Inhalt

Subgruppenanalysen: binäre Endpunkte

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

Project Code / Study Number / Analysis: SAR231893 / EFC14153 / CSR_RWE

2 PRO endpoints

2.1 Responder analysis for ACQ-5-IA (value<= 0.75) at week 52 - ITT type 2 inflammatory asthma phenotype population

Type 2 inflammatory asthma phenotype population	**Placebo (N=114)**	**Dupilumab (N=236)**
Responder status at Week 52 based on value of ACQ-5-IA <=0.75 [n(%)] [a]		
Responder	61 (53.5%)	180 (76.3%)
Non-responder	53 (46.5%)	56 (23.7%)
Odds Ratio (95% CI)	-	2.94 (1.74 to 4.97)
p-value for Odds Ratio		<0.001
Risk Ratio (95% CI)	-	1.38 (1.16 to 1.64)
Reversed Risk ratio (95% CI)	-	0.72 (0.61 to 0.86)
p-value for Risk Ratio		<0.001
Risk Difference (95% CI)	-	21.62 (11.40 to 31.85)
p-value for Risk Difference		<0.001

[a] Patients who met the corresponding criterion are considered as responders. Patients who did not meet the criterion or had missing value are considered as non-responders. OR, RR and RD are derived from a logistic regression model with treatment, age, weight group, region, baseline eosinophil level, baseline FeNO level, baseline ICS dose level, and baseline ACQ-5-IA score as covariates.
Peto OR calculation is based on Yusuf S et al. (Prog Cardiovasc Dis. 1985 Mar-Apr;27(5):335-71) and its p-value is derived using a normal approximation.
PGM=DEVOPS/SAR231893/EFC14153/CSR_RWE/REPORT/PGM/eff_pro_evt_ger_i_t.sas OUT=REPORT/OUTPUT/eff_pro_acq5aw52_ger_t2_t_x.rtf (30JUN2021 - 8:13)

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

Project Code / Study Number / Analysis: SAR231893 / EFC14153 / CSR_RWE

2 PRO endpoints

2.1 Responder analysis for ACQ-5-IA (value<= 0.75) at week 52 - ITT type 2 inflammatory asthma phenotype population

2.1.1 By gender (Male, Female)

	Gender			
	Male		Female	
Type 2 inflammatory asthma phenotype population	**Placebo (N=78)**	**Dupilumab (N=152)**	**Placebo (N=36)**	**Dupilumab (N=84)**
Responder status at Week 52 based on value of ACQ-5-IA <=0.75 [n(%)] [a]				
Responder	38 (48.7%)	119 (78.3%)	23 (63.9%)	61 (72.6%)
Non-responder	40 (51.3%)	33 (21.7%)	13 (36.1%)	23 (27.4%)
Odds Ratio (95% CI) vs placebo	-	3.69 (1.94 to 7.01)	-	1.87 (0.71 to 4.94)
p-value for Odds Ratio	-	<0.001	-	0.204
p-value for heterogeneity of Odds Ratio				0.160
Risk Ratio (95% CI) vs placebo	-	1.53 (1.21 to 1.94)	-	1.22 (0.84 to 1.76)
Reversed Risk ratio (95% CI) vs placebo	-	0.65 (0.51 to 0.83)	-	0.82 (0.57 to 1.19)
p-value for Risk Ratio	-	<0.001	-	0.292

[a] Patients who met the corresponding criterion are considered as responders. Patients who did not meet the criterion or had missing value are considered as non-responders.
OR, RR and RD are derived from a logistic regression model with treatment, age, weight group, region, baseline eosinophil level, baseline FeNO level, baseline ICS dose level, and baseline ACQ-5-IA score as covariates.
Peto OR calculation is based on Yusuf S et al. (Prog Cardiovasc Dis. 1985 Mar-Apr;27(5):335-71) and its p-value is derived using a normal approximation.
p-values for heterogeneity are estimated by using the same logistic model as the one used to estimate OR, RR and RD, with subgroup and treatment-by-subgroup interaction as additional covariates.
p-value for heterogeneity of Peto OR is estimated by using normal approximation.
PGM=DEVOPS/SAR231893/EFC14153/CSR_RWE/REPORT/PGM/eff_pro_evt_ger_subg_i_t.sas OUT=REPORT/OUTPUT/eff_pro_acq5aw52_ger_sex_t2_t_x.rtf (29JUN2021 - 17:41)

Project Code / Study Number / Analysis: SAR231893 / EFC14153 / CSR_RWE

2 PRO endpoints

2.1 Responder analysis for ACQ-5-IA (value<= 0.75) at week 52 - ITT type 2 inflammatory asthma phenotype population

2.1.1 By gender (Male, Female)

	Gender			
	Male		Female	
Type 2 inflammatory asthma phenotype population	**Placebo (N=78)**	**Dupilumab (N=152)**	**Placebo (N=36)**	**Dupilumab (N=84)**
p-value for heterogeneity of Risk Ratio				0.152
Risk Difference (95% CI) vs placebo	-	27.43 (14.61 to 40.25)	-	11.78 (-6.70 to 30.26)
p-value for Risk Difference	-	<0.001	-	0.209
p-value for heterogeneity of Risk Difference				0.151

[a] Patients who met the corresponding criterion are considered as responders. Patients who did not meet the criterion or had missing value are considered as non-responders.
OR, RR and RD are derived from a logistic regression model with treatment, age, weight group, region, baseline eosinophil level, baseline FeNO level, baseline ICS dose level, and baseline ACQ-5-IA score as covariates.
Peto OR calculation is based on Yusuf S et al. (Prog Cardiovasc Dis. 1985 Mar-Apr;27(5):335-71) and its p-value is derived using a normal approximation.
p-values for heterogeneity are estimated by using the same logistic model as the one used to estimate OR, RR and RD, with subgroup and treatment-by-subgroup interaction as additional covariates.
p-value for heterogeneity of Peto OR is estimated by using normal approximation.
PGM=DEVOPS/SAR231893/EFC14153/CSR_RWE/REPORT/PGM/eff_pro_evt_ger_subg_i_t.sas OUT=REPORT/OUTPUT/eff_pro_acq5aw52_ger_sex_t2_t_x.rtf (29JUN2021 - 17:41)

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

Project Code / Study Number / Analysis: SAR231893 / EFC14153 / CSR_RWE

2 PRO endpoints

2.1 Responder analysis for ACQ-5-IA (value<= 0.75) at week 52 - ITT type 2 inflammatory asthma phenotype population

2.1.2 By region (Latin America, East Europe, Western Countries)

	Region					
	Latin America		East Europe		Western countries	
Type 2 inflammatory asthma phenotype population	**Placebo (N=51)**	**Dupilumab (N=106)**	**Placebo (N=43)**	**Dupilumab (N=78)**	**Placebo (N=20)**	**Dupilumab (N=52)**
Responder status at Week 52 based on value of ACQ-5-IA <=0.75 [n(%)] [a]						
Responder	33 (64.7%)	93 (87.7%)	20 (46.5%)	57 (73.1%)	8 (40.0%)	30 (57.7%)
Non-responder	18 (35.3%)	13 (12.3%)	23 (53.5%)	21 (26.9%)	12 (60.0%)	22 (42.3%)
Odds Ratio (95% CI) vs placebo	-	3.81 (1.54 to 9.42)	-	3.40 (1.48 to 7.85)	-	1.85 (0.56 to 6.15)
p-value for Odds Ratio	-	0.004	-	0.004	-	0.308
p-value for heterogeneity of Odds Ratio:						
Latin America, East Europe						0.893
Latin America, Western countries						0.360
East Europe, Western countries						0.405
overall						0.624

[a] Patients who met the corresponding criterion are considered as responders. Patients who did not meet the criterion or had missing value are considered as non-responders.
OR, RR and RD are derived from a logistic regression model with treatment, age, weight group, baseline eosinophil level, baseline FeNO level, baseline ICS dose level, and baseline ACQ-5-IA score as covariates.
Peto OR calculation is based on Yusuf S et al. (Prog Cardiovasc Dis. 1985 Mar-Apr;27(5):335-71) and its p-value is derived using a normal approximation.
p-values for heterogeneity are estimated by using the same logistic model as the one used to estimate OR, RR and RD, with subgroup and treatment-by-subgroup interaction as additional covariates.
p-value for heterogeneity of Peto OR is estimated by using normal approximation.
PGM=DEVOPS/SAR231893/EFC14153/CSR_RWE/REPORT/PGM/eff_pro_evt_ger_subg_i_t.sas OUT=REPORT/OUTPUT/eff_pro_acq5aw52_ger_cty_t2_t_x.rtf (29JUN2021 - 17:42)

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

Project Code / Study Number / Analysis: SAR231893 / EFC14153 / CSR_RWE

2 PRO endpoints

2.1 Responder analysis for ACQ-5-IA (value<= 0.75) at week 52 - ITT type 2 inflammatory asthma phenotype population

2.1.2 By region (Latin America, East Europe, Western Countries)

	Region					
	Latin America		East Europe		Western countries	
Type 2 inflammatory asthma phenotype population	**Placebo (N=51)**	**Dupilumab (N=106)**	**Placebo (N=43)**	**Dupilumab (N=78)**	**Placebo (N=20)**	**Dupilumab (N=52)**
Risk Ratio (95% CI) vs placebo	-	1.37 (1.07 to 1.75)	-	1.60 (1.11 to 2.31)	-	1.31 (0.65 to 2.61)
Reversed Risk ratio (95% CI) vs placebo	-	0.73 (0.57 to 0.94)	-	0.63 (0.43 to 0.90)	-	0.77 (0.38 to 1.53)
p-value for Risk Ratio	-	0.014	-	0.013	-	0.444
p-value for heterogeneity of Risk Ratio:						
Latin America, East Europe						0.530
Latin America, Western countries						0.922
East Europe, Western countries						0.630
overall						0.798
Risk Difference (95% CI) vs placebo	-	24.09 (7.97 to 40.22)	-	28.17 (10.14 to 46.19)	-	10.26 (-17.36 to 37.88)
p-value for Risk Difference	-	0.004	-	0.002	-	0.460

[a] Patients who met the corresponding criterion are considered as responders. Patients who did not meet the criterion or had missing value are considered as non-responders.
OR, RR and RD are derived from a logistic regression model with treatment, age, weight group, baseline eosinophil level, baseline FeNO level, baseline ICS dose level, and baseline ACQ-5-IA score as covariates.
Peto OR calculation is based on Yusuf S et al. (Prog Cardiovasc Dis. 1985 Mar-Apr;27(5):335-71) and its p-value is derived using a normal approximation.
p-values for heterogeneity are estimated by using the same logistic model as the one used to estimate OR, RR and RD, with subgroup and treatment-by-subgroup interaction as additional covariates.
p-value for heterogeneity of Peto OR is estimated by using normal approximation.
PGM=DEVOPS/SAR231893/EFC14153/CSR_RWE/REPORT/PGM/eff_pro_evt_ger_subg_i_t.sas OUT=REPORT/OUTPUT/eff_pro_acq5aw52_ger_cty_t2_t_x.rtf (29JUN2021 - 17:42)

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

Project Code / Study Number / Analysis: SAR231893 / EFC14153 / CSR_RWE

2 PRO endpoints

2.1 Responder analysis for ACQ-5-IA (value<= 0.75) at week 52 - ITT type 2 inflammatory asthma phenotype population

2.1.2 By region (Latin America, East Europe, Western Countries)

	Region					
	Latin America		East Europe		Western countries	
Type 2 inflammatory asthma phenotype population	**Placebo (N=51)**	**Dupilumab (N=106)**	**Placebo (N=43)**	**Dupilumab (N=78)**	**Placebo (N=20)**	**Dupilumab (N=52)**
p-value for heterogeneity of Risk Difference:						
Latin America, East Europe						0.742
Latin America, Western countries						0.595
East Europe, Western countries						0.446
overall						0.748

[a] Patients who met the corresponding criterion are considered as responders. Patients who did not meet the criterion or had missing value are considered as non-responders.
OR, RR and RD are derived from a logistic regression model with treatment, age, weight group, baseline eosinophil level, baseline FeNO level, baseline ICS dose level, and baseline ACQ-5-IA score as covariates.
Peto OR calculation is based on Yusuf S et al. (Prog Cardiovasc Dis. 1985 Mar-Apr;27(5):335-71) and its p-value is derived using a normal approximation.
p-values for heterogeneity are estimated by using the same logistic model as the one used to estimate OR, RR and RD, with subgroup and treatment-by-subgroup interaction as additional covariates.
p-value for heterogeneity of Peto OR is estimated by using normal approximation.
PGM=DEVOPS/SAR231893/EFC14153/CSR_RWE/REPORT/PGM/eff_pro_evt_ger_subg_i_t.sas OUT=REPORT/OUTPUT/eff_pro_acq5aw52_ger_cty_t2_t_x.rtf (29JUN2021 - 17:42)

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

Project Code / Study Number / Analysis: SAR231893 / EFC14153 / CSR_RWE

2 PRO endpoints

2.1 Responder analysis for ACQ-5-IA (value<= 0.75) at week 52 - ITT type 2 inflammatory asthma phenotype population

2.1.3 By race (Caucasian/white, Black/of African descent, Other)

	Race					
	Caucasian/White		Black/of African descent		Other	
Type 2 inflammatory asthma phenotype population	**Placebo (N=102)**	**Dupilumab (N=208)**	**Placebo (N=5)**	**Dupilumab (N=9)**	**Placebo (N=7)**	**Dupilumab (N=19)**
Responder status at Week 52 based on value of ACQ-5-IA <=0.75 [n(%)] [a]						
Responder	58 (56.9%)	165 (79.3%)	0	3 (33.3%)	3 (42.9%)	12 (63.2%)
Non-responder	44 (43.1%)	43 (20.7%)	5 (100%)	6 (66.7%)	4 (57.1%)	7 (36.8%)
Odds Ratio (95% CI) vs placebo	-	2.83 (1.61 to 4.98)	-	5.6944E8 (0.00 to NE)	-	5.90 (0.04 to 892.39)
p-value for Odds Ratio	-	<0.001	-	0.997	-	0.465
Peto Odds Ratio (95% CI) vs placebo	-	3.03 (1.79 to 5.13)	-	6.29 (0.48 to 81.92)	-	2.22 (0.40 to 12.42)
Reversed Peto Odds Ratio (95% CI)	-	0.33 (0.19 to 0.56)	-	0.16 (0.01 to 2.08)	-	0.45 (0.08 to 2.50)
p-value for Peto Odds Ratio		<0.001		0.160		0.362

[a] Patients who met the corresponding criterion are considered as responders. Patients who did not meet the criterion or had missing value are considered as non-responders.
OR, RR and RD are derived from a logistic regression model with treatment, age, weight group, region, baseline eosinophil level, baseline FeNO level, baseline ICS dose level, and baseline ACQ-5-IA score as covariates.
Peto OR calculation is based on Yusuf S et al. (Prog Cardiovasc Dis. 1985 Mar-Apr;27(5):335-71) and its p-value is derived using a normal approximation.
p-values for heterogeneity are estimated by using the same logistic model as the one used to estimate OR, RR and RD, with subgroup and treatment-by-subgroup interaction as additional covariates.
p-value for heterogeneity of Peto OR is estimated by using normal approximation.
PGM=DEVOPS/SAR231893/EFC14153/CSR_RWE/REPORT/PGM/eff_pro_evt_ger_subg_i_t.sas OUT=REPORT/OUTPUT/eff_pro_acq5aw52_ger_race_t2_t_x.rtf (29JUN2021 - 17:42)

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

Project Code / Study Number / Analysis: SAR231893 / EFC14153 / CSR_RWE

2 PRO endpoints

2.1 Responder analysis for ACQ-5-IA (value<= 0.75) at week 52 - ITT type 2 inflammatory asthma phenotype population

2.1.3 By race (Caucasian/white, Black/of African descent, Other)

	Race					
	Caucasian/White		Black/of African descent		Other	
Type 2 inflammatory asthma phenotype population	**Placebo (N=102)**	**Dupilumab (N=208)**	**Placebo (N=5)**	**Dupilumab (N=9)**	**Placebo (N=7)**	**Dupilumab (N=19)**
p-value for heterogeneity of Peto Odds Ratio:						
Caucasian/White, Black/of African descent						0.585
Caucasian/White, Other						0.736
Black/of African descent, Other						0.510
overall						0.805
Risk Ratio (95% CI) vs placebo	-	1.31 (1.10 to 1.57)	-	2.74 (0.00 to 1762.77)	-	0.94 (0.00 to 4522.60)
Reversed Risk ratio (95% CI) vs placebo	-	0.76 (0.64 to 0.91)	-	0.37 (0.00 to 235.12)		
p-value for Risk Ratio	-	0.003	-	0.688	-	0.988

[a] Patients who met the corresponding criterion are considered as responders. Patients who did not meet the criterion or had missing value are considered as non-responders.
OR, RR and RD are derived from a logistic regression model with treatment, age, weight group, region, baseline eosinophil level, baseline FeNO level, baseline ICS dose level, and baseline ACQ-5-IA score as covariates.
Peto OR calculation is based on Yusuf S et al. (Prog Cardiovasc Dis. 1985 Mar-Apr;27(5):335-71) and its p-value is derived using a normal approximation.
p-values for heterogeneity are estimated by using the same logistic model as the one used to estimate OR, RR and RD, with subgroup and treatment-by-subgroup interaction as additional covariates.
p-value for heterogeneity of Peto OR is estimated by using normal approximation.
PGM=DEVOPS/SAR231893/EFC14153/CSR_RWE/REPORT/PGM/eff_pro_evt_ger_subg_i_t.sas OUT=REPORT/OUTPUT/eff_pro_acq5aw52_ger_race_t2_t_x.rtf (29JUN2021 - 17:42)

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

Project Code / Study Number / Analysis: SAR231893 / EFC14153 / CSR_RWE

2 PRO endpoints

2.1 Responder analysis for ACQ-5-IA (value<= 0.75) at week 52 - ITT type 2 inflammatory asthma phenotype population

2.1.3 By race (Caucasian/white, Black/of African descent, Other)

	Race					
	Caucasian/White		Black/of African descent		Other	
Type 2 inflammatory asthma phenotype population	**Placebo (N=102)**	**Dupilumab (N=208)**	**Placebo (N=5)**	**Dupilumab (N=9)**	**Placebo (N=7)**	**Dupilumab (N=19)**
p-value for heterogeneity of Risk Ratio:						
Caucasian/White, Black/of African descent						0.902
Caucasian/White, Other						0.648
Black/of African descent, Other						0.904
overall						0.894
Risk Difference (95% CI) vs placebo	-	19.31 (8.27 to 30.35)	-	27.34 (-288.65 to 343.33)	-	20.64 (-84.45 to 125.73)
p-value for Risk Difference	-	<0.001	-	0.822	-	0.683
p-value for heterogeneity of Risk Difference:						

[a] Patients who met the corresponding criterion are considered as responders. Patients who did not meet the criterion or had missing value are considered as non-responders.
OR, RR and RD are derived from a logistic regression model with treatment, age, weight group, region, baseline eosinophil level, baseline FeNO level, baseline ICS dose level, and baseline ACQ-5-IA score as covariates.
Peto OR calculation is based on Yusuf S et al. (Prog Cardiovasc Dis. 1985 Mar-Apr;27(5):335-71) and its p-value is derived using a normal approximation.
p-values for heterogeneity are estimated by using the same logistic model as the one used to estimate OR, RR and RD, with subgroup and treatment-by-subgroup interaction as additional covariates.
p-value for heterogeneity of Peto OR is estimated by using normal approximation.
PGM=DEVOPS/SAR231893/EFC14153/CSR_RWE/REPORT/PGM/eff_pro_evt_ger_subg_i_t.sas OUT=REPORT/OUTPUT/eff_pro_acq5aw52_ger_race_t2_t_x.rtf (29JUN2021 - 17:42)

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

Project Code / Study Number / Analysis: SAR231893 / EFC14153 / CSR_RWE

2 PRO endpoints

2.1 Responder analysis for ACQ-5-IA (value<= 0.75) at week 52 - ITT type 2 inflammatory asthma phenotype population

2.1.3 By race (Caucasian/white, Black/of African descent, Other)

	Race					
	Caucasian/White		Black/of African descent		Other	
Type 2 inflammatory asthma phenotype population	**Placebo (N=102)**	**Dupilumab (N=208)**	**Placebo (N=5)**	**Dupilumab (N=9)**	**Placebo (N=7)**	**Dupilumab (N=19)**
Caucasian/White, Black/of African descent						0.844
Caucasian/White, Other						0.882
Black/of African descent, Other						0.870
overall						0.970

[a] Patients who met the corresponding criterion are considered as responders. Patients who did not meet the criterion or had missing value are considered as non-responders.
OR, RR and RD are derived from a logistic regression model with treatment, age, weight group, region, baseline eosinophil level, baseline FeNO level, baseline ICS dose level, and baseline ACQ-5-IA score as covariates.
Peto OR calculation is based on Yusuf S et al. (Prog Cardiovasc Dis. 1985 Mar-Apr;27(5):335-71) and its p-value is derived using a normal approximation.
p-values for heterogeneity are estimated by using the same logistic model as the one used to estimate OR, RR and RD, with subgroup and treatment-by-subgroup interaction as additional covariates.
p-value for heterogeneity of Peto OR is estimated by using normal approximation.
PGM=DEVOPS/SAR231893/EFC14153/CSR_RWE/REPORT/PGM/eff_pro_evt_ger_subg_i_t.sas OUT=REPORT/OUTPUT/eff_pro_acq5aw52_ger_race_t2_t_x.rtf (29JUN2021 - 17:42)

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

Project Code / Study Number / Analysis: SAR231893 / EFC14153 / CSR_RWE

2 PRO endpoints

2.1 Responder analysis for ACQ-5-IA (value<= 0.75) at week 52 - ITT type 2 inflammatory asthma phenotype population

2.1.4 By baseline ICS dose level (Medium, High)

	Baseline ICS dose level			
	High		Medium	
Type 2 inflammatory asthma phenotype population	**Placebo (N=50)**	**Dupilumab (N=102)**	**Placebo (N=64)**	**Dupilumab (N=131)**
Responder status at Week 52 based on value of ACQ-5-IA <=0.75 [n(%)] [a]				
Responder	23 (46.0%)	75 (73.5%)	38 (59.4%)	104 (79.4%)
Non-responder	27 (54.0%)	27 (26.5%)	26 (40.6%)	27 (20.6%)
Odds Ratio (95% CI) vs placebo	-	3.79 (1.67 to 8.60)	-	2.63 (1.28 to 5.41)
p-value for Odds Ratio	-	0.002	-	0.009
p-value for heterogeneity of Odds Ratio				0.512
Risk Ratio (95% CI) vs placebo	-	1.51 (1.08 to 2.12)	-	1.35 (1.08 to 1.69)
Reversed Risk ratio (95% CI) vs placebo	-	0.66 (0.47 to 0.92)	-	0.74 (0.59 to 0.92)

[a] Patients who met the corresponding criterion are considered as responders. Patients who did not meet the criterion or had missing value are considered as non-responders.
OR, RR and RD are derived from a logistic regression model with treatment, age, weight group, region, baseline eosinophil level, baseline FeNO level and baseline ACQ-5-IA score as covariates.
Peto OR calculation is based on Yusuf S et al. (Prog Cardiovasc Dis. 1985 Mar-Apr;27(5):335-71) and its p-value is derived using a normal approximation.
p-values for heterogeneity are estimated by using the same logistic model as the one used to estimate OR, RR and RD, with subgroup and treatment-by-subgroup interaction as additional covariates.
p-value for heterogeneity of Peto OR is estimated by using normal approximation.
PGM=DEVOPS/SAR231893/EFC14153/CSR_RWE/REPORT/PGM/eff_pro_evt_ger_subg_i_t.sas OUT=REPORT/OUTPUT/eff_pro_acq5aw52_ger_ics_t2_t_x.rtf (29JUN2021 - 17:42)

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

Project Code / Study Number / Analysis: SAR231893 / EFC14153 / CSR_RWE

2 PRO endpoints

2.1 Responder analysis for ACQ-5-IA (value<= 0.75) at week 52 - ITT type 2 inflammatory asthma phenotype population

2.1.4 By baseline ICS dose level (Medium, High)

	Baseline ICS dose level			
	High		Medium	
Type 2 inflammatory asthma phenotype population	**Placebo (N=50)**	**Dupilumab (N=102)**	**Placebo (N=64)**	**Dupilumab (N=131)**
p-value for Risk Ratio	-	0.016	-	0.008
p-value for heterogeneity of Risk Ratio				0.604
Risk Difference (95% CI) vs placebo	-	25.79 (9.23 to 42.35)	-	20.55 (7.31 to 33.79)
p-value for Risk Difference	-	0.002	-	0.003
p-value for heterogeneity of Risk Difference				0.501

[a] Patients who met the corresponding criterion are considered as responders. Patients who did not meet the criterion or had missing value are considered as non-responders.
OR, RR and RD are derived from a logistic regression model with treatment, age, weight group, region, baseline eosinophil level, baseline FeNO level and baseline ACQ-5-IA score as covariates.
Peto OR calculation is based on Yusuf S et al. (Prog Cardiovasc Dis. 1985 Mar-Apr;27(5):335-71) and its p-value is derived using a normal approximation.
p-values for heterogeneity are estimated by using the same logistic model as the one used to estimate OR, RR and RD, with subgroup and treatment-by-subgroup interaction as additional covariates.
p-value for heterogeneity of Peto OR is estimated by using normal approximation.
PGM=DEVOPS/SAR231893/EFC14153/CSR_RWE/REPORT/PGM/eff_pro_evt_ger_subg_i_t.sas OUT=REPORT/OUTPUT/eff_pro_acq5aw52_ger_ics_t2_t_x.rtf (29JUN2021 - 17:42)

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

Project Code / Study Number / Analysis: SAR231893 / EFC14153 / CSR_RWE

2 PRO endpoints

2.1 Responder analysis for ACQ-5-IA (value<= 0.75) at week 52 - ITT type 2 inflammatory asthma phenotype population

2.1.5 By baseline ICS dose level 2 (Medium, High)

	Baseline ICS dose level 2			
	High		Medium	
Type 2 inflammatory asthma phenotype population	**Placebo (N=95)**	**Dupilumab (N=200)**	**Placebo (N=19)**	**Dupilumab (N=36)**
Responder status at Week 52 based on value of ACQ-5-IA <=0.75 [n(%)] [a]				
Responder	48 (50.5%)	156 (78.0%)	13 (68.4%)	24 (66.7%)
Non-responder	47 (49.5%)	44 (22.0%)	6 (31.6%)	12 (33.3%)
Odds Ratio (95% CI) vs placebo	-	3.99 (2.23 to 7.15)	-	0.69 (0.15 to 3.13)
p-value for Odds Ratio	-	<0.001	-	0.625
p-value for heterogeneity of Odds Ratio				0.028
Risk Ratio (95% CI) vs placebo	-	1.51 (1.23 to 1.86)	-	0.90 (0.48 to 1.68)
Reversed Risk ratio (95% CI) vs placebo	-	0.66 (0.54 to 0.81)		
p-value for Risk Ratio	-	<0.001	-	0.730

[a] Patients who met the corresponding criterion are considered as responders. Patients who did not meet the criterion or had missing value are considered as non-responders.
OR, RR and RD are derived from a logistic regression model with treatment, age, weight group, region, baseline eosinophil level, baseline FeNO level and baseline ACQ-5-IA score as covariates.
Peto OR calculation is based on Yusuf S et al. (Prog Cardiovasc Dis. 1985 Mar-Apr;27(5):335-71) and its p-value is derived using a normal approximation.
p-values for heterogeneity are estimated by using the same logistic model as the one used to estimate OR, RR and RD, with subgroup and treatment-by-subgroup interaction as additional covariates.
p-value for heterogeneity of Peto OR is estimated by using normal approximation.
PGM=DEVOPS/SAR231893/EFC14153/CSR_RWE/REPORT/PGM/eff_pro_evt_ger_subg_i_t.sas OUT=REPORT/OUTPUT/eff_pro_acq5aw52_ger_ics2_t2_t_x.rtf (01SEP2021 - 15:26)

Project Code / Study Number / Analysis: SAR231893 / EFC14153 / CSR_RWE

2 PRO endpoints

2.1 Responder analysis for ACQ-5-IA (value<= 0.75) at week 52 - ITT type 2 inflammatory asthma phenotype population

2.1.5 By baseline ICS dose level 2 (Medium, High)

	Baseline ICS dose level 2			
	High		Medium	
Type 2 inflammatory asthma phenotype population	**Placebo (N=95)**	**Dupilumab (N=200)**	**Placebo (N=19)**	**Dupilumab (N=36)**
p-value for heterogeneity of Risk Ratio				0.044
Risk Difference (95% CI) vs placebo	-	26.34 (15.27 to 37.42)	-	-6.83 (-37.89 to 24.23)
p-value for Risk Difference	-	<0.001	-	0.660
p-value for heterogeneity of Risk Difference				0.034

[a] Patients who met the corresponding criterion are considered as responders. Patients who did not meet the criterion or had missing value are considered as non-responders.
OR, RR and RD are derived from a logistic regression model with treatment, age, weight group, region, baseline eosinophil level, baseline FeNO level and baseline ACQ-5-IA score as covariates.
Peto OR calculation is based on Yusuf S et al. (Prog Cardiovasc Dis. 1985 Mar-Apr;27(5):335-71) and its p-value is derived using a normal approximation.
p-values for heterogeneity are estimated by using the same logistic model as the one used to estimate OR, RR and RD, with subgroup and treatment-by-subgroup interaction as additional covariates.
p-value for heterogeneity of Peto OR is estimated by using normal approximation.
PGM=DEVOPS/SAR231893/EFC14153/CSR_RWE/REPORT/PGM/eff_pro_evt_ger_subg_i_t.sas OUT=REPORT/OUTPUT/eff_pro_acq5aw52_ger_ics2_t2_t_x.rtf (01SEP2021 - 15:26)

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

Project Code / Study Number / Analysis: SAR231893 / EFC14153 / CSR_RWE

2 PRO endpoints

2.1 Responder analysis for ACQ-5-IA (value<= 0.75) at week 52 - ITT type 2 inflammatory asthma phenotype population

2.1.6 By baseline predicted FEV1 (<80%, >=80%)

	Baseline Predicted FEV1			
	<80%		>=80%	
Type 2 inflammatory asthma phenotype population	**Placebo (N=59)**	**Dupilumab (N=116)**	**Placebo (N=55)**	**Dupilumab (N=120)**
Responder status at Week 52 based on value of ACQ-5-IA <=0.75 [n(%)] [a]				
Responder	26 (44.1%)	91 (78.4%)	35 (63.6%)	89 (74.2%)
Non-responder	33 (55.9%)	25 (21.6%)	20 (36.4%)	31 (25.8%)
Odds Ratio (95% CI) vs placebo	-	5.75 (2.61 to 12.64)	-	1.88 (0.86 to 4.13)
p-value for Odds Ratio	-	<0.001	-	0.114
p-value for heterogeneity of Odds Ratio				0.028
Risk Ratio (95% CI) vs placebo	-	1.82 (1.31 to 2.53)	-	1.12 (0.89 to 1.42)
Reversed Risk ratio (95% CI) vs placebo	-	0.55 (0.40 to 0.76)	-	0.89 (0.70 to 1.12)
p-value for Risk Ratio	-	<0.001	-	0.322

