

Dossier zur Nutzenbewertung gemäß § 35a SGB V

Vimseltinib (ROMVIMZA®)

Deciphera Pharmaceuticals (Netherlands) B.V.

Modul 4 A – Anhang 4-G

*Behandlung von erwachsenen Patienten mit
symptomatischen tenosynovialen Riesenzelltumoren
(Tenosynovial Giant Cell Tumours, TGCT), die mit
einer klinisch relevanten Verschlechterung der
körperlichen Funktionsfähigkeit assoziiert sind und bei
denen chirurgische Optionen ausgeschöpft sind oder zu
einer inakzeptablen Morbidität oder Behinderung
führen würden*

Ergänzende Informationen zur Studie MOTION

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4 Subgruppenanalysen für die Studie MOTION

4.1 Subgruppenanalysen für Morbiditätsendpunkte

4.1.1 Subgruppenanalysen für Schmerzen gemessen mittels BPI

4.1.1.1 Subgruppenanalysen für die Veränderung der Skalenwerte der NRS für stärkste Schmerzen des BPI gegenüber dem Ausgangswert während der randomisierten, kontrollierten Studienphase

Subgroup Level Analysis Visit		Vimseltinib (N=83)	Placebo (N=40)
Sex	Interaction p-value [1]	0.4849	
Male			
Overall treatment effect	n'	37	13
	LS mean (SE) [2]	-1.4 (0.26)	-0.4 (0.31)
	LS mean difference (95% CI) p-value [2]	-1.0 (-1.8; -0.2) 0.0116	
	Hedges' g (95% CI)	-0.822 (-1.470; -0.174)	
Female			
Overall treatment effect	n'	46	26
	LS mean (SE) [2]	-1.9 (0.21)	-0.5 (0.25)
	LS mean difference (95% CI) p-value [2]	-1.4 (-2.0; -0.7) <.0001	
	Hedges' g (95% CI)	-0.999 (-1.503; -0.494)	
Age group	Interaction p-value [1]	NC	
18 - < 50			
Overall treatment effect	n'	54	27
	LS mean (SE) [2]	NC (NC)	NC (NC)
	LS mean difference (95% CI) p-value [2]	NC (NC; NC) NC	
	Hedges' g (95% CI)	NC (NC; NC)	
50 - < 65			
Overall treatment effect	n'	24	9
	LS mean (SE) [2]	NC (NC)	NC (NC)
	LS mean difference (95% CI) p-value [2]	NC (NC; NC) NC	

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

Subgroup Level Analysis Visit		Vimseltinib (N=83)	Placebo (N=40)
	Hedges' g (95% CI)	NC (NC; NC)	
≥ 65			
Overall treatment effect	n'	5	4
	LS mean (SE) [2]	NC (NC)	NC (NC)
	LS mean difference (95% CI) p-value [2]	NC (NC; NC) NC	
	Hedges' g (95% CI)	NC (NC; NC)	
Region	Interaction p-value [1]	0.3317	
U.S.			
Overall treatment effect	n'	9	4
	LS mean (SE) [2]	-1.4 (0.50)	-0.8 (0.53)
	LS mean difference (95% CI) p-value [2]	-0.5 (-2.0; 0.9) 0.4619	
	Hedges' g (95% CI)	-0.441 (-1.623; 0.742)	
Non-U.S.			
Overall treatment effect	n'	74	35
	LS mean (SE) [2]	-1.7 (0.18)	-0.4 (0.23)
	LS mean difference (95% CI) p-value [2]	-1.3 (-1.8; -0.7) <.0001	
	Hedges' g (95% CI)	-0.887 (-1.303; -0.470)	
Site in Europe	Interaction p-value [1]	0.8814	
Yes			
Overall treatment effect	n'	57	31
	LS mean (SE) [2]	-1.7 (0.21)	-0.5 (0.25)
	LS mean difference (95% CI) p-value [2]	-1.2 (-1.9; -0.6) 0.0002	
	Hedges' g (95% CI)	-0.843 (-1.295; -0.391)	
No			
Overall treatment effect	n'	26	8
	LS mean (SE) [2]	-1.6 (0.28)	-0.4 (0.35)
	LS mean difference (95% CI) p-value [2]	-1.2 (-2.1; -0.3) 0.0127	
	Hedges' g (95% CI)	-1.017 (-1.840; -0.193)	
Disease subtype	Interaction p-value [1]	0.9088	

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

Subgroup Level Analysis Visit		Vimseltinib (N=83)	Placebo (N=40)
Localized			
Overall treatment effect	n'	26	10
	LS mean (SE) [2]	-1.7 (0.24)	-0.4 (0.45)
	LS mean difference (95% CI) p-value [2]	-1.3 (-2.3; -0.3) 0.0122	
	Hedges' g (95% CI)	-0.941 (-1.697; -0.185)	
Diffuse			
Overall treatment effect	n'	57	27
	LS mean (SE) [2]	-1.7 (0.22)	-0.5 (0.23)
	LS mean difference (95% CI) p-value [2]	-1.2 (-1.9; -0.6) 0.0002	
	Hedges' g (95% CI)	-0.891 (-1.365; -0.416)	
Missing			
Overall treatment effect	n'	0	2
	LS mean (SE) [2]	NC (NC)	NC (NC)
	LS mean difference (95% CI) p-value [2]	NC (NC; NC) NC	
	Hedges' g (95% CI)	NC (NC; NC)	
Tumour location	Interaction p-value [1]	0.0023	
Lower Limb			
Overall treatment effect	n'	77	34
	LS mean (SE) [2]	-1.6 (0.18)	-0.6 (0.23)
	LS mean difference (95% CI) p-value [2]	-1.0 (-1.5; -0.4) 0.0013	
	Hedges' g (95% CI)	-0.674 (-1.084; -0.263)	
All Other			
Overall treatment effect	n'	6	5
	LS mean (SE) [2]	-3.3 (0.76)	0.2 (0.30)
	LS mean difference (95% CI) p-value [2]	-3.6 (-5.2; -2.0) <.0001	
	Hedges' g (95% CI)	-2.635 (-4.249; -1.022)	
Disease location joint size	Interaction p-value [1]	0.0930	
Large Joints			
Overall treatment effect	n'	69	28
	LS mean (SE) [2]	-1.6 (0.18)	-0.6 (0.24)

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

Subgroup Level Analysis Visit		Vimseltinib (N=83)	Placebo (N=40)
	LS mean difference (95% CI) p-value [2]	-1.0 (-1.6; -0.4) 0.0014	
	Hedges' g (95% CI)	-0.729 (-1.177; -0.281)	
Small Joints			
Overall treatment effect	n'	14	11
	LS mean (SE) [2]	-2.2 (0.52)	-0.2 (0.33)
	LS mean difference (95% CI) p-value [2]	-2.1 (-3.3; -0.8) 0.0013	
	Hedges' g (95% CI)	-1.319 (-2.185; -0.453)	
Disease location knee	Interaction p-value [1]	0.0517	
Yes			
Overall treatment effect	n'	56	26
	LS mean (SE) [2]	-1.5 (0.19)	-0.6 (0.25)
	LS mean difference (95% CI) p-value [2]	-0.9 (-1.5; -0.3) 0.0056	
	Hedges' g (95% CI)	-0.666 (-1.139; -0.193)	
No			
Overall treatment effect	n'	27	13
	LS mean (SE) [2]	-2.1 (0.33)	-0.3 (0.31)
	LS mean difference (95% CI) p-value [2]	-1.8 (-2.8; -0.9) 0.0001	
	Hedges' g (95% CI)	-1.344 (-2.064; -0.624)	
Prior surgery	Interaction p-value [1]	0.8943	
Yes			
Overall treatment effect	n'	64	26
	LS mean (SE) [2]	-1.6 (0.19)	-0.4 (0.25)
	LS mean difference (95% CI) p-value [2]	-1.2 (-1.8; -0.6) 0.0002	
	Hedges' g (95% CI)	-0.881 (-1.352; -0.410)	
No			
Overall treatment effect	n'	19	13
	LS mean (SE) [2]	-1.9 (0.39)	-0.6 (0.30)
	LS mean difference (95% CI) p-value [2]	-1.3 (-2.3; -0.3) 0.0118	
	Hedges' g (95% CI)	-0.914 (-1.650; -0.179)	

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

Subgroup Level Analysis Visit		Vimseltinib (N=83)	Placebo (N=40)
Prior imatinib/nilotinib treatment	Interaction p-value [1]	0.1031	
Yes			
Overall treatment effect	n'	19	9
	LS mean (SE) [2]	-1.8 (0.36)	0.2 (0.39)
	LS mean difference (95% CI) p-value [2]	-1.9 (-3.0; -0.8) 0.0006	
	Hedges' g (95% CI)	-1.424 (-2.296; -0.553)	
No			
Overall treatment effect	n'	64	30
	LS mean (SE) [2]	-1.7 (0.20)	-0.7 (0.23)
	LS mean difference (95% CI) p-value [2]	-1.0 (-1.6; -0.4) 0.0012	
	Hedges' g (95% CI)	-0.730 (-1.174; -0.287)	

N: Number of subjects in analysis set. n: Number of subjects with non-missing data. n': Number of subjects analysed. SD: Standard deviation. SE: Standard error. Min: Minimum. Max: Maximum. NC: Not calculated. NE: Not estimable. CI: Confidence interval.

Reference is Placebo.

[1] Treatment*Subgroup interaction p-value from MMRM model.

[2] MMRM model using unstructured covariance matrix with terms Treatment, Visit, Subgroup, Baseline value, Treatment by Visit, and Treatment by Subgroup interactions.

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

4.1.1.2 Subgruppenanalysen für die Veränderung der Skalenwerte der NRS für durchschnittliche Schmerzen des BPI gegenüber dem Ausgangswert während der randomisierten, kontrollierten Studienphase

Subgroup Level Analysis Visit		Vimseltinib (N=83)	Placebo (N=40)
Sex	Interaction p-value [1]	0.5426	
Male			
Overall treatment effect	n'	37	13
	LS mean (SE) [2]	-1.3 (0.22)	-0.3 (0.26)
	LS mean difference (95% CI) p-value [2]	-0.9 (-1.6; -0.3) 0.0073	
	Hedges' g (95% CI)	-0.874 (-1.525; -0.224)	
Female			
Overall treatment effect	n'	46	26
	LS mean (SE) [2]	-1.7 (0.19)	-0.5 (0.23)
	LS mean difference (95% CI) p-value [2]	-1.2 (-1.8; -0.6) 0.0001	
	Hedges' g (95% CI)	-0.961 (-1.463; -0.458)	
Age group	Interaction p-value [1]	NC	
18 - < 50			
Overall treatment effect	n'	54	27
	LS mean (SE) [2]	NC (NC)	NC (NC)
	LS mean difference (95% CI) p-value [2]	NC (NC; NC) NC	
	Hedges' g (95% CI)	NC (NC; NC)	
50 - < 65			
Overall treatment effect	n'	24	9
	LS mean (SE) [2]	NC (NC)	NC (NC)
	LS mean difference (95% CI) p-value [2]	NC (NC; NC) NC	
	Hedges' g (95% CI)	NC (NC; NC)	
≥ 65			
Overall treatment effect	n'	5	4
	LS mean (SE) [2]	NC (NC)	NC (NC)
	LS mean difference (95% CI) p-value [2]	NC (NC; NC) NC	
	Hedges' g (95% CI)	NC (NC; NC)	

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

Subgroup Level Analysis Visit		Vimseltinib (N=83)	Placebo (N=40)
Region		Interaction p-value [1]	0.3144
U.S.			
Overall treatment effect	n'	9	4
	LS mean (SE) [2]	-1.4 (0.45)	-1.0 (0.46)
	LS mean difference (95% CI) p-value [2]	-0.4 (-1.8; 0.9) 0.5109	
	Hedges' g (95% CI)	-0.394 (-1.574; 0.786)	
Non-U.S.			
Overall treatment effect	n'	74	35
	LS mean (SE) [2]	-1.5 (0.16)	-0.4 (0.20)
	LS mean difference (95% CI) p-value [2]	-1.1 (-1.6; -0.6) <.0001	
	Hedges' g (95% CI)	-0.863 (-1.278; -0.447)	
Site in Europe		Interaction p-value [1]	0.3769
Yes			
Overall treatment effect	n'	57	31
	LS mean (SE) [2]	-1.5 (0.19)	-0.4 (0.22)
	LS mean difference (95% CI) p-value [2]	-1.1 (-1.7; -0.5) 0.0002	
	Hedges' g (95% CI)	-0.861 (-1.314; -0.408)	
No			
Overall treatment effect	n'	26	8
	LS mean (SE) [2]	-1.5 (0.23)	-0.7 (0.29)
	LS mean difference (95% CI) p-value [2]	-0.8 (-1.5; -0.0) 0.0388	
	Hedges' g (95% CI)	-0.839 (-1.652; -0.027)	
Disease subtype		Interaction p-value [1]	0.9450
Localized			
Overall treatment effect	n'	26	10
	LS mean (SE) [2]	-1.5 (0.22)	-0.5 (0.39)
	LS mean difference (95% CI) p-value [2]	-1.0 (-1.9; -0.2) 0.0214	
	Hedges' g (95% CI)	-0.862 (-1.614; -0.111)	
Diffuse			

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

Subgroup Level Analysis Visit		Vimseltinib (N=83)	Placebo (N=40)
Overall treatment effect	n'	57	27
	LS mean (SE) [2]	-1.5 (0.19)	-0.4 (0.21)
	LS mean difference (95% CI) p-value [2]	-1.1 (-1.6; -0.5) 0.0002	
	Hedges' g (95% CI)	-0.881 (-1.355; -0.407)	
Missing			
Overall treatment effect	n'	0	2
	LS mean (SE) [2]	NC (NC)	NC (NC)
	LS mean difference (95% CI) p-value [2]	NC (NC; NC) NC	
	Hedges' g (95% CI)	NC (NC; NC)	
Tumour location		0.0022	
Lower Limb			
Overall treatment effect	n'	77	34
	LS mean (SE) [2]	-1.4 (0.16)	-0.5 (0.21)
	LS mean difference (95% CI) p-value [2]	-0.9 (-1.4; -0.3) 0.0017	
	Hedges' g (95% CI)	-0.657 (-1.067; -0.247)	
All Other			
Overall treatment effect	n'	6	5
	LS mean (SE) [2]	-3.1 (0.66)	-0.0 (0.27)
	LS mean difference (95% CI) p-value [2]	-3.1 (-4.5; -1.7) <.0001	
	Hedges' g (95% CI)	-2.610 (-4.217; -1.004)	
Disease location joint size		0.0284	
Large Joints			
Overall treatment effect	n'	69	28
	LS mean (SE) [2]	-1.4 (0.16)	-0.6 (0.22)
	LS mean difference (95% CI) p-value [2]	-0.8 (-1.4; -0.3) 0.0033	
	Hedges' g (95% CI)	-0.669 (-1.115; -0.222)	
Small Joints			
Overall treatment effect	n'	14	11
	LS mean (SE) [2]	-2.1 (0.40)	-0.2 (0.28)
	LS mean difference (95% CI) p-value [2]	-1.9 (-2.9; -0.9) 0.0002	

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

Subgroup Level Analysis Visit		Vimseltinib (N=83)	Placebo (N=40)
Hedges' g (95% CI)		-1.542 (-2.435; -0.648)	
Disease location knee		Interaction p-value [1]	
		0.0034	
Yes			
Overall treatment effect	n'	56	26
	LS mean (SE) [2]	-1.2 (0.17)	-0.6 (0.23)
	LS mean difference (95% CI) p-value [2]	-0.7 (-1.2; -0.1) 0.0227	
	Hedges' g (95% CI)	-0.545 (-1.014; -0.075)	
No			
Overall treatment effect	n'	27	13
	LS mean (SE) [2]	-2.0 (0.27)	-0.2 (0.26)
	LS mean difference (95% CI) p-value [2]	-1.8 (-2.6; -1.1) <.0001	
	Hedges' g (95% CI)	-1.598 (-2.343; -0.853)	
Prior surgery		Interaction p-value [1]	
		0.6761	
Yes			
Overall treatment effect	n'	64	26
	LS mean (SE) [2]	-1.5 (0.16)	-0.5 (0.22)
	LS mean difference (95% CI) p-value [2]	-1.0 (-1.5; -0.4) 0.0005	
	Hedges' g (95% CI)	-0.829 (-1.298; -0.360)	
No			
Overall treatment effect	n'	19	13
	LS mean (SE) [2]	-1.7 (0.38)	-0.5 (0.29)
	LS mean difference (95% CI) p-value [2]	-1.2 (-2.2; -0.2) 0.0145	
	Hedges' g (95% CI)	-0.888 (-1.622; -0.154)	
Prior imatinib/nilotinib treatment		Interaction p-value [1]	
		0.1927	
Yes			
Overall treatment effect	n'	19	9
	LS mean (SE) [2]	-1.6 (0.34)	-0.0 (0.34)
	LS mean difference (95% CI) p-value [2]	-1.6 (-2.5; -0.6) 0.0019	

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

Subgroup Level Analysis Visit		Vimseltinib (N=83)	Placebo (N=40)
No Overall treatment effect	Hedges' g (95% CI)	-1.275 (-2.131; -0.419)	
	n'	64	30
	LS mean (SE) [2]	-1.5 (0.17)	-0.6 (0.21)
	LS mean difference (95% CI) p-value [2]	-0.9 (-1.4; -0.4) 0.0014	
	Hedges' g (95% CI)	-0.721 (-1.164; -0.278)	

N: Number of subjects in analysis set. n: Number of subjects with non-missing data. n': Number of subjects analysed. SD: Standard deviation. SE: Standard error. Min: Minimum. Max: Maximum. NC: Not calculated. NE: Not estimable. CI: Confidence interval.

Reference is Placebo.

[1] Treatment*Subgroup interaction p-value from MMRM model.

[2] MMRM model using unstructured covariance matrix with terms Treatment, Visit, Subgroup, Baseline value, Treatment by Visit, and Treatment by Subgroup interactions.

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

4.1.1.3 Subgruppenanalysen für das Ansprechen mit mindestens 30 % Verbesserung im mittleren Wert der NRS für stärkste Schmerzen des BPI zu Woche 25, ohne eine Zunahme des Gebrauchs narkotischer Analgetika um 30 % oder mehr

Subgroup Level	Vimseltinib (N=83)		Placebo (N=40)		RR [1] (95% CI) p-value	OR [2] (95% CI) p-value	RD [3] (95% CI)
	N/N'	n (%)	N/N'	n (%)			
Sex	Interaction p-value [4]		0.1085				
Male	37/ 37	18 (48.6)	13/ 13	1 (7.7)	6.324 (0.935;42.792) 0.0587	11.368 (1.338;96.570) 0.0260	0.410 (0.193;0.626)
Female	46/ 46	22 (47.8)	27/ 27	8 (29.6)	1.614 (0.838;3.107) 0.1519	2.177 (0.794;5.968) 0.1305	0.182 (-0.043;0.407)
Age group	Interaction p-value [4]		NC				
18 - < 50	54/ 54	25 (46.3)	27/ 27	6 (22.2)	NC (NC;NC) NC	NC (NC;NC) NC	NC (NC;NC)
50 - < 65	24/ 24	14 (58.3)	9/ 9	2 (22.2)	NC (NC;NC) NC	NC (NC;NC) NC	NC (NC;NC)
≥ 65	5/ 5	1 (20.0)	4/ 4	1 (25.0)	NC (NC;NC) NC	NC (NC;NC) NC	NC (NC;NC)
Region	Interaction p-value [4]		0.3037				
U.S.	9/ 9	5 (55.6)	4/ 4	2 (50.0)	1.111 (0.355;3.478) 0.8564	1.250 (0.118;13.240) 0.8530	0.056 (-0.532;0.643)

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

Subgroup Level	Vimseltinib (N=83)		Placebo (N=40)		RR [1] (95% CI) p-value	OR [2] (95% CI) p-value	RD [3] (95% CI)
	N/N'	n (%)	N/N'	n (%)			
Non-U.S.	74/ 74	35 (47.3)	36/ 36	7 (19.4)	2.432 (1.199;4.933) 0.0137	3.718 (1.448;9.548) 0.0064	0.279 (0.106;0.451)
Site in Europe	Interaction p-value [4]		0.7963				
Yes	57/ 57	28 (49.1)	32/ 32	7 (21.9)	2.246 (1.108;4.550) 0.0247	3.448 (1.286;9.243) 0.0139	0.272 (0.079;0.466)
No	26/ 26	12 (46.2)	8/ 8	2 (25.0)	1.846 (0.518;6.574) 0.3441	2.571 (0.435;15.193) 0.2974	0.212 (-0.144;0.568)
Disease subtype	Interaction p-value [4]		0.1720				
Localized	26/ 26	12 (46.2)	10/ 10	4 (40.0)	1.154 (0.486;2.741) 0.7458	1.286 (0.292;5.657) 0.7395	0.062 (-0.298;0.421)
Diffuse	57/ 57	28 (49.1)	28/ 28	5 (17.9)	2.751 (1.191;6.354) 0.0178	4.441 (1.482;13.312) 0.0078	0.313 (0.120;0.505)
Missing	0/ 0	0	2/ 2	0 (0.0)	NC (NC;NC) NC	NC (NC;NC) NC	NC (NC;NC)
Tumour location	Interaction p-value [4]		0.3344				
Lower Limb	77/ 77	37 (48.1)	35/ 35	9 (25.7)	1.869 (1.016;3.436)	2.672 (1.108;6.443)	0.223 (0.041;0.406)

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

Subgroup Level	Vimseltinib (N=83)		Placebo (N=40)		RR [1] (95% CI) p-value	OR [2] (95% CI) p-value	RD [3] (95% CI)
	N/N'	n (%)	N/N'	n (%)			
					0.0442	0.0286	
All Other	6/ 6	3 (50.0)	5/ 5	0 (0.0)	6.000 (0.382;94.351) 0.2025	11.000 (0.426;284.305) 0.1484	0.500 (0.100;0.900)
Disease location joint size	Interaction p-value [4]		0.5585				
Large Joints	69/ 69	34 (49.3)	29/ 29	6 (20.7)	2.382 (1.123;5.051) 0.0237	3.724 (1.350;10.274) 0.0111	0.286 (0.097;0.475)
Small Joints	14/ 14	6 (42.9)	11/ 11	3 (27.3)	1.571 (0.503;4.908) 0.4367	2.000 (0.366;10.919) 0.4235	0.156 (-0.214;0.525)
Disease location knee	Interaction p-value [4]		0.3325				
Yes	56/ 56	28 (50.0)	27/ 27	5 (18.5)	2.700 (1.173;6.213) 0.0195	4.400 (1.460;13.262) 0.0085	0.315 (0.118;0.511)
No	27/ 27	12 (44.4)	13/ 13	4 (30.8)	1.444 (0.577;3.617) 0.4324	1.800 (0.443;7.308) 0.4110	0.137 (-0.176;0.450)
Prior surgery	Interaction p-value [4]		0.4484				
Yes	64/ 64	34 (53.1)	27/ 27	6 (22.2)	2.391 (1.138;5.022) 0.0214	3.967 (1.414;11.129) 0.0088	0.309 (0.110;0.508)

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

Subgroup Level	Vimseltinib (N=83)		Placebo (N=40)		RR [1] (95% CI) p-value	OR [2] (95% CI) p-value	RD [3] (95% CI)
	N/N'	n (%)	N/N'	n (%)			
No	19/ 19	6 (31.6)	13/ 13	3 (23.1)	1.368 (0.415;4.511) 0.6063	1.538 (0.307;7.716) 0.6006	0.085 (-0.225;0.395)
Prior imatinib/nilotinib treatment	Interaction p-value [4]		0.6032				
Yes	19/ 19	7 (36.8)	9/ 9	1 (11.1)	3.316 (0.477;23.060) 0.2257	4.667 (0.478;45.546) 0.1851	0.257 (-0.041;0.556)
No	64/ 64	33 (51.6)	31/ 31	8 (25.8)	1.998 (1.051;3.798) 0.0347	3.060 (1.193;7.851) 0.0200	0.258 (0.061;0.454)

N: Number of subjects in analysis set. N': Number of subjects analysed. n: Number of subjects with event. NC: Not calculated. NE: Not estimable. CI: Confidence interval. OR: Odds ratio. RD: Risk difference. RR: Risk ratio. Int.: Interaction.

Percentages based on N. Reference is Placebo.

[1] Log-binomial regression with terms Treatment, Subgroup, and Treatment by Subgroup interaction.

[2] Logistic regression with terms Treatment, Subgroup, and Treatment by Subgroup interaction.

[3] Cochran-Mantel-Haenszel method stratified by Subgroup.

[4] Treatment*Subgroup interaction p-value from log-binomial regression.

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

4.1.1.4 Subgruppenanalysen für das Ansprechen mit mindestens 30 % Verbesserung im mittleren Wert der NRS für stärkste Schmerzen des BPI zu Woche 25, ohne eine Zunahme des Gebrauchs narkotischer Analgetika um 30 % oder mehr

Subgroup Level	Vimseltinib (N=83)		Placebo (N=40)		RR [1] (95% CI) p-value	OR [2] (95% CI) p-value	RD [3] (95% CI)
	N/N'	n (%)	N/N'	n (%)			
Sex	Interaction p-value [4]		0.1085				
Male	37/ 37	18 (48.6)	13/ 13	1 (7.7)	6.324 (0.935;42.792) 0.0587	11.368 (1.338;96.570) 0.0260	0.410 (0.193;0.626)
Female	46/ 46	22 (47.8)	27/ 27	8 (29.6)	1.614 (0.838;3.107) 0.1519	2.177 (0.794;5.968) 0.1305	0.182 (-0.043;0.407)
Age group	Interaction p-value [4]		NC				
18 - < 50	54/ 54	25 (46.3)	27/ 27	6 (22.2)	NC (NC;NC) NC	NC (NC;NC) NC	NC (NC;NC)
50 - < 65	24/ 24	14 (58.3)	9/ 9	2 (22.2)	NC (NC;NC) NC	NC (NC;NC) NC	NC (NC;NC)
≥ 65	5/ 5	1 (20.0)	4/ 4	1 (25.0)	NC (NC;NC) NC	NC (NC;NC) NC	NC (NC;NC)
Region	Interaction p-value [4]		0.3037				
U.S.	9/ 9	5 (55.6)	4/ 4	2 (50.0)	1.111 (0.355;3.478) 0.8564	1.250 (0.118;13.240) 0.8530	0.056 (-0.532;0.643)

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

Subgroup Level	Vimseltinib (N=83)		Placebo (N=40)		RR [1] (95% CI) p-value	OR [2] (95% CI) p-value	RD [3] (95% CI)
	N/N'	n (%)	N/N'	n (%)			
Non-U.S.	74/ 74	35 (47.3)	36/ 36	7 (19.4)	2.432 (1.199;4.933) 0.0137	3.718 (1.448;9.548) 0.0064	0.279 (0.106;0.451)
Site in Europe	Interaction p-value [4]		0.7963				
Yes	57/ 57	28 (49.1)	32/ 32	7 (21.9)	2.246 (1.108;4.550) 0.0247	3.448 (1.286;9.243) 0.0139	0.272 (0.079;0.466)
No	26/ 26	12 (46.2)	8/ 8	2 (25.0)	1.846 (0.518;6.574) 0.3441	2.571 (0.435;15.193) 0.2974	0.212 (-0.144;0.568)
Disease subtype	Interaction p-value [4]		0.1720				
Localized	26/ 26	12 (46.2)	10/ 10	4 (40.0)	1.154 (0.486;2.741) 0.7458	1.286 (0.292;5.657) 0.7395	0.062 (-0.298;0.421)
Diffuse	57/ 57	28 (49.1)	28/ 28	5 (17.9)	2.751 (1.191;6.354) 0.0178	4.441 (1.482;13.312) 0.0078	0.313 (0.120;0.505)
Missing	0/ 0	0	2/ 2	0 (0.0)	NC (NC;NC) NC	NC (NC;NC) NC	NC (NC;NC)
Tumour location	Interaction p-value [4]		0.3344				
Lower Limb	77/ 77	37 (48.1)	35/ 35	9 (25.7)	1.869 (1.016;3.436)	2.672 (1.108;6.443)	0.223 (0.041;0.406)

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

Subgroup Level	Vimseltinib (N=83)		Placebo (N=40)		RR [1] (95% CI) p-value	OR [2] (95% CI) p-value	RD [3] (95% CI)
	N/N'	n (%)	N/N'	n (%)			
					0.0442	0.0286	
All Other	6/ 6	3 (50.0)	5/ 5	0 (0.0)	6.000 (0.382;94.351) 0.2025	11.000 (0.426;284.305) 0.1484	0.500 (0.100;0.900)
Disease location joint size	Interaction p-value [4]		0.5585				
Large Joints	69/ 69	34 (49.3)	29/ 29	6 (20.7)	2.382 (1.123;5.051) 0.0237	3.724 (1.350;10.274) 0.0111	0.286 (0.097;0.475)
Small Joints	14/ 14	6 (42.9)	11/ 11	3 (27.3)	1.571 (0.503;4.908) 0.4367	2.000 (0.366;10.919) 0.4235	0.156 (-0.214;0.525)
Disease location knee	Interaction p-value [4]		0.3325				
Yes	56/ 56	28 (50.0)	27/ 27	5 (18.5)	2.700 (1.173;6.213) 0.0195	4.400 (1.460;13.262) 0.0085	0.315 (0.118;0.511)
No	27/ 27	12 (44.4)	13/ 13	4 (30.8)	1.444 (0.577;3.617) 0.4324	1.800 (0.443;7.308) 0.4110	0.137 (-0.176;0.450)
Prior surgery	Interaction p-value [4]		0.4484				
Yes	64/ 64	34 (53.1)	27/ 27	6 (22.2)	2.391 (1.138;5.022) 0.0214	3.967 (1.414;11.129) 0.0088	0.309 (0.110;0.508)
No	19/ 19	6 (31.6)	13/ 13	3 (23.1)	1.368	1.538	0.085

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

Subgroup Level	Vimseltinib (N=83)		Placebo (N=40)		RR [1] (95% CI) p-value	OR [2] (95% CI) p-value	RD [3] (95% CI)
	N/N'	n (%)	N/N'	n (%)			
					(0.415;4.511) 0.6063	(0.307;7.716) 0.6006	(-0.225;0.395)
Prior imatinib/nilotinib treatment	Interaction p-value [4]		0.6032				
Yes	19/ 19	7 (36.8)	9/ 9	1 (11.1)	3.316 (0.477;23.060) 0.2257	4.667 (0.478;45.546) 0.1851	0.257 (-0.041;0.556)
No	64/ 64	33 (51.6)	31/ 31	8 (25.8)	1.998 (1.051;3.798) 0.0347	3.060 (1.193;7.851) 0.0200	0.258 (0.061;0.454)

N: Number of subjects in analysis set. N': Number of subjects analysed. n: Number of subjects with event. NC: Not calculated. NE: Not estimable. CI: Confidence interval. OR: Odds ratio. RD: Risk difference. RR: Risk ratio. Int.: Interaction.

