR650984/EFC15246/CIR_RWE/REPORT/PGM/ae_km_socpt_subgp_sr_s_t.sas OUT=REPORT/OUTPUT/ae_km_teaept_plne_s_t_x.rtf (12FEB2021 8:25)

16.2.7.1 Safety endpoints
16.2.7.1.75 Subgroup analysis by number of prior lines of therapy (IRT)
16.2.7.1.75.3 Treatment emergent adverse event per PT by treatment group according to number of prior lines of therapy (IRT) - Safety population

	1		>1		
	Kd (N=54)	**IKd (N=78)**	**Kd (N=68)**	**IKd (N=99)**	**p-value of treatment-by-sub group interaction[c]**
30 Months	0.9796 (0.8638 to 0.9971)	0.9443 (0.8580 to 0.9788)	0.8328 (0.7182 to 0.9038)	0.9898 (0.9298 to 0.9986)	
Number of patients at risk[b]					
3 Months	54	77	60	94	
6 Months	53	74	54	91	
9 Months	52	74	47	86	
12 Months	51	72	47	84	
15 Months	49	67	44	78	
18 Months	48	64	42	73	
21 Months	38	54	33	67	
24 Months	14	18	13	21	
27 Months	2	1	2	1	
30 Months	0	0	0	0	
Traumatic fracture (days)					
Number (%) of events	2 (3.7)	6 (7.7)	3 (4.4)	7 (7.1)	0.7560
Number (%) of patients censored	52 (96.3)	72 (92.3)	65 (95.6)	92 (92.9)	

PT are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.75 Subgroup analysis by number of prior lines of therapy (IRT)
16.2.7.1.75.3 Treatment emergent adverse event per PT by treatment group according to number of prior lines of therapy (IRT) - Safety population

	1		>1		
	Kd (N=54)	**IKd (N=78)**	**Kd (N=68)**	**IKd (N=99)**	**p-value of treatment-by-sub group interaction[c]**
6 Months	52	73	60	89	
9 Months	51	70	55	83	
12 Months	50	69	54	81	
15 Months	48	64	49	75	
18 Months	48	62	46	70	
21 Months	38	52	37	64	
24 Months	13	14	14	20	
27 Months	1	0	2	1	
30 Months	0	0	0	0	
Upper respiratory tract infection (days)					
Number (%) of events	18 (33.3)	29 (37.2)	11 (16.2)	35 (35.4)	0.1109
Number (%) of patients censored	36 (66.7)	49 (62.8)	57 (83.8)	64 (64.6)	
Kaplan-Meier estimates of event in months					
25% quantile (95% CI)	9.7906 (3.8768 to NC)	10.4148 (4.4025 to 13.3717)	NC (11.1376 to NC)	6.5051 (4.0411 to 12.8789)	
Median (95% CI)	NC (NC to NC)	NC (17.9055 to NC)	NC (NC to NC)	NC (NC to NC)	

PT are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.75 Subgroup analysis by number of prior lines of therapy (IRT)
16.2.7.1.75.3 Treatment emergent adverse event per PT by treatment group according to number of prior lines of therapy (IRT) - Safety population

	1		>1		
	Kd (N=54)	**IKd (N=78)**	**Kd (N=68)**	**IKd (N=99)**	**p-value of treatment-by-sub group interaction[c]**
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.6371		0.0101	
Hazard ratio (95% CI) vs Kd	-	1.15 (0.64 to 2.07)		2.37 (1.20 to 4.67)	
P-value	-	0.6374		0.0126	
Hazard ratio inverted (95% CI) vs IKd			0.42 (0.21 to 0.83)		
Events probability (95% CI)[b]					
3 Months	0.9074 (0.7917 to 0.9604)	0.8974 (0.8054 to 0.9473)	0.9398 (0.8475 to 0.9770)	0.8962 (0.8156 to 0.9428)	
6 Months	0.8519 (0.7255 to 0.9230)	0.8041 (0.6961 to 0.8771)	0.8768 (0.7685 to 0.9365)	0.7681 (0.6694 to 0.8408)	
9 Months	0.7593 (0.6218 to 0.8524)	0.7632 (0.6506 to 0.8438)	0.8768 (0.7685 to 0.9365)	0.6900 (0.5852 to 0.7734)	
12 Months	0.7213 (0.5808 to 0.8216)	0.7087 (0.5918 to 0.7978)	0.8585 (0.7451 to 0.9240)	0.6666 (0.5604 to 0.7527)	

PT are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.75 Subgroup analysis by number of prior lines of therapy (IRT)
16.2.7.1.75.3 Treatment emergent adverse event per PT by treatment group according to number of prior lines of therapy (IRT) - Safety population

	1		>1		
	Kd (N=54)	**IKd (N=78)**	**Kd (N=68)**	**IKd (N=99)**	**p-value of treatment-by-sub group interaction[c]**
15 Months	0.6616 (0.5175 to 0.7718)	0.6531 (0.5333 to 0.7492)	0.8399 (0.7218 to 0.9108)	0.6295 (0.5211 to 0.7198)	
18 Months	0.6616 (0.5175 to 0.7718)	0.6095 (0.4883 to 0.7104)	0.8199 (0.6967 to 0.8966)	0.6155 (0.5061 to 0.7076)	
21 Months	0.6616 (0.5175 to 0.7718)	0.6095 (0.4883 to 0.7104)	0.8199 (0.6967 to 0.8966)	0.6155 (0.5061 to 0.7076)	
24 Months	0.6616 (0.5175 to 0.7718)	0.6095 (0.4883 to 0.7104)	0.8199 (0.6967 to 0.8966)	0.6155 (0.5061 to 0.7076)	
27 Months	0.6616 (0.5175 to 0.7718)	0.6095 (0.4883 to 0.7104)	0.8199 (0.6967 to 0.8966)	0.6155 (0.5061 to 0.7076)	
30 Months	0.6616 (0.5175 to 0.7718)	0.6095 (0.4883 to 0.7104)	0.8199 (0.6967 to 0.8966)	0.6155 (0.5061 to 0.7076)	
Number of patients at risk[b]					
3 Months	49	70	61	85	
6 Months	46	59	53	71	
9 Months	40	56	48	60	
12 Months	37	52	46	56	
15 Months	32	45	42	47	

PT are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.75 Subgroup analysis by number of prior lines of therapy (IRT)
16.2.7.1.75.3 Treatment emergent adverse event per PT by treatment group according to number of prior lines of therapy (IRT) - Safety population

	1		>1		
	Kd (N=54)	**IKd (N=78)**	**Kd (N=68)**	**IKd (N=99)**	**p-value of treatment-by-sub group interaction[c]**
18 Months	32	42	40	42	
21 Months	24	35	33	40	
24 Months	6	9	15	13	
27 Months	1	1	2	0	
30 Months	0	0	0	0	
Urinary tract infection (days)					
Number (%) of events	1 (1.9)	7 (9.0)	10 (14.7)	5 (5.1)	0.0207
Number (%) of patients censored	53 (98.1)	71 (91.0)	58 (85.3)	94 (94.9)	
Kaplan-Meier estimates of event in months					
25% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (13.0103 to NC)	NC (NC to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.0910		0.0258	

PT are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.76 Subgroup analysis by cytogenetic abnormality (del(17p), t(4,14), t(14,16))
16.2.7.1.76.3 Treatment emergent adverse event per PT by treatment group according to cytogenetic abnormality (del(17p), t(4,14), t(14,16)) - Safety population

	At least one		None		
	Kd (N=30)	**IKd (N=42)**	**Kd (N=77)**	**IKd (N=113)**	**p-value of treatment-by-sub group interaction[c]**
18 Months	20	31	59	87	
21 Months	16	26	46	78	
24 Months	7	9	17	25	
27 Months	0	0	4	2	
30 Months	0	0	0	0	
Bronchitis (days)					
Number (%) of events	6 (20.0)	9 (21.4)	7 (9.1)	26 (23.0)	0.1655
Number (%) of patients censored	24 (80.0)	33 (78.6)	70 (90.9)	87 (77.0)	
Kaplan-Meier estimates of event in months					
25% quantile (95% CI)	21.7495 (6.1766 to NC)	NC (8.6735 to NC)	NC (NC to NC)	NC (10.9076 to NC)	
Median (95% CI)	NC (21.7495 to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.9648		0.0174	

PT are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.76 Subgroup analysis by cytogenetic abnormality (del(17p), t(4,14), t(14,16))
16.2.7.1.76.3 Treatment emergent adverse event per PT by treatment group according to cytogenetic abnormality (del(17p), t(4,14), t(14,16)) - Safety population

	At least one		None		
	Kd (N=30)	**IKd (N=42)**	**Kd (N=77)**	**IKd (N=113)**	**p-value of treatment-by-sub group interaction[c]**
Hazard ratio (95% CI) vs Kd	-	1.02 (0.36 to 2.88)		2.65 (1.15 to 6.10)	
P-value	-	0.9649		0.0222	
Hazard ratio inverted (95% CI) vs IKd			0.38 (0.16 to 0.87)		
Events probability (95% CI)[b]					
3 Months	0.9667 (0.7861 to 0.9952)	0.9762 (0.8428 to 0.9966)	0.9603 (0.8820 to 0.9870)	0.9377 (0.8738 to 0.9698)	
6 Months	0.9333 (0.7589 to 0.9829)	0.9029 (0.7614 to 0.9624)	0.9329 (0.8462 to 0.9715)	0.8913 (0.8164 to 0.9368)	
9 Months	0.8615 (0.6715 to 0.9458)	0.8763 (0.7276 to 0.9467)	0.9329 (0.8462 to 0.9715)	0.8632 (0.7833 to 0.9152)	
12 Months	0.8224 (0.6234 to 0.9223)	0.8232 (0.6639 to 0.9117)	0.9042 (0.8093 to 0.9532)	0.7968 (0.7079 to 0.8613)	
15 Months	0.8224 (0.6234 to 0.9223)	0.8232 (0.6639 to 0.9117)	0.9042 (0.8093 to 0.9532)	0.7871 (0.6971 to 0.8532)	
18 Months	0.8224 (0.6234 to 0.9223)	0.7644 (0.5943 to 0.8705)	0.9042 (0.8093 to 0.9532)	0.7558 (0.6620 to 0.8269)	
21 Months	0.8224 (0.6234 to 0.9223)	0.7644 (0.5943 to 0.8705)	0.9042 (0.8093 to 0.9532)	0.7558 (0.6620 to 0.8269)	

PT are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.76 Subgroup analysis by cytogenetic abnormality (del(17p), t(4,14), t(14,16))
16.2.7.1.76.3 Treatment emergent adverse event per PT by treatment group according to cytogenetic abnormality (del(17p), t(4,14), t(14,16)) - Safety population

	At least one		None		
	Kd (N=30)	**IKd (N=42)**	**Kd (N=77)**	**IKd (N=113)**	**p-value of treatment-by-sub group interaction[c]**
24 Months	0.7401 (0.4790 to 0.8843)	0.7644 (0.5943 to 0.8705)	0.9042 (0.8093 to 0.9532)	0.7558 (0.6620 to 0.8269)	
27 Months	0.7401 (0.4790 to 0.8843)	0.7644 (0.5943 to 0.8705)	0.9042 (0.8093 to 0.9532)	0.7558 (0.6620 to 0.8269)	
30 Months	0.7401 (0.4790 to 0.8843)	0.7644 (0.5943 to 0.8705)	0.9042 (0.8093 to 0.9532)	0.7558 (0.6620 to 0.8269)	
Number of patients at risk[b]					
3 Months	29	41	72	104	
6 Months	26	35	68	96	
9 Months	22	33	65	91	
12 Months	20	31	63	82	
15 Months	18	28	59	77	
18 Months	18	25	57	71	
21 Months	14	20	45	62	
24 Months	5	6	16	20	
27 Months	0	0	4	1	
30 Months	0	0	0	0	

PT are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.76 Subgroup analysis by cytogenetic abnormality (del(17p), t(4,14), t(14,16))
16.2.7.1.76.3 Treatment emergent adverse event per PT by treatment group according to cytogenetic abnormality (del(17p), t(4,14), t(14,16)) - Safety population

	At least one		None		
	Kd (N=30)	**IKd (N=42)**	**Kd (N=77)**	**IKd (N=113)**	**p-value of treatment-by-sub group interaction[c]**
21 Months	16	27	42	71	
24 Months	5	9	14	24	
27 Months	0	0	2	0	
30 Months	0	0	0	0	
Infusion related reaction (days)					
Number (%) of events	0 (0.0)	23 (54.8)	4 (5.2)	44 (38.9)	0.9846
Number (%) of patients censored	30 (100.0)	19 (45.2)	73 (94.8)	69 (61.1)	
Kaplan-Meier estimates of event in months					
25% quantile (95% CI)	NC (NC to NC)	0.0657 (0.0657 to 0.1314)	NC (NC to NC)	0.1314 (0.0986 to 0.1971)	
Median (95% CI)	NC (NC to NC)	2.4148 (0.1314 to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	<.0001		<.0001	

PT are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.76 Subgroup analysis by cytogenetic abnormality (del(17p), t(4,14), t(14,16))
16.2.7.1.76.3 Treatment emergent adverse event per PT by treatment group according to cytogenetic abnormality (del(17p), t(4,14), t(14,16)) - Safety population

	At least one		None		
	Kd (N=30)	**IKd (N=42)**	**Kd (N=77)**	**IKd (N=113)**	**p-value of treatment-by-sub group interaction[c]**
Hazard ratio (95% CI) vs Kd	-	NC		9.04 (3.25 to 25.18)	
P-value	-	0.9880		<.0001	
Hazard ratio inverted (95% CI) vs IKd			0.11 (0.04 to 0.31)		
Events probability (95% CI)[b]					
3 Months	1.0000 (1.0000 to 1.0000)	0.5000 (0.3422 to 0.6389)	0.9479 (0.8670 to 0.9801)	0.6282 (0.5322 to 0.7099)	
6 Months	1.0000 (1.0000 to 1.0000)	0.4762 (0.3205 to 0.6164)	0.9479 (0.8670 to 0.9801)	0.6282 (0.5322 to 0.7099)	
9 Months	1.0000 (1.0000 to 1.0000)	0.4762 (0.3205 to 0.6164)	0.9479 (0.8670 to 0.9801)	0.6282 (0.5322 to 0.7099)	
12 Months	1.0000 (1.0000 to 1.0000)	0.4762 (0.3205 to 0.6164)	0.9479 (0.8670 to 0.9801)	0.6282 (0.5322 to 0.7099)	
15 Months	1.0000 (1.0000 to 1.0000)	0.4762 (0.3205 to 0.6164)	0.9479 (0.8670 to 0.9801)	0.6188 (0.5225 to 0.7013)	
18 Months	1.0000 (1.0000 to 1.0000)	0.4762 (0.3205 to 0.6164)	0.9479 (0.8670 to 0.9801)	0.6188 (0.5225 to 0.7013)	
21 Months	1.0000 (1.0000 to 1.0000)	0.4444 (0.2892 to 0.5886)	0.9479 (0.8670 to 0.9801)	0.6085 (0.5117 to 0.6919)	

PT are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
PGM=DEVOPS/SAR650984/EFC15246/CIR_RWE/REPORT/PGM/ae_km_socpt_subgp_sr_s_t.sas OUT=REPORT/OUTPUT/ae_km_teaept_cyto_s_t_x.rtf (12FEB2021 8:25)

16.2.7.1 Safety endpoints
16.2.7.1.76 Subgroup analysis by cytogenetic abnormality (del(17p), t(4,14), t(14,16))
16.2.7.1.76.3 Treatment emergent adverse event per PT by treatment group according to cytogenetic abnormality (del(17p), t(4,14), t(14,16)) - Safety population

	At least one		None		
	Kd (N=30)	**IKd (N=42)**	**Kd (N=77)**	**IKd (N=113)**	**p-value of treatment-by-sub group interaction[c]**
24 Months	1.0000 (1.0000 to 1.0000)	0.4444 (0.2892 to 0.5886)	0.9479 (0.8670 to 0.9801)	0.6085 (0.5117 to 0.6919)	
27 Months	1.0000 (1.0000 to 1.0000)	0.4444 (0.2892 to 0.5886)	0.9479 (0.8670 to 0.9801)	0.6085 (0.5117 to 0.6919)	
30 Months	1.0000 (1.0000 to 1.0000)	0.4444 (0.2892 to 0.5886)	0.9479 (0.8670 to 0.9801)	0.6085 (0.5117 to 0.6919)	
Number of patients at risk[b]					
3 Months	30	21	72	70	
6 Months	28	19	69	69	
9 Months	26	19	65	68	
12 Months	25	19	65	67	
15 Months	23	16	61	63	
18 Months	23	15	59	60	
21 Months	19	12	46	51	
24 Months	7	5	17	17	
27 Months	0	0	4	1	
30 Months	0	0	0	0	

PT are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.76 Subgroup analysis by cytogenetic abnormality (del(17p), t(4,14), t(14,16))
16.2.7.1.76.3 Treatment emergent adverse event per PT by treatment group according to cytogenetic abnormality (del(17p), t(4,14), t(14,16)) - Safety population

	At least one		None		
	Kd (N=30)	**IKd (N=42)**	**Kd (N=77)**	**IKd (N=113)**	**p-value of treatment-by-sub group interaction[c]**
30 Months	0.9643 (0.7724 to 0.9949)	1.0000 (1.0000 to 1.0000)	0.9724 (0.8939 to 0.9930)	0.9156 (0.8441 to 0.9552)	
Number of patients at risk[b]					
3 Months	30	42	74	109	
6 Months	28	39	71	102	
9 Months	25	37	66	98	
12 Months	24	37	66	94	
15 Months	22	34	63	89	
18 Months	22	33	61	85	
21 Months	18	28	48	76	
24 Months	6	10	18	22	
27 Months	0	0	4	1	
30 Months	0	0	0	0	
Thrombocytopenia (days)					
Number (%) of events	5 (16.7)	2 (4.8)	7 (9.1)	3 (2.7)	0.9810
Number (%) of patients censored	25 (83.3)	40 (95.2)	70 (90.9)	110 (97.3)	

PT are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.76 Subgroup analysis by cytogenetic abnormality (del(17p), t(4,14), t(14,16))
16.2.7.1.76.3 Treatment emergent adverse event per PT by treatment group according to cytogenetic abnormality (del(17p), t(4,14), t(14,16)) - Safety population

	At least one		None		
	Kd (N=30)	**IKd (N=42)**	**Kd (N=77)**	**IKd (N=113)**	**p-value of treatment-by-sub group interaction[c]**
Kaplan-Meier estimates of event in months					
25% quantile (95% CI)	NC (3.2526 to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.0943		0.0475	
Hazard ratio (95% CI) vs Kd	-	0.27 (0.05 to 1.40)		0.28 (0.07 to 1.08)	
P-value	-	0.1188		0.0639	
Events probability (95% CI)[b]					
3 Months	0.9333 (0.7589 to 0.9829)	0.9762 (0.8428 to 0.9966)	0.9477 (0.8666 to 0.9800)	0.9912 (0.9388 to 0.9987)	
6 Months	0.8667 (0.6828 to 0.9478)	0.9762 (0.8428 to 0.9966)	0.9342 (0.8490 to 0.9721)	0.9912 (0.9388 to 0.9987)	

PT are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1.76.3 Treatment emergent adverse event per PT by treatment group according to cytogenetic abnormality (del(17p), t(4,14), t(14,16)) - Safety population

	At least one		None		
	Kd (N=30)	**IKd (N=42)**	**Kd (N=77)**	**IKd (N=113)**	**p-value of treatment-by-sub group interaction[c]**
9 Months	0.8320 (0.6423 to 0.9264)	0.9762 (0.8428 to 0.9966)	0.9204 (0.8313 to 0.9635)	0.9912 (0.9388 to 0.9987)	
12 Months	0.8320 (0.6423 to 0.9264)	0.9762 (0.8428 to 0.9966)	0.9204 (0.8313 to 0.9635)	0.9816 (0.9284 to 0.9954)	
15 Months	0.8320 (0.6423 to 0.9264)	0.9762 (0.8428 to 0.9966)	0.9204 (0.8313 to 0.9635)	0.9816 (0.9284 to 0.9954)	
18 Months	0.8320 (0.6423 to 0.9264)	0.9475 (0.8046 to 0.9867)	0.9048 (0.8102 to 0.9536)	0.9816 (0.9284 to 0.9954)	
21 Months	0.8320 (0.6423 to 0.9264)	0.9475 (0.8046 to 0.9867)	0.9048 (0.8102 to 0.9536)	0.9708 (0.9119 to 0.9905)	
24 Months	0.8320 (0.6423 to 0.9264)	0.9475 (0.8046 to 0.9867)	0.9048 (0.8102 to 0.9536)	0.9708 (0.9119 to 0.9905)	
27 Months	0.8320 (0.6423 to 0.9264)	0.9475 (0.8046 to 0.9867)	0.9048 (0.8102 to 0.9536)	0.9708 (0.9119 to 0.9905)	
30 Months	0.8320 (0.6423 to 0.9264)	0.9475 (0.8046 to 0.9867)	0.9048 (0.8102 to 0.9536)	0.9708 (0.9119 to 0.9905)	
Number of patients at risk[b]					
3 Months	28	41	72	109	

PT are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.76 Subgroup analysis by cytogenetic abnormality (del(17p), t(4,14), t(14,16))
16.2.7.1.76.3 Treatment emergent adverse event per PT by treatment group according to cytogenetic abnormality (del(17p), t(4,14), t(14,16)) - Safety population

	At least one		None		
	Kd (N=30)	**IKd (N=42)**	**Kd (N=77)**	**IKd (N=113)**	**p-value of treatment-by-sub group interaction[c]**
6 Months	25	39	68	106	
9 Months	22	37	63	104	
12 Months	22	37	63	101	
15 Months	21	34	59	95	
18 Months	21	32	56	91	
21 Months	17	27	44	80	
24 Months	7	10	16	25	
27 Months	0	0	4	2	
30 Months	0	0	0	0	
Traumatic fracture (days)					
Number (%) of events	1 (3.3)	3 (7.1)	4 (5.2)	8 (7.1)	0.7290
Number (%) of patients censored	29 (96.7)	39 (92.9)	73 (94.8)	105 (92.9)	
Kaplan-Meier estimates of event in months					
25% quantile (95% CI)	NC (NC to NC)	NC (21.4867 to NC)	NC (NC to NC)	NC (NC to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	

PT are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.76 Subgroup analysis by cytogenetic abnormality (del(17p), t(4,14), t(14,16))
16.2.7.1.76.3 Treatment emergent adverse event per PT by treatment group according to cytogenetic abnormality (del(17p), t(4,14), t(14,16)) - Safety population

	At least one		None		
	Kd (N=30)	**IKd (N=42)**	**Kd (N=77)**	**IKd (N=113)**	**p-value of treatment-by-sub group interaction[c]**
21 Months	18	26	47	76	
24 Months	6	9	17	21	
27 Months	0	0	3	1	
30 Months	0	0	0	0	
Upper respiratory tract infection (days)					
Number (%) of events	2 (6.7)	16 (38.1)	23 (29.9)	41 (36.3)	0.0321
Number (%) of patients censored	28 (93.3)	26 (61.9)	54 (70.1)	72 (63.7)	
Kaplan-Meier estimates of event in months					
25% quantile (95% CI)	NC (11.1376 to NC)	8.0821 (3.6140 to 13.3717)	10.9405 (3.8768 to NC)	8.4107 (4.0082 to 12.1561)	
Median (95% CI)	NC (NC to NC)	NC (13.2402 to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.0027		0.4225	

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CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
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16.2.7.1.76.3 Treatment emergent adverse event per PT by treatment group according to cytogenetic abnormality (del(17p), t(4,14), t(14,16)) - Safety population

	At least one		None		
	Kd (N=30)	**IKd (N=42)**	**Kd (N=77)**	**IKd (N=113)**	**p-value of treatment-by-sub group interaction[c]**
Hazard ratio (95% CI) vs Kd	-	6.95 (1.60 to 30.25)		1.23 (0.74 to 2.05)	
P-value	-	0.0098		0.4234	
Hazard ratio inverted (95% CI) vs IKd	0.14 (0.03 to 0.63)				
Events probability (95% CI)[b]					
3 Months	1.0000 (1.0000 to 1.0000)	0.9286 (0.7947 to 0.9764)	0.8943 (0.7997 to 0.9457)	0.8747 (0.7975 to 0.9238)	
6 Months	1.0000 (1.0000 to 1.0000)	0.8067 (0.6502 to 0.8984)	0.7996 (0.6896 to 0.8740)	0.7812 (0.6914 to 0.8477)	
9 Months	0.9643 (0.7724 to 0.9949)	0.7277 (0.5615 to 0.8394)	0.7718 (0.6586 to 0.8515)	0.7142 (0.6188 to 0.7898)	
12 Months	0.9257 (0.7339 to 0.9809)	0.6738 (0.5041 to 0.7965)	0.7421 (0.6255 to 0.8273)	0.6752 (0.5776 to 0.7550)	
15 Months	0.9257 (0.7339 to 0.9809)	0.5883 (0.4161 to 0.7253)	0.6966 (0.5758 to 0.7891)	0.6355 (0.5361 to 0.7191)	
18 Months	0.9257 (0.7339 to 0.9809)	0.5883 (0.4161 to 0.7253)	0.6807 (0.5587 to 0.7757)	0.6141 (0.5138 to 0.6997)	
21 Months	0.9257 (0.7339 to 0.9809)	0.5883 (0.4161 to 0.7253)	0.6807 (0.5587 to 0.7757)	0.6141 (0.5138 to 0.6997)	

PT are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.76 Subgroup analysis by cytogenetic abnormality (del(17p), t(4,14), t(14,16))
16.2.7.1.76.3 Treatment emergent adverse event per PT by treatment group according to cytogenetic abnormality (del(17p), t(4,14), t(14,16)) - Safety population

	At least one		None		
	Kd (N=30)	**IKd (N=42)**	**Kd (N=77)**	**IKd (N=113)**	**p-value of treatment-by-sub group interaction[c]**
24 Months	0.9257 (0.7339 to 0.9809)	0.5883 (0.4161 to 0.7253)	0.6807 (0.5587 to 0.7757)	0.6141 (0.5138 to 0.6997)	
27 Months	0.9257 (0.7339 to 0.9809)	0.5883 (0.4161 to 0.7253)	0.6807 (0.5587 to 0.7757)	0.6141 (0.5138 to 0.6997)	
30 Months	0.9257 (0.7339 to 0.9809)	0.5883 (0.4161 to 0.7253)	0.6807 (0.5587 to 0.7757)	0.6141 (0.5138 to 0.6997)	
Number of patients at risk[b]					
3 Months	30	39	67	96	
6 Months	28	31	58	83	
9 Months	25	27	52	74	
12 Months	23	25	50	69	
15 Months	21	19	44	61	
18 Months	21	19	42	56	
21 Months	17	16	34	50	
24 Months	7	7	12	13	
27 Months	0	0	3	1	
30 Months	0	0	0	0	

PT are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.77 Subgroup analysis by MM type
16.2.7.1.77.2 Treatment emergent adverse event per PT by treatment group according to MM type - Safety population

	IgG		Non-IgG		
	Kd (N=85)	**IKd (N=124)**	**Kd (N=37)**	**IKd (N=53)**	**p-value of treatment-by-sub group interaction[c]**
18 Months	65	94	25	37	
21 Months	54	87	17	30	
24 Months	20	28	7	10	
27 Months	3	2	1	0	
30 Months	0	0	0	0	
Bronchitis (days)					
Number (%) of events	12 (14.1)	31 (25.0)	3 (8.1)	9 (17.0)	0.9078
Number (%) of patients censored	73 (85.9)	93 (75.0)	34 (91.9)	44 (83.0)	
Kaplan-Meier estimates of event in months					
25% quantile (95% CI)	NC (21.7495 to NC)	17.5113 (9.1335 to NC)	NC (NC to NC)	NC (11.2361 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.0538		0.2576	

PT are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.77 Subgroup analysis by MM type
16.2.7.1.77.2 Treatment emergent adverse event per PT by treatment group according to MM type - Safety population

	IgG		Non-IgG		
	Kd (N=85)	**IKd (N=124)**	**Kd (N=37)**	**IKd (N=53)**	**p-value of treatment-by-sub group interaction[c]**
Hazard ratio (95% CI) vs Kd	-	1.90 (0.98 to 3.71)		2.09 (0.57 to 7.73)	
P-value	-	0.0581		0.2684	
Events probability (95% CI)[b]					
3 Months	0.9763 (0.9086 to 0.9940)	0.9429 (0.8839 to 0.9724)	0.9444 (0.7957 to 0.9858)	0.9623 (0.8574 to 0.9904)	
6 Months	0.9400 (0.8618 to 0.9746)	0.8678 (0.7932 to 0.9168)	0.9444 (0.7957 to 0.9858)	0.9422 (0.8313 to 0.9810)	
9 Months	0.9154 (0.8307 to 0.9588)	0.8336 (0.7539 to 0.8893)	0.9444 (0.7957 to 0.9858)	0.9208 (0.8022 to 0.9696)	
12 Months	0.8767 (0.7828 to 0.9318)	0.7819 (0.6963 to 0.8460)	0.9130 (0.7532 to 0.9712)	0.8351 (0.6967 to 0.9141)	
15 Months	0.8635 (0.7668 to 0.9221)	0.7730 (0.6865 to 0.8384)	0.9130 (0.7532 to 0.9712)	0.8351 (0.6967 to 0.9141)	
18 Months	0.8635 (0.7668 to 0.9221)	0.7336 (0.6426 to 0.8049)	0.9130 (0.7532 to 0.9712)	0.8113 (0.6676 to 0.8974)	
21 Months	0.8635 (0.7668 to 0.9221)	0.7336 (0.6426 to 0.8049)	0.9130 (0.7532 to 0.9712)	0.8113 (0.6676 to 0.8974)	

PT are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
PGM=DEVOPS/SAR650984/EFC15246/CIR_RWE/REPORT/PGM/ae_km_socpt_subgp_sr_s_t.sas OUT=REPORT/OUTPUT/ae_km_teaept_semm_s_t_x.rtf (12FEB2021 8:25)

16.2.7.1 Safety endpoints
16.2.7.1.77 Subgroup analysis by MM type
16.2.7.1.77.2 Treatment emergent adverse event per PT by treatment group according to MM type - Safety population