[a] Patients who met the corresponding criterion are considered as responders. Patients who did not meet the criterion or had missing value are considered as non-responders.
OR, RR and RD are derived from a logistic regression model with treatment, age, weight group, region, baseline eosinophil level, baseline FeNO level, baseline ICS dose level, and baseline ACQ-5-IA score as covariates.
Peto OR calculation is based on Yusuf S et al. (Prog Cardiovasc Dis. 1985 Mar-Apr;27(5):335-71) and its p-value is derived using a normal approximation.
p-values for heterogeneity are estimated by using the same logistic model as the one used to estimate OR, RR and RD, with subgroup and treatment-by-subgroup interaction as additional covariates.
p-value for heterogeneity of Peto OR is estimated by using normal approximation.
PGM=DEVOPS/SAR231893/EFC14153/CSR_RWE/REPORT/PGM/eff_pro_evt_ger_subg_i_t.sas OUT=REPORT/OUTPUT/eff_pro_acq5aw52_ger_pfev1_t2_t_x.rtf (29JUN2021 - 17:43)

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

Project Code / Study Number / Analysis: SAR231893 / EFC14153 / CSR_RWE

2 PRO endpoints

2.1 Responder analysis for ACQ-5-IA (value<= 0.75) at week 52 - ITT type 2 inflammatory asthma phenotype population

2.1.6 By baseline predicted FEV1 (<80%, >=80%)

	Baseline Predicted FEV1			
	<80%		>=80%	
Type 2 inflammatory asthma phenotype population	**Placebo (N=59)**	**Dupilumab (N=116)**	**Placebo (N=55)**	**Dupilumab (N=120)**
p-value for heterogeneity of Risk Ratio				0.018
Risk Difference (95% CI) vs placebo	-	36.57 (21.58 to 51.55)	-	9.03 (-6.17 to 24.22)
p-value for Risk Difference	-	<0.001	-	0.243
p-value for heterogeneity of Risk Difference				0.017

[a] Patients who met the corresponding criterion are considered as responders. Patients who did not meet the criterion or had missing value are considered as non-responders.
OR, RR and RD are derived from a logistic regression model with treatment, age, weight group, region, baseline eosinophil level, baseline FeNO level, baseline ICS dose level, and baseline ACQ-5-IA score as covariates.
Peto OR calculation is based on Yusuf S et al. (Prog Cardiovasc Dis. 1985 Mar-Apr;27(5):335-71) and its p-value is derived using a normal approximation.
p-values for heterogeneity are estimated by using the same logistic model as the one used to estimate OR, RR and RD, with subgroup and treatment-by-subgroup interaction as additional covariates.
p-value for heterogeneity of Peto OR is estimated by using normal approximation.
PGM=DEVOPS/SAR231893/EFC14153/CSR_RWE/REPORT/PGM/eff_pro_evt_ger_subg_i_t.sas OUT=REPORT/OUTPUT/eff_pro_acq5aw52_ger_pfev1_t2_t_x.rtf (29JUN2021 - 17:43)

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

Project Code / Study Number / Analysis: SAR231893 / EFC14153 / CSR_RWE

2 PRO endpoints

2.1 Responder analysis for ACQ-5-IA (value<= 0.75) at week 52 - ITT type 2 inflammatory asthma phenotype population

2.1.7 By baseline ACQ-7-IA (<=2, >2)

	Baseline ACQ-7-IA			
	<=2		>2	
Type 2 inflammatory asthma phenotype population	**Placebo (N=61)**	**Dupilumab (N=126)**	**Placebo (N=53)**	**Dupilumab (N=110)**
Responder status at Week 52 based on value of ACQ-5-IA <=0.75 [n(%)] [a]				
Responder	38 (62.3%)	98 (77.8%)	23 (43.4%)	82 (74.5%)
Non-responder	23 (37.7%)	28 (22.2%)	30 (56.6%)	28 (25.5%)
Odds Ratio (95% CI) vs placebo	-	2.30 (1.08 to 4.87)	-	3.95 (1.82 to 8.55)
p-value for Odds Ratio	-	0.030	-	<0.001
p-value for heterogeneity of Odds Ratio				0.212
Risk Ratio (95% CI) vs placebo	-	1.26 (1.00 to 1.58)	-	1.70 (1.20 to 2.41)
Reversed Risk ratio (95% CI) vs placebo	-	0.79 (0.63 to 1.00)	-	0.59 (0.42 to 0.83)
p-value for Risk Ratio	-	0.046	-	0.003

[a] Patients who met the corresponding criterion are considered as responders. Patients who did not meet the criterion or had missing value are considered as non-responders.
OR, RR and RD are derived from a logistic regression model with treatment, age, weight group, region, baseline eosinophil level, baseline FeNO level, baseline ICS dose level, and baseline ACQ-5-IA score as covariates.
Peto OR calculation is based on Yusuf S et al. (Prog Cardiovasc Dis. 1985 Mar-Apr;27(5):335-71) and its p-value is derived using a normal approximation.
p-values for heterogeneity are estimated by using the same logistic model as the one used to estimate OR, RR and RD, with subgroup and treatment-by-subgroup interaction as additional covariates.
p-value for heterogeneity of Peto OR is estimated by using normal approximation.
PGM=DEVOPS/SAR231893/EFC14153/CSR_RWE/REPORT/PGM/eff_pro_evt_ger_subg_i_t.sas OUT=REPORT/OUTPUT/eff_pro_acq5aw52_ger_acq7_t2_t_x.rtf (29JUN2021 - 17:43)

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

Project Code / Study Number / Analysis: SAR231893 / EFC14153 / CSR_RWE

2 PRO endpoints

2.1 Responder analysis for ACQ-5-IA (value<= 0.75) at week 52 - ITT type 2 inflammatory asthma phenotype population

2.1.7 By baseline ACQ-7-IA (<=2, >2)

	Baseline ACQ-7-IA			
	<=2		**>2**	
Type 2 inflammatory asthma phenotype population	**Placebo (N=61)**	**Dupilumab (N=126)**	**Placebo (N=53)**	**Dupilumab (N=110)**
p-value for heterogeneity of Risk Ratio				0.180
Risk Difference (95% CI) vs placebo	-	16.24 (2.39 to 30.09)	-	29.38 (14.01 to 44.75)
p-value for Risk Difference	-	0.022	-	<0.001
p-value for heterogeneity of Risk Difference				0.192

[a] Patients who met the corresponding criterion are considered as responders. Patients who did not meet the criterion or had missing value are considered as non-responders.
OR, RR and RD are derived from a logistic regression model with treatment, age, weight group, region, baseline eosinophil level, baseline FeNO level, baseline ICS dose level, and baseline ACQ-5-IA score as covariates.
Peto OR calculation is based on Yusuf S et al. (Prog Cardiovasc Dis. 1985 Mar-Apr;27(5):335-71) and its p-value is derived using a normal approximation.
p-values for heterogeneity are estimated by using the same logistic model as the one used to estimate OR, RR and RD, with subgroup and treatment-by-subgroup interaction as additional covariates.
p-value for heterogeneity of Peto OR is estimated by using normal approximation.
PGM=DEVOPS/SAR231893/EFC14153/CSR_RWE/REPORT/PGM/eff_pro_evt_ger_subg_i_t.sas OUT=REPORT/OUTPUT/eff_pro_acq5aw52_ger_acq7_t2_t_x.rtf (29JUN2021 - 17:43)

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

Project Code / Study Number / Analysis: SAR231893 / EFC14153 / CSR_RWE

2 PRO endpoints

2.1 Responder analysis for ACQ-5-IA (value<= 0.75) at week 52 - ITT type 2 inflammatory asthma phenotype population

2.1.8 By baseline weight (<=30 kg, >30 kg)

	Baseline weight (kg)			
	<=30		>30	
Type 2 inflammatory asthma phenotype population	**Placebo (N=36)**	**Dupilumab (N=76)**	**Placebo (N=78)**	**Dupilumab (N=160)**
Responder status at Week 52 based on value of ACQ-5-IA <=0.75 [n(%)] [a]				
Responder	20 (55.6%)	58 (76.3%)	41 (52.6%)	122 (76.3%)
Non-responder	16 (44.4%)	18 (23.7%)	37 (47.4%)	38 (23.8%)
Odds Ratio (95% CI) vs placebo	-	2.21 (0.89 to 5.49)	-	3.45 (1.77 to 6.74)
p-value for Odds Ratio	-	0.086	-	<0.001
p-value for heterogeneity of Odds Ratio				0.573
Risk Ratio (95% CI) vs placebo	-	1.27 (0.93 to 1.72)	-	1.45 (1.16 to 1.81)
Reversed Risk ratio (95% CI) vs placebo	-	0.79 (0.58 to 1.07)	-	0.69 (0.55 to 0.86)
p-value for Risk Ratio	-	0.130	-	0.001

[a] Patients who met the corresponding criterion are considered as responders. Patients who did not meet the criterion or had missing value are considered as non-responders.
OR, RR and RD are derived from a logistic regression model with treatment, age, region, baseline eosinophil level, baseline FeNO level, baseline ICS dose level, and baseline ACQ-5-IA score as covariates.
Peto OR calculation is based on Yusuf S et al. (Prog Cardiovasc Dis. 1985 Mar-Apr;27(5):335-71) and its p-value is derived using a normal approximation.
p-values for heterogeneity are estimated by using the same logistic model as the one used to estimate OR, RR and RD, with subgroup and treatment-by-subgroup interaction as additional covariates.
p-value for heterogeneity of Peto OR is estimated by using normal approximation.
PGM=DEVOPS/SAR231893/EFC14153/CSR_RWE/REPORT/PGM/eff_pro_evt_ger_subg_i_t.sas OUT=REPORT/OUTPUT/eff_pro_acq5aw52_ger_wgt_t2_t_x.rtf (29JUN2021 - 17:43)

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

Project Code / Study Number / Analysis: SAR231893 / EFC14153 / CSR_RWE

2 PRO endpoints

2.1 Responder analysis for ACQ-5-IA (value<= 0.75) at week 52 - ITT type 2 inflammatory asthma phenotype population

2.1.8 By baseline weight (<=30 kg, >30 kg)

	Baseline weight (kg)			
	<=30		>30	
Type 2 inflammatory asthma phenotype population	**Placebo (N=36)**	**Dupilumab (N=76)**	**Placebo (N=78)**	**Dupilumab (N=160)**
p-value for heterogeneity of Risk Ratio				0.377
Risk Difference (95% CI) vs placebo	-	16.17 (-2.79 to 35.13)	-	25.48 (13.07 to 37.88)
p-value for Risk Difference	-	0.094	-	<0.001
p-value for heterogeneity of Risk Difference				0.309

[a] Patients who met the corresponding criterion are considered as responders. Patients who did not meet the criterion or had missing value are considered as non-responders.
OR, RR and RD are derived from a logistic regression model with treatment, age, region, baseline eosinophil level, baseline FeNO level, baseline ICS dose level, and baseline ACQ-5-IA score as covariates.
Peto OR calculation is based on Yusuf S et al. (Prog Cardiovasc Dis. 1985 Mar-Apr;27(5):335-71) and its p-value is derived using a normal approximation.
p-values for heterogeneity are estimated by using the same logistic model as the one used to estimate OR, RR and RD, with subgroup and treatment-by-subgroup interaction as additional covariates.
p-value for heterogeneity of Peto OR is estimated by using normal approximation.
PGM=DEVOPS/SAR231893/EFC14153/CSR_RWE/REPORT/PGM/eff_pro_evt_ger_subg_i_t.sas OUT=REPORT/OUTPUT/eff_pro_acq5aw52_ger_wgt_t2_t_x.rtf (29JUN2021 - 17:43)

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

Project Code / Study Number / Analysis: SAR231893 / EFC14153 / CSR_RWE

2 PRO endpoints

2.1 Responder analysis for ACQ-5-IA (value<= 0.75) at week 52 - ITT type 2 inflammatory asthma phenotype population

2.1.9 By atopic medical condition (Yes, No)

	Atopic medical condition			
	Yes		No	
Type 2 inflammatory asthma phenotype population	**Placebo (N=103)**	**Dupilumab (N=227)**	**Placebo (N=11)**	**Dupilumab (N=9)**
Responder status at Week 52 based on value of ACQ-5-IA <=0.75 [n(%)] [a]				
Responder	53 (51.5%)	171 (75.3%)	8 (72.7%)	9 (100%)
Non-responder	50 (48.5%)	56 (24.7%)	3 (27.3%)	0
Odds Ratio (95% CI) vs placebo	-	3.04 (1.76 to 5.24)	-	3.3702E8 (0.00 to NE)
p-value for Odds Ratio	-	<0.001	-	0.995
Peto Odds Ratio (95% CI) vs placebo	-	2.98 (1.81 to 4.90)	-	7.63 (0.69 to 84.50)
Reversed Peto Odds Ratio (95% CI)	-	0.34 (0.20 to 0.55)	-	0.13 (0.01 to 1.45)
p-value for Peto Odds Ratio		<0.001		0.098
p-value for heterogeneity of Peto Odds Ratio				0.453
Risk Ratio (95% CI) vs placebo	-	1.39 (1.15 to 1.69)	-	1.23 (NE to NE)

[a] Patients who met the corresponding criterion are considered as responders. Patients who did not meet the criterion or had missing value are considered as non-responders. OR, RR and RD are derived from a logistic regression model with treatment, age, weight group, region, baseline eosinophil level, baseline FeNO level, baseline ICS dose level, and baseline ACQ-5-IA score as covariates.
Peto OR calculation is based on Yusuf S et al. (Prog Cardiovasc Dis. 1985 Mar-Apr;27(5):335-71) and its p-value is derived using a normal approximation.
p-values for heterogeneity are estimated by using the same logistic model as the one used to estimate OR, RR and RD, with subgroup and treatment-by-subgroup interaction as additional covariates.
p-value for heterogeneity of Peto OR is estimated by using normal approximation.

PGM=DEVOPS/SAR231893/EFC14153/CSR_RWE/REPORT/PGM/eff_pro_evt_ger_subg_i_t.sas OUT=REPORT/OUTPUT/eff_pro_acq5aw52_ger_amc_t2_t_x.rtf (29JUN2021 - 17:44)

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

Project Code / Study Number / Analysis: SAR231893 / EFC14153 / CSR_RWE

2 PRO endpoints

2.1 Responder analysis for ACQ-5-IA (value<= 0.75) at week 52 - ITT type 2 inflammatory asthma phenotype population

2.1.9 By atopic medical condition (Yes, No)

	Atopic medical condition			
	Yes		No	
Type 2 inflammatory asthma phenotype population	**Placebo (N=103)**	**Dupilumab (N=227)**	**Placebo (N=11)**	**Dupilumab (N=9)**
Reversed Risk ratio (95% CI) vs placebo	-	0.72 (0.59 to 0.87)	-	0.81 (NE to NE)
p-value for Risk Ratio	-	<0.001	-	<0.001
p-value for heterogeneity of Risk Ratio				<0.001
Risk Difference (95% CI) vs placebo	-	21.93 (11.12 to 32.73)	-	31.91 (-136.47 to 200.30)
p-value for Risk Difference	-	<0.001	-	0.682
p-value for heterogeneity of Risk Difference				0.785

[a] Patients who met the corresponding criterion are considered as responders. Patients who did not meet the criterion or had missing value are considered as non-responders.
OR, RR and RD are derived from a logistic regression model with treatment, age, weight group, region, baseline eosinophil level, baseline FeNO level, baseline ICS dose level, and baseline ACQ-5-IA score as covariates.
Peto OR calculation is based on Yusuf S et al. (Prog Cardiovasc Dis. 1985 Mar-Apr;27(5):335-71) and its p-value is derived using a normal approximation.
p-values for heterogeneity are estimated by using the same logistic model as the one used to estimate OR, RR and RD, with subgroup and treatment-by-subgroup interaction as additional covariates.
p-value for heterogeneity of Peto OR is estimated by using normal approximation.
PGM=DEVOPS/SAR231893/EFC14153/CSR_RWE/REPORT/PGM/eff_pro_evt_ger_subg_i_t.sas OUT=REPORT/OUTPUT/eff_pro_acq5aw52_ger_amc_t2_t_x.rtf (29JUN2021 - 17:44)

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

Project Code / Study Number / Analysis: SAR231893 / EFC14153 / CSR_RWE

2 PRO endpoints

2.1 Responder analysis for ACQ-5-IA (value<= 0.75) at week 52 - ITT type 2 inflammatory asthma phenotype population

2.1.10 By baseline total IgE (<median, >= median)

	Baseline Total IgE (IU/mL)			
	<median		>=median	
Type 2 inflammatory asthma phenotype population	**Placebo (N=66)**	**Dupilumab (N=105)**	**Placebo (N=47)**	**Dupilumab (N=125)**
Responder status at Week 52 based on value of ACQ-5-IA <=0.75 [n(%)] [a]				
Responder	38 (57.6%)	83 (79.0%)	23 (48.9%)	94 (75.2%)
Non-responder	28 (42.4%)	22 (21.0%)	24 (51.1%)	31 (24.8%)
Odds Ratio (95% CI) vs placebo	-	2.75 (1.31 to 5.81)	-	3.42 (1.57 to 7.44)
p-value for Odds Ratio	-	0.008	-	0.002
p-value for heterogeneity of Odds Ratio				0.814
Risk Ratio (95% CI) vs placebo	-	1.31 (1.03 to 1.66)	-	1.53 (1.12 to 2.08)
Reversed Risk ratio (95% CI) vs placebo	-	0.76 (0.60 to 0.97)	-	0.65 (0.48 to 0.89)
p-value for Risk Ratio	-	0.026	-	0.007

[a] Patients who met the corresponding criterion are considered as responders. Patients who did not meet the criterion or had missing value are considered as non-responders.
OR, RR and RD are derived from a logistic regression model with treatment, age, weight group, region, baseline eosinophil level, baseline FeNO level, baseline ICS dose level, and baseline ACQ-5-IA score as covariates.
Peto OR calculation is based on Yusuf S et al. (Prog Cardiovasc Dis. 1985 Mar-Apr;27(5):335-71) and its p-value is derived using a normal approximation.
p-values for heterogeneity are estimated by using the same logistic model as the one used to estimate OR, RR and RD, with subgroup and treatment-by-subgroup interaction as additional covariates.
p-value for heterogeneity of Peto OR is estimated by using normal approximation.
PGM=DEVOPS/SAR231893/EFC14153/CSR_RWE/REPORT/PGM/eff_pro_evt_ger_subg_i_t.sas OUT=REPORT/OUTPUT/eff_pro_acq5aw52_ger_igem_t2_t_x.rtf (29JUN2021 - 17:44)

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

Project Code / Study Number / Analysis: SAR231893 / EFC14153 / CSR_RWE

2 PRO endpoints

2.1 Responder analysis for ACQ-5-IA (value<= 0.75) at week 52 - ITT type 2 inflammatory asthma phenotype population

2.1.10 By baseline total IgE (<median, >= median)

	Baseline Total IgE (IU/mL)			
	<median		>=median	
Type 2 inflammatory asthma phenotype population	**Placebo (N=66)**	**Dupilumab (N=105)**	**Placebo (N=47)**	**Dupilumab (N=125)**
p-value for heterogeneity of Risk Ratio				0.365
Risk Difference (95% CI) vs placebo	-	19.94 (5.19 to 34.68)	-	24.43 (8.76 to 40.09)
p-value for Risk Difference	-	0.008	-	0.002
p-value for heterogeneity of Risk Difference				0.577

[a] Patients who met the corresponding criterion are considered as responders. Patients who did not meet the criterion or had missing value are considered as non-responders.
OR, RR and RD are derived from a logistic regression model with treatment, age, weight group, region, baseline eosinophil level, baseline FeNO level, baseline ICS dose level, and baseline ACQ-5-IA score as covariates.
Peto OR calculation is based on Yusuf S et al. (Prog Cardiovasc Dis. 1985 Mar-Apr;27(5):335-71) and its p-value is derived using a normal approximation.
p-values for heterogeneity are estimated by using the same logistic model as the one used to estimate OR, RR and RD, with subgroup and treatment-by-subgroup interaction as additional covariates.
p-value for heterogeneity of Peto OR is estimated by using normal approximation.
PGM=DEVOPS/SAR231893/EFC14153/CSR_RWE/REPORT/PGM/eff_pro_evt_ger_subg_i_t.sas OUT=REPORT/OUTPUT/eff_pro_acq5aw52_ger_igem_t2_t_x.rtf (29JUN2021 - 17:44)

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

Project Code / Study Number / Analysis: SAR231893 / EFC14153 / CSR_RWE

2 PRO endpoints

2.1 Responder analysis for ACQ-5-IA (value<= 0.75) at week 52 - ITT type 2 inflammatory asthma phenotype population

2.1.11 By baseline total IgE (<100 IU/ml, >= 100 IU/ml)

	Baseline Total IgE (IU/mL)			
	< 100		**>= 100**	
Type 2 inflammatory asthma phenotype population	**Placebo (N=22)**	**Dupilumab (N=29)**	**Placebo (N=91)**	**Dupilumab (N=201)**
Responder status at Week 52 based on value of ACQ-5-IA <=0.75 [n(%)] [a]				
Responder	11 (50.0%)	23 (79.3%)	50 (54.9%)	154 (76.6%)
Non-responder	11 (50.0%)	6 (20.7%)	41 (45.1%)	47 (23.4%)
Odds Ratio (95% CI) vs placebo	-	3.17 (0.73 to 13.71)	-	2.84 (1.58 to 5.11)
p-value for Odds Ratio	-	0.120	-	<0.001
p-value for heterogeneity of Odds Ratio				0.774
Risk Ratio (95% CI) vs placebo	-	1.49 (0.45 to 4.91)	-	1.31 (1.09 to 1.59)
Reversed Risk ratio (95% CI) vs placebo	-	0.67 (0.20 to 2.23)	-	0.76 (0.63 to 0.92)
p-value for Risk Ratio	-	0.508	-	0.005

[a] Patients who met the corresponding criterion are considered as responders. Patients who did not meet the criterion or had missing value are considered as non-responders.
OR, RR and RD are derived from a logistic regression model with treatment, age, weight group, region, baseline eosinophil level, baseline FeNO level, baseline ICS dose level, and baseline ACQ-5-IA score as covariates.
Peto OR calculation is based on Yusuf S et al. (Prog Cardiovasc Dis. 1985 Mar-Apr;27(5):335-71) and its p-value is derived using a normal approximation.
p-values for heterogeneity are estimated by using the same logistic model as the one used to estimate OR, RR and RD, with subgroup and treatment-by-subgroup interaction as additional covariates.
p-value for heterogeneity of Peto OR is estimated by using normal approximation.
PGM=DEVOPS/SAR231893/EFC14153/CSR_RWE/REPORT/PGM/eff_pro_evt_ger_subg_i_t.sas OUT=REPORT/OUTPUT/eff_pro_acq5aw52_ger_ige_t2_t_x.rtf (29JUN2021 - 17:44)

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

Project Code / Study Number / Analysis: SAR231893 / EFC14153 / CSR_RWE

2 PRO endpoints

2.1 Responder analysis for ACQ-5-IA (value<= 0.75) at week 52 - ITT type 2 inflammatory asthma phenotype population

2.1.11 By baseline total IgE (<100 IU/ml, >= 100 IU/ml)

	Baseline Total IgE (IU/mL)			
	< 100		>= 100	
Type 2 inflammatory asthma phenotype population	**Placebo (N=22)**	**Dupilumab (N=29)**	**Placebo (N=91)**	**Dupilumab (N=201)**
p-value for heterogeneity of Risk Ratio				0.453
Risk Difference (95% CI) vs placebo	-	24.47 (-10.83 to 59.78)	-	19.11 (7.61 to 30.60)
p-value for Risk Difference	-	0.169	-	0.001
p-value for heterogeneity of Risk Difference				0.477

[a] Patients who met the corresponding criterion are considered as responders. Patients who did not meet the criterion or had missing value are considered as non-responders.
OR, RR and RD are derived from a logistic regression model with treatment, age, weight group, region, baseline eosinophil level, baseline FeNO level, baseline ICS dose level, and baseline ACQ-5-IA score as covariates.
Peto OR calculation is based on Yusuf S et al. (Prog Cardiovasc Dis. 1985 Mar-Apr;27(5):335-71) and its p-value is derived using a normal approximation.
p-values for heterogeneity are estimated by using the same logistic model as the one used to estimate OR, RR and RD, with subgroup and treatment-by-subgroup interaction as additional covariates.
p-value for heterogeneity of Peto OR is estimated by using normal approximation.
PGM=DEVOPS/SAR231893/EFC14153/CSR_RWE/REPORT/PGM/eff_pro_evt_ger_subg_i_t.sas OUT=REPORT/OUTPUT/eff_pro_acq5aw52_ger_ige_t2_t_x.rtf (29JUN2021 - 17:44)

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

Project Code / Study Number / Analysis: SAR231893 / EFC14153 / CSR_RWE

2 PRO endpoints

2.1 Responder analysis for ACQ-5-IA (value<= 0.75) at week 52 - ITT type 2 inflammatory asthma phenotype population

2.1.12 By age at onset of asthma (0-2, 3-5, >=6 years)

	Age of onset of asthma (years)					
	0-2		3-5		>= 6	
Type 2 inflammatory asthma phenotype population	**Placebo (N=40)**	**Dupilumab (N=105)**	**Placebo (N=39)**	**Dupilumab (N=86)**	**Placebo (N=35)**	**Dupilumab (N=45)**
Responder status at Week 52 based on value of ACQ-5-IA <=0.75 [n(%)] [a]						
Responder	21 (52.5%)	80 (76.2%)	22 (56.4%)	64 (74.4%)	18 (51.4%)	36 (80.0%)
Non-responder	19 (47.5%)	25 (23.8%)	17 (43.6%)	22 (25.6%)	17 (48.6%)	9 (20.0%)
Odds Ratio (95% CI) vs placebo	-	2.78 (1.17 to 6.61)	-	2.42 (0.93 to 6.27)	-	4.46 (1.40 to 14.23)
p-value for Odds Ratio	-	0.021	-	0.070	-	0.012
p-value for heterogeneity of Odds Ratio:						
0-2, 3-5						0.614
0-2, >= 6						0.540
3-5, >= 6						0.296
overall						0.578

[a] Patients who met the corresponding criterion are considered as responders. Patients who did not meet the criterion or had missing value are considered as non-responders. OR, RR and RD are derived from a logistic regression model with treatment, age, weight group, region, baseline eosinophil level, baseline FeNO level, baseline ICS dose level, and baseline ACQ-5-IA score as covariates.
Peto OR calculation is based on Yusuf S et al. (Prog Cardiovasc Dis. 1985 Mar-Apr;27(5):335-71) and its p-value is derived using a normal approximation.
p-values for heterogeneity are estimated by using the same logistic model as the one used to estimate OR, RR and RD, with subgroup and treatment-by-subgroup interaction as additional covariates.
p-value for heterogeneity of Peto OR is estimated by using normal approximation.