Percentages based on N. Reference is Placebo.

[1] Log-binomial regression with terms Treatment, Subgroup, and Treatment by Subgroup interaction.

[2] Logistic regression with terms Treatment, Subgroup, and Treatment by Subgroup interaction.

[3] Cochran-Mantel-Haenszel method stratified by Subgroup.

[4] Treatment*Subgroup interaction p-value from log-binomial regression.

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

4.1.1.5 Subgruppenanalysen für das Ansprechen mit mindestens 30 % Verbesserung im mittleren Wert der NRS für durchschnittliche Schmerzen des BPI zu Woche 25, ohne eine Zunahme des Gebrauchs narkotischer Analgetika um 30 % oder mehr

Subgroup Level	Vimseltinib (N=83)		Placebo (N=40)		RR [1] (95% CI) p-value	OR [2] (95% CI) p-value	RD [3] (95% CI)
	N/N'	n (%)	N/N'	n (%)			
Sex	Interaction p-value [4]		0.3782				
Male	37/ 37	17 (45.9)	13/ 13	2 (15.4)	2.986 (0.796;11.201) 0.1048	4.675 (0.907;24.089) 0.0652	0.306 (0.052;0.559)
Female	46/ 46	25 (54.3)	27/ 27	9 (33.3)	1.630 (0.899;2.958) 0.1077	2.381 (0.886;6.397) 0.0854	0.210 (-0.019;0.439)
Age group	Interaction p-value [4]		NC				
18 - < 50	54/ 54	27 (50.0)	27/ 27	9 (33.3)	NC (NC;NC) NC	NC (NC;NC) NC	NC (NC;NC)
50 - < 65	24/ 24	14 (58.3)	9/ 9	1 (11.1)	NC (NC;NC) NC	NC (NC;NC) NC	NC (NC;NC)
≥ 65	5/ 5	1 (20.0)	4/ 4	1 (25.0)	NC (NC;NC) NC	NC (NC;NC) NC	NC (NC;NC)
Region	Interaction p-value [4]		0.2790				
U.S.	9/ 9	4 (44.4)	4/ 4	2 (50.0)	0.889 (0.262;3.018)	0.800 (0.076;8.474)	-0.056 (-0.643;0.532)

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

Subgroup Level	Vimseltinib (N=83)		Placebo (N=40)		RR [1] (95% CI) p-value	OR [2] (95% CI) p-value	RD [3] (95% CI)
	N/N'	n (%)	N/N'	n (%)			
					0.8502	0.8530	
Non-U.S.	74/ 74	38 (51.4)	36/ 36	9 (25.0)	2.054 (1.119;3.772) 0.0203	3.167 (1.312;7.645) 0.0104	0.264 (0.082;0.445)
Site in Europe	Interaction p-value [4]		0.0101				
Yes	57/ 57	31 (54.4)	32/ 32	6 (18.8)	2.901 (1.357;6.199) 0.0060	5.167 (1.846;14.463) 0.0018	0.356 (0.169;0.543)
No	26/ 26	11 (42.3)	8/ 8	5 (62.5)	0.677 (0.336;1.363) 0.2744	0.440 (0.086;2.244) 0.3233	-0.202 (-0.587;0.184)
Disease subtype	Interaction p-value [4]		0.3060				
Localized	26/ 26	12 (46.2)	10/ 10	4 (40.0)	1.154 (0.486;2.741) 0.7458	1.286 (0.292;5.657) 0.7395	0.062 (-0.298;0.421)
Diffuse	57/ 57	30 (52.6)	28/ 28	7 (25.0)	2.105 (1.059;4.186) 0.0337	3.333 (1.225;9.070) 0.0184	0.276 (0.070;0.483)
Missing	0/ 0	0	2/ 2	0 (0.0)	NC (NC;NC) NC	NC (NC;NC) NC	NC (NC;NC)
Tumour location	Interaction p-value [4]		0.7263				
Lower Limb	77/ 77	39 (50.6)	35/ 35	10 (28.6)	1.773	2.566	0.221

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

Subgroup Level	Vimseltinib (N=83)		Placebo (N=40)		RR [1] (95% CI) p-value	OR [2] (95% CI) p-value	RD [3] (95% CI)
	N/N'	n (%)	N/N'	n (%)			
					(1.004;3.129) 0.0483	(1.087;6.056) 0.0315	(0.034;0.408)
All Other	6/ 6	3 (50.0)	5/ 5	1 (20.0)	2.500 (0.364;17.173) 0.3514	4.000 (0.265;60.325) 0.3167	0.300 (-0.232;0.832)
Disease location joint size	Interaction p-value [4]		0.7828				
Large Joints	69/ 69	36 (52.2)	29/ 29	8 (27.6)	1.891 (1.006;3.556) 0.0479	2.864 (1.117;7.341) 0.0285	0.246 (0.045;0.447)
Small Joints	14/ 14	6 (42.9)	11/ 11	3 (27.3)	1.571 (0.503;4.908) 0.4367	2.000 (0.366;10.919) 0.4235	0.156 (-0.214;0.525)
Disease location knee	Interaction p-value [4]		0.2723				
Yes	56/ 56	29 (51.8)	27/ 27	6 (22.2)	2.330 (1.101;4.931) 0.0270	3.759 (1.318;10.719) 0.0132	0.296 (0.091;0.500)
No	27/ 27	13 (48.1)	13/ 13	5 (38.5)	1.252 (0.567;2.762) 0.5779	1.486 (0.386;5.722) 0.5650	0.097 (-0.228;0.422)
Prior surgery	Interaction p-value [4]		0.7959				
Yes	64/ 64	33 (51.6)	27/ 27	8 (29.6)	1.740 (0.929;3.261) 0.0838	2.528 (0.967;6.607) 0.0584	0.219 (0.008;0.431)

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

Subgroup Level	Vimseltinib (N=83)		Placebo (N=40)		RR [1] (95% CI) p-value	OR [2] (95% CI) p-value	RD [3] (95% CI)
	N/N'	n (%)	N/N'	n (%)			
No	19/ 19	9 (47.4)	13/ 13	3 (23.1)	2.053 (0.683;6.165) 0.2000	3.000 (0.622;14.469) 0.1711	0.243 (-0.078;0.564)
Prior imatinib/nilotinib treatment	Interaction p-value [4]		0.4738				
Yes	19/ 19	7 (36.8)	9/ 9	1 (11.1)	3.316 (0.477;23.060) 0.2257	4.667 (0.478;45.546) 0.1851	0.257 (-0.041;0.556)
No	64/ 64	35 (54.7)	31/ 31	10 (32.3)	1.695 (0.972;2.958) 0.0631	2.534 (1.031;6.231) 0.0427	0.224 (0.019;0.429)

N: Number of subjects in analysis set. N': Number of subjects analysed. n: Number of subjects with event. NC: Not calculated. NE: Not estimable. CI: Confidence interval. OR: Odds ratio. RD: Risk difference. RR: Risk ratio. Int.: Interaction.

Percentages based on N. Reference is Placebo.

[1] Log-binomial regression with terms Treatment, Subgroup, and Treatment by Subgroup interaction.

[2] Logistic regression with terms Treatment, Subgroup, and Treatment by Subgroup interaction.

[3] Cochran-Mantel-Haenszel method stratified by Subgroup.

[4] Treatment*Subgroup interaction p-value from log-binomial regression.

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

4.1.1.6 Subgruppenanalysen für das Ansprechen mit mindestens 30 % Verbesserung im mittleren Wert der NRS für durchschnittliche Schmerzen des BPI zu Woche 25, unabhängig vom Gebrauch narkotischer Analgetika

Subgroup Level	Vimseltinib (N=83)		Placebo (N=40)		RR [1] (95% CI) p-value	OR [2] (95% CI) p-value	RD [3] (95% CI)
	N/N'	n (%)	N/N'	n (%)			
Sex	Interaction p-value [4]		0.3782				
Male	37/ 37	17 (45.9)	13/ 13	2 (15.4)	2.986 (0.796;11.201) 0.1048	4.675 (0.907;24.089) 0.0652	0.306 (0.052;0.559)
Female	46/ 46	25 (54.3)	27/ 27	9 (33.3)	1.630 (0.899;2.958) 0.1077	2.381 (0.886;6.397) 0.0854	0.210 (-0.019;0.439)
Age group	Interaction p-value [4]		NC				
18 - < 50	54/ 54	27 (50.0)	27/ 27	9 (33.3)	NC (NC;NC) NC	NC (NC;NC) NC	NC (NC;NC)
50 - < 65	24/ 24	14 (58.3)	9/ 9	1 (11.1)	NC (NC;NC) NC	NC (NC;NC) NC	NC (NC;NC)
≥ 65	5/ 5	1 (20.0)	4/ 4	1 (25.0)	NC (NC;NC) NC	NC (NC;NC) NC	NC (NC;NC)
Region	Interaction p-value [4]		0.2790				
U.S.	9/ 9	4 (44.4)	4/ 4	2 (50.0)	0.889 (0.262;3.018) 0.8502	0.800 (0.076;8.474) 0.8530	-0.056 (-0.643;0.532)

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

Subgroup Level	Vimseltinib (N=83)		Placebo (N=40)		RR [1] (95% CI) p-value	OR [2] (95% CI) p-value	RD [3] (95% CI)
	N/N'	n (%)	N/N'	n (%)			
Non-U.S.	74/ 74	38 (51.4)	36/ 36	9 (25.0)	2.054 (1.119;3.772) 0.0203	3.167 (1.312;7.645) 0.0104	0.264 (0.082;0.445)
Site in Europe	Interaction p-value [4]		0.0101				
Yes	57/ 57	31 (54.4)	32/ 32	6 (18.8)	2.901 (1.357;6.199) 0.0060	5.167 (1.846;14.463) 0.0018	0.356 (0.169;0.543)
No	26/ 26	11 (42.3)	8/ 8	5 (62.5)	0.677 (0.336;1.363) 0.2744	0.440 (0.086;2.244) 0.3233	-0.202 (-0.587;0.184)
Disease subtype	Interaction p-value [4]		0.3060				
Localized	26/ 26	12 (46.2)	10/ 10	4 (40.0)	1.154 (0.486;2.741) 0.7458	1.286 (0.292;5.657) 0.7395	0.062 (-0.298;0.421)
Diffuse	57/ 57	30 (52.6)	28/ 28	7 (25.0)	2.105 (1.059;4.186) 0.0337	3.333 (1.225;9.070) 0.0184	0.276 (0.070;0.483)
Missing	0/ 0	0	2/ 2	0 (0.0)	NC (NC;NC) NC	NC (NC;NC) NC	NC (NC;NC)
Tumour location	Interaction p-value [4]		0.7263				
Lower Limb	77/ 77	39 (50.6)	35/ 35	10 (28.6)	1.773 (1.004;3.129)	2.566 (1.087;6.056)	0.221 (0.034;0.408)

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

Subgroup Level	Vimseltinib (N=83)		Placebo (N=40)		RR [1] (95% CI) p-value	OR [2] (95% CI) p-value	RD [3] (95% CI)
	N/N'	n (%)	N/N'	n (%)			
					0.0483	0.0315	
All Other	6/ 6	3 (50.0)	5/ 5	1 (20.0)	2.500 (0.364;17.173) 0.3514	4.000 (0.265;60.325) 0.3167	0.300 (-0.232;0.832)
Disease location joint size	Interaction p-value [4]		0.7828				
Large Joints	69/ 69	36 (52.2)	29/ 29	8 (27.6)	1.891 (1.006;3.556) 0.0479	2.864 (1.117;7.341) 0.0285	0.246 (0.045;0.447)
Small Joints	14/ 14	6 (42.9)	11/ 11	3 (27.3)	1.571 (0.503;4.908) 0.4367	2.000 (0.366;10.919) 0.4235	0.156 (-0.214;0.525)
Disease location knee	Interaction p-value [4]		0.2723				
Yes	56/ 56	29 (51.8)	27/ 27	6 (22.2)	2.330 (1.101;4.931) 0.0270	3.759 (1.318;10.719) 0.0132	0.296 (0.091;0.500)
No	27/ 27	13 (48.1)	13/ 13	5 (38.5)	1.252 (0.567;2.762) 0.5779	1.486 (0.386;5.722) 0.5650	0.097 (-0.228;0.422)
Prior surgery	Interaction p-value [4]		0.7959				
Yes	64/ 64	33 (51.6)	27/ 27	8 (29.6)	1.740 (0.929;3.261) 0.0838	2.528 (0.967;6.607) 0.0584	0.219 (0.008;0.431)
No	19/ 19	9 (47.4)	13/ 13	3 (23.1)	2.053	3.000	0.243

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

Subgroup Level	Vimseltinib (N=83)		Placebo (N=40)		RR [1] (95% CI) p-value	OR [2] (95% CI) p-value	RD [3] (95% CI)
	N/N'	n (%)	N/N'	n (%)			
					(0.683;6.165) 0.2000	(0.622;14.469) 0.1711	(-0.078;0.564)
Prior imatinib/nilotinib treatment	Interaction p-value [4]		0.4738				
Yes	19/ 19	7 (36.8)	9/ 9	1 (11.1)	3.316 (0.477;23.060) 0.2257	4.667 (0.478;45.546) 0.1851	0.257 (-0.041;0.556)
No	64/ 64	35 (54.7)	31/ 31	10 (32.3)	1.695 (0.972;2.958) 0.0631	2.534 (1.031;6.231) 0.0427	0.224 (0.019;0.429)

N: Number of subjects in analysis set. N': Number of subjects analysed. n: Number of subjects with event. NC: Not calculated. NE: Not estimable. CI: Confidence interval. OR: Odds ratio. RD: Risk difference. RR: Risk ratio. Int.: Interaction.

Percentages based on N. Reference is Placebo.

[1] Log-binomial regression with terms Treatment, Subgroup, and Treatment by Subgroup interaction.

[2] Logistic regression with terms Treatment, Subgroup, and Treatment by Subgroup interaction.

[3] Cochran-Mantel-Haenszel method stratified by Subgroup.

[4] Treatment*Subgroup interaction p-value from log-binomial regression.

4.1.2 Subgruppenanalysen für die körperliche Funktionsfähigkeit gemessen mittels PROMIS-PF

4.1.2.1 Subgruppenanalysen für die Veränderung des PROMIS-PF-Skalenwertes gegenüber dem Ausgangswert während der randomisierten, kontrollierten Studienphase

Subgroup Level Analysis Visit		Vimseltinib (N=83)	Placebo (N=40)
Sex	Interaction p-value [1]	0.2169	
Male			
Overall treatment effect	n'	37	12
	LS mean (SE) [2]	3.2 (0.73)	1.6 (1.14)
	LS mean difference (95% CI) p-value [2]	1.6 (-1.1; 4.3) 0.2458	
	Hedges' g (95% CI)	0.385 (-0.266; 1.036)	
Female			
Overall treatment effect	n'	46	25
	LS mean (SE) [2]	4.3 (0.52)	0.9 (0.63)
	LS mean difference (95% CI) p-value [2]	3.5 (1.8; 5.1) <.0001	
	Hedges' g (95% CI)	1.046 (0.533; 1.560)	
Age group	Interaction p-value [1]	NC	
18 - < 50			
Overall treatment effect	n'	54	27
	LS mean (SE) [2]	NC (NC)	NC (NC)
	LS mean difference (95% CI) p-value [2]	NC (NC; NC) NC	
	Hedges' g (95% CI)	NC (NC; NC)	
50 - < 65			
Overall treatment effect	n'	24	9
	LS mean (SE) [2]	NC (NC)	NC (NC)
	LS mean difference (95% CI) p-value [2]	NC (NC; NC) NC	
	Hedges' g (95% CI)	NC (NC; NC)	
≥ 65			
Overall treatment effect	n'	5	4
	LS mean (SE) [2]	NC (NC)	NC (NC)

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

Subgroup Level Analysis Visit		Vimseltinib (N=83)	Placebo (N=40)
LS mean difference (95% CI) p-value [2]		NC (NC; NC) NC	
Hedges' g (95% CI)		NC (NC; NC)	
Region		Interaction p-value [1]	
U.S.		0.0155	
Overall treatment effect	n'	9	3
	LS mean (SE) [2]	2.7 (0.98)	3.2 (0.97)
	LS mean difference (95% CI) p-value [2]	-0.5 (-3.1; 2.1) 0.7111	
	Hedges' g (95% CI)	-0.246 (-1.548; 1.056)	
Non-U.S.			
Overall treatment effect	n'	74	34
	LS mean (SE) [2]	4.0 (0.50)	0.9 (0.63)
	LS mean difference (95% CI) p-value [2]	3.0 (1.5; 4.6) 0.0002	
	Hedges' g (95% CI)	0.783 (0.366; 1.200)	
Site in Europe		Interaction p-value [1]	
Yes		0.1025	
Overall treatment effect	n'	57	30
	LS mean (SE) [2]	3.8 (0.52)	0.6 (0.62)
	LS mean difference (95% CI) p-value [2]	3.2 (1.6; 4.8) 0.0001	
	Hedges' g (95% CI)	0.894 (0.435; 1.353)	
No			
Overall treatment effect	n'	26	7
	LS mean (SE) [2]	3.8 (0.79)	3.2 (1.25)
	LS mean difference (95% CI) p-value [2]	0.6 (-2.3; 3.5) 0.6716	
	Hedges' g (95% CI)	0.180 (-0.650; 1.010)	
Disease subtype		Interaction p-value [1]	
Localized		0.2082	
Overall treatment effect	n'	26	9
	LS mean (SE) [2]	4.5 (0.80)	0.3 (0.94)
	LS mean difference (95% CI) p-value [2]	4.3 (1.8; 6.7) 0.0008	

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Subgroup Level Analysis Visit		Vimseltinib (N=83)	Placebo (N=40)
	Hedges' g (95% CI)	1.326 (0.511; 2.140)	
Diffuse			
Overall treatment effect	n'	57	26
	LS mean (SE) [2]	3.5 (0.50)	0.9 (0.65)
	LS mean difference (95% CI) p-value [2]	2.6 (1.0; 4.2) 0.0022	
	Hedges' g (95% CI)	0.738 (0.264; 1.212)	
Missing			
Overall treatment effect	n'	0	2
	LS mean (SE) [2]	NC (NC)	NC (NC)
	LS mean difference (95% CI) p-value [2]	NC (NC; NC) NC	
	Hedges' g (95% CI)	NC (NC; NC)	
Tumour location	Interaction p-value [1]	0.1612	
Lower Limb			
Overall treatment effect	n'	77	32
	LS mean (SE) [2]	3.7 (0.46)	1.3 (0.64)
	LS mean difference (95% CI) p-value [2]	2.4 (0.8; 3.9) 0.0034	
	Hedges' g (95% CI)	0.625 (0.207; 1.043)	
All Other			
Overall treatment effect	n'	6	5
	LS mean (SE) [2]	5.5 (2.24)	-0.3 (0.86)
	LS mean difference (95% CI) p-value [2]	5.8 (1.1; 10.5) 0.0165	
	Hedges' g (95% CI)	1.464 (0.136; 2.792)	
Disease location joint size	Interaction p-value [1]	0.3093	
Large Joints			
Overall treatment effect	n'	69	26
	LS mean (SE) [2]	3.7 (0.50)	1.4 (0.70)
	LS mean difference (95% CI) p-value [2]	2.3 (0.7; 4.0) 0.0070	
	Hedges' g (95% CI)	0.628 (0.171; 1.085)	
Small Joints			
Overall treatment effect	n'	14	11

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Subgroup Level Analysis Visit		Vimseltinib (N=83)	Placebo (N=40)
	LS mean (SE) [2]	4.3 (1.15)	0.4 (0.89)
	LS mean difference (95% CI) p-value [2]	3.9 (1.1; 6.7) 0.0074	
	Hedges' g (95% CI)	1.092 (0.251; 1.933)	
Disease location knee	Interaction p-value [1]	0.2624	
Yes			
Overall treatment effect	n'	56	24
	LS mean (SE) [2]	3.8 (0.53)	1.6 (0.73)
	LS mean difference (95% CI) p-value [2]	2.2 (0.5; 4.0) 0.0140	
	Hedges' g (95% CI)	0.605 (0.120; 1.089)	
No			
Overall treatment effect	n'	27	13
	LS mean (SE) [2]	3.9 (0.79)	0.2 (0.79)
	LS mean difference (95% CI) p-value [2]	3.7 (1.5; 5.9) 0.0013	
	Hedges' g (95% CI)	1.105 (0.404; 1.805)	
Prior surgery	Interaction p-value [1]	0.9880	
Yes			
Overall treatment effect	n'	64	24
	LS mean (SE) [2]	3.5 (0.50)	0.5 (0.69)
	LS mean difference (95% CI) p-value [2]	2.9 (1.3; 4.6) 0.0008	
	Hedges' g (95% CI)	0.821 (0.339; 1.302)	
No			
Overall treatment effect	n'	19	13
	LS mean (SE) [2]	5.1 (0.93)	2.2 (0.89)
	LS mean difference (95% CI) p-value [2]	2.9 (0.4; 5.4) 0.0234	
	Hedges' g (95% CI)	0.822 (0.092; 1.551)	
Prior imatinib/nilotinib treatment	Interaction p-value [1]	0.0438	
Yes			
Overall treatment effect	n'	19	8
	LS mean (SE) [2]	3.6 (0.92)	-1.1 (0.50)

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Subgroup		Vimseltinib (N=83)	Placebo (N=40)
Level	Analysis Visit		
No	LS mean difference (95% CI) p-value [2]	4.7 (2.6; 6.9) <.0001	
	Hedges' g (95% CI)	1.801 (0.850; 2.752)	
	n'	64	29
	Overall treatment effect		
	LS mean (SE) [2]	3.9 (0.50)	1.7 (0.67)
	LS mean difference (95% CI) p-value [2]	2.2 (0.5; 3.8) 0.0108	
	Hedges' g (95% CI)	0.576 (0.133; 1.020)	

N: Number of subjects in analysis set. n: Number of subjects with non-missing data. n': Number of subjects analysed. SD: Standard deviation. SE: Standard error. Min: Minimum. Max: Maximum. NC: Not calculated. NE: Not estimable. CI: Confidence interval.

Reference is Placebo.

[1] Treatment*Subgroup interaction p-value from MMRM model.

[2] MMRM model using unstructured covariance matrix with terms Treatment, Visit, Subgroup, Baseline value, Treatment by Visit, and Treatment by Subgroup interactions.

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

4.1.2.2 Subgruppenanalysen für den Anteil der Patienten mit einer Verbesserung des PROMIS-PF-Skalenwertes um mindestens 8,025 Punkte gegenüber dem Ausgangswert zu Woche 25

Subgroup Level	Vimseltinib (N=83)		Placebo (N=40)		RR [1] (95% CI) p-value	OR [2] (95% CI) p-value	RD [3] (95% CI)
	N/N'	n (%)	N/N'	n (%)			
Sex	Interaction p-value [4]		NC				
Male	37/ 37	6 (16.2)	13/ 13	0 (0.0)	NC (NC;NC) NC	NC (NC;NC) NC	NC (NC;NC)
Female	46/ 46	7 (15.2)	27/ 27	1 (3.7)	NC (NC;NC) NC	NC (NC;NC) NC	NC (NC;NC)
Age group	Interaction p-value [4]		NC				
18 - < 50	54/ 54	10 (18.5)	27/ 27	1 (3.7)	NC (NC;NC) NC	NC (NC;NC) NC	NC (NC;NC)
50 - < 65	24/ 24	3 (12.5)	9/ 9	0 (0.0)	NC (NC;NC) NC	NC (NC;NC) NC	NC (NC;NC)
≥ 65	5/ 5	0 (0.0)	4/ 4	0 (0.0)	NC (NC;NC) NC	NC (NC;NC) NC	NC (NC;NC)
Region	Interaction p-value [4]		0.4940				
U.S.	9/ 9	1 (11.1)	4/ 4	0 (0.0)	1.500 (0.074;30.590) 0.7921	1.588 (0.053;47.516) 0.7896	0.111 (-0.094;0.316)

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

Subgroup Level	Vimseltinib (N=83)		Placebo (N=40)		RR [1] (95% CI) p-value	OR [2] (95% CI) p-value	RD [3] (95% CI)
	N/N'	n (%)	N/N'	n (%)			
Non-U.S.	74/ 74	12 (16.2)	36/ 36	1 (2.8)	5.838 (0.789;43.168) 0.0839	6.774 (0.845;54.314) 0.0717	0.134 (0.035;0.234)
Site in Europe	Interaction p-value [4]		0.6408				
Yes	57/ 57	10 (17.5)	32/ 32	1 (3.1)	5.614 (0.753;41.879) 0.0924	6.596 (0.804;54.135) 0.0790	0.144 (0.029;0.260)
No	26/ 26	3 (11.5)	8/ 8	0 (0.0)	2.333 (0.133;40.970) 0.5622	2.532 (0.118;54.285) 0.5525	0.115 (-0.007;0.238)
Disease subtype	Interaction p-value [4]		0.2049				
Localized	26/ 26	3 (11.5)	10/ 10	1 (10.0)	1.154 (0.135;9.831) 0.8958	1.174 (0.107;12.821) 0.8954	0.015 (-0.207;0.238)
Diffuse	57/ 57	10 (17.5)	28/ 28	0 (0.0)	10.500 (0.637;172.980) 0.1000	12.600 (0.711;223.294) 0.0841	0.175 (0.077;0.274)
Missing	0/ 0	0	2/ 2	0 (0.0)	NC (NC;NC) NC	NC (NC;NC) NC	NC (NC;NC)
Tumour location	Interaction p-value [4]		0.8717				
Lower Limb	77/ 77	10 (13.0)	35/ 35	1 (2.9)	4.545 (0.605;34.143)	5.075 (0.624;41.302)	0.101 (0.008;0.194)

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

Subgroup Level	Vimseltinib (N=83)		Placebo (N=40)		RR [1] (95% CI) p-value	OR [2] (95% CI) p-value	RD [3] (95% CI)
	N/N'	n (%)	N/N'	n (%)			
					0.1411	0.1289	
All Other	6/ 6	3 (50.0)	5/ 5	0 (0.0)	6.000 (0.382;94.351) 0.2025	11.000 (0.426;284.305) 0.1484	0.500 (0.100;0.900)
Disease location joint size	Interaction p-value [4]		0.9368				
Large Joints	69/ 69	11 (15.9)	29/ 29	1 (3.4)	4.623 (0.625;34.183) 0.1336	5.310 (0.653;43.201) 0.1185	0.125 (0.016;0.234)
Small Joints	14/ 14	2 (14.3)	11/ 11	0 (0.0)	4.000 (0.211;75.659) 0.3554	4.600 (0.199;106.299) 0.3408	0.143 (-0.040;0.326)
Disease location knee	Interaction p-value [4]		NC				
Yes	56/ 56	7 (12.5)	27/ 27	1 (3.7)	NC (NC;NC) NC	NC (NC;NC) NC	NC (NC;NC)
No	27/ 27	6 (22.2)	13/ 13	0 (0.0)	NC (NC;NC) NC	NC (NC;NC) NC	NC (NC;NC)
Prior surgery	Interaction p-value [4]		NC				
Yes	64/ 64	8 (12.5)	27/ 27	1 (3.7)	NC (NC;NC) NC	NC (NC;NC) NC	NC (NC;NC)
No	19/ 19	5 (26.3)	13/ 13	0 (0.0)	NC	NC	NC

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

Subgroup Level	Vimseltinib (N=83)		Placebo (N=40)		RR [1] (95% CI) p-value	OR [2] (95% CI) p-value	RD [3] (95% CI)
	N/N'	n (%)	N/N'	n (%)	(NC;NC) NC	(NC;NC) NC	(NC;NC)
Prior imatinib/nilotinib treatment		Interaction p-value [4]		0.5018			
Yes	19/ 19	1 (5.3)	9/ 9	0 (0.0)	1.500 (0.067;33.608) 0.7983	1.541 (0.057;41.553) 0.7971	0.053 (-0.048;0.153)
No	64/ 64	12 (18.8)	31/ 31	1 (3.2)	5.813 (0.791;42.709) 0.0837	6.923 (0.857;55.911) 0.0695	0.155 (0.041;0.269)

N: Number of subjects in analysis set. N': Number of subjects analysed. n: Number of subjects with event. NC: Not calculated. NE: Not estimable. CI: Confidence interval. OR: Odds ratio. RD: Risk difference. RR: Risk ratio. Int.: Interaction.

Percentages based on N. Reference is Placebo.

[1] Log-binomial regression with terms Treatment, Subgroup, and Treatment by Subgroup interaction.

[2] Logistic regression with terms Treatment, Subgroup, and Treatment by Subgroup interaction.

[3] Cochran-Mantel-Haenszel method stratified by Subgroup.

[4] Treatment*Subgroup interaction p-value from log-binomial regression.