	IgG		Non-IgG		
	Kd (N=85)	**IKd (N=124)**	**Kd (N=37)**	**IKd (N=53)**	**p-value of treatment-by-sub group interaction[c]**
24 Months	0.8429 (0.7371 to 0.9087)	0.7336 (0.6426 to 0.8049)	0.9130 (0.7532 to 0.9712)	0.8113 (0.6676 to 0.8974)	
27 Months	0.8429 (0.7371 to 0.9087)	0.7336 (0.6426 to 0.8049)	0.9130 (0.7532 to 0.9712)	0.8113 (0.6676 to 0.8974)	
30 Months	0.8429 (0.7371 to 0.9087)	0.7336 (0.6426 to 0.8049)	0.9130 (0.7532 to 0.9712)	0.8113 (0.6676 to 0.8974)	
Number of patients at risk[b]					
3 Months	82	114	33	51	
6 Months	77	102	31	46	
9 Months	71	97	30	43	
12 Months	67	88	28	39	
15 Months	61	81	27	36	
18 Months	60	72	26	34	
21 Months	49	65	18	27	
24 Months	16	22	8	8	
27 Months	3	1	1	0	
30 Months	0	0	0	0	

PT are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.77 Subgroup analysis by MM type
16.2.7.1.77.2 Treatment emergent adverse event per PT by treatment group according to MM type - Safety population

	IgG		Non-IgG		
	Kd (N=85)	**IKd (N=124)**	**Kd (N=37)**	**IKd (N=53)**	**p-value of treatment-by-sub group interaction[c]**
18 Months	60	87	26	39	
21 Months	47	78	20	33	
24 Months	15	26	8	11	
27 Months	2	0	0	0	
30 Months	0	0	0	0	
Infusion related reaction (days)					
Number (%) of events	3 (3.5)	48 (38.7)	1 (2.7)	31 (58.5)	0.4392
Number (%) of patients censored	82 (96.5)	76 (61.3)	36 (97.3)	22 (41.5)	
Kaplan-Meier estimates of event in months					
25% quantile (95% CI)	NC (NC to NC)	0.1314 (0.0986 to 0.1643)	NC (NC to NC)	0.0657 (0.0329 to 0.0986)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	0.1971 (0.0986 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	<.0001		<.0001	

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CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.77 Subgroup analysis by MM type
16.2.7.1.77.2 Treatment emergent adverse event per PT by treatment group according to MM type - Safety population

	IgG		Non-IgG		
	Kd (N=85)	**IKd (N=124)**	**Kd (N=37)**	**IKd (N=53)**	**p-value of treatment-by-sub group interaction[c]**
Hazard ratio (95% CI) vs Kd	-	13.13 (4.09 to 42.17)		30.22 (4.12 to 221.83)	
P-value	-	<.0001		0.0008	
Hazard ratio inverted (95% CI) vs IKd	0.08 (0.02 to 0.24)		0.03 (0.00 to 0.24)		
Events probability (95% CI)[b]					
3 Months	0.9647 (0.8946 to 0.9885)	0.6288 (0.5374 to 0.7071)	0.9722 (0.8187 to 0.9960)	0.4528 (0.3163 to 0.5797)	
6 Months	0.9647 (0.8946 to 0.9885)	0.6205 (0.5290 to 0.6994)	0.9722 (0.8187 to 0.9960)	0.4528 (0.3163 to 0.5797)	
9 Months	0.9647 (0.8946 to 0.9885)	0.6205 (0.5290 to 0.6994)	0.9722 (0.8187 to 0.9960)	0.4528 (0.3163 to 0.5797)	
12 Months	0.9647 (0.8946 to 0.9885)	0.6205 (0.5290 to 0.6994)	0.9722 (0.8187 to 0.9960)	0.4528 (0.3163 to 0.5797)	
15 Months	0.9647 (0.8946 to 0.9885)	0.6205 (0.5290 to 0.6994)	0.9722 (0.8187 to 0.9960)	0.4331 (0.2983 to 0.5606)	
18 Months	0.9647 (0.8946 to 0.9885)	0.6205 (0.5290 to 0.6994)	0.9722 (0.8187 to 0.9960)	0.4331 (0.2983 to 0.5606)	

PT are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.77 Subgroup analysis by MM type
16.2.7.1.77.2 Treatment emergent adverse event per PT by treatment group according to MM type - Safety population

	IgG		Non-IgG		
	Kd (N=85)	**IKd (N=124)**	**Kd (N=37)**	**IKd (N=53)**	**p-value of treatment-by-sub group interaction[c]**
21 Months	0.9647 (0.8946 to 0.9885)	0.6102 (0.5179 to 0.6902)	0.9722 (0.8187 to 0.9960)	0.4115 (0.2781 to 0.5400)	
24 Months	0.9647 (0.8946 to 0.9885)	0.6102 (0.5179 to 0.6902)	0.9722 (0.8187 to 0.9960)	0.4115 (0.2781 to 0.5400)	
27 Months	0.9647 (0.8946 to 0.9885)	0.6102 (0.5179 to 0.6902)	0.9722 (0.8187 to 0.9960)	0.4115 (0.2781 to 0.5400)	
30 Months	0.9647 (0.8946 to 0.9885)	0.6102 (0.5179 to 0.6902)	0.9722 (0.8187 to 0.9960)	0.4115 (0.2781 to 0.5400)	
Number of patients at risk[b]					
3 Months	82	76	34	24	
6 Months	79	74	32	23	
9 Months	75	73	30	23	
12 Months	74	71	29	23	
15 Months	69	65	28	20	
18 Months	68	60	27	20	
21 Months	56	54	19	14	
24 Months	21	21	7	2	

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CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.77 Subgroup analysis by MM type
16.2.7.1.77.2 Treatment emergent adverse event per PT by treatment group according to MM type - Safety population

	IgG		Non-IgG		
	Kd (N=85)	**IKd (N=124)**	**Kd (N=37)**	**IKd (N=53)**	**p-value of treatment-by-sub group interaction[c]**
30 Months	0.9629 (0.8894 to 0.9879)	0.9324 (0.8693 to 0.9656)	1.0000 (1.0000 to 1.0000)	0.9556 (0.8338 to 0.9887)	
Number of patients at risk[b]					
3 Months	83	119	35	53	
6 Months	80	111	33	49	
9 Months	74	108	31	45	
12 Months	73	106	30	43	
15 Months	69	99	29	40	
18 Months	68	93	28	39	
21 Months	56	85	20	33	
24 Months	20	25	8	11	
27 Months	3	1	1	0	
30 Months	0	0	0	0	
Thrombocytopenia (days)					
Number (%) of events	6 (7.1)	2 (1.6)	6 (16.2)	3 (5.7)	0.7412
Number (%) of patients censored	79 (92.9)	122 (98.4)	31 (83.8)	50 (94.3)	

PT are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.77 Subgroup analysis by MM type
16.2.7.1.77.2 Treatment emergent adverse event per PT by treatment group according to MM type - Safety population

	IgG		Non-IgG		
	Kd (N=85)	**IKd (N=124)**	**Kd (N=37)**	**IKd (N=53)**	**p-value of treatment-by-sub group interaction[c]**
Kaplan-Meier estimates of event in months					
25% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (2.3326 to NC)	NC (NC to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.0447		0.0936	
Hazard ratio (95% CI) vs Kd	-	0.22 (0.05 to 1.11)		0.32 (0.08 to 1.30)	
P-value	-	0.0670		0.1115	
Events probability (95% CI)[b]					
3 Months	0.9762 (0.9081 to 0.9940)	0.9919 (0.9437 to 0.9989)	0.8911 (0.7352 to 0.9577)	0.9811 (0.8735 to 0.9973)	
6 Months	0.9521 (0.8773 to 0.9817)	0.9919 (0.9437 to 0.9989)	0.8632 (0.7020 to 0.9407)	0.9811 (0.8735 to 0.9973)	

PT are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.77 Subgroup analysis by MM type
16.2.7.1.77.2 Treatment emergent adverse event per PT by treatment group according to MM type - Safety population

	IgG		Non-IgG		
	Kd (N=85)	**IKd (N=124)**	**Kd (N=37)**	**IKd (N=53)**	**p-value of treatment-by-sub group interaction[c]**
9 Months	0.9397 (0.8612 to 0.9745)	0.9919 (0.9437 to 0.9989)	0.8345 (0.6678 to 0.9221)	0.9811 (0.8735 to 0.9973)	
12 Months	0.9397 (0.8612 to 0.9745)	0.9832 (0.9346 to 0.9958)	0.8345 (0.6678 to 0.9221)	0.9811 (0.8735 to 0.9973)	
15 Months	0.9397 (0.8612 to 0.9745)	0.9832 (0.9346 to 0.9958)	0.8345 (0.6678 to 0.9221)	0.9811 (0.8735 to 0.9973)	
18 Months	0.9257 (0.8417 to 0.9660)	0.9832 (0.9346 to 0.9958)	0.8345 (0.6678 to 0.9221)	0.9578 (0.8402 to 0.9894)	
21 Months	0.9257 (0.8417 to 0.9660)	0.9832 (0.9346 to 0.9958)	0.8345 (0.6678 to 0.9221)	0.9338 (0.8074 to 0.9783)	
24 Months	0.9257 (0.8417 to 0.9660)	0.9832 (0.9346 to 0.9958)	0.8345 (0.6678 to 0.9221)	0.9338 (0.8074 to 0.9783)	
27 Months	0.9257 (0.8417 to 0.9660)	0.9832 (0.9346 to 0.9958)	0.8345 (0.6678 to 0.9221)	0.9338 (0.8074 to 0.9783)	
30 Months	0.9257 (0.8417 to 0.9660)	0.9832 (0.9346 to 0.9958)	0.8345 (0.6678 to 0.9221)	0.9338 (0.8074 to 0.9783)	
Number of patients at risk[b]					
3 Months	82	119	32	52	

PT are presented if at least 10 events in a arm
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CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.77 Subgroup analysis by MM type
16.2.7.1.77.2 Treatment emergent adverse event per PT by treatment group according to MM type - Safety population

	IgG		Non-IgG		
	Kd (N=85)	**IKd (N=124)**	**Kd (N=37)**	**IKd (N=53)**	**p-value of treatment-by-sub group interaction[c]**
6 Months	77	116	30	49	
9 Months	72	115	27	45	
12 Months	71	111	27	45	
15 Months	67	103	26	42	
18 Months	65	97	25	40	
21 Months	54	89	17	32	
24 Months	19	28	8	11	
27 Months	3	2	1	0	
30 Months	0	0	0	0	
Traumatic fracture (days)					
Number (%) of events	4 (4.7)	10 (8.1)	1 (2.7)	3 (5.7)	0.9045
Number (%) of patients censored	81 (95.3)	114 (91.9)	36 (97.3)	50 (94.3)	
Kaplan-Meier estimates of event in months					
25% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	

PT are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.77 Subgroup analysis by MM type
16.2.7.1.77.2 Treatment emergent adverse event per PT by treatment group according to MM type - Safety population

	IgG		Non-IgG		
	Kd (N=85)	**IKd (N=124)**	**Kd (N=37)**	**IKd (N=53)**	**p-value of treatment-by-sub group interaction[c]**
21 Months	55	84	20	32	
24 Months	19	25	8	9	
27 Months	2	1	1	0	
30 Months	0	0	0	0	
Upper respiratory tract infection (days)					
Number (%) of events	21 (24.7)	52 (41.9)	8 (21.6)	12 (22.6)	0.2415
Number (%) of patients censored	64 (75.3)	72 (58.1)	29 (78.4)	41 (77.4)	
Kaplan-Meier estimates of event in months					
25% quantile (95% CI)	12.7803 (7.4908 to NC)	6.8008 (4.0411 to 10.5791)	NC (3.2197 to NC)	NC (4.2053 to NC)	
Median (95% CI)	NC (NC to NC)	NC (13.3717 to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.0124		0.9594	

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CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.77 Subgroup analysis by MM type
16.2.7.1.77.2 Treatment emergent adverse event per PT by treatment group according to MM type - Safety population

	IgG		Non-IgG		
	Kd (N=85)	**IKd (N=124)**	**Kd (N=37)**	**IKd (N=53)**	**p-value of treatment-by-sub group interaction[c]**
Hazard ratio (95% CI) vs Kd	-	1.89 (1.14 to 3.13)		1.02 (0.42 to 2.50)	
P-value	-	0.0140		0.9595	
Hazard ratio inverted (95% CI) vs IKd	0.53 (0.32 to 0.88)				
Events probability (95% CI)[b]					
3 Months	0.9171 (0.8339 to 0.9596)	0.8933 (0.8234 to 0.9366)	0.9459 (0.8007 to 0.9862)	0.9057 (0.7881 to 0.9596)	
6 Months	0.8688 (0.7755 to 0.9251)	0.7663 (0.6796 to 0.8323)	0.8580 (0.6912 to 0.9384)	0.8268 (0.6932 to 0.9059)	
9 Months	0.8195 (0.7184 to 0.8871)	0.6882 (0.5962 to 0.7633)	0.8273 (0.6546 to 0.9187)	0.8066 (0.6700 to 0.8911)	
12 Months	0.7805 (0.6741 to 0.8557)	0.6439 (0.5500 to 0.7231)	0.8273 (0.6546 to 0.9187)	0.7848 (0.6445 to 0.8749)	
15 Months	0.7403 (0.6294 to 0.8226)	0.5794 (0.4838 to 0.6635)	0.7929 (0.6121 to 0.8960)	0.7848 (0.6445 to 0.8749)	
18 Months	0.7403 (0.6294 to 0.8226)	0.5491 (0.4527 to 0.6354)	0.7584 (0.5720 to 0.8720)	0.7603 (0.6151 to 0.8568)	
21 Months	0.7403 (0.6294 to 0.8226)	0.5491 (0.4527 to 0.6354)	0.7584 (0.5720 to 0.8720)	0.7603 (0.6151 to 0.8568)	

PT are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.77 Subgroup analysis by MM type
16.2.7.1.77.2 Treatment emergent adverse event per PT by treatment group according to MM type - Safety population

	IgG		Non-IgG		
	Kd (N=85)	**IKd (N=124)**	**Kd (N=37)**	**IKd (N=53)**	**p-value of treatment-by-sub group interaction[c]**
24 Months	0.7403 (0.6294 to 0.8226)	0.5491 (0.4527 to 0.6354)	0.7584 (0.5720 to 0.8720)	0.7603 (0.6151 to 0.8568)	
27 Months	0.7403 (0.6294 to 0.8226)	0.5491 (0.4527 to 0.6354)	0.7584 (0.5720 to 0.8720)	0.7603 (0.6151 to 0.8568)	
30 Months	0.7403 (0.6294 to 0.8226)	0.5491 (0.4527 to 0.6354)	0.7584 (0.5720 to 0.8720)	0.7603 (0.6151 to 0.8568)	
Number of patients at risk[b]					
3 Months	77	107	33	48	
6 Months	71	89	28	41	
9 Months	63	79	25	37	
12 Months	59	72	24	36	
15 Months	51	59	23	33	
18 Months	51	53	21	31	
21 Months	43	49	14	26	
24 Months	17	13	4	9	
27 Months	2	1	1	0	
30 Months	0	0	0	0	

PT are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.78 Subgroup analysis by previous autologous stem-cell
16.2.7.1.78.3 Treatment emergent adverse event per PT by treatment group according to previous autologous stem-cell - Safety population

	Yes		No		
	Kd (N=68)	**IKd (N=115)**	**Kd (N=54)**	**IKd (N=62)**	**p-value of treatment-by-sub group interaction[c]**
18 Months	53	86	37	45	
21 Months	41	77	30	40	
24 Months	17	23	10	15	
27 Months	1	1	3	1	
30 Months	0	0	0	0	
Bronchitis (days)					
Number (%) of events	10 (14.7)	29 (25.2)	5 (9.3)	11 (17.7)	0.9383
Number (%) of patients censored	58 (85.3)	86 (74.8)	49 (90.7)	51 (82.3)	
Kaplan-Meier estimates of event in months					
25% quantile (95% CI)	NC (21.7495 to NC)	17.5113 (8.2793 to NC)	NC (NC to NC)	NC (11.2361 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.0925		0.2089	

PT are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.78 Subgroup analysis by previous autologous stem-cell
16.2.7.1.78.3 Treatment emergent adverse event per PT by treatment group according to previous autologous stem-cell - Safety population

	Yes		No		
	Kd (N=68)	**IKd (N=115)**	**Kd (N=54)**	**IKd (N=62)**	**p-value of treatment-by-sub group interaction[c]**
Hazard ratio (95% CI) vs Kd	-	1.84 (0.89 to 3.77)		1.94 (0.68 to 5.60)	
P-value	-	0.0975		0.2175	
Events probability (95% CI)[b]					
3 Months	0.9557 (0.8688 to 0.9855)	0.9385 (0.8753 to 0.9702)	0.9808 (0.8712 to 0.9973)	0.9675 (0.8761 to 0.9918)	
6 Months	0.9256 (0.8303 to 0.9683)	0.8667 (0.7887 to 0.9174)	0.9612 (0.8535 to 0.9901)	0.9335 (0.8324 to 0.9745)	
9 Months	0.8949 (0.7921 to 0.9485)	0.8298 (0.7462 to 0.8879)	0.9612 (0.8535 to 0.9901)	0.9159 (0.8095 to 0.9641)	
12 Months	0.8630 (0.7530 to 0.9263)	0.7827 (0.6933 to 0.8488)	0.9184 (0.7967 to 0.9686)	0.8275 (0.7027 to 0.9033)	
15 Months	0.8630 (0.7530 to 0.9263)	0.7827 (0.6933 to 0.8488)	0.8960 (0.7675 to 0.9555)	0.8095 (0.6821 to 0.8898)	
18 Months	0.8630 (0.7530 to 0.9263)	0.7287 (0.6328 to 0.8035)	0.8960 (0.7675 to 0.9555)	0.8095 (0.6821 to 0.8898)	
21 Months	0.8630 (0.7530 to 0.9263)	0.7287 (0.6328 to 0.8035)	0.8960 (0.7675 to 0.9555)	0.8095 (0.6821 to 0.8898)	

PT are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.78 Subgroup analysis by previous autologous stem-cell
16.2.7.1.78.3 Treatment emergent adverse event per PT by treatment group according to previous autologous stem-cell - Safety population

	Yes		No		
	Kd (N=68)	**IKd (N=115)**	**Kd (N=54)**	**IKd (N=62)**	**p-value of treatment-by-sub group interaction[c]**
24 Months	0.8368 (0.7136 to 0.9103)	0.7287 (0.6328 to 0.8035)	0.8960 (0.7675 to 0.9555)	0.8095 (0.6821 to 0.8898)	
27 Months	0.8368 (0.7136 to 0.9103)	0.7287 (0.6328 to 0.8035)	0.8960 (0.7675 to 0.9555)	0.8095 (0.6821 to 0.8898)	
30 Months	0.8368 (0.7136 to 0.9103)	0.7287 (0.6328 to 0.8035)	0.8960 (0.7675 to 0.9555)	0.8095 (0.6821 to 0.8898)	
Number of patients at risk[b]					
3 Months	64	106	51	59	
6 Months	61	95	47	53	
9 Months	56	88	45	52	
12 Months	53	81	42	46	
15 Months	50	76	38	41	
18 Months	49	67	37	39	
21 Months	37	59	30	33	
24 Months	15	16	9	14	
27 Months	1	0	3	1	
30 Months	0	0	0	0	

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CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.78 Subgroup analysis by previous autologous stem-cell
16.2.7.1.78.3 Treatment emergent adverse event per PT by treatment group according to previous autologous stem-cell - Safety population

	Yes		No		
	Kd (N=68)	**IKd (N=115)**	**Kd (N=54)**	**IKd (N=62)**	**p-value of treatment-by-sub group interaction[c]**
18 Months	48	82	38	44	
21 Months	35	72	32	39	
24 Months	13	21	10	16	
27 Months	0	0	2	0	
30 Months	0	0	0	0	
Infusion related reaction (days)					
Number (%) of events	1 (1.5)	61 (53.0)	3 (5.6)	18 (29.0)	0.0670
Number (%) of patients censored	67 (98.5)	54 (47.0)	51 (94.4)	44 (71.0)	
Kaplan-Meier estimates of event in months					
25% quantile (95% CI)	NC (NC to NC)	0.0657 (0.0657 to 0.1314)	NC (NC to NC)	0.2300 (0.0986 to NC)	
Median (95% CI)	NC (NC to NC)	0.2957 (0.1643 to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	<.0001		0.0014	

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CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.78 Subgroup analysis by previous autologous stem-cell
16.2.7.1.78.3 Treatment emergent adverse event per PT by treatment group according to previous autologous stem-cell - Safety population

	Yes		No		
	Kd (N=68)	**IKd (N=115)**	**Kd (N=54)**	**IKd (N=62)**	**p-value of treatment-by-sub group interaction[c]**
Hazard ratio (95% CI) vs Kd	-	48.68 (6.74 to 351.46)		5.81 (1.71 to 19.73)	
P-value	-	0.0001		0.0048	
Hazard ratio inverted (95% CI) vs IKd	0.02 (0.00 to 0.15)		0.17 (0.05 to 0.58)		
Events probability (95% CI)[b]					
3 Months	0.9853 (0.9002 to 0.9979)	0.4868 (0.3928 to 0.5743)	0.9441 (0.8365 to 0.9816)	0.7419 (0.6138 to 0.8332)	
6 Months	0.9853 (0.9002 to 0.9979)	0.4780 (0.3843 to 0.5656)	0.9441 (0.8365 to 0.9816)	0.7419 (0.6138 to 0.8332)	
9 Months	0.9853 (0.9002 to 0.9979)	0.4780 (0.3843 to 0.5656)	0.9441 (0.8365 to 0.9816)	0.7419 (0.6138 to 0.8332)	
12 Months	0.9853 (0.9002 to 0.9979)	0.4780 (0.3843 to 0.5656)	0.9441 (0.8365 to 0.9816)	0.7419 (0.6138 to 0.8332)	
15 Months	0.9853 (0.9002 to 0.9979)	0.4688 (0.3753 to 0.5566)	0.9441 (0.8365 to 0.9816)	0.7419 (0.6138 to 0.8332)	
18 Months	0.9853 (0.9002 to 0.9979)	0.4688 (0.3753 to 0.5566)	0.9441 (0.8365 to 0.9816)	0.7419 (0.6138 to 0.8332)	

PT are presented if at least 10 events in a arm
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CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.78 Subgroup analysis by previous autologous stem-cell
16.2.7.1.78.3 Treatment emergent adverse event per PT by treatment group according to previous autologous stem-cell - Safety population

	Yes		No		
	Kd (N=68)	**IKd (N=115)**	**Kd (N=54)**	**IKd (N=62)**	**p-value of treatment-by-sub group interaction[c]**
21 Months	0.9853 (0.9002 to 0.9979)	0.4688 (0.3753 to 0.5566)	0.9441 (0.8365 to 0.9816)	0.7018 (0.5681 to 0.8012)	
24 Months	0.9853 (0.9002 to 0.9979)	0.4688 (0.3753 to 0.5566)	0.9441 (0.8365 to 0.9816)	0.7018 (0.5681 to 0.8012)	
27 Months	0.9853 (0.9002 to 0.9979)	0.4688 (0.3753 to 0.5566)	0.9441 (0.8365 to 0.9816)	0.7018 (0.5681 to 0.8012)	
30 Months	0.9853 (0.9002 to 0.9979)	0.4688 (0.3753 to 0.5566)	0.9441 (0.8365 to 0.9816)	0.7018 (0.5681 to 0.8012)	
Number of patients at risk[b]					
3 Months	66	55	50	45	
6 Months	64	54	47	43	
9 Months	60	53	45	43	
12 Months	59	52	44	42	
15 Months	56	46	41	39	
18 Months	55	43	40	37	
21 Months	42	37	33	31	
24 Months	18	10	10	13	

PT are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.78 Subgroup analysis by previous autologous stem-cell
16.2.7.1.78.3 Treatment emergent adverse event per PT by treatment group according to previous autologous stem-cell - Safety population

	Yes		No		
	Kd (N=68)	**IKd (N=115)**	**Kd (N=54)**	**IKd (N=62)**	**p-value of treatment-by-sub group interaction[c]**
30 Months	0.9841 (0.8926 to 0.9977)	0.9175 (0.8473 to 0.9562)	0.9599 (0.8488 to 0.9898)	0.9836 (0.8893 to 0.9977)	
Number of patients at risk[b]					
3 Months	67	113	51	59	
6 Months	65	105	48	55	
9 Months	60	99	45	54	
12 Months	59	96	44	53	
15 Months	56	90	42	49	
18 Months	55	85	41	47	
21 Months	42	77	34	41	
24 Months	17	20	11	16	
27 Months	1	0	3	1	
30 Months	0	0	0	0	
Thrombocytopenia (days)					
Number (%) of events	7 (10.3)	3 (2.6)	5 (9.3)	2 (3.2)	0.7559
Number (%) of patients censored	61 (89.7)	112 (97.4)	49 (90.7)	60 (96.8)	

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CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1.78 Subgroup analysis by previous autologous stem-cell
16.2.7.1.78.3 Treatment emergent adverse event per PT by treatment group according to previous autologous stem-cell - Safety population

	Yes		No		
	Kd (N=68)	**IKd (N=115)**	**Kd (N=54)**	**IKd (N=62)**	**p-value of treatment-by-sub group interaction[c]**
Kaplan-Meier estimates of event in months					
25% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.0257		0.1796	
Hazard ratio (95% CI) vs Kd	-	0.24 (0.06 to 0.94)		0.34 (0.07 to 1.77)	
P-value	-	0.0400		0.2005	
Events probability (95% CI)[b]					
3 Months	0.9409 (0.8503 to 0.9774)	0.9913 (0.9399 to 0.9988)	0.9630 (0.8599 to 0.9906)	0.9839 (0.8910 to 0.9977)	
6 Months	0.9258 (0.8308 to 0.9684)	0.9913 (0.9399 to 0.9988)	0.9252 (0.8128 to 0.9713)	0.9839 (0.8910 to 0.9977)	

PT are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.78 Subgroup analysis by previous autologous stem-cell
16.2.7.1.78.3 Treatment emergent adverse event per PT by treatment group according to previous autologous stem-cell - Safety population

	Yes		No		
	Kd (N=68)	**IKd (N=115)**	**Kd (N=54)**	**IKd (N=62)**	**p-value of treatment-by-sub group interaction[c]**
9 Months	0.9103 (0.8112 to 0.9587)	0.9913 (0.9399 to 0.9988)	0.9055 (0.7876 to 0.9596)	0.9839 (0.8910 to 0.9977)	
12 Months	0.9103 (0.8112 to 0.9587)	0.9820 (0.9297 to 0.9955)	0.9055 (0.7876 to 0.9596)	0.9839 (0.8910 to 0.9977)	
15 Months	0.9103 (0.8112 to 0.9587)	0.9820 (0.9297 to 0.9955)	0.9055 (0.7876 to 0.9596)	0.9839 (0.8910 to 0.9977)	
18 Months	0.8928 (0.7878 to 0.9475)	0.9820 (0.9297 to 0.9955)	0.9055 (0.7876 to 0.9596)	0.9638 (0.8617 to 0.9909)	
21 Months	0.8928 (0.7878 to 0.9475)	0.9712 (0.9128 to 0.9907)	0.9055 (0.7876 to 0.9596)	0.9638 (0.8617 to 0.9909)	
24 Months	0.8928 (0.7878 to 0.9475)	0.9712 (0.9128 to 0.9907)	0.9055 (0.7876 to 0.9596)	0.9638 (0.8617 to 0.9909)	
27 Months	0.8928 (0.7878 to 0.9475)	0.9712 (0.9128 to 0.9907)	0.9055 (0.7876 to 0.9596)	0.9638 (0.8617 to 0.9909)	
30 Months	0.8928 (0.7878 to 0.9475)	0.9712 (0.9128 to 0.9907)	0.9055 (0.7876 to 0.9596)	0.9638 (0.8617 to 0.9909)	
Number of patients at risk[b]					
3 Months	63	112	51	59	

PT are presented if at least 10 events in a arm
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CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.78 Subgroup analysis by previous autologous stem-cell
16.2.7.1.78.3 Treatment emergent adverse event per PT by treatment group according to previous autologous stem-cell - Safety population

	Yes		No		
	Kd (N=68)	**IKd (N=115)**	**Kd (N=54)**	**IKd (N=62)**	**p-value of treatment-by-sub group interaction[c]**
6 Months	60	110	47	55	
9 Months	55	106	44	54	
12 Months	55	103	43	53	
15 Months	52	96	41	49	
18 Months	50	91	40	46	
21 Months	38	81	33	40	
24 Months	16	23	11	16	
27 Months	1	1	3	1	
30 Months	0	0	0	0	
Traumatic fracture (days)					
Number (%) of events	4 (5.9)	8 (7.0)	1 (1.9)	5 (8.1)	0.2868
Number (%) of patients censored	64 (94.1)	107 (93.0)	53 (98.1)	57 (91.9)	
Kaplan-Meier estimates of event in months					
25% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	

PT are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1.78 Subgroup analysis by previous autologous stem-cell
16.2.7.1.78.3 Treatment emergent adverse event per PT by treatment group according to previous autologous stem-cell - Safety population

	Yes		No		
	Kd (N=68)	**IKd (N=115)**	**Kd (N=54)**	**IKd (N=62)**	**p-value of treatment-by-sub group interaction[c]**
21 Months	41	78	34	38	
24 Months	17	19	10	15	
27 Months	1	0	2	1	
30 Months	0	0	0	0	
Upper respiratory tract infection (days)					
Number (%) of events	14 (20.6)	35 (30.4)	15 (27.8)	29 (46.8)	0.6924
Number (%) of patients censored	54 (79.4)	80 (69.6)	39 (72.2)	33 (53.2)	
Kaplan-Meier estimates of event in months					
25% quantile (95% CI)	NC (10.9405 to NC)	11.4661 (6.5051 to NC)	9.7906 (1.5113 to NC)	4.2382 (2.1355 to 8.9692)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	17.9055 (8.9692 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.1459		0.0531	

PT are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
PGM=DEVOPS/SAR650984/EFC15246/CIR_RWE/REPORT/PGM/ae_km_socpt_subgp_sr_s_t.sas OUT=REPORT/OUTPUT/ae_km_teaept_auto_s_t_x.rtf (12FEB2021 8:24)

16.2.7.1 Safety endpoints
16.2.7.1.78 Subgroup analysis by previous autologous stem-cell
16.2.7.1.78.3 Treatment emergent adverse event per PT by treatment group according to previous autologous stem-cell - Safety population