PGM=DEVOPS/SAR231893/EFC14153/CSR_RWE/REPORT/PGM/eff_pro_evt_ger_subg_i_t.sas OUT=REPORT/OUTPUT/eff_pro_acq5aw52_ger_onsa_t2_t_x.rtf (01SEP2021 - 15:26)

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

Project Code / Study Number / Analysis: SAR231893 / EFC14153 / CSR_RWE

2 PRO endpoints

2.1 Responder analysis for ACQ-5-IA (value<= 0.75) at week 52 - ITT type 2 inflammatory asthma phenotype population

2.1.12 By age at onset of asthma (0-2, 3-5, >=6 years)

	Age of onset of asthma (years)					
	0-2		3-5		>= 6	
Type 2 inflammatory asthma phenotype population	**Placebo (N=40)**	**Dupilumab (N=105)**	**Placebo (N=39)**	**Dupilumab (N=86)**	**Placebo (N=35)**	**Dupilumab (N=45)**
Risk Ratio (95% CI) vs placebo	-	1.44 (0.98 to 2.11)	-	1.21 (0.83 to 1.78)	-	1.57 (0.88 to 2.79)
Reversed Risk ratio (95% CI) vs placebo	-	0.69 (0.47 to 1.02)	-	0.82 (0.56 to 1.21)	-	0.64 (0.36 to 1.14)
p-value for Risk Ratio	-	0.060	-	0.316	-	0.125
p-value for heterogeneity of Risk Ratio:						
0-2, 3-5						0.580
0-2, >= 6						0.602
3-5, >= 6						0.278
overall						0.553
Risk Difference (95% CI) vs placebo	-	20.95 (3.63 to 38.27)	-	14.05 (-6.47 to 34.57)	-	30.12 (5.84 to 54.40)
p-value for Risk Difference	-	0.018	-	0.178	-	0.016
p-value for heterogeneity of Risk Difference:						

[a] Patients who met the corresponding criterion are considered as responders. Patients who did not meet the criterion or had missing value are considered as non-responders.
OR, RR and RD are derived from a logistic regression model with treatment, age, weight group, region, baseline eosinophil level, baseline FeNO level, baseline ICS dose level, and baseline ACQ-5-IA score as covariates.
Peto OR calculation is based on Yusuf S et al. (Prog Cardiovasc Dis. 1985 Mar-Apr;27(5):335-71) and its p-value is derived using a normal approximation.
p-values for heterogeneity are estimated by using the same logistic model as the one used to estimate OR, RR and RD, with subgroup and treatment-by-subgroup interaction as additional covariates.
p-value for heterogeneity of Peto OR is estimated by using normal approximation.
PGM=DEVOPS/SAR231893/EFC14153/CSR_RWE/REPORT/PGM/eff_pro_evt_ger_subg_i_t.sas OUT=REPORT/OUTPUT/eff_pro_acq5aw52_ger_onsa_t2_t_x.rtf (01SEP2021 - 15:26)

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

Project Code / Study Number / Analysis: SAR231893 / EFC14153 / CSR_RWE

2 PRO endpoints

2.1 Responder analysis for ACQ-5-IA (value<= 0.75) at week 52 - ITT type 2 inflammatory asthma phenotype population

2.1.12 By age at onset of asthma (0-2, 3-5, >=6 years)

	Age of onset of asthma (years)					
	0-2		3-5		>= 6	
Type 2 inflammatory asthma phenotype population	**Placebo (N=40)**	**Dupilumab (N=105)**	**Placebo (N=39)**	**Dupilumab (N=86)**	**Placebo (N=35)**	**Dupilumab (N=45)**
0-2, 3-5						0.693
0-2, >= 6						0.445
3-5, >= 6						0.268
overall						0.532

[a] Patients who met the corresponding criterion are considered as responders. Patients who did not meet the criterion or had missing value are considered as non-responders.
OR, RR and RD are derived from a logistic regression model with treatment, age, weight group, region, baseline eosinophil level, baseline FeNO level, baseline ICS dose level, and baseline ACQ-5-IA score as covariates.
Peto OR calculation is based on Yusuf S et al. (Prog Cardiovasc Dis. 1985 Mar-Apr;27(5):335-71) and its p-value is derived using a normal approximation.
p-values for heterogeneity are estimated by using the same logistic model as the one used to estimate OR, RR and RD, with subgroup and treatment-by-subgroup interaction as additional covariates.
p-value for heterogeneity of Peto OR is estimated by using normal approximation.
PGM=DEVOPS/SAR231893/EFC14153/CSR_RWE/REPORT/PGM/eff_pro_evt_ger_subg_i_t.sas OUT=REPORT/OUTPUT/eff_pro_acq5aw52_ger_onsa_t2_t_x.rtf (01SEP2021 - 15:26)

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

Project Code / Study Number / Analysis: SAR231893 / EFC14153 / CSR_RWE

2 PRO endpoints

2.1 Responder analysis for ACQ-5-IA (value<= 0.75) at week 52 - ITT type 2 inflammatory asthma phenotype population

2.1.13 By number of severe asthma exacerbation prior to the study (<=1, 2, >2)

	Number of severe asthma exacerbation prior to the study					
	<=1		2		>2	
Type 2 inflammatory asthma phenotype population	**Placebo (N=47)**	**Dupilumab (N=85)**	**Placebo (N=32)**	**Dupilumab (N=75)**	**Placebo (N=35)**	**Dupilumab (N=76)**
Responder status at Week 52 based on value of ACQ-5-IA <=0.75 [n(%)] [a]						
Responder	28 (59.6%)	63 (74.1%)	19 (59.4%)	61 (81.3%)	14 (40.0%)	56 (73.7%)
Non-responder	19 (40.4%)	22 (25.9%)	13 (40.6%)	14 (18.7%)	21 (60.0%)	20 (26.3%)
Odds Ratio (95% CI) vs placebo	-	2.85 (1.16 to 7.01)	-	3.29 (1.09 to 9.96)	-	3.62 (1.40 to 9.40)
p-value for Odds Ratio	-	0.023	-	0.035	-	0.009
p-value for heterogeneity of Odds Ratio:						
<=1, 2						0.668
<=1, >2						0.607
2, >2						0.954
overall						0.852

[a] Patients who met the corresponding criterion are considered as responders. Patients who did not meet the criterion or had missing value are considered as non-responders. OR, RR and RD are derived from a logistic regression model with treatment, age, weight group, region, baseline eosinophil level, baseline FeNO level, baseline ICS dose level, and baseline ACQ-5-IA score as covariates.
Peto OR calculation is based on Yusuf S et al. (Prog Cardiovasc Dis. 1985 Mar-Apr;27(5):335-71) and its p-value is derived using a normal approximation.
p-values for heterogeneity are estimated by using the same logistic model as the one used to estimate OR, RR and RD, with subgroup and treatment-by-subgroup interaction as additional covariates.
p-value for heterogeneity of Peto OR is estimated by using normal approximation.
PGM=DEVOPS/SAR231893/EFC14153/CSR_RWE/REPORT/PGM/eff_pro_evt_ger_subg_i_t.sas OUT=REPORT/OUTPUT/eff_pro_acq5aw52_ger_exa_t2_t_x.rtf (29JUN2021 - 17:45)

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

Project Code / Study Number / Analysis: SAR231893 / EFC14153 / CSR_RWE

2 PRO endpoints

2.1 Responder analysis for ACQ-5-IA (value<= 0.75) at week 52 - ITT type 2 inflammatory asthma phenotype population

2.1.13 By number of severe asthma exacerbation prior to the study (<=1, 2, >2)

	Number of severe asthma exacerbation prior to the study					
	<=1		**2**		**>2**	
Type 2 inflammatory asthma phenotype population	**Placebo (N=47)**	**Dupilumab (N=85)**	**Placebo (N=32)**	**Dupilumab (N=75)**	**Placebo (N=35)**	**Dupilumab (N=76)**
Risk Ratio (95% CI) vs placebo	-	1.19 (0.89 to 1.60)	-	1.47 (0.64 to 3.36)	-	1.61 (1.05 to 2.46)
Reversed Risk ratio (95% CI) vs placebo	-	0.84 (0.63 to 1.12)	-	0.68 (0.30 to 1.56)	-	0.62 (0.41 to 0.95)
p-value for Risk Ratio	-	0.227	-	0.360	-	0.029
p-value for heterogeneity of Risk Ratio:						
<=1, 2						0.277
<=1, >2						0.412
2, >2						0.840
overall						0.473
Risk Difference (95% CI) vs placebo	-	15.18 (-2.70 to 33.07)	-	26.29 (-0.67 to 53.25)	-	27.99 (8.06 to 47.92)
p-value for Risk Difference	-	0.095	-	0.056	-	0.006

[a] Patients who met the corresponding criterion are considered as responders. Patients who did not meet the criterion or had missing value are considered as non-responders.
OR, RR and RD are derived from a logistic regression model with treatment, age, weight group, region, baseline eosinophil level, baseline FeNO level, baseline ICS dose level, and baseline ACQ-5-IA score as covariates.
Peto OR calculation is based on Yusuf S et al. (Prog Cardiovasc Dis. 1985 Mar-Apr;27(5):335-71) and its p-value is derived using a normal approximation.
p-values for heterogeneity are estimated by using the same logistic model as the one used to estimate OR, RR and RD, with subgroup and treatment-by-subgroup interaction as additional covariates.
p-value for heterogeneity of Peto OR is estimated by using normal approximation.
PGM=DEVOPS/SAR231893/EFC14153/CSR_RWE/REPORT/PGM/eff_pro_evt_ger_subg_i_t.sas OUT=REPORT/OUTPUT/eff_pro_acq5aw52_ger_exa_t2_t_x.rtf (29JUN2021 - 17:45)

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

Project Code / Study Number / Analysis: SAR231893 / EFC14153 / CSR_RWE

2 PRO endpoints

2.1 Responder analysis for ACQ-5-IA (value<= 0.75) at week 52 - ITT type 2 inflammatory asthma phenotype population

2.1.13 By number of severe asthma exacerbation prior to the study (<=1, 2, >2)

	Number of severe asthma exacerbation prior to the study					
	<=1		2		>2	
Type 2 inflammatory asthma phenotype population	**Placebo (N=47)**	**Dupilumab (N=85)**	**Placebo (N=32)**	**Dupilumab (N=75)**	**Placebo (N=35)**	**Dupilumab (N=76)**
p-value for heterogeneity of Risk Difference:						
<=1, 2						0.262
<=1, >2						0.315
2, >2						0.881
overall						0.438

[a] Patients who met the corresponding criterion are considered as responders. Patients who did not meet the criterion or had missing value are considered as non-responders.
OR, RR and RD are derived from a logistic regression model with treatment, age, weight group, region, baseline eosinophil level, baseline FeNO level, baseline ICS dose level, and baseline ACQ-5-IA score as covariates.
Peto OR calculation is based on Yusuf S et al. (Prog Cardiovasc Dis. 1985 Mar-Apr;27(5):335-71) and its p-value is derived using a normal approximation.
p-values for heterogeneity are estimated by using the same logistic model as the one used to estimate OR, RR and RD, with subgroup and treatment-by-subgroup interaction as additional covariates.
p-value for heterogeneity of Peto OR is estimated by using normal approximation.
PGM=DEVOPS/SAR231893/EFC14153/CSR_RWE/REPORT/PGM/eff_pro_evt_ger_subg_i_t.sas OUT=REPORT/OUTPUT/eff_pro_acq5aw52_ger_exa_t2_t_x.rtf (29JUN2021 - 17:45)

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

Project Code / Study Number / Analysis: SAR231893 / EFC14153 / CSR_RWE

2 PRO endpoints

2.2 Responder analysis for change from baseline in ACQ-5-IA (improvement >= 0.9) at week 52 - ITT type 2 inflammatory asthma phenotype population

Type 2 inflammatory asthma phenotype population	**Placebo (N=114)**	**Dupilumab (N=236)**
Responder status at Week 52 based on change from baseline in ACQ-5-IA <=-0.9 [n(%)] [a]		
Responder	79 (69.3%)	185 (78.4%)
Non-responder	35 (30.7%)	51 (21.6%)
Odds Ratio (95% CI)	-	1.76 (0.95 to 3.24)
p-value for Odds Ratio		0.070
Risk Ratio (95% CI)	-	1.11 (0.94 to 1.31)
Reversed Risk ratio (95% CI)	-	0.90 (0.76 to 1.07)
p-value for Risk Ratio		0.223
Risk Difference (95% CI)	-	7.73 (-2.92 to 18.38)
p-value for Risk Difference		0.154

[a] Patients who met the corresponding criterion are considered as responders. Patients who did not meet the criterion or had missing value are considered as non-responders. OR, RR and RD are derived from a logistic regression model with treatment, age, weight group, region, baseline eosinophil level, baseline FeNO level, baseline ICS dose level, and baseline ACQ-5-IA score as covariates.
Peto OR calculation is based on Yusuf S et al. (Prog Cardiovasc Dis. 1985 Mar-Apr;27(5):335-71) and its p-value is derived using a normal approximation.
PGM=DEVOPS/SAR231893/EFC14153/CSR_RWE/REPORT/PGM/eff_pro_evt_ger_i_t.sas OUT=REPORT/OUTPUT/eff_pro_acq5bw52_ger_t2_t_x.rtf (30JUN2021 - 8:13)

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

Project Code / Study Number / Analysis: SAR231893 / EFC14153 / CSR_RWE

2 PRO endpoints

2.2 Responder analysis for change from baseline in ACQ-5-IA (improvement >= 0.9) at week 52 - ITT type 2 inflammatory asthma phenotype population

2.2.1 By gender (Male, Female)

	Gender			
	Male		Female	
Type 2 inflammatory asthma phenotype population	**Placebo (N=78)**	**Dupilumab (N=152)**	**Placebo (N=36)**	**Dupilumab (N=84)**
Responder status at Week 52 based on change from baseline in ACQ-5-IA <=-0.9 [n(%)] [a]				
Responder	53 (67.9%)	123 (80.9%)	26 (72.2%)	62 (73.8%)
Non-responder	25 (32.1%)	29 (19.1%)	10 (27.8%)	22 (26.2%)
Odds Ratio (95% CI) vs placebo	-	2.31 (1.04 to 5.12)	-	1.34 (0.46 to 3.90)
p-value for Odds Ratio	-	0.039	-	0.584
p-value for heterogeneity of Odds Ratio				0.502
Risk Ratio (95% CI) vs placebo	-	1.13 (0.90 to 1.42)	-	0.97 (0.68 to 1.37)
Reversed Risk ratio (95% CI) vs placebo	-	0.88 (0.70 to 1.11)		

[a] Patients who met the corresponding criterion are considered as responders. Patients who did not meet the criterion or had missing value are considered as non-responders.
OR, RR and RD are derived from a logistic regression model with treatment, age, weight group, region, baseline eosinophil level, baseline FeNO level, baseline ICS dose level, and baseline ACQ-5-IA score as covariates.
Peto OR calculation is based on Yusuf S et al. (Prog Cardiovasc Dis. 1985 Mar-Apr;27(5):335-71) and its p-value is derived using a normal approximation.
p-values for heterogeneity are estimated by using the same logistic model as the one used to estimate OR, RR and RD, with subgroup and treatment-by-subgroup interaction as additional covariates.
p-value for heterogeneity of Peto OR is estimated by using normal approximation.
PGM=DEVOPS/SAR231893/EFC14153/CSR_RWE/REPORT/PGM/eff_pro_evt_ger_subg_i_t.sas OUT=REPORT/OUTPUT/eff_pro_acq5bw52_ger_sex_t2_t_x.rtf (29JUN2021 - 17:41)

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

Project Code / Study Number / Analysis: SAR231893 / EFC14153 / CSR_RWE

2 PRO endpoints

2.2 Responder analysis for change from baseline in ACQ-5-IA (improvement >= 0.9) at week 52 - ITT type 2 inflammatory asthma phenotype population

2.2.1 By gender (Male, Female)

	Gender			
	Male		Female	
Type 2 inflammatory asthma phenotype population	**Placebo (N=78)**	**Dupilumab (N=152)**	**Placebo (N=36)**	**Dupilumab (N=84)**
p-value for Risk Ratio	-	0.289	-	0.860
p-value for heterogeneity of Risk Ratio				0.633
Risk Difference (95% CI) vs placebo	-	9.69 (-4.52 to 23.90)	-	-0.22 (-21.02 to 20.58)
p-value for Risk Difference	-	0.180	-	0.983
p-value for heterogeneity of Risk Difference				0.778

[a] Patients who met the corresponding criterion are considered as responders. Patients who did not meet the criterion or had missing value are considered as non-responders.
OR, RR and RD are derived from a logistic regression model with treatment, age, weight group, region, baseline eosinophil level, baseline FeNO level, baseline ICS dose level, and baseline ACQ-5-IA score as covariates.
Peto OR calculation is based on Yusuf S et al. (Prog Cardiovasc Dis. 1985 Mar-Apr;27(5):335-71) and its p-value is derived using a normal approximation.
p-values for heterogeneity are estimated by using the same logistic model as the one used to estimate OR, RR and RD, with subgroup and treatment-by-subgroup interaction as additional covariates.
p-value for heterogeneity of Peto OR is estimated by using normal approximation.
PGM=DEVOPS/SAR231893/EFC14153/CSR_RWE/REPORT/PGM/eff_pro_evt_ger_subg_i_t.sas OUT=REPORT/OUTPUT/eff_pro_acq5bw52_ger_sex_t2_t_x.rtf (29JUN2021 - 17:41)

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

Project Code / Study Number / Analysis: SAR231893 / EFC14153 / CSR_RWE

2 PRO endpoints

2.2 Responder analysis for change from baseline in ACQ-5-IA (improvement >= 0.9) at week 52 - ITT type 2 inflammatory asthma phenotype population

2.2.2 By region (Latin America, East Europe, Western Countries)

	Region					
	Latin America		East Europe		Western countries	
Type 2 inflammatory asthma phenotype population	**Placebo (N=51)**	**Dupilumab (N=106)**	**Placebo (N=43)**	**Dupilumab (N=78)**	**Placebo (N=20)**	**Dupilumab (N=52)**
Responder status at Week 52 based on change from baseline in ACQ-5-IA <=-0.9 [n(%)] [a]						
Responder	44 (86.3%)	93 (87.7%)	27 (62.8%)	62 (79.5%)	8 (40.0%)	30 (57.7%)
Non-responder	7 (13.7%)	13 (12.3%)	16 (37.2%)	16 (20.5%)	12 (60.0%)	22 (42.3%)
Odds Ratio (95% CI) vs placebo	-	1.45 (0.43 to 4.81)	-	2.11 (0.84 to 5.28)	-	3.47 (0.77 to 15.69)
p-value for Odds Ratio	-	0.545	-	0.110	-	0.105
p-value for heterogeneity of Odds Ratio:						
Latin America, East Europe						0.413
Latin America, Western countries						0.333

[a] Patients who met the corresponding criterion are considered as responders. Patients who did not meet the criterion or had missing value are considered as non-responders. OR, RR and RD are derived from a logistic regression model with treatment, age, weight group, baseline eosinophil level, baseline FeNO level, baseline ICS dose level, and baseline ACQ-5-IA score as covariates.
Peto OR calculation is based on Yusuf S et al. (Prog Cardiovasc Dis. 1985 Mar-Apr;27(5):335-71) and its p-value is derived using a normal approximation.
p-values for heterogeneity are estimated by using the same logistic model as the one used to estimate OR, RR and RD, with subgroup and treatment-by-subgroup interaction as additional covariates.
p-value for heterogeneity of Peto OR is estimated by using normal approximation.
PGM=DEVOPS/SAR231893/EFC14153/CSR_RWE/REPORT/PGM/eff_pro_evt_ger_subg_i_t.sas OUT=REPORT/OUTPUT/eff_pro_acq5bw52_ger_cty_t2_t_x.rtf (29JUN2021 - 17:42)

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

Project Code / Study Number / Analysis: SAR231893 / EFC14153 / CSR_RWE

2 PRO endpoints

2.2 population Responder analysis for change from baseline in ACQ-5-IA (improvement >= 0.9) at week 52 - ITT type 2 inflammatory asthma phenotype

2.2.2 By region (Latin America, East Europe, Western Countries)

	Region					
	Latin America		East Europe		Western countries	
Type 2 inflammatory asthma phenotype population	**Placebo (N=51)**	**Dupilumab (N=106)**	**Placebo (N=43)**	**Dupilumab (N=78)**	**Placebo (N=20)**	**Dupilumab (N=52)**
East Europe, Western countries						0.742
overall						0.578
Risk Ratio (95% CI) vs placebo	-	1.07 (0.82 to 1.41)	-	1.27 (0.94 to 1.72)	-	1.33 (0.63 to 2.81)
Reversed Risk ratio (95% CI) vs placebo	-	0.93 (0.71 to 1.22)	-	0.79 (0.58 to 1.07)	-	0.75 (0.36 to 1.58)
p-value for Risk Ratio	-	0.600	-	0.121	-	0.442
p-value for heterogeneity of Risk Ratio:						
Latin America, East Europe						0.400
Latin America, Western countries						0.346
East Europe, Western countries						0.599
overall						0.516

[a] Patients who met the corresponding criterion are considered as responders. Patients who did not meet the criterion or had missing value are considered as non-responders.
OR, RR and RD are derived from a logistic regression model with treatment, age, weight group, baseline eosinophil level, baseline FeNO level, baseline ICS dose level, and baseline ACQ-5-IA score as covariates.
Peto OR calculation is based on Yusuf S et al. (Prog Cardiovasc Dis. 1985 Mar-Apr;27(5):335-71) and its p-value is derived using a normal approximation.
p-values for heterogeneity are estimated by using the same logistic model as the one used to estimate OR, RR and RD, with subgroup and treatment-by-subgroup interaction as additional covariates.
p-value for heterogeneity of Peto OR is estimated by using normal approximation.
PGM=DEVOPS/SAR231893/EFC14153/CSR_RWE/REPORT/PGM/eff_pro_evt_ger_subg_i_t.sas OUT=REPORT/OUTPUT/eff_pro_acq5bw52_ger_cty_t2_t_x.rtf (29JUN2021 - 17:42)

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

Project Code / Study Number / Analysis: SAR231893 / EFC14153 / CSR_RWE

2 PRO endpoints

2.2 population Responder analysis for change from baseline in ACQ-5-IA (improvement >= 0.9) at week 52 - ITT type 2 inflammatory asthma phenotype

2.2.2 By region (Latin America, East Europe, Western Countries)

	Region					
	Latin America		East Europe		Western countries	
Type 2 inflammatory asthma phenotype population	**Placebo (N=51)**	**Dupilumab (N=106)**	**Placebo (N=43)**	**Dupilumab (N=78)**	**Placebo (N=20)**	**Dupilumab (N=52)**
Risk Difference (95% CI) vs placebo	-	5.51 (-12.37 to 23.40)	-	17.45 (-0.44 to 35.34)	-	23.91 (-13.97 to 61.79)
p-value for Risk Difference	-	0.543	-	0.056	-	0.212
p-value for heterogeneity of Risk Difference:						
Latin America, East Europe						0.243
Latin America, Western countries						0.257
East Europe, Western countries						0.753
overall						0.365

[a] Patients who met the corresponding criterion are considered as responders. Patients who did not meet the criterion or had missing value are considered as non-responders.
OR, RR and RD are derived from a logistic regression model with treatment, age, weight group, baseline eosinophil level, baseline FeNO level, baseline ICS dose level, and baseline ACQ-5-IA score as covariates.
Peto OR calculation is based on Yusuf S et al. (Prog Cardiovasc Dis. 1985 Mar-Apr;27(5):335-71) and its p-value is derived using a normal approximation.
p-values for heterogeneity are estimated by using the same logistic model as the one used to estimate OR, RR and RD, with subgroup and treatment-by-subgroup interaction as additional covariates.
p-value for heterogeneity of Peto OR is estimated by using normal approximation.
PGM=DEVOPS/SAR231893/EFC14153/CSR_RWE/REPORT/PGM/eff_pro_evt_ger_subg_i_t.sas OUT=REPORT/OUTPUT/eff_pro_acq5bw52_ger_cty_t2_t_x.rtf (29JUN2021 - 17:42)

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

Project Code / Study Number / Analysis: SAR231893 / EFC14153 / CSR_RWE

2 PRO endpoints

2.2 Responder analysis for change from baseline in ACQ-5-IA (improvement >= 0.9) at week 52 - ITT type 2 inflammatory asthma phenotype population

2.2.3 By race (Caucasian/white, Black/of African descent, Other)

	Race					
	Caucasian/White		Black/of African descent		Other	
Type 2 inflammatory asthma phenotype population	**Placebo (N=102)**	**Dupilumab (N=208)**	**Placebo (N=5)**	**Dupilumab (N=9)**	**Placebo (N=7)**	**Dupilumab (N=19)**
Responder status at Week 52 based on change from baseline in ACQ-5-IA <=-0.9 [n(%)] [a]						
Responder	76 (74.5%)	170 (81.7%)	0	4 (44.4%)	3 (42.9%)	11 (57.9%)
Non-responder	26 (25.5%)	38 (18.3%)	5 (100%)	5 (55.6%)	4 (57.1%)	8 (42.1%)
Odds Ratio (95% CI) vs placebo	-	1.45 (0.75 to 2.83)	-	19.44 (0.00 to NE)	-	6.484E37 (0.00 to NE)
p-value for Odds Ratio	-	0.271	-	0.996	-	0.790
Peto Odds Ratio (95% CI) vs placebo	-	1.55 (0.86 to 2.78)	-	7.56 (0.73 to 77.80)	-	1.79 (0.33 to 9.84)
Reversed Peto Odds Ratio (95% CI)	-	0.65 (0.36 to 1.16)	-	0.13 (0.01 to 1.37)	-	0.56 (0.10 to 3.03)
p-value for Peto Odds Ratio		0.141		0.089		0.504

[a] Patients who met the corresponding criterion are considered as responders. Patients who did not meet the criterion or had missing value are considered as non-responders.
OR, RR and RD are derived from a logistic regression model with treatment, age, weight group, region, baseline eosinophil level, baseline FeNO level, baseline ICS dose level, and baseline ACQ-5-IA score as covariates.
Peto OR calculation is based on Yusuf S et al. (Prog Cardiovasc Dis. 1985 Mar-Apr;27(5):335-71) and its p-value is derived using a normal approximation.
p-values for heterogeneity are estimated by using the same logistic model as the one used to estimate OR, RR and RD, with subgroup and treatment-by-subgroup interaction as additional covariates.
p-value for heterogeneity of Peto OR is estimated by using normal approximation.
PGM=DEVOPS/SAR231893/EFC14153/CSR_RWE/REPORT/PGM/eff_pro_evt_ger_subg_i_t.sas OUT=REPORT/OUTPUT/eff_pro_acq5bw52_ger_race_t2_t_x.rtf (29JUN2021 - 17:42)

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

Project Code / Study Number / Analysis: SAR231893 / EFC14153 / CSR_RWE

2 PRO endpoints

2.2 Responder analysis for change from baseline in ACQ-5-IA (improvement >= 0.9) at week 52 - ITT type 2 inflammatory asthma phenotype population

2.2.3 By race (Caucasian/white, Black/of African descent, Other)

	Race					
	Caucasian/White		Black/of African descent		Other	
Type 2 inflammatory asthma phenotype population	**Placebo (N=102)**	**Dupilumab (N=208)**	**Placebo (N=5)**	**Dupilumab (N=9)**	**Placebo (N=7)**	**Dupilumab (N=19)**
p-value for heterogeneity of Peto Odds Ratio:						
Caucasian/White, Black/of African descent						0.197
Caucasian/White, Other						0.877
Black/of African descent, Other						0.328
overall						0.434
Risk Ratio (95% CI) vs placebo	-	1.06 (0.89 to 1.25)	-	2.39 (0.00 to 8.44E134)	-	1.63 (0.13 to 20.69)
Reversed Risk ratio (95% CI) vs placebo	-	0.95 (0.80 to 1.12)	-	0.42 (0.00 to 1.47E134)	-	0.61 (0.05 to 7.78)
p-value for Risk Ratio	-	0.525	-	0.994	-	0.688

[a] Patients who met the corresponding criterion are considered as responders. Patients who did not meet the criterion or had missing value are considered as non-responders. OR, RR and RD are derived from a logistic regression model with treatment, age, weight group, region, baseline eosinophil level, baseline FeNO level, baseline ICS dose level, and baseline ACQ-5-IA score as covariates.
Peto OR calculation is based on Yusuf S et al. (Prog Cardiovasc Dis. 1985 Mar-Apr;27(5):335-71) and its p-value is derived using a normal approximation.
p-values for heterogeneity are estimated by using the same logistic model as the one used to estimate OR, RR and RD, with subgroup and treatment-by-subgroup interaction as additional covariates.
p-value for heterogeneity of Peto OR is estimated by using normal approximation.
PGM=DEVOPS/SAR231893/EFC14153/CSR_RWE/REPORT/PGM/eff_pro_evt_ger_subg_i_t.sas OUT=REPORT/OUTPUT/eff_pro_acq5bw52_ger_race_t2_t_x.rtf (29JUN2021 - 17:42)

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

Project Code / Study Number / Analysis: SAR231893 / EFC14153 / CSR_RWE

2 PRO endpoints

2.2 Responder analysis for change from baseline in ACQ-5-IA (improvement >= 0.9) at week 52 - ITT type 2 inflammatory asthma phenotype population

2.2.3 By race (Caucasian/white, Black/of African descent, Other)

	Race					
	Caucasian/White		Black/of African descent		Other	
Type 2 inflammatory asthma phenotype population	**Placebo (N=102)**	**Dupilumab (N=208)**	**Placebo (N=5)**	**Dupilumab (N=9)**	**Placebo (N=7)**	**Dupilumab (N=19)**
p-value for heterogeneity of Risk Ratio:						
Caucasian/White, Black/of African descent						0.757
Caucasian/White, Other						0.598
Black/of African descent, Other						0.764
overall						0.829
Risk Difference (95% CI) vs placebo	-	4.19 (-7.12 to 15.51)	-	28.63 (-363.19 to 420.46)	-	43.03 (-35.66 to 121.72)
p-value for Risk Difference	-	0.466	-	0.849	-	0.263
p-value for heterogeneity of Risk Difference:						

[a] Patients who met the corresponding criterion are considered as responders. Patients who did not meet the criterion or had missing value are considered as non-responders.
OR, RR and RD are derived from a logistic regression model with treatment, age, weight group, region, baseline eosinophil level, baseline FeNO level, baseline ICS dose level, and baseline ACQ-5-IA score as covariates.
Peto OR calculation is based on Yusuf S et al. (Prog Cardiovasc Dis. 1985 Mar-Apr;27(5):335-71) and its p-value is derived using a normal approximation.
p-values for heterogeneity are estimated by using the same logistic model as the one used to estimate OR, RR and RD, with subgroup and treatment-by-subgroup interaction as additional covariates.
p-value for heterogeneity of Peto OR is estimated by using normal approximation.
PGM=DEVOPS/SAR231893/EFC14153/CSR_RWE/REPORT/PGM/eff_pro_evt_ger_subg_i_t.sas OUT=REPORT/OUTPUT/eff_pro_acq5bw52_ger_race_t2_t_x.rtf (29JUN2021 - 17:42)

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

Project Code / Study Number / Analysis: SAR231893 / EFC14153 / CSR_RWE

2 PRO endpoints

2.2 Responder analysis for change from baseline in ACQ-5-IA (improvement >= 0.9) at week 52 - ITT type 2 inflammatory asthma phenotype population

2.2.3 By race (Caucasian/white, Black/of African descent, Other)

	Race					
	Caucasian/White		Black/of African descent		Other	
Type 2 inflammatory asthma phenotype population	**Placebo (N=102)**	**Dupilumab (N=208)**	**Placebo (N=5)**	**Dupilumab (N=9)**	**Placebo (N=7)**	**Dupilumab (N=19)**
Caucasian/White, Black/of African descent						0.541
Caucasian/White, Other						0.503
Black/of African descent, Other						0.724
overall						0.668

[a] Patients who met the corresponding criterion are considered as responders. Patients who did not meet the criterion or had missing value are considered as non-responders.
OR, RR and RD are derived from a logistic regression model with treatment, age, weight group, region, baseline eosinophil level, baseline FeNO level, baseline ICS dose level, and baseline ACQ-5-IA score as covariates.
Peto OR calculation is based on Yusuf S et al. (Prog Cardiovasc Dis. 1985 Mar-Apr;27(5):335-71) and its p-value is derived using a normal approximation.
p-values for heterogeneity are estimated by using the same logistic model as the one used to estimate OR, RR and RD, with subgroup and treatment-by-subgroup interaction as additional covariates.
p-value for heterogeneity of Peto OR is estimated by using normal approximation.
PGM=DEVOPS/SAR231893/EFC14153/CSR_RWE/REPORT/PGM/eff_pro_evt_ger_subg_i_t.sas OUT=REPORT/OUTPUT/eff_pro_acq5bw52_ger_race_t2_t_x.rtf (29JUN2021 - 17:42)

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

Project Code / Study Number / Analysis: SAR231893 / EFC14153 / CSR_RWE

2 PRO endpoints

2.2 population Responder analysis for change from baseline in ACQ-5-IA (improvement >= 0.9) at week 52 - ITT type 2 inflammatory asthma phenotype

2.2.4 By baseline ICS dose level (Medium, High)

	Baseline ICS dose level			
	High		Medium	
Type 2 inflammatory asthma phenotype population	**Placebo (N=50)**	**Dupilumab (N=102)**	**Placebo (N=64)**	**Dupilumab (N=131)**
Responder status at Week 52 based on change from baseline in ACQ-5-IA <=-0.9 [n(%)] [a]				
Responder	32 (64.0%)	76 (74.5%)	47 (73.4%)	108 (82.4%)
Non-responder	18 (36.0%)	26 (25.5%)	17 (26.6%)	23 (17.6%)
Odds Ratio (95% CI) vs placebo	-	1.68 (0.66 to 4.27)	-	2.37 (1.00 to 5.61)
p-value for Odds Ratio	-	0.272	-	0.049
p-value for heterogeneity of Odds Ratio				0.609
Risk Ratio (95% CI) vs placebo	-	1.09 (0.79 to 1.50)	-	1.12 (0.91 to 1.38)
Reversed Risk ratio (95% CI) vs placebo	-	0.92 (0.67 to 1.27)	-	0.89 (0.72 to 1.10)

[a] Patients who met the corresponding criterion are considered as responders. Patients who did not meet the criterion or had missing value are considered as non-responders.
OR, RR and RD are derived from a logistic regression model with treatment, age, weight group, region, baseline eosinophil level, baseline FeNO level and baseline ACQ-5-IA score as covariates.
Peto OR calculation is based on Yusuf S et al. (Prog Cardiovasc Dis. 1985 Mar-Apr;27(5):335-71) and its p-value is derived using a normal approximation.
p-values for heterogeneity are estimated by using the same logistic model as the one used to estimate OR, RR and RD, with subgroup and treatment-by-subgroup interaction as additional covariates.
p-value for heterogeneity of Peto OR is estimated by using normal approximation.
PGM=DEVOPS/SAR231893/EFC14153/CSR_RWE/REPORT/PGM/eff_pro_evt_ger_subg_i_t.sas OUT=REPORT/OUTPUT/eff_pro_acq5bw52_ger_ics_t2_t_x.rtf (29JUN2021 - 17:43)

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

Project Code / Study Number / Analysis: SAR231893 / EFC14153 / CSR_RWE

2 PRO endpoints

2.2 Responder analysis for change from baseline in ACQ-5-IA (improvement >= 0.9) at week 52 - ITT type 2 inflammatory asthma phenotype population