4.1.3 Subgruppenanalysen für den ROM

4.1.3.1 Subgruppenanalysen für die Veränderung des aktiven ROM des betroffenen Gelenks im Vergleich zu einer Referenznorm gegenüber dem Ausgangswert während der randomisierten, kontrollierten Studienphase

Subgroup Level Analysis Visit		Vimseltinib (N=83)	Placebo (N=40)
Sex	Interaction p-value [1]	0.9990	
Male			
Overall treatment effect	n'	34	12
	LS mean (SE) [2]	15.9 (2.82)	1.0 (5.73)
	LS mean difference (95% CI) p-value [2]	15.0 (2.6; 27.3) 0.0180	
	Hedges' g (95% CI)	0.801 (0.127; 1.475)	
Female			
Overall treatment effect	n'	43	24
	LS mean (SE) [2]	20.9 (4.08)	5.9 (5.20)
	LS mean difference (95% CI) p-value [2]	14.9 (1.3; 28.6) 0.0320	
	Hedges' g (95% CI)	0.550 (0.045; 1.054)	
Age group	Interaction p-value [1]	NC	
18 - < 50			
Overall treatment effect	n'	52	26
	LS mean (SE) [2]	NC (NC)	NC (NC)
	LS mean difference (95% CI) p-value [2]	NC (NC; NC) NC	
	Hedges' g (95% CI)	NC (NC; NC)	
50 - < 65			
Overall treatment effect	n'	23	8
	LS mean (SE) [2]	NC (NC)	NC (NC)
	LS mean difference (95% CI) p-value [2]	NC (NC; NC) NC	
	Hedges' g (95% CI)	NC (NC; NC)	
≥ 65			
Overall treatment effect	n'	4	4
	LS mean (SE) [2]	NC (NC)	NC (NC)

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Subgroup Level Analysis Visit		Vimseltinib (N=83)	Placebo (N=40)
LS mean difference (95% CI) p-value [2]		NC (NC; NC) NC	
Hedges' g (95% CI)		NC (NC; NC)	
Region		Interaction p-value [1]	
U.S.		NC	
Overall treatment effect	n'	8	4
	LS mean (SE) [2]	NC (NC)	NC (NC)
	LS mean difference (95% CI) p-value [2]	NC (NC; NC) NC	
	Hedges' g (95% CI)	NC (NC; NC)	
Non-U.S.			
Overall treatment effect	n'	71	34
	LS mean (SE) [2]	NC (NC)	NC (NC)
	LS mean difference (95% CI) p-value [2]	NC (NC; NC) NC	
	Hedges' g (95% CI)	NC (NC; NC)	
Site in Europe		Interaction p-value [1]	
Yes		0.7088	
Overall treatment effect	n'	54	29
	LS mean (SE) [2]	17.0 (3.21)	4.4 (3.65)
	LS mean difference (95% CI) p-value [2]	12.6 (3.0; 22.2) 0.0104	
	Hedges' g (95% CI)	0.596 (0.139; 1.053)	
No			
Overall treatment effect	n'	23	7
	LS mean (SE) [2]	22.5 (5.84)	3.9 (14.05)
	LS mean difference (95% CI) p-value [2]	18.6 (-11.8; 49.1) 0.2274	
	Hedges' g (95% CI)	0.520 (-0.330; 1.371)	
Disease subtype		Interaction p-value [1]	
Localized		0.3487	
Overall treatment effect	n'	23	8
	LS mean (SE) [2]	17.4 (4.41)	9.5 (5.44)
	LS mean difference (95% CI) p-value [2]	7.9 (-5.5; 21.3) 0.2447	

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Subgroup Level Analysis Visit		Vimseltinib (N=83)	Placebo (N=40)
	Hedges' g (95% CI)	0.477 (-0.331; 1.284)	
Diffuse			
Overall treatment effect	n'	54	26
	LS mean (SE) [2]	19.4 (3.51)	2.7 (5.09)
	LS mean difference (95% CI) p-value [2]	16.7 (4.0; 29.4) 0.0104	
	Hedges' g (95% CI)	0.618 (0.144; 1.092)	
Missing			
Overall treatment effect	n'	0	2
	LS mean (SE) [2]	NC (NC)	NC (NC)
	LS mean difference (95% CI) p-value [2]	NC (NC; NC) NC	
	Hedges' g (95% CI)	NC (NC; NC)	
Tumour location	Interaction p-value [1]	0.5829	
Lower Limb			
Overall treatment effect	n'	72	31
	LS mean (SE) [2]	17.2 (2.72)	3.2 (3.91)
	LS mean difference (95% CI) p-value [2]	14.0 (5.1; 22.9) 0.0024	
	Hedges' g (95% CI)	0.663 (0.236; 1.091)	
All Other			
Overall treatment effect	n'	5	5
	LS mean (SE) [2]	40.6 (19.87)	11.7 (16.51)
	LS mean difference (95% CI) p-value [2]	28.9 (-24.0; 81.9) 0.2813	
	Hedges' g (95% CI)	0.680 (-0.587; 1.947)	
Disease location joint size	Interaction p-value [1]	0.0306	
Large Joints			
Overall treatment effect	n'	65	25
	LS mean (SE) [2]	16.3 (2.69)	10.0 (5.32)
	LS mean difference (95% CI) p-value [2]	6.2 (-4.2; 16.7) 0.2407	
	Hedges' g (95% CI)	0.276 (-0.184; 0.736)	
Small Joints			
Overall treatment effect	n'	12	11

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Subgroup Level Analysis Visit		Vimseltinib (N=83)	Placebo (N=40)
	LS mean (SE) [2]	32.0 (12.64)	-9.0 (7.35)
	LS mean difference (95% CI) p-value [2]	40.9 (11.8; 70.0) 0.0062	
	Hedges' g (95% CI)	1.157 (0.278; 2.035)	
Disease location knee		Interaction p-value [1]	0.1290
Yes			
Overall treatment effect	n'	53	23
	LS mean (SE) [2]	15.9 (2.83)	7.9 (5.06)
	LS mean difference (95% CI) p-value [2]	8.0 (-0.9; 16.9) 0.0789	
	Hedges' g (95% CI)	0.440 (-0.051; 0.931)	
No			
Overall treatment effect	n'	24	13
	LS mean (SE) [2]	24.9 (6.78)	-2.1 (8.26)
	LS mean difference (95% CI) p-value [2]	27.0 (4.2; 49.9) 0.0207	
	Hedges' g (95% CI)	0.803 (0.108; 1.497)	
Prior surgery		Interaction p-value [1]	0.1305
Yes			
Overall treatment effect	n'	59	23
	LS mean (SE) [2]	16.5 (3.45)	6.9 (4.66)
	LS mean difference (95% CI) p-value [2]	9.6 (-1.4; 20.6) 0.0879	
	Hedges' g (95% CI)	0.420 (-0.062; 0.903)	
No			
Overall treatment effect	n'	18	13
	LS mean (SE) [2]	26.0 (4.87)	-0.6 (8.01)
	LS mean difference (95% CI) p-value [2]	26.6 (7.7; 45.5) 0.0063	
	Hedges' g (95% CI)	1.007 (0.256; 1.759)	
Prior imatinib/nilotinib treatment		Interaction p-value [1]	0.2502
Yes			
Overall treatment effect	n'	18	7
	LS mean (SE) [2]	13.3 (3.22)	6.2 (4.74)

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

Subgroup		Vimseltinib (N=83)	Placebo (N=40)
Level	Analysis Visit		
No	LS mean difference (95% CI) p-value [2]	7.1 (-4.2; 18.4) 0.2164	
	Hedges' g (95% CI)	0.550 (-0.330; 1.430)	
	Overall treatment effect		
	n'	59	29
	LS mean (SE) [2]	20.3 (3.40)	3.8 (4.77)
	LS mean difference (95% CI) p-value [2]	16.5 (4.7; 28.3) 0.0066	
	Hedges' g (95% CI)	0.624 (0.173; 1.075)	

N: Number of subjects in analysis set. n: Number of subjects with non-missing data. n': Number of subjects analysed. SD: Standard deviation. SE: Standard error. Min: Minimum. Max: Maximum. NC: Not calculated. NE: Not estimable. CI: Confidence interval.

Reference is Placebo.

[1] Treatment*Subgroup interaction p-value from MMRM model.

[2] MMRM model using unstructured covariance matrix with terms Treatment, Visit, Subgroup, Baseline value, Treatment by Visit, and Treatment by Subgroup interactions.

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

4.1.3.2 Subgruppenanalysen für den Anteil der Patienten mit einer Verbesserung des aktiven ROM des betroffenen Gelenks um mindestens 10 Prozentpunkte im Vergleich zu einer Referenznorm gegenüber dem Ausgangswert zu Woche 25

Subgroup Level	Vimseltinib (N=83)		Placebo (N=40)		RR [1] (95% CI) p-value	OR [2] (95% CI) p-value	RD [3] (95% CI)
	N/N'	n (%)	N/N'	n (%)			
Sex	Interaction p-value [4]		0.2061				
Male	37/ 37	17 (45.9)	13/ 13	1 (7.7)	5.973 (0.880;40.548) 0.0674	10.200 (1.200;86.695) 0.0334	0.383 (0.166;0.599)
Female	46/ 46	23 (50.0)	27/ 27	7 (25.9)	1.929 (0.958;3.884) 0.0659	2.857 (1.013;8.057) 0.0472	0.241 (0.021;0.460)
Age group	Interaction p-value [4]		NC				
18 - < 50	54/ 54	30 (55.6)	27/ 27	7 (25.9)	NC (NC;NC) NC	NC (NC;NC) NC	NC (NC;NC)
50 - < 65	24/ 24	8 (33.3)	9/ 9	1 (11.1)	NC (NC;NC) NC	NC (NC;NC) NC	NC (NC;NC)
≥ 65	5/ 5	2 (40.0)	4/ 4	0 (0.0)	NC (NC;NC) NC	NC (NC;NC) NC	NC (NC;NC)
Region	Interaction p-value [4]		0.3814				
U.S.	9/ 9	2 (22.2)	4/ 4	1 (25.0)	0.889 (0.110;7.198) 0.9121	0.857 (0.055;13.479) 0.9127	-0.028 (-0.532;0.476)

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

Subgroup Level	Vimseltinib (N=83)		Placebo (N=40)		RR [1] (95% CI) p-value	OR [2] (95% CI) p-value	RD [3] (95% CI)
	N/N'	n (%)	N/N'	n (%)			
Non-U.S.	74/ 74	38 (51.4)	36/ 36	7 (19.4)	2.641 (1.310;5.323) 0.0066	4.373 (1.703;11.227) 0.0022	0.319 (0.147;0.491)
Site in Europe	Interaction p-value [4]		0.6563				
Yes	57/ 57	28 (49.1)	32/ 32	6 (18.8)	2.620 (1.215;5.648) 0.0140	4.184 (1.496;11.701) 0.0064	0.304 (0.116;0.491)
No	26/ 26	12 (46.2)	8/ 8	2 (25.0)	1.846 (0.518;6.574) 0.3441	2.571 (0.435;15.193) 0.2974	0.212 (-0.144;0.568)
Disease subtype	Interaction p-value [4]		0.9931				
Localized	26/ 26	12 (46.2)	10/ 10	2 (20.0)	2.308 (0.624;8.529) 0.2099	3.429 (0.607;19.353) 0.1629	0.262 (-0.052;0.575)
Diffuse	57/ 57	28 (49.1)	28/ 28	(21.4)	2.292 (1.075;4.886) 0.0317	3.540 (1.250;10.030) 0.0173	0.277 (0.077;0.477)
Missing	0/ 0	0 (0.0)	2/ 2	0 (0.0)	NC (NC;NC) NC	NC (NC;NC) NC	NC (NC;NC)
Tumour location	Interaction p-value [4]		0.9696				
Lower Limb	77/ 77	37 (48.1)	35/ 35	7 (20.0)	2.403 (1.191;4.848)	3.700 (1.444;9.483)	0.281 (0.107;0.454)

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

Subgroup Level	Vimseltinib (N=83)		Placebo (N=40)		RR [1] (95% CI) p-value	OR [2] (95% CI) p-value	RD [3] (95% CI)
	N/N'	n (%)	N/N'	n (%)			
					0.0144	0.0064	
All Other	6/ 6	3 (50.0)	5/ 5	1 (20.0)	2.500 (0.364;17.173) 0.3514	4.000 (0.265;60.325) 0.3167	0.300 (-0.232;0.832)
Disease location joint size	Interaction p-value [4]		0.4176				
Large Joints	69/ 69	34 (49.3)	29/ 29	5 (17.2)	2.858 (1.243;6.571) 0.0134	4.663 (1.595;13.633) 0.0049	0.320 (0.139;0.501)
Small Joints	14/ 14	6 (42.9)	11/ 11	3 (27.3)	1.571 (0.503;4.908) 0.4367	2.000 (0.366;10.919) 0.4235	0.156 (-0.214;0.525)
Disease location knee	Interaction p-value [4]		0.4413				
Yes	56/ 56	25 (44.6)	27/ 27	4 (14.8)	3.013 (1.165;7.794) 0.0229	4.637 (1.417;15.171) 0.0112	0.298 (0.111;0.485)
No	27/ 27	15 (55.6)	13/ 13	4 (30.8)	1.806 (0.747;4.364) 0.1894	2.812 (0.693;11.419) 0.1481	0.248 (-0.065;0.561)
Prior surgery	Interaction p-value [4]		0.4670				
Yes	64/ 64	29 (45.3)	27/ 27	4 (14.8)	3.059 (1.190;7.859) 0.0202	4.764 (1.478;15.355) 0.0089	0.305 (0.124;0.486)
No	19/ 19	11 (57.9)	13/ 13	4 (30.8)	1.882	3.094	0.271

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Subgroup Level	Vimseltinib (N=83)		Placebo (N=40)		RR [1] (95% CI) p-value	OR [2] (95% CI) p-value	RD [3] (95% CI)
	N/N'	n (%)	N/N'	n (%)			
					(0.764;4.633) 0.1691	(0.698;13.711) 0.1371	(-0.064;0.606)
Prior imatinib/nilotinib treatment	Interaction p-value [4]		0.7097				
Yes	19/ 19	7 (36.8)	9/ 9	1 (11.1)	3.316 (0.477;23.060) 0.2257	4.667 (0.478;45.546) 0.1851	0.257 (-0.041;0.556)
No	64/ 64	33 (51.6)	31/ 31	7 (22.6)	2.283 (1.141;4.570) 0.0197	3.650 (1.378;9.669) 0.0092	0.290 (0.098;0.481)

N: Number of subjects in analysis set. N': Number of subjects analysed. n: Number of subjects with event. NC: Not calculated. NE: Not estimable. CI: Confidence interval. OR: Odds ratio. RD: Risk difference. RR: Risk ratio. Int.: Interaction.

Percentages based on N. Reference is Placebo.

[1] Log-binomial regression with terms Treatment, Subgroup, and Treatment by Subgroup interaction.

[2] Logistic regression with terms Treatment, Subgroup, and Treatment by Subgroup interaction.

[3] Cochran-Mantel-Haenszel method stratified by Subgroup.

[4] Treatment*Subgroup interaction p-value from log-binomial regression.

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

4.1.4 Subgruppenanalysen für Steifheit gemessen mittels NRS für stärkste Steifheit**4.1.4.1 Subgruppenanalysen für die Veränderung des Skalenwertes der NRS für stärkste Steifheit gegenüber dem Ausgangswert während der randomisierten, kontrollierten Studienphase**

Subgroup Level Analysis Visit		Vimseltinib (N=83)	Placebo (N=40)
Sex	Interaction p-value [1]	0.9233	
Male			
Overall treatment effect	n'	36	12
	LS mean (SE) [2]	-1.3 (0.21)	-0.2 (0.24)
	LS mean difference (95% CI) p-value [2]	-1.1 (-1.8; -0.5) 0.0003	
	Hedges' g (95% CI)	-1.223 (-1.917; -0.529)	
Female			
Overall treatment effect	n'	46	25
	LS mean (SE) [2]	-1.8 (0.18)	-0.6 (0.23)
	LS mean difference (95% CI) p-value [2]	-1.2 (-1.7; -0.6) <.0001	
	Hedges' g (95% CI)	-1.010 (-1.522; -0.499)	
Age group	Interaction p-value [1]	NC	
18 - < 50			
Overall treatment effect	n'	54	27
	LS mean (SE) [2]	NC (NC)	NC (NC)
	LS mean difference (95% CI) p-value [2]	NC (NC; NC) NC	
	Hedges' g (95% CI)	NC (NC; NC)	
50 - < 65			
Overall treatment effect	n'	24	9
	LS mean (SE) [2]	NC (NC)	NC (NC)
	LS mean difference (95% CI) p-value [2]	NC (NC; NC) NC	
	Hedges' g (95% CI)	NC (NC; NC)	
≥ 65			
Overall treatment effect	n'	5	4
	LS mean (SE) [2]	NC (NC)	NC (NC)

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Subgroup Level Analysis Visit		Vimseltinib (N=83)	Placebo (N=40)
LS mean difference (95% CI) p-value [2]		NC (NC; NC) NC	
Hedges' g (95% CI)		NC (NC; NC)	
Region		Interaction p-value [1]	
U.S.		0.4513	
Overall treatment effect	n'	9	3
	LS mean (SE) [2]	-1.2 (0.33)	0.3 (0.36)
	LS mean difference (95% CI) p-value [2]	-1.5 (-2.5; -0.5) 0.0028	
	Hedges' g (95% CI)	-2.024 (-3.553; -0.494)	
Non-U.S.			
Overall treatment effect	n'	73	34
	LS mean (SE) [2]	-1.6 (0.17)	-0.5 (0.21)
	LS mean difference (95% CI) p-value [2]	-1.1 (-1.6; -0.6) <.0001	
	Hedges' g (95% CI)	-0.839 (-1.258; -0.419)	
Site in Europe		Interaction p-value [1]	
Yes		0.0672	
Overall treatment effect	n'	56	30
	LS mean (SE) [2]	-1.6 (0.18)	-0.6 (0.23)
	LS mean difference (95% CI) p-value [2]	-1.0 (-1.6; -0.4) 0.0010	
	Hedges' g (95% CI)	-0.758 (-1.213; -0.303)	
No			
Overall treatment effect	n'	26	7
	LS mean (SE) [2]	-1.6 (0.23)	0.0 (0.24)
	LS mean difference (95% CI) p-value [2]	-1.7 (-2.3; -1.0) <.0001	
	Hedges' g (95% CI)	-2.132 (-3.108; -1.156)	
Disease subtype		Interaction p-value [1]	
Localized		0.1314	
Overall treatment effect	n'	25	9
	LS mean (SE) [2]	-1.5 (0.21)	-0.8 (0.37)
	LS mean difference (95% CI) p-value [2]	-0.7 (-1.6; 0.1) 0.0911	

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Subgroup Level Analysis Visit		Vimseltinib (N=83)	Placebo (N=40)
Diffuse		Hedges' g (95% CI)	-0.658 (-1.431; 0.115)
Overall treatment effect	n'	57	26
	LS mean (SE) [2]	-1.6 (0.18)	-0.3 (0.18)
	LS mean difference (95% CI) p-value [2]	-1.4 (-1.9; -0.9) <.0001	
	Hedges' g (95% CI)	-1.247 (-1.746; -0.749)	
Missing			
Overall treatment effect	n'	0	2
	LS mean (SE) [2]	NC (NC)	NC (NC)
	LS mean difference (95% CI) p-value [2]	NC (NC; NC) NC	
	Hedges' g (95% CI)	NC (NC; NC)	
Tumour location		Interaction p-value [1]	0.1051
Lower Limb			
Overall treatment effect	n'	76	32
	LS mean (SE) [2]	-1.6 (0.16)	-0.5 (0.20)
	LS mean difference (95% CI) p-value [2]	-1.0 (-1.5; -0.5) 0.0001	
	Hedges' g (95% CI)	-0.843 (-1.269; -0.418)	
All Other			
Overall treatment effect	n'	6	5
	LS mean (SE) [2]	-1.6 (0.36)	0.1 (0.23)
	LS mean difference (95% CI) p-value [2]	-1.8 (-2.6; -0.9) <.0001	
	Hedges' g (95% CI)	-2.472 (-4.039; -0.904)	
Disease location joint size		Interaction p-value [1]	0.7828
Large Joints			
Overall treatment effect	n'	68	26
	LS mean (SE) [2]	-1.6 (0.17)	-0.5 (0.21)
	LS mean difference (95% CI) p-value [2]	-1.1 (-1.6; -0.6) <.0001	
	Hedges' g (95% CI)	-0.927 (-1.395; -0.459)	
Small Joints			
Overall treatment effect	n'	14	11

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Subgroup Level Analysis Visit		Vimseltinib (N=83)	Placebo (N=40)
	LS mean (SE) [2]	-1.6 (0.35)	-0.4 (0.32)
	LS mean difference (95% CI) p-value [2]	-1.2 (-2.2; -0.3) 0.0108	
	Hedges' g (95% CI)	-1.038 (-1.873; -0.202)	
Disease location knee		0.3640	
Yes			
Overall treatment effect	n'	55	24
	LS mean (SE) [2]	-1.5 (0.18)	-0.5 (0.22)
	LS mean difference (95% CI) p-value [2]	-1.0 (-1.6; -0.4) 0.0005	
	Hedges' g (95% CI)	-0.868 (-1.363; -0.373)	
No			
Overall treatment effect	n'	27	13
	LS mean (SE) [2]	-1.7 (0.23)	-0.3 (0.29)
	LS mean difference (95% CI) p-value [2]	-1.4 (-2.1; -0.6) 0.0004	
	Hedges' g (95% CI)	-1.236 (-1.946; -0.525)	
Prior surgery		0.6867	
Yes			
Overall treatment effect	n'	63	24
	LS mean (SE) [2]	-1.5 (0.17)	-0.3 (0.21)
	LS mean difference (95% CI) p-value [2]	-1.2 (-1.7; -0.7) <.0001	
	Hedges' g (95% CI)	-1.083 (-1.577; -0.589)	
No			
Overall treatment effect	n'	19	13
	LS mean (SE) [2]	-1.8 (0.27)	-0.7 (0.29)
	LS mean difference (95% CI) p-value [2]	-1.0 (-1.8; -0.3) 0.0098	
	Hedges' g (95% CI)	-0.939 (-1.676; -0.201)	
Prior imatinib/nilotinib treatment		0.7156	
Yes			
Overall treatment effect	n'	18	8
	LS mean (SE) [2]	-1.2 (0.19)	-0.2 (0.40)

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Subgroup		Vimseltinib (N=83)	Placebo (N=40)
Level	Analysis Visit		
No	LS mean difference (95% CI) p-value [2]	-1.0 (-1.9; -0.1) 0.0309	
	Hedges' g (95% CI)	-0.923 (-1.787; -0.058)	
	Overall treatment effect		
	n'	64	29
	LS mean (SE) [2]	-1.7 (0.18)	-0.5 (0.20)
	LS mean difference (95% CI) p-value [2]	-1.2 (-1.7; -0.6) <.0001	
	Hedges' g (95% CI)	-0.966 (-1.424; -0.509)	

N: Number of subjects in analysis set. n: Number of subjects with non-missing data. n': Number of subjects analysed. SD: Standard deviation. SE: Standard error. Min: Minimum. Max: Maximum. NC: Not calculated. NE: Not estimable. CI: Confidence interval.

Reference is Placebo.

[1] Treatment*Subgroup interaction p-value from MMRM model.

[2] MMRM model using unstructured covariance matrix with terms Treatment, Visit, Subgroup, Baseline value, Treatment by Visit, and Treatment by Subgroup interactions.

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

4.1.4.2 Subgruppenanalysen für den Anteil der Patienten mit einer Reduktion des Skalenwertes der NRS für stärkste Steifheit um mindestens 2 Punkte gegenüber dem Ausgangswert zu Woche 25

Subgroup Level	Vimseltinib (N=83)		Placebo (N=40)		RR [1] (95% CI) p-value	OR [2] (95% CI) p-value	RD [3] (95% CI)
	N/N'	n (%)	N/N'	n (%)			
Sex	Interaction p-value [4]		0.1095				
Male	37/ 37	14 (37.8)	13/ 13	0 (0.0)	10.684 (0.682;167.429) 0.0916	16.660 (0.919;302.036) 0.0571	0.378 (0.222;0.535)
Female	46/ 46	18 (39.1)	27/ 27	6 (22.2)	1.761 (0.797;3.889) 0.1617	2.250 (0.761;6.648) 0.1424	0.169 (-0.042;0.380)
Age group	Interaction p-value [4]		NC				
18 - < 50	54/ 54	20 (37.0)	27/ 27	2 (7.4)	NC (NC;NC) NC	NC (NC;NC) NC	NC (NC;NC)
50 - < 65	24/ 24	11 (45.8)	9/ 9	3 (33.3)	NC (NC;NC) NC	NC (NC;NC) NC	NC (NC;NC)
≥ 65	5/ 5	1 (20.0)	4/ 4	1 (25.0)	NC (NC;NC) NC	NC (NC;NC) NC	NC (NC;NC)
Region	Interaction p-value [4]		0.0145				
U.S.	9/ 9	1 (11.1)	4/ 4	2 (50.0)	0.222 (0.027;1.800) 0.1587	0.125 (0.007;2.176) 0.1537	-0.389 (-0.920;0.142)

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Subgroup Level	Vimseltinib (N=83)		Placebo (N=40)		RR [1] (95% CI) p-value	OR [2] (95% CI) p-value	RD [3] (95% CI)
	N/N'	n (%)	N/N'	n (%)			
Non-U.S.	74/ 74	31 (41.9)	36/ 36	4 (11.1)	3.770 (1.441;9.868) 0.0069	5.767 (1.849;17.987) 0.0025	0.308 (0.156;0.460)
Site in Europe	Interaction p-value [4]		0.2650				
Yes	57/ 57	24 (42.1)	32/ 32	4 (12.5)	3.368 (1.282;8.849) 0.0137	5.091 (1.577;16.439) 0.0065	0.296 (0.124;0.468)
No	26/ 26	8 (30.8)	8/ 8	2 (25.0)	1.231 (0.325;4.661) 0.7599	1.333 (0.220;8.099) 0.7546	0.058 (-0.291;0.406)
Disease subtype	Interaction p-value [4]		0.2461				
Localized	26/ 26	7 (26.9)	10/ 10	2 (20.0)	1.346 (0.335;5.415) 0.6756	1.474 (0.250;8.698) 0.6686	0.069 (-0.232;0.370)
Diffuse	57/ 57	25 (43.9)	28/ 28	3 (10.7)	4.094 (1.351;12.407) 0.0127	6.510 (1.762;24.053) 0.0050	0.331 (0.159;0.504)
Missing	0/ 0	0	2/ 2	1 (50.0)	NC (NC;NC) NC	NC (NC;NC) NC	NC (NC;NC)
Tumour location	Interaction p-value [4]		0.4293				
Lower Limb	77/ 77	29 (37.7)	35/ 35	6 (17.1)	2.197 (1.004;4.807) 0.0488	2.920 (1.082;7.879) 0.0343	0.205 (0.040;0.370)

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Subgroup Level	Vimseltinib (N=83)		Placebo (N=40)		RR [1] (95% CI) p-value	OR [2] (95% CI) p-value	RD [3] (95% CI)
	N/N'	n (%)	N/N'	n (%)			
All Other	6/ 6	3 (50.0)	5/ 5	0 (0.0)	6.000 (0.382;94.351) 0.2025	11.000 (0.426;284.305) 0.1484	0.500 (0.100;0.900)
Disease location joint size	Interaction p-value [4]		0.3043				
Large Joints	69/ 69	26 (37.7)	29/ 29	3 (10.3)	3.643 (1.196;11.093) 0.0229	5.240 (1.442;19.046) 0.0119	0.273 (0.114;0.433)
Small Joints	14/ 14	6 (42.9)	11/ 11	3 (27.3)	1.571 (0.503;4.908) 0.4367	2.000 (0.366;10.919) 0.4235	0.156 (-0.214;0.525)
Disease location knee	Interaction p-value [4]		0.3300				
Yes	56/ 56	22 (39.3)	27/ 27	3 (11.1)	3.536 (1.159;10.787) 0.0265	5.176 (1.390;19.273) 0.0142	0.282 (0.107;0.456)
No	27/ 27	10 (37.0)	13/ 13	3 (23.1)	1.605 (0.530;4.858) 0.4025	1.961 (0.434;8.860) 0.3816	0.140 (-0.153;0.432)
Prior surgery	Interaction p-value [4]		0.9120				
Yes	64/ 64	25 (39.1)	27/ 27	4 (14.8)	2.637 (1.015;6.851) 0.0466	3.686 (1.139;11.930) 0.0295	0.242 (0.063;0.422)
No	19/ 19	7 (36.8)	13/ 13	2 (15.4)	2.395 (0.588;9.752)	3.208 (0.546;18.867)	0.215 (-0.078;0.507)

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

Subgroup Level	Vimseltinib (N=83)		Placebo (N=40)		RR [1] (95% CI) p-value	OR [2] (95% CI) p-value	RD [3] (95% CI)
	N/N'	n (%)	N/N'	n (%)			
					0.2229	0.1972	
Prior imatinib/nilotinib treatment	Interaction p-value [4]		0.9108				
Yes	19/ 19	6 (31.6)	9/ 9	1 (11.1)	2.842 (0.399;20.234) 0.2969	3.692 (0.373;36.567) 0.2642	0.205 (-0.088;0.498)
No	64/ 64	26 (40.6)	31/ 31	5 (16.1)	2.519 (1.071;5.926) 0.0343	3.558 (1.209;10.469) 0.0212	0.245 (0.068;0.422)

N: Number of subjects in analysis set. N': Number of subjects analysed. n: Number of subjects with event. NC: Not calculated. NE: Not estimable. CI: Confidence interval. OR: Odds ratio. RD: Risk difference. RR: Risk ratio. Int.: Interaction.

Percentages based on N. Reference is Placebo.

[1] Log-binomial regression with terms Treatment, Subgroup, and Treatment by Subgroup interaction.

[2] Logistic regression with terms Treatment, Subgroup, and Treatment by Subgroup interaction.

[3] Cochran-Mantel-Haenszel method stratified by Subgroup.

[4] Treatment*Subgroup interaction p-value from log-binomial regression.