	Yes		No		
	Kd (N=68)	**IKd (N=115)**	**Kd (N=54)**	**IKd (N=62)**	**p-value of treatment-by-sub group interaction[c]**
Hazard ratio (95% CI) vs Kd	-	1.58 (0.85 to 2.93)		1.83 (0.98 to 3.42)	
P-value	-	0.1495		0.0568	
Events probability (95% CI)[b]					
3 Months	0.9706 (0.8875 to 0.9926)	0.9474 (0.8866 to 0.9760)	0.8674 (0.7417 to 0.9345)	0.8022 (0.6779 to 0.8825)	
6 Months	0.9099 (0.8103 to 0.9585)	0.8487 (0.7678 to 0.9031)	0.8086 (0.6732 to 0.8922)	0.6623 (0.5263 to 0.7676)	
9 Months	0.8625 (0.7522 to 0.9261)	0.7739 (0.6839 to 0.8413)	0.7682 (0.6276 to 0.8613)	0.6265 (0.4894 to 0.7364)	
12 Months	0.8294 (0.7126 to 0.9018)	0.7350 (0.6413 to 0.8079)	0.7468 (0.6036 to 0.8447)	0.5907 (0.4534 to 0.7044)	
15 Months	0.7786 (0.6542 to 0.8627)	0.6947 (0.5977 to 0.7726)	0.7235 (0.5770 to 0.8266)	0.5358 (0.3992 to 0.6545)	
18 Months	0.7786 (0.6542 to 0.8627)	0.6724 (0.5736 to 0.7532)	0.7002 (0.5510 to 0.8080)	0.4954 (0.3592 to 0.6176)	
21 Months	0.7786 (0.6542 to 0.8627)	0.6724 (0.5736 to 0.7532)	0.7002 (0.5510 to 0.8080)	0.4954 (0.3592 to 0.6176)	

PT are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.78 Subgroup analysis by previous autologous stem-cell
16.2.7.1.78.3 Treatment emergent adverse event per PT by treatment group according to previous autologous stem-cell - Safety population

	Yes		No		
	Kd (N=68)	**IKd (N=115)**	**Kd (N=54)**	**IKd (N=62)**	**p-value of treatment-by-sub group interaction[c]**
24 Months	0.7786 (0.6542 to 0.8627)	0.6724 (0.5736 to 0.7532)	0.7002 (0.5510 to 0.8080)	0.4954 (0.3592 to 0.6176)	
27 Months	0.7786 (0.6542 to 0.8627)	0.6724 (0.5736 to 0.7532)	0.7002 (0.5510 to 0.8080)	0.4954 (0.3592 to 0.6176)	
30 Months	0.7786 (0.6542 to 0.8627)	0.6724 (0.5736 to 0.7532)	0.7002 (0.5510 to 0.8080)	0.4954 (0.3592 to 0.6176)	
Number of patients at risk[b]					
3 Months	65	107	45	48	
6 Months	59	93	40	37	
9 Months	52	81	36	35	
12 Months	49	75	34	33	
15 Months	43	65	31	27	
18 Months	42	60	30	24	
21 Months	32	56	25	19	
24 Months	13	16	8	6	
27 Months	1	1	2	0	
30 Months	0	0	0	0	

PT are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.79 Subgroup analysis by baseline creatinine clearance (MDRD)
16.2.7.1.79.2 Treatment emergent adverse event per PT by treatment group according to baseline creatinine clearance (MDRD) - Safety population

	>=60 mL/min/1.73m2		<60 mL/min/1.73m2		
	Kd (N=92)	**IKd (N=120)**	**Kd (N=18)**	**IKd (N=43)**	**p-value of treatment-by-sub group interaction[c]**
18 Months	72	89	10	34	
21 Months	55	80	9	30	
24 Months	20	28	4	8	
27 Months	4	1	0	1	
30 Months	0	0	0	0	
Bronchitis (days)					
Number (%) of events	10 (10.9)	25 (20.8)	1 (5.6)	7 (16.3)	0.9062
Number (%) of patients censored	82 (89.1)	95 (79.2)	17 (94.4)	36 (83.7)	
Kaplan-Meier estimates of event in months					
25% quantile (95% CI)	NC (NC to NC)	NC (9.1335 to NC)	NC (2.2012 to NC)	NC (10.9076 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.0364		0.3875	

PT are presented if at least 10 events in a arm
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CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.79 Subgroup analysis by baseline creatinine clearance (MDRD)
16.2.7.1.79.2 Treatment emergent adverse event per PT by treatment group according to baseline creatinine clearance (MDRD) - Safety population

	>=60 mL/min/1.73m2		<60 mL/min/1.73m2		
	Kd (N=92)	**IKd (N=120)**	**Kd (N=18)**	**IKd (N=43)**	**p-value of treatment-by-sub group interaction[c]**
Hazard ratio (95% CI) vs Kd	-	2.15 (1.03 to 4.47)		2.44 (0.30 to 19.87)	
P-value	-	0.0411		0.4032	
Hazard ratio inverted (95% CI) vs IKd	0.47 (0.22 to 0.97)				
Events probability (95% CI)[b]					
3 Months	0.9783 (0.9159 to 0.9945)	0.9412 (0.8807 to 0.9715)	0.9375 (0.6323 to 0.9910)	0.9767 (0.8462 to 0.9967)	
6 Months	0.9565 (0.8883 to 0.9835)	0.8627 (0.7856 to 0.9136)	0.9375 (0.6323 to 0.9910)	0.9529 (0.8246 to 0.9880)	
9 Months	0.9344 (0.8598 to 0.9700)	0.8356 (0.7543 to 0.8919)	0.9375 (0.6323 to 0.9910)	0.9285 (0.7943 to 0.9764)	
12 Months	0.9113 (0.8304 to 0.9547)	0.7897 (0.7026 to 0.8539)	0.9375 (0.6323 to 0.9910)	0.8796 (0.7345 to 0.9481)	
15 Months	0.8993 (0.8153 to 0.9464)	0.7897 (0.7026 to 0.8539)	0.9375 (0.6323 to 0.9910)	0.8552 (0.7056 to 0.9322)	
18 Months	0.8993 (0.8153 to 0.9464)	0.7793 (0.6907 to 0.8453)	0.9375 (0.6323 to 0.9910)	0.8285 (0.6730 to 0.9144)	
21 Months	0.8993 (0.8153 to 0.9464)	0.7793 (0.6907 to 0.8453)	0.9375 (0.6323 to 0.9910)	0.8285 (0.6730 to 0.9144)	

PT are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.79 Subgroup analysis by baseline creatinine clearance (MDRD)
16.2.7.1.79.2 Treatment emergent adverse event per PT by treatment group according to baseline creatinine clearance (MDRD) - Safety population

	>=60 mL/min/1.73m2		<60 mL/min/1.73m2		
	Kd (N=92)	**IKd (N=120)**	**Kd (N=18)**	**IKd (N=43)**	**p-value of treatment-by-sub group interaction[c]**
24 Months	0.8798 (0.7847 to 0.9346)	0.7793 (0.6907 to 0.8453)	0.9375 (0.6323 to 0.9910)	0.8285 (0.6730 to 0.9144)	
27 Months	0.8798 (0.7847 to 0.9346)	0.7793 (0.6907 to 0.8453)	0.9375 (0.6323 to 0.9910)	0.8285 (0.6730 to 0.9144)	
30 Months	0.8798 (0.7847 to 0.9346)	0.7793 (0.6907 to 0.8453)	0.9375 (0.6323 to 0.9910)	0.8285 (0.6730 to 0.9144)	
Number of patients at risk[b]					
3 Months	90	110	15	42	
6 Months	87	96	13	40	
9 Months	81	91	13	38	
12 Months	77	85	13	36	
15 Months	71	78	12	33	
18 Months	71	73	10	30	
21 Months	53	65	9	25	
24 Months	19	23	4	7	
27 Months	4	1	0	0	
30 Months	0	0	0	0	

PT are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.79 Subgroup analysis by baseline creatinine clearance (MDRD)
16.2.7.1.79.2 Treatment emergent adverse event per PT by treatment group according to baseline creatinine clearance (MDRD) - Safety population

	>=60 mL/min/1.73m2		<60 mL/min/1.73m2		
	Kd (N=92)	**IKd (N=120)**	**Kd (N=18)**	**IKd (N=43)**	**p-value of treatment-by-sub group interaction[c]**
21 Months	51	74	9	28	
24 Months	16	26	4	9	
27 Months	2	0	0	0	
30 Months	0	0	0	0	
Infusion related reaction (days)					
Number (%) of events	3 (3.3)	55 (45.8)	1 (5.6)	16 (37.2)	0.4545
Number (%) of patients censored	89 (96.7)	65 (54.2)	17 (94.4)	27 (62.8)	
Kaplan-Meier estimates of event in months					
25% quantile (95% CI)	NC (NC to NC)	0.0986 (0.0657 to 0.1314)	NC (0.0986 to NC)	0.1314 (0.0657 to NC)	
Median (95% CI)	NC (NC to NC)	NC (0.1643 to NC)	NC (NC to NC)	NC (0.2300 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	<.0001		0.0219	

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CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.79 Subgroup analysis by baseline creatinine clearance (MDRD)
16.2.7.1.79.2 Treatment emergent adverse event per PT by treatment group according to baseline creatinine clearance (MDRD) - Safety population

	>=60 mL/min/1.73m2		<60 mL/min/1.73m2		
	Kd (N=92)	**IKd (N=120)**	**Kd (N=18)**	**IKd (N=43)**	**p-value of treatment-by-sub group interaction[c]**
Hazard ratio (95% CI) vs Kd	-	17.86 (5.58 to 57.16)		7.46 (0.99 to 56.27)	
P-value	-	<.0001		0.0513	
Hazard ratio inverted (95% CI) vs IKd	0.06 (0.02 to 0.18)				
Events probability (95% CI)[b]					
3 Months	0.9674 (0.9023 to 0.9894)	0.5497 (0.4564 to 0.6336)	0.9444 (0.6664 to 0.9920)	0.6512 (0.4895 to 0.7729)	
6 Months	0.9674 (0.9023 to 0.9894)	0.5497 (0.4564 to 0.6336)	0.9444 (0.6664 to 0.9920)	0.6512 (0.4895 to 0.7729)	
9 Months	0.9674 (0.9023 to 0.9894)	0.5497 (0.4564 to 0.6336)	0.9444 (0.6664 to 0.9920)	0.6512 (0.4895 to 0.7729)	
12 Months	0.9674 (0.9023 to 0.9894)	0.5497 (0.4564 to 0.6336)	0.9444 (0.6664 to 0.9920)	0.6512 (0.4895 to 0.7729)	
15 Months	0.9674 (0.9023 to 0.9894)	0.5497 (0.4564 to 0.6336)	0.9444 (0.6664 to 0.9920)	0.6512 (0.4895 to 0.7729)	
18 Months	0.9674 (0.9023 to 0.9894)	0.5497 (0.4564 to 0.6336)	0.9444 (0.6664 to 0.9920)	0.6512 (0.4895 to 0.7729)	
21 Months	0.9674 (0.9023 to 0.9894)	0.5394 (0.4457 to 0.6240)	0.9444 (0.6664 to 0.9920)	0.6240 (0.4608 to 0.7505)	

PT are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.79 Subgroup analysis by baseline creatinine clearance (MDRD)
16.2.7.1.79.2 Treatment emergent adverse event per PT by treatment group according to baseline creatinine clearance (MDRD) - Safety population

	>=60 mL/min/1.73m2		<60 mL/min/1.73m2		
	Kd (N=92)	**IKd (N=120)**	**Kd (N=18)**	**IKd (N=43)**	**p-value of treatment-by-sub group interaction[c]**
24 Months	0.9674 (0.9023 to 0.9894)	0.5394 (0.4457 to 0.6240)	0.9444 (0.6664 to 0.9920)	0.6240 (0.4608 to 0.7505)	
27 Months	0.9674 (0.9023 to 0.9894)	0.5394 (0.4457 to 0.6240)	0.9444 (0.6664 to 0.9920)	0.6240 (0.4608 to 0.7505)	
30 Months	0.9674 (0.9023 to 0.9894)	0.5394 (0.4457 to 0.6240)	0.9444 (0.6664 to 0.9920)	0.6240 (0.4608 to 0.7505)	
Number of patients at risk[b]					
3 Months	89	64	16	28	
6 Months	88	64	14	27	
9 Months	84	63	13	27	
12 Months	82	62	13	27	
15 Months	77	57	12	25	
18 Months	77	53	10	24	
21 Months	59	46	9	20	
24 Months	21	18	4	4	
27 Months	4	1	0	0	
30 Months	0	0	0	0	

PT are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.79 Subgroup analysis by baseline creatinine clearance (MDRD)
16.2.7.1.79.2 Treatment emergent adverse event per PT by treatment group according to baseline creatinine clearance (MDRD) - Safety population

	>=60 mL/min/1.73m2		<60 mL/min/1.73m2		
	Kd (N=92)	**IKd (N=120)**	**Kd (N=18)**	**IKd (N=43)**	**p-value of treatment-by-sub group interaction[c]**
30 Months	0.9666 (0.9001 to 0.9891)	0.9650 (0.9095 to 0.9867)	1.0000 (1.0000 to 1.0000)	0.9762 (0.8428 to 0.9966)	
Number of patients at risk[b]					
3 Months	91	115	16	43	
6 Months	90	107	14	41	
9 Months	84	103	13	40	
12 Months	82	102	13	40	
15 Months	78	95	12	38	
18 Months	78	90	10	36	
21 Months	60	81	9	31	
24 Months	21	27	4	9	
27 Months	4	1	0	0	
30 Months	0	0	0	0	
Thrombocytopenia (days)					
Number (%) of events	8 (8.7)	3 (2.5)	3 (16.7)	0 (0.0)	0.9928
Number (%) of patients censored	84 (91.3)	117 (97.5)	15 (83.3)	43 (100.0)	

PT are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.79 Subgroup analysis by baseline creatinine clearance (MDRD)
16.2.7.1.79.2 Treatment emergent adverse event per PT by treatment group according to baseline creatinine clearance (MDRD) - Safety population

	>=60 mL/min/1.73m2		<60 mL/min/1.73m2		
	Kd (N=92)	**IKd (N=120)**	**Kd (N=18)**	**IKd (N=43)**	**p-value of treatment-by-sub group interaction[c]**
Kaplan-Meier estimates of event in months					
25% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (0.2300 to NC)	NC (NC to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.0523		0.0035	
Hazard ratio (95% CI) vs Kd	-	0.29 (0.08 to 1.10)		NC	
P-value	-	0.0683		0.9966	
Events probability (95% CI)[b]					
3 Months	0.9565 (0.8883 to 0.9835)	0.9833 (0.9347 to 0.9958)	0.9444 (0.6664 to 0.9920)	1.0000 (1.0000 to 1.0000)	
6 Months	0.9239 (0.8470 to 0.9630)	0.9833 (0.9347 to 0.9958)	0.9444 (0.6664 to 0.9920)	1.0000 (1.0000 to 1.0000)	

PT are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
PGM=DEVOPS/SAR650984/EFC15246/CIR_RWE/REPORT/PGM/ae_km_socpt_subgp_sr_s_t.sas OUT=REPORT/OUTPUT/ae_km_teaept_crcl_s_t_x.rtf (12FEB2021 8:25)

16.2.7.1 Safety endpoints
16.2.7.1.79 Subgroup analysis by baseline creatinine clearance (MDRD)
16.2.7.1.79.2 Treatment emergent adverse event per PT by treatment group according to baseline creatinine clearance (MDRD) - Safety population

	>=60 mL/min/1.73m2		<60 mL/min/1.73m2		
	Kd (N=92)	**IKd (N=120)**	**Kd (N=18)**	**IKd (N=43)**	**p-value of treatment-by-sub group interaction[c]**
9 Months	0.9239 (0.8470 to 0.9630)	0.9833 (0.9347 to 0.9958)	0.8095 (0.5156 to 0.9348)	1.0000 (1.0000 to 1.0000)	
12 Months	0.9239 (0.8470 to 0.9630)	0.9740 (0.9214 to 0.9916)	0.8095 (0.5156 to 0.9348)	1.0000 (1.0000 to 1.0000)	
15 Months	0.9239 (0.8470 to 0.9630)	0.9740 (0.9214 to 0.9916)	0.8095 (0.5156 to 0.9348)	1.0000 (1.0000 to 1.0000)	
18 Months	0.9118 (0.8311 to 0.9549)	0.9740 (0.9214 to 0.9916)	0.8095 (0.5156 to 0.9348)	1.0000 (1.0000 to 1.0000)	
21 Months	0.9118 (0.8311 to 0.9549)	0.9740 (0.9214 to 0.9916)	0.8095 (0.5156 to 0.9348)	1.0000 (1.0000 to 1.0000)	
24 Months	0.9118 (0.8311 to 0.9549)	0.9740 (0.9214 to 0.9916)	0.8095 (0.5156 to 0.9348)	1.0000 (1.0000 to 1.0000)	
27 Months	0.9118 (0.8311 to 0.9549)	0.9740 (0.9214 to 0.9916)	0.8095 (0.5156 to 0.9348)	1.0000 (1.0000 to 1.0000)	
30 Months	0.9118 (0.8311 to 0.9549)	0.9740 (0.9214 to 0.9916)	0.8095 (0.5156 to 0.9348)	1.0000 (1.0000 to 1.0000)	
Number of patients at risk[b]					
3 Months	88	114	16	43	

PT are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.79 Subgroup analysis by baseline creatinine clearance (MDRD)
16.2.7.1.79.2 Treatment emergent adverse event per PT by treatment group according to baseline creatinine clearance (MDRD) - Safety population

	>=60 mL/min/1.73m2		<60 mL/min/1.73m2		
	Kd (N=92)	**IKd (N=120)**	**Kd (N=18)**	**IKd (N=43)**	**p-value of treatment-by-sub group interaction[c]**
6 Months	85	110	14	42	
9 Months	81	106	11	41	
12 Months	80	104	11	41	
15 Months	76	96	10	39	
18 Months	75	91	8	37	
21 Months	57	82	7	32	
24 Months	20	27	4	10	
27 Months	4	1	0	1	
30 Months	0	0	0	0	
Traumatic fracture (days)					
Number (%) of events	4 (4.3)	8 (6.7)	1 (5.6)	3 (7.0)	0.6767
Number (%) of patients censored	88 (95.7)	112 (93.3)	17 (94.4)	40 (93.0)	
Kaplan-Meier estimates of event in months					
25% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (14.6858 to NC)	NC (NC to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	

PT are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.79 Subgroup analysis by baseline creatinine clearance (MDRD)
16.2.7.1.79.2 Treatment emergent adverse event per PT by treatment group according to baseline creatinine clearance (MDRD) - Safety population

	>=60 mL/min/1.73m2		<60 mL/min/1.73m2		
	Kd (N=92)	**IKd (N=120)**	**Kd (N=18)**	**IKd (N=43)**	**p-value of treatment-by-sub group interaction[c]**
21 Months	60	78	8	30	
24 Months	20	24	4	8	
27 Months	3	1	0	0	
30 Months	0	0	0	0	
Upper respiratory tract infection (days)					
Number (%) of events	24 (26.1)	47 (39.2)	5 (27.8)	17 (39.5)	0.5988
Number (%) of patients censored	68 (73.9)	73 (60.8)	13 (72.2)	26 (60.5)	
Kaplan-Meier estimates of event in months					
25% quantile (95% CI)	13.8645 (7.4908 to NC)	7.2936 (4.2382 to 12.1561)	12.7803 (0.4600 to NC)	5.9795 (2.2012 to 11.7290)	
Median (95% CI)	NC (NC to NC)	NC (16.3285 to NC)	NC (6.4723 to NC)	NC (10.4148 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.0327		0.6500	

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CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.79 Subgroup analysis by baseline creatinine clearance (MDRD)
16.2.7.1.79.2 Treatment emergent adverse event per PT by treatment group according to baseline creatinine clearance (MDRD) - Safety population

	>=60 mL/min/1.73m2		<60 mL/min/1.73m2		
	Kd (N=92)	**IKd (N=120)**	**Kd (N=18)**	**IKd (N=43)**	**p-value of treatment-by-sub group interaction[c]**
Hazard ratio (95% CI) vs Kd	-	1.70 (1.04 to 2.78)		1.26 (0.46 to 3.41)	
P-value	-	0.0348		0.6507	
Hazard ratio inverted (95% CI) vs IKd	0.59 (0.36 to 0.96)				
Events probability (95% CI)[b]					
3 Months	0.9348 (0.8606 to 0.9702)	0.8893 (0.8170 to 0.9342)	0.8185 (0.5352 to 0.9379)	0.8837 (0.7429 to 0.9499)	
6 Months	0.8584 (0.7687 to 0.9152)	0.7835 (0.6965 to 0.8482)	0.8185 (0.5352 to 0.9379)	0.7171 (0.5557 to 0.8284)	
9 Months	0.8141 (0.7181 to 0.8801)	0.7099 (0.6167 to 0.7844)	0.7503 (0.4612 to 0.8989)	0.6684 (0.5049 to 0.7886)	
12 Months	0.7792 (0.6788 to 0.8516)	0.6725 (0.5772 to 0.7510)	0.7503 (0.4612 to 0.8989)	0.6189 (0.4547 to 0.7467)	
15 Months	0.7423 (0.6376 to 0.8209)	0.6049 (0.5069 to 0.6893)	0.6753 (0.3822 to 0.8519)	0.6189 (0.4547 to 0.7467)	
18 Months	0.7295 (0.6234 to 0.8101)	0.5728 (0.4738 to 0.6600)	0.6753 (0.3822 to 0.8519)	0.5920 (0.4272 to 0.7238)	
21 Months	0.7295 (0.6234 to 0.8101)	0.5728 (0.4738 to 0.6600)	0.6753 (0.3822 to 0.8519)	0.5920 (0.4272 to 0.7238)	

PT are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.79 Subgroup analysis by baseline creatinine clearance (MDRD)
16.2.7.1.79.2 Treatment emergent adverse event per PT by treatment group according to baseline creatinine clearance (MDRD) - Safety population

	>=60 mL/min/1.73m2		<60 mL/min/1.73m2		
	Kd (N=92)	**IKd (N=120)**	**Kd (N=18)**	**IKd (N=43)**	**p-value of treatment-by-sub group interaction[c]**
24 Months	0.7295 (0.6234 to 0.8101)	0.5728 (0.4738 to 0.6600)	0.6753 (0.3822 to 0.8519)	0.5920 (0.4272 to 0.7238)	
27 Months	0.7295 (0.6234 to 0.8101)	0.5728 (0.4738 to 0.6600)	0.6753 (0.3822 to 0.8519)	0.5920 (0.4272 to 0.7238)	
30 Months	0.7295 (0.6234 to 0.8101)	0.5728 (0.4738 to 0.6600)	0.6753 (0.3822 to 0.8519)	0.5920 (0.4272 to 0.7238)	
Number of patients at risk[b]					
3 Months	86	103	13	38	
6 Months	78	87	12	30	
9 Months	70	76	10	27	
12 Months	65	72	10	25	
15 Months	58	59	8	23	
18 Months	57	53	7	21	
21 Months	44	48	6	18	
24 Months	16	15	2	5	
27 Months	3	0	0	1	
30 Months	0	0	0	0	

PT are presented if at least 10 events in a arm
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CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.80 Subgroup analysis by previous treament with PI
16.2.7.1.80.2 Treatment emergent adverse event per PT by treatment group according to previous treament with PI - Safety population

	Yes		No		
	Kd (N=47)	**IKd (N=79)**	**Kd (N=75)**	**IKd (N=98)**	**p-value of treatment-by-sub group interaction[c]**
18 Months	32	55	58	76	
21 Months	26	48	45	69	
24 Months	10	13	17	25	
27 Months	2	0	2	2	
30 Months	0	0	0	0	
Bronchitis (days)					
Number (%) of events	9 (19.1)	18 (22.8)	6 (8.0)	22 (22.4)	0.1641
Number (%) of patients censored	38 (80.9)	61 (77.2)	69 (92.0)	76 (77.6)	
Kaplan-Meier estimates of event in months					
25% quantile (95% CI)	NC (9.9877 to NC)	NC (9.1335 to NC)	NC (NC to NC)	NC (10.9076 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.5863		0.0147	

PT are presented if at least 10 events in a arm
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CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.80 Subgroup analysis by previous treament with PI
16.2.7.1.80.2 Treatment emergent adverse event per PT by treatment group according to previous treament with PI - Safety population

	Yes		No		
	Kd (N=47)	**IKd (N=79)**	**Kd (N=75)**	**IKd (N=98)**	**p-value of treatment-by-sub group interaction[c]**
Hazard ratio (95% CI) vs Kd	-	1.25 (0.56 to 2.78)		2.92 (1.18 to 7.21)	
P-value	-	0.5871		0.0199	
Hazard ratio inverted (95% CI) vs IKd			0.34 (0.14 to 0.84)		
Events probability (95% CI)[b]					
3 Months	0.9565 (0.8371 to 0.9889)	0.9615 (0.8854 to 0.9874)	0.9732 (0.8969 to 0.9932)	0.9386 (0.8683 to 0.9719)	
6 Months	0.9343 (0.8099 to 0.9783)	0.8815 (0.7846 to 0.9366)	0.9455 (0.8613 to 0.9792)	0.8967 (0.8165 to 0.9431)	
9 Months	0.8892 (0.7540 to 0.9524)	0.8538 (0.7513 to 0.9163)	0.9455 (0.8613 to 0.9792)	0.8644 (0.7779 to 0.9190)	
12 Months	0.8190 (0.6702 to 0.9052)	0.7830 (0.6700 to 0.8612)	0.9305 (0.8409 to 0.9705)	0.8097 (0.7149 to 0.8757)	
15 Months	0.7942 (0.6412 to 0.8874)	0.7682 (0.6534 to 0.8493)	0.9305 (0.8409 to 0.9705)	0.8097 (0.7149 to 0.8757)	
18 Months	0.7942 (0.6412 to 0.8874)	0.7512 (0.6335 to 0.8358)	0.9305 (0.8409 to 0.9705)	0.7622 (0.6611 to 0.8368)	
21 Months	0.7942 (0.6412 to 0.8874)	0.7512 (0.6335 to 0.8358)	0.9305 (0.8409 to 0.9705)	0.7622 (0.6611 to 0.8368)	

PT are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.80 Subgroup analysis by previous treament with PI
16.2.7.1.80.2 Treatment emergent adverse event per PT by treatment group according to previous treament with PI - Safety population

	Yes		No		
	Kd (N=47)	**IKd (N=79)**	**Kd (N=75)**	**IKd (N=98)**	**p-value of treatment-by-sub group interaction[c]**
24 Months	0.7942 (0.6412 to 0.8874)	0.7512 (0.6335 to 0.8358)	0.9067 (0.7990 to 0.9581)	0.7622 (0.6611 to 0.8368)	
27 Months	0.7942 (0.6412 to 0.8874)	0.7512 (0.6335 to 0.8358)	0.9067 (0.7990 to 0.9581)	0.7622 (0.6611 to 0.8368)	
30 Months	0.7942 (0.6412 to 0.8874)	0.7512 (0.6335 to 0.8358)	0.9067 (0.7990 to 0.9581)	0.7622 (0.6611 to 0.8368)	
Number of patients at risk[b]					
3 Months	44	74	71	91	
6 Months	42	64	66	84	
9 Months	38	61	63	79	
12 Months	34	53	61	74	
15 Months	30	47	58	70	
18 Months	29	42	57	64	
21 Months	22	34	45	58	
24 Months	8	9	16	21	
27 Months	2	0	2	1	
30 Months	0	0	0	0	

PT are presented if at least 10 events in a arm
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CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.80 Subgroup analysis by previous treament with PI
16.2.7.1.80.2 Treatment emergent adverse event per PT by treatment group according to previous treament with PI - Safety population

	Yes		No		
	Kd (N=47)	**IKd (N=79)**	**Kd (N=75)**	**IKd (N=98)**	**p-value of treatment-by-sub group interaction[c]**
21 Months	26	48	41	63	
24 Months	11	12	12	25	
27 Months	1	0	1	0	
30 Months	0	0	0	0	
Infusion related reaction (days)					
Number (%) of events	1 (2.1)	30 (38.0)	3 (4.0)	49 (50.0)	0.8293
Number (%) of patients censored	46 (97.9)	49 (62.0)	72 (96.0)	49 (50.0)	
Kaplan-Meier estimates of event in months					
25% quantile (95% CI)	NC (NC to NC)	0.1314 (0.0657 to 4.6324)	NC (NC to NC)	0.0986 (0.0657 to 0.1314)	
Median (95% CI)	NC (NC to NC)	NC (18.9240 to NC)	NC (NC to NC)	19.3840 (0.1643 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	<.0001		<.0001	

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[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1.80 Subgroup analysis by previous treament with PI
16.2.7.1.80.2 Treatment emergent adverse event per PT by treatment group according to previous treament with PI - Safety population

	Yes		No		
	Kd (N=47)	**IKd (N=79)**	**Kd (N=75)**	**IKd (N=98)**	**p-value of treatment-by-sub group interaction[c]**
Hazard ratio (95% CI) vs Kd	-	21.65 (2.95 to 158.85)		16.20 (5.05 to 52.04)	
P-value	-	0.0025		<.0001	
Hazard ratio inverted (95% CI) vs IKd	0.05 (0.01 to 0.34)		0.06 (0.02 to 0.20)		
Events probability (95% CI)[b]					
3 Months	0.9783 (0.8555 to 0.9969)	0.6582 (0.5425 to 0.7513)	0.9600 (0.8811 to 0.9869)	0.5100 (0.4072 to 0.6037)	
6 Months	0.9783 (0.8555 to 0.9969)	0.6451 (0.5289 to 0.7395)	0.9600 (0.8811 to 0.9869)	0.5100 (0.4072 to 0.6037)	
9 Months	0.9783 (0.8555 to 0.9969)	0.6451 (0.5289 to 0.7395)	0.9600 (0.8811 to 0.9869)	0.5100 (0.4072 to 0.6037)	
12 Months	0.9783 (0.8555 to 0.9969)	0.6451 (0.5289 to 0.7395)	0.9600 (0.8811 to 0.9869)	0.5100 (0.4072 to 0.6037)	
15 Months	0.9783 (0.8555 to 0.9969)	0.6307 (0.5138 to 0.7269)	0.9600 (0.8811 to 0.9869)	0.5100 (0.4072 to 0.6037)	
18 Months	0.9783 (0.8555 to 0.9969)	0.6307 (0.5138 to 0.7269)	0.9600 (0.8811 to 0.9869)	0.5100 (0.4072 to 0.6037)	
21 Months	0.9783 (0.8555 to 0.9969)	0.6141 (0.4958 to 0.7126)	0.9600 (0.8811 to 0.9869)	0.4979 (0.3950 to 0.5923)	