2.2.4 By baseline ICS dose level (Medium, High)

	Baseline ICS dose level			
	High		Medium	
Type 2 inflammatory asthma phenotype population	**Placebo (N=50)**	**Dupilumab (N=102)**	**Placebo (N=64)**	**Dupilumab (N=131)**
p-value for Risk Ratio	-	0.606	-	0.273
p-value for heterogeneity of Risk Ratio				0.911
Risk Difference (95% CI) vs placebo	-	11.74 (-6.78 to 30.26)	-	10.95 (-4.22 to 26.13)
p-value for Risk Difference	-	0.212	-	0.156
p-value for heterogeneity of Risk Difference				0.926

[a] Patients who met the corresponding criterion are considered as responders. Patients who did not meet the criterion or had missing value are considered as non-responders.
OR, RR and RD are derived from a logistic regression model with treatment, age, weight group, region, baseline eosinophil level, baseline FeNO level and baseline ACQ-5-IA score as covariates.
Peto OR calculation is based on Yusuf S et al. (Prog Cardiovasc Dis. 1985 Mar-Apr;27(5):335-71) and its p-value is derived using a normal approximation.
p-values for heterogeneity are estimated by using the same logistic model as the one used to estimate OR, RR and RD, with subgroup and treatment-by-subgroup interaction as additional covariates.
p-value for heterogeneity of Peto OR is estimated by using normal approximation.
PGM=DEVOPS/SAR231893/EFC14153/CSR_RWE/REPORT/PGM/eff_pro_evt_ger_subg_i_t.sas OUT=REPORT/OUTPUT/eff_pro_acq5bw52_ger_ics_t2_t_x.rtf (29JUN2021 - 17:43)

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

Project Code / Study Number / Analysis: SAR231893 / EFC14153 / CSR_RWE

2 PRO endpoints

2.2 Responder analysis for change from baseline in ACQ-5-IA (improvement >= 0.9) at week 52 - ITT type 2 inflammatory asthma phenotype population

2.2.5 By baseline ICS dose level 2 (Medium, High)

	Baseline ICS dose level 2			
	High		Medium	
Type 2 inflammatory asthma phenotype population	**Placebo (N=95)**	**Dupilumab (N=200)**	**Placebo (N=19)**	**Dupilumab (N=36)**
Responder status at Week 52 based on change from baseline in ACQ-5-IA <=-0.9 [n(%)] [a]				
Responder	66 (69.5%)	158 (79.0%)	13 (68.4%)	27 (75.0%)
Non-responder	29 (30.5%)	42 (21.0%)	6 (31.6%)	9 (25.0%)
Odds Ratio (95% CI) vs placebo	-	1.78 (0.93 to 3.42)	-	2.50 (0.19 to 32.73)
p-value for Odds Ratio	-	0.081	-	0.475
p-value for heterogeneity of Odds Ratio				0.945
Risk Ratio (95% CI) vs placebo	-	1.12 (0.94 to 1.34)	-	1.30 (0.39 to 4.28)
Reversed Risk ratio (95% CI) vs placebo	-	0.89 (0.75 to 1.07)	-	0.77 (0.23 to 2.53)

[a] Patients who met the corresponding criterion are considered as responders. Patients who did not meet the criterion or had missing value are considered as non-responders.
OR, RR and RD are derived from a logistic regression model with treatment, age, weight group, region, baseline eosinophil level, baseline FeNO level and baseline ACQ-5-IA score as covariates.
Peto OR calculation is based on Yusuf S et al. (Prog Cardiovasc Dis. 1985 Mar-Apr;27(5):335-71) and its p-value is derived using a normal approximation.
p-values for heterogeneity are estimated by using the same logistic model as the one used to estimate OR, RR and RD, with subgroup and treatment-by-subgroup interaction as additional covariates.
p-value for heterogeneity of Peto OR is estimated by using normal approximation.
PGM=DEVOPS/SAR231893/EFC14153/CSR_RWE/REPORT/PGM/eff_pro_evt_ger_subg_i_t.sas OUT=REPORT/OUTPUT/eff_pro_acq5bw52_ger_ics2_t2_t_x.rtf (01SEP2021 - 15:26)

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

Project Code / Study Number / Analysis: SAR231893 / EFC14153 / CSR_RWE

2 PRO endpoints

2.2 population Responder analysis for change from baseline in ACQ-5-IA (improvement >= 0.9) at week 52 - ITT type 2 inflammatory asthma phenotype

2.2.5 By baseline ICS dose level 2 (Medium, High)

	Baseline ICS dose level 2			
	High		Medium	
Type 2 inflammatory asthma phenotype population	**Placebo (N=95)**	**Dupilumab (N=200)**	**Placebo (N=19)**	**Dupilumab (N=36)**
p-value for Risk Ratio	-	0.209	-	0.660
p-value for heterogeneity of Risk Ratio				0.873
Risk Difference (95% CI) vs placebo	-	8.11 (-3.05 to 19.27)	-	23.02 (-41.33 to 87.38)
p-value for Risk Difference	-	0.154	-	0.474
p-value for heterogeneity of Risk Difference				0.726

[a] Patients who met the corresponding criterion are considered as responders. Patients who did not meet the criterion or had missing value are considered as non-responders.
OR, RR and RD are derived from a logistic regression model with treatment, age, weight group, region, baseline eosinophil level, baseline FeNO level and baseline ACQ-5-IA score as covariates.
Peto OR calculation is based on Yusuf S et al. (Prog Cardiovasc Dis. 1985 Mar-Apr;27(5):335-71) and its p-value is derived using a normal approximation.
p-values for heterogeneity are estimated by using the same logistic model as the one used to estimate OR, RR and RD, with subgroup and treatment-by-subgroup interaction as additional covariates.
p-value for heterogeneity of Peto OR is estimated by using normal approximation.
PGM=DEVOPS/SAR231893/EFC14153/CSR_RWE/REPORT/PGM/eff_pro_evt_ger_subg_i_t.sas OUT=REPORT/OUTPUT/eff_pro_acq5bw52_ger_ics2_t2_t_x.rtf (01SEP2021 - 15:26)

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

Project Code / Study Number / Analysis: SAR231893 / EFC14153 / CSR_RWE

2 PRO endpoints

2.2 population Responder analysis for change from baseline in ACQ-5-IA (improvement >= 0.9) at week 52 - ITT type 2 inflammatory asthma phenotype

2.2.6 By baseline predicted FEV1 (<80%, >=80%)

	Baseline Predicted FEV1			
	<80%		>=80%	
Type 2 inflammatory asthma phenotype population	**Placebo (N=59)**	**Dupilumab (N=116)**	**Placebo (N=55)**	**Dupilumab (N=120)**
Responder status at Week 52 based on change from baseline in ACQ-5-IA <=-0.9 [n(%)] [a]				
Responder	38 (64.4%)	91 (78.4%)	41 (74.5%)	94 (78.3%)
Non-responder	21 (35.6%)	25 (21.6%)	14 (25.5%)	26 (21.7%)
Odds Ratio (95% CI) vs placebo	-	2.92 (1.10 to 7.74)	-	1.50 (0.61 to 3.66)
p-value for Odds Ratio	-	0.031	-	0.372
p-value for heterogeneity of Odds Ratio				0.430
Risk Ratio (95% CI) vs placebo	-	1.18 (0.89 to 1.55)	-	1.04 (0.82 to 1.33)
Reversed Risk ratio (95% CI) vs placebo	-	0.85 (0.64 to 1.12)	-	0.96 (0.75 to 1.22)

[a] Patients who met the corresponding criterion are considered as responders. Patients who did not meet the criterion or had missing value are considered as non-responders.
OR, RR and RD are derived from a logistic regression model with treatment, age, weight group, region, baseline eosinophil level, baseline FeNO level, baseline ICS dose level, and baseline ACQ-5-IA score as covariates.
Peto OR calculation is based on Yusuf S et al. (Prog Cardiovasc Dis. 1985 Mar-Apr;27(5):335-71) and its p-value is derived using a normal approximation.
p-values for heterogeneity are estimated by using the same logistic model as the one used to estimate OR, RR and RD, with subgroup and treatment-by-subgroup interaction as additional covariates.
p-value for heterogeneity of Peto OR is estimated by using normal approximation.
PGM=DEVOPS/SAR231893/EFC14153/CSR_RWE/REPORT/PGM/eff_pro_evt_ger_subg_i_t.sas OUT=REPORT/OUTPUT/eff_pro_acq5bw52_ger_pfev1_t2_t_x.rtf (29JUN2021 - 17:43)

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

Project Code / Study Number / Analysis: SAR231893 / EFC14153 / CSR_RWE

2 PRO endpoints

2.2 population Responder analysis for change from baseline in ACQ-5-IA (improvement >= 0.9) at week 52 - ITT type 2 inflammatory asthma phenotype

2.2.6 By baseline predicted FEV1 (<80%, >=80%)

	Baseline Predicted FEV1			
	<80%		>=80%	
Type 2 inflammatory asthma phenotype population	**Placebo (N=59)**	**Dupilumab (N=116)**	**Placebo (N=55)**	**Dupilumab (N=120)**
p-value for Risk Ratio	-	0.245	-	0.725
p-value for heterogeneity of Risk Ratio				0.199
Risk Difference (95% CI) vs placebo	-	13.82 (-2.70 to 30.34)	-	4.23 (-10.77 to 19.22)
p-value for Risk Difference	-	0.101	-	0.579
p-value for heterogeneity of Risk Difference				0.151

[a] Patients who met the corresponding criterion are considered as responders. Patients who did not meet the criterion or had missing value are considered as non-responders.
OR, RR and RD are derived from a logistic regression model with treatment, age, weight group, region, baseline eosinophil level, baseline FeNO level, baseline ICS dose level, and baseline ACQ-5-IA score as covariates.
Peto OR calculation is based on Yusuf S et al. (Prog Cardiovasc Dis. 1985 Mar-Apr;27(5):335-71) and its p-value is derived using a normal approximation.
p-values for heterogeneity are estimated by using the same logistic model as the one used to estimate OR, RR and RD, with subgroup and treatment-by-subgroup interaction as additional covariates.
p-value for heterogeneity of Peto OR is estimated by using normal approximation.
PGM=DEVOPS/SAR231893/EFC14153/CSR_RWE/REPORT/PGM/eff_pro_evt_ger_subg_i_t.sas OUT=REPORT/OUTPUT/eff_pro_acq5bw52_ger_pfev1_t2_t_x.rtf (29JUN2021 - 17:43)

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

Project Code / Study Number / Analysis: SAR231893 / EFC14153 / CSR_RWE

2 PRO endpoints

2.2 population Responder analysis for change from baseline in ACQ-5-IA (improvement >= 0.9) at week 52 - ITT type 2 inflammatory asthma phenotype

2.2.7 By baseline ACQ-7-IA (<=2, >2)

	Baseline ACQ-7-IA			
	<=2		>2	
Type 2 inflammatory asthma phenotype population	**Placebo (N=61)**	**Dupilumab (N=126)**	**Placebo (N=53)**	**Dupilumab (N=110)**
Responder status at Week 52 based on change from baseline in ACQ-5-IA <=-0.9 [n(%)] [a]				
Responder	36 (59.0%)	89 (70.6%)	43 (81.1%)	96 (87.3%)
Non-responder	25 (41.0%)	37 (29.4%)	10 (18.9%)	14 (12.7%)
Odds Ratio (95% CI) vs placebo	-	1.76 (0.78 to 3.97)	-	1.67 (0.63 to 4.43)
p-value for Odds Ratio	-	0.175	-	0.301
p-value for heterogeneity of Odds Ratio				0.957
Risk Ratio (95% CI) vs placebo	-	1.13 (0.85 to 1.50)	-	1.10 (0.82 to 1.48)
Reversed Risk ratio (95% CI) vs placebo	-	0.89 (0.67 to 1.18)	-	0.91 (0.67 to 1.23)

[a] Patients who met the corresponding criterion are considered as responders. Patients who did not meet the criterion or had missing value are considered as non-responders.
OR, RR and RD are derived from a logistic regression model with treatment, age, weight group, region, baseline eosinophil level, baseline FeNO level, baseline ICS dose level, and baseline ACQ-5-IA score as covariates.
Peto OR calculation is based on Yusuf S et al. (Prog Cardiovasc Dis. 1985 Mar-Apr;27(5):335-71) and its p-value is derived using a normal approximation.
p-values for heterogeneity are estimated by using the same logistic model as the one used to estimate OR, RR and RD, with subgroup and treatment-by-subgroup interaction as additional covariates.
p-value for heterogeneity of Peto OR is estimated by using normal approximation.
PGM=DEVOPS/SAR231893/EFC14153/CSR_RWE/REPORT/PGM/eff_pro_evt_ger_subg_i_t.sas OUT=REPORT/OUTPUT/eff_pro_acq5bw52_ger_acq7_t2_t_x.rtf (29JUN2021 - 17:43)

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

Project Code / Study Number / Analysis: SAR231893 / EFC14153 / CSR_RWE

2 PRO endpoints

2.2 population Responder analysis for change from baseline in ACQ-5-IA (improvement >= 0.9) at week 52 - ITT type 2 inflammatory asthma phenotype

2.2.7 By baseline ACQ-7-IA (<=2, >2)

	Baseline ACQ-7-IA			
	<=2		>2	
Type 2 inflammatory asthma phenotype population	**Placebo (N=61)**	**Dupilumab (N=126)**	**Placebo (N=53)**	**Dupilumab (N=110)**
p-value for Risk Ratio	-	0.406	-	0.527
p-value for heterogeneity of Risk Ratio				0.574
Risk Difference (95% CI) vs placebo	-	10.94 (-5.56 to 27.44)	-	7.38 (-9.86 to 24.62)
p-value for Risk Difference	-	0.192	-	0.399
p-value for heterogeneity of Risk Difference				0.427

[a] Patients who met the corresponding criterion are considered as responders. Patients who did not meet the criterion or had missing value are considered as non-responders.
OR, RR and RD are derived from a logistic regression model with treatment, age, weight group, region, baseline eosinophil level, baseline FeNO level, baseline ICS dose level, and baseline ACQ-5-IA score as covariates.
Peto OR calculation is based on Yusuf S et al. (Prog Cardiovasc Dis. 1985 Mar-Apr;27(5):335-71) and its p-value is derived using a normal approximation.
p-values for heterogeneity are estimated by using the same logistic model as the one used to estimate OR, RR and RD, with subgroup and treatment-by-subgroup interaction as additional covariates.
p-value for heterogeneity of Peto OR is estimated by using normal approximation.
PGM=DEVOPS/SAR231893/EFC14153/CSR_RWE/REPORT/PGM/eff_pro_evt_ger_subg_i_t.sas OUT=REPORT/OUTPUT/eff_pro_acq5bw52_ger_acq7_t2_t_x.rtf (29JUN2021 - 17:43)

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

Project Code / Study Number / Analysis: SAR231893 / EFC14153 / CSR_RWE

2 PRO endpoints

2.2 population Responder analysis for change from baseline in ACQ-5-IA (improvement >= 0.9) at week 52 - ITT type 2 inflammatory asthma phenotype

2.2.8 By baseline weight (<=30 kg, >30 kg)

	Baseline weight (kg)			
	<=30		>30	
Type 2 inflammatory asthma phenotype population	**Placebo (N=36)**	**Dupilumab (N=76)**	**Placebo (N=78)**	**Dupilumab (N=160)**
Responder status at Week 52 based on change from baseline in ACQ-5-IA <=-0.9 [n(%)] [a]				
Responder	26 (72.2%)	60 (78.9%)	53 (67.9%)	125 (78.1%)
Non-responder	10 (27.8%)	16 (21.1%)	25 (32.1%)	35 (21.9%)
Odds Ratio (95% CI) vs placebo	-	1.64 (0.48 to 5.64)	-	2.03 (0.95 to 4.33)
p-value for Odds Ratio	-	0.428	-	0.067
p-value for heterogeneity of Odds Ratio				0.590
Risk Ratio (95% CI) vs placebo	-	0.93 (0.63 to 1.38)	-	1.17 (0.92 to 1.49)
Reversed Risk ratio (95% CI) vs placebo			-	0.86 (0.67 to 1.09)

[a] Patients who met the corresponding criterion are considered as responders. Patients who did not meet the criterion or had missing value are considered as non-responders.
OR, RR and RD are derived from a logistic regression model with treatment, age, region, baseline eosinophil level, baseline FeNO level, baseline ICS dose level, and baseline ACQ-5-IA score as covariates.
Peto OR calculation is based on Yusuf S et al. (Prog Cardiovasc Dis. 1985 Mar-Apr;27(5):335-71) and its p-value is derived using a normal approximation.
p-values for heterogeneity are estimated by using the same logistic model as the one used to estimate OR, RR and RD, with subgroup and treatment-by-subgroup interaction as additional covariates.
p-value for heterogeneity of Peto OR is estimated by using normal approximation.
PGM=DEVOPS/SAR231893/EFC14153/CSR_RWE/REPORT/PGM/eff_pro_evt_ger_subg_i_t.sas OUT=REPORT/OUTPUT/eff_pro_acq5bw52_ger_wgt_t2_t_x.rtf (29JUN2021 - 17:44)

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

Project Code / Study Number / Analysis: SAR231893 / EFC14153 / CSR_RWE

2 PRO endpoints

2.2 population Responder analysis for change from baseline in ACQ-5-IA (improvement >= 0.9) at week 52 - ITT type 2 inflammatory asthma phenotype

2.2.8 By baseline weight (<=30 kg, >30 kg)

	Baseline weight (kg)			
	<=30		>30	
Type 2 inflammatory asthma phenotype population	**Placebo (N=36)**	**Dupilumab (N=76)**	**Placebo (N=78)**	**Dupilumab (N=160)**
p-value for Risk Ratio	-	0.725	-	0.204
p-value for heterogeneity of Risk Ratio				0.194
Risk Difference (95% CI) vs placebo	-	-2.96 (-25.65 to 19.73)	-	14.32 (-0.67 to 29.32)
p-value for Risk Difference	-	0.797	-	0.061
p-value for heterogeneity of Risk Difference				0.141

[a] Patients who met the corresponding criterion are considered as responders. Patients who did not meet the criterion or had missing value are considered as non-responders.
OR, RR and RD are derived from a logistic regression model with treatment, age, region, baseline eosinophil level, baseline FeNO level, baseline ICS dose level, and baseline ACQ-5-IA score as covariates.
Peto OR calculation is based on Yusuf S et al. (Prog Cardiovasc Dis. 1985 Mar-Apr;27(5):335-71) and its p-value is derived using a normal approximation.
p-values for heterogeneity are estimated by using the same logistic model as the one used to estimate OR, RR and RD, with subgroup and treatment-by-subgroup interaction as additional covariates.
p-value for heterogeneity of Peto OR is estimated by using normal approximation.
PGM=DEVOPS/SAR231893/EFC14153/CSR_RWE/REPORT/PGM/eff_pro_evt_ger_subg_i_t.sas OUT=REPORT/OUTPUT/eff_pro_acq5bw52_ger_wgt_t2_t_x.rtf (29JUN2021 - 17:44)

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

Project Code / Study Number / Analysis: SAR231893 / EFC14153 / CSR_RWE

2 PRO endpoints

2.2 population Responder analysis for change from baseline in ACQ-5-IA (improvement >= 0.9) at week 52 - ITT type 2 inflammatory asthma phenotype

2.2.9 By atopic medical condition (Yes, No)

	Atopic medical condition			
	Yes		No	
Type 2 inflammatory asthma phenotype population	**Placebo (N=103)**	**Dupilumab (N=227)**	**Placebo (N=11)**	**Dupilumab (N=9)**
Responder status at Week 52 based on change from baseline in ACQ-5-IA <=-0.9 [n(%)] [a]				
Responder	70 (68.0%)	176 (77.5%)	9 (81.8%)	9 (100%)
Non-responder	33 (32.0%)	51 (22.5%)	2 (18.2%)	0
Odds Ratio (95% CI) vs placebo	-	1.76 (0.94 to 3.30)	-	206.76 (0.00 to NE)
p-value for Odds Ratio	-	0.078	-	0.998
Peto Odds Ratio (95% CI) vs placebo	-	1.65 (0.97 to 2.82)	-	6.82 (0.39 to 119.26)
Reversed Peto Odds Ratio (95% CI)	-	0.61 (0.35 to 1.03)	-	0.15 (0.01 to 2.56)
p-value for Peto Odds Ratio		0.065		0.189
p-value for heterogeneity of Peto Odds Ratio				0.340

[a] Patients who met the corresponding criterion are considered as responders. Patients who did not meet the criterion or had missing value are considered as non-responders. OR, RR and RD are derived from a logistic regression model with treatment, age, weight group, region, baseline eosinophil level, baseline FeNO level, baseline ICS dose level, and baseline ACQ-5-IA score as covariates.
Peto OR calculation is based on Yusuf S et al. (Prog Cardiovasc Dis. 1985 Mar-Apr;27(5):335-71) and its p-value is derived using a normal approximation.
p-values for heterogeneity are estimated by using the same logistic model as the one used to estimate OR, RR and RD, with subgroup and treatment-by-subgroup interaction as additional covariates.
p-value for heterogeneity of Peto OR is estimated by using normal approximation.
PGM=DEVOPS/SAR231893/EFC14153/CSR_RWE/REPORT/PGM/eff_pro_evt_ger_subg_i_t.sas OUT=REPORT/OUTPUT/eff_pro_acq5bw52_ger_amc_t2_t_x.rtf (29JUN2021 - 17:44)

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

Project Code / Study Number / Analysis: SAR231893 / EFC14153 / CSR_RWE

2 PRO endpoints

2.2 population Responder analysis for change from baseline in ACQ-5-IA (improvement >= 0.9) at week 52 - ITT type 2 inflammatory asthma phenotype

2.2.9 By atopic medical condition (Yes, No)

	Atopic medical condition			
	Yes		No	
Type 2 inflammatory asthma phenotype population	**Placebo (N=103)**	**Dupilumab (N=227)**	**Placebo (N=11)**	**Dupilumab (N=9)**
Risk Ratio (95% CI) vs placebo	-	1.11 (0.93 to 1.32)	-	1.13 (NE to NE)
Reversed Risk ratio (95% CI) vs placebo	-	0.90 (0.76 to 1.08)	-	0.89 (NE to NE)
p-value for Risk Ratio	-	0.259	-	<0.001
p-value for heterogeneity of Risk Ratio				<0.001
Risk Difference (95% CI) vs placebo	-	7.96 (-3.16 to 19.07)	-	18.12 (-595.89 to 632.13)
p-value for Risk Difference	-	0.160	-	0.949
p-value for heterogeneity of Risk Difference				0.769

[a] Patients who met the corresponding criterion are considered as responders. Patients who did not meet the criterion or had missing value are considered as non-responders.
OR, RR and RD are derived from a logistic regression model with treatment, age, weight group, region, baseline eosinophil level, baseline FeNO level, baseline ICS dose level, and baseline ACQ-5-IA score as covariates.
Peto OR calculation is based on Yusuf S et al. (Prog Cardiovasc Dis. 1985 Mar-Apr;27(5):335-71) and its p-value is derived using a normal approximation.
p-values for heterogeneity are estimated by using the same logistic model as the one used to estimate OR, RR and RD, with subgroup and treatment-by-subgroup interaction as additional covariates.
p-value for heterogeneity of Peto OR is estimated by using normal approximation.
PGM=DEVOPS/SAR231893/EFC14153/CSR_RWE/REPORT/PGM/eff_pro_evt_ger_subg_i_t.sas OUT=REPORT/OUTPUT/eff_pro_acq5bw52_ger_amc_t2_t_x.rtf (29JUN2021 - 17:44)

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

Project Code / Study Number / Analysis: SAR231893 / EFC14153 / CSR_RWE

2 PRO endpoints

2.2 population Responder analysis for change from baseline in ACQ-5-IA (improvement >= 0.9) at week 52 - ITT type 2 inflammatory asthma phenotype

2.2.10 By baseline total IgE (<median, >= median)

	Baseline Total IgE (IU/mL)			
	<median		>=median	
Type 2 inflammatory asthma phenotype population	**Placebo (N=66)**	**Dupilumab (N=105)**	**Placebo (N=47)**	**Dupilumab (N=125)**
Responder status at Week 52 based on change from baseline in ACQ-5-IA <=-0.9 [n(%)] [a]				
Responder	47 (71.2%)	84 (80.0%)	31 (66.0%)	98 (78.4%)
Non-responder	19 (28.8%)	21 (20.0%)	16 (34.0%)	27 (21.6%)
Odds Ratio (95% CI) vs placebo	-	1.44 (0.59 to 3.49)	-	2.36 (0.93 to 5.96)
p-value for Odds Ratio	-	0.420	-	0.070
p-value for heterogeneity of Odds Ratio				0.666
Risk Ratio (95% CI) vs placebo	-	1.09 (0.83 to 1.41)	-	1.17 (0.86 to 1.60)
Reversed Risk ratio (95% CI) vs placebo	-	0.92 (0.71 to 1.20)	-	0.85 (0.62 to 1.16)

[a] Patients who met the corresponding criterion are considered as responders. Patients who did not meet the criterion or had missing value are considered as non-responders.
OR, RR and RD are derived from a logistic regression model with treatment, age, weight group, region, baseline eosinophil level, baseline FeNO level, baseline ICS dose level, and baseline ACQ-5-IA score as covariates.
Peto OR calculation is based on Yusuf S et al. (Prog Cardiovasc Dis. 1985 Mar-Apr;27(5):335-71) and its p-value is derived using a normal approximation.
p-values for heterogeneity are estimated by using the same logistic model as the one used to estimate OR, RR and RD, with subgroup and treatment-by-subgroup interaction as additional covariates.
p-value for heterogeneity of Peto OR is estimated by using normal approximation.
PGM=DEVOPS/SAR231893/EFC14153/CSR_RWE/REPORT/PGM/eff_pro_evt_ger_subg_i_t.sas OUT=REPORT/OUTPUT/eff_pro_acq5bw52_ger_igem_t2_t_x.rtf (29JUN2021 - 17:44)

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

Project Code / Study Number / Analysis: SAR231893 / EFC14153 / CSR_RWE

2 PRO endpoints

2.2 population Responder analysis for change from baseline in ACQ-5-IA (improvement >= 0.9) at week 52 - ITT type 2 inflammatory asthma phenotype

2.2.10 By baseline total IgE (<median, >= median)

	Baseline Total IgE (IU/mL)			
	<median		>=median	
Type 2 inflammatory asthma phenotype population	**Placebo (N=66)**	**Dupilumab (N=105)**	**Placebo (N=47)**	**Dupilumab (N=125)**
p-value for Risk Ratio	-	0.539	-	0.312
p-value for heterogeneity of Risk Ratio				0.551
Risk Difference (95% CI) vs placebo	-	5.85 (-10.78 to 22.47)	-	12.14 (-4.04 to 28.32)
p-value for Risk Difference	-	0.488	-	0.140
p-value for heterogeneity of Risk Difference				0.513

[a] Patients who met the corresponding criterion are considered as responders. Patients who did not meet the criterion or had missing value are considered as non-responders.
OR, RR and RD are derived from a logistic regression model with treatment, age, weight group, region, baseline eosinophil level, baseline FeNO level, baseline ICS dose level, and baseline ACQ-5-IA score as covariates.
Peto OR calculation is based on Yusuf S et al. (Prog Cardiovasc Dis. 1985 Mar-Apr;27(5):335-71) and its p-value is derived using a normal approximation.
p-values for heterogeneity are estimated by using the same logistic model as the one used to estimate OR, RR and RD, with subgroup and treatment-by-subgroup interaction as additional covariates.
p-value for heterogeneity of Peto OR is estimated by using normal approximation.
PGM=DEVOPS/SAR231893/EFC14153/CSR_RWE/REPORT/PGM/eff_pro_evt_ger_subg_i_t.sas OUT=REPORT/OUTPUT/eff_pro_acq5bw52_ger_igem_t2_t_x.rtf (29JUN2021 - 17:44)

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

Project Code / Study Number / Analysis: SAR231893 / EFC14153 / CSR_RWE

2 PRO endpoints

2.2 population Responder analysis for change from baseline in ACQ-5-IA (improvement >= 0.9) at week 52 - ITT type 2 inflammatory asthma phenotype

2.2.11 By baseline total IgE (<100 IU/ml, >= 100 IU/ml)

	Baseline Total IgE (IU/mL)			
	< 100		>= 100	
Type 2 inflammatory asthma phenotype population	**Placebo (N=22)**	**Dupilumab (N=29)**	**Placebo (N=91)**	**Dupilumab (N=201)**
Responder status at Week 52 based on change from baseline in ACQ-5-IA <=-0.9 [n(%)] [a]				
Responder	17 (77.3%)	23 (79.3%)	61 (67.0%)	159 (79.1%)
Non-responder	5 (22.7%)	6 (20.7%)	30 (33.0%)	42 (20.9%)
Odds Ratio (95% CI) vs placebo	-	0.41 (0.05 to 3.34)	-	2.22 (1.12 to 4.38)
p-value for Odds Ratio	-	0.397	-	0.022
p-value for heterogeneity of Odds Ratio				0.144
Risk Ratio (95% CI) vs placebo	-	0.93 (0.05 to 18.89)	-	1.14 (0.94 to 1.38)
Reversed Risk ratio (95% CI) vs placebo			-	0.88 (0.72 to 1.06)

[a] Patients who met the corresponding criterion are considered as responders. Patients who did not meet the criterion or had missing value are considered as non-responders.
OR, RR and RD are derived from a logistic regression model with treatment, age, weight group, region, baseline eosinophil level, baseline FeNO level, baseline ICS dose level, and baseline ACQ-5-IA score as covariates.
Peto OR calculation is based on Yusuf S et al. (Prog Cardiovasc Dis. 1985 Mar-Apr;27(5):335-71) and its p-value is derived using a normal approximation.
p-values for heterogeneity are estimated by using the same logistic model as the one used to estimate OR, RR and RD, with subgroup and treatment-by-subgroup interaction as additional covariates.
p-value for heterogeneity of Peto OR is estimated by using normal approximation.
PGM=DEVOPS/SAR231893/EFC14153/CSR_RWE/REPORT/PGM/eff_pro_evt_ger_subg_i_t.sas OUT=REPORT/OUTPUT/eff_pro_acq5bw52_ger_ige_t2_t_x.rtf (29JUN2021 - 17:45)

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

Project Code / Study Number / Analysis: SAR231893 / EFC14153 / CSR_RWE

2 PRO endpoints

2.2 Responder analysis for change from baseline in ACQ-5-IA (improvement >= 0.9) at week 52 - ITT type 2 inflammatory asthma phenotype population

2.2.11 By baseline total IgE (<100 IU/ml, >= 100 IU/ml)

	Baseline Total IgE (IU/mL)			
	< 100		>= 100	
Type 2 inflammatory asthma phenotype population	**Placebo (N=22)**	**Dupilumab (N=29)**	**Placebo (N=91)**	**Dupilumab (N=201)**
p-value for Risk Ratio	-	0.963	-	0.184
p-value for heterogeneity of Risk Ratio				0.567
Risk Difference (95% CI) vs placebo	-	-7.14 (-58.95 to 44.67)	-	10.54 (-1.68 to 22.75)
p-value for Risk Difference	-	0.782	-	0.091
p-value for heterogeneity of Risk Difference				0.502