4.1.5 Subgruppenanalysen für den Schweregrad der Erkrankung gemessen mittels PGIS

4.1.5.1 Subgruppenanalysen für die Veränderung des PGIS-ROM-Skalenwertes gegenüber dem Ausgangswert während der randomisierten, kontrollierten Studienphase

Subgroup Level Analysis Visit		Vimseltinib (N=83)	Placebo (N=40)
Sex	Interaction p-value [1]	0.8588	
Male			
Overall treatment effect	n'	37	12
	LS mean (SE) [2]	-0.4 (0.10)	-0.1 (0.15)
	LS mean difference (95% CI) p-value [2]	-0.3 (-0.7; 0.0) 0.0652	
	Hedges' g (95% CI)	-0.614 (-1.273; 0.044)	
Female			
Overall treatment effect	n'	46	24
	LS mean (SE) [2]	-0.8 (0.10)	-0.4 (0.11)
	LS mean difference (95% CI) p-value [2]	-0.4 (-0.7; -0.1) 0.0158	
	Hedges' g (95% CI)	-0.613 (-1.114; -0.112)	
Age group	Interaction p-value [1]	NC	
18 - < 50			
Overall treatment effect	n'	54	27
	LS mean (SE) [2]	NC (NC)	NC (NC)
	LS mean difference (95% CI) p-value [2]	NC (NC; NC) NC	
	Hedges' g (95% CI)	NC (NC; NC)	
50 - < 65			
Overall treatment effect	n'	24	9
	LS mean (SE) [2]	NC (NC)	NC (NC)
	LS mean difference (95% CI) p-value [2]	NC (NC; NC) NC	
	Hedges' g (95% CI)	NC (NC; NC)	
≥ 65			
Overall treatment effect	n'	5	4
	LS mean (SE) [2]	NC (NC)	NC (NC)

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

Subgroup Level Analysis Visit		Vimseltinib (N=83)	Placebo (N=40)
LS mean difference (95% CI) p-value [2]		NC (NC; NC) NC	
Hedges' g (95% CI)		NC (NC; NC)	
Region		Interaction p-value [1]	
U.S.		0.0234	
Overall treatment effect	n'	9	3
	LS mean (SE) [2]	-0.7 (0.14)	-1.1 (0.26)
	LS mean difference (95% CI) p-value [2]	0.4 (-0.2; 0.9) 0.2246	
	Hedges' g (95% CI)	0.809 (-0.529; 2.146)	
Non-U.S.			
Overall treatment effect	n'	74	33
	LS mean (SE) [2]	-0.6 (0.08)	-0.2 (0.09)
	LS mean difference (95% CI) p-value [2]	-0.4 (-0.6; -0.1) 0.0029	
	Hedges' g (95% CI)	-0.634 (-1.050; -0.218)	
Site in Europe		Interaction p-value [1]	
Yes		0.5524	
Overall treatment effect	n'	57	29
	LS mean (SE) [2]	-0.6 (0.10)	-0.3 (0.09)
	LS mean difference (95% CI) p-value [2]	-0.3 (-0.5; 0.0) 0.0603	
	Hedges' g (95% CI)	-0.430 (-0.879; 0.019)	
No			
Overall treatment effect	n'	26	7
	LS mean (SE) [2]	-0.7 (0.11)	-0.3 (0.29)
	LS mean difference (95% CI) p-value [2]	-0.5 (-1.1; 0.2) 0.1404	
	Hedges' g (95% CI)	-0.628 (-1.471; 0.215)	
Disease subtype		Interaction p-value [1]	
Localized		0.4789	
Overall treatment effect	n'	26	9
	LS mean (SE) [2]	-0.6 (0.14)	-0.4 (0.18)
	LS mean difference (95% CI) p-value [2]	-0.2 (-0.7; 0.3) 0.3886	

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

Subgroup		Vimseltinib (N=83)	Placebo (N=40)
Level	Analysis Visit		
Diffuse		Hedges' g (95% CI)	-0.332 (-1.089; 0.424)
Overall treatment effect	n'	57	25
	LS mean (SE) [2]	-0.6 (0.08)	-0.2 (0.11)
	LS mean difference (95% CI) p-value [2]	-0.4 (-0.7; -0.1) 0.0058	
	Hedges' g (95% CI)	-0.671 (-1.149; -0.192)	
Missing			
Overall treatment effect	n'	0	2
	LS mean (SE) [2]	NC (NC)	NC (NC)
	LS mean difference (95% CI) p-value [2]	NC (NC; NC) NC	
	Hedges' g (95% CI)	NC (NC; NC)	
Tumour location		Interaction p-value [1]	0.4825
Lower Limb			
Overall treatment effect	n'	77	31
	LS mean (SE) [2]	-0.6 (0.08)	-0.3 (0.10)
	LS mean difference (95% CI) p-value [2]	-0.3 (-0.5; -0.0) 0.0209	
	Hedges' g (95% CI)	-0.495 (-0.914; -0.075)	
All Other			
Overall treatment effect	n'	6	5
	LS mean (SE) [2]	-0.6 (0.23)	-0.1 (0.28)
	LS mean difference (95% CI) p-value [2]	-0.6 (-1.3; 0.2) 0.1278	
	Hedges' g (95% CI)	-0.923 (-2.163; 0.318)	
Disease location joint size		Interaction p-value [1]	0.2311
Large Joints			
Overall treatment effect	n'	69	25
	LS mean (SE) [2]	-0.6 (0.08)	-0.3 (0.10)
	LS mean difference (95% CI) p-value [2]	-0.3 (-0.5; -0.0) 0.0423	
	Hedges' g (95% CI)	-0.476 (-0.936; -0.017)	
Small Joints			
Overall treatment effect	n'	14	11

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

Subgroup Level Analysis Visit		Vimseltinib (N=83)	Placebo (N=40)
	LS mean (SE) [2]	-0.9 (0.13)	-0.3 (0.21)
	LS mean difference (95% CI) p-value [2]	-0.6 (-1.1; -0.1) 0.0154	
	Hedges' g (95% CI)	-0.984 (-1.815; -0.154)	
Disease location knee		Interaction p-value [1]	0.4246
Yes			
Overall treatment effect	n'	56	23
	LS mean (SE) [2]	-0.6 (0.08)	-0.4 (0.08)
	LS mean difference (95% CI) p-value [2]	-0.2 (-0.5; -0.0) 0.0429	
	Hedges' g (95% CI)	-0.504 (-0.992; -0.015)	
No			
Overall treatment effect	n'	27	13
	LS mean (SE) [2]	-0.6 (0.14)	-0.1 (0.21)
	LS mean difference (95% CI) p-value [2]	-0.5 (-1.0; 0.0) 0.0650	
	Hedges' g (95% CI)	-0.625 (-1.296; 0.046)	
Prior surgery		Interaction p-value [1]	0.1556
Yes			
Overall treatment effect	n'	64	23
	LS mean (SE) [2]	-0.6 (0.08)	-0.2 (0.11)
	LS mean difference (95% CI) p-value [2]	-0.5 (-0.7; -0.2) 0.0011	
	Hedges' g (95% CI)	-0.806 (-1.294; -0.318)	
No			
Overall treatment effect	n'	19	13
	LS mean (SE) [2]	-0.6 (0.18)	-0.5 (0.16)
	LS mean difference (95% CI) p-value [2]	-0.1 (-0.5; 0.4) 0.7828	
	Hedges' g (95% CI)	-0.099 (-0.800; 0.602)	
Prior imatinib/nilotinib treatment		Interaction p-value [1]	0.4794
Yes			
Overall treatment effect	n'	19	8
	LS mean (SE) [2]	-0.7 (0.16)	-0.2 (0.13)

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

Subgroup		Vimseltinib (N=83)	Placebo (N=40)
Level	Analysis Visit		
No	LS mean difference (95% CI) p-value [2]	-0.5 (-0.9; -0.1) 0.0257	
	Hedges' g (95% CI)		
	Overall treatment effect		
	n'	64	28
	LS mean (SE) [2]	-0.6 (0.08)	-0.3 (0.11)
	LS mean difference (95% CI) p-value [2]	-0.3 (-0.6; -0.0) 0.0475	
	Hedges' g (95% CI)	-0.451 (-0.897; -0.005)	

N: Number of subjects in analysis set. n: Number of subjects with non-missing data. n': Number of subjects analysed. SD: Standard deviation. SE: Standard error. Min: Minimum. Max: Maximum. NC: Not calculated. NE: Not estimable. CI: Confidence interval.

Reference is Placebo.

[1] Treatment*Subgroup interaction p-value from MMRM model.

[2] MMRM model using unstructured covariance matrix with terms Treatment, Visit, Subgroup, Baseline value, Treatment by Visit, and Treatment by Subgroup interactions.

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

4.1.5.2 Subgruppenanalysen für die Veränderung des PGIS-PF-Skalenwertes gegenüber dem Ausgangswert während der randomisierten, kontrollierten Studienphase

Subgroup Level Analysis Visit		Vimseltinib (N=83)	Placebo (N=40)
Sex	Interaction p-value [1]	0.4620	
Male			
Overall treatment effect	n'	37	12
	LS mean (SE) [2]	-0.5 (0.10)	-0.3 (0.11)
	LS mean difference (95% CI) p-value [2]	-0.2 (-0.5; 0.1) 0.1862	
	Hedges' g (95% CI)	-0.439 (-1.092; 0.214)	
Female			
Overall treatment effect	n'	46	25
	LS mean (SE) [2]	-0.6 (0.09)	-0.3 (0.14)
	LS mean difference (95% CI) p-value [2]	-0.4 (-0.7; -0.0) 0.0346	
	Hedges' g (95% CI)	-0.528 (-1.019; -0.036)	
Age group	Interaction p-value [1]	NC	
18 - < 50			
Overall treatment effect	n'	54	27
	LS mean (SE) [2]	NC (NC)	NC (NC)
	LS mean difference (95% CI) p-value [2]	NC (NC; NC) NC	
	Hedges' g (95% CI)	NC (NC; NC)	
50 - < 65			
Overall treatment effect	n'	24	9
	LS mean (SE) [2]	NC (NC)	NC (NC)
	LS mean difference (95% CI) p-value [2]	NC (NC; NC) NC	
	Hedges' g (95% CI)	NC (NC; NC)	
≥ 65			
Overall treatment effect	n'	5	4
	LS mean (SE) [2]	NC (NC)	NC (NC)
	LS mean difference (95% CI) p-value [2]	NC (NC; NC) NC	
	Hedges' g (95% CI)	NC (NC; NC)	

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

Subgroup Level Analysis Visit		Vimseltinib (N=83)	Placebo (N=40)
Region		Interaction p-value [1]	0.0065
U.S.			
Overall treatment effect	n'	9	3
	LS mean (SE) [2]	-0.7 (0.20)	-1.2 (0.20)
	LS mean difference (95% CI) p-value [2]	0.5 (-0.1; 1.0) 0.1014	
	Hedges' g (95% CI)	1.094 (-0.276; 2.463)	
Non-U.S.			
Overall treatment effect	n'	74	34
	LS mean (SE) [2]	-0.6 (0.07)	-0.2 (0.10)
	LS mean difference (95% CI) p-value [2]	-0.4 (-0.6; -0.1) 0.0052	
	Hedges' g (95% CI)	-0.587 (-0.998; -0.176)	
Site in Europe		Interaction p-value [1]	0.5978
Yes			
Overall treatment effect	n'	57	30
	LS mean (SE) [2]	-0.6 (0.09)	-0.2 (0.09)
	LS mean difference (95% CI) p-value [2]	-0.3 (-0.6; -0.1) 0.0147	
	Hedges' g (95% CI)	-0.555 (-1.002; -0.108)	
No			
Overall treatment effect	n'	26	7
	LS mean (SE) [2]	-0.6 (0.12)	-0.4 (0.31)
	LS mean difference (95% CI) p-value [2]	-0.1 (-0.8; 0.5) 0.6747	
	Hedges' g (95% CI)	-0.178 (-1.008; 0.652)	
Disease subtype		Interaction p-value [1]	0.6856
Localized			
Overall treatment effect	n'	26	9
	LS mean (SE) [2]	-0.6 (0.12)	-0.4 (0.20)
	LS mean difference (95% CI) p-value [2]	-0.2 (-0.7; 0.2) 0.3345	
	Hedges' g (95% CI)	-0.372 (-1.130; 0.386)	
Diffuse			

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

Subgroup Level Analysis Visit		Vimseltinib (N=83)	Placebo (N=40)
Overall treatment effect	n'	57	26
	LS mean (SE) [2]	-0.6 (0.09)	-0.2 (0.12)
	LS mean difference (95% CI) p-value [2]	-0.3 (-0.6; -0.0) 0.0302	
	Hedges' g (95% CI)	-0.516 (-0.984; -0.049)	
Missing			
Overall treatment effect	n'	0	2
	LS mean (SE) [2]	NC (NC)	NC (NC)
	LS mean difference (95% CI) p-value [2]	NC (NC; NC) NC	
	Hedges' g (95% CI)	NC (NC; NC)	
Tumour location		Interaction p-value [1]	0.0347
Lower Limb			
Overall treatment effect	n'	77	32
	LS mean (SE) [2]	-0.5 (0.08)	-0.3 (0.10)
	LS mean difference (95% CI) p-value [2]	-0.2 (-0.5; 0.0) 0.1048	
	Hedges' g (95% CI)	-0.342 (-0.754; 0.070)	
All Other			
Overall treatment effect	n'	6	5
	LS mean (SE) [2]	-1.0 (0.16)	0.0 (0.36)
	LS mean difference (95% CI) p-value [2]	-1.1 (-1.9; -0.3) 0.0068	
	Hedges' g (95% CI)	-1.657 (-3.024; -0.289)	
Disease location joint size		Interaction p-value [1]	0.2621
Large Joints			
Overall treatment effect	n'	69	26
	LS mean (SE) [2]	-0.6 (0.08)	-0.2 (0.11)
	LS mean difference (95% CI) p-value [2]	-0.4 (-0.7; -0.1) 0.0076	
	Hedges' g (95% CI)	-0.621 (-1.078; -0.164)	
Small Joints			
Overall treatment effect	n'	14	11
	LS mean (SE) [2]	-0.6 (0.12)	-0.5 (0.21)
	LS mean difference (95% CI) p-value [2]	-0.1 (-0.5; 0.4) 0.7348	

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

Subgroup Level Analysis Visit		Vimseltinib (N=83)	Placebo (N=40)
	Hedges' g (95% CI)	-0.136 (-0.921; 0.649)	
Disease location knee	Interaction p-value [1]	0.8165	
Yes			
Overall treatment effect	n'	56	24
	LS mean (SE) [2]	-0.6 (0.08)	-0.3 (0.10)
	LS mean difference (95% CI) p-value [2]	-0.3 (-0.6; -0.0) 0.0227	
	Hedges' g (95% CI)	-0.560 (-1.043; -0.077)	
No			
Overall treatment effect	n'	27	13
	LS mean (SE) [2]	-0.5 (0.12)	-0.3 (0.21)
	LS mean difference (95% CI) p-value [2]	-0.2 (-0.7; 0.2) 0.3181	
	Hedges' g (95% CI)	-0.336 (-0.998; 0.325)	
Prior surgery	Interaction p-value [1]	0.2096	
Yes			
Overall treatment effect	n'	64	24
	LS mean (SE) [2]	-0.6 (0.08)	-0.2 (0.10)
	LS mean difference (95% CI) p-value [2]	-0.4 (-0.7; -0.1) 0.0028	
	Hedges' g (95% CI)	-0.727 (-1.205; -0.248)	
No			
Overall treatment effect	n'	19	13
	LS mean (SE) [2]	-0.5 (0.15)	-0.4 (0.21)
	LS mean difference (95% CI) p-value [2]	-0.0 (-0.5; 0.4) 0.8481	
	Hedges' g (95% CI)	-0.069 (-0.770; 0.632)	
Prior imatinib/nilotinib treatment	Interaction p-value [1]	0.3025	
Yes			
Overall treatment effect	n'	19	8
	LS mean (SE) [2]	-0.6 (0.17)	-0.1 (0.12)
	LS mean difference (95% CI) p-value [2]	-0.5 (-0.9; -0.1) 0.0211	

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

Subgroup Level Analysis Visit		Vimseltinib (N=83)	Placebo (N=40)
No Overall treatment effect	Hedges' g (95% CI)	-0.979 (-1.841; -0.118)	
	n'	64	29
	LS mean (SE) [2]	-0.6 (0.08)	-0.3 (0.12)
	LS mean difference (95% CI) p-value [2]	-0.2 (-0.5; 0.1) 0.1054	
	Hedges' g (95% CI)	-0.363 (-0.802; 0.076)	

N: Number of subjects in analysis set. n: Number of subjects with non-missing data. n': Number of subjects analysed. SD: Standard deviation. SE: Standard error. Min: Minimum. Max: Maximum. NC: Not calculated. NE: Not estimable. CI: Confidence interval.

Reference is Placebo.

[1] Treatment*Subgroup interaction p-value from MMRM model.

[2] MMRM model using unstructured covariance matrix with terms Treatment, Visit, Subgroup, Baseline value, Treatment by Visit, and Treatment by Subgroup interactions.

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

4.1.5.3 Subgruppenanalysen für den Anteil der Patienten mit einer Senkung des PGIS-ROM-Skalenwertes um mindestens 1 Punkt gegenüber dem Ausgangswert zu Woche 25

Subgroup Level	Vimseltinib (N=83)		Placebo (N=40)		RR [1] (95% CI) p-value	OR [2] (95% CI) p-value	RD [3] (95% CI)
	N/N'	n (%)	N/N'	n (%)			
Sex	Interaction p-value [4]		0.1265				
Male	37/ 37	11 (29.7)	13/ 13	0 (0.0)	8.474 (0.534;134.463) 0.1297	11.717 (0.641;214.288) 0.0970	0.297 (0.150;0.445)
Female	46/ 46	21 (45.7)	27/ 27	8 (29.6)	1.541 (0.795;2.985) 0.2001	1.995 (0.727;5.474) 0.1799	0.160 (-0.064;0.385)
Age group	Interaction p-value [4]		NC				
18 - < 50	54/ 54	20 (37.0)	27/ 27	6 (22.2)	NC (NC;NC) NC	NC (NC;NC) NC	NC (NC;NC)
50 - < 65	24/ 24	11 (45.8)	9/ 9	2 (22.2)	NC (NC;NC) NC	NC (NC;NC) NC	NC (NC;NC)
≥ 65	5/ 5	1 (20.0)	4/ 4	0 (0.0)	NC (NC;NC) NC	NC (NC;NC) NC	NC (NC;NC)
Region	Interaction p-value [4]		0.7085				
U.S.	9/ 9	3 (33.3)	4/ 4	1 (25.0)	1.333 (0.193;9.209) 0.7705	1.500 (0.106;21.312) 0.7646	0.083 (-0.441;0.608)

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

Subgroup Level	Vimseltinib (N=83)		Placebo (N=40)		RR [1] (95% CI) p-value	OR [2] (95% CI) p-value	RD [3] (95% CI)
	N/N'	n (%)	N/N'	n (%)			
Non-U.S.	74/ 74	29 (39.2)	36/ 36	7 (19.4)	2.015 (0.978;4.153) 0.0574	2.670 (1.034;6.891) 0.0424	0.197 (0.027;0.368)
Site in Europe	Interaction p-value [4]		0.5631				
Yes	57/ 57	22 (38.6)	32/ 32	7 (21.9)	1.764 (0.849;3.669) 0.1285	2.245 (0.831;6.062) 0.1106	0.167 (-0.024;0.358)
No	26/ 26	10 (38.5)	8/ 8	1 (12.5)	3.077 (0.462;20.505) 0.2455	4.375 (0.466;41.067) 0.1964	0.260 (-0.036;0.555)
Disease subtype	Interaction p-value [4]		0.2466				
Localized	26/ 26	11 (42.3)	10/ 10	1 (10.0)	4.231 (0.625;28.651) 0.1394	6.600 (0.726;60.021) 0.0939	0.323 (0.057;0.589)
Diffuse	57/ 57	21 (36.8)	28/ 28	7 (25.0)	1.474 (0.713;3.046) 0.2952	1.750 (0.637;4.808) 0.2778	0.118 (-0.085;0.322)
Missing	0/ 0	0	2/ 2	0 (0.0)	NC (NC;NC) NC	NC (NC;NC) NC	NC (NC;NC)
Tumour location	Interaction p-value [4]		0.4869				
Lower Limb	77/ 77	30 (39.0)	35/ 35	8 (22.9)	1.705 (0.872;3.330)	2.154 (0.865;5.364)	0.161 (-0.016;0.338)

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

Subgroup Level	Vimseltinib (N=83)		Placebo (N=40)		RR [1] (95% CI) p-value	OR [2] (95% CI) p-value	RD [3] (95% CI)
	N/N'	n (%)	N/N'	n (%)			
					0.1186	0.0992	
All Other	6/ 6	2 (33.3)	5/ 5	0 (0.0)	4.286 (0.252;72.901) 0.3142	6.111 (0.229;162.735) 0.2797	0.333 (-0.044;0.711)
Disease location joint size	Interaction p-value [4]		0.9636				
Large Joints	69/ 69	27 (39.1)	29/ 29	6 (20.7)	1.891 (0.875;4.089) 0.1052	2.464 (0.888;6.836) 0.0832	0.184 (-0.003;0.371)
Small Joints	14/ 14	5 (35.7)	11/ 11	2 (18.2)	1.964 (0.467;8.267) 0.3572	2.500 (0.381;16.420) 0.3400	0.175 (-0.164;0.514)
Disease location knee	Interaction p-value [4]		0.9987				
Yes	56/ 56	24 (42.9)	27/ 27	6 (22.2)	1.929 (0.895;4.156) 0.0936	2.625 (0.918;7.504) 0.0717	0.206 (0.003;0.410)
No	27/ 27	8 (29.6)	13/ 13	2 (15.4)	1.926 (0.474;7.819) 0.3592	2.316 (0.415;12.910) 0.3381	0.142 (-0.119;0.403)
Prior surgery	Interaction p-value [4]		0.6989				
Yes	64/ 64	25 (39.1)	27/ 27	6 (22.2)	1.758 (0.815;3.793) 0.1506	2.244 (0.795;6.328) 0.1267	0.168 (-0.029;0.366)
No	19/ 19	7 (36.8)	13/ 13	2 (15.4)	2.395	3.208	0.215

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

Subgroup Level	Vimseltinib (N=83)		Placebo (N=40)		RR [1] (95% CI) p-value	OR [2] (95% CI) p-value	RD [3] (95% CI)
	N/N'	n (%)	N/N'	n (%)			
					(0.588;9.752) 0.2229	(0.546;18.867) 0.1972	(-0.078;0.507)
Prior imatinib/nilotinib treatment	Interaction p-value [4]		0.5041				
Yes	19/ 19	7 (36.8)	9/ 9	1 (11.1)	3.316 (0.477;23.060) 0.2257	4.667 (0.478;45.546) 0.1851	0.257 (-0.041;0.556)
No	64/ 64	25 (39.1)	31/ 31	7 (22.6)	1.730 (0.842;3.554) 0.1358	2.198 (0.825;5.858) 0.1154	0.165 (-0.025;0.354)

N: Number of subjects in analysis set. N': Number of subjects analysed. n: Number of subjects with event. NC: Not calculated. NE: Not estimable. CI: Confidence interval. OR: Odds ratio. RD: Risk difference. RR: Risk ratio. Int.: Interaction.

Percentages based on N. Reference is Placebo.

[1] Log-binomial regression with terms Treatment, Subgroup, and Treatment by Subgroup interaction.

[2] Logistic regression with terms Treatment, Subgroup, and Treatment by Subgroup interaction.

[3] Cochran-Mantel-Haenszel method stratified by Subgroup.

[4] Treatment*Subgroup interaction p-value from log-binomial regression.

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

4.1.5.4 Subgruppenanalysen für den Anteil der Patienten mit einer Senkung des PGIS-PF-Skalenwertes um mindestens 1 Punkt gegenüber dem Ausgangswert zu Woche 25

Subgroup Level	Vimseltinib (N=83)		Placebo (N=40)		RR [1] (95% CI) p-value	OR [2] (95% CI) p-value	RD [3] (95% CI)
	N/N'	n (%)	N/N'	n (%)			
Sex	Interaction p-value [4]		0.7461				
Male	37/ 37	15 (40.5)	13/ 13	2 (15.4)	2.635 (0.695;9.996) 0.1543	3.750 (0.725;19.397) 0.1149	0.252 (-0.000;0.504)
Female	46/ 46	21 (45.7)	27/ 27	6 (22.2)	2.054 (0.948;4.450) 0.0679	2.940 (1.001;8.631) 0.0497	0.234 (0.021;0.447)
Age group	Interaction p-value [4]		NC				
18 - < 50	54/ 54	21 (38.9)	27/ 27	6 (22.2)	NC (NC;NC) NC	NC (NC;NC) NC	NC (NC;NC)
50 - < 65	24/ 24	13 (54.2)	9/ 9	2 (22.2)	NC (NC;NC) NC	NC (NC;NC) NC	NC (NC;NC)
≥ 65	5/ 5	2 (40.0)	4/ 4	0 (0.0)	NC (NC;NC) NC	NC (NC;NC) NC	NC (NC;NC)
Region	Interaction p-value [4]		0.6286				
U.S.	9/ 9	3 (33.3)	4/ 4	1 (25.0)	1.333 (0.193;9.209) 0.7705	1.500 (0.106;21.312) 0.7646	0.083 (-0.441;0.608)

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

Subgroup Level	Vimseltinib (N=83)		Placebo (N=40)		RR [1] (95% CI) p-value	OR [2] (95% CI) p-value	RD [3] (95% CI)
	N/N'	n (%)	N/N'	n (%)			
Non-U.S.	74/ 74	33 (44.6)	36/ 36	7 (19.4)	2.293 (1.126;4.673) 0.0223	3.334 (1.297;8.571) 0.0124	0.252 (0.080;0.423)
Site in Europe	Interaction p-value [4]		0.3709				
Yes	57/ 57	28 (49.1)	32/ 32	6 (18.8)	2.620 (1.215;5.648) 0.0140	4.184 (1.496;11.701) 0.0064	0.304 (0.116;0.491)
No	26/ 26	8 (30.8)	8/ 8	2 (25.0)	1.231 (0.325;4.661) 0.7599	1.333 (0.220;8.099) 0.7546	0.058 (-0.291;0.406)
Disease subtype	Interaction p-value [4]		0.2031				
Localized	26/ 26	13 (50.0)	10/ 10	1 (10.0)	5.000 (0.749;33.386) 0.0966	9.000 (0.993;81.581) 0.0507	0.400 (0.133;0.667)
Diffuse	57/ 57	23 (40.4)	28/ 28	7 (25.0)	1.614 (0.790;3.299) 0.1894	2.029 (0.742;5.549) 0.1679	0.154 (-0.051;0.358)
Missing	0/ 0	0	2/ 2	0 (0.0)	NC (NC;NC) NC	NC (NC;NC) NC	NC (NC;NC)
Tumour location	Interaction p-value [4]		0.4049				
Lower Limb	77/ 77	31 (40.3)	35/ 35	7 (20.0)	2.013 (0.983;4.120)	2.696 (1.048;6.937)	0.203 (0.031;0.375)

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

Subgroup Level	Vimseltinib (N=83)		Placebo (N=40)		RR [1] (95% CI) p-value	OR [2] (95% CI) p-value	RD [3] (95% CI)
	N/N'	n (%)	N/N'	n (%)			
					0.0556	0.0398	
All Other	6/ 6	5 (83.3)	5/ 5	1 (20.0)	4.167 (0.696;24.936) 0.1180	20.000 (0.930;429.904) 0.0556	0.633 (0.173;1.000)
Disease location joint size	Interaction p-value [4]		0.5202				
Large Joints	69/ 69	30 (43.5)	29/ 29	5 (17.2)	2.522 (1.087;5.850) 0.0312	3.692 (1.261;10.815) 0.0172	0.262 (0.082;0.443)
Small Joints	14/ 14	6 (42.9)	11/ 11	3 (27.3)	1.571 (0.503;4.908) 0.4367	2.000 (0.366;10.919) 0.4235	0.156 (-0.214;0.525)
Disease location knee	Interaction p-value [4]		0.2317				
Yes	56/ 56	25 (44.6)	27/ 27	4 (14.8)	3.013 (1.165;7.794) 0.0229	4.637 (1.417;15.171) 0.0112	0.298 (0.111;0.485)
No	27/ 27	11 (40.7)	13/ 13	4 (30.8)	1.324 (0.520;3.368) 0.5557	1.547 (0.379;6.310) 0.5431	0.100 (-0.212;0.412)
Prior surgery	Interaction p-value [4]		0.5636				
Yes	64/ 64	29 (45.3)	27/ 27	5 (18.5)	2.447 (1.061;5.644) 0.0359	3.646 (1.227;10.829) 0.0199	0.268 (0.077;0.459)
No	19/ 19	7 (36.8)	13/ 13	3 (23.1)	1.596	1.944	0.138

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

Subgroup Level	Vimseltinib (N=83)		Placebo (N=40)		RR [1] (95% CI) p-value	OR [2] (95% CI) p-value	RD [3] (95% CI)
	N/N'	n (%)	N/N'	n (%)			
					(0.504;5.062) 0.4269	(0.396;9.551) 0.4129	(-0.178;0.453)
Prior imatinib/nilotinib treatment	Interaction p-value [4]		0.3754				
Yes	19/ 19	9 (47.4)	9/ 9	1 (11.1)	4.263 (0.633;28.723) 0.1363	7.200 (0.747;69.381) 0.0877	0.363 (0.058;0.667)
No	64/ 64	27 (42.2)	31/ 31	7 (22.6)	1.868 (0.917;3.808) 0.0854	2.502 (0.942;6.648) 0.0659	0.196 (0.006;0.387)

N: Number of subjects in analysis set. N': Number of subjects analysed. n: Number of subjects with event. NC: Not calculated. NE: Not estimable. CI: Confidence interval. OR: Odds ratio. RD: Risk difference. RR: Risk ratio. Int.: Interaction.

Percentages based on N. Reference is Placebo.

[1] Log-binomial regression with terms Treatment, Subgroup, and Treatment by Subgroup interaction.

[2] Logistic regression with terms Treatment, Subgroup, and Treatment by Subgroup interaction.

[3] Cochran-Mantel-Haenszel method stratified by Subgroup.

[4] Treatment*Subgroup interaction p-value from log-binomial regression.