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CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.80 Subgroup analysis by previous treament with PI
16.2.7.1.80.2 Treatment emergent adverse event per PT by treatment group according to previous treament with PI - Safety population

	Yes		No		
	Kd (N=47)	**IKd (N=79)**	**Kd (N=75)**	**IKd (N=98)**	**p-value of treatment-by-sub group interaction[c]**
24 Months	0.9783 (0.8555 to 0.9969)	0.6141 (0.4958 to 0.7126)	0.9600 (0.8811 to 0.9869)	0.4979 (0.3950 to 0.5923)	
27 Months	0.9783 (0.8555 to 0.9969)	0.6141 (0.4958 to 0.7126)	0.9600 (0.8811 to 0.9869)	0.4979 (0.3950 to 0.5923)	
30 Months	0.9783 (0.8555 to 0.9969)	0.6141 (0.4958 to 0.7126)	0.9600 (0.8811 to 0.9869)	0.4979 (0.3950 to 0.5923)	
Number of patients at risk[b]					
3 Months	45	51	71	49	
6 Months	44	48	67	49	
9 Months	41	47	64	49	
12 Months	40	45	63	49	
15 Months	37	41	60	44	
18 Months	36	38	59	42	
21 Months	29	32	46	36	
24 Months	11	9	17	14	
27 Months	2	0	2	1	
30 Months	0	0	0	0	

PT are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.80 Subgroup analysis by previous treament with PI
16.2.7.1.80.2 Treatment emergent adverse event per PT by treatment group according to previous treament with PI - Safety population

	Yes		No		
	Kd (N=47)	**IKd (N=79)**	**Kd (N=75)**	**IKd (N=98)**	**p-value of treatment-by-sub group interaction[c]**
30 Months	0.9783 (0.8555 to 0.9969)	0.9449 (0.8598 to 0.9790)	0.9708 (0.8882 to 0.9926)	0.9360 (0.8630 to 0.9707)	
Number of patients at risk[b]					
3 Months	45	77	73	95	
6 Months	44	71	69	89	
9 Months	41	68	64	85	
12 Months	40	65	63	84	
15 Months	37	60	61	79	
18 Months	36	56	60	76	
21 Months	29	48	47	70	
24 Months	12	12	16	24	
27 Months	2	0	2	1	
30 Months	0	0	0	0	
Thrombocytopenia (days)					
Number (%) of events	4 (8.5)	3 (3.8)	8 (10.7)	2 (2.0)	0.4167
Number (%) of patients censored	43 (91.5)	76 (96.2)	67 (89.3)	96 (98.0)	

PT are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.80 Subgroup analysis by previous treament with PI
16.2.7.1.80.2 Treatment emergent adverse event per PT by treatment group according to previous treament with PI - Safety population

	Yes		No		
	Kd (N=47)	**IKd (N=79)**	**Kd (N=75)**	**IKd (N=98)**	**p-value of treatment-by-sub group interaction[c]**
Kaplan-Meier estimates of event in months					
25% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.2779		0.0151	
Hazard ratio (95% CI) vs Kd	-	0.45 (0.10 to 1.99)		0.18 (0.04 to 0.86)	
P-value	-	0.2909		0.0309	
Events probability (95% CI)[b]					
3 Months	0.9574 (0.8404 to 0.9892)	0.9872 (0.9125 to 0.9982)	0.9459 (0.8623 to 0.9794)	0.9898 (0.9298 to 0.9986)	
6 Months	0.9362 (0.8150 to 0.9790)	0.9872 (0.9125 to 0.9982)	0.9183 (0.8271 to 0.9625)	0.9898 (0.9298 to 0.9986)	

PT are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.80 Subgroup analysis by previous treament with PI
16.2.7.1.80.2 Treatment emergent adverse event per PT by treatment group according to previous treament with PI - Safety population

	Yes		No		
	Kd (N=47)	**IKd (N=79)**	**Kd (N=75)**	**IKd (N=98)**	**p-value of treatment-by-sub group interaction[c]**
9 Months	0.9144 (0.7878 to 0.9670)	0.9872 (0.9125 to 0.9982)	0.9040 (0.8090 to 0.9530)	0.9898 (0.9298 to 0.9986)	
12 Months	0.9144 (0.7878 to 0.9670)	0.9872 (0.9125 to 0.9982)	0.9040 (0.8090 to 0.9530)	0.9788 (0.9178 to 0.9947)	
15 Months	0.9144 (0.7878 to 0.9670)	0.9872 (0.9125 to 0.9982)	0.9040 (0.8090 to 0.9530)	0.9788 (0.9178 to 0.9947)	
18 Months	0.9144 (0.7878 to 0.9670)	0.9713 (0.8890 to 0.9928)	0.8881 (0.7883 to 0.9425)	0.9788 (0.9178 to 0.9947)	
21 Months	0.9144 (0.7878 to 0.9670)	0.9542 (0.8636 to 0.9851)	0.8881 (0.7883 to 0.9425)	0.9788 (0.9178 to 0.9947)	
24 Months	0.9144 (0.7878 to 0.9670)	0.9542 (0.8636 to 0.9851)	0.8881 (0.7883 to 0.9425)	0.9788 (0.9178 to 0.9947)	
27 Months	0.9144 (0.7878 to 0.9670)	0.9542 (0.8636 to 0.9851)	0.8881 (0.7883 to 0.9425)	0.9788 (0.9178 to 0.9947)	
30 Months	0.9144 (0.7878 to 0.9670)	0.9542 (0.8636 to 0.9851)	0.8881 (0.7883 to 0.9425)	0.9788 (0.9178 to 0.9947)	
Number of patients at risk[b]					
3 Months	45	76	69	95	

PT are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.80 Subgroup analysis by previous treament with PI
16.2.7.1.80.2 Treatment emergent adverse event per PT by treatment group according to previous treament with PI - Safety population

	Yes		No		
	Kd (N=47)	**IKd (N=79)**	**Kd (N=75)**	**IKd (N=98)**	**p-value of treatment-by-sub group interaction[c]**
6 Months	43	72	64	93	
9 Months	39	70	60	90	
12 Months	38	67	60	89	
15 Months	36	62	57	83	
18 Months	35	57	55	80	
21 Months	28	48	43	73	
24 Months	11	12	16	27	
27 Months	2	0	2	2	
30 Months	0	0	0	0	
Traumatic fracture (days)					
Number (%) of events	1 (2.1)	7 (8.9)	4 (5.3)	6 (6.1)	0.2679
Number (%) of patients censored	46 (97.9)	72 (91.1)	71 (94.7)	92 (93.9)	
Kaplan-Meier estimates of event in months					
25% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	

PT are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.80 Subgroup analysis by previous treament with PI
16.2.7.1.80.2 Treatment emergent adverse event per PT by treatment group according to previous treament with PI - Safety population

	Yes		No		
	Kd (N=47)	**IKd (N=79)**	**Kd (N=75)**	**IKd (N=98)**	**p-value of treatment-by-sub group interaction[c]**
21 Months	30	47	45	69	
24 Months	12	11	15	23	
27 Months	2	0	1	1	
30 Months	0	0	0	0	
Upper respiratory tract infection (days)					
Number (%) of events	12 (25.5)	27 (34.2)	17 (22.7)	37 (37.8)	0.5815
Number (%) of patients censored	35 (74.5)	52 (65.8)	58 (77.3)	61 (62.2)	
Kaplan-Meier estimates of event in months					
25% quantile (95% CI)	13.8645 (1.8727 to NC)	7.2936 (4.0082 to 16.0986)	NC (7.4908 to NC)	8.4107 (5.2238 to 12.1561)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (17.3142 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.3494		0.0427	

PT are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.80 Subgroup analysis by previous treament with PI
16.2.7.1.80.2 Treatment emergent adverse event per PT by treatment group according to previous treament with PI - Safety population

	Yes		No		
	Kd (N=47)	**IKd (N=79)**	**Kd (N=75)**	**IKd (N=98)**	**p-value of treatment-by-sub group interaction[c]**
Hazard ratio (95% CI) vs Kd	-	1.38 (0.70 to 2.73)		1.80 (1.01 to 3.19)	
P-value	-	0.3516		0.0458	
Hazard ratio inverted (95% CI) vs IKd			0.56 (0.31 to 0.99)		
Events probability (95% CI)[b]					
3 Months	0.8704 (0.7340 to 0.9396)	0.9099 (0.8203 to 0.9560)	0.9600 (0.8811 to 0.9869)	0.8863 (0.8041 to 0.9354)	
6 Months	0.8486 (0.7085 to 0.9248)	0.7769 (0.6657 to 0.8550)	0.8755 (0.7743 to 0.9333)	0.7904 (0.6941 to 0.8594)	
9 Months	0.8039 (0.6568 to 0.8929)	0.7350 (0.6196 to 0.8203)	0.8318 (0.7225 to 0.9009)	0.7133 (0.6102 to 0.7938)	
12 Months	0.7566 (0.6032 to 0.8574)	0.7067 (0.5891 to 0.7964)	0.8164 (0.7044 to 0.8892)	0.6688 (0.5631 to 0.7544)	
15 Months	0.7296 (0.5718 to 0.8371)	0.6626 (0.5420 to 0.7583)	0.7693 (0.6505 to 0.8521)	0.6225 (0.5149 to 0.7128)	
18 Months	0.7296 (0.5718 to 0.8371)	0.6298 (0.5069 to 0.7301)	0.7529 (0.6320 to 0.8390)	0.5968 (0.4880 to 0.6898)	
21 Months	0.7296 (0.5718 to 0.8371)	0.6298 (0.5069 to 0.7301)	0.7529 (0.6320 to 0.8390)	0.5968 (0.4880 to 0.6898)	

PT are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.80 Subgroup analysis by previous treament with PI
16.2.7.1.80.2 Treatment emergent adverse event per PT by treatment group according to previous treament with PI - Safety population

	Yes		No		
	Kd (N=47)	**IKd (N=79)**	**Kd (N=75)**	**IKd (N=98)**	**p-value of treatment-by-sub group interaction[c]**
24 Months	0.7296 (0.5718 to 0.8371)	0.6298 (0.5069 to 0.7301)	0.7529 (0.6320 to 0.8390)	0.5968 (0.4880 to 0.6898)	
27 Months	0.7296 (0.5718 to 0.8371)	0.6298 (0.5069 to 0.7301)	0.7529 (0.6320 to 0.8390)	0.5968 (0.4880 to 0.6898)	
30 Months	0.7296 (0.5718 to 0.8371)	0.6298 (0.5069 to 0.7301)	0.7529 (0.6320 to 0.8390)	0.5968 (0.4880 to 0.6898)	
Number of patients at risk[b]					
3 Months	40	70	70	85	
6 Months	39	57	60	73	
9 Months	34	52	54	64	
12 Months	31	48	52	60	
15 Months	27	42	47	50	
18 Months	27	38	45	46	
21 Months	22	32	35	43	
24 Months	10	9	11	13	
27 Months	2	0	1	1	
30 Months	0	0	0	0	

PT are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.81 Subgroup analysis by previous treatment with IMiD
16.2.7.1.81.2 Treatment emergent adverse event per PT by treatment group according to previous treatment with IMiD - Safety population

	Yes		No		
	Kd (N=62)	**IKd (N=80)**	**Kd (N=60)**	**IKd (N=97)**	**p-value of treatment-by-sub group interaction[c]**
6 Months	52	69	55	89	
9 Months	49	66	51	87	
12 Months	47	65	50	84	
15 Months	47	59	45	78	
18 Months	46	58	44	73	
21 Months	37	50	34	67	
24 Months	15	21	12	17	
27 Months	3	1	1	1	
30 Months	0	0	0	0	
Bronchitis (days)					
Number (%) of events	9 (14.5)	21 (26.3)	6 (10.0)	19 (19.6)	0.8386
Number (%) of patients censored	53 (85.5)	59 (73.8)	54 (90.0)	78 (80.4)	
Kaplan-Meier estimates of event in months					
25% quantile (95% CI)	NC (11.2361 to NC)	16.3943 (8.6735 to NC)	NC (NC to NC)	NC (10.7105 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	

PT are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.81 Subgroup analysis by previous treatment with IMiD
16.2.7.1.81.2 Treatment emergent adverse event per PT by treatment group according to previous treatment with IMiD - Safety population

	Yes		No		
	Kd (N=62)	**IKd (N=80)**	**Kd (N=60)**	**IKd (N=97)**	**p-value of treatment-by-sub group interaction[c]**
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.1163		0.1068	
Hazard ratio (95% CI) vs Kd	-	1.85 (0.85 to 4.04)		2.09 (0.84 to 5.24)	
P-value	-	0.1222		0.1149	
Events probability (95% CI)[b]					
3 Months	0.9664 (0.8722 to 0.9915)	0.9245 (0.8396 to 0.9654)	0.9667 (0.8732 to 0.9916)	0.9690 (0.9069 to 0.9899)	
6 Months	0.9488 (0.8495 to 0.9832)	0.8984 (0.8071 to 0.9479)	0.9333 (0.8321 to 0.9744)	0.8834 (0.7993 to 0.9337)	
9 Months	0.9306 (0.8253 to 0.9734)	0.8448 (0.7426 to 0.9088)	0.9167 (0.8113 to 0.9644)	0.8722 (0.7858 to 0.9254)	
12 Months	0.8546 (0.7297 to 0.9246)	0.7630 (0.6502 to 0.8437)	0.9167 (0.8113 to 0.9644)	0.8272 (0.7332 to 0.8904)	
15 Months	0.8546 (0.7297 to 0.9246)	0.7630 (0.6502 to 0.8437)	0.8983 (0.7874 to 0.9530)	0.8157 (0.7201 to 0.8813)	

PT are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.81 Subgroup analysis by previous treatment with IMiD
16.2.7.1.81.2 Treatment emergent adverse event per PT by treatment group according to previous treatment with IMiD - Safety population

	Yes		No		
	Kd (N=62)	**IKd (N=80)**	**Kd (N=60)**	**IKd (N=97)**	**p-value of treatment-by-sub group interaction[c]**
18 Months	0.8546 (0.7297 to 0.9246)	0.7178 (0.5999 to 0.8065)	0.8983 (0.7874 to 0.9530)	0.7898 (0.6897 to 0.8608)	
21 Months	0.8546 (0.7297 to 0.9246)	0.7178 (0.5999 to 0.8065)	0.8983 (0.7874 to 0.9530)	0.7898 (0.6897 to 0.8608)	
24 Months	0.8229 (0.6813 to 0.9058)	0.7178 (0.5999 to 0.8065)	0.8983 (0.7874 to 0.9530)	0.7898 (0.6897 to 0.8608)	
27 Months	0.8229 (0.6813 to 0.9058)	0.7178 (0.5999 to 0.8065)	0.8983 (0.7874 to 0.9530)	0.7898 (0.6897 to 0.8608)	
30 Months	0.8229 (0.6813 to 0.9058)	0.7178 (0.5999 to 0.8065)	0.8983 (0.7874 to 0.9530)	0.7898 (0.6897 to 0.8608)	
Number of patients at risk[b]					
3 Months	57	72	58	93	
6 Months	52	68	56	80	
9 Months	49	62	52	78	
12 Months	44	55	51	72	
15 Months	43	51	45	66	
18 Months	42	47	44	59	

PT are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.81 Subgroup analysis by previous treatment with IMiD
16.2.7.1.81.2 Treatment emergent adverse event per PT by treatment group according to previous treatment with IMiD - Safety population

	Yes		No		
	Kd (N=62)	**IKd (N=80)**	**Kd (N=60)**	**IKd (N=97)**	**p-value of treatment-by-sub group interaction[c]**
6 Months	53	75	55	88	
9 Months	51	71	50	81	
12 Months	50	68	43	80	
15 Months	49	59	39	75	
18 Months	48	57	38	69	
21 Months	38	48	29	63	
24 Months	12	22	11	15	
27 Months	1	0	1	0	
30 Months	0	0	0	0	
Infusion related reaction (days)					
Number (%) of events	3 (4.8)	40 (50.0)	1 (1.7)	39 (40.2)	0.4814
Number (%) of patients censored	59 (95.2)	40 (50.0)	59 (98.3)	58 (59.8)	
Kaplan-Meier estimates of event in months					
25% quantile (95% CI)	NC (NC to NC)	0.0986 (0.0657 to 0.1643)	NC (NC to NC)	0.1314 (0.0657 to 0.1643)	
Median (95% CI)	NC (NC to NC)	19.3840 (0.1643 to NC)	NC (NC to NC)	NC (18.9240 to NC)	

PT are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.81 Subgroup analysis by previous treatment with IMiD
16.2.7.1.81.2 Treatment emergent adverse event per PT by treatment group according to previous treatment with IMiD - Safety population

	Yes		No		
	Kd (N=62)	**IKd (N=80)**	**Kd (N=60)**	**IKd (N=97)**	**p-value of treatment-by-sub group interaction[c]**
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	<.0001		<.0001	
Hazard ratio (95% CI) vs Kd	-	13.39 (4.14 to 43.33)		29.27 (4.02 to 213.12)	
P-value	-	<.0001		0.0009	
Hazard ratio inverted (95% CI) vs IKd	0.07 (0.02 to 0.24)		0.03 (0.00 to 0.25)		
Events probability (95% CI)[b]					
3 Months	0.9513 (0.8567 to 0.9840)	0.5375 (0.4226 to 0.6392)	0.9833 (0.8875 to 0.9976)	0.6082 (0.5038 to 0.6973)	
6 Months	0.9513 (0.8567 to 0.9840)	0.5250 (0.4105 to 0.6273)	0.9833 (0.8875 to 0.9976)	0.6082 (0.5038 to 0.6973)	
9 Months	0.9513 (0.8567 to 0.9840)	0.5250 (0.4105 to 0.6273)	0.9833 (0.8875 to 0.9976)	0.6082 (0.5038 to 0.6973)	
12 Months	0.9513 (0.8567 to 0.9840)	0.5250 (0.4105 to 0.6273)	0.9833 (0.8875 to 0.9976)	0.6082 (0.5038 to 0.6973)	

PT are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.

16.2.7.1 Safety endpoints
16.2.7.1.81 Subgroup analysis by previous treatment with IMiD
16.2.7.1.81.2 Treatment emergent adverse event per PT by treatment group according to previous treatment with IMiD - Safety population

	Yes		No		
	Kd (N=62)	**IKd (N=80)**	**Kd (N=60)**	**IKd (N=97)**	**p-value of treatment-by-sub group interaction[c]**
15 Months	0.9513 (0.8567 to 0.9840)	0.5122 (0.3980 to 0.6151)	0.9833 (0.8875 to 0.9976)	0.6082 (0.5038 to 0.6973)	
18 Months	0.9513 (0.8567 to 0.9840)	0.5122 (0.3980 to 0.6151)	0.9833 (0.8875 to 0.9976)	0.6082 (0.5038 to 0.6973)	
21 Months	0.9513 (0.8567 to 0.9840)	0.4962 (0.3817 to 0.6006)	0.9833 (0.8875 to 0.9976)	0.5956 (0.4904 to 0.6860)	
24 Months	0.9513 (0.8567 to 0.9840)	0.4962 (0.3817 to 0.6006)	0.9833 (0.8875 to 0.9976)	0.5956 (0.4904 to 0.6860)	
27 Months	0.9513 (0.8567 to 0.9840)	0.4962 (0.3817 to 0.6006)	0.9833 (0.8875 to 0.9976)	0.5956 (0.4904 to 0.6860)	
30 Months	0.9513 (0.8567 to 0.9840)	0.4962 (0.3817 to 0.6006)	0.9833 (0.8875 to 0.9976)	0.5956 (0.4904 to 0.6860)	
Number of patients at risk[b]					
3 Months	57	43	59	57	
6 Months	53	41	58	56	
9 Months	51	41	54	55	
12 Months	50	41	53	53	
15 Months	49	34	48	51	

PT are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.81 Subgroup analysis by previous treatment with IMiD
16.2.7.1.81.2 Treatment emergent adverse event per PT by treatment group according to previous treatment with IMiD - Safety population

	Yes		No		
	Kd (N=62)	**IKd (N=80)**	**Kd (N=60)**	**IKd (N=97)**	**p-value of treatment-by-sub group interaction[c]**
18 Months	48	32	47	48	
21 Months	39	25	36	43	
24 Months	14	14	14	9	
27 Months	3	1	1	0	
30 Months	0	0	0	0	
Insomnia (days)					
Number (%) of events	15 (24.2)	22 (27.5)	13 (21.7)	20 (20.6)	0.7290
Number (%) of patients censored	47 (75.8)	58 (72.5)	47 (78.3)	77 (79.4)	
Kaplan-Meier estimates of event in months					
25% quantile (95% CI)	17.9384 (2.8583 to NC)	14.1602 (4.1068 to NC)	NC (3.9754 to NC)	NC (7.5893 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.7458		0.8544	

PT are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.81 Subgroup analysis by previous treatment with IMiD
16.2.7.1.81.2 Treatment emergent adverse event per PT by treatment group according to previous treatment with IMiD - Safety population

	Yes		No		
	Kd (N=62)	**IKd (N=80)**	**Kd (N=60)**	**IKd (N=97)**	**p-value of treatment-by-sub group interaction[c]**
Thrombocytopenia (days)					
Number (%) of events	9 (14.5)	2 (2.5)	3 (5.0)	3 (3.1)	0.2228
Number (%) of patients censored	53 (85.5)	78 (97.5)	57 (95.0)	94 (96.9)	
Kaplan-Meier estimates of event in months					
25% quantile (95% CI)	NC (6.5051 to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.0074		0.5522	
Hazard ratio (95% CI) vs Kd	-	0.16 (0.03 to 0.74)		0.62 (0.12 to 3.06)	
P-value	-	0.0193		0.5560	
Events probability (95% CI)[b]					

PT are presented if at least 10 events in a arm
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CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.81 Subgroup analysis by previous treatment with IMiD
16.2.7.1.81.2 Treatment emergent adverse event per PT by treatment group according to previous treatment with IMiD - Safety population

	Yes		No		
	Kd (N=62)	**IKd (N=80)**	**Kd (N=60)**	**IKd (N=97)**	**p-value of treatment-by-sub group interaction[c]**
3 Months	0.9018 (0.7944 to 0.9547)	0.9875 (0.9146 to 0.9982)	1.0000 (1.0000 to 1.0000)	0.9897 (0.9291 to 0.9985)	
6 Months	0.8681 (0.7534 to 0.9318)	0.9875 (0.9146 to 0.9982)	0.9833 (0.8875 to 0.9976)	0.9897 (0.9291 to 0.9985)	
9 Months	0.8504 (0.7320 to 0.9193)	0.9875 (0.9146 to 0.9982)	0.9664 (0.8722 to 0.9915)	0.9897 (0.9291 to 0.9985)	
12 Months	0.8504 (0.7320 to 0.9193)	0.9875 (0.9146 to 0.9982)	0.9664 (0.8722 to 0.9915)	0.9784 (0.9164 to 0.9946)	
15 Months	0.8504 (0.7320 to 0.9193)	0.9875 (0.9146 to 0.9982)	0.9664 (0.8722 to 0.9915)	0.9784 (0.9164 to 0.9946)	
18 Months	0.8504 (0.7320 to 0.9193)	0.9875 (0.9146 to 0.9982)	0.9462 (0.8417 to 0.9824)	0.9662 (0.8986 to 0.9890)	
21 Months	0.8504 (0.7320 to 0.9193)	0.9718 (0.8910 to 0.9929)	0.9462 (0.8417 to 0.9824)	0.9662 (0.8986 to 0.9890)	
24 Months	0.8504 (0.7320 to 0.9193)	0.9718 (0.8910 to 0.9929)	0.9462 (0.8417 to 0.9824)	0.9662 (0.8986 to 0.9890)	
27 Months	0.8504 (0.7320 to 0.9193)	0.9718 (0.8910 to 0.9929)	0.9462 (0.8417 to 0.9824)	0.9662 (0.8986 to 0.9890)	

PT are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.81 Subgroup analysis by previous treatment with IMiD
16.2.7.1.81.2 Treatment emergent adverse event per PT by treatment group according to previous treatment with IMiD - Safety population

	Yes		No		
	Kd (N=62)	**IKd (N=80)**	**Kd (N=60)**	**IKd (N=97)**	**p-value of treatment-by-sub group interaction[c]**
30 Months	0.8504 (0.7320 to 0.9193)	0.9718 (0.8910 to 0.9929)	0.9462 (0.8417 to 0.9824)	0.9662 (0.8986 to 0.9890)	
Number of patients at risk[b]					
3 Months	54	77	60	94	
6 Months	49	75	58	90	
9 Months	46	72	53	88	
12 Months	46	71	52	85	
15 Months	45	65	48	80	
18 Months	44	63	46	74	
21 Months	36	54	35	67	
24 Months	13	22	14	17	
27 Months	3	1	1	1	
30 Months	0	0	0	0	
Traumatic fracture (days)					
Number (%) of events	1 (1.6)	6 (7.5)	4 (6.7)	7 (7.2)	0.2468
Number (%) of patients censored	61 (98.4)	74 (92.5)	56 (93.3)	90 (92.8)	

PT are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.81 Subgroup analysis by previous treatment with IMiD
16.2.7.1.81.2 Treatment emergent adverse event per PT by treatment group according to previous treatment with IMiD - Safety population

	Yes		No		
	Kd (N=62)	**IKd (N=80)**	**Kd (N=60)**	**IKd (N=97)**	**p-value of treatment-by-sub group interaction[c]**
6 Months	55	74	57	88	
9 Months	53	70	53	83	
12 Months	52	68	52	82	
15 Months	51	62	46	77	
18 Months	50	60	44	72	
21 Months	40	52	35	64	
24 Months	14	20	13	14	
27 Months	2	1	1	0	
30 Months	0	0	0	0	
Upper respiratory tract infection (days)					
Number (%) of events	15 (24.2)	28 (35.0)	14 (23.3)	36 (37.1)	0.8284
Number (%) of patients censored	47 (75.8)	52 (65.0)	46 (76.7)	61 (62.9)	
Kaplan-Meier estimates of event in months					
25% quantile (95% CI)	15.7372 (7.4908 to NC)	8.4764 (3.6468 to 12.8789)	NC (5.9138 to NC)	8.0821 (4.4025 to 13.2402)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (17.9055 to NC)	

PT are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.81 Subgroup analysis by previous treatment with IMiD
16.2.7.1.81.2 Treatment emergent adverse event per PT by treatment group according to previous treatment with IMiD - Safety population

	Yes		No		
	Kd (N=62)	**IKd (N=80)**	**Kd (N=60)**	**IKd (N=97)**	**p-value of treatment-by-sub group interaction[c]**
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.1779		0.0884	
Hazard ratio (95% CI) vs Kd	-	1.53 (0.82 to 2.87)		1.70 (0.92 to 3.15)	
P-value	-	0.1812		0.0924	
Events probability (95% CI)[b]					
3 Months	0.9344 (0.8345 to 0.9749)	0.8866 (0.7934 to 0.9394)	0.9167 (0.8113 to 0.9644)	0.9056 (0.8264 to 0.9497)	
6 Months	0.8824 (0.7688 to 0.9422)	0.7685 (0.6577 to 0.8474)	0.8494 (0.7305 to 0.9186)	0.7975 (0.7010 to 0.8658)	
9 Months	0.8284 (0.7040 to 0.9039)	0.7140 (0.5985 to 0.8017)	0.8154 (0.6914 to 0.8933)	0.7300 (0.6269 to 0.8090)	
12 Months	0.8096 (0.6819 to 0.8899)	0.6723 (0.5542 to 0.7656)	0.7783 (0.6486 to 0.8650)	0.6955 (0.5898 to 0.7789)	

PT are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.