[a] Patients who met the corresponding criterion are considered as responders. Patients who did not meet the criterion or had missing value are considered as non-responders.
OR, RR and RD are derived from a logistic regression model with treatment, age, weight group, region, baseline eosinophil level, baseline FeNO level, baseline ICS dose level, and baseline ACQ-5-IA score as covariates.
Peto OR calculation is based on Yusuf S et al. (Prog Cardiovasc Dis. 1985 Mar-Apr;27(5):335-71) and its p-value is derived using a normal approximation.
p-values for heterogeneity are estimated by using the same logistic model as the one used to estimate OR, RR and RD, with subgroup and treatment-by-subgroup interaction as additional covariates.
p-value for heterogeneity of Peto OR is estimated by using normal approximation.
PGM=DEVOPS/SAR231893/EFC14153/CSR_RWE/REPORT/PGM/eff_pro_evt_ger_subg_i_t.sas OUT=REPORT/OUTPUT/eff_pro_acq5bw52_ger_ige_t2_t_x.rtf (29JUN2021 - 17:45)

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

Project Code / Study Number / Analysis: SAR231893 / EFC14153 / CSR_RWE

2 PRO endpoints

2.2 population Responder analysis for change from baseline in ACQ-5-IA (improvement >= 0.9) at week 52 - ITT type 2 inflammatory asthma phenotype

2.2.12 By age at onset of asthma (0-2, 3-5, >=6 years)

	Age of onset of asthma (years)					
	0-2		3-5		>= 6	
Type 2 inflammatory asthma phenotype population	**Placebo (N=40)**	**Dupilumab (N=105)**	**Placebo (N=39)**	**Dupilumab (N=86)**	**Placebo (N=35)**	**Dupilumab (N=45)**
Responder status at Week 52 based on change from baseline in ACQ-5-IA <=-0.9 [n(%)] [a]						
Responder	26 (65.0%)	81 (77.1%)	28 (71.8%)	67 (77.9%)	25 (71.4%)	37 (82.2%)
Non-responder	14 (35.0%)	24 (22.9%)	11 (28.2%)	19 (22.1%)	10 (28.6%)	8 (17.8%)
Odds Ratio (95% CI) vs placebo	-	2.22 (0.81 to 6.10)	-	1.73 (0.52 to 5.80)	-	2.22 (0.58 to 8.58)
p-value for Odds Ratio	-	0.121	-	0.369	-	0.242
p-value for heterogeneity of Odds Ratio:						
0-2, 3-5						0.696
0-2, >= 6						0.932

[a] Patients who met the corresponding criterion are considered as responders. Patients who did not meet the criterion or had missing value are considered as non-responders. OR, RR and RD are derived from a logistic regression model with treatment, age, weight group, region, baseline eosinophil level, baseline FeNO level, baseline ICS dose level, and baseline ACQ-5-IA score as covariates.
Peto OR calculation is based on Yusuf S et al. (Prog Cardiovasc Dis. 1985 Mar-Apr;27(5):335-71) and its p-value is derived using a normal approximation.
p-values for heterogeneity are estimated by using the same logistic model as the one used to estimate OR, RR and RD, with subgroup and treatment-by-subgroup interaction as additional covariates.
p-value for heterogeneity of Peto OR is estimated by using normal approximation.
PGM=DEVOPS/SAR231893/EFC14153/CSR_RWE/REPORT/PGM/eff_pro_evt_ger_subg_i_t.sas OUT=REPORT/OUTPUT/eff_pro_acq5bw52_ger_onsa_t2_t_x.rtf (01SEP2021 - 15:26)

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

Project Code / Study Number / Analysis: SAR231893 / EFC14153 / CSR_RWE

2 PRO endpoints

2.2 population Responder analysis for change from baseline in ACQ-5-IA (improvement >= 0.9) at week 52 - ITT type 2 inflammatory asthma phenotype

2.2.12 By age at onset of asthma (0-2, 3-5, >=6 years)

	Age of onset of asthma (years)					
	0-2		3-5		>= 6	
Type 2 inflammatory asthma phenotype population	**Placebo (N=40)**	**Dupilumab (N=105)**	**Placebo (N=39)**	**Dupilumab (N=86)**	**Placebo (N=35)**	**Dupilumab (N=45)**
3-5, >= 6						0.791
overall						0.922
Risk Ratio (95% CI) vs placebo	-	1.10 (0.79 to 1.53)	-	1.01 (0.66 to 1.54)	-	1.18 (0.74 to 1.88)
Reversed Risk ratio (95% CI) vs placebo	-	0.91 (0.65 to 1.27)	-	0.99 (0.65 to 1.51)	-	0.85 (0.53 to 1.35)
p-value for Risk Ratio	-	0.588	-	0.962	-	0.473
p-value for heterogeneity of Risk Ratio:						
0-2, 3-5						0.981
0-2, >= 6						0.440
3-5, >= 6						0.451
overall						0.689

[a] Patients who met the corresponding criterion are considered as responders. Patients who did not meet the criterion or had missing value are considered as non-responders.
OR, RR and RD are derived from a logistic regression model with treatment, age, weight group, region, baseline eosinophil level, baseline FeNO level, baseline ICS dose level, and baseline ACQ-5-IA score as covariates.
Peto OR calculation is based on Yusuf S et al. (Prog Cardiovasc Dis. 1985 Mar-Apr;27(5):335-71) and its p-value is derived using a normal approximation.
p-values for heterogeneity are estimated by using the same logistic model as the one used to estimate OR, RR and RD, with subgroup and treatment-by-subgroup interaction as additional covariates.
p-value for heterogeneity of Peto OR is estimated by using normal approximation.
PGM=DEVOPS/SAR231893/EFC14153/CSR_RWE/REPORT/PGM/eff_pro_evt_ger_subg_i_t.sas OUT=REPORT/OUTPUT/eff_pro_acq5bw52_ger_onsa_t2_t_x.rtf (01SEP2021 - 15:26)

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

Project Code / Study Number / Analysis: SAR231893 / EFC14153 / CSR_RWE

2 PRO endpoints

2.2 Responder analysis for change from baseline in ACQ-5-IA (improvement >= 0.9) at week 52 - ITT type 2 inflammatory asthma phenotype population

2.2.12 By age at onset of asthma (0-2, 3-5, >=6 years)

	Age of onset of asthma (years)					
	0-2		3-5		>= 6	
Type 2 inflammatory asthma phenotype population	**Placebo (N=40)**	**Dupilumab (N=105)**	**Placebo (N=39)**	**Dupilumab (N=86)**	**Placebo (N=35)**	**Dupilumab (N=45)**
Risk Difference (95% CI) vs placebo	-	6.66 (-12.89 to 26.21)	-	5.99 (-19.51 to 31.49)	-	13.61 (-15.51 to 42.74)
p-value for Risk Difference	-	0.501	-	0.642	-	0.354
p-value for heterogeneity of Risk Difference:						
0-2, 3-5						0.811
0-2, >= 6						0.319
3-5, >= 6						0.449
overall						0.590

[a] Patients who met the corresponding criterion are considered as responders. Patients who did not meet the criterion or had missing value are considered as non-responders.
OR, RR and RD are derived from a logistic regression model with treatment, age, weight group, region, baseline eosinophil level, baseline FeNO level, baseline ICS dose level, and baseline ACQ-5-IA score as covariates.
Peto OR calculation is based on Yusuf S et al. (Prog Cardiovasc Dis. 1985 Mar-Apr;27(5):335-71) and its p-value is derived using a normal approximation.
p-values for heterogeneity are estimated by using the same logistic model as the one used to estimate OR, RR and RD, with subgroup and treatment-by-subgroup interaction as additional covariates.
p-value for heterogeneity of Peto OR is estimated by using normal approximation.
PGM=DEVOPS/SAR231893/EFC14153/CSR_RWE/REPORT/PGM/eff_pro_evt_ger_subg_i_t.sas OUT=REPORT/OUTPUT/eff_pro_acq5bw52_ger_onsa_t2_t_x.rtf (01SEP2021 - 15:26)

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

Project Code / Study Number / Analysis: SAR231893 / EFC14153 / CSR_RWE

2 PRO endpoints

2.2 population Responder analysis for change from baseline in ACQ-5-IA (improvement >= 0.9) at week 52 - ITT type 2 inflammatory asthma phenotype

2.2.13 By number of severe asthma exacerbation prior to the study (<=1, 2, >2)

	Number of severe asthma exacerbation prior to the study					
	<=1		2		>2	
Type 2 inflammatory asthma phenotype population	**Placebo (N=47)**	**Dupilumab (N=85)**	**Placebo (N=32)**	**Dupilumab (N=75)**	**Placebo (N=35)**	**Dupilumab (N=76)**
Responder status at Week 52 based on change from baseline in ACQ-5-IA <=-0.9 [n(%)] [a]						
Responder	33 (70.2%)	66 (77.6%)	22 (68.8%)	60 (80.0%)	24 (68.6%)	59 (77.6%)
Non-responder	14 (29.8%)	19 (22.4%)	10 (31.3%)	15 (20.0%)	11 (31.4%)	17 (22.4%)
Odds Ratio (95% CI) vs placebo	-	2.57 (0.90 to 7.29)	-	1.04 (0.27 to 4.10)	-	1.75 (0.55 to 5.55)
p-value for Odds Ratio	-	0.077	-	0.950	-	0.336
p-value for heterogeneity of Odds Ratio:						
<=1, 2						0.513
<=1, >2						0.540

[a] Patients who met the corresponding criterion are considered as responders. Patients who did not meet the criterion or had missing value are considered as non-responders. OR, RR and RD are derived from a logistic regression model with treatment, age, weight group, region, baseline eosinophil level, baseline FeNO level, baseline ICS dose level, and baseline ACQ-5-IA score as covariates.
Peto OR calculation is based on Yusuf S et al. (Prog Cardiovasc Dis. 1985 Mar-Apr;27(5):335-71) and its p-value is derived using a normal approximation.
p-values for heterogeneity are estimated by using the same logistic model as the one used to estimate OR, RR and RD, with subgroup and treatment-by-subgroup interaction as additional covariates.
p-value for heterogeneity of Peto OR is estimated by using normal approximation.
PGM=DEVOPS/SAR231893/EFC14153/CSR_RWE/REPORT/PGM/eff_pro_evt_ger_subg_i_t.sas OUT=REPORT/OUTPUT/eff_pro_acq5bw52_ger_exa_t2_t_x.rtf (29JUN2021 - 17:46)

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

Project Code / Study Number / Analysis: SAR231893 / EFC14153 / CSR_RWE

2 PRO endpoints

2.2 population Responder analysis for change from baseline in ACQ-5-IA (improvement >= 0.9) at week 52 - ITT type 2 inflammatory asthma phenotype

2.2.13 By number of severe asthma exacerbation prior to the study (<=1, 2, >2)

	Number of severe asthma exacerbation prior to the study					
	<=1		2		>2	
Type 2 inflammatory asthma phenotype population	**Placebo (N=47)**	**Dupilumab (N=85)**	**Placebo (N=32)**	**Dupilumab (N=75)**	**Placebo (N=35)**	**Dupilumab (N=76)**
2, >2						0.970
overall						0.751
Risk Ratio (95% CI) vs placebo	-	1.19 (0.86 to 1.65)	-	1.10 (0.66 to 1.83)	-	1.08 (0.72 to 1.61)
Reversed Risk ratio (95% CI) vs placebo	-	0.84 (0.61 to 1.16)	-	0.91 (0.55 to 1.52)	-	0.93 (0.62 to 1.39)
p-value for Risk Ratio	-	0.281	-	0.720	-	0.712
p-value for heterogeneity of Risk Ratio:						
<=1, 2						0.997
<=1, >2						0.444
2, >2						0.497
overall						0.686

[a] Patients who met the corresponding criterion are considered as responders. Patients who did not meet the criterion or had missing value are considered as non-responders.
OR, RR and RD are derived from a logistic regression model with treatment, age, weight group, region, baseline eosinophil level, baseline FeNO level, baseline ICS dose level, and baseline ACQ-5-IA score as covariates.
Peto OR calculation is based on Yusuf S et al. (Prog Cardiovasc Dis. 1985 Mar-Apr;27(5):335-71) and its p-value is derived using a normal approximation.
p-values for heterogeneity are estimated by using the same logistic model as the one used to estimate OR, RR and RD, with subgroup and treatment-by-subgroup interaction as additional covariates.
p-value for heterogeneity of Peto OR is estimated by using normal approximation.
PGM=DEVOPS/SAR231893/EFC14153/CSR_RWE/REPORT/PGM/eff_pro_evt_ger_subg_i_t.sas OUT=REPORT/OUTPUT/eff_pro_acq5bw52_ger_exa_t2_t_x.rtf (29JUN2021 - 17:46)

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

Project Code / Study Number / Analysis: SAR231893 / EFC14153 / CSR_RWE

2 PRO endpoints

2.2 population Responder analysis for change from baseline in ACQ-5-IA (improvement >= 0.9) at week 52 - ITT type 2 inflammatory asthma phenotype

2.2.13 By number of severe asthma exacerbation prior to the study (<=1, 2, >2)

	Number of severe asthma exacerbation prior to the study					
	<=1		2		>2	
Type 2 inflammatory asthma phenotype population	**Placebo (N=47)**	**Dupilumab (N=85)**	**Placebo (N=32)**	**Dupilumab (N=75)**	**Placebo (N=35)**	**Dupilumab (N=76)**
Risk Difference (95% CI) vs placebo	-	17.57 (-3.95 to 39.09)	-	10.51 (-15.31 to 36.33)	-	5.83 (-15.77 to 27.43)
p-value for Risk Difference	-	0.109	-	0.421	-	0.593
p-value for heterogeneity of Risk Difference:						
<=1, 2						0.893
<=1, >2						0.342
2, >2						0.480
overall						0.598

[a] Patients who met the corresponding criterion are considered as responders. Patients who did not meet the criterion or had missing value are considered as non-responders.
OR, RR and RD are derived from a logistic regression model with treatment, age, weight group, region, baseline eosinophil level, baseline FeNO level, baseline ICS dose level, and baseline ACQ-5-IA score as covariates.
Peto OR calculation is based on Yusuf S et al. (Prog Cardiovasc Dis. 1985 Mar-Apr;27(5):335-71) and its p-value is derived using a normal approximation.
p-values for heterogeneity are estimated by using the same logistic model as the one used to estimate OR, RR and RD, with subgroup and treatment-by-subgroup interaction as additional covariates.
p-value for heterogeneity of Peto OR is estimated by using normal approximation.
PGM=DEVOPS/SAR231893/EFC14153/CSR_RWE/REPORT/PGM/eff_pro_evt_ger_subg_i_t.sas OUT=REPORT/OUTPUT/eff_pro_acq5bw52_ger_exa_t2_t_x.rtf (29JUN2021 - 17:46)

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

Project Code / Study Number / Analysis: SAR231893 / EFC14153 / CSR_RWE

2 PRO endpoints

2.3 Responder analysis for change from baseline in PAQLQ(S)-IA global score (improvement >= 0.5) at week 52 - ITT type 2 inflammatory asthma phenotype population

Type 2 inflammatory asthma phenotype population	Placebo (N=107)	Dupilumab (N=211)
Responder status at Week 52 based on change from baseline in PAQLQ(S)-IA global score >=0.5 [n(%)] [a]		
Responder	73 (68.2%)	161 (76.3%)
Non-responder	34 (31.8%)	50 (23.7%)
Odds Ratio (95% CI)	-	1.89 (1.02 to 3.53)
p-value for Odds Ratio		0.044
Risk Ratio (95% CI)	-	1.18 (1.02 to 1.36)
Reversed Risk ratio (95% CI)	-	0.85 (0.74 to 0.98)
p-value for Risk Ratio		0.026
Risk Difference (95% CI)	-	11.73 (2.11 to 21.35)
p-value for Risk Difference		0.017

[a] Patients who met the corresponding criterion are considered as responders. Patients who did not meet the criterion or had missing value are considered as non-responders.
OR, RR and RD are derived from a logistic regression model with treatment, age, weight group, region, baseline eosinophil level, baseline FeNO level, baseline ICS dose level, and baseline PAQLQ(S)-IA global score as covariates.
Peto OR calculation is based on Yusuf S et al. (Prog Cardiovasc Dis. 1985 Mar-Apr;27(5):335-71) and its p-value is derived using a normal approximation.
Only patients of age >=7 years old at randomization are included in the analysis.
PGM=DEVOPS/SAR231893/EFC14153/CSR_RWE/REPORT/PGM/eff_pro_evt_ger_i_t.sas OUT=REPORT/OUTPUT/eff_pro_aqlqaw52_ger_t2_t_x.rtf (30JUN2021 - 8:13)

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

Project Code / Study Number / Analysis: SAR231893 / EFC14153 / CSR_RWE

2 PRO endpoints

2.3 Responder analysis for change from baseline in PAQLQ(S)-IA global score (improvement >= 0.5) at week 52 - ITT type 2 inflammatory asthma phenotype population

2.3.1 By gender (Male, Female)

	Gender			
	Male		Female	
Type 2 inflammatory asthma phenotype population	**Placebo (N=72)**	**Dupilumab (N=134)**	**Placebo (N=35)**	**Dupilumab (N=77)**
Responder status at Week 52 based on change from baseline in PAQLQ(S)-IA global score >=0.5 [n(%)] [a]				
Responder	48 (66.7%)	102 (76.1%)	25 (71.4%)	59 (76.6%)
Non-responder	24 (33.3%)	32 (23.9%)	10 (28.6%)	18 (23.4%)
Odds Ratio (95% CI) vs placebo	-	2.14 (0.98 to 4.68)	-	1.73 (0.55 to 5.44)
p-value for Odds Ratio	-	0.056	-	0.342
p-value for heterogeneity of Odds Ratio				0.576
Risk Ratio (95% CI) vs placebo	-	1.18 (0.95 to 1.48)	-	1.10 (0.75 to 1.61)

[a] Patients who met the corresponding criterion are considered as responders. Patients who did not meet the criterion or had missing value are considered as non-responders.
OR, RR and RD are derived from a logistic regression model with treatment, age, weight group, region, baseline eosinophil level, baseline FeNO level, baseline ICS dose level, and baseline PAQLQ(S)-IA global score as covariates.
Peto OR calculation is based on Yusuf S et al. (Prog Cardiovasc Dis. 1985 Mar-Apr;27(5):335-71) and its p-value is derived using a normal approximation.
p-values for heterogeneity are estimated by using the same logistic model as the one used to estimate OR, RR and RD, with subgroup and treatment-by-subgroup interaction as additional covariates.
p-value for heterogeneity of Peto OR is estimated by using normal approximation.
Only patients of age >=7 years old at randomization are included in the analysis.
PGM=DEVOPS/SAR231893/EFC14153/CSR_RWE/REPORT/PGM/eff_pro_evt_ger_subg_i_t.sas OUT=REPORT/OUTPUT/eff_pro_aqlqaw52_ger_sex_t2_t_x.rtf (29JUN2021 - 17:46)

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

Project Code / Study Number / Analysis: SAR231893 / EFC14153 / CSR_RWE

2 PRO endpoints

2.3 Responder analysis for change from baseline in PAQLQ(S)-IA global score (improvement >= 0.5) at week 52 - ITT type 2 inflammatory asthma phenotype population

2.3.1 By gender (Male, Female)

	Gender			
	Male		Female	
Type 2 inflammatory asthma phenotype population	**Placebo (N=72)**	**Dupilumab (N=134)**	**Placebo (N=35)**	**Dupilumab (N=77)**
Reversed Risk ratio (95% CI) vs placebo	-	0.84 (0.68 to 1.05)	-	0.91 (0.62 to 1.32)
p-value for Risk Ratio	-	0.130	-	0.611
p-value for heterogeneity of Risk Ratio				0.833
Risk Difference (95% CI) vs placebo	-	12.36 (-0.77 to 25.49)	-	7.06 (-13.73 to 27.85)
p-value for Risk Difference	-	0.065	-	0.502
p-value for heterogeneity of Risk Difference				0.771

[a] Patients who met the corresponding criterion are considered as responders. Patients who did not meet the criterion or had missing value are considered as non-responders.
OR, RR and RD are derived from a logistic regression model with treatment, age, weight group, region, baseline eosinophil level, baseline FeNO level, baseline ICS dose level, and baseline PAQLQ(S)-IA global score as covariates.
Peto OR calculation is based on Yusuf S et al. (Prog Cardiovasc Dis. 1985 Mar-Apr;27(5):335-71) and its p-value is derived using a normal approximation.
p-values for heterogeneity are estimated by using the same logistic model as the one used to estimate OR, RR and RD, with subgroup and treatment-by-subgroup interaction as additional covariates.
p-value for heterogeneity of Peto OR is estimated by using normal approximation.
Only patients of age >=7 years old at randomization are included in the analysis.
PGM=DEVOPS/SAR231893/EFC14153/CSR_RWE/REPORT/PGM/eff_pro_evt_ger_subg_i_t.sas OUT=REPORT/OUTPUT/eff_pro_aqlqaw52_ger_sex_t2_t_x.rtf (29JUN2021 - 17:46)

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

Project Code / Study Number / Analysis: SAR231893 / EFC14153 / CSR_RWE

2 PRO endpoints

2.3 Responder analysis for change from baseline in PAQLQ(S)-IA global score (improvement >= 0.5) at week 52 - ITT type 2 inflammatory asthma phenotype population

2.3.2 By region (Latin America, East Europe, Western Countries)

	Region					
	Latin America		East Europe		Western countries	
Type 2 inflammatory asthma phenotype population	**Placebo (N=50)**	**Dupilumab (N=94)**	**Placebo (N=37)**	**Dupilumab (N=68)**	**Placebo (N=20)**	**Dupilumab (N=49)**
Responder status at Week 52 based on change from baseline in PAQLQ(S)-IA global score >=0.5 [n(%)] [a]						
Responder	38 (76.0%)	79 (84.0%)	25 (67.6%)	54 (79.4%)	10 (50.0%)	28 (57.1%)
Non-responder	12 (24.0%)	15 (16.0%)	12 (32.4%)	14 (20.6%)	10 (50.0%)	21 (42.9%)
Odds Ratio (95% CI) vs placebo	-	1.92 (0.63 to 5.87)	-	2.59 (0.82 to 8.19)	-	2.00 (0.60 to 6.73)
p-value for Odds Ratio	-	0.248	-	0.103	-	0.255
p-value for heterogeneity of Odds Ratio:						
Latin America, East Europe						0.895
Latin America, Western countries						0.934

[a] Patients who met the corresponding criterion are considered as responders. Patients who did not meet the criterion or had missing value are considered as non-responders.
OR, RR and RD are derived from a logistic regression model with treatment, age, weight group, baseline eosinophil level, baseline FeNO level, baseline ICS dose level, and baseline PAQLQ(S)-IA global score as covariates.
Peto OR calculation is based on Yusuf S et al. (Prog Cardiovasc Dis. 1985 Mar-Apr;27(5):335-71) and its p-value is derived using a normal approximation.
p-values for heterogeneity are estimated by using the same logistic model as the one used to estimate OR, RR and RD, with subgroup and treatment-by-subgroup interaction as additional covariates.
p-value for heterogeneity of Peto OR is estimated by using normal approximation.
Only patients of age >=7 years old at randomization are included in the analysis.
PGM=DEVOPS/SAR231893/EFC14153/CSR_RWE/REPORT/PGM/eff_pro_evt_ger_subg_i_t.sas OUT=REPORT/OUTPUT/eff_pro_aqlqaw52_ger_cty_t2_t_x.rtf (29JUN2021 - 17:46)

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

Project Code / Study Number / Analysis: SAR231893 / EFC14153 / CSR_RWE

2 PRO endpoints

2.3 Responder analysis for change from baseline in PAQLQ(S)-IA global score (improvement >= 0.5) at week 52 - ITT type 2 inflammatory asthma phenotype population

2.3.2 By region (Latin America, East Europe, Western Countries)

	Region					
	Latin America		East Europe		Western countries	
Type 2 inflammatory asthma phenotype population	**Placebo (N=50)**	**Dupilumab (N=94)**	**Placebo (N=37)**	**Dupilumab (N=68)**	**Placebo (N=20)**	**Dupilumab (N=49)**
East Europe, Western countries						0.837
overall						0.978
Risk Ratio (95% CI) vs placebo	-	1.14 (0.92 to 1.41)	-	1.18 (0.84 to 1.66)	-	1.33 (0.76 to 2.32)
Reversed Risk ratio (95% CI) vs placebo	-	0.88 (0.71 to 1.09)	-	0.85 (0.60 to 1.19)	-	0.75 (0.43 to 1.31)
p-value for Risk Ratio	-	0.232	-	0.335	-	0.310
p-value for heterogeneity of Risk Ratio:						
Latin America, East Europe						0.907
Latin America, Western countries						0.855
East Europe, Western countries						0.909

[a] Patients who met the corresponding criterion are considered as responders. Patients who did not meet the criterion or had missing value are considered as non-responders.
OR, RR and RD are derived from a logistic regression model with treatment, age, weight group, baseline eosinophil level, baseline FeNO level, baseline ICS dose level, and baseline PAQLQ(S)-IA global score as covariates.
Peto OR calculation is based on Yusuf S et al. (Prog Cardiovasc Dis. 1985 Mar-Apr;27(5):335-71) and its p-value is derived using a normal approximation.
p-values for heterogeneity are estimated by using the same logistic model as the one used to estimate OR, RR and RD, with subgroup and treatment-by-subgroup interaction as additional covariates.
p-value for heterogeneity of Peto OR is estimated by using normal approximation.
Only patients of age >=7 years old at randomization are included in the analysis.
PGM=DEVOPS/SAR231893/EFC14153/CSR_RWE/REPORT/PGM/eff_pro_evt_ger_subg_i_t.sas OUT=REPORT/OUTPUT/eff_pro_aqlqaw52_ger_cty_t2_t_x.rtf (29JUN2021 - 17:46)

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

Project Code / Study Number / Analysis: SAR231893 / EFC14153 / CSR_RWE

2 PRO endpoints

2.3 Responder analysis for change from baseline in PAQLQ(S)-IA global score (improvement >= 0.5) at week 52 - ITT type 2 inflammatory asthma phenotype population

2.3.2 By region (Latin America, East Europe, Western Countries)

	Region					
	Latin America		East Europe		Western countries	
Type 2 inflammatory asthma phenotype population	**Placebo (N=50)**	**Dupilumab (N=94)**	**Placebo (N=37)**	**Dupilumab (N=68)**	**Placebo (N=20)**	**Dupilumab (N=49)**
overall						0.980
Risk Difference (95% CI) vs placebo	-	10.68 (-4.59 to 25.95)	-	14.40 (-6.79 to 35.58)	-	16.52 (-10.18 to 43.21)
p-value for Risk Difference	-	0.169	-	0.180	-	0.220
p-value for heterogeneity of Risk Difference:						
Latin America, East Europe						0.816
Latin America, Western countries						0.822
East Europe, Western countries						0.709
overall						0.930

[a] Patients who met the corresponding criterion are considered as responders. Patients who did not meet the criterion or had missing value are considered as non-responders.
OR, RR and RD are derived from a logistic regression model with treatment, age, weight group, baseline eosinophil level, baseline FeNO level, baseline ICS dose level, and baseline PAQLQ(S)-IA global score as covariates.
Peto OR calculation is based on Yusuf S et al. (Prog Cardiovasc Dis. 1985 Mar-Apr;27(5):335-71) and its p-value is derived using a normal approximation.
p-values for heterogeneity are estimated by using the same logistic model as the one used to estimate OR, RR and RD, with subgroup and treatment-by-subgroup interaction as additional covariates.
p-value for heterogeneity of Peto OR is estimated by using normal approximation.
Only patients of age >=7 years old at randomization are included in the analysis.
PGM=DEVOPS/SAR231893/EFC14153/CSR_RWE/REPORT/PGM/eff_pro_evt_ger_subg_i_t.sas OUT=REPORT/OUTPUT/eff_pro_aqlqaw52_ger_cty_t2_t_x.rtf (29JUN2021 - 17:46)

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

Project Code / Study Number / Analysis: SAR231893 / EFC14153 / CSR_RWE

2 PRO endpoints

2.3 Responder analysis for change from baseline in PAQLQ(S)-IA global score (improvement >= 0.5) at week 52 - ITT type 2 inflammatory asthma phenotype population

2.3.3 By race (Caucasian/white, Black/of African descent, Other)

	Race					
	Caucasian/White		Black/of African descent		Other	
Type 2 inflammatory asthma phenotype population	**Placebo (N=95)**	**Dupilumab (N=183)**	**Placebo (N=5)**	**Dupilumab (N=9)**	**Placebo (N=7)**	**Dupilumab (N=19)**
Responder status at Week 52 based on change from baseline in PAQLQ(S)-IA global score >=0.5 [n(%)] [a]						
Responder	70 (73.7%)	146 (79.8%)	0	6 (66.7%)	3 (42.9%)	9 (47.4%)
Non-responder	25 (26.3%)	37 (20.2%)	5 (100%)	3 (33.3%)	4 (57.1%)	10 (52.6%)
Odds Ratio (95% CI) vs placebo	-	1.84 (0.92 to 3.70)	-	1.348E24 (0.00 to NE)	-	2.70 (0.18 to 39.70)
p-value for Odds Ratio	-	0.086	-	0.985	-	0.445
Peto Odds Ratio (95% CI) vs placebo	-	1.42 (0.78 to 2.57)	-	12.53 (1.49 to 105.27)	-	1.19 (0.22 to 6.55)
Reversed Peto Odds Ratio (95% CI)	-	0.70 (0.39 to 1.28)	-	0.08 (0.01 to 0.67)	-	0.84 (0.15 to 4.55)

[a] Patients who met the corresponding criterion are considered as responders. Patients who did not meet the criterion or had missing value are considered as non-responders. OR, RR and RD are derived from a logistic regression model with treatment, age, weight group, region, baseline eosinophil level, baseline FeNO level, baseline ICS dose level, and baseline PAQLQ(S)-IA global score as covariates.
Peto OR calculation is based on Yusuf S et al. (Prog Cardiovasc Dis. 1985 Mar-Apr;27(5):335-71) and its p-value is derived using a normal approximation.
p-values for heterogeneity are estimated by using the same logistic model as the one used to estimate OR, RR and RD, with subgroup and treatment-by-subgroup interaction as additional covariates.
p-value for heterogeneity of Peto OR is estimated by using normal approximation.
Only patients of age >=7 years old at randomization are included in the analysis.
PGM=DEVOPS/SAR231893/EFC14153/CSR_RWE/REPORT/PGM/eff_pro_evt_ger_subg_i_t.sas OUT=REPORT/OUTPUT/eff_pro_aqlqaw52_ger_race_t2_t_x.rtf (29JUN2021 - 17:47)

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

Project Code / Study Number / Analysis: SAR231893 / EFC14153 / CSR_RWE

2 PRO endpoints

2.3 Responder analysis for change from baseline in PAQLQ(S)-IA global score (improvement >= 0.5) at week 52 - ITT type 2 inflammatory asthma phenotype population

2.3.3 By race (Caucasian/white, Black/of African descent, Other)

	Race					
	Caucasian/White		Black/of African descent		Other	
Type 2 inflammatory asthma phenotype population	**Placebo (N=95)**	**Dupilumab (N=183)**	**Placebo (N=5)**	**Dupilumab (N=9)**	**Placebo (N=7)**	**Dupilumab (N=19)**
p-value for Peto Odds Ratio		0.248		0.020		0.841
p-value for heterogeneity of Peto Odds Ratio:						
Caucasian/White, Black/of African descent						0.054
Caucasian/White, Other						0.848
Black/of African descent, Other						0.091
overall						0.145
Risk Ratio (95% CI) vs placebo	-	1.11 (0.95 to 1.30)	-	10.51 (0.00 to 3.3313E9)	-	0.00 (NE to NE)