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

4.1.6 Subgruppenanalysen für die Veränderung des Gesundheitszustandes gemessen mittels PGIC**4.1.6.1 Subgruppenanalysen für den Anteil der Patienten, die den PGIC-ROM zu Woche 25 mit „wenig besser“, „viel besser“ oder „sehr viel besser“ beantwortet haben**

Subgroup Level	Vimseltinib (N=83)		Placebo (N=40)		RR [1] (95% CI) p-value	OR [2] (95% CI) p-value	RD [3] (95% CI)
	N/N'	n (%)	N/N'	n (%)			
Sex	Interaction p-value [4]		0.7770				
Male	37/ 37	24 (64.9)	13/ 13	3 (23.1)	2.811 (1.013;7.798) 0.0471	6.154 (1.435;26.395) 0.0145	0.418 (0.142;0.694)
Female	46/ 46	29 (63.0)	27/ 27	5 (18.5)	3.404 (1.497;7.742) 0.0035	7.506 (2.399;23.487) 0.0005	0.445 (0.243;0.648)
Age group	Interaction p-value [4]		NC				
18 - < 50	54/ 54	31 (57.4)	27/ 27	7 (25.9)	NC (NC;NC) NC	NC (NC;NC) NC	NC (NC;NC)
50 - < 65	24/ 24	19 (79.2)	24/ 24	19 (79.2)	NC (NC;NC) NC	NC (NC;NC) NC	NC (NC;NC)
≥ 65	5/ 5	3 (60.0)	4/ 4	0 (0.0)	NC (NC;NC) NC	NC (NC;NC) NC	NC (NC;NC)
Region	Interaction p-value [4]		0.3937				
U.S.	9/ 9	7 (77.8)	4/ 4	0 (0.0)	7.500	27.000	0.778

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

Subgroup Level	Vimseltinib (N=83)		Placebo (N=40)		RR [1] (95% CI) p-value	OR [2] (95% CI) p-value	RD [3] (95% CI)
	N/N'	n (%)	N/N'	n (%)			
					(0.528;106.560) 0.1367	(1.043;698.790) 0.0471	(0.506;1.000)
Non-U.S.	74/ 74	46 (62.2)	36/ 36	8 (22.2)	2.797 (1.480;5.286) 0.0015	5.750 (2.302;14.363) 0.0002	0.399 (0.224;0.574)
Site in Europe	Interaction p-value [4]		0.8228				
Yes	57/ 57	35 (61.4)	32/ 32	6 (18.8)	3.275 (1.547;6.933) 0.0019	6.894 (2.448;19.418) 0.0003	0.427 (0.241;0.612)
No	26/ 26	18 (69.2)	8/ 8	2 (25.0)	2.769 (0.812;9.448) 0.1038	6.750 (1.111;41.001) 0.0380	0.442 (0.094;0.791)
Disease subtype	Interaction p-value [4]		0.2248				
Localized	26/ 26	15 (57.7)	10/ 10	3 (30.0)	1.923 (0.706;5.240) 0.2010	3.182 (0.668;15.146) 0.1460	0.277 (-0.065;0.619)
Diffuse	57/ 57	38 (66.7)	28/ 28	4 (14.3)	4.667 (1.849;11.777) 0.0011	12.000 (3.639;39.571) <.0001	0.524 (0.346;0.702)
Missing	0/ 0	0	2/ 2	1 (50.0)	NC (NC;NC) NC	NC (NC;NC) NC	NC (NC;NC)
Tumour location	Interaction p-value [4]		0.2698				

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

Subgroup Level	Vimseltinib (N=83)		Placebo (N=40)		RR [1] (95% CI) p-value	OR [2] (95% CI) p-value	RD [3] (95% CI)
	N/N'	n (%)	N/N'	n (%)			
Lower Limb	77/ 77	48 (62.3)	35/ 35	8 (22.9)	2.727 (1.448;5.136) 0.0019	5.586 (2.240;13.930) 0.0002	0.395 (0.219;0.571)
All Other	6/ 6	5 (83.3)	5/ 5	0 (0.0)	9.429 (0.645;137.772) 0.1011	40.333 (1.330;1222.97) 0.0337	0.833 (0.535;1.000)
Disease location joint size	Interaction p-value [4]		0.7199				
Large Joints	69/ 69	43 (62.3)	29/ 29	6 (20.7)	3.012 (1.443;6.287) 0.0033	6.340 (2.282;17.615) 0.0004	0.416 (0.230;0.603)
Small Joints	14/ 14	10 (71.4)	11/ 11	2 (18.2)	3.929 (1.074;14.367) 0.0386	11.250 (1.647;76.849) 0.0136	0.532 (0.204;0.861)
Disease location knee	Interaction p-value [4]		0.6386				
Yes	56/ 56	36 (64.3)	27/ 27	6 (22.2)	2.893 (1.391;6.016) 0.0045	6.300 (2.184;18.170) 0.0007	0.421 (0.220;0.621)
No	27/ 27	17 (63.0)	13/ 13	2 (15.4)	4.093 (1.107;15.126) 0.0346	9.350 (1.713;51.032) 0.0098	0.476 (0.208;0.743)
Prior surgery	Interaction p-value [4]		0.4103				
Yes	64/ 64	44 (68.8)	27/ 27	5 (18.5)	3.713 (1.654;8.331) 0.0015	9.680 (3.204;29.243) <.0001	0.502 (0.317;0.688)

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

Subgroup Level	Vimseltinib (N=83)		Placebo (N=40)		RR [1] (95% CI) p-value	OR [2] (95% CI) p-value	RD [3] (95% CI)
	N/N'	n (%)	N/N'	n (%)			
No	19/ 19	9 (47.4)	13/ 13	3 (23.1)	2.053 (0.683;6.165) 0.2000	3.000 (0.622;14.469) 0.1711	0.243 (-0.078;0.564)
Prior imatinib/nilotinib treatment	Interaction p-value [4]		0.8460				
Yes	19/ 19	8 (42.1)	9/ 9	1 (11.1)	3.789 (0.555;25.890) 0.1742	5.818 (0.601;56.294) 0.1283	0.310 (0.008;0.612)
No	64/ 64	45 (70.3)	31/ 31	7 (22.6)	3.114 (1.592;6.091) 0.0009	8.120 (2.993;22.033) <.0001	0.477 (0.292;0.662)

N: Number of subjects in analysis set. N': Number of subjects analysed. n: Number of subjects with event. NC: Not calculated. NE: Not estimable. CI: Confidence interval. OR: Odds ratio. RD: Risk difference. RR: Risk ratio. Int.: Interaction.

Percentages based on N. Reference is Placebo.

[1] Log-binomial regression with terms Treatment, Subgroup, and Treatment by Subgroup interaction.

[2] Logistic regression with terms Treatment, Subgroup, and Treatment by Subgroup interaction.

[3] Cochran-Mantel-Haenszel method stratified by Subgroup.

[4] Treatment*Subgroup interaction p-value from log-binomial regression.

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

4.1.6.2 Subgruppenanalysen für den Anteil der Patienten, die den PGIC-PF zu Woche 25 mit „wenig besser“, „viel besser“ oder „sehr viel besser“ beantwortet haben

Subgroup Level	Vimseltinib (N=83)		Placebo (N=40)		RR [1] (95% CI) p-value	OR [2] (95% CI) p-value	RD [3] (95% CI)
	N/N'	n (%)	N/N'	n (%)			
Sex	Interaction p-value [4]		0.5908				
Male	37/ 37	27 (73.0)	13/ 13	4 (30.8)	2.372 (1.025;5.486) 0.0436	6.075 (1.523;24.228) 0.0106	0.422 (0.133;0.711)
Female	46/ 46	28 (60.9)	27/ 27	5 (18.5)	3.287 (1.441;7.496) 0.0047	6.844 (2.195;21.344) 0.0009	0.424 (0.220;0.627)
Age group	Interaction p-value [4]		NC				
18 - < 50	54/ 54	33 (61.1)	27/ 27	8 (29.6)	NC (NC;NC) NC	NC (NC;NC) NC	NC (NC;NC)
50 - < 65	24/ 24	20 (83.3)	9/ 9	1 (11.1)	NC (NC;NC) NC	NC (NC;NC) NC	NC (NC;NC)
≥ 65	5/ 5	2 (40.0)	4/ 4	0 (0.0)	NC (NC;NC) NC	NC (NC;NC) NC	NC (NC;NC)
Region	Interaction p-value [4]		0.3470				
U.S.	9/ 9	7 (77.8)	4/ 4	0 (0.0)	7.500 (0.528;106.560) 0.1367	27.000 (1.043;698.790) 0.0471	0.778 (0.506;1.000)

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

Subgroup Level	Vimseltinib (N=83)		Placebo (N=40)		RR [1] (95% CI) p-value	OR [2] (95% CI) p-value	RD [3] (95% CI)
	N/N'	n (%)	N/N'	n (%)			
Non-U.S.	74/ 74	48 (64.9)	36/ 36	9 (25.0)	2.595 (1.438;4.681) 0.0015	5.538 (2.268;13.523) 0.0002	0.399 (0.220;0.577)
Site in Europe	Interaction p-value [4]		0.9238				
Yes	57/ 57	37 (64.9)	32/ 32	7 (21.9)	2.967 (1.500;5.869) 0.0018	6.607 (2.433;17.945) 0.0002	0.430 (0.241;0.620)
No	26/ 26	18 (69.2)	8/ 8	2 (25.0)	2.769 (0.812;9.448) 0.1038	6.750 (1.111;41.001) 0.0380	0.442 (0.094;0.791)
Disease subtype	Interaction p-value [4]		0.3032				
Localized	26/ 26	15 (57.7)	10/ 10	3 (30.0)	1.923 (0.706;5.240) 0.2010	3.182 (0.668;15.146) 0.1460	0.277 (-0.065;0.619)
Diffuse	57/ 57	40 (70.2)	28/ 28	5 (17.9)	3.930 (1.744;8.854) 0.0010	10.824 (3.527;33.216) <.0001	0.523 (0.338;0.708)
Missing	0/ 0	0	2/ 2	1 (50.0)	NC (NC;NC) NC	NC (NC;NC) NC	NC (NC;NC)
Tumour location	Interaction p-value [4]		0.2297				
Lower Limb	77/ 77	50 (64.9)	35/ 35	9 (25.7)	2.525 (1.405;4.540)	5.350 (2.195;13.039)	0.392 (0.212;0.572)

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

Subgroup Level	Vimseltinib (N=83)		Placebo (N=40)		RR [1] (95% CI) p-value	OR [2] (95% CI) p-value	RD [3] (95% CI)
	N/N'	n (%)	N/N'	n (%)			
					0.0020	0.0002	
All Other	6/ 6	5 (83.3)	5/ 5	0 (0.0)	9.429 (0.645;137.772) 0.1011	40.333 (1.330;1222.97) 0.0337	0.833 (0.535;1.000)
Disease location joint size	Interaction p-value [4]		0.7356				
Large Joints	69/ 69	46 (66.7)	29/ 29	7 (24.1)	2.762 (1.418;5.378) 0.0028	6.286 (2.343;16.864) 0.0003	0.425 (0.234;0.617)
Small Joints	14/ 14	9 (64.3)	11/ 11	2 (18.2)	3.536 (0.951;13.143) 0.0594	8.100 (1.233;53.200) 0.0294	0.461 (0.122;0.800)
Disease location knee	Interaction p-value [4]		0.9644				
Yes	56/ 56	37 (66.1)	27/ 27	6 (22.2)	2.973 (1.433;6.171) 0.0034	6.816 (2.355;19.725) 0.0004	0.438 (0.239;0.638)
No	27/ 27	18 (66.7)	13/ 13	3 (23.1)	2.889 (1.034;8.073) 0.0430	6.667 (1.461;30.426) 0.0143	0.436 (0.146;0.726)
Prior surgery	Interaction p-value [4]		0.2833				
Yes	64/ 64	44 (68.8)	27/ 27	5 (18.5)	3.713 (1.654;8.331) 0.0015	9.680 (3.204;29.243) <.0001	0.502 (0.317;0.688)
No	19/ 19	11 (57.9)	13/ 13	4 (30.8)	1.882	3.094	0.271

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

Subgroup Level	Vimseltinib (N=83)		Placebo (N=40)		RR [1] (95% CI) p-value	OR [2] (95% CI) p-value	RD [3] (95% CI)
	N/N'	n (%)	N/N'	n (%)			
					(0.764;4.633) 0.1691	(0.698;13.711) 0.1371	(-0.064;0.606)
Prior imatinib/nilotinib treatment	Interaction p-value [4]		0.4630				
Yes	19/ 19	11 (57.9)	9/ 9	1 (11.1)	5.211 (0.789;34.395) 0.0865	11.000 (1.137;106.430) 0.0384	0.468 (0.165;0.770)
No	64/ 64	44 (68.8)	31/ 31	8 (25.8)	2.664 (1.434;4.949) 0.0019	6.325 (2.416;16.562) 0.0002	0.429 (0.238;0.621)

N: Number of subjects in analysis set. N': Number of subjects analysed. n: Number of subjects with event. NC: Not calculated. NE: Not estimable. CI: Confidence interval. OR: Odds ratio. RD: Risk difference. RR: Risk ratio. Int.: Interaction.

Percentages based on N. Reference is Placebo.

[1] Log-binomial regression with terms Treatment, Subgroup, and Treatment by Subgroup interaction.

[2] Logistic regression with terms Treatment, Subgroup, and Treatment by Subgroup interaction.

[3] Cochran-Mantel-Haenszel method stratified by Subgroup.

[4] Treatment*Subgroup interaction p-value from log-binomial regression.

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

4.1.6.3 Subgruppenanalysen für den Anteil der Patienten, die den PGIC-gesamt zu Woche 25 mit „wenig besser“, „viel besser“ oder „sehr viel besser“ beantwortet haben

Subgroup Level	Vimseltinib (N=83)		Placebo (N=40)		RR [1] (95% CI) p-value	OR [2] (95% CI) p-value	RD [3] (95% CI)
	N/N'	n (%)	N/N'	n (%)			
Sex	Interaction p-value [4]		0.5908				
Male	37/ 37	27 (73.0)	13/ 13	4 (30.8)	2.372 (1.025;5.486) 0.0436	6.075 (1.523;24.228) 0.0106	0.422 (0.133;0.711)
Female	46/ 46	28 (60.9)	27/ 27	5 (18.5)	3.287 (1.441;7.496) 0.0047	6.844 (2.195;21.344) 0.0009	0.424 (0.220;0.627)
Age group	Interaction p-value [4]		NC				
18 - < 50	54/ 54	33 (61.1)	27/ 27	8 (29.6)	NC (NC;NC) NC	NC (NC;NC) NC	NC (NC;NC)
50 - < 65	24/ 24	19 (79.2)	9/ 9	1 (11.1)	NC (NC;NC) NC	NC (NC;NC) NC	NC (NC;NC)
≥ 65	5/ 5	3 (60.0)	4/ 4	0 (0.0)	NC (NC;NC) NC	NC (NC;NC) NC	NC (NC;NC)
Region	Interaction p-value [4]		0.3470				
U.S.	9/ 9	7 (77.8)	4/ 4	0 (0.0)	7.500 (0.528;106.560) 0.1367	27.000 (1.043;698.790) 0.0471	0.778 (0.506;1.000)

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Subgroup Level	Vimseltinib (N=83)		Placebo (N=40)		RR [1] (95% CI) p-value	OR [2] (95% CI) p-value	RD [3] (95% CI)
	N/N'	n (%)	N/N'	n (%)			
Non-U.S.	74/ 74	48 (64.9)	36/ 36	9 (25.0)	2.595 (1.438;4.681) 0.0015	5.538 (2.268;13.523) 0.0002	0.399 (0.220;0.577)
Site in Europe	Interaction p-value [4]		0.9238				
Yes	57/ 57	37 (64.9)	32/ 32	7 (21.9)	2.967 (1.500;5.869) 0.0018	6.607 (2.433;17.945) 0.0002	0.430 (0.241;0.620)
No	26/ 26	18 (69.2)	8/ 8	2 (25.0)	2.769 (0.812;9.448) 0.1038	6.750 (1.111;41.001) 0.0380	0.442 (0.094;0.791)
Disease subtype	Interaction p-value [4]		0.3032				
Localized	26/ 26	15 (57.7)	10/ 10	3 (30.0)	1.923 (0.706;5.240) 0.2010	3.182 (0.668;15.146) 0.1460	0.277 (-0.065;0.619)
Diffuse	57/ 57	40 (70.2)	28/ 28	5 (17.9)	3.930 (1.744;8.854) 0.0010	10.824 (3.527;33.216) <.0001	0.523 (0.338;0.708)
Missing	0/ 0	0	2/ 2	1 (50.0)	NC (NC;NC) NC	NC (NC;NC) NC	NC (NC;NC)
Tumour location	Interaction p-value [4]		0.1442				
Lower Limb	77/ 77	49 (63.6)	35/ 35	9 (25.7)	2.475 (1.375;4.455)	5.056 (2.078;12.298)	0.379 (0.199;0.560)

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Subgroup Level	Vimseltinib (N=83)		Placebo (N=40)		RR [1] (95% CI) p-value	OR [2] (95% CI) p-value	RD [3] (95% CI)
	N/N'	n (%)	N/N'	n (%)			
					0.0025	0.0004	
All Other	6/ 6	6 (100.0)	5/ 5	0 (0.0)	11.143 (0.778;159.580) 0.0759	143.000 (2.415;8467.01) 0.0172	1.000 (NC;NC)
Disease location joint size	Interaction p-value [4]		0.7356				
Large Joints	69/ 69	46 (66.7)	29/ 29	7 (24.1)	2.762 (1.418;5.378) 0.0028	6.286 (2.343;16.864) 0.0003	0.425 (0.234;0.617)
Small Joints	14/ 14	9 (64.3)	11/ 11	2 (18.2)	3.536 (0.951;13.143) 0.0594	8.100 (1.233;53.200) 0.0294	0.461 (0.122;0.800)
Disease location knee	Interaction p-value [4]		0.9644				
Yes	56/ 56	37 (66.1)	27/ 27	6 (22.2)	2.973 (1.433;6.171) 0.0034	6.816 (2.355;19.725) 0.0004	0.438 (0.239;0.638)
No	27/ 27	18 (66.7)	13/ 13	3 (23.1)	2.889 (1.034;8.073) 0.0430	6.667 (1.461;30.426) 0.0143	0.436 (0.146;0.726)
Prior surgery	Interaction p-value [4]		0.2833				
Yes	64/ 64	44 (68.8)	27/ 27	5 (18.5)	3.713 (1.654;8.331) 0.0015	9.680 (3.204;29.243) <.0001	0.502 (0.317;0.688)
No	19/ 19	11 (57.9)	13/ 13	4 (30.8)	1.882	3.094	0.271

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Subgroup Level	Vimseltinib (N=83)		Placebo (N=40)		RR [1] (95% CI) p-value	OR [2] (95% CI) p-value	RD [3] (95% CI)
	N/N'	n (%)	N/N'	n (%)			
					(0.764;4.633) 0.1691	(0.698;13.711) 0.1371	(-0.064;0.606)
Prior imatinib/nilotinib treatment	Interaction p-value [4]						
Yes	19/ 19	10 (52.6)	9/ 9	1 (11.1)	4.737 (0.711;31.558) 0.1080	8.889 (0.922;85.655) 0.0587	0.415 (0.111;0.719)
No	64/ 64	45 (70.3)	31/ 31	8 (25.8)	2.725 (1.469;5.053) 0.0015	6.809 (2.589;17.905) 0.0001	0.445 (0.255;0.635)

N: Number of subjects in analysis set. N': Number of subjects analysed. n: Number of subjects with event. NC: Not calculated. NE: Not estimable. CI: Confidence interval. OR: Odds ratio. RD: Risk difference. RR: Risk ratio. Int.: Interaction.

Percentages based on N. Reference is Placebo.

[1] Log-binomial regression with terms Treatment, Subgroup, and Treatment by Subgroup interaction.

[2] Logistic regression with terms Treatment, Subgroup, and Treatment by Subgroup interaction.

[3] Cochran-Mantel-Haenszel method stratified by Subgroup.

[4] Treatment*Subgroup interaction p-value from log-binomial regression.

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

4.1.7 Subgruppenanalysen für den allgemeinen Gesundheitszustand gemessen mittels EQ-5D-5L VAS**4.1.7.1 Subgruppenanalysen für die Veränderung des Skalenwertes der EQ 5D-5L VAS gegenüber dem Ausgangswert während der randomisierten, kontrollierten Studienphase**

Subgroup Level Analysis Visit		Vimseltinib (N=83)	Placebo (N=40)
Sex	Interaction p-value [1]	0.3306	
Male			
Overall treatment effect	n'	37	12
	LS mean (SE) [2]	10.0 (2.18)	0.9 (1.66)
	LS mean difference (95% CI) p-value [2]	9.1 (3.5; 14.6) 0.0016	
	Hedges' g (95% CI)	1.068 (0.388; 1.749)	
Female			
Overall treatment effect	n'	46	24
	LS mean (SE) [2]	9.6 (1.55)	4.4 (2.46)
	LS mean difference (95% CI) p-value [2]	5.2 (-0.6; 10.9) 0.0782	
	Hedges' g (95% CI)	0.445 (-0.051; 0.940)	
Age group	Interaction p-value [1]	NC	
18 - < 50			
Overall treatment effect	n'	54	27
	LS mean (SE) [2]	NC (NC)	NC (NC)
	LS mean difference (95% CI) p-value [2]	NC (NC; NC) NC	
	Hedges' g (95% CI)	NC (NC; NC)	
50 - < 65			
Overall treatment effect	n'	24	9
	LS mean (SE) [2]	NC (NC)	NC (NC)
	LS mean difference (95% CI) p-value [2]	NC (NC; NC) NC	
	Hedges' g (95% CI)	NC (NC; NC)	
≥ 65			
Overall treatment effect	n'	5	4
	LS mean (SE) [2]	NC (NC)	NC (NC)

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

Subgroup Level Analysis Visit		Vimseltinib (N=83)	Placebo (N=40)
LS mean difference (95% CI) p-value [2]		NC (NC; NC) NC	
Hedges' g (95% CI)		NC (NC; NC)	
Region		Interaction p-value [1]	
U.S.		0.0774	
Overall treatment effect	n'	9	3
	LS mean (SE) [2]	9.9 (2.63)	10.3 (2.81)
	LS mean difference (95% CI) p-value [2]	-0.4 (-7.4; 6.6) 0.9155	
	Hedges' g (95% CI)	-0.070 (-1.369; 1.228)	
Non-U.S.			
Overall treatment effect	n'	74	33
	LS mean (SE) [2]	9.7 (1.40)	2.5 (1.89)
	LS mean difference (95% CI) p-value [2]	7.2 (2.4; 11.9) 0.0033	
	Hedges' g (95% CI)	0.625 (0.209; 1.041)	
Site in Europe		Interaction p-value [1]	
Yes		0.5483	
Overall treatment effect	n'	57	29
	LS mean (SE) [2]	10.0 (1.66)	2.9 (2.00)
	LS mean difference (95% CI) p-value [2]	7.2 (2.0; 12.4) 0.0074	
	Hedges' g (95% CI)	0.618 (0.164; 1.072)	
No			
Overall treatment effect	n'	26	7
	LS mean (SE) [2]	9.1 (1.96)	4.7 (3.52)
	LS mean difference (95% CI) p-value [2]	4.3 (-3.5; 12.2) 0.2753	
	Hedges' g (95% CI)	0.464 (-0.373; 1.300)	
Disease subtype		Interaction p-value [1]	
Localized		0.0562	
Overall treatment effect	n'	26	9
	LS mean (SE) [2]	11.1 (2.13)	-2.6 (3.53)
	LS mean difference (95% CI) p-value [2]	13.7 (5.5; 22.0) 0.0014	

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

Subgroup Level Analysis Visit		Vimseltinib (N=83)	Placebo (N=40)
	Hedges' g (95% CI)	1.262 (0.453; 2.071)	
Diffuse			
Overall treatment effect	n'	57	25
	LS mean (SE) [2]	9.4 (1.59)	4.7 (2.07)
	LS mean difference (95% CI) p-value [2]	4.7 (-0.4; 9.8) 0.0710	
	Hedges' g (95% CI)	0.434 (-0.037; 0.906)	
Missing			
Overall treatment effect	n'	0	2
	LS mean (SE) [2]	NC (NC)	NC (NC)
	LS mean difference (95% CI) p-value [2]	NC (NC; NC) NC	
	Hedges' g (95% CI)	NC (NC; NC)	
Tumour location	Interaction p-value [1]	0.6995	
Lower Limb			
Overall treatment effect	n'	77	31
	LS mean (SE) [2]	9.5 (1.36)	3.1 (1.92)
	LS mean difference (95% CI) p-value [2]	6.4 (1.7; 11.1) 0.0083	
	Hedges' g (95% CI)	0.567 (0.146; 0.988)	
All Other			
Overall treatment effect	n'	6	5
	LS mean (SE) [2]	13.3 (5.19)	4.2 (4.21)
	LS mean difference (95% CI) p-value [2]	9.1 (-4.1; 22.3) 0.1740	
	Hedges' g (95% CI)	0.823 (-0.405; 2.051)	
Disease location joint size	Interaction p-value [1]	0.0497	
Large Joints			
Overall treatment effect	n'	69	25
	LS mean (SE) [2]	8.6 (1.45)	4.4 (1.85)
	LS mean difference (95% CI) p-value [2]	4.2 (-0.4; 8.8) 0.0741	
	Hedges' g (95% CI)	0.418 (-0.040; 0.876)	
Small Joints			
Overall treatment effect	n'	14	11

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Subgroup Level Analysis Visit		Vimseltinib (N=83)	Placebo (N=40)
	LS mean (SE) [2]	15.2 (2.83)	0.6 (3.79)
	LS mean difference (95% CI) p-value [2]	14.7 (5.2; 24.1) 0.0027	
	Hedges' g (95% CI)	1.229 (0.374; 2.085)	
Disease location knee	Interaction p-value [1]	0.0844	
Yes			
Overall treatment effect	n'	56	23
	LS mean (SE) [2]	8.8 (1.66)	5.0 (1.94)
	LS mean difference (95% CI) p-value [2]	3.7 (-1.3; 8.8) 0.1476	
	Hedges' g (95% CI)	0.359 (-0.127; 0.844)	
No			
Overall treatment effect	n'	27	13
	LS mean (SE) [2]	11.8 (2.02)	-0.0 (3.35)
	LS mean difference (95% CI) p-value [2]	11.8 (4.0; 19.6) 0.0033	
	Hedges' g (95% CI)	1.006 (0.313; 1.700)	
Prior surgery	Interaction p-value [1]	0.6369	
Yes			
Overall treatment effect	n'	64	23
	LS mean (SE) [2]	9.0 (1.51)	1.4 (2.36)
	LS mean difference (95% CI) p-value [2]	7.7 (2.1; 13.2) 0.0074	
	Hedges' g (95% CI)	0.659 (0.176; 1.142)	
No			
Overall treatment effect	n'	19	13
	LS mean (SE) [2]	12.1 (2.54)	6.5 (2.13)
	LS mean difference (95% CI) p-value [2]	5.7 (-0.9; 12.2) 0.0903	
	Hedges' g (95% CI)	0.611 (-0.106; 1.327)	
Prior imatinib/nilotinib treatment	Interaction p-value [1]	0.2472	
Yes			
Overall treatment effect	n'	19	8
	LS mean (SE) [2]	9.6 (3.30)	-1.8 (3.58)

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

Subgroup		Vimseltinib (N=83)	Placebo (N=40)
Level	Analysis Visit		
No	LS mean difference (95% CI) p-value [2]	11.4 (1.5; 21.4) 0.0246	
	Hedges' g (95% CI)	0.954 (0.095; 1.813)	
	n'	64	28
	Overall treatment effect		
	LS mean (SE) [2]	9.8 (1.35)	4.6 (1.95)
	LS mean difference (95% CI) p-value [2]	5.1 (0.5; 9.8) 0.0319	
	Hedges' g (95% CI)	0.489 (0.042; 0.936)	

N: Number of subjects in analysis set. n: Number of subjects with non-missing data. n': Number of subjects analysed. SD: Standard deviation. SE: Standard error. Min: Minimum. Max: Maximum. NC: Not calculated. NE: Not estimable. CI: Confidence interval.

Reference is Placebo.

[1] Treatment*Subgroup interaction p-value from MMRM model.

[2] MMRM model using unstructured covariance matrix with terms Treatment, Visit, Subgroup, Baseline value, Treatment by Visit, and Treatment by Subgroup interactions.

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

4.1.7.2 Subgruppenanalysen für den Anteil der Patienten mit einer Verbesserung der EQ-5D-5L VAS um mindestens 15 Punkte gegenüber dem Ausgangswert zu Woche 25

Subgroup Level	Vimseltinib (N=83)		Placebo (N=40)		RR [1] (95% CI) p-value	OR [2] (95% CI) p-value	RD [3] (95% CI)
	N/N'	n (%)	N/N'	n (%)			
Sex	Interaction p-value [4]		0.1783				
Male	37/ 37	13 (35.1)	13/ 13	0 (0.0)	9.947 (0.633;156.439) 0.1022	14.878 (0.819;270.332) 0.0680	0.351 (0.198;0.505)
Female	46/ 46	13 (28.3)	27/ 27	4 (14.8)	1.908 (0.691;5.263) 0.2123	2.265 (0.655;7.833) 0.1965	0.134 (-0.052;0.321)
Age group	Interaction p-value [4]		NC				
18 - < 50	54/ 54	18 (33.3)	27/ 27	2 (7.4)	NC (NC;NC) NC	NC (NC;NC) NC	NC (NC;NC)
50 - < 65	24/ 24	8 (33.3)	9/ 9	2 (22.2)	NC (NC;NC) NC	NC (NC;NC) NC	NC (NC;NC)
≥ 65	5/ 5	0 (0.0)	4/ 4	0 (0.0)	NC (NC;NC) NC	NC (NC;NC) NC	NC (NC;NC)
Region	Interaction p-value [4]		0.3833				
U.S.	9/ 9	0 (0.0)	4/ 4	0 (0.0)	0.500 (0.012;21.691) 0.7186	0.474 (0.008;27.939) 0.7195	NC (NC;NC)

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Subgroup Level	Vimseltinib (N=83)		Placebo (N=40)		RR [1] (95% CI) p-value	OR [2] (95% CI) p-value	RD [3] (95% CI)
	N/N'	n (%)	N/N'	n (%)			
Non-U.S.	74/ 74	26 (35.1)	36/ 36	4 (11.1)	3.162 (1.193;8.379) 0.0206	4.333 (1.381;13.600) 0.0120	0.240 (0.091;0.390)
Site in Europe	Interaction p-value [4]		0.8819				
Yes	57/ 57	21 (36.8)	32/ 32	4 (12.5)	2.947 (1.109;7.835) 0.0302	4.083 (1.257;13.259) 0.0192	0.243 (0.074;0.413)
No	26/ 26	5 (19.2)	8/ 8	0 (0.0)	3.667 (0.224;59.999) 0.3622	4.349 (0.216;87.523) 0.3372	0.192 (0.041;0.344)
Disease subtype	Interaction p-value [4]		0.2981				
Localized	26/ 26	8 (30.8)	10/ 10	2 (20.0)	1.538 (0.392;6.037) 0.5368	1.778 (0.306;10.324) 0.5215	0.108 (-0.197;0.413)
Diffuse	57/ 57	18 (31.6)	28/ 28	2 (7.1)	4.421 (1.102;17.734) 0.0360	6.000 (1.283;28.067) 0.0228	0.244 (0.091;0.398)
Missing	0/ 0	0	2/ 2	0 (0.0)	NC (NC;NC) NC	NC (NC;NC) NC	NC (NC;NC)
Tumour location	Interaction p-value [4]		0.3740				
Lower Limb	77/ 77	22 (28.6)	35/ 35	4 (11.4)	2.500 (0.931;6.712)	3.100 (0.979;9.817)	0.171 (0.026;0.317)

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Subgroup Level	Vimseltinib (N=83)		Placebo (N=40)		RR [1] (95% CI) p-value	OR [2] (95% CI) p-value	RD [3] (95% CI)
	N/N'	n (%)	N/N'	n (%)			
					0.0690	0.0544	
All Other	6/ 6	4 (66.7)	5/ 5	0 (0.0)	7.714 (0.513;116.014) 0.1396	19.800 (0.744;527.260) 0.0746	0.667 (0.289;1.000)
Disease location joint size	Interaction p-value [4]		0.5658				
Large Joints	69/ 69	20 (29.0)	29/ 29	2 (6.9)	4.203 (1.050;16.829) 0.0425	5.510 (1.196;25.385) 0.0285	0.221 (0.080;0.362)
Small Joints	14/ 14	6 (42.9)	11/ 11	2 (18.2)	2.357 (0.586;9.481) 0.2273	3.375 (0.524;21.729) 0.2005	0.247 (-0.098;0.592)
Disease location knee	Interaction p-value [4]		0.7545				
Yes	56/ 56	15 (26.8)	27/ 27	2 (7.4)	3.616 (0.890;14.695) 0.0724	4.573 (0.964;21.697) 0.0557	0.194 (0.041;0.346)
No	27/ 27	11 (40.7)	13/ 13	2 (15.4)	2.648 (0.684;10.252) 0.1585	3.781 (0.697;20.512) 0.1232	0.254 (-0.016;0.523)
Prior surgery	Interaction p-value [4]		0.7435				
Yes	64/ 64	18 (28.1)	27/ 27	2 (7.4)	3.797 (0.946;15.242) 0.0599	4.891 (1.049;22.814) 0.0433	0.207 (0.059;0.355)
No	19/ 19	8 (42.1)	13/ 13	2 (15.4)	2.737	4.000	0.267

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Subgroup Level	Vimseltinib (N=83)		Placebo (N=40)		RR [1] (95% CI) p-value	OR [2] (95% CI) p-value	RD [3] (95% CI)
	N/N'	n (%)	N/N'	n (%)			
					(0.689;10.874) 0.1526	(0.688;23.261) 0.1227	(-0.029;0.563)
Prior imatinib/nilotinib treatment	Interaction p-value [4]		0.6148				
Yes	19/ 19	4 (21.1)	9/ 9	1 (11.1)	1.895 (0.246;14.612) 0.5398	2.133 (0.203;22.444) 0.5280	0.099 (-0.176;0.375)
No	64/ 64	22 (34.4)	31/ 31	3 (9.7)	3.552 (1.150;10.968) 0.0276	4.889 (1.336;17.896) 0.0165	0.247 (0.091;0.403)

N: Number of subjects in analysis set. N': Number of subjects analysed. n: Number of subjects with event. NC: Not calculated. NE: Not estimable. CI: Confidence interval. OR: Odds ratio. RD: Risk difference. RR: Risk ratio. Int.: Interaction.