16.2.7.1 Safety endpoints
16.2.7.1.81 Subgroup analysis by previous treatment with IMiD
16.2.7.1.81.2 Treatment emergent adverse event per PT by treatment group according to previous treatment with IMiD - Safety population

	Yes		No		
	Kd (N=62)	**IKd (N=80)**	**Kd (N=60)**	**IKd (N=97)**	**p-value of treatment-by-sub group interaction[c]**
15 Months	0.7512 (0.6153 to 0.8450)	0.6436 (0.5241 to 0.7404)	0.7589 (0.6263 to 0.8498)	0.6371 (0.5287 to 0.7269)	
18 Months	0.7315 (0.5933 to 0.8292)	0.6271 (0.5063 to 0.7262)	0.7589 (0.6263 to 0.8498)	0.5988 (0.4887 to 0.6926)	
21 Months	0.7315 (0.5933 to 0.8292)	0.6271 (0.5063 to 0.7262)	0.7589 (0.6263 to 0.8498)	0.5988 (0.4887 to 0.6926)	
24 Months	0.7315 (0.5933 to 0.8292)	0.6271 (0.5063 to 0.7262)	0.7589 (0.6263 to 0.8498)	0.5988 (0.4887 to 0.6926)	
27 Months	0.7315 (0.5933 to 0.8292)	0.6271 (0.5063 to 0.7262)	0.7589 (0.6263 to 0.8498)	0.5988 (0.4887 to 0.6926)	
30 Months	0.7315 (0.5933 to 0.8292)	0.6271 (0.5063 to 0.7262)	0.7589 (0.6263 to 0.8498)	0.5988 (0.4887 to 0.6926)	
Number of patients at risk[b]					
3 Months	55	69	55	86	
6 Months	49	58	50	72	
9 Months	44	52	44	64	
12 Months	42	48	41	60	
15 Months	38	40	36	52	

PT are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.82 Subgroup analysis by previous treatment with PI and IMiD
16.2.7.1.82.2 Treatment emergent adverse event per PT by treatment group according to previous treatment with PI and IMiD - Safety population

	Yes		No		
	Kd (N=17)	**IKd (N=22)**	**Kd (N=105)**	**IKd (N=155)**	**p-value of treatment-by-sub group interaction[c]**
18 Months	14	14	76	117	
21 Months	12	13	59	104	
24 Months	6	6	21	32	
27 Months	1	0	3	2	
30 Months	0	0	0	0	
Bronchitis (days)					
Number (%) of events	5 (29.4)	6 (27.3)	10 (9.5)	34 (21.9)	0.1539
Number (%) of patients censored	12 (70.6)	16 (72.7)	95 (90.5)	121 (78.1)	
Kaplan-Meier estimates of event in months					
25% quantile (95% CI)	10.5133 (2.6612 to NC)	17.5113 (1.1828 to NC)	NC (NC to NC)	NC (11.2361 to NC)	
Median (95% CI)	NC (10.5133 to NC)	NC (17.5113 to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.8830		0.0103	

PT are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.82 Subgroup analysis by previous treatment with PI and IMiD
16.2.7.1.82.2 Treatment emergent adverse event per PT by treatment group according to previous treatment with PI and IMiD - Safety population

	Yes		No		
	Kd (N=17)	**IKd (N=22)**	**Kd (N=105)**	**IKd (N=155)**	**p-value of treatment-by-sub group interaction[c]**
Hazard ratio (95% CI) vs Kd	-	0.91 (0.28 to 3.00)		2.44 (1.21 to 4.94)	
P-value	-	0.8831		0.0131	
Hazard ratio inverted (95% CI) vs IKd			0.41 (0.20 to 0.83)		
Events probability (95% CI)[b]					
3 Months	0.9375 (0.6323 to 0.9910)	0.9545 (0.7187 to 0.9935)	0.9712 (0.9135 to 0.9906)	0.9480 (0.8987 to 0.9737)	
6 Months	0.9375 (0.6323 to 0.9910)	0.9545 (0.7187 to 0.9935)	0.9419 (0.8752 to 0.9735)	0.8812 (0.8180 to 0.9234)	
9 Months	0.8705 (0.5733 to 0.9660)	0.8541 (0.6119 to 0.9506)	0.9319 (0.8624 to 0.9669)	0.8605 (0.7940 to 0.9067)	
12 Months	0.6696 (0.3787 to 0.8474)	0.7536 (0.5050 to 0.8895)	0.9213 (0.8487 to 0.9599)	0.8043 (0.7306 to 0.8598)	
15 Months	0.6696 (0.3787 to 0.8474)	0.7536 (0.5050 to 0.8895)	0.9103 (0.8345 to 0.9524)	0.7972 (0.7227 to 0.8537)	
18 Months	0.6696 (0.3787 to 0.8474)	0.6908 (0.4329 to 0.8492)	0.9103 (0.8345 to 0.9524)	0.7657 (0.6874 to 0.8268)	
21 Months	0.6696 (0.3787 to 0.8474)	0.6908 (0.4329 to 0.8492)	0.9103 (0.8345 to 0.9524)	0.7657 (0.6874 to 0.8268)	

PT are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.82 Subgroup analysis by previous treatment with PI and IMiD
16.2.7.1.82.2 Treatment emergent adverse event per PT by treatment group according to previous treatment with PI and IMiD - Safety population

	Yes		No		
	Kd (N=17)	**IKd (N=22)**	**Kd (N=105)**	**IKd (N=155)**	**p-value of treatment-by-sub group interaction[c]**
24 Months	0.6696 (0.3787 to 0.8474)	0.6908 (0.4329 to 0.8492)	0.8921 (0.8052 to 0.9416)	0.7657 (0.6874 to 0.8268)	
27 Months	0.6696 (0.3787 to 0.8474)	0.6908 (0.4329 to 0.8492)	0.8921 (0.8052 to 0.9416)	0.7657 (0.6874 to 0.8268)	
30 Months	0.6696 (0.3787 to 0.8474)	0.6908 (0.4329 to 0.8492)	0.8921 (0.8052 to 0.9416)	0.7657 (0.6874 to 0.8268)	
Number of patients at risk[b]					
3 Months	15	20	100	145	
6 Months	14	19	94	129	
9 Months	13	17	88	123	
12 Months	10	14	85	113	
15 Months	10	13	78	104	
18 Months	10	11	76	95	
21 Months	8	10	59	82	
24 Months	3	4	21	26	
27 Months	1	0	3	1	
30 Months	0	0	0	0	

PT are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.82 Subgroup analysis by previous treatment with PI and IMiD
16.2.7.1.82.2 Treatment emergent adverse event per PT by treatment group according to previous treatment with PI and IMiD - Safety population

	Yes		No		
	Kd (N=17)	**IKd (N=22)**	**Kd (N=105)**	**IKd (N=155)**	**p-value of treatment-by-sub group interaction[c]**
21 Months	12	16	55	95	
24 Months	5	6	18	31	
27 Months	0	0	2	0	
30 Months	0	0	0	0	
Infusion related reaction (days)					
Number (%) of events	1 (5.9)	8 (36.4)	3 (2.9)	71 (45.8)	0.3872
Number (%) of patients censored	16 (94.1)	14 (63.6)	102 (97.1)	84 (54.2)	
Kaplan-Meier estimates of event in months					
25% quantile (95% CI)	NC (2.1684 to NC)	0.2957 (0.0329 to NC)	NC (NC to NC)	0.0986 (0.0657 to 0.1314)	
Median (95% CI)	NC (NC to NC)	NC (0.2957 to NC)	NC (NC to NC)	NC (0.1971 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.0302		<.0001	

PT are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.82 Subgroup analysis by previous treatment with PI and IMiD
16.2.7.1.82.2 Treatment emergent adverse event per PT by treatment group according to previous treatment with PI and IMiD - Safety population

	Yes		No		
	Kd (N=17)	**IKd (N=22)**	**Kd (N=105)**	**IKd (N=155)**	**p-value of treatment-by-sub group interaction[c]**
Hazard ratio (95% CI) vs Kd	-	7.15 (0.89 to 57.25)		20.17 (6.35 to 64.08)	
P-value	-	0.0637		<.0001	
Hazard ratio inverted (95% CI) vs IKd			0.05 (0.02 to 0.16)		
Events probability (95% CI)[b]					
3 Months	0.9375 (0.6323 to 0.9910)	0.7273 (0.4910 to 0.8671)	0.9714 (0.9140 to 0.9907)	0.5547 (0.4729 to 0.6288)	
6 Months	0.9375 (0.6323 to 0.9910)	0.6818 (0.4462 to 0.8338)	0.9714 (0.9140 to 0.9907)	0.5547 (0.4729 to 0.6288)	
9 Months	0.9375 (0.6323 to 0.9910)	0.6818 (0.4462 to 0.8338)	0.9714 (0.9140 to 0.9907)	0.5547 (0.4729 to 0.6288)	
12 Months	0.9375 (0.6323 to 0.9910)	0.6818 (0.4462 to 0.8338)	0.9714 (0.9140 to 0.9907)	0.5547 (0.4729 to 0.6288)	
15 Months	0.9375 (0.6323 to 0.9910)	0.6331 (0.3981 to 0.7971)	0.9714 (0.9140 to 0.9907)	0.5547 (0.4729 to 0.6288)	
18 Months	0.9375 (0.6323 to 0.9910)	0.6331 (0.3981 to 0.7971)	0.9714 (0.9140 to 0.9907)	0.5547 (0.4729 to 0.6288)	
21 Months	0.9375 (0.6323 to 0.9910)	0.6331 (0.3981 to 0.7971)	0.9714 (0.9140 to 0.9907)	0.5386 (0.4563 to 0.6138)	

PT are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.82 Subgroup analysis by previous treatment with PI and IMiD
16.2.7.1.82.2 Treatment emergent adverse event per PT by treatment group according to previous treatment with PI and IMiD - Safety population

	Yes		No		
	Kd (N=17)	**IKd (N=22)**	**Kd (N=105)**	**IKd (N=155)**	**p-value of treatment-by-sub group interaction[c]**
24 Months	0.9375 (0.6323 to 0.9910)	0.6331 (0.3981 to 0.7971)	0.9714 (0.9140 to 0.9907)	0.5386 (0.4563 to 0.6138)	
27 Months	0.9375 (0.6323 to 0.9910)	0.6331 (0.3981 to 0.7971)	0.9714 (0.9140 to 0.9907)	0.5386 (0.4563 to 0.6138)	
30 Months	0.9375 (0.6323 to 0.9910)	0.6331 (0.3981 to 0.7971)	0.9714 (0.9140 to 0.9907)	0.5386 (0.4563 to 0.6138)	
Number of patients at risk[b]					
3 Months	15	16	101	84	
6 Months	14	14	97	83	
9 Months	14	14	91	82	
12 Months	14	14	89	80	
15 Months	14	12	83	73	
18 Months	14	11	81	69	
21 Months	12	10	63	58	
24 Months	5	5	23	18	
27 Months	1	0	3	1	
30 Months	0	0	0	0	

PT are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.82 Subgroup analysis by previous treatment with PI and IMiD
16.2.7.1.82.2 Treatment emergent adverse event per PT by treatment group according to previous treatment with PI and IMiD - Safety population

	Yes		No		
	Kd (N=17)	**IKd (N=22)**	**Kd (N=105)**	**IKd (N=155)**	**p-value of treatment-by-sub group interaction[c]**
30 Months	1.0000 (1.0000 to 1.0000)	0.8500 (0.6038 to 0.9490)	0.9695 (0.9084 to 0.9901)	0.9525 (0.9028 to 0.9771)	
Number of patients at risk[b]					
3 Months	16	21	102	151	
6 Months	15	19	98	141	
9 Months	15	18	90	135	
12 Months	15	16	88	133	
15 Months	15	15	83	124	
18 Months	15	14	81	118	
21 Months	13	13	63	105	
24 Months	6	5	22	31	
27 Months	1	0	3	1	
30 Months	0	0	0	0	
Thrombocytopenia (days)					
Number (%) of events	3 (17.6)	2 (9.1)	9 (8.6)	3 (1.9)	0.4665
Number (%) of patients censored	14 (82.4)	20 (90.9)	96 (91.4)	152 (98.1)	

PT are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1.82 Subgroup analysis by previous treatment with PI and IMiD
16.2.7.1.82.2 Treatment emergent adverse event per PT by treatment group according to previous treatment with PI and IMiD - Safety population

	Yes		No		
	Kd (N=17)	**IKd (N=22)**	**Kd (N=105)**	**IKd (N=155)**	**p-value of treatment-by-sub group interaction[c]**
Kaplan-Meier estimates of event in months					
25% quantile (95% CI)	NC (0.2300 to NC)	NC (0.4600 to NC)	NC (NC to NC)	NC (NC to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.4492		0.0118	
Hazard ratio (95% CI) vs Kd	-	0.51 (0.08 to 3.04)		0.22 (0.06 to 0.80)	
P-value	-	0.4578		0.0221	
Events probability (95% CI)[b]					
3 Months	0.8824 (0.6060 to 0.9692)	0.9545 (0.7187 to 0.9935)	0.9615 (0.9007 to 0.9854)	0.9935 (0.9551 to 0.9991)	
6 Months	0.8824 (0.6060 to 0.9692)	0.9545 (0.7187 to 0.9935)	0.9323 (0.8632 to 0.9671)	0.9935 (0.9551 to 0.9991)	

PT are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.82 Subgroup analysis by previous treatment with PI and IMiD
16.2.7.1.82.2 Treatment emergent adverse event per PT by treatment group according to previous treatment with PI and IMiD - Safety population

	Yes		No		
	Kd (N=17)	**IKd (N=22)**	**Kd (N=105)**	**IKd (N=155)**	**p-value of treatment-by-sub group interaction[c]**
9 Months	0.8193 (0.5377 to 0.9380)	0.9545 (0.7187 to 0.9935)	0.9223 (0.8505 to 0.9604)	0.9935 (0.9551 to 0.9991)	
12 Months	0.8193 (0.5377 to 0.9380)	0.9545 (0.7187 to 0.9935)	0.9223 (0.8505 to 0.9604)	0.9865 (0.9470 to 0.9966)	
15 Months	0.8193 (0.5377 to 0.9380)	0.9545 (0.7187 to 0.9935)	0.9223 (0.8505 to 0.9604)	0.9865 (0.9470 to 0.9966)	
18 Months	0.8193 (0.5377 to 0.9380)	0.9545 (0.7187 to 0.9935)	0.9107 (0.8352 to 0.9526)	0.9788 (0.9355 to 0.9931)	
21 Months	0.8193 (0.5377 to 0.9380)	0.8949 (0.6362 to 0.9731)	0.9107 (0.8352 to 0.9526)	0.9788 (0.9355 to 0.9931)	
24 Months	0.8193 (0.5377 to 0.9380)	0.8949 (0.6362 to 0.9731)	0.9107 (0.8352 to 0.9526)	0.9788 (0.9355 to 0.9931)	
27 Months	0.8193 (0.5377 to 0.9380)	0.8949 (0.6362 to 0.9731)	0.9107 (0.8352 to 0.9526)	0.9788 (0.9355 to 0.9931)	
30 Months	0.8193 (0.5377 to 0.9380)	0.8949 (0.6362 to 0.9731)	0.9107 (0.8352 to 0.9526)	0.9788 (0.9355 to 0.9931)	
Number of patients at risk[b]					
3 Months	15	20	99	151	

PT are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.82 Subgroup analysis by previous treatment with PI and IMiD
16.2.7.1.82.2 Treatment emergent adverse event per PT by treatment group according to previous treatment with PI and IMiD - Safety population

	Yes		No		
	Kd (N=17)	**IKd (N=22)**	**Kd (N=105)**	**IKd (N=155)**	**p-value of treatment-by-sub group interaction[c]**
6 Months	14	19	93	146	
9 Months	13	19	86	141	
12 Months	13	18	85	138	
15 Months	13	17	80	128	
18 Months	13	16	77	121	
21 Months	11	14	60	107	
24 Months	5	5	22	34	
27 Months	1	0	3	2	
30 Months	0	0	0	0	
Traumatic fracture (days)					
Number (%) of events	0 (0.0)	4 (18.2)	5 (4.8)	9 (5.8)	0.9909
Number (%) of patients censored	17 (100.0)	18 (81.8)	100 (95.2)	146 (94.2)	
Kaplan-Meier estimates of event in months					
25% quantile (95% CI)	NC (NC to NC)	NC (0.6242 to NC)	NC (NC to NC)	NC (NC to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	

PT are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.82 Subgroup analysis by previous treatment with PI and IMiD
16.2.7.1.82.2 Treatment emergent adverse event per PT by treatment group according to previous treatment with PI and IMiD - Safety population

	Yes		No		
	Kd (N=17)	**IKd (N=22)**	**Kd (N=105)**	**IKd (N=155)**	**p-value of treatment-by-sub group interaction[c]**
21 Months	13	14	62	102	
24 Months	6	4	21	30	
27 Months	1	0	2	1	
30 Months	0	0	0	0	
Upper respiratory tract infection (days)					
Number (%) of events	3 (17.6)	3 (13.6)	26 (24.8)	61 (39.4)	0.3680
Number (%) of patients censored	14 (82.4)	19 (86.4)	79 (75.2)	94 (60.6)	
Kaplan-Meier estimates of event in months					
25% quantile (95% CI)	NC (1.5113 to NC)	NC (3.4497 to NC)	12.7803 (6.8665 to NC)	6.8008 (4.4025 to 11.4661)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (17.3142 to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.7575		0.0217	

PT are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.82 Subgroup analysis by previous treatment with PI and IMiD
16.2.7.1.82.2 Treatment emergent adverse event per PT by treatment group according to previous treatment with PI and IMiD - Safety population

	Yes		No		
	Kd (N=17)	**IKd (N=22)**	**Kd (N=105)**	**IKd (N=155)**	**p-value of treatment-by-sub group interaction[c]**
Hazard ratio (95% CI) vs Kd	-	0.78 (0.16 to 3.86)		1.70 (1.07 to 2.69)	
P-value	-	0.7581		0.0233	
Hazard ratio inverted (95% CI) vs IKd			0.59 (0.37 to 0.93)		
Events probability (95% CI)[b]					
3 Months	0.9375 (0.6323 to 0.9910)	1.0000 (1.0000 to 1.0000)	0.9235 (0.8529 to 0.9610)	0.8822 (0.8196 to 0.9241)	
6 Months	0.9375 (0.6323 to 0.9910)	0.9048 (0.6700 to 0.9753)	0.8544 (0.7700 to 0.9096)	0.7675 (0.6914 to 0.8272)	
9 Months	0.8750 (0.5860 to 0.9672)	0.9048 (0.6700 to 0.9753)	0.8133 (0.7228 to 0.8767)	0.6975 (0.6165 to 0.7647)	
12 Months	0.8750 (0.5860 to 0.9672)	0.8545 (0.6133 to 0.9507)	0.7803 (0.6853 to 0.8497)	0.6617 (0.5789 to 0.7320)	
15 Months	0.8125 (0.5246 to 0.9354)	0.8545 (0.6133 to 0.9507)	0.7461 (0.6470 to 0.8211)	0.6094 (0.5246 to 0.6837)	
18 Months	0.8125 (0.5246 to 0.9354)	0.8545 (0.6133 to 0.9507)	0.7338 (0.6333 to 0.8109)	0.5766 (0.4905 to 0.6533)	
21 Months	0.8125 (0.5246 to 0.9354)	0.8545 (0.6133 to 0.9507)	0.7338 (0.6333 to 0.8109)	0.5766 (0.4905 to 0.6533)	

PT are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
PGM=DEVOPS/SAR650984/EFC15246/CIR_RWE/REPORT/PGM/ae_km_socpt_subgp_sr_s_t.sas OUT=REPORT/OUTPUT/ae_km_teaept_piimid_s_t_x.rtf (12FEB2021 8:25)

16.2.7.1 Safety endpoints
16.2.7.1.82 Subgroup analysis by previous treatment with PI and IMiD
16.2.7.1.82.2 Treatment emergent adverse event per PT by treatment group according to previous treatment with PI and IMiD - Safety population

	Yes		No		
	Kd (N=17)	**IKd (N=22)**	**Kd (N=105)**	**IKd (N=155)**	**p-value of treatment-by-sub group interaction[c]**
24 Months	0.8125 (0.5246 to 0.9354)	0.8545 (0.6133 to 0.9507)	0.7338 (0.6333 to 0.8109)	0.5766 (0.4905 to 0.6533)	
27 Months	0.8125 (0.5246 to 0.9354)	0.8545 (0.6133 to 0.9507)	0.7338 (0.6333 to 0.8109)	0.5766 (0.4905 to 0.6533)	
30 Months	0.8125 (0.5246 to 0.9354)	0.8545 (0.6133 to 0.9507)	0.7338 (0.6333 to 0.8109)	0.5766 (0.4905 to 0.6533)	
Number of patients at risk[b]					
3 Months	15	21	95	134	
6 Months	15	18	84	112	
9 Months	14	18	74	98	
12 Months	14	16	69	92	
15 Months	13	15	61	77	
18 Months	13	15	59	69	
21 Months	11	14	46	61	
24 Months	5	4	16	18	
27 Months	1	0	2	1	
30 Months	0	0	0	0	

PT are presented if at least 10 events in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.67 Subgroup analysis by age
16.2.7.1.67.14 Treatment emergent severe adverse event per PT by treatment group according to age - Safety population

	<65 years		>=65 years		
	Kd (N=65)	**IKd (N=87)**	**Kd (N=57)**	**IKd (N=90)**	**p-value of treatment-by-sub group interaction[c]**
27 Months	0.9517 (0.8573 to 0.9842)	0.8362 (0.7340 to 0.9017)	0.7939 (0.6583 to 0.8803)	0.8362 (0.7388 to 0.8997)	
30 Months	0.9517 (0.8573 to 0.9842)	0.8362 (0.7340 to 0.9017)	0.7939 (0.6583 to 0.8803)	0.8362 (0.7388 to 0.8997)	
Number of patients at risk[b]					
3 Months	62	83	51	83	
6 Months	59	81	48	75	
9 Months	56	76	42	73	
12 Months	54	72	41	70	
15 Months	50	63	38	67	
18 Months	49	58	37	65	
21 Months	36	53	32	56	
24 Months	17	18	10	17	
27 Months	1	0	2	1	
30 Months	0	0	0	0	
Thrombocytopenia (days)					

PT are presented if at least 5% of patients in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
PGM=DEVOPS/SAR650984/EFC15246/CIR_RWE/REPORT/PGM/ae_km_socpt_subgp_sr_s_t.sas OUT=REPORT/OUTPUT/ae_km_sevae34pt_age_s_t_x.rtf (12FEB2021 8:23)

16.2.7.1 Safety endpoints
16.2.7.1.67 Subgroup analysis by age
16.2.7.1.67.14 Treatment emergent severe adverse event per PT by treatment group according to age - Safety population

	<65 years		>=65 years		
	Kd (N=65)	**IKd (N=87)**	**Kd (N=57)**	**IKd (N=90)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	7 (10.8)	2 (2.3)	3 (5.3)	2 (2.2)	0.5522
Number (%) of patients censored	58 (89.2)	85 (97.7)	54 (94.7)	88 (97.8)	
Kaplan-Meier estimates of event in months					
25% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.0284		0.3254	
Hazard ratio (95% CI) vs Kd	-	0.20 (0.04 to 0.99)		0.42 (0.07 to 2.51)	
P-value	-	0.0479		0.3406	
Events probability (95% CI)[b]					
3 Months	0.9228 (0.8244 to 0.9671)	0.9885 (0.9212 to 0.9984)	0.9825 (0.8819 to 0.9975)	0.9888 (0.9229 to 0.9984)	

PT are presented if at least 5% of patients in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.67 Subgroup analysis by age
16.2.7.1.67.14 Treatment emergent severe adverse event per PT by treatment group according to age - Safety population

	<65 years		>=65 years		
	Kd (N=65)	**IKd (N=87)**	**Kd (N=57)**	**IKd (N=90)**	**p-value of treatment-by-sub group interaction[c]**
6 Months	0.8915 (0.7859 to 0.9468)	0.9885 (0.9212 to 0.9984)	0.9825 (0.8819 to 0.9975)	0.9888 (0.9229 to 0.9984)	
9 Months	0.8915 (0.7859 to 0.9468)	0.9885 (0.9212 to 0.9984)	0.9454 (0.8400 to 0.9821)	0.9888 (0.9229 to 0.9984)	
12 Months	0.8915 (0.7859 to 0.9468)	0.9761 (0.9079 to 0.9940)	0.9454 (0.8400 to 0.9821)	0.9888 (0.9229 to 0.9984)	
15 Months	0.8915 (0.7859 to 0.9468)	0.9761 (0.9079 to 0.9940)	0.9454 (0.8400 to 0.9821)	0.9888 (0.9229 to 0.9984)	
18 Months	0.8915 (0.7859 to 0.9468)	0.9761 (0.9079 to 0.9940)	0.9454 (0.8400 to 0.9821)	0.9756 (0.9054 to 0.9939)	
21 Months	0.8915 (0.7859 to 0.9468)	0.9761 (0.9079 to 0.9940)	0.9454 (0.8400 to 0.9821)	0.9756 (0.9054 to 0.9939)	
24 Months	0.8915 (0.7859 to 0.9468)	0.9761 (0.9079 to 0.9940)	0.9454 (0.8400 to 0.9821)	0.9756 (0.9054 to 0.9939)	
27 Months	0.8915 (0.7859 to 0.9468)	0.9761 (0.9079 to 0.9940)	0.9454 (0.8400 to 0.9821)	0.9756 (0.9054 to 0.9939)	
30 Months	0.8915 (0.7859 to 0.9468)	0.9761 (0.9079 to 0.9940)	0.9454 (0.8400 to 0.9821)	0.9756 (0.9054 to 0.9939)	

PT are presented if at least 5% of patients in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.67 Subgroup analysis by age
16.2.7.1.67.14 Treatment emergent severe adverse event per PT by treatment group according to age - Safety population

	<65 years		>=65 years		
	Kd (N=65)	**IKd (N=87)**	**Kd (N=57)**	**IKd (N=90)**	**p-value of treatment-by-sub group interaction[c]**
Number of patients at risk[b]					
3 Months	59	84	55	87	
6 Months	55	83	53	82	
9 Months	52	80	48	80	
12 Months	52	78	47	78	
15 Months	49	70	45	75	
18 Months	48	66	44	71	
21 Months	35	61	38	61	
24 Months	17	20	11	19	
27 Months	1	0	3	2	
30 Months	0	0	0	0	

PT are presented if at least 5% of patients in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.68 Subgroup analysis by gender
16.2.7.1.68.13 Treatment emergent severe adverse event per PT by treatment group according to gender - Safety population

	Male		Female		
	Kd (N=68)	**IKd (N=99)**	**Kd (N=54)**	**IKd (N=78)**	**p-value of treatment-by-sub group interaction[c]**
27 Months	0.8214 (0.6999 to 0.8972)	0.7858 (0.6842 to 0.8581)	0.9437 (0.8355 to 0.9815)	0.8946 (0.8001 to 0.9459)	
30 Months	0.8214 (0.6999 to 0.8972)	0.7858 (0.6842 to 0.8581)	0.9437 (0.8355 to 0.9815)	0.8946 (0.8001 to 0.9459)	
Number of patients at risk[b]					
3 Months	60	93	53	73	
6 Months	54	85	53	71	
9 Months	50	80	48	69	
12 Months	47	74	48	68	
15 Months	44	68	44	62	
18 Months	43	62	43	61	
21 Months	32	52	36	57	
24 Months	15	17	12	18	
27 Months	1	0	2	1	
30 Months	0	0	0	0	
Thrombocytopenia (days)					

PT are presented if at least 5% of patients in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
PGM=DEVOPS/SAR650984/EFC15246/CIR_RWE/REPORT/PGM/ae_km_socpt_subgp_sr_s_t.sas OUT=REPORT/OUTPUT/ae_km_sevae34pt_sex_s_t_x.rtf (12FEB2021 8:24)

16.2.7.1 Safety endpoints
16.2.7.1.68 Subgroup analysis by gender
16.2.7.1.68.13 Treatment emergent severe adverse event per PT by treatment group according to gender - Safety population

	Male		Female		
	Kd (N=68)	**IKd (N=99)**	**Kd (N=54)**	**IKd (N=78)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	4 (5.9)	3 (3.0)	6 (11.1)	1 (1.3)	0.2533
Number (%) of patients censored	64 (94.1)	96 (97.0)	48 (88.9)	77 (98.7)	
Kaplan-Meier estimates of event in months					
25% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.3571		0.0149	
Hazard ratio (95% CI) vs Kd	-	0.50 (0.11 to 2.24)		0.11 (0.01 to 0.94)	
P-value	-	0.3666		0.0441	
Events probability (95% CI)[b]					
3 Months	0.9704 (0.8867 to 0.9925)	0.9899 (0.9305 to 0.9986)	0.9259 (0.8146 to 0.9715)	0.9870 (0.9114 to 0.9982)	

PT are presented if at least 5% of patients in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.68 Subgroup analysis by gender
16.2.7.1.68.13 Treatment emergent severe adverse event per PT by treatment group according to gender - Safety population

	Male		Female		
	Kd (N=68)	**IKd (N=99)**	**Kd (N=54)**	**IKd (N=78)**	**p-value of treatment-by-sub group interaction[c]**
6 Months	0.9552 (0.8675 to 0.9853)	0.9899 (0.9305 to 0.9986)	0.9074 (0.7917 to 0.9604)	0.9870 (0.9114 to 0.9982)	
9 Months	0.9390 (0.8454 to 0.9767)	0.9899 (0.9305 to 0.9986)	0.8889 (0.7693 to 0.9485)	0.9870 (0.9114 to 0.9982)	
12 Months	0.9390 (0.8454 to 0.9767)	0.9785 (0.9166 to 0.9946)	0.8889 (0.7693 to 0.9485)	0.9870 (0.9114 to 0.9982)	
15 Months	0.9390 (0.8454 to 0.9767)	0.9785 (0.9166 to 0.9946)	0.8889 (0.7693 to 0.9485)	0.9870 (0.9114 to 0.9982)	
18 Months	0.9390 (0.8454 to 0.9767)	0.9660 (0.8977 to 0.9890)	0.8889 (0.7693 to 0.9485)	0.9870 (0.9114 to 0.9982)	
21 Months	0.9390 (0.8454 to 0.9767)	0.9660 (0.8977 to 0.9890)	0.8889 (0.7693 to 0.9485)	0.9870 (0.9114 to 0.9982)	
24 Months	0.9390 (0.8454 to 0.9767)	0.9660 (0.8977 to 0.9890)	0.8889 (0.7693 to 0.9485)	0.9870 (0.9114 to 0.9982)	
27 Months	0.9390 (0.8454 to 0.9767)	0.9660 (0.8977 to 0.9890)	0.8889 (0.7693 to 0.9485)	0.9870 (0.9114 to 0.9982)	
30 Months	0.9390 (0.8454 to 0.9767)	0.9660 (0.8977 to 0.9890)	0.8889 (0.7693 to 0.9485)	0.9870 (0.9114 to 0.9982)	

PT are presented if at least 5% of patients in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
PGM=DEVOPS/SAR650984/EFC15246/CIR_RWE/REPORT/PGM/ae_km_socpt_subgp_sr_s_t.sas OUT=REPORT/OUTPUT/ae_km_sevae34pt_sex_s_t_x.rtf (12FEB2021 8:24)

16.2.7.1 Safety endpoints
16.2.7.1.68 Subgroup analysis by gender
16.2.7.1.68.13 Treatment emergent severe adverse event per PT by treatment group according to gender - Safety population

	Male		Female		
	Kd (N=68)	**IKd (N=99)**	**Kd (N=54)**	**IKd (N=78)**	**p-value of treatment-by-sub group interaction[c]**
Number of patients at risk[b]					
3 Months	64	95	50	76	
6 Months	59	90	49	75	
9 Months	55	87	45	73	
12 Months	55	85	44	71	
15 Months	53	78	41	67	
18 Months	52	72	40	65	
21 Months	39	64	34	58	
24 Months	16	21	12	18	
27 Months	1	1	3	1	
30 Months	0	0	0	0	

PT are presented if at least 5% of patients in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.69 Subgroup analysis by ethnic origin
16.2.7.1.69.12 Treatment emergent severe adverse event per PT by treatment group according to ethnic origin - Safety population

	White		Other		
	Kd (N=83)	**IKd (N=130)**	**Kd (N=27)**	**IKd (N=33)**	**p-value of treatment-by-sub group interaction[c]**
27 Months	0.8749 (0.7798 to 0.9307)	0.8530 (0.7766 to 0.9049)	0.8371 (0.6209 to 0.9358)	0.7635 (0.5644 to 0.8804)	
30 Months	0.8749 (0.7798 to 0.9307)	0.8530 (0.7766 to 0.9049)	0.8371 (0.6209 to 0.9358)	0.7635 (0.5644 to 0.8804)	
Number of patients at risk[b]					
3 Months	75	122	27	30	
6 Months	72	115	26	29	
9 Months	68	110	22	27	
12 Months	66	107	21	25	
15 Months	63	99	17	22	
18 Months	61	93	17	21	
21 Months	45	81	16	20	
24 Months	17	27	7	6	
27 Months	1	1	2	0	
30 Months	0	0	0	0	
Thrombocytopenia (days)					

PT are presented if at least 5% of patients in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.69 Subgroup analysis by ethnic origin
16.2.7.1.69.12 Treatment emergent severe adverse event per PT by treatment group according to ethnic origin - Safety population

	White		Other		
	Kd (N=83)	**IKd (N=130)**	**Kd (N=27)**	**IKd (N=33)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	7 (8.4)	3 (2.3)	2 (7.4)	0 (0.0)	0.9933
Number (%) of patients censored	76 (91.6)	127 (97.7)	25 (92.6)	33 (100.0)	
Kaplan-Meier estimates of event in months					
25% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (6.5051 to NC)	NC (NC to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.0413		0.1194	
Hazard ratio (95% CI) vs Kd	-	0.27 (0.07 to 1.04)		NC	
P-value	-	0.0573		0.9977	
Events probability (95% CI)[b]					
3 Months	0.9393 (0.8603 to 0.9743)	0.9846 (0.9397 to 0.9961)	1.0000 (1.0000 to 1.0000)	1.0000 (1.0000 to 1.0000)	

PT are presented if at least 5% of patients in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
PGM=DEVOPS/SAR650984/EFC15246/CIR_RWE/REPORT/PGM/ae_km_socpt_subgp_sr_s_t.sas OUT=REPORT/OUTPUT/ae_km_sevae34pt_race_s_t_x.rtf (12FEB2021 8:24)

16.2.7.1 Safety endpoints
16.2.7.1.69 Subgroup analysis by ethnic origin
16.2.7.1.69.12 Treatment emergent severe adverse event per PT by treatment group according to ethnic origin - Safety population

	White		Other		
	Kd (N=83)	**IKd (N=130)**	**Kd (N=27)**	**IKd (N=33)**	**p-value of treatment-by-sub group interaction[c]**
6 Months	0.9271 (0.8449 to 0.9666)	0.9846 (0.9397 to 0.9961)	0.9630 (0.7649 to 0.9947)	1.0000 (1.0000 to 1.0000)	
9 Months	0.9147 (0.8295 to 0.9584)	0.9846 (0.9397 to 0.9961)	0.9244 (0.7302 to 0.9806)	1.0000 (1.0000 to 1.0000)	
12 Months	0.9147 (0.8295 to 0.9584)	0.9761 (0.9278 to 0.9923)	0.9244 (0.7302 to 0.9806)	1.0000 (1.0000 to 1.0000)	
15 Months	0.9147 (0.8295 to 0.9584)	0.9761 (0.9278 to 0.9923)	0.9244 (0.7302 to 0.9806)	1.0000 (1.0000 to 1.0000)	
18 Months	0.9147 (0.8295 to 0.9584)	0.9761 (0.9278 to 0.9923)	0.9244 (0.7302 to 0.9806)	1.0000 (1.0000 to 1.0000)	
21 Months	0.9147 (0.8295 to 0.9584)	0.9761 (0.9278 to 0.9923)	0.9244 (0.7302 to 0.9806)	1.0000 (1.0000 to 1.0000)	
24 Months	0.9147 (0.8295 to 0.9584)	0.9761 (0.9278 to 0.9923)	0.9244 (0.7302 to 0.9806)	1.0000 (1.0000 to 1.0000)	
27 Months	0.9147 (0.8295 to 0.9584)	0.9761 (0.9278 to 0.9923)	0.9244 (0.7302 to 0.9806)	1.0000 (1.0000 to 1.0000)	
30 Months	0.9147 (0.8295 to 0.9584)	0.9761 (0.9278 to 0.9923)	0.9244 (0.7302 to 0.9806)	1.0000 (1.0000 to 1.0000)	

PT are presented if at least 5% of patients in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.