[a] Patients who met the corresponding criterion are considered as responders. Patients who did not meet the criterion or had missing value are considered as non-responders.
OR, RR and RD are derived from a logistic regression model with treatment, age, weight group, region, baseline eosinophil level, baseline FeNO level, baseline ICS dose level, and baseline PAQLQ(S)-IA global score as covariates.
Peto OR calculation is based on Yusuf S et al. (Prog Cardiovasc Dis. 1985 Mar-Apr;27(5):335-71) and its p-value is derived using a normal approximation.
p-values for heterogeneity are estimated by using the same logistic model as the one used to estimate OR, RR and RD, with subgroup and treatment-by-subgroup interaction as additional covariates.
p-value for heterogeneity of Peto OR is estimated by using normal approximation.
Only patients of age >=7 years old at randomization are included in the analysis.
PGM=DEVOPS/SAR231893/EFC14153/CSR_RWE/REPORT/PGM/eff_pro_evt_ger_subg_i_t.sas OUT=REPORT/OUTPUT/eff_pro_aqlqaw52_ger_race_t2_t_x.rtf (29JUN2021 - 17:47)

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

Project Code / Study Number / Analysis: SAR231893 / EFC14153 / CSR_RWE

2 PRO endpoints

2.3 Responder analysis for change from baseline in PAQLQ(S)-IA global score (improvement >= 0.5) at week 52 - ITT type 2 inflammatory asthma phenotype population

2.3.3 By race (Caucasian/white, Black/of African descent, Other)

	Race					
	Caucasian/White		Black/of African descent		Other	
Type 2 inflammatory asthma phenotype population	**Placebo (N=95)**	**Dupilumab (N=183)**	**Placebo (N=5)**	**Dupilumab (N=9)**	**Placebo (N=7)**	**Dupilumab (N=19)**
Reversed Risk ratio (95% CI) vs placebo	-	0.90 (0.77 to 1.05)	-	0.10 (0.00 to 30132616)		
p-value for Risk Ratio	-	0.184	-	0.755	-	<0.001
p-value for heterogeneity of Risk Ratio:						
Caucasian/White, Black/of African descent						0.962
Caucasian/White, Other						0.748
Black/of African descent, Other						0.963
overall						0.948

[a] Patients who met the corresponding criterion are considered as responders. Patients who did not meet the criterion or had missing value are considered as non-responders.
OR, RR and RD are derived from a logistic regression model with treatment, age, weight group, region, baseline eosinophil level, baseline FeNO level, baseline ICS dose level, and baseline PAQLQ(S)-IA global score as covariates.
Peto OR calculation is based on Yusuf S et al. (Prog Cardiovasc Dis. 1985 Mar-Apr;27(5):335-71) and its p-value is derived using a normal approximation.
p-values for heterogeneity are estimated by using the same logistic model as the one used to estimate OR, RR and RD, with subgroup and treatment-by-subgroup interaction as additional covariates.
p-value for heterogeneity of Peto OR is estimated by using normal approximation.
Only patients of age >=7 years old at randomization are included in the analysis.
PGM=DEVOPS/SAR231893/EFC14153/CSR_RWE/REPORT/PGM/eff_pro_evt_ger_subg_i_t.sas OUT=REPORT/OUTPUT/eff_pro_aqlqaw52_ger_race_t2_t_x.rtf (29JUN2021 - 17:47)

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

Project Code / Study Number / Analysis: SAR231893 / EFC14153 / CSR_RWE

2 PRO endpoints

2.3 Responder analysis for change from baseline in PAQLQ(S)-IA global score (improvement >= 0.5) at week 52 - ITT type 2 inflammatory asthma phenotype population

2.3.3 By race (Caucasian/white, Black/of African descent, Other)

	Race					
	Caucasian/White		Black/of African descent		Other	
Type 2 inflammatory asthma phenotype population	**Placebo (N=95)**	**Dupilumab (N=183)**	**Placebo (N=5)**	**Dupilumab (N=9)**	**Placebo (N=7)**	**Dupilumab (N=19)**
Risk Difference (95% CI) vs placebo	-	7.43 (-3.81 to 18.67)	-	66.55 (-604.74 to 737.84)	-	14.70 (-42.54 to 71.93)
p-value for Risk Difference	-	0.194	-	0.797	-	0.594
p-value for heterogeneity of Risk Difference:						
Caucasian/White, Black/of African descent						0.550
Caucasian/White, Other						0.965
Black/of African descent, Other						0.563
overall						0.835

[a] Patients who met the corresponding criterion are considered as responders. Patients who did not meet the criterion or had missing value are considered as non-responders.
OR, RR and RD are derived from a logistic regression model with treatment, age, weight group, region, baseline eosinophil level, baseline FeNO level, baseline ICS dose level, and baseline PAQLQ(S)-IA global score as covariates.
Peto OR calculation is based on Yusuf S et al. (Prog Cardiovasc Dis. 1985 Mar-Apr;27(5):335-71) and its p-value is derived using a normal approximation.
p-values for heterogeneity are estimated by using the same logistic model as the one used to estimate OR, RR and RD, with subgroup and treatment-by-subgroup interaction as additional covariates.
p-value for heterogeneity of Peto OR is estimated by using normal approximation.
Only patients of age >=7 years old at randomization are included in the analysis.
PGM=DEVOPS/SAR231893/EFC14153/CSR_RWE/REPORT/PGM/eff_pro_evt_ger_subg_i_t.sas OUT=REPORT/OUTPUT/eff_pro_aqlqaw52_ger_race_t2_t_x.rtf (29JUN2021 - 17:47)

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

Project Code / Study Number / Analysis: SAR231893 / EFC14153 / CSR_RWE

2 PRO endpoints

2.3 Responder analysis for change from baseline in PAQLQ(S)-IA global score (improvement >= 0.5) at week 52 - ITT type 2 inflammatory asthma phenotype population

2.3.4 By baseline ICS dose level (Medium, High)

	Baseline ICS dose level			
	High		Medium	
Type 2 inflammatory asthma phenotype population	**Placebo (N=45)**	**Dupilumab (N=92)**	**Placebo (N=62)**	**Dupilumab (N=118)**
Responder status at Week 52 based on change from baseline in PAQLQ(S)-IA global score >=0.5 [n(%)] [a]				
Responder	28 (62.2%)	66 (71.7%)	45 (72.6%)	95 (80.5%)
Non-responder	17 (37.8%)	26 (28.3%)	17 (27.4%)	23 (19.5%)
Odds Ratio (95% CI) vs placebo	-	2.03 (0.79 to 5.22)	-	2.09 (0.87 to 5.01)
p-value for Odds Ratio	-	0.139	-	0.097
p-value for heterogeneity of Odds Ratio				0.882
Risk Ratio (95% CI) vs placebo	-	1.16 (0.89 to 1.51)	-	1.14 (0.95 to 1.36)

[a] Patients who met the corresponding criterion are considered as responders. Patients who did not meet the criterion or had missing value are considered as non-responders.
OR, RR and RD are derived from a logistic regression model with treatment, age, weight group, region, baseline eosinophil level, baseline FeNO level and baseline PAQLQ(S)-IA global score as covariates.
Peto OR calculation is based on Yusuf S et al. (Prog Cardiovasc Dis. 1985 Mar-Apr;27(5):335-71) and its p-value is derived using a normal approximation.
p-values for heterogeneity are estimated by using the same logistic model as the one used to estimate OR, RR and RD, with subgroup and treatment-by-subgroup interaction as additional covariates.
p-value for heterogeneity of Peto OR is estimated by using normal approximation.
Only patients of age >=7 years old at randomization are included in the analysis.
PGM=DEVOPS/SAR231893/EFC14153/CSR_RWE/REPORT/PGM/eff_pro_evt_ger_subg_i_t.sas OUT=REPORT/OUTPUT/eff_pro_aqlqaw52_ger_ics_t2_t_x.rtf (29JUN2021 - 17:47)

Project Code / Study Number / Analysis: SAR231893 / EFC14153 / CSR_RWE

2 PRO endpoints

2.3 Responder analysis for change from baseline in PAQLQ(S)-IA global score (improvement >= 0.5) at week 52 - ITT type 2 inflammatory asthma phenotype population

2.3.4 By baseline ICS dose level (Medium, High)

	Baseline ICS dose level			
	High		Medium	
Type 2 inflammatory asthma phenotype population	**Placebo (N=45)**	**Dupilumab (N=92)**	**Placebo (N=62)**	**Dupilumab (N=118)**
Reversed Risk ratio (95% CI) vs placebo	-	0.86 (0.66 to 1.12)	-	0.88 (0.74 to 1.05)
p-value for Risk Ratio	-	0.260	-	0.152
p-value for heterogeneity of Risk Ratio				0.857
Risk Difference (95% CI) vs placebo	-	10.80 (-6.21 to 27.82)	-	10.27 (-2.76 to 23.31)
p-value for Risk Difference	-	0.211	-	0.122
p-value for heterogeneity of Risk Difference				0.998

[a] Patients who met the corresponding criterion are considered as responders. Patients who did not meet the criterion or had missing value are considered as non-responders.
OR, RR and RD are derived from a logistic regression model with treatment, age, weight group, region, baseline eosinophil level, baseline FeNO level and baseline PAQLQ(S)-IA global score as covariates.
Peto OR calculation is based on Yusuf S et al. (Prog Cardiovasc Dis. 1985 Mar-Apr;27(5):335-71) and its p-value is derived using a normal approximation.
p-values for heterogeneity are estimated by using the same logistic model as the one used to estimate OR, RR and RD, with subgroup and treatment-by-subgroup interaction as additional covariates.
p-value for heterogeneity of Peto OR is estimated by using normal approximation.
Only patients of age >=7 years old at randomization are included in the analysis.
PGM=DEVOPS/SAR231893/EFC14153/CSR_RWE/REPORT/PGM/eff_pro_evt_ger_subg_i_t.sas OUT=REPORT/OUTPUT/eff_pro_aqlqaw52_ger_ics_t2_t_x.rtf (29JUN2021 - 17:47)

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

Project Code / Study Number / Analysis: SAR231893 / EFC14153 / CSR_RWE

2 PRO endpoints

2.3 Responder analysis for change from baseline in PAQLQ(S)-IA global score (improvement >= 0.5) at week 52 - ITT type 2 inflammatory asthma phenotype population

2.3.5 By baseline ICS dose level 2 (Medium, High)

	Baseline ICS dose level 2			
	High		Medium	
Type 2 inflammatory asthma phenotype population	**Placebo (N=88)**	**Dupilumab (N=182)**	**Placebo (N=19)**	**Dupilumab (N=29)**
Responder status at Week 52 based on change from baseline in PAQLQ(S)-IA global score >=0.5 [n(%)] [a]				
Responder	59 (67.0%)	141 (77.5%)	14 (73.7%)	20 (69.0%)
Non-responder	29 (33.0%)	41 (22.5%)	5 (26.3%)	9 (31.0%)
Odds Ratio (95% CI) vs placebo	-	2.17 (1.12 to 4.20)	-	0.71 (0.08 to 6.62)
p-value for Odds Ratio	-	0.022	-	0.758
p-value for heterogeneity of Odds Ratio				0.256
Risk Ratio (95% CI) vs placebo	-	1.19 (1.02 to 1.40)	-	1.06 (0.38 to 2.98)

[a] Patients who met the corresponding criterion are considered as responders. Patients who did not meet the criterion or had missing value are considered as non-responders.
OR, RR and RD are derived from a logistic regression model with treatment, age, weight group, region, baseline eosinophil level, baseline FeNO level and baseline PAQLQ(S)-IA global score as covariates.
Peto OR calculation is based on Yusuf S et al. (Prog Cardiovasc Dis. 1985 Mar-Apr;27(5):335-71) and its p-value is derived using a normal approximation.
p-values for heterogeneity are estimated by using the same logistic model as the one used to estimate OR, RR and RD, with subgroup and treatment-by-subgroup interaction as additional covariates.
p-value for heterogeneity of Peto OR is estimated by using normal approximation.
Only patients of age >=7 years old at randomization are included in the analysis.
PGM=DEVOPS/SAR231893/EFC14153/CSR_RWE/REPORT/PGM/eff_pro_evt_ger_subg_i_t.sas OUT=REPORT/OUTPUT/eff_pro_aqlqaw52_ger_ics2_t2_t_x.rtf (01SEP2021 - 15:26)

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

Project Code / Study Number / Analysis: SAR231893 / EFC14153 / CSR_RWE

2 PRO endpoints

2.3 Responder analysis for change from baseline in PAQLQ(S)-IA global score (improvement >= 0.5) at week 52 - ITT type 2 inflammatory asthma phenotype population

2.3.5 By baseline ICS dose level 2 (Medium, High)

	Baseline ICS dose level 2			
	High		Medium	
Type 2 inflammatory asthma phenotype population	**Placebo (N=88)**	**Dupilumab (N=182)**	**Placebo (N=19)**	**Dupilumab (N=29)**
Reversed Risk ratio (95% CI) vs placebo	-	0.84 (0.71 to 0.98)	-	0.95 (0.34 to 2.66)
p-value for Risk Ratio	-	0.030	-	0.913
p-value for heterogeneity of Risk Ratio				0.579
Risk Difference (95% CI) vs placebo	-	13.39 (2.51 to 24.27)	-	4.86 (-43.47 to 53.18)
p-value for Risk Difference	-	0.016	-	0.840
p-value for heterogeneity of Risk Difference				0.402

[a] Patients who met the corresponding criterion are considered as responders. Patients who did not meet the criterion or had missing value are considered as non-responders.
OR, RR and RD are derived from a logistic regression model with treatment, age, weight group, region, baseline eosinophil level, baseline FeNO level and baseline PAQLQ(S)-IA global score as covariates.
Peto OR calculation is based on Yusuf S et al. (Prog Cardiovasc Dis. 1985 Mar-Apr;27(5):335-71) and its p-value is derived using a normal approximation.
p-values for heterogeneity are estimated by using the same logistic model as the one used to estimate OR, RR and RD, with subgroup and treatment-by-subgroup interaction as additional covariates.
p-value for heterogeneity of Peto OR is estimated by using normal approximation.
Only patients of age >=7 years old at randomization are included in the analysis.
PGM=DEVOPS/SAR231893/EFC14153/CSR_RWE/REPORT/PGM/eff_pro_evt_ger_subg_i_t.sas OUT=REPORT/OUTPUT/eff_pro_aqlqaw52_ger_ics2_t2_t_x.rtf (01SEP2021 - 15:26)

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

Project Code / Study Number / Analysis: SAR231893 / EFC14153 / CSR_RWE

2 PRO endpoints

2.3 Responder analysis for change from baseline in PAQLQ(S)-IA global score (improvement >= 0.5) at week 52 - ITT type 2 inflammatory asthma phenotype population

2.3.6 By baseline predicted FEV1 (<80%, >=80%)

	Baseline Predicted FEV1			
	<80%		>=80%	
Type 2 inflammatory asthma phenotype population	**Placebo (N=59)**	**Dupilumab (N=98)**	**Placebo (N=48)**	**Dupilumab (N=113)**
Responder status at Week 52 based on change from baseline in PAQLQ(S)-IA global score >=0.5 [n(%)] [a]				
Responder	38 (64.4%)	79 (80.6%)	35 (72.9%)	82 (72.6%)
Non-responder	21 (35.6%)	19 (19.4%)	13 (27.1%)	31 (27.4%)
Odds Ratio (95% CI) vs placebo	-	2.93 (1.17 to 7.34)	-	1.25 (0.48 to 3.23)
p-value for Odds Ratio	-	0.023	-	0.643
p-value for heterogeneity of Odds Ratio				0.109
Risk Ratio (95% CI) vs placebo	-	1.32 (0.95 to 1.82)	-	0.97 (0.76 to 1.24)

[a] Patients who met the corresponding criterion are considered as responders. Patients who did not meet the criterion or had missing value are considered as non-responders.
OR, RR and RD are derived from a logistic regression model with treatment, age, weight group, region, baseline eosinophil level, baseline FeNO level, baseline ICS dose level, and baseline PAQLQ(S)-IA global score as covariates.
Peto OR calculation is based on Yusuf S et al. (Prog Cardiovasc Dis. 1985 Mar-Apr;27(5):335-71) and its p-value is derived using a normal approximation.
p-values for heterogeneity are estimated by using the same logistic model as the one used to estimate OR, RR and RD, with subgroup and treatment-by-subgroup interaction as additional covariates.
p-value for heterogeneity of Peto OR is estimated by using normal approximation.
Only patients of age >=7 years old at randomization are included in the analysis.
PGM=DEVOPS/SAR231893/EFC14153/CSR_RWE/REPORT/PGM/eff_pro_evt_ger_subg_i_t.sas OUT=REPORT/OUTPUT/eff_pro_aqlqaw52_ger_pfev1_t2_t_x.rtf (29JUN2021 - 17:47)

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

Project Code / Study Number / Analysis: SAR231893 / EFC14153 / CSR_RWE

2 PRO endpoints

2.3 Responder analysis for change from baseline in PAQLQ(S)-IA global score (improvement >= 0.5) at week 52 - ITT type 2 inflammatory asthma phenotype population

2.3.6 By baseline predicted FEV1 (<80%, >=80%)

	Baseline Predicted FEV1			
	<80%		>=80%	
Type 2 inflammatory asthma phenotype population	**Placebo (N=59)**	**Dupilumab (N=98)**	**Placebo (N=48)**	**Dupilumab (N=113)**
Reversed Risk ratio (95% CI) vs placebo	-	0.76 (0.55 to 1.05)		
p-value for Risk Ratio	-	0.097	-	0.814
p-value for heterogeneity of Risk Ratio				0.089
Risk Difference (95% CI) vs placebo	-	20.53 (2.84 to 38.21)	-	-1.41 (-17.11 to 14.29)
p-value for Risk Difference	-	0.023	-	0.859
p-value for heterogeneity of Risk Difference				0.055

[a] Patients who met the corresponding criterion are considered as responders. Patients who did not meet the criterion or had missing value are considered as non-responders.
OR, RR and RD are derived from a logistic regression model with treatment, age, weight group, region, baseline eosinophil level, baseline FeNO level, baseline ICS dose level, and baseline PAQLQ(S)-IA global score as covariates.
Peto OR calculation is based on Yusuf S et al. (Prog Cardiovasc Dis. 1985 Mar-Apr;27(5):335-71) and its p-value is derived using a normal approximation.
p-values for heterogeneity are estimated by using the same logistic model as the one used to estimate OR, RR and RD, with subgroup and treatment-by-subgroup interaction as additional covariates.
p-value for heterogeneity of Peto OR is estimated by using normal approximation.
Only patients of age >=7 years old at randomization are included in the analysis.
PGM=DEVOPS/SAR231893/EFC14153/CSR_RWE/REPORT/PGM/eff_pro_evt_ger_subg_i_t.sas OUT=REPORT/OUTPUT/eff_pro_aqlqaw52_ger_pfev1_t2_t_x.rtf (29JUN2021 - 17:47)

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

Project Code / Study Number / Analysis: SAR231893 / EFC14153 / CSR_RWE

2 PRO endpoints

2.3 Responder analysis for change from baseline in PAQLQ(S)-IA global score (improvement >= 0.5) at week 52 - ITT type 2 inflammatory asthma phenotype population

2.3.7 By baseline ACQ-7-IA (<=2, >2)

	Baseline ACQ-7-IA			
	<=2		**>2**	
Type 2 inflammatory asthma phenotype population	**Placebo (N=58)**	**Dupilumab (N=116)**	**Placebo (N=49)**	**Dupilumab (N=95)**
Responder status at Week 52 based on change from baseline in PAQLQ(S)-IA global score >=0.5 [n(%)] [a]				
Responder	37 (63.8%)	82 (70.7%)	36 (73.5%)	79 (83.2%)
Non-responder	21 (36.2%)	34 (29.3%)	13 (26.5%)	16 (16.8%)
Odds Ratio (95% CI) vs placebo	-	1.52 (0.67 to 3.45)	-	2.43 (0.87 to 6.80)
p-value for Odds Ratio	-	0.317	-	0.090
p-value for heterogeneity of Odds Ratio				0.402
Risk Ratio (95% CI) vs placebo	-	1.11 (0.84 to 1.46)	-	1.20 (0.89 to 1.61)

[a] Patients who met the corresponding criterion are considered as responders. Patients who did not meet the criterion or had missing value are considered as non-responders.
OR, RR and RD are derived from a logistic regression model with treatment, age, weight group, region, baseline eosinophil level, baseline FeNO level, baseline ICS dose level, and baseline PAQLQ(S)-IA global score as covariates.
Peto OR calculation is based on Yusuf S et al. (Prog Cardiovasc Dis. 1985 Mar-Apr;27(5):335-71) and its p-value is derived using a normal approximation.
p-values for heterogeneity are estimated by using the same logistic model as the one used to estimate OR, RR and RD, with subgroup and treatment-by-subgroup interaction as additional covariates.
p-value for heterogeneity of Peto OR is estimated by using normal approximation.
Only patients of age >=7 years old at randomization are included in the analysis.
PGM=DEVOPS/SAR231893/EFC14153/CSR_RWE/REPORT/PGM/eff_pro_evt_ger_subg_i_t.sas OUT=REPORT/OUTPUT/eff_pro_aqlqaw52_ger_acq7_t2_t_x.rtf (29JUN2021 - 17:48)

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

Project Code / Study Number / Analysis: SAR231893 / EFC14153 / CSR_RWE

2 PRO endpoints

2.3 Responder analysis for change from baseline in PAQLQ(S)-IA global score (improvement >= 0.5) at week 52 - ITT type 2 inflammatory asthma phenotype population

2.3.7 By baseline ACQ-7-IA (<=2, >2)

	Baseline ACQ-7-IA			
	<=2		>2	
Type 2 inflammatory asthma phenotype population	**Placebo (N=58)**	**Dupilumab (N=116)**	**Placebo (N=49)**	**Dupilumab (N=95)**
Reversed Risk ratio (95% CI) vs placebo	-	0.90 (0.69 to 1.19)	-	0.83 (0.62 to 1.12)
p-value for Risk Ratio	-	0.471	-	0.223
p-value for heterogeneity of Risk Ratio				0.574
Risk Difference (95% CI) vs placebo	-	5.91 (-11.25 to 23.07)	-	14.31 (-2.32 to 30.93)
p-value for Risk Difference	-	0.498	-	0.091
p-value for heterogeneity of Risk Difference				0.516

[a] Patients who met the corresponding criterion are considered as responders. Patients who did not meet the criterion or had missing value are considered as non-responders.
OR, RR and RD are derived from a logistic regression model with treatment, age, weight group, region, baseline eosinophil level, baseline FeNO level, baseline ICS dose level, and baseline PAQLQ(S)-IA global score as covariates.
Peto OR calculation is based on Yusuf S et al. (Prog Cardiovasc Dis. 1985 Mar-Apr;27(5):335-71) and its p-value is derived using a normal approximation.
p-values for heterogeneity are estimated by using the same logistic model as the one used to estimate OR, RR and RD, with subgroup and treatment-by-subgroup interaction as additional covariates.
p-value for heterogeneity of Peto OR is estimated by using normal approximation.
Only patients of age >=7 years old at randomization are included in the analysis.
PGM=DEVOPS/SAR231893/EFC14153/CSR_RWE/REPORT/PGM/eff_pro_evt_ger_subg_i_t.sas OUT=REPORT/OUTPUT/eff_pro_aqlqaw52_ger_acq7_t2_t_x.rtf (29JUN2021 - 17:48)

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

Project Code / Study Number / Analysis: SAR231893 / EFC14153 / CSR_RWE

2 PRO endpoints

2.3 Responder analysis for change from baseline in PAQLQ(S)-IA global score (improvement >= 0.5) at week 52 - ITT type 2 inflammatory asthma phenotype population

2.3.8 By baseline weight (<=30 kg, >30 kg)

	Baseline weight (kg)			
	<=30		>30	
Type 2 inflammatory asthma phenotype population	**Placebo (N=29)**	**Dupilumab (N=56)**	**Placebo (N=78)**	**Dupilumab (N=155)**
Responder status at Week 52 based on change from baseline in PAQLQ(S)-IA global score >=0.5 [n(%)] [a]				
Responder	20 (69.0%)	42 (75.0%)	53 (67.9%)	119 (76.8%)
Non-responder	9 (31.0%)	14 (25.0%)	25 (32.1%)	36 (23.2%)
Odds Ratio (95% CI) vs placebo	-	1.36 (0.38 to 4.87)	-	2.33 (1.09 to 5.01)
p-value for Odds Ratio	-	0.631	-	0.030
p-value for heterogeneity of Odds Ratio				0.602
Risk Ratio (95% CI) vs placebo	-	1.10 (0.61 to 1.98)	-	1.19 (0.98 to 1.45)

[a] Patients who met the corresponding criterion are considered as responders. Patients who did not meet the criterion or had missing value are considered as non-responders.
OR, RR and RD are derived from a logistic regression model with treatment, age, region, baseline eosinophil level, baseline FeNO level, baseline ICS dose level, and baseline PAQLQ(S)-IA global score as covariates.
Peto OR calculation is based on Yusuf S et al. (Prog Cardiovasc Dis. 1985 Mar-Apr;27(5):335-71) and its p-value is derived using a normal approximation.
p-values for heterogeneity are estimated by using the same logistic model as the one used to estimate OR, RR and RD, with subgroup and treatment-by-subgroup interaction as additional covariates.
p-value for heterogeneity of Peto OR is estimated by using normal approximation.
Only patients of age >=7 years old at randomization are included in the analysis.
PGM=DEVOPS/SAR231893/EFC14153/CSR_RWE/REPORT/PGM/eff_pro_evt_ger_subg_i_t.sas OUT=REPORT/OUTPUT/eff_pro_aqlqaw52_ger_wgt_t2_t_x.rtf (29JUN2021 - 17:48)

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

Project Code / Study Number / Analysis: SAR231893 / EFC14153 / CSR_RWE

2 PRO endpoints

2.3 Responder analysis for change from baseline in PAQLQ(S)-IA global score (improvement >= 0.5) at week 52 - ITT type 2 inflammatory asthma phenotype population

2.3.8 By baseline weight (<=30 kg, >30 kg)

	Baseline weight (kg)			
	<=30		>30	
Type 2 inflammatory asthma phenotype population	**Placebo (N=29)**	**Dupilumab (N=56)**	**Placebo (N=78)**	**Dupilumab (N=155)**
Reversed Risk ratio (95% CI) vs placebo	-	0.91 (0.50 to 1.63)	-	0.84 (0.69 to 1.02)
p-value for Risk Ratio	-	0.743	-	0.082
p-value for heterogeneity of Risk Ratio				0.771
Risk Difference (95% CI) vs placebo	-	7.17 (-18.91 to 33.25)	-	14.03 (1.05 to 27.01)
p-value for Risk Difference	-	0.585	-	0.034
p-value for heterogeneity of Risk Difference				0.947

[a] Patients who met the corresponding criterion are considered as responders. Patients who did not meet the criterion or had missing value are considered as non-responders. OR, RR and RD are derived from a logistic regression model with treatment, age, region, baseline eosinophil level, baseline FeNO level, baseline ICS dose level, and baseline PAQLQ(S)-IA global score as covariates.
Peto OR calculation is based on Yusuf S et al. (Prog Cardiovasc Dis. 1985 Mar-Apr;27(5):335-71) and its p-value is derived using a normal approximation.
p-values for heterogeneity are estimated by using the same logistic model as the one used to estimate OR, RR and RD, with subgroup and treatment-by-subgroup interaction as additional covariates.
p-value for heterogeneity of Peto OR is estimated by using normal approximation.
Only patients of age >=7 years old at randomization are included in the analysis.
PGM=DEVOPS/SAR231893/EFC14153/CSR_RWE/REPORT/PGM/eff_pro_evt_ger_subg_i_t.sas OUT=REPORT/OUTPUT/eff_pro_aqlqaw52_ger_wgt_t2_t_x.rtf (29JUN2021 - 17:48)

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

Project Code / Study Number / Analysis: SAR231893 / EFC14153 / CSR_RWE

2 PRO endpoints

2.3 Responder analysis for change from baseline in PAQLQ(S)-IA global score (improvement >= 0.5) at week 52 - ITT type 2 inflammatory asthma phenotype population

2.3.9 By atopic medical condition (Yes, No)

	Atopic medical condition			
	Yes		No	
Type 2 inflammatory asthma phenotype population	**Placebo (N=97)**	**Dupilumab (N=205)**	**Placebo (N=10)**	**Dupilumab (N=6)**
Responder status at Week 52 based on change from baseline in PAQLQ(S)-IA global score >=0.5 [n(%)] [a]				
Responder	65 (67.0%)	155 (75.6%)	8 (80.0%)	6 (100%)
Non-responder	32 (33.0%)	50 (24.4%)	2 (20.0%)	0
Odds Ratio (95% CI) vs placebo	-	1.92 (1.01 to 3.64)	-	1413073 (0.00 to NE)
p-value for Odds Ratio	-	0.046	-	0.995
Peto Odds Ratio (95% CI) vs placebo	-	1.54 (0.90 to 2.65)	-	5.55 (0.29 to 107.50)
Reversed Peto Odds Ratio (95% CI)	-	0.65 (0.38 to 1.11)	-	0.18 (0.01 to 3.45)
p-value for Peto Odds Ratio		0.117		0.257

[a] Patients who met the corresponding criterion are considered as responders. Patients who did not meet the criterion or had missing value are considered as non-responders.
OR, RR and RD are derived from a logistic regression model with treatment, age, weight group, region, baseline eosinophil level, baseline FeNO level, baseline ICS dose level, and baseline PAQLQ(S)-IA global score as covariates.
Peto OR calculation is based on Yusuf S et al. (Prog Cardiovasc Dis. 1985 Mar-Apr;27(5):335-71) and its p-value is derived using a normal approximation.
p-values for heterogeneity are estimated by using the same logistic model as the one used to estimate OR, RR and RD, with subgroup and treatment-by-subgroup interaction as additional covariates.
p-value for heterogeneity of Peto OR is estimated by using normal approximation.
Only patients of age >=7 years old at randomization are included in the analysis.
PGM=DEVOPS/SAR231893/EFC14153/CSR_RWE/REPORT/PGM/eff_pro_evt_ger_subg_i_t.sas OUT=REPORT/OUTPUT/eff_pro_aqlqaw52_ger_amc_t2_t_x.rtf (29JUN2021 - 17:48)

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

Project Code / Study Number / Analysis: SAR231893 / EFC14153 / CSR_RWE

2 PRO endpoints

2.3 Responder analysis for change from baseline in PAQLQ(S)-IA global score (improvement >= 0.5) at week 52 - ITT type 2 inflammatory asthma phenotype population

2.3.9 By atopic medical condition (Yes, No)

	Atopic medical condition			
	Yes		No	
Type 2 inflammatory asthma phenotype population	**Placebo (N=97)**	**Dupilumab (N=205)**	**Placebo (N=10)**	**Dupilumab (N=6)**
p-value for heterogeneity of Peto Odds Ratio				0.405
Risk Ratio (95% CI) vs placebo	-	1.19 (1.02 to 1.39)	-	1.40 (NE to NE)
Reversed Risk ratio (95% CI) vs placebo	-	0.84 (0.72 to 0.98)	-	0.72 (NE to NE)
p-value for Risk Ratio	-	0.027	-	<0.001
p-value for heterogeneity of Risk Ratio				<0.001
Risk Difference (95% CI) vs placebo	-	12.14 (1.98 to 22.30)	-	41.15 (-214.48 to 296.78)
p-value for Risk Difference	-	0.019	-	0.707
p-value for heterogeneity of Risk Difference				0.915