Percentages based on N. Reference is Placebo.

[1] Log-binomial regression with terms Treatment, Subgroup, and Treatment by Subgroup interaction.

[2] Logistic regression with terms Treatment, Subgroup, and Treatment by Subgroup interaction.

[3] Cochran-Mantel-Haenszel method stratified by Subgroup.

[4] Treatment*Subgroup interaction p-value from log-binomial regression.

4.2 Subgruppenanalysen für Sicherheitsendpunkte

4.2.1 Subgruppenanalysen für die Gesamtrate der UEs (unabhängig vom Schweregrad) während der randomisierten, kontrollierten Studienphase

Subgroup Level	Vimseltinib (N=83)		Placebo (N=40)		RR [1] (95% CI) p-value	OR [2] (95% CI) p-value	RD [3] (95% CI)
	N/N'	n (%)	N/N'	n (%)			
Sex	Interaction p-value [4]		0.4798				
Male	37/ 37	37 (100.0)	13/ 13	13 (100.0)	1.023 (0.919;1.139) 0.6727	2.778 (0.052;147.030) 0.6139	NC (NC;NC)
Female	46/ 46	46 (100.0)	26/ 26	24 (92.3)	1.090 (0.963;1.234) 0.1720	9.490 (0.438;205.563) 0.1516	0.077 (-0.026;0.179)
Age group	Interaction p-value [4]		NC				
18 - < 50	54/ 54	54 (100.0)	26/ 26	24 (92.3)	NC (NC;NC) NC	NC (NC;NC) NC	NC (NC;NC)
50 - < 65	24/ 24	24 (100.0)	9/ 9	9 (100.0)	NC (NC;NC) NC	NC (NC;NC) NC	NC (NC;NC)
≥ 65	5/ 5	5 (100.0)	4/ 4	4 (100.0)	NC (NC;NC) NC	NC (NC;NC) NC	NC (NC;NC)
Region	Interaction p-value [4]		0.9490				
U.S.	9/ 9	9 (100.0)	4/ 4	4 (100.0)	1.056	2.111	NC

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

Subgroup Level	Vimseltinib (N=83)		Placebo (N=40)		RR [1] (95% CI) p-value	OR [2] (95% CI) p-value	RD [3] (95% CI)
	N/N'	n (%)	N/N'	n (%)			
					(0.763;1.461) 0.7443	(0.036;124.518) 0.7195	(NC;NC)
Non-U.S.	74/ 74	74 (100.0)	35/ 35	33 (94.3)	1.067 (0.974;1.169) 0.1603	11.119 (0.519;238.008) 0.1233	0.057 (-0.020;0.134)
Site in Europe	Interaction p-value [4]		0.7516				
Yes	57/ 57	57 (100.0)	31/ 31	29 (93.5)	1.075 (0.969;1.193) 0.1694	9.746 (0.453;209.656) 0.1459	0.065 (-0.022;0.151)
No	26/ 26	26 (100.0)	8/ 8	8 (100.0)	1.039 (0.880;1.228) 0.6511	3.118 (0.057;169.426) 0.5770	NC (NC;NC)
Disease subtype	Interaction p-value [4]		0.5762				
Localized	26/ 26	26 (100.0)	10/ 10	10 (100.0)	1.028 (0.895;1.182) 0.6947	2.524 (0.047;135.683) 0.6488	NC (NC;NC)
Diffuse	57/ 57	57 (100.0)	27/ 27	25 (92.6)	1.089 (0.967;1.225) 0.1602	11.275 (0.522;243.352) 0.1222	0.074 (-0.025;0.173)
Missing	0/ 0	0	2/ 2	2 (100.0)	NC (NC;NC) NC	NC (NC;NC) NC	NC (NC;NC)
Tumour location	Interaction p-value [4]		0.4635				

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

Subgroup Level	Vimseltinib (N=83)		Placebo (N=40)		RR [1] (95% CI) p-value	OR [2] (95% CI) p-value	RD [3] (95% CI)
	N/N'	n (%)	N/N'	n (%)			
Lower Limb	77/ 77	77 (100.0)	34/ 34	33 (97.1)	1.038 (0.966;1.116) 0.3112	6.940 (0.276;174.776) 0.2392	0.029 (-0.027;0.086)
All Other	6/ 6	6 (100.0)	5/ 5	4 (80.0)	1.238 (0.747;2.053) 0.4077	4.333 (0.142;132.315) 0.4006	0.200 (-0.151;0.551)
Disease location joint size	Interaction p-value [4]		0.1714				
Large Joints	69/ 69	69 (100.0)	28/ 28	28 (100.0)	1.010 (0.959;1.064) 0.7008	2.439 (0.047;125.904) 0.6578	NC (NC;NC)
Small Joints	14/ 14	14 (100.0)	11/ 11	9 (81.8)	1.221 (0.900;1.657) 0.1995	7.632 (0.329;177.140) 0.2053	0.182 (-0.046;0.410)
Disease location knee	Interaction p-value [4]		0.1102				
Yes	56/ 56	56 (100.0)	26/ 26	26 (100.0)	1.010 (0.954;1.069) 0.7353	2.132 (0.041;110.398) 0.7070	NC (NC;NC)
No	27/ 27	27 (100.0)	13/ 13	11 (84.6)	1.196 (0.932;1.534) 0.1600	11.957 (0.531;268.989) 0.1183	0.154 (-0.042;0.350)
Prior surgery	Interaction p-value [4]		0.1608				
Yes	64/ 64	64 (100.0)	26/ 26	26 (100.0)	1.011 (0.956;1.069)	2.434 (0.047;125.895)	NC (NC;NC)

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

Subgroup Level	Vimseltinib (N=83)		Placebo (N=40)		RR [1] (95% CI) p-value	OR [2] (95% CI) p-value	RD [3] (95% CI)
	N/N'	n (%)	N/N'	n (%)			
					0.7013	0.6586	
No	19/ 19	19 (100.0)	13/ 13	11 (84.6)	1.187 (0.921;1.530) 0.1862	8.478 (0.373;192.499) 0.1797	0.154 (-0.042;0.350)
Prior imatinib/nilotinib treatment	Interaction p-value [4]		0.6364				
Yes	19/ 19	19 (100.0)	9/ 9	9 (100.0)	1.026 (0.876;1.203) 0.7482	2.053 (0.038;111.611) 0.7243	NC (NC;NC)
No	64/ 64	64 (100.0)	30/ 30	28 (93.3)	1.079 (0.970;1.201) 0.1597	11.316 (0.526;243.325) 0.1212	0.067 (-0.023;0.156)

N: Number of subjects in analysis set. N': Number of subjects analysed. n: Number of subjects with event. NC: Not calculated. NE: Not estimable. CI: Confidence interval. OR: Odds ratio. RD: Risk difference. RR: Risk ratio. Int.: Interaction.

Percentages based on N. Reference is Placebo.

[1] Log-binomial regression with terms Treatment, Subgroup, and Treatment by Subgroup interaction.

[2] Logistic regression with terms Treatment, Subgroup, and Treatment by Subgroup interaction.

[3] Cochran-Mantel-Haenszel method stratified by Subgroup.

[4] Treatment*Subgroup interaction p-value from log-binomial regression.

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

4.2.2 Subgruppenanalysen für die Gesamtrate der SUEs während der randomisierten, kontrollierten Studienphase

Subgroup Level	Vimseltinib (N=83)		Placebo (N=40)		RR [1] (95% CI) p-value	OR [2] (95% CI) p-value	RD [3] (95% CI)
	N/N'	n (%)	N/N'	n (%)			
Sex	Interaction p-value [4]		NC				
Male	37/ 37	2 (5.4)	13/ 13	0 (0.0)	NC (NC;NC) NC	NC (NC;NC) NC	NC (NC;NC)
Female	46/ 46	4 (8.7)	26/ 26	1 (3.8)	NC (NC;NC) NC	NC (NC;NC) NC	NC (NC;NC)
Age group	Interaction p-value [4]		NC				
18 - < 50	54/ 54	4 (7.4)	26/ 26	1 (3.8)	NC (NC;NC) NC	NC (NC;NC) NC	NC (NC;NC)
50 - < 65	24/ 24	1 (4.2)	9/ 9	0 (0.0)	NC (NC;NC) NC	NC (NC;NC) NC	NC (NC;NC)
≥ 65	5/ 5	1 (20.0)	4/ 4	0 (0.0)	NC (NC;NC) NC	NC (NC;NC) NC	NC (NC;NC)
Region	Interaction p-value [4]		NC				
U.S.	9/ 9	0 (0.0)	4/ 4	0 (0.0)	NC (NC;NC) NC	NC (NC;NC) NC	NC (NC;NC)

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

Subgroup Level	Vimseltinib (N=83)		Placebo (N=40)		RR [1] (95% CI) p-value	OR [2] (95% CI) p-value	RD [3] (95% CI)
	N/N'	n (%)	N/N'	n (%)			
Non-U.S.	74/ 74	6 (8.1)	35/ 35	1 (2.9)	NC (NC;NC) NC	NC (NC;NC) NC	NC (NC;NC)
Site in Europe	Interaction p-value [4]		NC				
Yes	57/ 57	4 (7.0)	31/ 31	1 (3.2)	NC (NC;NC) NC	NC (NC;NC) NC	NC (NC;NC)
No	26/ 26	2 (7.7)	8/ 8	0 (0.0)	NC (NC;NC) NC	NC (NC;NC) NC	NC (NC;NC)
Disease subtype	Interaction p-value [4]		NC				
Localized	26/ 26	2 (7.7)	10/ 10	1 (10.0)	NC (NC;NC) NC	NC (NC;NC) NC	NC (NC;NC)
Diffuse	57/ 57	4 (7.0)	27/ 27	0 (0.0)	NC (NC;NC) NC	NC (NC;NC) NC	NC (NC;NC)
Missing	0/ 0	0	2/ 2	0 (0.0)	NC (NC;NC) NC	NC (NC;NC) NC	NC (NC;NC)
Tumour location	Interaction p-value [4]		NC				
Lower Limb	77/ 77	6 (7.8)	34/ 34	1 (2.9)	NC (NC;NC) NC	NC (NC;NC) NC	NC (NC;NC)

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

Subgroup Level	Vimseltinib (N=83)		Placebo (N=40)		RR [1] (95% CI) p-value	OR [2] (95% CI) p-value	RD [3] (95% CI)
	N/N'	n (%)	N/N'	n (%)			
All Other	6/ 6	0 (0.0)	5/ 5	0 (0.0)	NC (NC;NC) NC	NC (NC;NC) NC	NC (NC;NC)
Disease location joint size	Interaction p-value [4]		NC				
Large Joints	69/ 69	6 (8.7)	28/ 28	0 (0.0)	NC (NC;NC) NC	NC (NC;NC) NC	NC (NC;NC)
Small Joints	14/ 14	0 (0.0)	11/ 11	1 (9.1)	NC (NC;NC) NC	NC (NC;NC) NC	NC (NC;NC)
Disease location knee	Interaction p-value [4]		NC				
Yes	56/ 56	5 (8.9)	26/ 26	0 (0.0)	NC (NC;NC) NC	NC (NC;NC) NC	NC (NC;NC)
No	27/ 27	1 (3.7)	13/ 13	1 (7.7)	NC (NC;NC) NC	NC (NC;NC) NC	NC (NC;NC)
Prior surgery	Interaction p-value [4]		NC				
Yes	64/ 64	3 (4.7)	26/ 26	1 (3.8)	NC (NC;NC) NC	NC (NC;NC) NC	NC (NC;NC)
No	19/ 19	3 (15.8)	13/ 13	0 (0.0)	NC (NC;NC)	NC (NC;NC)	NC (NC;NC)

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

Subgroup Level	Vimseltinib (N=83)		Placebo (N=40)		RR [1] (95% CI) p-value	OR [2] (95% CI) p-value	RD [3] (95% CI)
	N/N'	n (%)	N/N'	n (%)	NC	NC	
Prior imatinib/nilotinib treatment							
	Interaction p-value [4]		NC				
Yes	19/ 19	0 (0.0)	9/ 9	1 (11.1)	NC (NC;NC) NC	NC (NC;NC) NC	NC (NC;NC)
No	64/ 64	6 (9.4)	30/ 30	0 (0.0)	NC (NC;NC) NC	NC (NC;NC) NC	NC (NC;NC)

N: Number of subjects in analysis set. N': Number of subjects analysed. n: Number of subjects with event. NC: Not calculated. NE: Not estimable. CI: Confidence interval. OR: Odds ratio. RD: Risk difference. RR: Risk ratio. Int.: Interaction.

Percentages based on N. Reference is Placebo.

[1] Log-binomial regression with terms Treatment, Subgroup, and Treatment by Subgroup interaction.

[2] Logistic regression with terms Treatment, Subgroup, and Treatment by Subgroup interaction.

[3] Cochran-Mantel-Haenszel method stratified by Subgroup.

[4] Treatment*Subgroup interaction p-value from log-binomial regression.

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

4.2.3 Subgruppenanalysen für die Gesamtrate der schweren UEs während der randomisierten, kontrollierten Studienphase

Subgroup Level	Vimseltinib (N=83)		Placebo (N=40)		RR [1] (95% CI) p-value	OR [2] (95% CI) p-value	RD [3] (95% CI)
	N/N'	n (%)	N/N'	n (%)			
Sex	Interaction p-value [4]		0.5849				
Male	37/ 37	15 (40.5)	13/ 13	2 (15.4)	2.635 (0.695;9.996) 0.1543	3.750 (0.725;19.397) 0.1149	0.252 (-0.000;0.504)
Female	46/ 46	16 (34.8)	26/ 26	2 (7.7)	4.522 (1.127;18.138) 0.0333	6.400 (1.338;30.606) 0.0201	0.271 (0.099;0.442)
Age group	Interaction p-value [4]		NC				
18 - < 50	54/ 54	17 (31.5)	26/ 26	3 (11.5)	NC (NC;NC) NC	NC (NC;NC) NC	NC (NC;NC)
50 - < 65	24/ 24	10 (41.7)	9/ 9	1 (11.1)	NC (NC;NC) NC	NC (NC;NC) NC	NC (NC;NC)
≥ 65	5/ 5	4 (80.0)	4/ 4	0 (0.0)	NC (NC;NC) NC	NC (NC;NC) NC	NC (NC;NC)
Region	Interaction p-value [4]		0.8422				
U.S.	9/ 9	2 (22.2)	4/ 4	0 (0.0)	2.500 (0.146;42.800) 0.5272	3.000 (0.116;77.643) 0.5081	0.222 (-0.049;0.494)

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

Subgroup Level	Vimseltinib (N=83)		Placebo (N=40)		RR [1] (95% CI) p-value	OR [2] (95% CI) p-value	RD [3] (95% CI)
	N/N'	n (%)	N/N'	n (%)			
Non-U.S.	74/ 74	29 (39.2)	35/ 35	4 (11.4)	3.429 (1.306;9.000) 0.0123	4.994 (1.596;15.634) 0.0057	0.278 (0.124;0.431)
Site in Europe	Interaction p-value [4]		0.7624				
Yes	57/ 57	24 (42.1)	31/ 31	4 (12.9)	3.263 (1.245;8.556) 0.0162	4.909 (1.517;15.886) 0.0079	0.292 (0.118;0.466)
No	26/ 26	7 (26.9)	8/ 8	0 (0.0)	5.000 (0.316;79.120) 0.2533	6.538 (0.334;127.944) 0.2159	0.269 (0.099;0.440)
Disease subtype	Interaction p-value [4]		0.0617				
Localized	26/ 26	11 (42.3)	10/ 10	3 (30.0)	1.410 (0.495;4.021) 0.5202	1.711 (0.359;8.145) 0.4999	0.123 (-0.219;0.465)
Diffuse	57/ 57	20 (35.1)	27/ 27	1 (3.7)	9.474 (1.341;66.953) 0.0242	14.054 (1.773;111.381) 0.0123	0.314 (0.171;0.457)
Missing	0/ 0	0	2/ 2	0 (0.0)	NC (NC;NC) NC	NC (NC;NC) NC	NC (NC;NC)
Tumour location	Interaction p-value [4]		0.8435				
Lower Limb	77/ 77	29 (37.7)	34/ 34	4 (11.8)	3.201 (1.220;8.397) 0.0180	4.531 (1.448;14.176) 0.0094	0.259 (0.106;0.412)

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

Subgroup Level	Vimseltinib (N=83)		Placebo (N=40)		RR [1] (95% CI) p-value	OR [2] (95% CI) p-value	RD [3] (95% CI)
	N/N'	n (%)	N/N'	n (%)			
All Other	6/ 6	2 (33.3)	5/ 5	0 (0.0)	4.286 (0.252;72.901) 0.3142	6.111 (0.229;162.735) 0.2797	0.333 (-0.044;0.711)
Disease location joint size	Interaction p-value [4]		0.4462				
Large Joints	69/ 69	25 (36.2)	28/ 28	2 (7.1)	5.072 (1.287;19.996) 0.0203	7.386 (1.616;33.761) 0.0099	0.291 (0.143;0.439)
Small Joints	14/ 14	6 (42.9)	11/ 11	2 (18.2)	2.357 (0.586;9.481) 0.2273	3.375 (0.524;21.729) 0.2005	0.247 (-0.098;0.592)
Disease location knee	Interaction p-value [4]		0.3944				
Yes	56/ 56	22 (39.3)	26/ 26	2 (7.7)	5.107 (1.297;20.114) 0.0197	7.765 (1.666;36.181) 0.0090	0.316 (0.152;0.480)
No	27/ 27	9 (33.3)	13/ 13	2 (15.4)	2.167 (0.544;8.629) 0.2728	2.750 (0.499;15.143) 0.2451	0.179 (-0.085;0.444)
Prior surgery	Interaction p-value [4]		0.4114				
Yes	64/ 64	21 (32.8)	26/ 26	3 (11.5)	2.844 (0.927;8.721) 0.0675	3.744 (1.009;13.896) 0.0485	0.213 (0.044;0.381)
No	19/ 19	10 (52.6)	13/ 13	1 (7.7)	6.842 (0.992;47.176)	13.333 (1.434;123.989)	0.449 (0.182;0.717)

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

Subgroup Level	Vimseltinib (N=83)		Placebo (N=40)		RR [1] (95% CI) p-value	OR [2] (95% CI) p-value	RD [3] (95% CI)
	N/N'	n (%)	N/N'	n (%)			
					0.0509	0.0228	
Prior imatinib/nilotinib treatment	Interaction p-value [4]		0.0092				
Yes	19/ 19	5 (26.3)	9/ 9	3 (33.3)	0.789 (0.240;2.599) 0.6974	0.714 (0.128;3.995) 0.7017	-0.070 (-0.436;0.296)
No	64/ 64	26 (40.6)	30/ 30	1 (3.3)	12.187 (1.735;85.632) 0.0119	19.842 (2.542;154.894) 0.0044	0.373 (0.237;0.509)

N: Number of subjects in analysis set. N': Number of subjects analysed. n: Number of subjects with event. NC: Not calculated. NE: Not estimable. CI: Confidence interval. OR: Odds ratio. RD: Risk difference. RR: Risk ratio. Int.: Interaction.

Percentages based on N. Reference is Placebo.

[1] Log-binomial regression with terms Treatment, Subgroup, and Treatment by Subgroup interaction.

[2] Logistic regression with terms Treatment, Subgroup, and Treatment by Subgroup interaction.

[3] Cochran-Mantel-Haenszel method stratified by Subgroup.

[4] Treatment*Subgroup interaction p-value from log-binomial regression.

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

4.2.4 Subgruppenanalysen für die Gesamtrate der Abbrüche der Studienmedikation aufgrund von UEs während der randomisierten, kontrollierten Studienphase

Subgroup Level	Vimseltinib (N=83)		Placebo (N=40)		RR [1] (95% CI) p-value	OR [2] (95% CI) p-value	RD [3] (95% CI)
	N/N'	n (%)	N/N'	n (%)			
Sex	Interaction p-value [4]		NC				
Male	37/ 37	1 (2.7)	13/ 13	0 (0.0)	NC (NC;NC) NC	NC (NC;NC) NC	NC (NC;NC)
Female	46/ 46	4 (8.7)	26/ 26	0 (0.0)	NC (NC;NC) NC	NC (NC;NC) NC	NC (NC;NC)
Age group	Interaction p-value [4]		NC				
18 - < 50	54/ 54	3 (5.6)	26/ 26	0 (0.0)	NC (NC;NC) NC	NC (NC;NC) NC	NC (NC;NC)
50 - < 65	24/ 24	1 (4.2)	9/ 9	0 (0.0)	NC (NC;NC) NC	NC (NC;NC) NC	NC (NC;NC)
≥ 65	5/ 5	1 (20.0)	4/ 4	0 (0.0)	NC (NC;NC) NC	NC (NC;NC) NC	NC (NC;NC)
Region	Interaction p-value [4]		NC				
U.S.	9/ 9	1 (11.1)	4/ 4	0 (0.0)	NC (NC;NC) NC	NC (NC;NC) NC	NC (NC;NC)

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

Subgroup Level	Vimseltinib (N=83)		Placebo (N=40)		RR [1] (95% CI) p-value	OR [2] (95% CI) p-value	RD [3] (95% CI)
	N/N'	n (%)	N/N'	n (%)			
Non-U.S.	74/ 74	4 (5.4)	35/ 35	0 (0.0)	NC (NC;NC) NC	NC (NC;NC) NC	NC (NC;NC)
Site in Europe	Interaction p-value [4]		NC				
Yes	57/ 57	4 (7.0)	31/ 31	0 (0.0)	NC (NC;NC) NC	NC (NC;NC) NC	NC (NC;NC)
No	26/ 26	1 (3.8)	8/ 8	0 (0.0)	NC (NC;NC) NC	NC (NC;NC) NC	NC (NC;NC)
Disease subtype	Interaction p-value [4]		NC				
Localized	26/ 26	1 (3.8)	10/ 10	0 (0.0)	NC (NC;NC) NC	NC (NC;NC) NC	NC (NC;NC)
Diffuse	57/ 57	4 (7.0)	27/ 27	0 (0.0)	NC (NC;NC) NC	NC (NC;NC) NC	NC (NC;NC)
Missing	0/ 0	0	2/ 2	0 (0.0)	NC (NC;NC) NC	NC (NC;NC) NC	NC (NC;NC)
Tumour location	Interaction p-value [4]		NC				
Lower Limb	77/ 77	5 (6.5)	34/ 34	0 (0.0)	NC (NC;NC)	NC (NC;NC)	NC (NC;NC)

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

Subgroup Level	Vimseltinib (N=83)		Placebo (N=40)		RR [1] (95% CI) p-value	OR [2] (95% CI) p-value	RD [3] (95% CI)
	N/N'	n (%)	N/N'	n (%)			
					NC	NC	
All Other	6/ 6	0 (0.0)	5/ 5	0 (0.0)	NC (NC;NC) NC	NC (NC;NC) NC	NC (NC;NC)
Disease location joint size	Interaction p-value [4]		NC				
Large Joints	69/ 69	4 (5.8)	28/ 28	0 (0.0)	NC (NC;NC) NC	NC (NC;NC) NC	NC (NC;NC)
Small Joints	14/ 14	1 (7.1)	11/ 11	0 (0.0)	NC (NC;NC) NC	NC (NC;NC) NC	NC (NC;NC)
Disease location knee	Interaction p-value [4]		NC				
Yes	56/ 56	4 (7.1)	26/ 26	0 (0.0)	NC (NC;NC) NC	NC (NC;NC) NC	NC (NC;NC)
No	27/ 27	1 (3.7)	13/ 13	0 (0.0)	NC (NC;NC) NC	NC (NC;NC) NC	NC (NC;NC)
Prior surgery	Interaction p-value [4]		NC				
Yes	64/ 64	2 (3.1)	26/ 26	0 (0.0)	NC (NC;NC) NC	NC (NC;NC) NC	NC (NC;NC)
No	19/ 19	3 (15.8)	13/ 13	0 (0.0)	NC	NC	NC

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

Subgroup Level	Vimseltinib (N=83)		Placebo (N=40)		RR [1] (95% CI) p-value	OR [2] (95% CI) p-value	RD [3] (95% CI)
	N/N'	n (%)	N/N'	n (%)	(NC;NC) NC	(NC;NC) NC	(NC;NC)
Prior imatinib/nilotinib treatment					NC		
Yes	19/ 19	2 (10.5)	9/ 9	0 (0.0)	NC (NC;NC) NC	NC (NC;NC) NC	NC (NC;NC)
No	64/ 64	3 (4.7)	30/ 30	0 (0.0)	NC (NC;NC) NC	NC (NC;NC) NC	NC (NC;NC)

N: Number of subjects in analysis set. N': Number of subjects analysed. n: Number of subjects with event. NC: Not calculated. NE: Not estimable. CI: Confidence interval. OR: Odds ratio. RD: Risk difference. RR: Risk ratio. Int.: Interaction.

Percentages based on N. Reference is Placebo.

[1] Log-binomial regression with terms Treatment, Subgroup, and Treatment by Subgroup interaction.

[2] Logistic regression with terms Treatment, Subgroup, and Treatment by Subgroup interaction.

[3] Cochran-Mantel-Haenszel method stratified by Subgroup.

[4] Treatment*Subgroup interaction p-value from log-binomial regression.

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

4.2.5 Subgruppenanalysen für die Gesamtrate der Todesfälle aufgrund von UEs während der randomisierten, kontrollierten Studienphase

Subgroup Level	Vimseltinib (N=83)		Placebo (N=40)		RR [1] (95% CI) p-value	OR [2] (95% CI) p-value	RD [3] (95% CI)
	N/N'	n (%)	N/N'	n (%)			
Sex	Interaction p-value [4]		NC				
Male	37/ 37	0	13/ 13	0	NC (NC;NC) NC	NC (NC;NC) NC	NC (NC;NC)
Female	46/ 46	0	26/ 26	0	NC (NC;NC) NC	NC (NC;NC) NC	NC (NC;NC)
Age group	Interaction p-value [4]		NC				
18 - < 50	54/ 54	0	26/ 26	0	NC (NC;NC) NC	NC (NC;NC) NC	NC (NC;NC)
50 - < 65	24/ 24	0	9/ 9	0	NC (NC;NC) NC	NC (NC;NC) NC	NC (NC;NC)
≥ 65	5/ 5	0	4/ 4	0	NC (NC;NC) NC	NC (NC;NC) NC	NC (NC;NC)
Region	Interaction p-value [4]		NC				
U.S.	9/ 9	0	4/ 4	0	NC (NC;NC) NC	NC (NC;NC) NC	NC (NC;NC)

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

Subgroup Level	Vimseltinib (N=83)		Placebo (N=40)		RR [1] (95% CI) p-value	OR [2] (95% CI) p-value	RD [3] (95% CI)
	N/N'	n (%)	N/N'	n (%)			
Non-U.S.	74/ 74	0	35/ 35	0	NC (NC;NC) NC	NC (NC;NC) NC	NC (NC;NC)
Site in Europe	Interaction p-value [4]		NC				
Yes	57/ 57	0	31/ 31	0	NC (NC;NC) NC	NC (NC;NC) NC	NC (NC;NC)
No	26/ 26	0	8/ 8	0	NC (NC;NC) NC	NC (NC;NC) NC	NC (NC;NC)
Disease subtype	Interaction p-value [4]		NC				
Localized	26/ 26	0	10/ 10	0	NC (NC;NC) NC	NC (NC;NC) NC	NC (NC;NC)
Diffuse	57/ 57	0	27/ 27	0	NC (NC;NC) NC	NC (NC;NC) NC	NC (NC;NC)
Missing	0/ 0	0	2/ 2	0	NC (NC;NC) NC	NC (NC;NC) NC	NC (NC;NC)
Tumour location	Interaction p-value [4]		NC				
Lower Limb	77/ 77	0	34/ 34	0	NC (NC;NC)	NC (NC;NC)	NC (NC;NC)

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

Subgroup Level	Vimseltinib (N=83)		Placebo (N=40)		RR [1] (95% CI) p-value	OR [2] (95% CI) p-value	RD [3] (95% CI)
	N/N'	n (%)	N/N'	n (%)			
					NC	NC	
All Other	6/ 6	0	5/ 5	0	NC (NC;NC) NC	NC (NC;NC) NC	NC (NC;NC)
Disease location joint size	Interaction p-value [4]		NC				
Large Joints	69/ 69	0	28/ 28	0	NC (NC;NC) NC	NC (NC;NC) NC	NC (NC;NC)
Small Joints	14/ 14	0	11/ 11	0	NC (NC;NC) NC	NC (NC;NC) NC	NC (NC;NC)
Disease location knee	Interaction p-value [4]		NC				
Yes	56/ 56	0	26/ 26	0	NC (NC;NC) NC	NC (NC;NC) NC	NC (NC;NC)
No	27/ 27	0	13/ 13	0	NC (NC;NC) NC	NC (NC;NC) NC	NC (NC;NC)
Prior surgery	Interaction p-value [4]		NC				
Yes	64/ 64	0	26/ 26	0	NC (NC;NC) NC	NC (NC;NC) NC	NC (NC;NC)
No	19/ 19	0	13/ 13	0	NC	NC	NC

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

Subgroup Level	Vimseltinib (N=83)		Placebo (N=40)		RR [1] (95% CI) p-value	OR [2] (95% CI) p-value	RD [3] (95% CI)
	N/N'	n (%)	N/N'	n (%)			
					(NC;NC) NC	(NC;NC) NC	(NC;NC)
Prior imatinib/nilotinib treatment	Interaction p-value [4]		NC				
Yes	19/ 19	0	9/ 9	0	NC (NC;NC) NC	NC (NC;NC) NC	NC (NC;NC)
No	64/ 64	0	30/ 30	0	NC (NC;NC) NC	NC (NC;NC) NC	NC (NC;NC)

N: Number of subjects in analysis set. N': Number of subjects analysed. n: Number of subjects with event. NC: Not calculated. NE: Not estimable. CI: Confidence interval. OR: Odds ratio. RD: Risk difference. RR: Risk ratio. Int.: Interaction.