16.2.7.1 Safety endpoints
16.2.7.1.69 Subgroup analysis by ethnic origin
16.2.7.1.69.12 Treatment emergent severe adverse event per PT by treatment group according to ethnic origin - Safety population

	White		Other		
	Kd (N=83)	**IKd (N=130)**	**Kd (N=27)**	**IKd (N=33)**	**p-value of treatment-by-sub group interaction[c]**
Number of patients at risk[b]					
3 Months	77	125	27	32	
6 Months	75	121	25	31	
9 Months	71	117	22	30	
12 Months	70	116	22	29	
15 Months	67	110	20	25	
18 Months	65	104	20	24	
21 Months	47	90	19	24	
24 Months	17	29	8	8	
27 Months	1	1	3	1	
30 Months	0	0	0	0	

PT are presented if at least 5% of patients in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.70 Subgroup analysis by geographical region
16.2.7.1.70.11 Treatment emergent severe adverse event per PT by treatment group according to geographical region - Safety population

	Europe		America		Asia		Other countries		
	Pd (N=60)	**IPd (N=85)**	**Pd (N=20)**	**IPd (N=23)**	**Pd (N=20)**	**IPd (N=24)**	**Pd (N=22)**	**IPd (N=45)**	**p-value of treatment-by-subgroup interaction[c]**
Thrombocytopenia (days)									
Number (%) of events	7 (11.7)	3 (3.5)	0 (0.0)	0 (0.0)	2 (10.0)	0 (0.0)	1 (4.5)	1 (2.2)	0.9886
Number (%) of patients censored	53 (88.3)	82 (96.5)	20 (100.0)	23 (100.0)	18 (90.0)	24 (100.0)	21 (95.5)	44 (97.8)	
Kaplan-Meier estimates of event in months									
25% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (3.3840 to NC)	NC (NC to NC)	NC (2.3326 to NC)	NC (NC to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	

PT are presented if at least 5% of patients in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.70 Subgroup analysis by geographical region
16.2.7.1.70.11 Treatment emergent severe adverse event per PT by treatment group according to geographical region - Safety population

	Europe		America		Asia		Other countries		
	Pd (N=60)	**IPd (N=85)**	**Pd (N=20)**	**IPd (N=23)**	**Pd (N=20)**	**IPd (N=24)**	**Pd (N=22)**	**IPd (N=45)**	**p-value of treatment-by-subgroup interaction[c]**
Comparison vs. Pd									
Log-Rank test p-value[a] vs Kd	-	0.0521				0.1155		0.6112	
Hazard ratio (95% CI) vs Kd	-	0.28 (0.07 to 1.10)		NC		NC		0.49 (0.03 to 7.91)	
P-value	-	0.0687				0.9977		0.6185	
Events probability (95% CI)[b]									
3 Months	0.9158 (0.8094 to 0.9641)	0.9882 (0.9194 to 0.9983)	1.0000 (1.0000 to 1.0000)	1.0000 (1.0000 to 1.0000)	1.0000 (1.0000 to 1.0000)	1.0000 (1.0000 to 1.0000)	0.9545 (0.7187 to 0.9935)	0.9778 (0.8525 to 0.9968)	
6 Months	0.8985 (0.7879 to 0.9531)	0.9882 (0.9194 to 0.9983)	1.0000 (1.0000 to 1.0000)	1.0000 (1.0000 to 1.0000)	0.9500 (0.6947 to 0.9928)	1.0000 (1.0000 to 1.0000)	0.9545 (0.7187 to 0.9935)	0.9778 (0.8525 to 0.9968)	

PT are presented if at least 5% of patients in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.70 Subgroup analysis by geographical region
16.2.7.1.70.11 Treatment emergent severe adverse event per PT by treatment group according to geographical region - Safety population

	Europe		America		Asia		Other countries		
	Pd (N=60)	IPd (N=85)	Pd (N=20)	IPd (N=23)	Pd (N=20)	IPd (N=24)	Pd (N=22)	IPd (N=45)	p-value of treatment-by-subgroup interaction[c]
9 Months	0.8802 (0.7648 to 0.9411)	0.9882 (0.9194 to 0.9983)	1.0000 (1.0000 to 1.0000)	1.0000 (1.0000 to 1.0000)	0.8972 (0.6475 to 0.9733)	1.0000 (1.0000 to 1.0000)	0.9545 (0.7187 to 0.9935)	0.9778 (0.8525 to 0.9968)	
12 Months	0.8802 (0.7648 to 0.9411)	0.9756 (0.9057 to 0.9938)	1.0000 (1.0000 to 1.0000)	1.0000 (1.0000 to 1.0000)	0.8972 (0.6475 to 0.9733)	1.0000 (1.0000 to 1.0000)	0.9545 (0.7187 to 0.9935)	0.9778 (0.8525 to 0.9968)	
15 Months	0.8802 (0.7648 to 0.9411)	0.9756 (0.9057 to 0.9938)	1.0000 (1.0000 to 1.0000)	1.0000 (1.0000 to 1.0000)	0.8972 (0.6475 to 0.9733)	1.0000 (1.0000 to 1.0000)	0.9545 (0.7187 to 0.9935)	0.9778 (0.8525 to 0.9968)	
18 Months	0.8802 (0.7648 to 0.9411)	0.9620 (0.8866 to 0.9876)	1.0000 (1.0000 to 1.0000)	1.0000 (1.0000 to 1.0000)	0.8972 (0.6475 to 0.9733)	1.0000 (1.0000 to 1.0000)	0.9545 (0.7187 to 0.9935)	0.9778 (0.8525 to 0.9968)	
21 Months	0.8802 (0.7648 to 0.9411)	0.9620 (0.8866 to 0.9876)	1.0000 (1.0000 to 1.0000)	1.0000 (1.0000 to 1.0000)	0.8972 (0.6475 to 0.9733)	1.0000 (1.0000 to 1.0000)	0.9545 (0.7187 to 0.9935)	0.9778 (0.8525 to 0.9968)	

PT are presented if at least 5% of patients in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.70 Subgroup analysis by geographical region
16.2.7.1.70.11 Treatment emergent severe adverse event per PT by treatment group according to geographical region - Safety population

	Europe		America		Asia		Other countries		
	Pd (N=60)	**IPd (N=85)**	**Pd (N=20)**	**IPd (N=23)**	**Pd (N=20)**	**IPd (N=24)**	**Pd (N=22)**	**IPd (N=45)**	**p-value of treatment-by-subgroup interaction[c]**
24 Months	0.8802 (0.7648 to 0.9411)	0.9620 (0.8866 to 0.9876)	1.0000 (1.0000 to 1.0000)	1.0000 (1.0000 to 1.0000)	0.8972 (0.6475 to 0.9733)	1.0000 (1.0000 to 1.0000)	0.9545 (0.7187 to 0.9935)	0.9778 (0.8525 to 0.9968)	
27 Months	0.8802 (0.7648 to 0.9411)	0.9620 (0.8866 to 0.9876)	1.0000 (1.0000 to 1.0000)	1.0000 (1.0000 to 1.0000)	0.8972 (0.6475 to 0.9733)	1.0000 (1.0000 to 1.0000)	0.9545 (0.7187 to 0.9935)	0.9778 (0.8525 to 0.9968)	
30 Months	0.8802 (0.7648 to 0.9411)	0.9620 (0.8866 to 0.9876)	1.0000 (1.0000 to 1.0000)	1.0000 (1.0000 to 1.0000)	0.8972 (0.6475 to 0.9733)	1.0000 (1.0000 to 1.0000)	0.9545 (0.7187 to 0.9935)	0.9778 (0.8525 to 0.9968)	
Number of patients at risk[b]									
3 Months	53	81	20	22	20	24	21	44	
6 Months	49	78	20	22	18	23	21	42	
9 Months	47	78	19	21	15	22	19	39	
12 Months	46	75	19	21	15	21	19	39	

PT are presented if at least 5% of patients in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.71 Subgroup analysis by regulatory region
16.2.7.1.71.13 Treatment emergent severe adverse event per PT by treatment group according to regulatory region - Safety population

	Western countries		Other countries		
	Kd (N=55)	**IKd (N=97)**	**Kd (N=67)**	**IKd (N=80)**	**p-value of treatment-by-sub group interaction[c]**
27 Months	0.9414 (0.8291 to 0.9808)	0.8566 (0.7656 to 0.9142)	0.8271 (0.7090 to 0.9005)	0.8114 (0.7015 to 0.8841)	
30 Months	0.9414 (0.8291 to 0.9808)	0.8566 (0.7656 to 0.9142)	0.8271 (0.7090 to 0.9005)	0.8114 (0.7015 to 0.8841)	
Number of patients at risk[b]					
3 Months	50	93	63	73	
6 Months	47	85	60	71	
9 Months	45	83	53	66	
12 Months	45	78	50	64	
15 Months	43	72	45	58	
18 Months	43	68	43	55	
21 Months	35	60	33	49	
24 Months	12	18	15	17	
27 Months	1	0	2	1	
30 Months	0	0	0	0	
Thrombocytopenia (days)					

PT are presented if at least 5% of patients in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.71 Subgroup analysis by regulatory region
16.2.7.1.71.13 Treatment emergent severe adverse event per PT by treatment group according to regulatory region - Safety population

	Western countries		Other countries		
	Kd (N=55)	**IKd (N=97)**	**Kd (N=67)**	**IKd (N=80)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	4 (7.3)	4 (4.1)	6 (9.0)	0 (0.0)	0.9926
Number (%) of patients censored	51 (92.7)	93 (95.9)	61 (91.0)	80 (100.0)	
Kaplan-Meier estimates of event in months					
25% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.3955		0.0068	
Hazard ratio (95% CI) vs Kd	-	0.55 (0.14 to 2.21)		NC	
P-value	-	0.4024		0.9938	
Events probability (95% CI)[b]					
3 Months	0.9448 (0.8384 to 0.9818)	0.9793 (0.9197 to 0.9948)	0.9552 (0.8676 to 0.9853)	1.0000 (1.0000 to 1.0000)	

PT are presented if at least 5% of patients in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.

16.2.7.1 Safety endpoints
16.2.7.1.71 Subgroup analysis by regulatory region
16.2.7.1.71.13 Treatment emergent severe adverse event per PT by treatment group according to regulatory region - Safety population

	Western countries		Other countries		
	Kd (N=55)	**IKd (N=97)**	**Kd (N=67)**	**IKd (N=80)**	**p-value of treatment-by-sub group interaction[c]**
6 Months	0.9259 (0.8144 to 0.9715)	0.9793 (0.9197 to 0.9948)	0.9403 (0.8487 to 0.9772)	1.0000 (1.0000 to 1.0000)	
9 Months	0.9259 (0.8144 to 0.9715)	0.9793 (0.9197 to 0.9948)	0.9095 (0.8095 to 0.9583)	1.0000 (1.0000 to 1.0000)	
12 Months	0.9259 (0.8144 to 0.9715)	0.9681 (0.9044 to 0.9896)	0.9095 (0.8095 to 0.9583)	1.0000 (1.0000 to 1.0000)	
15 Months	0.9259 (0.8144 to 0.9715)	0.9681 (0.9044 to 0.9896)	0.9095 (0.8095 to 0.9583)	1.0000 (1.0000 to 1.0000)	
18 Months	0.9259 (0.8144 to 0.9715)	0.9559 (0.8864 to 0.9833)	0.9095 (0.8095 to 0.9583)	1.0000 (1.0000 to 1.0000)	
21 Months	0.9259 (0.8144 to 0.9715)	0.9559 (0.8864 to 0.9833)	0.9095 (0.8095 to 0.9583)	1.0000 (1.0000 to 1.0000)	
24 Months	0.9259 (0.8144 to 0.9715)	0.9559 (0.8864 to 0.9833)	0.9095 (0.8095 to 0.9583)	1.0000 (1.0000 to 1.0000)	
27 Months	0.9259 (0.8144 to 0.9715)	0.9559 (0.8864 to 0.9833)	0.9095 (0.8095 to 0.9583)	1.0000 (1.0000 to 1.0000)	
30 Months	0.9259 (0.8144 to 0.9715)	0.9559 (0.8864 to 0.9833)	0.9095 (0.8095 to 0.9583)	1.0000 (1.0000 to 1.0000)	

PT are presented if at least 5% of patients in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.71 Subgroup analysis by regulatory region
16.2.7.1.71.13 Treatment emergent severe adverse event per PT by treatment group according to regulatory region - Safety population

	Western countries		Other countries		
	Kd (N=55)	**IKd (N=97)**	**Kd (N=67)**	**IKd (N=80)**	**p-value of treatment-by-sub group interaction[c]**
Number of patients at risk[b]					
3 Months	50	93	64	78	
6 Months	47	89	61	76	
9 Months	46	88	54	72	
12 Months	46	85	53	71	
15 Months	44	79	50	66	
18 Months	44	74	48	63	
21 Months	36	64	37	58	
24 Months	11	19	17	20	
27 Months	1	0	3	2	
30 Months	0	0	0	0	

PT are presented if at least 5% of patients in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.72 Subgroup analysis by baseline ECOG PS
16.2.7.1.72.10 Treatment emergent severe adverse event per PT by treatment group according to baseline ECOG PS - Safety population

	0 or 1		>1		
	Kd (N=117)	**IKd (N=167)**	**Kd (N=5)**	**IKd (N=10)**	**p-value of treatment-by-sub group interaction[c]**
27 Months	0.8730 (0.7948 to 0.9229)	0.8273 (0.7580 to 0.8783)	1.0000 (1.0000 to 1.0000)	1.0000 (1.0000 to 1.0000)	
30 Months	0.8730 (0.7948 to 0.9229)	0.8273 (0.7580 to 0.8783)	1.0000 (1.0000 to 1.0000)	1.0000 (1.0000 to 1.0000)	
Number of patients at risk[b]					
3 Months	108	157	5	9	
6 Months	103	147	4	9	
9 Months	94	140	4	9	
12 Months	91	134	4	8	
15 Months	86	122	2	8	
18 Months	84	116	2	7	
21 Months	66	103	2	6	
24 Months	26	35	1	0	
27 Months	3	1	0	0	
30 Months	0	0	0	0	
Thrombocytopenia (days)					

PT are presented if at least 5% of patients in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
PGM=DEVOPS/SAR650984/EFC15246/CIR_RWE/REPORT/PGM/ae_km_socpt_subgp_sr_s_t.sas OUT=REPORT/OUTPUT/ae_km_sevae34pt_ecog_s_t_x.rtf (12FEB2021 8:23)

16.2.7.1 Safety endpoints
16.2.7.1.72 Subgroup analysis by baseline ECOG PS
16.2.7.1.72.10 Treatment emergent severe adverse event per PT by treatment group according to baseline ECOG PS - Safety population

	0 or 1		>1		
	Kd (N=117)	**IKd (N=167)**	**Kd (N=5)**	**IKd (N=10)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	9 (7.7)	4 (2.4)	1 (20.0)	0 (0.0)	0.9918
Number (%) of patients censored	108 (92.3)	163 (97.6)	4 (80.0)	10 (100.0)	
Kaplan-Meier estimates of event in months					
25% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (3.2526 to NC)	NC (NC to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (3.2526 to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (3.2526 to NC)	NC (NC to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.0349		0.1797	
Hazard ratio (95% CI) vs Kd	-	0.30 (0.09 to 0.98)		NC	
P-value	-	0.0467		0.9985	
Events probability (95% CI)[b]					
3 Months	0.9483 (0.8886 to 0.9765)	0.9880 (0.9530 to 0.9970)	1.0000 (1.0000 to 1.0000)	1.0000 (1.0000 to 1.0000)	

PT are presented if at least 5% of patients in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.72 Subgroup analysis by baseline ECOG PS
16.2.7.1.72.10 Treatment emergent severe adverse event per PT by treatment group according to baseline ECOG PS - Safety population

	0 or 1		>1		
	Kd (N=117)	**IKd (N=167)**	**Kd (N=5)**	**IKd (N=10)**	**p-value of treatment-by-sub group interaction[c]**
6 Months	0.9396 (0.8775 to 0.9708)	0.9880 (0.9530 to 0.9970)	0.8000 (0.2038 to 0.9692)	1.0000 (1.0000 to 1.0000)	
9 Months	0.9216 (0.8546 to 0.9584)	0.9880 (0.9530 to 0.9970)	0.8000 (0.2038 to 0.9692)	1.0000 (1.0000 to 1.0000)	
12 Months	0.9216 (0.8546 to 0.9584)	0.9815 (0.9436 to 0.9940)	0.8000 (0.2038 to 0.9692)	1.0000 (1.0000 to 1.0000)	
15 Months	0.9216 (0.8546 to 0.9584)	0.9815 (0.9436 to 0.9940)	0.8000 (0.2038 to 0.9692)	1.0000 (1.0000 to 1.0000)	
18 Months	0.9216 (0.8546 to 0.9584)	0.9743 (0.9328 to 0.9903)	0.8000 (0.2038 to 0.9692)	1.0000 (1.0000 to 1.0000)	
21 Months	0.9216 (0.8546 to 0.9584)	0.9743 (0.9328 to 0.9903)	0.8000 (0.2038 to 0.9692)	1.0000 (1.0000 to 1.0000)	
24 Months	0.9216 (0.8546 to 0.9584)	0.9743 (0.9328 to 0.9903)	0.8000 (0.2038 to 0.9692)	1.0000 (1.0000 to 1.0000)	
27 Months	0.9216 (0.8546 to 0.9584)	0.9743 (0.9328 to 0.9903)	0.8000 (0.2038 to 0.9692)	1.0000 (1.0000 to 1.0000)	
30 Months	0.9216 (0.8546 to 0.9584)	0.9743 (0.9328 to 0.9903)	0.8000 (0.2038 to 0.9692)	1.0000 (1.0000 to 1.0000)	

PT are presented if at least 5% of patients in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.72 Subgroup analysis by baseline ECOG PS
16.2.7.1.72.10 Treatment emergent severe adverse event per PT by treatment group according to baseline ECOG PS - Safety population

	0 or 1		>1		
	Kd (N=117)	**IKd (N=167)**	**Kd (N=5)**	**IKd (N=10)**	**p-value of treatment-by-sub group interaction[c]**
Number of patients at risk[b]					
3 Months	109	162	5	9	
6 Months	104	156	4	9	
9 Months	96	151	4	9	
12 Months	95	148	4	8	
15 Months	92	137	2	8	
18 Months	90	130	2	7	
21 Months	71	116	2	6	
24 Months	27	39	1	0	
27 Months	4	2	0	0	
30 Months	0	0	0	0	

PT are presented if at least 5% of patients in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.73 Subgroup analysis by ISS staging at study entry
16.2.7.1.73.10 Treatment emergent severe adverse event per PT by treatment group according to ISS staging at study entry - Safety population

	I		II		III		
	Kd (N=70)	**IKd (N=89)**	**Kd (N=31)**	**IKd (N=63)**	**Kd (N=20)**	**IKd (N=24)**	**p-value of treatment-by-sub group interaction[c]**
27 Months	2	1	1	0	0	0	
30 Months	0	0	0	0	0	0	
Thrombocytopenia (days)							
Number (%) of events	4 (5.7)	2 (2.2)	3 (9.7)	1 (1.6)	3 (15.0)	1 (4.2)	0.8115
Number (%) of patients censored	66 (94.3)	87 (97.8)	28 (90.3)	62 (98.4)	17 (85.0)	23 (95.8)	
Kaplan-Meier estimates of event in months							
25% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (6.5051 to NC)	NC (NC to NC)	NC (0.2300 to NC)	NC (15.0144 to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Kd							
Log-Rank test p-value[a] vs Kd	-	0.2575		0.0711		0.2242	
Hazard ratio (95% CI) vs Kd	-	0.39 (0.07 to 2.12)		0.16 (0.02 to 1.55)		0.27 (0.03 to 2.60)	
P-value	-	0.2752		0.1146		0.2572	

PT are presented if at least 5% of patients in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.73 Subgroup analysis by ISS staging at study entry
16.2.7.1.73.10 Treatment emergent severe adverse event per PT by treatment group according to ISS staging at study entry - Safety population

	I		II		III		
	Kd (N=70)	**IKd (N=89)**	**Kd (N=31)**	**IKd (N=63)**	**Kd (N=20)**	**IKd (N=24)**	**p-value of treatment-by-sub group interaction[c]**
Events probability (95% CI)[b]							
3 Months	0.9571 (0.8730 to 0.9860)	0.9888 (0.9229 to 0.9984)	0.9355 (0.7659 to 0.9835)	0.9841 (0.8926 to 0.9977)	0.9500 (0.6947 to 0.9928)	1.0000 (1.0000 to 1.0000)	
6 Months	0.9429 (0.8549 to 0.9782)	0.9888 (0.9229 to 0.9984)	0.9355 (0.7659 to 0.9835)	0.9841 (0.8926 to 0.9977)	0.8972 (0.6475 to 0.9733)	1.0000 (1.0000 to 1.0000)	
9 Months	0.9429 (0.8549 to 0.9782)	0.9888 (0.9229 to 0.9984)	0.9008 (0.7229 to 0.9669)	0.9841 (0.8926 to 0.9977)	0.8374 (0.5740 to 0.9449)	1.0000 (1.0000 to 1.0000)	
12 Months	0.9429 (0.8549 to 0.9782)	0.9769 (0.9105 to 0.9942)	0.9008 (0.7229 to 0.9669)	0.9841 (0.8926 to 0.9977)	0.8374 (0.5740 to 0.9449)	1.0000 (1.0000 to 1.0000)	
15 Months	0.9429 (0.8549 to 0.9782)	0.9769 (0.9105 to 0.9942)	0.9008 (0.7229 to 0.9669)	0.9841 (0.8926 to 0.9977)	0.8374 (0.5740 to 0.9449)	1.0000 (1.0000 to 1.0000)	
18 Months	0.9429 (0.8549 to 0.9782)	0.9769 (0.9105 to 0.9942)	0.9008 (0.7229 to 0.9669)	0.9841 (0.8926 to 0.9977)	0.8374 (0.5740 to 0.9449)	0.9231 (0.5664 to 0.9888)	
21 Months	0.9429 (0.8549 to 0.9782)	0.9769 (0.9105 to 0.9942)	0.9008 (0.7229 to 0.9669)	0.9841 (0.8926 to 0.9977)	0.8374 (0.5740 to 0.9449)	0.9231 (0.5664 to 0.9888)	
24 Months	0.9429 (0.8549 to 0.9782)	0.9769 (0.9105 to 0.9942)	0.9008 (0.7229 to 0.9669)	0.9841 (0.8926 to 0.9977)	0.8374 (0.5740 to 0.9449)	0.9231 (0.5664 to 0.9888)	

PT are presented if at least 5% of patients in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.73 Subgroup analysis by ISS staging at study entry
16.2.7.1.73.10 Treatment emergent severe adverse event per PT by treatment group according to ISS staging at study entry - Safety population

	I		II		III		
	Kd (N=70)	**IKd (N=89)**	**Kd (N=31)**	**IKd (N=63)**	**Kd (N=20)**	**IKd (N=24)**	**p-value of treatment-by-sub group interaction[c]**
27 Months	0.9429 (0.8549 to 0.9782)	0.9769 (0.9105 to 0.9942)	0.9008 (0.7229 to 0.9669)	0.9841 (0.8926 to 0.9977)	0.8374 (0.5740 to 0.9449)	0.9231 (0.5664 to 0.9888)	
30 Months	0.9429 (0.8549 to 0.9782)	0.9769 (0.9105 to 0.9942)	0.9008 (0.7229 to 0.9669)	0.9841 (0.8926 to 0.9977)	0.8374 (0.5740 to 0.9449)	0.9231 (0.5664 to 0.9888)	
Number of patients at risk[b]							
3 Months	67	87	28	61	18	22	
6 Months	65	86	27	58	15	20	
9 Months	62	83	24	58	13	18	
12 Months	62	80	23	58	13	17	
15 Months	62	75	20	56	11	13	
18 Months	62	71	20	55	9	10	
21 Months	48	64	17	49	7	8	
24 Months	18	21	8	17	2	1	
27 Months	3	2	1	0	0	0	
30 Months	0	0	0	0	0	0	

PT are presented if at least 5% of patients in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.74 Subgroup analysis by R-ISS staging
16.2.7.1.74.12 Treatment emergent severe adverse event per PT by treatment group according to R-ISS staging - Safety population

	I or II		III		Not classified		
	Kd (N=102)	**IKd (N=155)**	**Kd (N=8)**	**IKd (N=15)**	**Kd (N=12)**	**IKd (N=7)**	**p-value of treatment-by-sub group interaction[c]**
Thrombocytopenia (days)							
Number (%) of events	8 (7.8)	3 (1.9)	2 (25.0)	1 (6.7)	0 (0.0)	0 (0.0)	0.9994
Number (%) of patients censored	94 (92.2)	152 (98.1)	6 (75.0)	14 (93.3)	12 (100.0)	7 (100.0)	
Kaplan-Meier estimates of event in months							
25% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	6.2752 (3.2526 to NC)	NC (15.0144 to NC)	NC (NC to NC)	NC (NC to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (3.2526 to NC)	NC (15.0144 to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (6.2752 to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Kd							
Log-Rank test p-value[a] vs Kd	-	0.0217		0.2072			
Hazard ratio (95% CI) vs Kd	-	0.24 (0.06 to 0.90)		0.24 (0.02 to 2.66)		NC	
P-value	-	0.0348		0.2455			

PT are presented if at least 5% of patients in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.74 Subgroup analysis by R-ISS staging
16.2.7.1.74.12 Treatment emergent severe adverse event per PT by treatment group according to R-ISS staging - Safety population