[a] Patients who met the corresponding criterion are considered as responders. Patients who did not meet the criterion or had missing value are considered as non-responders.
OR, RR and RD are derived from a logistic regression model with treatment, age, weight group, region, baseline eosinophil level, baseline FeNO level, baseline ICS dose level, and baseline PAQLQ(S)-IA global score as covariates.
Peto OR calculation is based on Yusuf S et al. (Prog Cardiovasc Dis. 1985 Mar-Apr;27(5):335-71) and its p-value is derived using a normal approximation.
p-values for heterogeneity are estimated by using the same logistic model as the one used to estimate OR, RR and RD, with subgroup and treatment-by-subgroup interaction as additional covariates.
p-value for heterogeneity of Peto OR is estimated by using normal approximation.
Only patients of age >=7 years old at randomization are included in the analysis.
PGM=DEVOPS/SAR231893/EFC14153/CSR_RWE/REPORT/PGM/eff_pro_evt_ger_subg_i_t.sas OUT=REPORT/OUTPUT/eff_pro_aqlqaw52_ger_amc_t2_t_x.rtf (29JUN2021 - 17:48)

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

Project Code / Study Number / Analysis: SAR231893 / EFC14153 / CSR_RWE

2 PRO endpoints

2.3 Responder analysis for change from baseline in PAQLQ(S)-IA global score (improvement >= 0.5) at week 52 - ITT type 2 inflammatory asthma phenotype population

2.3.10 By baseline total IgE (<median, >= median)

	Baseline Total IgE (IU/mL)			
	<median		>=median	
Type 2 inflammatory asthma phenotype population	**Placebo (N=61)**	**Dupilumab (N=90)**	**Placebo (N=45)**	**Dupilumab (N=116)**
Responder status at Week 52 based on change from baseline in PAQLQ(S)-IA global score >=0.5 [n(%)] [a]				
Responder	43 (70.5%)	72 (80.0%)	29 (64.4%)	87 (75.0%)
Non-responder	18 (29.5%)	18 (20.0%)	16 (35.6%)	29 (25.0%)
Odds Ratio (95% CI) vs placebo	-	2.81 (1.06 to 7.50)	-	1.63 (0.67 to 3.98)
p-value for Odds Ratio	-	0.039	-	0.281
p-value for heterogeneity of Odds Ratio				0.330
Risk Ratio (95% CI) vs placebo	-	1.25 (0.92 to 1.70)	-	1.31 (0.93 to 1.83)

[a] Patients who met the corresponding criterion are considered as responders. Patients who did not meet the criterion or had missing value are considered as non-responders.
OR, RR and RD are derived from a logistic regression model with treatment, age, weight group, region, baseline eosinophil level, baseline FeNO level, baseline ICS dose level, and baseline PAQLQ(S)-IA global score as covariates.
Peto OR calculation is based on Yusuf S et al. (Prog Cardiovasc Dis. 1985 Mar-Apr;27(5):335-71) and its p-value is derived using a normal approximation.
p-values for heterogeneity are estimated by using the same logistic model as the one used to estimate OR, RR and RD, with subgroup and treatment-by-subgroup interaction as additional covariates.
p-value for heterogeneity of Peto OR is estimated by using normal approximation.
Only patients of age >=7 years old at randomization are included in the analysis.
PGM=DEVOPS/SAR231893/EFC14153/CSR_RWE/REPORT/PGM/eff_pro_evt_ger_subg_i_t.sas OUT=REPORT/OUTPUT/eff_pro_aqlqaw52_ger_igem_t2_t_x.rtf (29JUN2021 - 17:49)

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

Project Code / Study Number / Analysis: SAR231893 / EFC14153 / CSR_RWE

2 PRO endpoints

2.3 Responder analysis for change from baseline in PAQLQ(S)-IA global score (improvement >= 0.5) at week 52 - ITT type 2 inflammatory asthma phenotype population

2.3.10 By baseline total IgE (<median, >= median)

	Baseline Total IgE (IU/mL)			
	<median		>=median	
Type 2 inflammatory asthma phenotype population	**Placebo (N=61)**	**Dupilumab (N=90)**	**Placebo (N=45)**	**Dupilumab (N=116)**
Reversed Risk ratio (95% CI) vs placebo	-	0.80 (0.59 to 1.08)	-	0.77 (0.55 to 1.08)
p-value for Risk Ratio	-	0.148	-	0.122
p-value for heterogeneity of Risk Ratio				0.800
Risk Difference (95% CI) vs placebo	-	18.17 (-0.09 to 36.43)	-	16.12 (-0.97 to 33.21)
p-value for Risk Difference	-	0.051	-	0.064
p-value for heterogeneity of Risk Difference				0.599

[a] Patients who met the corresponding criterion are considered as responders. Patients who did not meet the criterion or had missing value are considered as non-responders. OR, RR and RD are derived from a logistic regression model with treatment, age, weight group, region, baseline eosinophil level, baseline FeNO level, baseline ICS dose level, and baseline PAQLQ(S)-IA global score as covariates.
Peto OR calculation is based on Yusuf S et al. (Prog Cardiovasc Dis. 1985 Mar-Apr;27(5):335-71) and its p-value is derived using a normal approximation.
p-values for heterogeneity are estimated by using the same logistic model as the one used to estimate OR, RR and RD, with subgroup and treatment-by-subgroup interaction as additional covariates.
p-value for heterogeneity of Peto OR is estimated by using normal approximation.
Only patients of age >=7 years old at randomization are included in the analysis.
PGM=DEVOPS/SAR231893/EFC14153/CSR_RWE/REPORT/PGM/eff_pro_evt_ger_subg_i_t.sas OUT=REPORT/OUTPUT/eff_pro_aqlqaw52_ger_igem_t2_t_x.rtf (29JUN2021 - 17:49)

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

Project Code / Study Number / Analysis: SAR231893 / EFC14153 / CSR_RWE

2 PRO endpoints

2.3 Responder analysis for change from baseline in PAQLQ(S)-IA global score (improvement >= 0.5) at week 52 - ITT type 2 inflammatory asthma phenotype population

2.3.11 By baseline total IgE (<100 IU/ml, >= 100 IU/ml)

	Baseline Total IgE (IU/mL)			
	< 100		>= 100	
Type 2 inflammatory asthma phenotype population	**Placebo (N=19)**	**Dupilumab (N=24)**	**Placebo (N=87)**	**Dupilumab (N=182)**
Responder status at Week 52 based on change from baseline in PAQLQ(S)-IA global score >=0.5 [n(%)] [a]				
Responder	13 (68.4%)	21 (87.5%)	59 (67.8%)	138 (75.8%)
Non-responder	6 (31.6%)	3 (12.5%)	28 (32.2%)	44 (24.2%)
Odds Ratio (95% CI) vs placebo	-	6.78 (0.85 to 54.15)	-	1.72 (0.86 to 3.44)
p-value for Odds Ratio	-	0.070	-	0.123
p-value for heterogeneity of Odds Ratio				0.180
Risk Ratio (95% CI) vs placebo	-	1.42 (0.19 to 10.78)	-	1.15 (0.96 to 1.38)

[a] Patients who met the corresponding criterion are considered as responders. Patients who did not meet the criterion or had missing value are considered as non-responders.
OR, RR and RD are derived from a logistic regression model with treatment, age, weight group, region, baseline eosinophil level, baseline FeNO level, baseline ICS dose level, and baseline PAQLQ(S)-IA global score as covariates.
Peto OR calculation is based on Yusuf S et al. (Prog Cardiovasc Dis. 1985 Mar-Apr;27(5):335-71) and its p-value is derived using a normal approximation.
p-values for heterogeneity are estimated by using the same logistic model as the one used to estimate OR, RR and RD, with subgroup and treatment-by-subgroup interaction as additional covariates.
p-value for heterogeneity of Peto OR is estimated by using normal approximation.
Only patients of age >=7 years old at randomization are included in the analysis.
PGM=DEVOPS/SAR231893/EFC14153/CSR_RWE/REPORT/PGM/eff_pro_evt_ger_subg_i_t.sas OUT=REPORT/OUTPUT/eff_pro_aqlqaw52_ger_ige_t2_t_x.rtf (29JUN2021 - 17:49)

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

Project Code / Study Number / Analysis: SAR231893 / EFC14153 / CSR_RWE

2 PRO endpoints

2.3 Responder analysis for change from baseline in PAQLQ(S)-IA global score (improvement >= 0.5) at week 52 - ITT type 2 inflammatory asthma phenotype population

2.3.11 By baseline total IgE (<100 IU/ml, >= 100 IU/ml)

	Baseline Total IgE (IU/mL)			
	< 100		**>= 100**	
Type 2 inflammatory asthma phenotype population	**Placebo (N=19)**	**Dupilumab (N=24)**	**Placebo (N=87)**	**Dupilumab (N=182)**
Reversed Risk ratio (95% CI) vs placebo	-	0.70 (0.09 to 5.35)	-	0.87 (0.73 to 1.05)
p-value for Risk Ratio	-	0.727	-	0.137
p-value for heterogeneity of Risk Ratio				0.234
Risk Difference (95% CI) vs placebo	-	29.14 (-13.39 to 71.67)	-	9.55 (-1.93 to 21.04)
p-value for Risk Difference	-	0.172	-	0.103
p-value for heterogeneity of Risk Difference				0.146

[a] Patients who met the corresponding criterion are considered as responders. Patients who did not meet the criterion or had missing value are considered as non-responders.
OR, RR and RD are derived from a logistic regression model with treatment, age, weight group, region, baseline eosinophil level, baseline FeNO level, baseline ICS dose level, and baseline PAQLQ(S)-IA global score as covariates.
Peto OR calculation is based on Yusuf S et al. (Prog Cardiovasc Dis. 1985 Mar-Apr;27(5):335-71) and its p-value is derived using a normal approximation.
p-values for heterogeneity are estimated by using the same logistic model as the one used to estimate OR, RR and RD, with subgroup and treatment-by-subgroup interaction as additional covariates.
p-value for heterogeneity of Peto OR is estimated by using normal approximation.
Only patients of age >=7 years old at randomization are included in the analysis.
PGM=DEVOPS/SAR231893/EFC14153/CSR_RWE/REPORT/PGM/eff_pro_evt_ger_subg_i_t.sas OUT=REPORT/OUTPUT/eff_pro_aqlqaw52_ger_ige_t2_t_x.rtf (29JUN2021 - 17:49)

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

Project Code / Study Number / Analysis: SAR231893 / EFC14153 / CSR_RWE

2 PRO endpoints

2.3 Responder analysis for change from baseline in PAQLQ(S)-IA global score (improvement >= 0.5) at week 52 - ITT type 2 inflammatory asthma phenotype population

2.3.12 By age at onset of asthma (0-2, 3-5, >=6 years)

	Age of onset of asthma (years)					
	0-2		3-5		>= 6	
Type 2 inflammatory asthma phenotype population	**Placebo (N=36)**	**Dupilumab (N=89)**	**Placebo (N=36)**	**Dupilumab (N=77)**	**Placebo (N=35)**	**Dupilumab (N=45)**
Responder status at Week 52 based on change from baseline in PAQLQ(S)-IA global score >=0.5 [n(%)] [a]						
Responder	19 (52.8%)	69 (77.5%)	27 (75.0%)	54 (70.1%)	27 (77.1%)	38 (84.4%)
Non-responder	17 (47.2%)	20 (22.5%)	9 (25.0%)	23 (29.9%)	8 (22.9%)	7 (15.6%)
Odds Ratio (95% CI) vs placebo	-	3.34 (1.28 to 8.71)	-	1.15 (0.36 to 3.63)	-	2.49 (0.34 to 18.21)
p-value for Odds Ratio	-	0.014	-	0.812	-	0.364
p-value for heterogeneity of Odds Ratio:						
0-2, 3-5						0.122
0-2, >= 6						0.417

[a] Patients who met the corresponding criterion are considered as responders. Patients who did not meet the criterion or had missing value are considered as non-responders.
OR, RR and RD are derived from a logistic regression model with treatment, age, weight group, region, baseline eosinophil level, baseline FeNO level, baseline ICS dose level, and baseline PAQLQ(S)-IA global score as covariates.
Peto OR calculation is based on Yusuf S et al. (Prog Cardiovasc Dis. 1985 Mar-Apr;27(5):335-71) and its p-value is derived using a normal approximation.
p-values for heterogeneity are estimated by using the same logistic model as the one used to estimate OR, RR and RD, with subgroup and treatment-by-subgroup interaction as additional covariates.
p-value for heterogeneity of Peto OR is estimated by using normal approximation.
Only patients of age >=7 years old at randomization are included in the analysis.
PGM=DEVOPS/SAR231893/EFC14153/CSR_RWE/REPORT/PGM/eff_pro_evt_ger_subg_i_t.sas OUT=REPORT/OUTPUT/eff_pro_aqlqaw52_ger_onsa_t2_t_x.rtf (01SEP2021 - 15:27)

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

Project Code / Study Number / Analysis: SAR231893 / EFC14153 / CSR_RWE

2 PRO endpoints

2.3 Responder analysis for change from baseline in PAQLQ(S)-IA global score (improvement >= 0.5) at week 52 - ITT type 2 inflammatory asthma phenotype population

2.3.12 By age at onset of asthma (0-2, 3-5, >=6 years)

	Age of onset of asthma (years)					
	0-2		3-5		>= 6	
Type 2 inflammatory asthma phenotype population	**Placebo (N=36)**	**Dupilumab (N=89)**	**Placebo (N=36)**	**Dupilumab (N=77)**	**Placebo (N=35)**	**Dupilumab (N=45)**
3-5, >= 6						0.581
overall						0.296
Risk Ratio (95% CI) vs placebo	-	1.39 (0.94 to 2.08)	-	1.00 (0.69 to 1.43)	-	1.15 (0.41 to 3.22)
Reversed Risk ratio (95% CI) vs placebo	-	0.72 (0.48 to 1.07)			-	0.87 (0.31 to 2.43)
p-value for Risk Ratio	-	0.100	-	0.986	-	0.785
p-value for heterogeneity of Risk Ratio:						
0-2, 3-5						0.198
0-2, >= 6						0.402
3-5, >= 6						0.616

[a] Patients who met the corresponding criterion are considered as responders. Patients who did not meet the criterion or had missing value are considered as non-responders.
OR, RR and RD are derived from a logistic regression model with treatment, age, weight group, region, baseline eosinophil level, baseline FeNO level, baseline ICS dose level, and baseline PAQLQ(S)-IA global score as covariates.
Peto OR calculation is based on Yusuf S et al. (Prog Cardiovasc Dis. 1985 Mar-Apr;27(5):335-71) and its p-value is derived using a normal approximation.
p-values for heterogeneity are estimated by using the same logistic model as the one used to estimate OR, RR and RD, with subgroup and treatment-by-subgroup interaction as additional covariates.
p-value for heterogeneity of Peto OR is estimated by using normal approximation.
Only patients of age >=7 years old at randomization are included in the analysis.
PGM=DEVOPS/SAR231893/EFC14153/CSR_RWE/REPORT/PGM/eff_pro_evt_ger_subg_i_t.sas OUT=REPORT/OUTPUT/eff_pro_aqlqaw52_ger_onsa_t2_t_x.rtf (01SEP2021 - 15:27)

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

Project Code / Study Number / Analysis: SAR231893 / EFC14153 / CSR_RWE

2 PRO endpoints

2.3 Responder analysis for change from baseline in PAQLQ(S)-IA global score (improvement >= 0.5) at week 52 - ITT type 2 inflammatory asthma phenotype population

2.3.12 By age at onset of asthma (0-2, 3-5, >=6 years)

	Age of onset of asthma (years)					
	0-2		3-5		>= 6	
Type 2 inflammatory asthma phenotype population	**Placebo (N=36)**	**Dupilumab (N=89)**	**Placebo (N=36)**	**Dupilumab (N=77)**	**Placebo (N=35)**	**Dupilumab (N=45)**
overall						0.436
Risk Difference (95% CI) vs placebo	-	21.38 (1.42 to 41.34)	-	1.77 (-20.12 to 23.66)	-	12.96 (-21.71 to 47.63)
p-value for Risk Difference	-	0.036	-	0.873	-	0.458
p-value for heterogeneity of Risk Difference:						
0-2, 3-5						0.217
0-2, >= 6						0.647
3-5, >= 6						0.504
overall						0.464

[a] Patients who met the corresponding criterion are considered as responders. Patients who did not meet the criterion or had missing value are considered as non-responders. OR, RR and RD are derived from a logistic regression model with treatment, age, weight group, region, baseline eosinophil level, baseline FeNO level, baseline ICS dose level, and baseline PAQLQ(S)-IA global score as covariates.
Peto OR calculation is based on Yusuf S et al. (Prog Cardiovasc Dis. 1985 Mar-Apr;27(5):335-71) and its p-value is derived using a normal approximation.
p-values for heterogeneity are estimated by using the same logistic model as the one used to estimate OR, RR and RD, with subgroup and treatment-by-subgroup interaction as additional covariates.
p-value for heterogeneity of Peto OR is estimated by using normal approximation.
Only patients of age >=7 years old at randomization are included in the analysis.
PGM=DEVOPS/SAR231893/EFC14153/CSR_RWE/REPORT/PGM/eff_pro_evt_ger_subg_i_t.sas OUT=REPORT/OUTPUT/eff_pro_aqlqaw52_ger_onsa_t2_t_x.rtf (01SEP2021 - 15:27)

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

Project Code / Study Number / Analysis: SAR231893 / EFC14153 / CSR_RWE

2 PRO endpoints

2.3 Responder analysis for change from baseline in PAQLQ(S)-IA global score (improvement >= 0.5) at week 52 - ITT type 2 inflammatory asthma phenotype population

2.3.13 By number of severe asthma exacerbation prior to the study (<=1, 2, >2)

	Number of severe asthma exacerbation prior to the study					
	<=1		**2**		**>2**	
Type 2 inflammatory asthma phenotype population	**Placebo (N=43)**	**Dupilumab (N=78)**	**Placebo (N=30)**	**Dupilumab (N=66)**	**Placebo (N=34)**	**Dupilumab (N=67)**
Responder status at Week 52 based on change from baseline in PAQLQ(S)-IA global score >=0.5 [n(%)] [a]						
Responder	30 (69.8%)	59 (75.6%)	20 (66.7%)	51 (77.3%)	23 (67.6%)	51 (76.1%)
Non-responder	13 (30.2%)	19 (24.4%)	10 (33.3%)	15 (22.7%)	11 (32.4%)	16 (23.9%)
Odds Ratio (95% CI) vs placebo	-	2.37 (0.84 to 6.73)	-	2.43 (0.62 to 9.47)	-	1.53 (0.40 to 5.82)
p-value for Odds Ratio	-	0.104	-	0.199	-	0.531
p-value for heterogeneity of Odds Ratio:						
<=1, 2						0.861
<=1, >2						0.291

[a] Patients who met the corresponding criterion are considered as responders. Patients who did not meet the criterion or had missing value are considered as non-responders. OR, RR and RD are derived from a logistic regression model with treatment, age, weight group, region, baseline eosinophil level, baseline FeNO level, baseline ICS dose level, and baseline PAQLQ(S)-IA global score as covariates.
Peto OR calculation is based on Yusuf S et al. (Prog Cardiovasc Dis. 1985 Mar-Apr;27(5):335-71) and its p-value is derived using a normal approximation.
p-values for heterogeneity are estimated by using the same logistic model as the one used to estimate OR, RR and RD, with subgroup and treatment-by-subgroup interaction as additional covariates.
p-value for heterogeneity of Peto OR is estimated by using normal approximation.
Only patients of age >=7 years old at randomization are included in the analysis.
PGM=DEVOPS/SAR231893/EFC14153/CSR_RWE/REPORT/PGM/eff_pro_evt_ger_subg_i_t.sas OUT=REPORT/OUTPUT/eff_pro_aqlqaw52_ger_exa_t2_t_x.rtf (29JUN2021 - 17:50)

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

Project Code / Study Number / Analysis: SAR231893 / EFC14153 / CSR_RWE

2 PRO endpoints

2.3 Responder analysis for change from baseline in PAQLQ(S)-IA global score (improvement >= 0.5) at week 52 - ITT type 2 inflammatory asthma phenotype population

2.3.13 By number of severe asthma exacerbation prior to the study (<=1, 2, >2)

	Number of severe asthma exacerbation prior to the study					
	<=1		2		>2	
Type 2 inflammatory asthma phenotype population	**Placebo (N=43)**	**Dupilumab (N=78)**	**Placebo (N=30)**	**Dupilumab (N=66)**	**Placebo (N=34)**	**Dupilumab (N=67)**
2, >2						0.403
overall						0.546
Risk Ratio (95% CI) vs placebo	-	1.21 (0.82 to 1.79)	-	1.29 (0.69 to 2.41)	-	1.11 (0.62 to 1.99)
Reversed Risk ratio (95% CI) vs placebo	-	0.82 (0.56 to 1.22)	-	0.77 (0.41 to 1.45)	-	0.90 (0.50 to 1.61)
p-value for Risk Ratio	-	0.326	-	0.419	-	0.719
p-value for heterogeneity of Risk Ratio:						
<=1, 2						0.951
<=1, >2						0.700
2, >2						0.841

[a] Patients who met the corresponding criterion are considered as responders. Patients who did not meet the criterion or had missing value are considered as non-responders.
OR, RR and RD are derived from a logistic regression model with treatment, age, weight group, region, baseline eosinophil level, baseline FeNO level, baseline ICS dose level, and baseline PAQLQ(S)-IA global score as covariates.
Peto OR calculation is based on Yusuf S et al. (Prog Cardiovasc Dis. 1985 Mar-Apr;27(5):335-71) and its p-value is derived using a normal approximation.
p-values for heterogeneity are estimated by using the same logistic model as the one used to estimate OR, RR and RD, with subgroup and treatment-by-subgroup interaction as additional covariates.
p-value for heterogeneity of Peto OR is estimated by using normal approximation.
Only patients of age >=7 years old at randomization are included in the analysis.
PGM=DEVOPS/SAR231893/EFC14153/CSR_RWE/REPORT/PGM/eff_pro_evt_ger_subg_i_t.sas OUT=REPORT/OUTPUT/eff_pro_aqlqaw52_ger_exa_t2_t_x.rtf (29JUN2021 - 17:50)

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

Project Code / Study Number / Analysis: SAR231893 / EFC14153 / CSR_RWE

2 PRO endpoints

2.3 Responder analysis for change from baseline in PAQLQ(S)-IA global score (improvement >= 0.5) at week 52 - ITT type 2 inflammatory asthma phenotype population

2.3.13 By number of severe asthma exacerbation prior to the study (<=1, 2, >2)

	Number of severe asthma exacerbation prior to the study					
	<=1		2		>2	
Type 2 inflammatory asthma phenotype population	**Placebo (N=43)**	**Dupilumab (N=78)**	**Placebo (N=30)**	**Dupilumab (N=66)**	**Placebo (N=34)**	**Dupilumab (N=67)**
overall						0.926
Risk Difference (95% CI) vs placebo	-	16.47 (-5.22 to 38.16)	-	8.85 (-16.52 to 34.23)	-	9.01 (-19.32 to 37.35)
p-value for Risk Difference	-	0.135	-	0.489	-	0.529
p-value for heterogeneity of Risk Difference:						
<=1, 2						0.976
<=1, >2						0.623
2, >2						0.685
overall						0.866

[a] Patients who met the corresponding criterion are considered as responders. Patients who did not meet the criterion or had missing value are considered as non-responders.
OR, RR and RD are derived from a logistic regression model with treatment, age, weight group, region, baseline eosinophil level, baseline FeNO level, baseline ICS dose level, and baseline PAQLQ(S)-IA global score as covariates.
Peto OR calculation is based on Yusuf S et al. (Prog Cardiovasc Dis. 1985 Mar-Apr;27(5):335-71) and its p-value is derived using a normal approximation.
p-values for heterogeneity are estimated by using the same logistic model as the one used to estimate OR, RR and RD, with subgroup and treatment-by-subgroup interaction as additional covariates.
p-value for heterogeneity of Peto OR is estimated by using normal approximation.
Only patients of age >=7 years old at randomization are included in the analysis.
PGM=DEVOPS/SAR231893/EFC14153/CSR_RWE/REPORT/PGM/eff_pro_evt_ger_subg_i_t.sas OUT=REPORT/OUTPUT/eff_pro_aqlqaw52_ger_exa_t2_t_x.rtf (29JUN2021 - 17:50)

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

Project Code / Study Number / Analysis: SAR231893 / EFC14153 / CSR_RWE

2 PRO endpoints

2.4 Responder analysis for change from baseline in PAQLQ(S)-IA global score (improvement >= 0.9) at week 52 - ITT type 2 inflammatory asthma phenotype population

Type 2 inflammatory asthma phenotype population	**Placebo (N=107)**	**Dupilumab (N=211)**
Responder status at Week 52 based on change from baseline in PAQLQ(S)-IA global score >=0.9 [n(%)] [a]		
Responder	56 (52.3%)	132 (62.6%)
Non-responder	51 (47.7%)	79 (37.4%)
Odds Ratio (95% CI)	-	2.07 (1.10 to 3.88)
p-value for Odds Ratio		0.023
Risk Ratio (95% CI)	-	1.25 (1.01 to 1.54)
Reversed Risk ratio (95% CI)	-	0.80 (0.65 to 0.99)
p-value for Risk Ratio		0.036
Risk Difference (95% CI)	-	13.92 (2.68 to 25.16)
p-value for Risk Difference		0.015

[a] Patients who met the corresponding criterion are considered as responders. Patients who did not meet the criterion or had missing value are considered as non-responders.
OR, RR and RD are derived from a logistic regression model with treatment, age, weight group, region, baseline eosinophil level, baseline FeNO level, baseline ICS dose level, and baseline PAQLQ(S)-IA global score as covariates.
Peto OR calculation is based on Yusuf S et al. (Prog Cardiovasc Dis. 1985 Mar-Apr;27(5):335-71) and its p-value is derived using a normal approximation.
Only patients of age >=7 years old at randomization are included in the analysis.
PGM=DEVOPS/SAR231893/EFC14153/CSR_RWE/REPORT/PGM/eff_pro_evt_ger_i_t.sas OUT=REPORT/OUTPUT/eff_pro_aqlqbw52_ger_t2_t_x.rtf (30JUN2021 - 8:14)

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

Project Code / Study Number / Analysis: SAR231893 / EFC14153 / CSR_RWE

2 PRO endpoints

2.4 Responder analysis for change from baseline in PAQLQ(S)-IA global score (improvement >= 0.9) at week 52 - ITT type 2 inflammatory asthma phenotype population

2.4.1 By gender (Male, Female)

	Gender			
	Male		Female	
Type 2 inflammatory asthma phenotype population	**Placebo (N=72)**	**Dupilumab (N=134)**	**Placebo (N=35)**	**Dupilumab (N=77)**
Responder status at Week 52 based on change from baseline in PAQLQ(S)-IA global score >=0.9 [n(%)] [a]				
Responder	35 (48.6%)	84 (62.7%)	21 (60.0%)	48 (62.3%)
Non-responder	37 (51.4%)	50 (37.3%)	14 (40.0%)	29 (37.7%)
Odds Ratio (95% CI) vs placebo	-	3.10 (1.38 to 6.94)	-	1.22 (0.41 to 3.64)
p-value for Odds Ratio	-	0.006	-	0.718
p-value for heterogeneity of Odds Ratio				0.133
Risk Ratio (95% CI) vs placebo	-	1.33 (0.97 to 1.82)	-	1.01 (0.62 to 1.63)

[a] Patients who met the corresponding criterion are considered as responders. Patients who did not meet the criterion or had missing value are considered as non-responders.
OR, RR and RD are derived from a logistic regression model with treatment, age, weight group, region, baseline eosinophil level, baseline FeNO level, baseline ICS dose level, and baseline PAQLQ(S)-IA global score as covariates.
Peto OR calculation is based on Yusuf S et al. (Prog Cardiovasc Dis. 1985 Mar-Apr;27(5):335-71) and its p-value is derived using a normal approximation.
p-values for heterogeneity are estimated by using the same logistic model as the one used to estimate OR, RR and RD, with subgroup and treatment-by-subgroup interaction as additional covariates.
p-value for heterogeneity of Peto OR is estimated by using normal approximation.
Only patients of age >=7 years old at randomization are included in the analysis.
PGM=DEVOPS/SAR231893/EFC14153/CSR_RWE/REPORT/PGM/eff_pro_evt_ger_subg_i_t.sas OUT=REPORT/OUTPUT/eff_pro_aqlqbw52_ger_sex_t2_t_x.rtf (29JUN2021 - 17:46)

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

Project Code / Study Number / Analysis: SAR231893 / EFC14153 / CSR_RWE

2 PRO endpoints

2.4 Responder analysis for change from baseline in PAQLQ(S)-IA global score (improvement >= 0.9) at week 52 - ITT type 2 inflammatory asthma phenotype population

2.4.1 By gender (Male, Female)

	Gender			
	Male		Female	
Type 2 inflammatory asthma phenotype population	**Placebo (N=72)**	**Dupilumab (N=134)**	**Placebo (N=35)**	**Dupilumab (N=77)**
Reversed Risk ratio (95% CI) vs placebo	-	0.75 (0.55 to 1.03)	-	0.99 (0.61 to 1.60)
p-value for Risk Ratio	-	0.078	-	0.965
p-value for heterogeneity of Risk Ratio				0.410
Risk Difference (95% CI) vs placebo	-	17.96 (2.34 to 33.57)	-	4.97 (-17.31 to 27.25)
p-value for Risk Difference	-	0.024	-	0.659
p-value for heterogeneity of Risk Difference				0.450

[a] Patients who met the corresponding criterion are considered as responders. Patients who did not meet the criterion or had missing value are considered as non-responders.
OR, RR and RD are derived from a logistic regression model with treatment, age, weight group, region, baseline eosinophil level, baseline FeNO level, baseline ICS dose level, and baseline PAQLQ(S)-IA global score as covariates.
Peto OR calculation is based on Yusuf S et al. (Prog Cardiovasc Dis. 1985 Mar-Apr;27(5):335-71) and its p-value is derived using a normal approximation.
p-values for heterogeneity are estimated by using the same logistic model as the one used to estimate OR, RR and RD, with subgroup and treatment-by-subgroup interaction as additional covariates.
p-value for heterogeneity of Peto OR is estimated by using normal approximation.
Only patients of age >=7 years old at randomization are included in the analysis.
PGM=DEVOPS/SAR231893/EFC14153/CSR_RWE/REPORT/PGM/eff_pro_evt_ger_subg_i_t.sas OUT=REPORT/OUTPUT/eff_pro_aqlqbw52_ger_sex_t2_t_x.rtf (29JUN2021 - 17:46)

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

Project Code / Study Number / Analysis: SAR231893 / EFC14153 / CSR_RWE

2 PRO endpoints

2.4 Responder analysis for change from baseline in PAQLQ(S)-IA global score (improvement >= 0.9) at week 52 - ITT type 2 inflammatory asthma phenotype population