Percentages based on N. Reference is Placebo.

[1] Log-binomial regression with terms Treatment, Subgroup, and Treatment by Subgroup interaction.

[2] Logistic regression with terms Treatment, Subgroup, and Treatment by Subgroup interaction.

[3] Cochran-Mantel-Haenszel method stratified by Subgroup.

[4] Treatment*Subgroup interaction p-value from log-binomial regression.

4.2.6 Subgruppenanalysen für UEs auf Ebene von SOC und PT während der randomisierten, kontrollierten Studienphase

4.2.6.1 Subgruppenanalysen für UEs auf Ebene der SOC „Augenerkrankungen“ während der randomisierten, kontrollierten Studienphase

Subgroup Level	Vimseltinib (N=83)		Placebo (N=40)		RR [1] (95% CI) p-value	OR [2] (95% CI) p-value	RD [3] (95% CI)
	N/N'	n (%)	N/N'	n (%)			
Sex	Interaction p-value [4]		0.9326				
Male	37/ 37	28 (75.7)	13/ 13	3 (23.1)	3.279 (1.195;8.996) 0.0211	10.370 (2.331;46.146) 0.0021	0.526 (0.258;0.794)
Female	46/ 46	33 (71.7)	26/ 26	6 (23.1)	3.109 (1.506;6.418) 0.0022	8.462 (2.773;25.816) 0.0002	0.487 (0.279;0.694)
Age group	Interaction p-value [4]						
18 - < 50	54/ 54	NC	26/ 26	NC	NC (NC;NC) NC	NC (NC;NC) NC	NC (NC;NC)
50 - < 65	24/ 24	NC	9/ 9	NC	NC (NC;NC) NC	NC (NC;NC) NC	NC (NC;NC)
≥ 65	5/ 5	NC	4/ 4	NC	NC (NC;NC) NC	NC (NC;NC) NC	NC (NC;NC)

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

Subgroup Level	Vimseltinib (N=83)		Placebo (N=40)		RR [1] (95% CI) p-value	OR [2] (95% CI) p-value	RD [3] (95% CI)
	N/N'	n (%)	N/N'	n (%)			
Region	Interaction p-value [4]		0.2401				
U.S.	9/ 9	9 (100.0)	4/ 4	0 (0.0)	9.500 (0.682;132.251) 0.0938	171.000 (2.899;10086.0) 0.0134	1.000 (NC;NC)
Non-U.S.	74/ 74	52 (70.3)	35/ 35	9 (25.7)	2.733 (1.527;4.892) 0.0007	6.828 (2.756;16.917) <.0001	0.446 (0.267;0.624)
Site in Europe	Interaction p-value [4]		0.4111				
Yes	57/ 57	40 (70.2)	31/ 31	6 (19.4)	3.626 (1.733;7.586) 0.0006	9.804 (3.409;28.195) <.0001	0.508 (0.325;0.691)
No	26/ 26	21 (80.8)	8/ 8	3 (37.5)	2.154 (0.863;5.373)	7.000 (1.238;39.566)	0.433 (0.065;0.801)
Disease subtype	Interaction p-value [4]		0.1984				
Localized	26/ 26	14 (53.8)	10/ 10	3 (30.0)	1.795 (0.653;4.935) 0.2570	2.722 (0.574;12.914) 0.2074	0.238 (-0.104;0.581)
Diffuse	57/ 57	47 (82.5)	27/ 27	5 (18.5)	4.453 (2.000;9.912) 0.0003	20.680 (6.311;67.768) <.0001	0.639 (0.463;0.816)
Missing	0/ 0	0	2/ 2	1 (50.0)	NC (NC;NC)	NC (NC;NC)	NC (NC;NC)

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

Subgroup Level	Vimseltinib (N=83)		Placebo (N=40)		RR [1] (95% CI) p-value	OR [2] (95% CI) p-value	RD [3] (95% CI)
	N/N'	n (%)	N/N'	n (%)	NC	NC	
Tumour location	Interaction p-value [4]		0.7443				
Lower Limb	77/ 77	56 (72.7)	34/ 34	8 (23.5)	3.091 (1.661;5.753) 0.0004	8.667 (3.393;22.138) <.0001	0.492 (0.318;0.666)
All Other	6/ 6	5 (83.3)	5/ 5	1 (20.0)	4.167 (0.696;24.936) 0.1180	20.000 (0.930;429.904) 0.0556	0.633 (0.173;1.000)
Disease location joint size	Interaction p-value [4]		0.1957				
Large Joints	69/ 69	51 (73.9)	28/ 28	8 (28.6)	2.587 (1.417;4.724) 0.0020	7.083 (2.658;18.879) <.0001	0.453 (0.257;0.650)
Small Joints	14/ 14	10 (71.4)	11/ 11	1 (9.1)	7.857 (1.178;52.421) 0.0333	25.000 (2.360;264.803) 0.0075	0.623 (0.332;0.915)
Disease location knee	Interaction p-value [4]		0.3469				
Yes	56/ 56	40 (71.4)	26/ 26	7 (26.9)	2.653 (1.379;5.105) 0.0035	6.786 (2.392;19.249) 0.0003	0.445 (0.238;0.653)
No	27/ 27	21 (77.8)	13/ 13	2 (15.4)	5.056 (1.391;18.378) 0.0139	19.250 (3.316;111.747) 0.0010	0.624 (0.373;0.875)
Prior surgery	Interaction p-value [4]		0.6540				

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

Subgroup Level	Vimseltinib (N=83)		Placebo (N=40)		RR [1] (95% CI) p-value	OR [2] (95% CI) p-value	RD [3] (95% CI)
	N/N'	n (%)	N/N'	n (%)			
Yes	64/ 64	50 (78.1)	26/ 26	6 (23.1)	3.385 (1.658;6.911) 0.0008	11.905 (4.011;35.334) <.0001	0.550 (0.359;0.741)
No	19/ 19	11 (57.9)	13/ 13	3 (23.1)	2.509 (0.866;7.270) 0.0902	4.583 (0.945;22.235) 0.0588	0.348 (0.029;0.667)
Prior imatinib/nilotinib treatment		Interaction p-value [4]		0.9531			
Yes	19/ 19	13 (68.4)	9/ 9	2 (22.2)	3.079 (0.873;10.853) 0.0802	7.583 (1.198;48.004) 0.0314	0.462 (0.119;0.805)
No	64/ 64	48 (75.0)	30/ 30	7 (23.3)	3.214 (1.655;6.243) 0.0006	9.857 (3.562;27.276) <.0001	0.517 (0.332;0.701)

N: Number of subjects in analysis set. N': Number of subjects analysed. n: Number of subjects with event. NC: Not calculated. NE: Not estimable. CI: Confidence interval. OR: Odds ratio. RD: Risk difference. RR: Risk ratio. Int.: Interaction.

Percentages based on N. Reference is Placebo.

[1] Log-binomial regression with terms Treatment, Subgroup, and Treatment by Subgroup interaction.

[2] Logistic regression with terms Treatment, Subgroup, and Treatment by Subgroup interaction.

[3] Cochran-Mantel-Haenszel method stratified by Subgroup.

[4] Treatment*Subgroup interaction p-value from log-binomial regression.

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

4.2.6.2 Subgruppenanalysen für UEs auf Ebene des PT „Periorbitalödem“ während der randomisierten, kontrollierten Studienphase

Subgroup Level	Vimseltinib (N=83)		Placebo (N=40)		RR [1] (95% CI) p-value	OR [2] (95% CI) p-value	RD [3] (95% CI)
	N/N'	n (%)	N/N'	n (%)			
Sex	Interaction p-value [4]		0.7796				
Male	37/ 37	13 (35.1)	13/ 13	1 (7.7)	4.568 (0.661;31.572) 0.1236	6.500 (0.758;55.732) 0.0878	0.274 (0.063;0.486)
Female	46/ 46	24 (52.2)	26/ 26	4 (15.4)	3.391 (1.321;8.707) 0.0111	6.000 (1.785;20.167) 0.0038	0.368 (0.168;0.568)
Age group	Interaction p-value [4]						
18 - < 50	54/ 54	NC	26/ 26	NC	NC (NC;NC) NC	NC (NC;NC) NC	NC (NC;NC)
50 - < 65	24/ 24	NC	9/ 9	NC	NC (NC;NC) NC	NC (NC;NC) NC	NC (NC;NC)
≥ 65	5/ 5	NC	4/ 4	NC	NC (NC;NC) NC	NC (NC;NC) NC	NC (NC;NC)
Region	Interaction p-value [4]		0.2617				
U.S.	9/ 9	9 (100.0)	4/ 4	0 (0.0)	9.500 (0.682;132.251) 0.0938	171.000 (2.899;10086.0) 0.0134	1.000 (NC;NC)

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

Subgroup Level	Vimseltinib (N=83)		Placebo (N=40)		RR [1] (95% CI) p-value	OR [2] (95% CI) p-value	RD [3] (95% CI)
	N/N'	n (%)	N/N'	n (%)			
Non-U.S.	74/ 74	28 (37.8)	35/ 35	5 (14.3)	2.649 (1.118;6.275) 0.0269	3.652 (1.269;10.509) 0.0163	0.236 (0.075;0.396)
Site in Europe	Interaction p-value [4]		0.7570				
Yes	57/ 57	23 (40.4)	31/ 31	4 (12.9)	3.127 (1.188;8.229) 0.0209	4.566 (1.409;14.799) 0.0114	0.274 (0.101;0.448)
No	26/ 26	14 (53.8)	8/ 8	1 (12.5)	4.308 (0.666;27.882) 0.1254	8.167 (0.876;76.151) 0.0652	0.413 (0.115;0.712)
Disease subtype	Interaction p-value [4]		0.8329				
Localized	26/ 26	9 (34.6)	10/ 10	1 (10.0)	3.462 (0.501;23.919) 0.2080	4.765 (0.518;43.798) 0.1678	0.246 (-0.015;0.507)
Diffuse	57/ 57	28 (49.1)	27/ 27	3 (11.1)	4.421 (1.473;13.270) 0.0080	7.724 (2.089;28.563) 0.0022	0.380 (0.204;0.556)
Missing	0/ 0	0	2/ 2	1 (50.0)	NC (NC;NC) NC	NC (NC;NC) NC	NC (NC;NC)
Tumour location	Interaction p-value [4]		0.7222				
Lower Limb	77/ 77	34 (44.2)	34/ 34	4 (11.8)	3.753 (1.445;9.746)	5.930 (1.904;18.470)	0.324 (0.169;0.479)

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

Subgroup Level	Vimseltinib (N=83)		Placebo (N=40)		RR [1] (95% CI) p-value	OR [2] (95% CI) p-value	RD [3] (95% CI)
	N/N'	n (%)	N/N'	n (%)			
					0.0066	0.0021	
All Other	6/ 6	3 (50.0)	5/ 5	1 (20.0)	2.500 (0.364;17.173) 0.3514	4.000 (0.265;60.325) 0.3167	0.300 (-0.232;0.832)
Disease location joint size	Interaction p-value [4]		0.9563				
Large Joints	69/ 69	33 (47.8)	28/ 28	4 (14.3)	3.348 (1.308;8.572) 0.0118	5.500 (1.726;17.529) 0.0039	0.335 (0.160;0.511)
Small Joints	14/ 14	4 (28.6)	11/ 11	1 (9.1)	3.143 (0.407;24.269) 0.2722	4.000 (0.378;42.368) 0.2496	0.195 (-0.097;0.486)
Disease location knee	Interaction p-value [4]		0.7448				
Yes	56/ 56	25 (44.6)	26/ 26	3 (11.5)	3.869 (1.283;11.664) 0.0163	6.183 (1.663;22.993) 0.0066	0.331 (0.152;0.510)
No	27/ 27	12 (44.4)	13/ 13	2 (15.4)	2.889 (0.754;11.064) 0.1215	4.400 (0.814;23.776) 0.0852	0.291 (0.019;0.562)
Prior surgery	Interaction p-value [4]		0.6922				
Yes	64/ 64	29 (45.3)	26/ 26	3 (11.5)	3.927 (1.310;11.772) 0.0146	6.352 (1.731;23.306) 0.0053	0.338 (0.165;0.511)
No	19/ 19	8 (42.1)	13/ 13	2 (15.4)	2.737	4.000	0.267

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

Subgroup Level	Vimseltinib (N=83)		Placebo (N=40)		RR [1] (95% CI) p-value	OR [2] (95% CI) p-value	RD [3] (95% CI)
	N/N'	n (%)	N/N'	n (%)			
					(0.689;10.874) 0.1526	(0.688;23.261) 0.1227	(-0.029;0.563)
Prior imatinib/nilotinib treatment	Interaction p-value [4]		0.5436				
Yes	19/ 19	6 (31.6)	9/ 9	0 (0.0)	6.500 (0.405;104.196) 0.1861	9.148 (0.458;182.609) 0.1473	0.316 (0.107;0.525)
No	64/ 64	31 (48.4)	30/ 30	5 (16.7)	2.906 (1.256;6.726) 0.0127	4.697 (1.598;13.805) 0.0049	0.318 (0.137;0.499)

N: Number of subjects in analysis set. N': Number of subjects analysed. n: Number of subjects with event. NC: Not calculated. NE: Not estimable. CI: Confidence interval. OR: Odds ratio. RD: Risk difference. RR: Risk ratio. Int.: Interaction.

Percentages based on N. Reference is Placebo.

[1] Log-binomial regression with terms Treatment, Subgroup, and Treatment by Subgroup interaction.

[2] Logistic regression with terms Treatment, Subgroup, and Treatment by Subgroup interaction.

[3] Cochran-Mantel-Haenszel method stratified by Subgroup.

[4] Treatment*Subgroup interaction p-value from log-binomial regression.

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

4.2.6.3 Subgruppenanalysen für UEs auf Ebene der SOC „Allgemeine Erkrankungen und Beschwerden am Verabreichungsort“ während der randomisierten, kontrollierten Studienphase

Subgroup Level	Vimseltinib (N=83)		Placebo (N=40)		RR [1] (95% CI) p-value	OR [2] (95% CI) p-value	RD [3] (95% CI)
	N/N'	n (%)	N/N'	n (%)			
Sex	Interaction p-value [4]		0.2910				
Male	37/ 37	26 (70.3)	13/ 13	7 (53.8)	1.305 (0.757;2.251) 0.3385	2.026 (0.553;7.422) 0.2865	0.164 (-0.144;0.473)
Female	46/ 46	38 (82.6)	26/ 26	11 (42.3)	1.953 (1.223;3.118) 0.0051	6.477 (2.179;19.252) 0.0008	0.403 (0.184;0.622)
Age group	Interaction p-value [4]						
18 - < 50	54/ 54	NC	26/ 26	NC	NC (NC;NC) NC	NC (NC;NC) NC	NC (NC;NC)
50 - < 65	24/ 24	NC	9/ 9	NC	NC (NC;NC) NC	NC (NC;NC) NC	NC (NC;NC)
≥ 65	5/ 5	NC	4/ 4	NC	NC (NC;NC) NC	NC (NC;NC) NC	NC (NC;NC)
Region	Interaction p-value [4]		0.2428				
U.S.	9/ 9	8 (88.9)	4/ 4	1 (25.0)	3.556 (0.641;19.718) 0.1467	24.000 (1.111;518.581) 0.0427	0.639 (0.167;1.000)

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

Subgroup Level	Vimseltinib (N=83)		Placebo (N=40)		RR [1] (95% CI) p-value	OR [2] (95% CI) p-value	RD [3] (95% CI)
	N/N'	n (%)	N/N'	n (%)			
Non-U.S.	74/ 74	56 (75.7)	35/ 35	17 (48.6)	1.558 (1.082;2.243) 0.0171	3.294 (1.409;7.702) 0.0059	0.271 (0.079;0.463)
Site in Europe	Interaction p-value [4]		0.1898				
Yes	57/ 57	44 (77.2)	31/ 31	16 (51.6)	1.496 (1.034;2.163) 0.0325	3.173 (1.243;8.103) 0.0158	0.256 (0.049;0.463)
No	26/ 26	20 (76.9)	8/ 8	2 (25.0)	3.077 (0.910;10.407) 0.0706	10.000 (1.585;63.097) 0.0143	0.519 (0.178;0.860)
Disease subtype	Interaction p-value [4]		0.2977				
Localized	26/ 26	21 (80.8)	10/ 10	6 (60.0)	1.346 (0.785;2.309) 0.2804	2.800 (0.567;13.833) 0.2065	0.208 (-0.132;0.547)
Diffuse	57/ 57	43 (75.4)	27/ 27	10 (37.0)	2.037 (1.219;3.404) 0.0066	5.221 (1.946;14.008) 0.0010	0.384 (0.170;0.598)
Missing	0/ 0	0	2/ 2	2 (100.0)	NC (NC;NC) NC	NC (NC;NC) NC	NC (NC;NC)
Tumour location	Interaction p-value [4]		NC				
Lower Limb	77/ 77	61 (79.2)	34/ 34	14 (41.2)	1.924 (1.267;2.921)	5.446 (2.265;13.094)	0.380 (0.192;0.569)

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

Subgroup Level	Vimseltinib (N=83)		Placebo (N=40)		RR [1] (95% CI) p-value	OR [2] (95% CI) p-value	RD [3] (95% CI)
	N/N'	n (%)	N/N'	n (%)			
					0.0021	0.0002	
All Other	6/ 6	3 (50.0)	5/ 5	4 (80.0)	0.625 (0.251;1.556) 0.3126	0.250 (0.017;3.770) 0.3167	-0.300 (-0.832;0.232)
Disease location joint size	Interaction p-value [4]		0.2811				
Large Joints	69/ 69	55 (79.7)	28/ 28	12 (42.9)	1.860 (1.193;2.899) 0.0062	5.238 (2.024;13.558) 0.0006	0.369 (0.162;0.575)
Small Joints	14/ 14	9 (64.3)	11/ 11	6 (54.5)	1.179 (0.606;2.294) 0.6287	1.500 (0.299;7.531) 0.6224	0.097 (-0.289;0.484)
Disease location knee	Interaction p-value [4]		0.3306				
Yes	56/ 56	45 (80.4)	26/ 26	11 (42.3)	1.899 (1.190;3.030) 0.0071	5.579 (2.012;15.467) 0.0010	0.380 (0.164;0.597)
No	27/ 27	19 (70.4)	13/ 13	7 (53.8)	1.307 (0.747;2.287) 0.3486	2.036 (0.518;7.995) 0.3085	0.165 (-0.156;0.486)
Prior surgery	Interaction p-value [4]		0.7097				
Yes	64/ 64	51 (79.7)	26/ 26	12 (46.2)	1.727 (1.120;2.663) 0.0135	4.577 (1.713;12.226) 0.0024	0.335 (0.120;0.551)
No	19/ 19	13 (68.4)	13/ 13	6 (46.2)	1.482	2.528	0.223

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

Subgroup Level	Vimseltinib (N=83)		Placebo (N=40)		RR [1] (95% CI) p-value	OR [2] (95% CI) p-value	RD [3] (95% CI)
	N/N'	n (%)	N/N'	n (%)			
					(0.765;2.874) 0.2437	(0.588;10.859) 0.2124	(-0.120;0.565)
Prior imatinib/nilotinib treatment	Interaction p-value [4]		0.0093				
Yes	19/ 19	12 (63.2)	9/ 9	7 (77.8)	0.812 (0.498;1.325) 0.4047	0.490 (0.079;3.045) 0.4439	-0.146 (-0.494;0.201)
No	64/ 64	52 (81.3)	30/ 30	11 (36.7)	2.216 (1.365;3.598) 0.0013	7.485 (2.831;19.790) <.0001	0.446 (0.249;0.643)

N: Number of subjects in analysis set. N': Number of subjects analysed. n: Number of subjects with event. NC: Not calculated. NE: Not estimable. CI: Confidence interval. OR: Odds ratio. RD: Risk difference. RR: Risk ratio. Int.: Interaction.

Percentages based on N. Reference is Placebo.

[1] Log-binomial regression with terms Treatment, Subgroup, and Treatment by Subgroup interaction.

[2] Logistic regression with terms Treatment, Subgroup, and Treatment by Subgroup interaction.

[3] Cochran-Mantel-Haenszel method stratified by Subgroup.

[4] Treatment*Subgroup interaction p-value from log-binomial regression.

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

4.2.6.4 Subgruppenanalysen für UEs auf Ebene des PT „Gesichtsödem“ während der randomisierten, kontrollierten Studienphase

Subgroup Level	Vimseltinib (N=83)		Placebo (N=40)		RR [1] (95% CI) p-value	OR [2] (95% CI) p-value	RD [3] (95% CI)
	N/N'	n (%)	N/N'	n (%)			
Sex	Interaction p-value [4]		0.4162				
Male	37/ 37	11 (29.7)	13/ 13	0 (0.0)	8.474 (0.534;134.463) 0.1297	11.717 (0.641;214.288) 0.0970	0.297 (0.150;0.445)
Female	46/ 46	15 (32.6)	26/ 26	3 (11.5)	2.826 (0.902;8.859) 0.0747	3.710 (0.960;14.336) 0.0573	0.211 (0.028;0.394)
Age group	Interaction p-value [4]						
18 - < 50	54/ 54	NC	26/ 26	NC	NC (NC;NC) NC	NC (NC;NC) NC	NC (NC;NC)
50 - < 65	24/ 24	NC	9/ 9	NC	NC (NC;NC) NC	NC (NC;NC) NC	NC (NC;NC)
≥ 65	5/ 5	NC	4/ 4	NC	NC (NC;NC) NC	NC (NC;NC) NC	NC (NC;NC)
Region	Interaction p-value [4]		0.7994				
U.S.	9/ 9	2 (22.2)	4/ 4	0 (0.0)	2.500 (0.146;42.800) 0.5272	3.000 (0.116;77.643) 0.5081	0.222 (-0.049;0.494)

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

Subgroup Level	Vimseltinib (N=83)		Placebo (N=40)		RR [1] (95% CI) p-value	OR [2] (95% CI) p-value	RD [3] (95% CI)
	N/N'	n (%)	N/N'	n (%)			
Non-U.S.	74/ 74	24 (32.4)	35/ 35	3 (8.6)	3.784 (1.221;11.724) 0.0211	5.120 (1.424;18.408) 0.0124	0.239 (0.097;0.380)
Site in Europe	Interaction p-value [4]		0.3326				
Yes	57/ 57	21 (36.8)	31/ 31	2 (6.5)	5.711 (1.433;22.764) 0.0135	8.458 (1.830;39.087) 0.0063	0.304 (0.152;0.456)
No	26/ 26	5 (19.2)	8/ 8	1 (12.5)	1.538 (0.209;11.316) 0.6722	1.667 (0.165;16.810) 0.6649	0.067 (-0.207;0.342)
Disease subtype	Interaction p-value [4]		0.3575				
Localized	26/ 26	10 (38.5)	10/ 10	0 (0.0)	8.556 (0.547;133.704) 0.1259	13.364 (0.706;252.950) 0.0840	0.385 (0.198;0.572)
Diffuse	57/ 57	16 (28.1)	27/ 27	3 (11.1)	2.526 (0.804;7.938) 0.1126	3.122 (0.824;11.828) 0.0939	0.170 (0.003;0.336)
Missing	0/ 0	0	2/ 2	0 (0.0)	NC (NC;NC) NC	NC (NC;NC) NC	NC (NC;NC)
Tumour location	Interaction p-value [4]		0.0361				
Lower Limb	77/ 77	24 (31.2)	34/ 34	1 (2.9)	10.597 (1.494;75.178)	14.943 (1.929;115.737)	0.282 (0.164;0.400)

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

Subgroup Level	Vimseltinib (N=83)		Placebo (N=40)		RR [1] (95% CI) p-value	OR [2] (95% CI) p-value	RD [3] (95% CI)
	N/N'	n (%)	N/N'	n (%)			
					0.0182	0.0096	
All Other	6/ 6	2 (33.3)	5/ 5	2 (40.0)	0.833 (0.175;3.965) 0.8188	0.750 (0.064;8.834) 0.8192	-0.067 (-0.638;0.505)
Disease location joint size	Interaction p-value [4]		0.4072				
Large Joints	69/ 69	21 (30.4)	28/ 28	3 (10.7)	2.841 (0.920;8.769) 0.0695	3.646 (0.991;13.414) 0.0516	0.197 (0.039;0.355)
Small Joints	14/ 14	5 (35.7)	11/ 11	0 (0.0)	8.800 (0.538;143.814) 0.1271	13.316 (0.650;272.829) 0.0929	0.357 (0.106;0.608)
Disease location knee	Interaction p-value [4]		0.9388				
Yes	56/ 56	17 (30.4)	26/ 26	2 (7.7)	3.946 (0.984;15.834) 0.0528	5.231 (1.109;24.667) 0.0365	0.227 (0.069;0.385)
No	27/ 27	9 (33.3)	13/ 13	1 (7.7)	4.333 (0.612;30.677) 0.1420	6.000 (0.671;53.681) 0.1090	0.256 (0.027;0.486)
Prior surgery	Interaction p-value [4]		0.8591				
Yes	64/ 64	19 (29.7)	26/ 26	2 (7.7)	3.859 (0.967;15.400) 0.0558	5.067 (1.087;23.609) 0.0388	0.220 (0.068;0.372)
No	19/ 19	7 (36.8)	13/ 13	1 (7.7)	4.789	7.000	0.291

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

Subgroup Level	Vimseltinib (N=83)		Placebo (N=40)		RR [1] (95% CI) p-value	OR [2] (95% CI) p-value	RD [3] (95% CI)
	N/N'	n (%)	N/N'	n (%)			
					(0.666;34.445) 0.1197	(0.743;65.943) 0.0890	(0.031;0.552)
Prior imatinib/nilotinib treatment	Interaction p-value [4]		0.6029				
Yes	19/ 19	6 (31.6)	9/ 9	0 (0.0)	6.500 (0.405;104.196) 0.1861	9.148 (0.458;182.609) 0.1473	0.316 (0.107;0.525)
No	64/ 64	20 (31.3)	30/ 30	3 (10.0)	3.125 (1.006;9.706) 0.0488	4.091 (1.110;15.081) 0.0343	0.213 (0.056;0.369)

N: Number of subjects in analysis set. N': Number of subjects analysed. n: Number of subjects with event. NC: Not calculated. NE: Not estimable. CI: Confidence interval. OR: Odds ratio. RD: Risk difference. RR: Risk ratio. Int.: Interaction.

Percentages based on N. Reference is Placebo.

[1] Log-binomial regression with terms Treatment, Subgroup, and Treatment by Subgroup interaction.

[2] Logistic regression with terms Treatment, Subgroup, and Treatment by Subgroup interaction.

[3] Cochran-Mantel-Haenszel method stratified by Subgroup.

[4] Treatment*Subgroup interaction p-value from log-binomial regression.