	I or II		III		Not classified		
	Kd (N=102)	**IKd (N=155)**	**Kd (N=8)**	**IKd (N=15)**	**Kd (N=12)**	**IKd (N=7)**	**p-value of treatment-by-sub group interaction[c]**
Events probability (95% CI)[b]							
3 Months	0.9411 (0.8735 to 0.9731)	0.9871 (0.9494 to 0.9968)	1.0000 (1.0000 to 1.0000)	1.0000 (1.0000 to 1.0000)	1.0000 (1.0000 to 1.0000)	1.0000 (1.0000 to 1.0000)	
6 Months	0.9312 (0.8610 to 0.9666)	0.9871 (0.9494 to 0.9968)	0.8571 (0.3341 to 0.9786)	1.0000 (1.0000 to 1.0000)	1.0000 (1.0000 to 1.0000)	1.0000 (1.0000 to 1.0000)	
9 Months	0.9209 (0.8481 to 0.9597)	0.9871 (0.9494 to 0.9968)	0.6857 (0.2128 to 0.9121)	1.0000 (1.0000 to 1.0000)	1.0000 (1.0000 to 1.0000)	1.0000 (1.0000 to 1.0000)	
12 Months	0.9209 (0.8481 to 0.9597)	0.9802 (0.9400 to 0.9936)	0.6857 (0.2128 to 0.9121)	1.0000 (1.0000 to 1.0000)	1.0000 (1.0000 to 1.0000)	1.0000 (1.0000 to 1.0000)	
15 Months	0.9209 (0.8481 to 0.9597)	0.9802 (0.9400 to 0.9936)	0.6857 (0.2128 to 0.9121)	1.0000 (1.0000 to 1.0000)	1.0000 (1.0000 to 1.0000)	1.0000 (1.0000 to 1.0000)	
18 Months	0.9209 (0.8481 to 0.9597)	0.9802 (0.9400 to 0.9936)	0.6857 (0.2128 to 0.9121)	0.8750 (0.3870 to 0.9814)	1.0000 (1.0000 to 1.0000)	1.0000 (1.0000 to 1.0000)	
21 Months	0.9209 (0.8481 to 0.9597)	0.9802 (0.9400 to 0.9936)	0.6857 (0.2128 to 0.9121)	0.8750 (0.3870 to 0.9814)	1.0000 (1.0000 to 1.0000)	1.0000 (1.0000 to 1.0000)	
24 Months	0.9209 (0.8481 to 0.9597)	0.9802 (0.9400 to 0.9936)	0.6857 (0.2128 to 0.9121)	0.8750 (0.3870 to 0.9814)	1.0000 (1.0000 to 1.0000)	1.0000 (1.0000 to 1.0000)	
27 Months	0.9209 (0.8481 to 0.9597)	0.9802 (0.9400 to 0.9936)	0.6857 (0.2128 to 0.9121)	0.8750 (0.3870 to 0.9814)	1.0000 (1.0000 to 1.0000)	1.0000 (1.0000 to 1.0000)	

PT are presented if at least 5% of patients in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.74 Subgroup analysis by R-ISS staging
16.2.7.1.74.12 Treatment emergent severe adverse event per PT by treatment group according to R-ISS staging - Safety population

	I or II		III		Not classified		
	Kd (N=102)	**IKd (N=155)**	**Kd (N=8)**	**IKd (N=15)**	**Kd (N=12)**	**IKd (N=7)**	**p-value of treatment-by-sub group interaction[c]**
30 Months	0.9209 (0.8481 to 0.9597)	0.9802 (0.9400 to 0.9936)	0.6857 (0.2128 to 0.9121)	0.8750 (0.3870 to 0.9814)	1.0000 (1.0000 to 1.0000)	1.0000 (1.0000 to 1.0000)	
Number of patients at risk[b]							
3 Months	95	152	7	13	12	6	
6 Months	91	147	5	12	12	6	
9 Months	84	144	4	11	12	5	
12 Months	83	141	4	10	12	5	
15 Months	78	133	4	8	12	4	
18 Months	76	128	4	5	12	4	
21 Months	60	115	3	3	10	4	
24 Months	24	39	1	0	3	0	
27 Months	4	2	0	0	0	0	
30 Months	0	0	0	0	0	0	

PT are presented if at least 5% of patients in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
PGM=DEVOPS/SAR650984/EFC15246/CIR_RWE/REPORT/PGM/ae_km_socpt_subgp_sr_s_t.sas OUT=REPORT/OUTPUT/ae_km_sevae34pt_seriss_s_t_x.rtf (12FEB2021 8:24)

16.2.7.1 Safety endpoints
16.2.7.1.75 Subgroup analysis by number of prior lines of therapy (IRT)
16.2.7.1.75.13 Treatment emergent severe adverse event per PT by treatment group according to number of prior lines of therapy (IRT) - Safety population

	1		>1		
	Kd (N=54)	**IKd (N=78)**	**Kd (N=68)**	**IKd (N=99)**	**p-value of treatment-by-sub group interaction[c]**
27 Months	0.9063 (0.7893 to 0.9599)	0.8412 (0.7371 to 0.9066)	0.8514 (0.7330 to 0.9201)	0.8316 (0.7356 to 0.8952)	
30 Months	0.9063 (0.7893 to 0.9599)	0.8412 (0.7371 to 0.9066)	0.8514 (0.7330 to 0.9201)	0.8316 (0.7356 to 0.8952)	
Number of patients at risk[b]					
3 Months	51	74	62	92	
6 Months	50	68	57	88	
9 Months	48	67	50	82	
12 Months	47	64	48	78	
15 Months	45	60	43	70	
18 Months	45	59	41	64	
21 Months	36	50	32	59	
24 Months	14	17	13	18	
27 Months	2	1	1	0	
30 Months	0	0	0	0	
Thrombocytopenia (days)					

PT are presented if at least 5% of patients in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
PGM=DEVOPS/SAR650984/EFC15246/CIR_RWE/REPORT/PGM/ae_km_socpt_subgp_sr_s_t.sas OUT=REPORT/OUTPUT/ae_km_sevae34pt_plne_s_t_x.rtf (12FEB2021 8:24)

16.2.7.1 Safety endpoints
16.2.7.1.75 Subgroup analysis by number of prior lines of therapy (IRT)
16.2.7.1.75.13 Treatment emergent severe adverse event per PT by treatment group according to number of prior lines of therapy (IRT) - Safety population

	1		>1		
	Kd (N=54)	**IKd (N=78)**	**Kd (N=68)**	**IKd (N=99)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	0 (0.0)	3 (3.8)	10 (14.7)	1 (1.0)	0.9887
Number (%) of patients censored	54 (100.0)	75 (96.2)	58 (85.3)	98 (99.0)	
Kaplan-Meier estimates of event in months					
25% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (6.5051 to NC)	NC (NC to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.1448		0.0005	
Hazard ratio (95% CI) vs Kd	-	NC		0.07 (0.01 to 0.51)	
P-value	-	0.9958		0.0092	
Events probability (95% CI)[b]					
3 Months	1.0000 (1.0000 to 1.0000)	0.9872 (0.9125 to 0.9982)	0.9106 (0.8118 to 0.9588)	0.9898 (0.9298 to 0.9986)	

PT are presented if at least 5% of patients in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.75 Subgroup analysis by number of prior lines of therapy (IRT)
16.2.7.1.75.13 Treatment emergent severe adverse event per PT by treatment group according to number of prior lines of therapy (IRT) - Safety population

	1		>1		
	Kd (N=54)	**IKd (N=78)**	**Kd (N=68)**	**IKd (N=99)**	**p-value of treatment-by-sub group interaction[c]**
6 Months	1.0000 (1.0000 to 1.0000)	0.9872 (0.9125 to 0.9982)	0.8803 (0.7747 to 0.9383)	0.9898 (0.9298 to 0.9986)	
9 Months	1.0000 (1.0000 to 1.0000)	0.9872 (0.9125 to 0.9982)	0.8483 (0.7361 to 0.9154)	0.9898 (0.9298 to 0.9986)	
12 Months	1.0000 (1.0000 to 1.0000)	0.9738 (0.8994 to 0.9934)	0.8483 (0.7361 to 0.9154)	0.9898 (0.9298 to 0.9986)	
15 Months	1.0000 (1.0000 to 1.0000)	0.9738 (0.8994 to 0.9934)	0.8483 (0.7361 to 0.9154)	0.9898 (0.9298 to 0.9986)	
18 Months	1.0000 (1.0000 to 1.0000)	0.9593 (0.8789 to 0.9867)	0.8483 (0.7361 to 0.9154)	0.9898 (0.9298 to 0.9986)	
21 Months	1.0000 (1.0000 to 1.0000)	0.9593 (0.8789 to 0.9867)	0.8483 (0.7361 to 0.9154)	0.9898 (0.9298 to 0.9986)	
24 Months	1.0000 (1.0000 to 1.0000)	0.9593 (0.8789 to 0.9867)	0.8483 (0.7361 to 0.9154)	0.9898 (0.9298 to 0.9986)	
27 Months	1.0000 (1.0000 to 1.0000)	0.9593 (0.8789 to 0.9867)	0.8483 (0.7361 to 0.9154)	0.9898 (0.9298 to 0.9986)	
30 Months	1.0000 (1.0000 to 1.0000)	0.9593 (0.8789 to 0.9867)	0.8483 (0.7361 to 0.9154)	0.9898 (0.9298 to 0.9986)	

PT are presented if at least 5% of patients in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.75 Subgroup analysis by number of prior lines of therapy (IRT)
16.2.7.1.75.13 Treatment emergent severe adverse event per PT by treatment group according to number of prior lines of therapy (IRT) - Safety population

	1		>1		
	Kd (N=54)	**IKd (N=78)**	**Kd (N=68)**	**IKd (N=99)**	**p-value of treatment-by-sub group interaction[c]**
Number of patients at risk[b]					
3 Months	54	77	60	94	
6 Months	53	74	55	91	
9 Months	52	74	48	86	
12 Months	51	72	48	84	
15 Months	49	67	45	78	
18 Months	49	64	43	73	
21 Months	39	55	34	67	
24 Months	14	18	14	21	
27 Months	2	1	2	1	
30 Months	0	0	0	0	

PT are presented if at least 5% of patients in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.76 Subgroup analysis by cytogenetic abnormality (del(17p), t(4,14), t(14,16))
16.2.7.1.76.14 Treatment emergent severe adverse event per PT by treatment group according to cytogenetic abnormality (del(17p), t(4,14), t(14,16)) - Safety population

	At least one		None		
	Kd (N=30)	**IKd (N=42)**	**Kd (N=77)**	**IKd (N=113)**	**p-value of treatment-by-sub group interaction[c]**
27 Months	0.9246 (0.7281 to 0.9808)	0.8175 (0.6535 to 0.9090)	0.8615 (0.7576 to 0.9231)	0.8410 (0.7563 to 0.8982)	
30 Months	0.9246 (0.7281 to 0.9808)	0.8175 (0.6535 to 0.9090)	0.8615 (0.7576 to 0.9231)	0.8410 (0.7563 to 0.8982)	
Number of patients at risk[b]					
3 Months	29	40	71	105	
6 Months	27	36	67	101	
9 Months	25	34	61	98	
12 Months	24	33	59	93	
15 Months	21	29	55	86	
18 Months	21	28	53	82	
21 Months	18	24	41	72	
24 Months	7	9	16	22	
27 Months	0	0	3	1	
30 Months	0	0	0	0	
Thrombocytopenia (days)					

PT are presented if at least 5% of patients in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.76 Subgroup analysis by cytogenetic abnormality (del(17p), t(4,14), t(14,16))
16.2.7.1.76.14 Treatment emergent severe adverse event per PT by treatment group according to cytogenetic abnormality (del(17p), t(4,14), t(14,16)) - Safety population

	At least one		None		
	Kd (N=30)	**IKd (N=42)**	**Kd (N=77)**	**IKd (N=113)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	5 (16.7)	2 (4.8)	5 (6.5)	2 (1.8)	0.9703
Number (%) of patients censored	25 (83.3)	40 (95.2)	72 (93.5)	111 (98.2)	
Kaplan-Meier estimates of event in months					
25% quantile (95% CI)	NC (3.2526 to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.0943		0.0869	
Hazard ratio (95% CI) vs Kd	-	0.27 (0.05 to 1.40)		0.26 (0.05 to 1.36)	
P-value	-	0.1188		0.1115	
Events probability (95% CI)[b]					
3 Months	0.9333 (0.7589 to 0.9829)	0.9762 (0.8428 to 0.9966)	0.9477 (0.8666 to 0.9800)	0.9912 (0.9388 to 0.9987)	

PT are presented if at least 5% of patients in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.76 Subgroup analysis by cytogenetic abnormality (del(17p), t(4,14), t(14,16))
16.2.7.1.76.14 Treatment emergent severe adverse event per PT by treatment group according to cytogenetic abnormality (del(17p), t(4,14), t(14,16)) - Safety population

	At least one		None		
	Kd (N=30)	**IKd (N=42)**	**Kd (N=77)**	**IKd (N=113)**	**p-value of treatment-by-sub group interaction[c]**
6 Months	0.8667 (0.6828 to 0.9478)	0.9762 (0.8428 to 0.9966)	0.9477 (0.8666 to 0.9800)	0.9912 (0.9388 to 0.9987)	
9 Months	0.8320 (0.6423 to 0.9264)	0.9762 (0.8428 to 0.9966)	0.9340 (0.8485 to 0.9720)	0.9912 (0.9388 to 0.9987)	
12 Months	0.8320 (0.6423 to 0.9264)	0.9762 (0.8428 to 0.9966)	0.9340 (0.8485 to 0.9720)	0.9816 (0.9284 to 0.9954)	
15 Months	0.8320 (0.6423 to 0.9264)	0.9762 (0.8428 to 0.9966)	0.9340 (0.8485 to 0.9720)	0.9816 (0.9284 to 0.9954)	
18 Months	0.8320 (0.6423 to 0.9264)	0.9475 (0.8046 to 0.9867)	0.9340 (0.8485 to 0.9720)	0.9816 (0.9284 to 0.9954)	
21 Months	0.8320 (0.6423 to 0.9264)	0.9475 (0.8046 to 0.9867)	0.9340 (0.8485 to 0.9720)	0.9816 (0.9284 to 0.9954)	
24 Months	0.8320 (0.6423 to 0.9264)	0.9475 (0.8046 to 0.9867)	0.9340 (0.8485 to 0.9720)	0.9816 (0.9284 to 0.9954)	
27 Months	0.8320 (0.6423 to 0.9264)	0.9475 (0.8046 to 0.9867)	0.9340 (0.8485 to 0.9720)	0.9816 (0.9284 to 0.9954)	
30 Months	0.8320 (0.6423 to 0.9264)	0.9475 (0.8046 to 0.9867)	0.9340 (0.8485 to 0.9720)	0.9816 (0.9284 to 0.9954)	

PT are presented if at least 5% of patients in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.76 Subgroup analysis by cytogenetic abnormality (del(17p), t(4,14), t(14,16))
16.2.7.1.76.14 Treatment emergent severe adverse event per PT by treatment group according to cytogenetic abnormality (del(17p), t(4,14), t(14,16)) - Safety population

	At least one		None		
	Kd (N=30)	**IKd (N=42)**	**Kd (N=77)**	**IKd (N=113)**	**p-value of treatment-by-sub group interaction[c]**
Number of patients at risk[b]					
3 Months	28	41	72	109	
6 Months	25	39	69	106	
9 Months	22	37	64	104	
12 Months	22	37	64	101	
15 Months	21	34	60	95	
18 Months	21	32	58	91	
21 Months	17	27	46	81	
24 Months	7	10	17	25	
27 Months	0	0	4	2	
30 Months	0	0	0	0	

PT are presented if at least 5% of patients in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.77 Subgroup analysis by MM type
16.2.7.1.77.14 Treatment emergent severe adverse event per PT by treatment group according to MM type - Safety population

	IgG		Non-IgG		
	Kd (N=85)	**IKd (N=124)**	**Kd (N=37)**	**IKd (N=53)**	**p-value of treatment-by-sub group interaction[c]**
27 Months	0.8528 (0.7552 to 0.9137)	0.8431 (0.7621 to 0.8983)	0.9387 (0.7749 to 0.9844)	0.8220 (0.6852 to 0.9034)	
30 Months	0.8528 (0.7552 to 0.9137)	0.8431 (0.7621 to 0.8983)	0.9387 (0.7749 to 0.9844)	0.8220 (0.6852 to 0.9034)	
Number of patients at risk[b]					
3 Months	79	116	34	50	
6 Months	75	110	32	46	
9 Months	68	108	30	41	
12 Months	66	103	29	39	
15 Months	61	94	27	36	
18 Months	60	88	26	35	
21 Months	50	80	18	29	
24 Months	20	24	7	11	
27 Months	2	1	1	0	
30 Months	0	0	0	0	
Thrombocytopenia (days)					

PT are presented if at least 5% of patients in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.77 Subgroup analysis by MM type
16.2.7.1.77.14 Treatment emergent severe adverse event per PT by treatment group according to MM type - Safety population

	IgG		Non-IgG		
	Kd (N=85)	**IKd (N=124)**	**Kd (N=37)**	**IKd (N=53)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	4 (4.7)	2 (1.6)	6 (16.2)	2 (3.8)	0.7026
Number (%) of patients censored	81 (95.3)	122 (98.4)	31 (83.8)	51 (96.2)	
Kaplan-Meier estimates of event in months					
25% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (2.3326 to NC)	NC (NC to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.1902		0.0398	
Hazard ratio (95% CI) vs Kd	-	0.34 (0.06 to 1.85)		0.22 (0.04 to 1.08)	
P-value	-	0.2120		0.0616	
Events probability (95% CI)[b]					
3 Months	0.9762 (0.9081 to 0.9940)	0.9919 (0.9437 to 0.9989)	0.8911 (0.7352 to 0.9577)	0.9811 (0.8735 to 0.9973)	

PT are presented if at least 5% of patients in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.77 Subgroup analysis by MM type
16.2.7.1.77.14 Treatment emergent severe adverse event per PT by treatment group according to MM type - Safety population

	IgG		Non-IgG		
	Kd (N=85)	**IKd (N=124)**	**Kd (N=37)**	**IKd (N=53)**	**p-value of treatment-by-sub group interaction[c]**
6 Months	0.9643 (0.8934 to 0.9883)	0.9919 (0.9437 to 0.9989)	0.8632 (0.7020 to 0.9407)	0.9811 (0.8735 to 0.9973)	
9 Months	0.9519 (0.8769 to 0.9817)	0.9919 (0.9437 to 0.9989)	0.8345 (0.6678 to 0.9221)	0.9811 (0.8735 to 0.9973)	
12 Months	0.9519 (0.8769 to 0.9817)	0.9832 (0.9346 to 0.9958)	0.8345 (0.6678 to 0.9221)	0.9811 (0.8735 to 0.9973)	
15 Months	0.9519 (0.8769 to 0.9817)	0.9832 (0.9346 to 0.9958)	0.8345 (0.6678 to 0.9221)	0.9811 (0.8735 to 0.9973)	
18 Months	0.9519 (0.8769 to 0.9817)	0.9832 (0.9346 to 0.9958)	0.8345 (0.6678 to 0.9221)	0.9578 (0.8402 to 0.9894)	
21 Months	0.9519 (0.8769 to 0.9817)	0.9832 (0.9346 to 0.9958)	0.8345 (0.6678 to 0.9221)	0.9578 (0.8402 to 0.9894)	
24 Months	0.9519 (0.8769 to 0.9817)	0.9832 (0.9346 to 0.9958)	0.8345 (0.6678 to 0.9221)	0.9578 (0.8402 to 0.9894)	
27 Months	0.9519 (0.8769 to 0.9817)	0.9832 (0.9346 to 0.9958)	0.8345 (0.6678 to 0.9221)	0.9578 (0.8402 to 0.9894)	
30 Months	0.9519 (0.8769 to 0.9817)	0.9832 (0.9346 to 0.9958)	0.8345 (0.6678 to 0.9221)	0.9578 (0.8402 to 0.9894)	

PT are presented if at least 5% of patients in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.77 Subgroup analysis by MM type
16.2.7.1.77.14 Treatment emergent severe adverse event per PT by treatment group according to MM type - Safety population

	IgG		Non-IgG		
	Kd (N=85)	**IKd (N=124)**	**Kd (N=37)**	**IKd (N=53)**	**p-value of treatment-by-sub group interaction[c]**
Number of patients at risk[b]					
3 Months	82	119	32	52	
6 Months	78	116	30	49	
9 Months	73	115	27	45	
12 Months	72	111	27	45	
15 Months	68	103	26	42	
18 Months	67	97	25	40	
21 Months	56	89	17	33	
24 Months	20	28	8	11	
27 Months	3	2	1	0	
30 Months	0	0	0	0	

PT are presented if at least 5% of patients in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
PGM=DEVOPS/SAR650984/EFC15246/CIR_RWE/REPORT/PGM/ae_km_socpt_subgp_sr_s_t.sas OUT=REPORT/OUTPUT/ae_km_sevae34pt_semm_s_t_x.rtf (12FEB2021 8:24)

16.2.7.1 Safety endpoints
16.2.7.1.78 Subgroup analysis by previous autologous stem-cell
16.2.7.1.78.14 Treatment emergent severe adverse event per PT by treatment group according to previous autologous stem-cell - Safety population

	Yes		No		
	Kd (N=68)	**IKd (N=115)**	**Kd (N=54)**	**IKd (N=62)**	**p-value of treatment-by-sub group interaction[c]**
27 Months	0.9082 (0.8068 to 0.9577)	0.8591 (0.7768 to 0.9128)	0.8391 (0.7031 to 0.9163)	0.7946 (0.6660 to 0.8780)	
30 Months	0.9082 (0.8068 to 0.9577)	0.8591 (0.7768 to 0.9128)	0.8391 (0.7031 to 0.9163)	0.7946 (0.6660 to 0.8780)	
Number of patients at risk[b]					
3 Months	65	110	48	56	
6 Months	62	105	45	51	
9 Months	57	99	41	50	
12 Months	55	94	40	48	
15 Months	52	86	36	44	
18 Months	51	80	35	43	
21 Months	39	72	29	37	
24 Months	16	21	11	14	
27 Months	0	1	3	0	
30 Months	0	0	0	0	
Thrombocytopenia (days)					

PT are presented if at least 5% of patients in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.78 Subgroup analysis by previous autologous stem-cell
16.2.7.1.78.14 Treatment emergent severe adverse event per PT by treatment group according to previous autologous stem-cell - Safety population

	Yes		No		
	Kd (N=68)	**IKd (N=115)**	**Kd (N=54)**	**IKd (N=62)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	5 (7.4)	2 (1.7)	5 (9.3)	2 (3.2)	0.7382
Number (%) of patients censored	63 (92.6)	113 (98.3)	49 (90.7)	60 (96.8)	
Kaplan-Meier estimates of event in months					
25% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.0548		0.1796	
Hazard ratio (95% CI) vs Kd	-	0.23 (0.04 to 1.18)		0.34 (0.07 to 1.77)	
P-value	-	0.0788		0.2005	
Events probability (95% CI)[b]					
3 Months	0.9409 (0.8503 to 0.9774)	0.9913 (0.9399 to 0.9988)	0.9630 (0.8599 to 0.9906)	0.9839 (0.8910 to 0.9977)	

PT are presented if at least 5% of patients in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.78 Subgroup analysis by previous autologous stem-cell
16.2.7.1.78.14 Treatment emergent severe adverse event per PT by treatment group according to previous autologous stem-cell - Safety population

	Yes		No		
	Kd (N=68)	**IKd (N=115)**	**Kd (N=54)**	**IKd (N=62)**	**p-value of treatment-by-sub group interaction[c]**
6 Months	0.9409 (0.8503 to 0.9774)	0.9913 (0.9399 to 0.9988)	0.9252 (0.8128 to 0.9713)	0.9839 (0.8910 to 0.9977)	
9 Months	0.9255 (0.8302 to 0.9683)	0.9913 (0.9399 to 0.9988)	0.9055 (0.7876 to 0.9596)	0.9839 (0.8910 to 0.9977)	
12 Months	0.9255 (0.8302 to 0.9683)	0.9820 (0.9297 to 0.9955)	0.9055 (0.7876 to 0.9596)	0.9839 (0.8910 to 0.9977)	
15 Months	0.9255 (0.8302 to 0.9683)	0.9820 (0.9297 to 0.9955)	0.9055 (0.7876 to 0.9596)	0.9839 (0.8910 to 0.9977)	
18 Months	0.9255 (0.8302 to 0.9683)	0.9820 (0.9297 to 0.9955)	0.9055 (0.7876 to 0.9596)	0.9638 (0.8617 to 0.9909)	
21 Months	0.9255 (0.8302 to 0.9683)	0.9820 (0.9297 to 0.9955)	0.9055 (0.7876 to 0.9596)	0.9638 (0.8617 to 0.9909)	
24 Months	0.9255 (0.8302 to 0.9683)	0.9820 (0.9297 to 0.9955)	0.9055 (0.7876 to 0.9596)	0.9638 (0.8617 to 0.9909)	
27 Months	0.9255 (0.8302 to 0.9683)	0.9820 (0.9297 to 0.9955)	0.9055 (0.7876 to 0.9596)	0.9638 (0.8617 to 0.9909)	
30 Months	0.9255 (0.8302 to 0.9683)	0.9820 (0.9297 to 0.9955)	0.9055 (0.7876 to 0.9596)	0.9638 (0.8617 to 0.9909)	

PT are presented if at least 5% of patients in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.78 Subgroup analysis by previous autologous stem-cell
16.2.7.1.78.14 Treatment emergent severe adverse event per PT by treatment group according to previous autologous stem-cell - Safety population

	Yes		No		
	Kd (N=68)	**IKd (N=115)**	**Kd (N=54)**	**IKd (N=62)**	**p-value of treatment-by-sub group interaction[c]**
Number of patients at risk[b]					
3 Months	63	112	51	59	
6 Months	61	110	47	55	
9 Months	56	106	44	54	
12 Months	56	103	43	53	
15 Months	53	96	41	49	
18 Months	52	91	40	46	
21 Months	40	82	33	40	
24 Months	17	23	11	16	
27 Months	1	1	3	1	
30 Months	0	0	0	0	

PT are presented if at least 5% of patients in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.79 Subgroup analysis by baseline creatinine clearance (MDRD)
16.2.7.1.79.10 Treatment emergent severe adverse event per PT by treatment group according to baseline creatinine clearance (MDRD) - Safety population

	>=60 mL/min/1.73m2		<60 mL/min/1.73m2		
	Kd (N=92)	**IKd (N=120)**	**Kd (N=18)**	**IKd (N=43)**	**p-value of treatment-by-sub group interaction[c]**
27 Months	0.8787 (0.7916 to 0.9309)	0.8155 (0.7282 to 0.8771)	0.7843 (0.4640 to 0.9260)	0.8837 (0.7429 to 0.9499)	
30 Months	0.8787 (0.7916 to 0.9309)	0.8155 (0.7282 to 0.8771)	0.7843 (0.4640 to 0.9260)	0.8837 (0.7429 to 0.9499)	
Number of patients at risk[b]					
3 Months	87	112	15	40	
6 Months	85	105	13	39	
9 Months	79	98	11	39	
12 Months	76	94	11	38	
15 Months	71	85	9	36	
18 Months	71	80	7	34	
21 Months	54	71	7	30	
24 Months	20	23	4	10	
27 Months	3	0	0	1	
30 Months	0	0	0	0	
Thrombocytopenia (days)					

PT are presented if at least 5% of patients in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.79 Subgroup analysis by baseline creatinine clearance (MDRD)
16.2.7.1.79.10 Treatment emergent severe adverse event per PT by treatment group according to baseline creatinine clearance (MDRD) - Safety population

	>=60 mL/min/1.73m2		<60 mL/min/1.73m2		
	Kd (N=92)	**IKd (N=120)**	**Kd (N=18)**	**IKd (N=43)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	6 (6.5)	3 (2.5)	3 (16.7)	0 (0.0)	0.9913
Number (%) of patients censored	86 (93.5)	117 (97.5)	15 (83.3)	43 (100.0)	
Kaplan-Meier estimates of event in months					
25% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (0.2300 to NC)	NC (NC to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.1650		0.0035	
Hazard ratio (95% CI) vs Kd	-	0.39 (0.10 to 1.55)		NC	
P-value	-	0.1809		0.9966	
Events probability (95% CI)[b]					
3 Months	0.9565 (0.8883 to 0.9835)	0.9833 (0.9347 to 0.9958)	0.9444 (0.6664 to 0.9920)	1.0000 (1.0000 to 1.0000)	

PT are presented if at least 5% of patients in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.79 Subgroup analysis by baseline creatinine clearance (MDRD)
16.2.7.1.79.10 Treatment emergent severe adverse event per PT by treatment group according to baseline creatinine clearance (MDRD) - Safety population

	>=60 mL/min/1.73m2		<60 mL/min/1.73m2		
	Kd (N=92)	**IKd (N=120)**	**Kd (N=18)**	**IKd (N=43)**	**p-value of treatment-by-sub group interaction[c]**
6 Months	0.9348 (0.8606 to 0.9702)	0.9833 (0.9347 to 0.9958)	0.9444 (0.6664 to 0.9920)	1.0000 (1.0000 to 1.0000)	
9 Months	0.9348 (0.8606 to 0.9702)	0.9833 (0.9347 to 0.9958)	0.8095 (0.5156 to 0.9348)	1.0000 (1.0000 to 1.0000)	
12 Months	0.9348 (0.8606 to 0.9702)	0.9740 (0.9214 to 0.9916)	0.8095 (0.5156 to 0.9348)	1.0000 (1.0000 to 1.0000)	
15 Months	0.9348 (0.8606 to 0.9702)	0.9740 (0.9214 to 0.9916)	0.8095 (0.5156 to 0.9348)	1.0000 (1.0000 to 1.0000)	
18 Months	0.9348 (0.8606 to 0.9702)	0.9740 (0.9214 to 0.9916)	0.8095 (0.5156 to 0.9348)	1.0000 (1.0000 to 1.0000)	
21 Months	0.9348 (0.8606 to 0.9702)	0.9740 (0.9214 to 0.9916)	0.8095 (0.5156 to 0.9348)	1.0000 (1.0000 to 1.0000)	
24 Months	0.9348 (0.8606 to 0.9702)	0.9740 (0.9214 to 0.9916)	0.8095 (0.5156 to 0.9348)	1.0000 (1.0000 to 1.0000)	
27 Months	0.9348 (0.8606 to 0.9702)	0.9740 (0.9214 to 0.9916)	0.8095 (0.5156 to 0.9348)	1.0000 (1.0000 to 1.0000)	
30 Months	0.9348 (0.8606 to 0.9702)	0.9740 (0.9214 to 0.9916)	0.8095 (0.5156 to 0.9348)	1.0000 (1.0000 to 1.0000)	

PT are presented if at least 5% of patients in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.

16.2.7.1 Safety endpoints
16.2.7.1.79 Subgroup analysis by baseline creatinine clearance (MDRD)
16.2.7.1.79.10 Treatment emergent severe adverse event per PT by treatment group according to baseline creatinine clearance (MDRD) - Safety population

	>=60 mL/min/1.73m2		<60 mL/min/1.73m2		
	Kd (N=92)	**IKd (N=120)**	**Kd (N=18)**	**IKd (N=43)**	**p-value of treatment-by-sub group interaction[c]**
Number of patients at risk[b]					
3 Months	88	114	16	43	
6 Months	86	110	14	42	
9 Months	82	106	11	41	
12 Months	81	104	11	41	
15 Months	77	96	10	39	
18 Months	77	91	8	37	
21 Months	59	82	7	32	
24 Months	21	27	4	10	
27 Months	4	1	0	1	
30 Months	0	0	0	0	

PT are presented if at least 5% of patients in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.80 Subgroup analysis by previous treament with PI
16.2.7.1.80.12 Treatment emergent severe adverse event per PT by treatment group according to previous treament with PI - Safety population

	Yes		No		
	Kd (N=47)	**IKd (N=79)**	**Kd (N=75)**	**IKd (N=98)**	**p-value of treatment-by-sub group interaction[c]**
27 Months	0.8196 (0.6707 to 0.9056)	0.8235 (0.7147 to 0.8938)	0.9132 (0.8167 to 0.9601)	0.8467 (0.7546 to 0.9064)	
30 Months	0.8196 (0.6707 to 0.9056)	0.8235 (0.7147 to 0.8938)	0.9132 (0.8167 to 0.9601)	0.8467 (0.7546 to 0.9064)	
Number of patients at risk[b]					
3 Months	41	73	72	93	
6 Months	40	69	67	87	
9 Months	35	65	63	84	
12 Months	35	61	60	81	
15 Months	31	57	57	73	
18 Months	30	53	56	70	
21 Months	24	45	44	64	
24 Months	11	12	16	23	
27 Months	2	0	1	1	
30 Months	0	0	0	0	
Thrombocytopenia (days)					

PT are presented if at least 5% of patients in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.80 Subgroup analysis by previous treament with PI
16.2.7.1.80.12 Treatment emergent severe adverse event per PT by treatment group according to previous treament with PI - Safety population

	Yes		No		
	Kd (N=47)	**IKd (N=79)**	**Kd (N=75)**	**IKd (N=98)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	4 (8.5)	2 (2.5)	6 (8.0)	2 (2.0)	0.8758
Number (%) of patients censored	43 (91.5)	77 (97.5)	69 (92.0)	96 (98.0)	
Kaplan-Meier estimates of event in months					
25% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.1351		0.0618	
Hazard ratio (95% CI) vs Kd	-	0.30 (0.05 to 1.62)		0.25 (0.05 to 1.21)	
P-value	-	0.1599		0.0850	
Events probability (95% CI)[b]					
3 Months	0.9574 (0.8404 to 0.9892)	0.9872 (0.9125 to 0.9982)	0.9459 (0.8623 to 0.9794)	0.9898 (0.9298 to 0.9986)	

PT are presented if at least 5% of patients in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.80 Subgroup analysis by previous treament with PI
16.2.7.1.80.12 Treatment emergent severe adverse event per PT by treatment group according to previous treament with PI - Safety population

	Yes		No		
	Kd (N=47)	**IKd (N=79)**	**Kd (N=75)**	**IKd (N=98)**	**p-value of treatment-by-sub group interaction[c]**
6 Months	0.9362 (0.8150 to 0.9790)	0.9872 (0.9125 to 0.9982)	0.9322 (0.8448 to 0.9712)	0.9898 (0.9298 to 0.9986)	
9 Months	0.9144 (0.7878 to 0.9670)	0.9872 (0.9125 to 0.9982)	0.9179 (0.8262 to 0.9623)	0.9898 (0.9298 to 0.9986)	
12 Months	0.9144 (0.7878 to 0.9670)	0.9872 (0.9125 to 0.9982)	0.9179 (0.8262 to 0.9623)	0.9788 (0.9178 to 0.9947)	
15 Months	0.9144 (0.7878 to 0.9670)	0.9872 (0.9125 to 0.9982)	0.9179 (0.8262 to 0.9623)	0.9788 (0.9178 to 0.9947)	
18 Months	0.9144 (0.7878 to 0.9670)	0.9713 (0.8890 to 0.9928)	0.9179 (0.8262 to 0.9623)	0.9788 (0.9178 to 0.9947)	
21 Months	0.9144 (0.7878 to 0.9670)	0.9713 (0.8890 to 0.9928)	0.9179 (0.8262 to 0.9623)	0.9788 (0.9178 to 0.9947)	
24 Months	0.9144 (0.7878 to 0.9670)	0.9713 (0.8890 to 0.9928)	0.9179 (0.8262 to 0.9623)	0.9788 (0.9178 to 0.9947)	
27 Months	0.9144 (0.7878 to 0.9670)	0.9713 (0.8890 to 0.9928)	0.9179 (0.8262 to 0.9623)	0.9788 (0.9178 to 0.9947)	
30 Months	0.9144 (0.7878 to 0.9670)	0.9713 (0.8890 to 0.9928)	0.9179 (0.8262 to 0.9623)	0.9788 (0.9178 to 0.9947)	

PT are presented if at least 5% of patients in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
PGM=DEVOPS/SAR650984/EFC15246/CIR_RWE/REPORT/PGM/ae_km_socpt_subgp_sr_s_t.sas OUT=REPORT/OUTPUT/ae_km_sevae34pt_pi_s_t_x.rtf (12FEB2021 8:24)

16.2.7.1 Safety endpoints
16.2.7.1.80 Subgroup analysis by previous treament with PI
16.2.7.1.80.12 Treatment emergent severe adverse event per PT by treatment group according to previous treament with PI - Safety population

	Yes		No		
	Kd (N=47)	**IKd (N=79)**	**Kd (N=75)**	**IKd (N=98)**	**p-value of treatment-by-sub group interaction[c]**
Number of patients at risk[b]					
3 Months	45	76	69	95	
6 Months	43	72	65	93	
9 Months	39	70	61	90	
12 Months	38	67	61	89	
15 Months	36	62	58	83	
18 Months	35	57	57	80	
21 Months	28	49	45	73	
24 Months	11	12	17	27	
27 Months	2	0	2	2	
30 Months	0	0	0	0	

PT are presented if at least 5% of patients in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.81 Subgroup analysis by previous treatment with IMiD
16.2.7.1.81.12 Treatment emergent severe adverse event per PT by treatment group according to previous treatment with IMiD - Safety population

	Yes		No		
	Kd (N=62)	**IKd (N=80)**	**Kd (N=60)**	**IKd (N=97)**	**p-value of treatment-by-sub group interaction[c]**
27 Months	0.8903 (0.7717 to 0.9492)	0.8500 (0.7449 to 0.9142)	0.8640 (0.7461 to 0.9296)	0.8248 (0.7296 to 0.8890)	
30 Months	0.8903 (0.7717 to 0.9492)	0.8500 (0.7449 to 0.9142)	0.8640 (0.7461 to 0.9296)	0.8248 (0.7296 to 0.8890)	
Number of patients at risk[b]					
3 Months	59	77	54	89	
6 Months	54	72	53	84	
9 Months	50	69	48	80	
12 Months	48	66	47	76	
15 Months	46	58	42	72	
18 Months	45	56	41	67	
21 Months	36	49	32	60	
24 Months	14	19	13	16	
27 Months	2	0	1	1	
30 Months	0	0	0	0	
Thrombocytopenia (days)					

PT are presented if at least 5% of patients in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.81 Subgroup analysis by previous treatment with IMiD
16.2.7.1.81.12 Treatment emergent severe adverse event per PT by treatment group according to previous treatment with IMiD - Safety population

	Yes		No		
	Kd (N=62)	**IKd (N=80)**	**Kd (N=60)**	**IKd (N=97)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	8 (12.9)	1 (1.3)	2 (3.3)	3 (3.1)	0.0929
Number (%) of patients censored	54 (87.1)	79 (98.8)	58 (96.7)	94 (96.9)	
Kaplan-Meier estimates of event in months					
25% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.0046		0.9373	
Hazard ratio (95% CI) vs Kd	-	0.09 (0.01 to 0.73)		0.93 (0.16 to 5.57)	
P-value	-	0.0241		0.9373	
Events probability (95% CI)[b]					
3 Months	0.9018 (0.7944 to 0.9547)	0.9875 (0.9146 to 0.9982)	1.0000 (1.0000 to 1.0000)	0.9897 (0.9291 to 0.9985)	

PT are presented if at least 5% of patients in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
PGM=DEVOPS/SAR650984/EFC15246/CIR_RWE/REPORT/PGM/ae_km_socpt_subgp_sr_s_t.sas OUT=REPORT/OUTPUT/ae_km_sevae34pt_imid_s_t_x.rtf (12FEB2021 8:24)

16.2.7.1 Safety endpoints
16.2.7.1.81 Subgroup analysis by previous treatment with IMiD
16.2.7.1.81.12 Treatment emergent severe adverse event per PT by treatment group according to previous treatment with IMiD - Safety population

	Yes		No		
	Kd (N=62)	**IKd (N=80)**	**Kd (N=60)**	**IKd (N=97)**	**p-value of treatment-by-sub group interaction[c]**
6 Months	0.8851 (0.7740 to 0.9435)	0.9875 (0.9146 to 0.9982)	0.9833 (0.8875 to 0.9976)	0.9897 (0.9291 to 0.9985)	
9 Months	0.8674 (0.7521 to 0.9315)	0.9875 (0.9146 to 0.9982)	0.9664 (0.8722 to 0.9915)	0.9897 (0.9291 to 0.9985)	
12 Months	0.8674 (0.7521 to 0.9315)	0.9875 (0.9146 to 0.9982)	0.9664 (0.8722 to 0.9915)	0.9784 (0.9164 to 0.9946)	
15 Months	0.8674 (0.7521 to 0.9315)	0.9875 (0.9146 to 0.9982)	0.9664 (0.8722 to 0.9915)	0.9784 (0.9164 to 0.9946)	
18 Months	0.8674 (0.7521 to 0.9315)	0.9875 (0.9146 to 0.9982)	0.9664 (0.8722 to 0.9915)	0.9662 (0.8986 to 0.9890)	
21 Months	0.8674 (0.7521 to 0.9315)	0.9875 (0.9146 to 0.9982)	0.9664 (0.8722 to 0.9915)	0.9662 (0.8986 to 0.9890)	
24 Months	0.8674 (0.7521 to 0.9315)	0.9875 (0.9146 to 0.9982)	0.9664 (0.8722 to 0.9915)	0.9662 (0.8986 to 0.9890)	
27 Months	0.8674 (0.7521 to 0.9315)	0.9875 (0.9146 to 0.9982)	0.9664 (0.8722 to 0.9915)	0.9662 (0.8986 to 0.9890)	
30 Months	0.8674 (0.7521 to 0.9315)	0.9875 (0.9146 to 0.9982)	0.9664 (0.8722 to 0.9915)	0.9662 (0.8986 to 0.9890)	

PT are presented if at least 5% of patients in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.81 Subgroup analysis by previous treatment with IMiD
16.2.7.1.81.12 Treatment emergent severe adverse event per PT by treatment group according to previous treatment with IMiD - Safety population

	Yes		No		
	Kd (N=62)	**IKd (N=80)**	**Kd (N=60)**	**IKd (N=97)**	**p-value of treatment-by-sub group interaction[c]**
Number of patients at risk[b]					
3 Months	54	77	60	94	
6 Months	50	75	58	90	
9 Months	47	72	53	88	
12 Months	47	71	52	85	
15 Months	46	65	48	80	
18 Months	45	63	47	74	
21 Months	37	55	36	67	
24 Months	14	22	14	17	
27 Months	3	1	1	1	
30 Months	0	0	0	0	

PT are presented if at least 5% of patients in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.82 Subgroup analysis by previous treatment with PI and IMiD
16.2.7.1.82.11 Treatment emergent severe adverse event per PT by treatment group according to previous treatment with PI and IMiD - Safety population

	Yes		No		
	Kd (N=17)	**IKd (N=22)**	**Kd (N=105)**	**IKd (N=155)**	**p-value of treatment-by-sub group interaction[c]**
27 Months	0.8667 (0.5639 to 0.9649)	0.9500 (0.6947 to 0.9928)	0.8803 (0.7986 to 0.9303)	0.8206 (0.7474 to 0.8743)	
30 Months	0.8667 (0.5639 to 0.9649)	0.9500 (0.6947 to 0.9928)	0.8803 (0.7986 to 0.9303)	0.8206 (0.7474 to 0.8743)	
Number of patients at risk[b]					
3 Months	16	21	97	145	
6 Months	15	20	92	136	
9 Months	14	19	84	130	
12 Months	14	18	81	124	
15 Months	13	17	75	113	
18 Months	13	16	73	107	
21 Months	11	15	57	94	
24 Months	6	6	21	29	
27 Months	1	0	2	1	
30 Months	0	0	0	0	
Thrombocytopenia (days)					

PT are presented if at least 5% of patients in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.82 Subgroup analysis by previous treatment with PI and IMiD
16.2.7.1.82.11 Treatment emergent severe adverse event per PT by treatment group according to previous treatment with PI and IMiD - Safety population

	Yes		No		
	Kd (N=17)	**IKd (N=22)**	**Kd (N=105)**	**IKd (N=155)**	**p-value of treatment-by-sub group interaction[c]**
Number (%) of events	3 (17.6)	1 (4.5)	7 (6.7)	3 (1.9)	0.9208
Number (%) of patients censored	14 (82.4)	21 (95.5)	98 (93.3)	152 (98.1)	
Kaplan-Meier estimates of event in months					
25% quantile (95% CI)	NC (0.2300 to NC)	NC (0.4600 to NC)	NC (NC to NC)	NC (NC to NC)	
Median (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
75% quantile (95% CI)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	NC (NC to NC)	
Comparison vs. Kd					
Log-Rank test p-value[a] vs Kd	-	0.1936		0.0499	
Hazard ratio (95% CI) vs Kd	-	0.25 (0.03 to 2.40)		0.28 (0.07 to 1.09)	
P-value	-	0.2297		0.0664	
Events probability (95% CI)[b]					
3 Months	0.8824 (0.6060 to 0.9692)	0.9545 (0.7187 to 0.9935)	0.9615 (0.9007 to 0.9854)	0.9935 (0.9551 to 0.9991)	

PT are presented if at least 5% of patients in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.82 Subgroup analysis by previous treatment with PI and IMiD
16.2.7.1.82.11 Treatment emergent severe adverse event per PT by treatment group according to previous treatment with PI and IMiD - Safety population

	Yes		No		
	Kd (N=17)	**IKd (N=22)**	**Kd (N=105)**	**IKd (N=155)**	**p-value of treatment-by-sub group interaction[c]**
6 Months	0.8824 (0.6060 to 0.9692)	0.9545 (0.7187 to 0.9935)	0.9421 (0.8757 to 0.9736)	0.9935 (0.9551 to 0.9991)	
9 Months	0.8193 (0.5377 to 0.9380)	0.9545 (0.7187 to 0.9935)	0.9321 (0.8628 to 0.9670)	0.9935 (0.9551 to 0.9991)	
12 Months	0.8193 (0.5377 to 0.9380)	0.9545 (0.7187 to 0.9935)	0.9321 (0.8628 to 0.9670)	0.9865 (0.9470 to 0.9966)	
15 Months	0.8193 (0.5377 to 0.9380)	0.9545 (0.7187 to 0.9935)	0.9321 (0.8628 to 0.9670)	0.9865 (0.9470 to 0.9966)	
18 Months	0.8193 (0.5377 to 0.9380)	0.9545 (0.7187 to 0.9935)	0.9321 (0.8628 to 0.9670)	0.9788 (0.9355 to 0.9931)	
21 Months	0.8193 (0.5377 to 0.9380)	0.9545 (0.7187 to 0.9935)	0.9321 (0.8628 to 0.9670)	0.9788 (0.9355 to 0.9931)	
24 Months	0.8193 (0.5377 to 0.9380)	0.9545 (0.7187 to 0.9935)	0.9321 (0.8628 to 0.9670)	0.9788 (0.9355 to 0.9931)	
27 Months	0.8193 (0.5377 to 0.9380)	0.9545 (0.7187 to 0.9935)	0.9321 (0.8628 to 0.9670)	0.9788 (0.9355 to 0.9931)	
30 Months	0.8193 (0.5377 to 0.9380)	0.9545 (0.7187 to 0.9935)	0.9321 (0.8628 to 0.9670)	0.9788 (0.9355 to 0.9931)	

PT are presented if at least 5% of patients in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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16.2.7.1 Safety endpoints
16.2.7.1.82 Subgroup analysis by previous treatment with PI and IMiD
16.2.7.1.82.11 Treatment emergent severe adverse event per PT by treatment group according to previous treatment with PI and IMiD - Safety population

	Yes		No		
	Kd (N=17)	**IKd (N=22)**	**Kd (N=105)**	**IKd (N=155)**	**p-value of treatment-by-sub group interaction[c]**
Number of patients at risk[b]					
3 Months	15	20	99	151	
6 Months	14	19	94	146	
9 Months	13	19	87	141	
12 Months	13	18	86	138	
15 Months	13	17	81	128	
18 Months	13	16	79	121	
21 Months	11	15	62	107	
24 Months	5	5	23	34	
27 Months	1	0	3	2	
30 Months	0	0	0	0	

PT are presented if at least 5% of patients in a arm
CI: Confidence interval, HR: Hazard ratio, NA:Not Applicable / Not Calculable
CI for Kaplan-Meier estimates are calculated with log-log transformation of survival function and methods of Brookmeyer and Crowley
[a] One-sided significance level is 0.025
[b] Estimated using the Kaplan-Meier method
[c] P-value for treatment-by-subgroup factor interaction are based on Cox proportional hazard model including treatment, subgroup variables, and the treatment-by-subgroup interaction as covariates.
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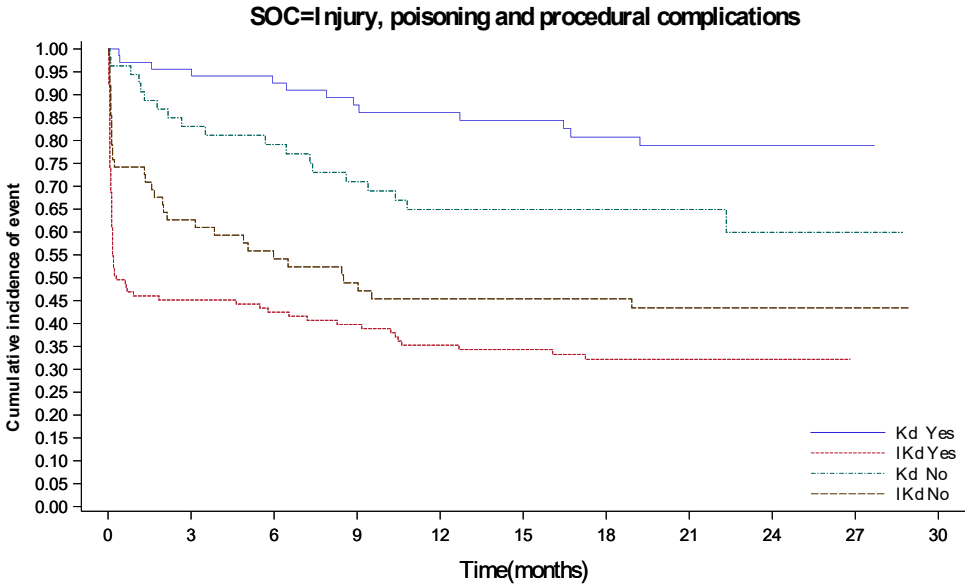
16.2.7.1 Safety endpoints
16.2.7.1.78 Subgroup analysis by previous autologous stem-cell
16.2.7.1.78.2 Kaplan-Meier cumulative incidence curve of treatment emergent adverse event per SOC by treatment group according to previous autologous stem-cell - Safety population

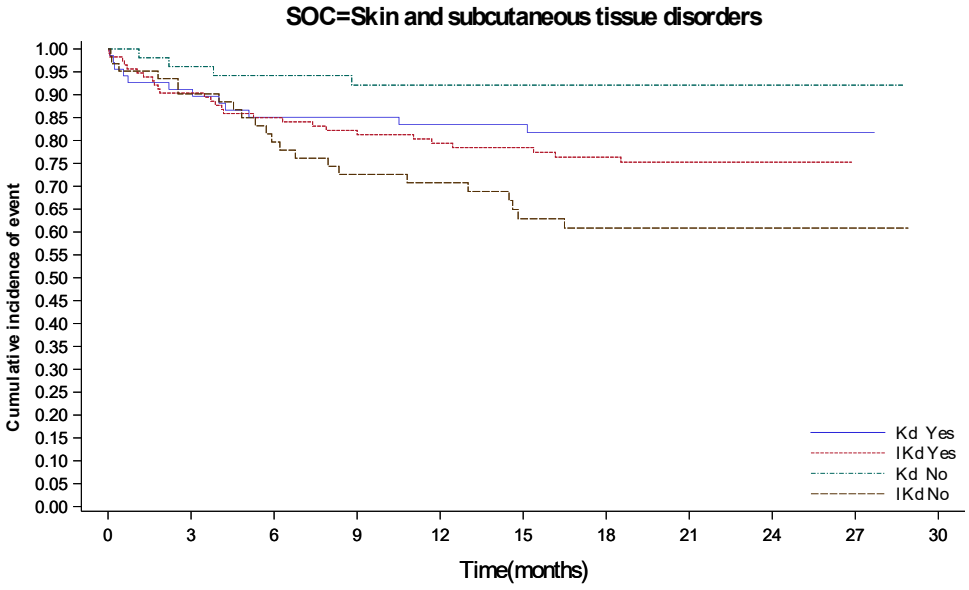


Number at Risk

Kd Yes	68	64	60	53	51	47	44	33	13	1	0
IKd Yes	115	51	48	44	39	34	30	27	6	0	
Kd No	54	44	39	35	31	29	28	22	7	2	0
IKd No	62	38	31	28	25	24	23	19	8	1	0

SOC are presented if at least 10 events in a arm
PGM=DEVOPS/SAR650984/EFC15246/CIR_RWE/REPORT/PGM/ae_km_socpt_subgrp_s_f.sas OUT=REPORT/OUTPUT/ae_km_teaesoc_auto_s_f_x.rtf (09FEB2021 12:44)

16.2.7.1 Safety endpoints
16.2.7.1.78 Subgroup analysis by previous autologous stem-cell
16.2.7.1.78.2 Kaplan-Meier cumulative incidence curve of treatment emergent adverse event per SOC by treatment group according to previous autologous stem-cell - Safety population

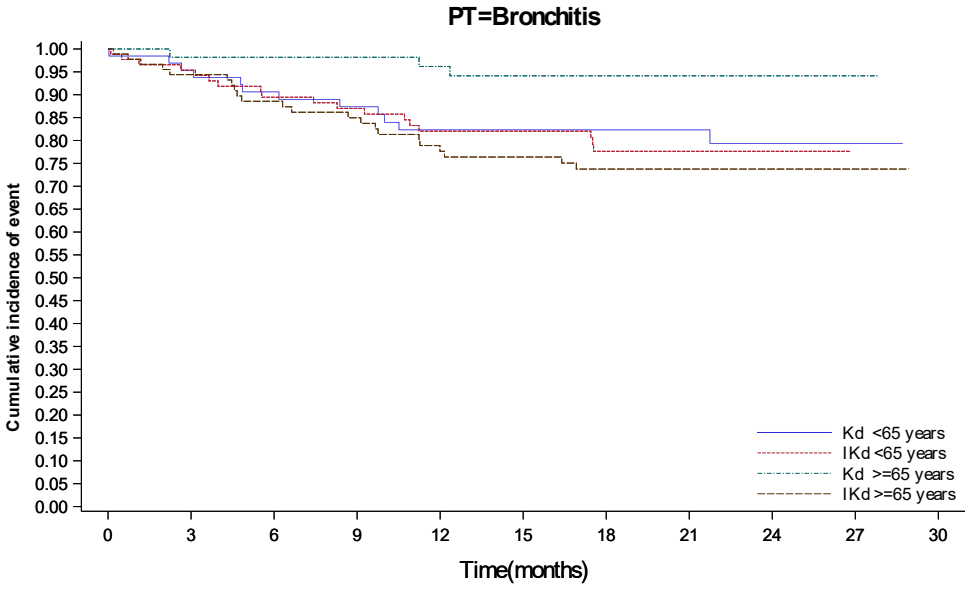


Number at Risk

Kd Yes	68	61	55	53	51	48	46	36	14	1	0
IKd Yes	115	102	93	88	84	77	70	61	17	0	
Kd No	54	50	46	43	42	39	38	32	10	2	0
IKd No	62	54	45	40	38	31	29	25	7	1	0

SOC are presented if at least 10 events in a arm

16.2.7.1 Safety endpoints
16.2.7.1.67 Subgroup analysis by age
16.2.7.1.67.4 Kaplan-Meier cumulative incidence curve of treatment emergent adverse event per PT by treatment group according to age - Safety population

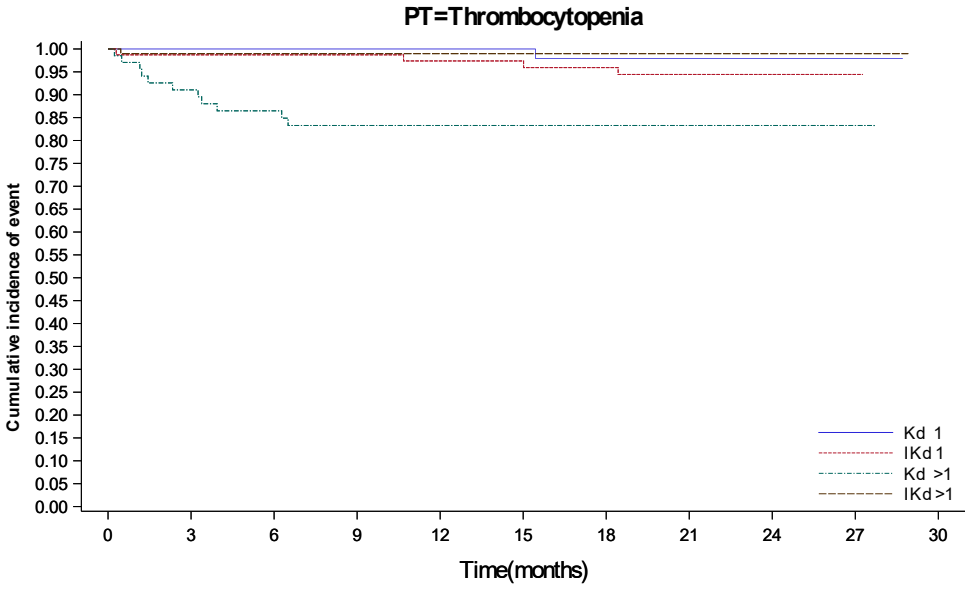


Number at Risk

Kd <65 years	65	61	56	52	48	44	43	30	15	1	0
IKd <65 years	87	81	74	70	65	59	53	48	15	0	
Kd >=65 years	57	54	52	49	47	44	43	37	9	3	0
IKd >=65 years	90	84	74	70	62	58	53	44	15	1	0

PT are presented if at least 10 events in a arm
PGM=DEVOPS/SAR650984/EFC15246/CIR_RWE/REPORT/PGM/ae_km_socpt_subgrp_s_f.sas OUT=REPORT/OUTPUT/ae_km_teaept_age_s_f_x.rtf (09FEB2021 12:44)

16.2.7.1 Safety endpoints
16.2.7.1.75 Subgroup analysis by number of prior lines of therapy (IRT)
16.2.7.1.75.4 Kaplan-Meier cumulative incidence curve of treatment emergent adverse event per PT by treatment group according to number of prior lines of therapy (IRT) - Safety population

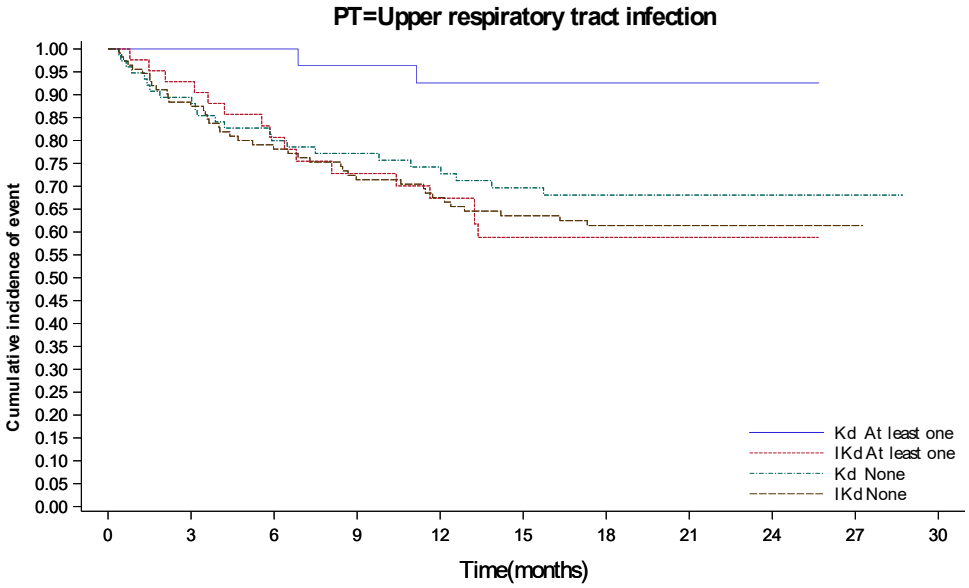


Number at Risk

Kd 1	54	54	53	52	51	49	48	38	14	2	0
IKd 1	78	77	74	74	72	67	64	54	18	1	0
Kd >1	68	60	54	47	47	44	42	33	13	2	0
IKd >1	99	94	91	86	84	78	73	67	21	1	0

PT are presented if at least 10 events in a arm
PGM=DEVOPS/SAR650984/EFC15246/CIR_RWE/REPORT/PGM/ae_km_socpt_subgrp_s_f.sas OUT=REPORT/OUTPUT/ae_km_teaept_plne_s_f_x.rtf (09FEB2021 12:45)

16.2.7.1 Safety endpoints
16.2.7.1.76 Subgroup analysis by cytogenetic abnormality (del(17p), t(4,14), t(14,16))
16.2.7.1.76.4 Kaplan-Meier cumulative incidence curve of treatment emergent adverse event per PT by treatment group according to cytogenetic abnormality (del(17p), t(4,14), t(14,16)) - Safety population



Number at Risk

Kd At least one	30	30	28	25	23	21	21	17	7	0	
IKd At least one	42	39	31	27	25	19	19	16	7	0	
Kd None	77	67	58	52	50	44	42	34	12	3	0
IKd None	113	96	83	74	69	61	56	50	13	1	0

PT are presented if at least 10 events in a arm
PGM=DEVOPS/SAR650984/EFC15246/CIR_RWE/REPORT/PGM/ae_km_socpt_subgrp_s_f.sas OUT=REPORT/OUTPUT/ae_km_teaept_cyto_s_f_x.rtf (09FEB2021 12:44)