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

4.2.6.5 Subgruppenanalysen für UEs auf Ebene der SOC „Untersuchungen“ während der randomisierten, kontrollierten Studienphase

Subgroup Level	Vimseltinib (N=83)		Placebo (N=40)		RR [1] (95% CI) p-value	OR [2] (95% CI) p-value	RD [3] (95% CI)
	N/N'	n (%)	N/N'	n (%)			
Sex	Interaction p-value [4]		0.7698				
Male	37/ 37	17 (45.9)	13/ 13	1 (7.7)	5.973 (0.880;40.548) 0.0674	10.200 (1.200;86.695) 0.0334	0.383 (0.166;0.599)
Female	46/ 46	23 (50.0)	26/ 26	3 (11.5)	4.333 (1.438;13.055) 0.0092	7.667 (2.018;29.126) 0.0028	0.385 (0.195;0.574)
Age group	Interaction p-value [4]						
18 - < 50	54/ 54	NC	26/ 26	NC	NC (NC;NC) NC	NC (NC;NC) NC	NC (NC;NC)
50 - < 65	24/ 24	NC	9/ 9	NC	NC (NC;NC) NC	NC (NC;NC) NC	NC (NC;NC)
≥ 65	5/ 5	NC	4/ 4	NC	NC (NC;NC) NC	NC (NC;NC) NC	NC (NC;NC)
Region	Interaction p-value [4]		0.0872				
U.S.	9/ 9	7 (77.8)	4/ 4	2 (50.0)	1.556 (0.550;4.403) 0.4052	3.500 (0.284;43.161) 0.3284	0.278 (-0.282;0.838)

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

Subgroup Level	Vimseltinib (N=83)		Placebo (N=40)		RR [1] (95% CI) p-value	OR [2] (95% CI) p-value	RD [3] (95% CI)
	N/N'	n (%)	N/N'	n (%)			
Non-U.S.	74/ 74	33 (44.6)	35/ 35	2 (5.7)	7.804 (1.984;30.696) 0.0033	13.280 (2.966;59.464) 0.0007	0.389 (0.252;0.526)
Site in Europe	Interaction p-value [4]		0.1550				
Yes	57/ 57	28 (49.1)	31/ 31	2 (6.5)	7.614 (1.942;29.851) 0.0036	14.000 (3.049;64.274) 0.0007	0.427 (0.271;0.583)
No	26/ 26	12 (46.2)	8/ 8	2 (25.0)	1.846 (0.518;6.574) 0.3441	2.571 (0.435;15.193) 0.2974	0.212 (-0.144;0.568)
Disease subtype	Interaction p-value [4]		0.9693				
Localized	26/ 26	12 (46.2)	10/ 10	1 (10.0)	4.615 (0.687;31.018) 0.1156	7.714 (0.850;69.983) 0.0694	0.362 (0.095;0.629)
Diffuse	57/ 57	28 (49.1)	27/ 27	3 (11.1)	4.421 (1.473;13.270) 0.0080	7.724 (2.089;28.563) 0.0022	0.380 (0.204;0.556)
Missing	0/ 0	0	2/ 2	0 (0.0)	NC (NC;NC) NC	NC (NC;NC) NC	NC (NC;NC)
Tumour location	Interaction p-value [4]		0.6867				
Lower Limb	77/ 77	36 (46.8)	34/ 34	3 (8.8)	5.299 (1.752;16.022)	9.073 (2.556;32.205)	0.379 (0.233;0.526)

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

Subgroup Level	Vimseltinib (N=83)		Placebo (N=40)		RR [1] (95% CI) p-value	OR [2] (95% CI) p-value	RD [3] (95% CI)
	N/N'	n (%)	N/N'	n (%)			
					0.0031	0.0006	
All Other	6/ 6	4 (66.7)	5/ 5	1 (20.0)	3.333 (0.528;21.032) 0.2002	8.000 (0.500;127.900) 0.1415	0.467 (-0.048;0.982)
Disease location joint size	Interaction p-value [4]		0.4599				
Large Joints	69/ 69	32 (46.4)	28/ 28	2 (7.1)	6.493 (1.667;25.281) 0.0070	11.243 (2.474;51.102) 0.0017	0.392 (0.241;0.544)
Small Joints	14/ 14	8 (57.1)	11/ 11	2 (18.2)	3.143 (0.829;11.921) 0.0923	6.000 (0.932;38.629) 0.0593	0.390 (0.044;0.735)
Disease location knee	Interaction p-value [4]		0.7034				
Yes	56/ 56	24 (42.9)	26/ 26	2 (7.7)	5.571 (1.422;21.826) 0.0137	9.000 (1.936;41.836) 0.0051	0.352 (0.186;0.517)
No	27/ 27	16 (59.3)	13/ 13	2 (15.4)	3.852 (1.037;14.313) 0.0441	8.000 (1.475;43.396) 0.0159	0.439 (0.169;0.709)
Prior surgery	Interaction p-value [4]		0.1310				
Yes	64/ 64	29 (45.3)	26/ 26	1 (3.8)	11.781 (1.692;82.037) 0.0127	20.714 (2.644;162.277) 0.0039	0.415 (0.272;0.557)
No	19/ 19	11 (57.9)	13/ 13	3 (23.1)	2.509	4.583	0.348

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

Subgroup Level	Vimseltinib (N=83)		Placebo (N=40)		RR [1] (95% CI) p-value	OR [2] (95% CI) p-value	RD [3] (95% CI)
	N/N'	n (%)	N/N'	n (%)			
					(0.866;7.270) 0.0902	(0.945;22.235) 0.0588	(0.029;0.667)
Prior imatinib/nilotinib treatment	Interaction p-value [4]		0.2762				
Yes	19/ 19	12 (63.2)	9/ 9	0 (0.0)	12.500 (0.821;190.299) 0.0691	31.667 (1.601;626.212) 0.0233	0.632 (0.415;0.848)
No	64/ 64	28 (43.8)	30/ 30	4 (13.3)	3.281 (1.264;8.516) 0.0146	5.056 (1.580;16.171) 0.0063	0.304 (0.132;0.476)

N: Number of subjects in analysis set. N': Number of subjects analysed. n: Number of subjects with event. NC: Not calculated. NE: Not estimable. CI: Confidence interval. OR: Odds ratio. RD: Risk difference. RR: Risk ratio. Int.: Interaction.

Percentages based on N. Reference is Placebo.

[1] Log-binomial regression with terms Treatment, Subgroup, and Treatment by Subgroup interaction.

[2] Logistic regression with terms Treatment, Subgroup, and Treatment by Subgroup interaction.

[3] Cochran-Mantel-Haenszel method stratified by Subgroup.

[4] Treatment*Subgroup interaction p-value from log-binomial regression.

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

4.2.6.6 Subgruppenanalysen für UEs auf Ebene des PT „Aspartataminotransferase erhöht“ während der randomisierten, kontrollierten Studienphase

Subgroup Level	Vimseltinib (N=83)		Placebo (N=40)		RR [1] (95% CI) p-value	OR [2] (95% CI) p-value	RD [3] (95% CI)
	N/N'	n (%)	N/N'	n (%)			
Sex	Interaction p-value [4]		0.7151				
Male	37/ 37	5 (13.5)	13/ 13	0 (0.0)	4.053 (0.239;68.637) 0.3324	4.569 (0.236;88.513) 0.3150	0.135 (0.025;0.245)
Female	46/ 46	14 (30.4)	26/ 26	1 (3.8)	7.913 (1.102;56.795) 0.0397	10.937 (1.346;88.883) 0.0252	0.266 (0.114;0.418)
Age group	Interaction p-value [4]						
18 - < 50	54/ 54	NC	26/ 26	NC	NC (NC;NC) NC	NC (NC;NC) NC	NC (NC;NC)
50 - < 65	24/ 24	NC	9/ 9	NC	NC (NC;NC) NC	NC (NC;NC) NC	NC (NC;NC)
≥ 65	5/ 5	NC	4/ 4	NC	NC (NC;NC) NC	NC (NC;NC) NC	NC (NC;NC)
Region	Interaction p-value [4]		0.9144				
U.S.	9/ 9	5 (55.6)	4/ 4	0 (0.0)	5.500 (0.374;80.916) 0.2140	11.000 (0.459;263.529) 0.1390	0.556 (0.231;0.880)

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

Subgroup Level	Vimseltinib (N=83)		Placebo (N=40)		RR [1] (95% CI) p-value	OR [2] (95% CI) p-value	RD [3] (95% CI)
	N/N'	n (%)	N/N'	n (%)			
Non-U.S.	74/ 74	14 (18.9)	35/ 35	1 (2.9)	6.622 (0.906;48.369) 0.0624	7.933 (0.999;62.991) 0.0501	0.161 (0.056;0.266)
Site in Europe	Interaction p-value [4]		0.7850				
Yes	57/ 57	13 (22.8)	31/ 31	1 (3.2)	7.070 (0.970;51.534) 0.0536	8.864 (1.100;71.391) 0.0404	0.196 (0.070;0.321)
No	26/ 26	6 (23.1)	8/ 8	0 (0.0)	4.333 (0.270;69.553) 0.3005	5.390 (0.272;106.708) 0.2688	0.231 (0.069;0.393)
Disease subtype	Interaction p-value [4]		0.9667				
Localized	26/ 26	7 (26.9)	10/ 10	0 (0.0)	6.111 (0.381;98.067) 0.2012	8.077 (0.419;155.773) 0.1665	0.269 (0.099;0.440)
Diffuse	57/ 57	12 (21.1)	27/ 27	1 (3.7)	5.684 (0.779;41.498) 0.0867	6.933 (0.852;56.413) 0.0702	0.173 (0.046;0.301)
Missing	0/ 0	0	2/ 2	0 (0.0)	NC (NC;NC) NC	NC (NC;NC) NC	NC (NC;NC)
Tumour location	Interaction p-value [4]		0.2837				
Lower Limb	77/ 77	16 (20.8)	34/ 34	0 (0.0)	14.808 (0.914;239.904)	18.512 (1.077;318.188)	0.208 (0.117;0.298)

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

Subgroup Level	Vimseltinib (N=83)		Placebo (N=40)		RR [1] (95% CI) p-value	OR [2] (95% CI) p-value	RD [3] (95% CI)
	N/N'	n (%)	N/N'	n (%)			
					0.0579	0.0443	
All Other	6/ 6	3 (50.0)	5/ 5	1 (20.0)	2.500 (0.364;17.173) 0.3514	4.000 (0.265;60.325) 0.3167	0.300 (-0.232;0.832)
Disease location joint size	Interaction p-value [4]		0.9232				
Large Joints	69/ 69	15 (21.7)	28/ 28	1 (3.6)	6.087 (0.844;43.912) 0.0732	7.500 (0.940;59.811) 0.0572	0.182 (0.063;0.301)
Small Joints	14/ 14	4 (28.6)	11/ 11	0 (0.0)	7.200 (0.429;120.964) 0.1703	9.857 (0.472;205.892) 0.1400	0.286 (0.049;0.522)
Disease location knee	Interaction p-value [4]		0.6725				
Yes	56/ 56	10 (17.9)	26/ 26	1 (3.8)	4.643 (0.627;34.386) 0.1329	5.435 (0.657;44.941) 0.1163	0.140 (0.016;0.265)
No	27/ 27	9 (33.3)	13/ 13	0 (0.0)	9.500 (0.595;151.684) 0.1112	13.865 (0.741;259.416) 0.0785	0.333 (0.156;0.511)
Prior surgery	Interaction p-value [4]		0.5514				
Yes	64/ 64	13 (20.3)	26/ 26	0 (0.0)	11.215 (0.691;182.009) 0.0891	13.893 (0.795;242.911) 0.0715	0.203 (0.105;0.302)
No	19/ 19	6 (31.6)	13/ 13	1 (7.7)	4.105	5.538	0.239

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

Subgroup Level	Vimseltinib (N=83)		Placebo (N=40)		RR [1] (95% CI) p-value	OR [2] (95% CI) p-value	RD [3] (95% CI)
	N/N'	n (%)	N/N'	n (%)			
					(0.558;30.213) 0.1655	(0.579;52.955) 0.1373	(-0.015;0.493)
Prior imatinib/nilotinib treatment	Interaction p-value [4]		0.5489				
Yes	19/ 19	2 (10.5)	9/ 9	0 (0.0)	2.500 (0.132;47.287) 0.5413	2.714 (0.118;62.549) 0.5328	0.105 (-0.033;0.243)
No	64/ 64	17 (26.6)	30/ 30	1 (3.3)	7.969 (1.112;57.119) 0.0389	10.489 (1.325;83.061) 0.0260	0.232 (0.106;0.358)

N: Number of subjects in analysis set. N': Number of subjects analysed. n: Number of subjects with event. NC: Not calculated. NE: Not estimable. CI: Confidence interval. OR: Odds ratio. RD: Risk difference. RR: Risk ratio. Int.: Interaction.

Percentages based on N. Reference is Placebo.

[1] Log-binomial regression with terms Treatment, Subgroup, and Treatment by Subgroup interaction.

[2] Logistic regression with terms Treatment, Subgroup, and Treatment by Subgroup interaction.

[3] Cochran-Mantel-Haenszel method stratified by Subgroup.

[4] Treatment*Subgroup interaction p-value from log-binomial regression.

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

4.2.6.7 Subgruppenanalysen für UEs auf Ebene des PT „Kreatinphosphokinase im Blut erhöht“ während der randomisierten, kontrollierten Studienphase

Subgroup Level	Vimseltinib (N=83)		Placebo (N=40)		RR [1] (95% CI) p-value	OR [2] (95% CI) p-value	RD [3] (95% CI)
	N/N'	n (%)	N/N'	n (%)			
Sex	Interaction p-value [4]		0.7538				
Male	37/ 37	9 (24.3)	13/ 13	0 (0.0)	7.000 (0.436;112.497) 0.1696	9.000 (0.487;166.307) 0.1398	0.243 (0.105;0.381)
Female	46/ 46	11 (23.9)	26/ 26	0 (0.0)	13.213 (0.810;215.459) 0.0699	17.169 (0.968;304.566) 0.0527	0.239 (0.116;0.362)
Age group	Interaction p-value [4]		0.2663				
18 - < 50	54/ 54	NC	26/ 26	NC	NC (NC;NC) NC	NC (NC;NC) NC	NC (NC;NC)
50 - < 65	24/ 24	NC	9/ 9	NC	NC (NC;NC) NC	NC (NC;NC) NC	NC (NC;NC)
≥ 65	5/ 5	NC	4/ 4	NC	NC (NC;NC) NC	NC (NC;NC) NC	NC (NC;NC)
Region	Interaction p-value [4]		0.2663				
U.S.	9/ 9	1 (11.1)	4/ 4	0 (0.0)	1.500 (0.074;30.590) 0.7921	1.588 (0.053;47.516) 0.7896	0.111 (-0.094;0.316)

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

Subgroup Level	Vimseltinib (N=83)		Placebo (N=40)		RR [1] (95% CI) p-value	OR [2] (95% CI) p-value	RD [3] (95% CI)
	N/N'	n (%)	N/N'	n (%)			
Non-U.S.	74/ 74	19 (25.7)	35/ 35	0 (0.0)	18.720 (1.163;301.400) 0.0388	24.946 (1.460;426.348) 0.0263	0.257 (0.157;0.356)
Site in Europe	Interaction p-value [4]		0.3988				
Yes	57/ 57	16 (28.1)	31/ 31	0 (0.0)	18.207 (1.129;293.533) 0.0408	25.048 (1.447;433.617) 0.0268	0.281 (0.164;0.397)
No	26/ 26	4 (15.4)	8/ 8	0 (0.0)	3.000 (0.178;50.465) 0.4456	3.400 (0.165;70.119) 0.4280	0.154 (0.015;0.293)
Disease subtype	Interaction p-value [4]		0.6349				
Localized	26/ 26	6 (23.1)	10/ 10	0 (0.0)	5.296 (0.325;86.203) 0.2415	6.659 (0.341;129.924) 0.2110	0.231 (0.069;0.393)
Diffuse	57/ 57	14 (24.6)	27/ 27	0 (0.0)	14.000 (0.866;226.317) 0.0631	18.333 (1.051;319.918) 0.0462	0.246 (0.134;0.357)
Missing	0/ 0	0	2/ 2	0 (0.0)	NC (NC;NC) NC	NC (NC;NC) NC	NC (NC;NC)
Tumour location	Interaction p-value [4]		0.5171				
Lower Limb	77/ 77	18 (23.4)	34/ 34	0 (0.0)	16.603 (1.029;267.769)	21.454 (1.253;367.254)	0.234 (0.139;0.328)

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

Subgroup Level	Vimseltinib (N=83)		Placebo (N=40)		RR [1] (95% CI) p-value	OR [2] (95% CI) p-value	RD [3] (95% CI)
	N/N'	n (%)	N/N'	n (%)			
					0.0477	0.0344	
All Other	6/ 6	2 (33.3)	5/ 5	0 (0.0)	4.286 (0.252;72.901) 0.3142	6.111 (0.229;162.735) 0.2797	0.333 (-0.044;0.711)
Disease location joint size	Interaction p-value [4]		0.9427				
Large Joints	69/ 69	14 (20.3)	28/ 28	0 (0.0)	12.014 (0.741;194.779) 0.0803	14.892 (0.857;258.776) 0.0637	0.203 (0.108;0.298)
Small Joints	14/ 14	6 (42.9)	11/ 11	0 (0.0)	10.400 (0.649;166.714) 0.0981	17.588 (0.867;356.807) 0.0619	0.429 (0.169;0.688)
Disease location knee	Interaction p-value [4]		0.8692				
Yes	56/ 56	12 (21.4)	26/ 26	0 (0.0)	11.842 (0.728;192.679) 0.0824	14.888 (0.846;261.871) 0.0649	0.214 (0.107;0.322)
No	27/ 27	8 (29.6)	13/ 13	0 (0.0)	8.500 (0.528;136.885) 0.1312	11.769 (0.625;221.597) 0.0997	0.296 (0.124;0.469)
Prior surgery	Interaction p-value [4]		0.7999				
Yes	64/ 64	15 (23.4)	26/ 26	0 (0.0)	12.877 (0.799;207.600) 0.0716	16.596 (0.955;288.461) 0.0538	0.234 (0.131;0.338)
No	19/ 19	5 (26.3)	13/ 13	0 (0.0)	7.700	10.241	0.263

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

Subgroup Level	Vimseltinib (N=83)		Placebo (N=40)		RR [1] (95% CI) p-value	OR [2] (95% CI) p-value	RD [3] (95% CI)
	N/N'	n (%)	N/N'	n (%)			
					(0.462;128.325) 0.1550	(0.516;203.342) 0.1271	(0.065;0.461)
Prior imatinib/nilotinib treatment	Interaction p-value [4]		0.8659				
Yes	19/ 19	8 (42.1)	9/ 9	0 (0.0)	8.500 (0.544;132.869) 0.1271	14.043 (0.714;276.154) 0.0821	0.421 (0.199;0.643)
No	64/ 64	12 (18.8)	30/ 30	0 (0.0)	11.923 (0.729;194.925) 0.0821	14.524 (0.830;254.041) 0.0669	0.188 (0.092;0.283)

N: Number of subjects in analysis set. N': Number of subjects analysed. n: Number of subjects with event. NC: Not calculated. NE: Not estimable. CI: Confidence interval. OR: Odds ratio. RD: Risk difference. RR: Risk ratio. Int.: Interaction.

Percentages based on N. Reference is Placebo.

[1] Log-binomial regression with terms Treatment, Subgroup, and Treatment by Subgroup interaction.

[2] Logistic regression with terms Treatment, Subgroup, and Treatment by Subgroup interaction.

[3] Cochran-Mantel-Haenszel method stratified by Subgroup.

[4] Treatment*Subgroup interaction p-value from log-binomial regression.

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

4.2.6.8 Subgruppenanalysen für UEs auf Ebene der SOC „Erkrankungen der Haut und des Unterhautgewebes“ während der randomisierten, kontrollierten Studienphase

Subgroup Level	Vimseltinib (N=83)		Placebo (N=40)		RR [1] (95% CI) p-value	OR [2] (95% CI) p-value	RD [3] (95% CI)
	N/N'	n (%)	N/N'	n (%)			
Sex	Interaction p-value [4]		0.6616				
Male	37/ 37	16 (43.2)	13/ 13	1 (7.7)	5.622 (0.825;38.303) 0.0778	9.143 (1.074;77.800) 0.0428	0.356 (0.140;0.571)
Female	46/ 46	32 (69.6)	26/ 26	5 (19.2)	3.617 (1.608;8.136) 0.0019	9.600 (3.009;30.624) 0.0001	0.503 (0.302;0.705)
Age group	Interaction p-value [4]		NC				
18 - < 50	54/ 54	NC	26/ 26	NC	NC (NC;NC) NC	NC (NC;NC) NC	NC (NC;NC)
50 - < 65	24/ 24	NC	9/ 9	NC	NC (NC;NC) NC	NC (NC;NC) NC	NC (NC;NC)
≥ 65	5/ 5	NC	4/ 4	NC	NC (NC;NC) NC	NC (NC;NC) NC	NC (NC;NC)
Region	Interaction p-value [4]		0.8284				
U.S.	9/ 9	7 (77.8)	4/ 4	1 (25.0)	3.111 (0.550;17.600) 0.1993	10.500 (0.668;165.114) 0.0944	0.528 (0.024;1.000)

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

Subgroup Level	Vimseltinib (N=83)		Placebo (N=40)		RR [1] (95% CI) p-value	OR [2] (95% CI) p-value	RD [3] (95% CI)
	N/N'	n (%)	N/N'	n (%)			
Non-U.S.	74/ 74	41 (55.4)	35/ 35	5 (14.3)	3.878 (1.680;8.955) 0.0015	7.455 (2.604;21.342) 0.0002	0.411 (0.249;0.573)
Site in Europe	Interaction p-value [4]		0.7269				
Yes	57/ 57	32 (56.1)	31/ 31	5 (16.1)	3.481 (1.510;8.021) 0.0034	6.656 (2.236;19.812) 0.0007	0.400 (0.217;0.583)
No	26/ 26	16 (61.5)	8/ 8	1 (12.5)	4.923 (0.768;31.574) 0.0928	11.200 (1.193;105.132) 0.0345	0.490 (0.195;0.786)
Disease subtype	Interaction p-value [4]		0.6304				
Localized	26/ 26	14 (53.8)	10/ 10	2 (20.0)	2.692 (0.741;9.777) 0.1323	4.667 (0.827;26.342) 0.0811	0.338 (0.025;0.652)
Diffuse	57/ 57	34 (59.6)	27/ 27	4 (14.8)	4.026 (1.590;10.198) 0.0033	8.500 (2.595;27.838) 0.0004	0.448 (0.263;0.633)
Missing	0/ 0	0	2/ 2	0 (0.0)	NC (NC;NC) NC	NC (NC;NC) NC	NC (NC;NC)
Tumour location	Interaction p-value [4]		0.9256				
Lower Limb	77/ 77	43 (55.8)	34/ 34	5 (14.7)	3.797 (1.650;8.739)	7.335 (2.566;20.967)	0.411 (0.249;0.574)

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

Subgroup Level	Vimseltinib (N=83)		Placebo (N=40)		RR [1] (95% CI) p-value	OR [2] (95% CI) p-value	RD [3] (95% CI)
	N/N'	n (%)	N/N'	n (%)			
					0.0017	0.0002	
All Other	6/ 6	5 (83.3)	5/ 5	1 (20.0)	4.167 (0.696;24.936) 0.1180	20.000 (0.930;429.904) 0.0556	0.633 (0.173;1.000)
Disease location joint size	Interaction p-value [4]		0.6313				
Large Joints	69/ 69	41 (59.4)	28/ 28	4 (14.3)	4.159 (1.644;10.521) 0.0026	8.786 (2.747;28.095) 0.0002	0.451 (0.277;0.625)
Small Joints	14/ 14	7 (50.0)	11/ 11	2 (18.2)	2.750 (0.707;10.700) 0.1445	4.500 (0.703;28.794) 0.1122	0.318 (-0.029;0.665)
Disease location knee	Interaction p-value [4]		0.3976				
Yes	56/ 56	32 (57.1)	26/ 26	3 (11.5)	4.952 (1.668;14.703) 0.0040	10.222 (2.746;38.052) 0.0005	0.456 (0.277;0.635)
No	27/ 27	16 (59.3)	13/ 13	3 (23.1)	2.568 (0.907;7.269) 0.0757	4.848 (1.080;21.758) 0.0393	0.362 (0.067;0.656)
Prior surgery	Interaction p-value [4]		0.5429				
Yes	64/ 64	35 (54.7)	26/ 26	3 (11.5)	4.740 (1.598;14.060) 0.0050	9.253 (2.522;33.948) 0.0008	0.431 (0.258;0.605)
No	19/ 19	13 (68.4)	13/ 13	3 (23.1)	2.965	7.222	0.453

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

Subgroup Level	Vimseltinib (N=83)		Placebo (N=40)		RR [1] (95% CI) p-value	OR [2] (95% CI) p-value	RD [3] (95% CI)
	N/N'	n (%)	N/N'	n (%)			
					(1.050;8.375) 0.0402	(1.440;36.224) 0.0163	(0.143;0.764)
Prior imatinib/nilotinib treatment	Interaction p-value [4]		0.2349				
Yes	19/ 19	11 (57.9)	9/ 9	0 (0.0)	11.500 (0.752;175.936) 0.0793	25.706 (1.307;505.486) 0.0327	0.579 (0.357;0.801)
No	64/ 64	37 (57.8)	30/ 30	6 (20.0)	2.891 (1.371;6.093) 0.0053	5.481 (1.971;15.246) 0.0011	0.378 (0.191;0.566)

N: Number of subjects in analysis set. N': Number of subjects analysed. n: Number of subjects with event. NC: Not calculated. NE: Not estimable. CI: Confidence interval. OR: Odds ratio. RD: Risk difference. RR: Risk ratio. Int.: Interaction.

Percentages based on N. Reference is Placebo.

[1] Log-binomial regression with terms Treatment, Subgroup, and Treatment by Subgroup interaction.

[2] Logistic regression with terms Treatment, Subgroup, and Treatment by Subgroup interaction.

[3] Cochran-Mantel-Haenszel method stratified by Subgroup.

[4] Treatment*Subgroup interaction p-value from log-binomial regression.

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

4.2.6.9 Subgruppenanalysen für UEs auf Ebene des PT „Pruritus“ während der randomisierten, kontrollierten Studienphase

Subgroup Level	Vimseltinib (N=83)		Placebo (N=40)		RR [1] (95% CI) p-value	OR [2] (95% CI) p-value	RD [3] (95% CI)
	N/N'	n (%)	N/N'	n (%)			
Sex	Interaction p-value [4]		0.8148				
Male	37/ 37	9 (24.3)	13/ 13	1 (7.7)	3.162 (0.442;22.606) 0.2513	3.857 (0.439;33.912) 0.2236	0.166 (-0.034;0.367)
Female	46/ 46	15 (32.6)	26/ 26	2 (7.7)	4.239 (1.051;17.102) 0.0424	5.806 (1.210;27.873) 0.0280	0.249 (0.079;0.419)
Age group	Interaction p-value [4]		NC				
18 - < 50	54/ 54	NC	26/ 26	NC	NC (NC;NC) NC	NC (NC;NC) NC	NC (NC;NC)
50 - < 65	24/ 24	NC	9/ 9	NC	NC (NC;NC) NC	NC (NC;NC) NC	NC (NC;NC)
≥ 65	5/ 5	NC	4/ 4	NC	NC (NC;NC) NC	NC (NC;NC) NC	NC (NC;NC)
Region	Interaction p-value [4]		0.3230				
U.S.	9/ 9	3 (33.3)	4/ 4	1 (25.0)	1.333 (0.193;9.209) 0.7705	1.500 (0.106;21.312) 0.7646	0.083 (-0.441;0.608)

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

Subgroup Level	Vimseltinib (N=83)		Placebo (N=40)		RR [1] (95% CI) p-value	OR [2] (95% CI) p-value	RD [3] (95% CI)
	N/N'	n (%)	N/N'	n (%)			
Non-U.S.	74/ 74	21 (28.4)	35/ 35	2 (5.7)	4.966 (1.233;20.010) 0.0242	6.538 (1.438;29.717) 0.0151	0.227 (0.098;0.355)
Site in Europe	Interaction p-value [4]		0.6512				
Yes	57/ 57	16 (28.1)	31/ 31	2 (6.5)	4.351 (1.069;17.704) 0.0400	5.659 (1.207;26.527) 0.0279	0.216 (0.071;0.361)
No	26/ 26	8 (30.8)	8/ 8	1 (12.5)	2.462 (0.360;16.822) 0.3583	3.111 (0.326;29.658) 0.3238	0.183 (-0.107;0.473)
Disease subtype	Interaction p-value [4]		0.5180				
Localized	26/ 26	5 (19.2)	10/ 10	1 (10.0)	1.923 (0.255;14.488) 0.5256	2.143 (0.218;21.047) 0.5132	0.092 (-0.148;0.332)
Diffuse	57/ 57	19 (33.3)	27/ 27	2 (7.4)	4.500 (1.128;17.944) 0.0331	6.250 (1.337;29.211) 0.0198	0.259 (0.102;0.417)
Missing	0/ 0	0	2/ 2	0 (0.0)	NC (NC;NC) NC	NC (NC;NC) NC	NC (NC;NC)
Tumour location	Interaction p-value [4]		0.8531				
Lower Limb	77/ 77	22 (28.6)	34/ 34	3 (8.8)	3.238 (1.039;10.092) 0.0428	4.133 (1.145;14.927) 0.0303	0.197 (0.059;0.336)

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

Subgroup Level	Vimseltinib (N=83)		Placebo (N=40)		RR [1] (95% CI) p-value	OR [2] (95% CI) p-value	RD [3] (95% CI)
	N/N'	n (%)	N/N'	n (%)			
All Other	6/ 6	2 (33.3)	5/ 5	0 (0.0)	4.286 (0.252;72.901) 0.3142	6.111 (0.229;162.735) 0.2797	0.333 (-0.044;0.711)
Disease location joint size	Interaction p-value [4]		0.2503				
Large Joints	69/ 69	19 (27.5)	28/ 28	1 (3.6)	7.710 (1.084;54.865) 0.0413	10.260 (1.302;80.874) 0.0271	0.240 (0.114;0.365)
Small Joints	14/ 14	5 (35.7)	11/ 11	2 (18.2)	1.964 (0.467;8.267) 0.3572	2.500 (0.381;16.420) 0.3400	0.175 (-0.164;0.514)
Disease location knee	Interaction p-value [4]		0.0839				
Yes	56/ 56	14 (25.0)	26/ 26	0 (0.0)	13.737 (0.851;221.814) 0.0649	18.082 (1.035;315.944) 0.0473	0.250 (0.137;0.363)
No	27/ 27	10 (37.0)	13/ 13	3 (23.1)	1.605 (0.530;4.858) 0.4025	1.961 (0.434;8.860) 0.3816	0.140 (-0.153;0.432)
Prior surgery	Interaction p-value [4]		0.2097				
Yes	64/ 64	19 (29.7)	26/ 26	1 (3.8)	7.719 (1.089;54.718) 0.0408	10.556 (1.333;83.606) 0.0256	0.258 (0.124;0.393)
No	19/ 19	5 (26.3)	13/ 13	2 (15.4)	1.711 (0.389;7.517)	1.964 (0.318;12.124)	0.109 (-0.169;0.388)

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

Subgroup Level	Vimseltinib (N=83)		Placebo (N=40)		RR [1] (95% CI) p-value	OR [2] (95% CI) p-value	RD [3] (95% CI)
	N/N'	n (%)	N/N'	n (%)			
					0.4772	0.4672	
Prior imatinib/nilotinib treatment	Interaction p-value [4]		0.5481				
Yes	19/ 19	6 (31.6)	9/ 9	0 (0.0)	6.500 (0.405;104.196) 0.1861	9.148 (0.458;182.609) 0.1473	0.316 (0.107;0.525)
No	64/ 64	18 (28.1)	30/ 30	3 (10.0)	2.813 (0.897;8.818) 0.0761	3.522 (0.949;13.070) 0.0599	0.181 (0.027;0.335)

N: Number of subjects in analysis set. N': Number of subjects analysed. n: Number of subjects with event. NC: Not calculated. NE: Not estimable. CI: Confidence interval. OR: Odds ratio. RD: Risk difference. RR: Risk ratio. Int.: Interaction.

Percentages based on N. Reference is Placebo.

[1] Log-binomial regression with terms Treatment, Subgroup, and Treatment by Subgroup interaction.

[2] Logistic regression with terms Treatment, Subgroup, and Treatment by Subgroup interaction.

[3] Cochran-Mantel-Haenszel method stratified by Subgroup.

[4] Treatment*Subgroup interaction p-value from log-binomial regression.