2.4.2 By region (Latin America, East Europe, Western Countries)

	Region					
	Latin America		East Europe		Western countries	
Type 2 inflammatory asthma phenotype population	**Placebo (N=50)**	**Dupilumab (N=94)**	**Placebo (N=37)**	**Dupilumab (N=68)**	**Placebo (N=20)**	**Dupilumab (N=49)**
Responder status at Week 52 based on change from baseline in PAQLQ(S)-IA global score >=0.9 [n(%)] [a]						
Responder	28 (56.0%)	65 (69.1%)	21 (56.8%)	44 (64.7%)	7 (35.0%)	23 (46.9%)
Non-responder	22 (44.0%)	29 (30.9%)	16 (43.2%)	24 (35.3%)	13 (65.0%)	26 (53.1%)
Odds Ratio (95% CI) vs placebo	-	2.12 (0.73 to 6.17)	-	1.92 (0.67 to 5.54)	-	3.04 (0.74 to 12.55)
p-value for Odds Ratio	-	0.168	-	0.224	-	0.122
p-value for heterogeneity of Odds Ratio:						
Latin America, East Europe						0.853
Latin America, Western countries						0.582

[a] Patients who met the corresponding criterion are considered as responders. Patients who did not meet the criterion or had missing value are considered as non-responders.
OR, RR and RD are derived from a logistic regression model with treatment, age, weight group, baseline eosinophil level, baseline FeNO level, baseline ICS dose level, and baseline PAQLQ(S)-IA global score as covariates.
Peto OR calculation is based on Yusuf S et al. (Prog Cardiovasc Dis. 1985 Mar-Apr;27(5):335-71) and its p-value is derived using a normal approximation.
p-values for heterogeneity are estimated by using the same logistic model as the one used to estimate OR, RR and RD, with subgroup and treatment-by-subgroup interaction as additional covariates.
p-value for heterogeneity of Peto OR is estimated by using normal approximation.
Only patients of age >=7 years old at randomization are included in the analysis.
PGM=DEVOPS/SAR231893/EFC14153/CSR_RWE/REPORT/PGM/eff_pro_evt_ger_subg_i_t.sas OUT=REPORT/OUTPUT/eff_pro_aqlqbw52_ger_cty_t2_t_x.rtf (29JUN2021 - 17:46)

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

Project Code / Study Number / Analysis: SAR231893 / EFC14153 / CSR_RWE

2 PRO endpoints

2.4 Responder analysis for change from baseline in PAQLQ(S)-IA global score (improvement >= 0.9) at week 52 - ITT type 2 inflammatory asthma phenotype population

2.4.2 By region (Latin America, East Europe, Western Countries)

	Region					
	Latin America		East Europe		Western countries	
Type 2 inflammatory asthma phenotype population	**Placebo (N=50)**	**Dupilumab (N=94)**	**Placebo (N=37)**	**Dupilumab (N=68)**	**Placebo (N=20)**	**Dupilumab (N=49)**
East Europe, Western countries						0.493
overall						0.787
Risk Ratio (95% CI) vs placebo	-	1.31 (0.90 to 1.90)	-	1.14 (0.74 to 1.75)	-	1.49 (0.68 to 3.24)
Reversed Risk ratio (95% CI) vs placebo	-	0.76 (0.53 to 1.11)	-	0.88 (0.57 to 1.35)	-	0.67 (0.31 to 1.47)
p-value for Risk Ratio	-	0.150	-	0.548	-	0.313
p-value for heterogeneity of Risk Ratio:						
Latin America, East Europe						0.545
Latin America, Western countries						0.824
East Europe, Western countries						0.904

[a] Patients who met the corresponding criterion are considered as responders. Patients who did not meet the criterion or had missing value are considered as non-responders.
OR, RR and RD are derived from a logistic regression model with treatment, age, weight group, baseline eosinophil level, baseline FeNO level, baseline ICS dose level, and baseline PAQLQ(S)-IA global score as covariates.
Peto OR calculation is based on Yusuf S et al. (Prog Cardiovasc Dis. 1985 Mar-Apr;27(5):335-71) and its p-value is derived using a normal approximation.
p-values for heterogeneity are estimated by using the same logistic model as the one used to estimate OR, RR and RD, with subgroup and treatment-by-subgroup interaction as additional covariates.
p-value for heterogeneity of Peto OR is estimated by using normal approximation.
Only patients of age >=7 years old at randomization are included in the analysis.
PGM=DEVOPS/SAR231893/EFC14153/CSR_RWE/REPORT/PGM/eff_pro_evt_ger_subg_i_t.sas OUT=REPORT/OUTPUT/eff_pro_aqlqbw52_ger_cty_t2_t_x.rtf (29JUN2021 - 17:46)

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

Project Code / Study Number / Analysis: SAR231893 / EFC14153 / CSR_RWE

2 PRO endpoints

2.4 Responder analysis for change from baseline in PAQLQ(S)-IA global score (improvement >= 0.9) at week 52 - ITT type 2 inflammatory asthma phenotype population

2.4.2 By region (Latin America, East Europe, Western Countries)

	Region					
	Latin America		East Europe		Western countries	
Type 2 inflammatory asthma phenotype population	**Placebo (N=50)**	**Dupilumab (N=94)**	**Placebo (N=37)**	**Dupilumab (N=68)**	**Placebo (N=20)**	**Dupilumab (N=49)**
overall						0.831
Risk Difference (95% CI) vs placebo	-	16.53 (-1.07 to 34.12)	-	13.47 (-8.56 to 35.50)	-	22.67 (-9.07 to 54.41)
p-value for Risk Difference	-	0.065	-	0.228	-	0.158
p-value for heterogeneity of Risk Difference:						
Latin America, East Europe						0.648
Latin America, Western countries						0.629
East Europe, Western countries						0.920
overall						0.846

[a] Patients who met the corresponding criterion are considered as responders. Patients who did not meet the criterion or had missing value are considered as non-responders.
OR, RR and RD are derived from a logistic regression model with treatment, age, weight group, baseline eosinophil level, baseline FeNO level, baseline ICS dose level, and baseline PAQLQ(S)-IA global score as covariates.
Peto OR calculation is based on Yusuf S et al. (Prog Cardiovasc Dis. 1985 Mar-Apr;27(5):335-71) and its p-value is derived using a normal approximation.
p-values for heterogeneity are estimated by using the same logistic model as the one used to estimate OR, RR and RD, with subgroup and treatment-by-subgroup interaction as additional covariates.
p-value for heterogeneity of Peto OR is estimated by using normal approximation.
Only patients of age >=7 years old at randomization are included in the analysis.
PGM=DEVOPS/SAR231893/EFC14153/CSR_RWE/REPORT/PGM/eff_pro_evt_ger_subg_i_t.sas OUT=REPORT/OUTPUT/eff_pro_aqlqbw52_ger_cty_t2_t_x.rtf (29JUN2021 - 17:46)

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

Project Code / Study Number / Analysis: SAR231893 / EFC14153 / CSR_RWE

2 PRO endpoints

2.4 Responder analysis for change from baseline in PAQLQ(S)-IA global score (improvement >= 0.9) at week 52 - ITT type 2 inflammatory asthma phenotype population

2.4.3 By race (Caucasian/white, Black/of African descent, Other)

	Race					
	Caucasian/White		Black/of African descent		Other	
Type 2 inflammatory asthma phenotype population	**Placebo (N=95)**	**Dupilumab (N=183)**	**Placebo (N=5)**	**Dupilumab (N=9)**	**Placebo (N=7)**	**Dupilumab (N=19)**
Responder status at Week 52 based on change from baseline in PAQLQ(S)-IA global score >=0.9 [n(%)] [a]						
Responder	55 (57.9%)	120 (65.6%)	0	4 (44.4%)	1 (14.3%)	8 (42.1%)
Non-responder	40 (42.1%)	63 (34.4%)	5 (100%)	5 (55.6%)	6 (85.7%)	11 (57.9%)
Odds Ratio (95% CI) vs placebo	-	1.78 (0.91 to 3.48)	-	0.66 (0.00 to NE)	-	28.94 (0.17 to 4863.15)
p-value for Odds Ratio	-	0.094	-	1.000	-	0.183
Peto Odds Ratio (95% CI) vs placebo	-	1.39 (0.83 to 2.32)	-	7.56 (0.73 to 77.80)	-	3.26 (0.55 to 19.45)

[a] Patients who met the corresponding criterion are considered as responders. Patients who did not meet the criterion or had missing value are considered as non-responders.
OR, RR and RD are derived from a logistic regression model with treatment, age, weight group, region, baseline eosinophil level, baseline FeNO level, baseline ICS dose level, and baseline PAQLQ(S)-IA global score as covariates.
Peto OR calculation is based on Yusuf S et al. (Prog Cardiovasc Dis. 1985 Mar-Apr;27(5):335-71) and its p-value is derived using a normal approximation.
p-values for heterogeneity are estimated by using the same logistic model as the one used to estimate OR, RR and RD, with subgroup and treatment-by-subgroup interaction as additional covariates.
p-value for heterogeneity of Peto OR is estimated by using normal approximation.
Only patients of age >=7 years old at randomization are included in the analysis.
PGM=DEVOPS/SAR231893/EFC14153/CSR_RWE/REPORT/PGM/eff_pro_evt_ger_subg_i_t.sas OUT=REPORT/OUTPUT/eff_pro_aqlqbw52_ger_race_t2_t_x.rtf (29JUN2021 - 17:47)

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

Project Code / Study Number / Analysis: SAR231893 / EFC14153 / CSR_RWE

2 PRO endpoints

2.4 Responder analysis for change from baseline in PAQLQ(S)-IA global score (improvement >= 0.9) at week 52 - ITT type 2 inflammatory asthma phenotype population

2.4.3 By race (Caucasian/white, Black/of African descent, Other)

	Race					
	Caucasian/White		Black/of African descent		Other	
Type 2 inflammatory asthma phenotype population	**Placebo (N=95)**	**Dupilumab (N=183)**	**Placebo (N=5)**	**Dupilumab (N=9)**	**Placebo (N=7)**	**Dupilumab (N=19)**
Reversed Peto Odds Ratio (95% CI)	-	0.72 (0.43 to 1.20)	-	0.13 (0.01 to 1.37)	-	0.31 (0.05 to 1.82)
p-value for Peto Odds Ratio		0.209		0.089		0.195
p-value for heterogeneity of Peto Odds Ratio:						
Caucasian/White, Black/of African descent						0.164
Caucasian/White, Other						0.368
Black/of African descent, Other						0.575
overall						0.272
Risk Ratio (95% CI) vs placebo	-	1.18 (0.94 to 1.47)	-	1.82 (0.00 to 4.749E14)	-	1.78 (0.13 to 25.28)

[a] Patients who met the corresponding criterion are considered as responders. Patients who did not meet the criterion or had missing value are considered as non-responders.
OR, RR and RD are derived from a logistic regression model with treatment, age, weight group, region, baseline eosinophil level, baseline FeNO level, baseline ICS dose level, and baseline PAQLQ(S)-IA global score as covariates.
Peto OR calculation is based on Yusuf S et al. (Prog Cardiovasc Dis. 1985 Mar-Apr;27(5):335-71) and its p-value is derived using a normal approximation.
p-values for heterogeneity are estimated by using the same logistic model as the one used to estimate OR, RR and RD, with subgroup and treatment-by-subgroup interaction as additional covariates.
p-value for heterogeneity of Peto OR is estimated by using normal approximation.
Only patients of age >=7 years old at randomization are included in the analysis.
PGM=DEVOPS/SAR231893/EFC14153/CSR_RWE/REPORT/PGM/eff_pro_evt_ger_subg_i_t.sas OUT=REPORT/OUTPUT/eff_pro_aqlqbw52_ger_race_t2_t_x.rtf (29JUN2021 - 17:47)

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

Project Code / Study Number / Analysis: SAR231893 / EFC14153 / CSR_RWE

2 PRO endpoints

2.4 Responder analysis for change from baseline in PAQLQ(S)-IA global score (improvement >= 0.9) at week 52 - ITT type 2 inflammatory asthma phenotype population

2.4.3 By race (Caucasian/white, Black/of African descent, Other)

	Race					
	Caucasian/White		Black/of African descent		Other	
Type 2 inflammatory asthma phenotype population	**Placebo (N=95)**	**Dupilumab (N=183)**	**Placebo (N=5)**	**Dupilumab (N=9)**	**Placebo (N=7)**	**Dupilumab (N=19)**
Reversed Risk ratio (95% CI) vs placebo	-	0.85 (0.68 to 1.07)	-	0.55 (0.00 to 1.439E14)	-	0.56 (0.04 to 7.97)
p-value for Risk Ratio	-	0.158	-	0.963	-	0.651
p-value for heterogeneity of Risk Ratio:						
Caucasian/White, Black/of African descent						0.853
Caucasian/White, Other						0.310
Black/of African descent, Other						0.871
overall						0.586

[a] Patients who met the corresponding criterion are considered as responders. Patients who did not meet the criterion or had missing value are considered as non-responders.
OR, RR and RD are derived from a logistic regression model with treatment, age, weight group, region, baseline eosinophil level, baseline FeNO level, baseline ICS dose level, and baseline PAQLQ(S)-IA global score as covariates.
Peto OR calculation is based on Yusuf S et al. (Prog Cardiovasc Dis. 1985 Mar-Apr;27(5):335-71) and its p-value is derived using a normal approximation.
p-values for heterogeneity are estimated by using the same logistic model as the one used to estimate OR, RR and RD, with subgroup and treatment-by-subgroup interaction as additional covariates.
p-value for heterogeneity of Peto OR is estimated by using normal approximation.
Only patients of age >=7 years old at randomization are included in the analysis.
PGM=DEVOPS/SAR231893/EFC14153/CSR_RWE/REPORT/PGM/eff_pro_evt_ger_subg_i_t.sas OUT=REPORT/OUTPUT/eff_pro_aqlqbw52_ger_race_t2_t_x.rtf (29JUN2021 - 17:47)

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

Project Code / Study Number / Analysis: SAR231893 / EFC14153 / CSR_RWE

2 PRO endpoints

2.4 Responder analysis for change from baseline in PAQLQ(S)-IA global score (improvement >= 0.9) at week 52 - ITT type 2 inflammatory asthma phenotype population

2.4.3 By race (Caucasian/white, Black/of African descent, Other)

	Race					
	Caucasian/White		Black/of African descent		Other	
Type 2 inflammatory asthma phenotype population	**Placebo (N=95)**	**Dupilumab (N=183)**	**Placebo (N=5)**	**Dupilumab (N=9)**	**Placebo (N=7)**	**Dupilumab (N=19)**
Risk Difference (95% CI) vs placebo	-	11.24 (-1.47 to 23.95)	-	23.33 (-458.42 to 505.08)	-	49.53 (-78.12 to 177.18)
p-value for Risk Difference	-	0.083	-	0.900	-	0.423
p-value for heterogeneity of Risk Difference:						
Caucasian/White, Black/of African descent						0.807
Caucasian/White, Other						0.435
Black/of African descent, Other						0.991
overall						0.720

[a] Patients who met the corresponding criterion are considered as responders. Patients who did not meet the criterion or had missing value are considered as non-responders.
OR, RR and RD are derived from a logistic regression model with treatment, age, weight group, region, baseline eosinophil level, baseline FeNO level, baseline ICS dose level, and baseline PAQLQ(S)-IA global score as covariates.
Peto OR calculation is based on Yusuf S et al. (Prog Cardiovasc Dis. 1985 Mar-Apr;27(5):335-71) and its p-value is derived using a normal approximation.
p-values for heterogeneity are estimated by using the same logistic model as the one used to estimate OR, RR and RD, with subgroup and treatment-by-subgroup interaction as additional covariates.
p-value for heterogeneity of Peto OR is estimated by using normal approximation.
Only patients of age >=7 years old at randomization are included in the analysis.
PGM=DEVOPS/SAR231893/EFC14153/CSR_RWE/REPORT/PGM/eff_pro_evt_ger_subg_i_t.sas OUT=REPORT/OUTPUT/eff_pro_aqlqbw52_ger_race_t2_t_x.rtf (29JUN2021 - 17:47)

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

Project Code / Study Number / Analysis: SAR231893 / EFC14153 / CSR_RWE

2 PRO endpoints

2.4 Responder analysis for change from baseline in PAQLQ(S)-IA global score (improvement >= 0.9) at week 52 - ITT type 2 inflammatory asthma phenotype population

2.4.4 By baseline ICS dose level (Medium, High)

	Baseline ICS dose level			
	High		Medium	
Type 2 inflammatory asthma phenotype population	**Placebo (N=45)**	**Dupilumab (N=92)**	**Placebo (N=62)**	**Dupilumab (N=118)**
Responder status at Week 52 based on change from baseline in PAQLQ(S)-IA global score >=0.9 [n(%)] [a]				
Responder	21 (46.7%)	60 (65.2%)	35 (56.5%)	72 (61.0%)
Non-responder	24 (53.3%)	32 (34.8%)	27 (43.5%)	46 (39.0%)
Odds Ratio (95% CI) vs placebo	-	3.90 (1.38 to 11.04)	-	1.58 (0.68 to 3.69)
p-value for Odds Ratio	-	0.011	-	0.288
p-value for heterogeneity of Odds Ratio				0.227
Risk Ratio (95% CI) vs placebo	-	1.28 (0.89 to 1.84)	-	1.23 (0.89 to 1.70)

[a] Patients who met the corresponding criterion are considered as responders. Patients who did not meet the criterion or had missing value are considered as non-responders.
OR, RR and RD are derived from a logistic regression model with treatment, age, weight group, region, baseline eosinophil level, baseline FeNO level and baseline PAQLQ(S)-IA global score as covariates.
Peto OR calculation is based on Yusuf S et al. (Prog Cardiovasc Dis. 1985 Mar-Apr;27(5):335-71) and its p-value is derived using a normal approximation.
p-values for heterogeneity are estimated by using the same logistic model as the one used to estimate OR, RR and RD, with subgroup and treatment-by-subgroup interaction as additional covariates.
p-value for heterogeneity of Peto OR is estimated by using normal approximation.
Only patients of age >=7 years old at randomization are included in the analysis.
PGM=DEVOPS/SAR231893/EFC14153/CSR_RWE/REPORT/PGM/eff_pro_evt_ger_subg_i_t.sas OUT=REPORT/OUTPUT/eff_pro_aqlqbw52_ger_ics_t2_t_x.rtf (29JUN2021 - 17:47)

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

Project Code / Study Number / Analysis: SAR231893 / EFC14153 / CSR_RWE

2 PRO endpoints

2.4 Responder analysis for change from baseline in PAQLQ(S)-IA global score (improvement >= 0.9) at week 52 - ITT type 2 inflammatory asthma phenotype population

2.4.4 By baseline ICS dose level (Medium, High)

	Baseline ICS dose level			
	High		Medium	
Type 2 inflammatory asthma phenotype population	**Placebo (N=45)**	**Dupilumab (N=92)**	**Placebo (N=62)**	**Dupilumab (N=118)**
Reversed Risk ratio (95% CI) vs placebo	-	0.78 (0.54 to 1.13)	-	0.81 (0.59 to 1.12)
p-value for Risk Ratio	-	0.185	-	0.208
p-value for heterogeneity of Risk Ratio				0.864
Risk Difference (95% CI) vs placebo	-	18.45 (-1.42 to 38.31)	-	12.76 (-3.73 to 29.25)
p-value for Risk Difference	-	0.068	-	0.128
p-value for heterogeneity of Risk Difference				0.704

[a] Patients who met the corresponding criterion are considered as responders. Patients who did not meet the criterion or had missing value are considered as non-responders.
OR, RR and RD are derived from a logistic regression model with treatment, age, weight group, region, baseline eosinophil level, baseline FeNO level and baseline PAQLQ(S)-IA global score as covariates.
Peto OR calculation is based on Yusuf S et al. (Prog Cardiovasc Dis. 1985 Mar-Apr;27(5):335-71) and its p-value is derived using a normal approximation.
p-values for heterogeneity are estimated by using the same logistic model as the one used to estimate OR, RR and RD, with subgroup and treatment-by-subgroup interaction as additional covariates.
p-value for heterogeneity of Peto OR is estimated by using normal approximation.
Only patients of age >=7 years old at randomization are included in the analysis.
PGM=DEVOPS/SAR231893/EFC14153/CSR_RWE/REPORT/PGM/eff_pro_evt_ger_subg_i_t.sas OUT=REPORT/OUTPUT/eff_pro_aqlqbw52_ger_ics_t2_t_x.rtf (29JUN2021 - 17:47)

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

Project Code / Study Number / Analysis: SAR231893 / EFC14153 / CSR_RWE

2 PRO endpoints

2.4 Responder analysis for change from baseline in PAQLQ(S)-IA global score (improvement >= 0.9) at week 52 - ITT type 2 inflammatory asthma phenotype population

2.4.5 By baseline ICS dose level 2 (Medium, High)

	Baseline ICS dose level 2			
	High		Medium	
Type 2 inflammatory asthma phenotype population	**Placebo (N=88)**	**Dupilumab (N=182)**	**Placebo (N=19)**	**Dupilumab (N=29)**
Responder status at Week 52 based on change from baseline in PAQLQ(S)-IA global score >=0.9 [n(%)] [a]				
Responder	45 (51.1%)	115 (63.2%)	11 (57.9%)	17 (58.6%)
Non-responder	43 (48.9%)	67 (36.8%)	8 (42.1%)	12 (41.4%)
Odds Ratio (95% CI) vs placebo	-	2.35 (1.20 to 4.59)	-	0.28 (0.01 to 9.93)
p-value for Odds Ratio	-	0.013	-	0.470
p-value for heterogeneity of Odds Ratio				0.216
Risk Ratio (95% CI) vs placebo	-	1.23 (0.98 to 1.55)	-	1.16 (0.35 to 3.86)

[a] Patients who met the corresponding criterion are considered as responders. Patients who did not meet the criterion or had missing value are considered as non-responders.
OR, RR and RD are derived from a logistic regression model with treatment, age, weight group, region, baseline eosinophil level, baseline FeNO level and baseline PAQLQ(S)-IA global score as covariates.
Peto OR calculation is based on Yusuf S et al. (Prog Cardiovasc Dis. 1985 Mar-Apr;27(5):335-71) and its p-value is derived using a normal approximation.
p-values for heterogeneity are estimated by using the same logistic model as the one used to estimate OR, RR and RD, with subgroup and treatment-by-subgroup interaction as additional covariates.
p-value for heterogeneity of Peto OR is estimated by using normal approximation.
Only patients of age >=7 years old at randomization are included in the analysis.
PGM=DEVOPS/SAR231893/EFC14153/CSR_RWE/REPORT/PGM/eff_pro_evt_ger_subg_i_t.sas OUT=REPORT/OUTPUT/eff_pro_aqlqbw52_ger_ics2_t2_t_x.rtf (01SEP2021 - 15:26)

Project Code / Study Number / Analysis: SAR231893 / EFC14153 / CSR_RWE

2 PRO endpoints

2.4 Responder analysis for change from baseline in PAQLQ(S)-IA global score (improvement >= 0.9) at week 52 - ITT type 2 inflammatory asthma phenotype population

2.4.5 By baseline ICS dose level 2 (Medium, High)

	Baseline ICS dose level 2			
	High		Medium	
Type 2 inflammatory asthma phenotype population	**Placebo (N=88)**	**Dupilumab (N=182)**	**Placebo (N=19)**	**Dupilumab (N=29)**
Reversed Risk ratio (95% CI) vs placebo	-	0.81 (0.65 to 1.02)	-	0.86 (0.26 to 2.86)
p-value for Risk Ratio	-	0.069	-	0.801
p-value for heterogeneity of Risk Ratio				0.772
Risk Difference (95% CI) vs placebo	-	14.61 (2.26 to 26.96)	-	7.95 (-53.72 to 69.62)
p-value for Risk Difference	-	0.021	-	0.795
p-value for heterogeneity of Risk Difference				0.513

[a] Patients who met the corresponding criterion are considered as responders. Patients who did not meet the criterion or had missing value are considered as non-responders.
OR, RR and RD are derived from a logistic regression model with treatment, age, weight group, region, baseline eosinophil level, baseline FeNO level and baseline PAQLQ(S)-IA global score as covariates.
Peto OR calculation is based on Yusuf S et al. (Prog Cardiovasc Dis. 1985 Mar-Apr;27(5):335-71) and its p-value is derived using a normal approximation.
p-values for heterogeneity are estimated by using the same logistic model as the one used to estimate OR, RR and RD, with subgroup and treatment-by-subgroup interaction as additional covariates.
p-value for heterogeneity of Peto OR is estimated by using normal approximation.
Only patients of age >=7 years old at randomization are included in the analysis.
PGM=DEVOPS/SAR231893/EFC14153/CSR_RWE/REPORT/PGM/eff_pro_evt_ger_subg_i_t.sas OUT=REPORT/OUTPUT/eff_pro_aqlqbw52_ger_ics2_t2_t_x.rtf (01SEP2021 - 15:26)

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

Project Code / Study Number / Analysis: SAR231893 / EFC14153 / CSR_RWE

2 PRO endpoints

2.4 Responder analysis for change from baseline in PAQLQ(S)-IA global score (improvement >= 0.9) at week 52 - ITT type 2 inflammatory asthma phenotype population

2.4.6 By baseline predicted FEV1 (<80%, >=80%)

	Baseline Predicted FEV1			
	<80%		>=80%	
Type 2 inflammatory asthma phenotype population	**Placebo (N=59)**	**Dupilumab (N=98)**	**Placebo (N=48)**	**Dupilumab (N=113)**
Responder status at Week 52 based on change from baseline in PAQLQ(S)-IA global score >=0.9 [n(%)] [a]				
Responder	30 (50.8%)	67 (68.4%)	26 (54.2%)	65 (57.5%)
Non-responder	29 (49.2%)	31 (31.6%)	22 (45.8%)	48 (42.5%)
Odds Ratio (95% CI) vs placebo	-	3.64 (1.41 to 9.43)	-	1.78 (0.67 to 4.75)
p-value for Odds Ratio	-	0.008	-	0.245
p-value for heterogeneity of Odds Ratio				0.175
Risk Ratio (95% CI) vs placebo	-	1.43 (1.00 to 2.05)	-	1.00 (0.66 to 1.50)

[a] Patients who met the corresponding criterion are considered as responders. Patients who did not meet the criterion or had missing value are considered as non-responders.
OR, RR and RD are derived from a logistic regression model with treatment, age, weight group, region, baseline eosinophil level, baseline FeNO level, baseline ICS dose level, and baseline PAQLQ(S)-IA global score as covariates.
Peto OR calculation is based on Yusuf S et al. (Prog Cardiovasc Dis. 1985 Mar-Apr;27(5):335-71) and its p-value is derived using a normal approximation.
p-values for heterogeneity are estimated by using the same logistic model as the one used to estimate OR, RR and RD, with subgroup and treatment-by-subgroup interaction as additional covariates.
p-value for heterogeneity of Peto OR is estimated by using normal approximation.
Only patients of age >=7 years old at randomization are included in the analysis.
PGM=DEVOPS/SAR231893/EFC14153/CSR_RWE/REPORT/PGM/eff_pro_evt_ger_subg_i_t.sas OUT=REPORT/OUTPUT/eff_pro_aqlqbw52_ger_pfev1_t2_t_x.rtf (29JUN2021 - 17:47)

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

Project Code / Study Number / Analysis: SAR231893 / EFC14153 / CSR_RWE

2 PRO endpoints

2.4 Responder analysis for change from baseline in PAQLQ(S)-IA global score (improvement >= 0.9) at week 52 - ITT type 2 inflammatory asthma phenotype population

2.4.6 By baseline predicted FEV1 (<80%, >=80%)

	Baseline Predicted FEV1			
	<80%		>=80%	
Type 2 inflammatory asthma phenotype population	**Placebo (N=59)**	**Dupilumab (N=98)**	**Placebo (N=48)**	**Dupilumab (N=113)**
Reversed Risk ratio (95% CI) vs placebo	-	0.70 (0.49 to 1.00)		
p-value for Risk Ratio	-	0.051	-	0.986
p-value for heterogeneity of Risk Ratio				0.115
Risk Difference (95% CI) vs placebo	-	21.81 (3.94 to 39.68)	-	5.88 (-15.80 to 27.55)
p-value for Risk Difference	-	0.017	-	0.593
p-value for heterogeneity of Risk Difference				0.228

[a] Patients who met the corresponding criterion are considered as responders. Patients who did not meet the criterion or had missing value are considered as non-responders.
OR, RR and RD are derived from a logistic regression model with treatment, age, weight group, region, baseline eosinophil level, baseline FeNO level, baseline ICS dose level, and baseline PAQLQ(S)-IA global score as covariates.
Peto OR calculation is based on Yusuf S et al. (Prog Cardiovasc Dis. 1985 Mar-Apr;27(5):335-71) and its p-value is derived using a normal approximation.
p-values for heterogeneity are estimated by using the same logistic model as the one used to estimate OR, RR and RD, with subgroup and treatment-by-subgroup interaction as additional covariates.
p-value for heterogeneity of Peto OR is estimated by using normal approximation.
Only patients of age >=7 years old at randomization are included in the analysis.
PGM=DEVOPS/SAR231893/EFC14153/CSR_RWE/REPORT/PGM/eff_pro_evt_ger_subg_i_t.sas OUT=REPORT/OUTPUT/eff_pro_aqlqbw52_ger_pfev1_t2_t_x.rtf (29JUN2021 - 17:47)

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

Project Code / Study Number / Analysis: SAR231893 / EFC14153 / CSR_RWE

2 PRO endpoints

2.4 Responder analysis for change from baseline in PAQLQ(S)-IA global score (improvement >= 0.9) at week 52 - ITT type 2 inflammatory asthma phenotype population

2.4.7 By baseline ACQ-7-IA (<=2, >2)

	Baseline ACQ-7-IA			
	<=2		>2	
Type 2 inflammatory asthma phenotype population	**Placebo (N=58)**	**Dupilumab (N=116)**	**Placebo (N=49)**	**Dupilumab (N=95)**
Responder status at Week 52 based on change from baseline in PAQLQ(S)-IA global score >=0.9 [n(%)] [a]				
Responder	25 (43.1%)	61 (52.6%)	31 (63.3%)	71 (74.7%)
Non-responder	33 (56.9%)	55 (47.4%)	18 (36.7%)	24 (25.3%)
Odds Ratio (95% CI) vs placebo	-	1.89 (0.75 to 4.76)	-	2.29 (0.91 to 5.75)
p-value for Odds Ratio	-	0.173	-	0.079
p-value for heterogeneity of Odds Ratio				0.457
Risk Ratio (95% CI) vs placebo	-	1.28 (0.82 to 2.01)	-	1.22 (0.92 to 1.63)

[a] Patients who met the corresponding criterion are considered as responders. Patients who did not meet the criterion or had missing value are considered as non-responders.
OR, RR and RD are derived from a logistic regression model with treatment, age, weight group, region, baseline eosinophil level, baseline FeNO level, baseline ICS dose level, and baseline PAQLQ(S)-IA global score as covariates.
Peto OR calculation is based on Yusuf S et al. (Prog Cardiovasc Dis. 1985 Mar-Apr;27(5):335-71) and its p-value is derived using a normal approximation.
p-values for heterogeneity are estimated by using the same logistic model as the one used to estimate OR, RR and RD, with subgroup and treatment-by-subgroup interaction as additional covariates.
p-value for heterogeneity of Peto OR is estimated by using normal approximation.
Only patients of age >=7 years old at randomization are included in the analysis.
PGM=DEVOPS/SAR231893/EFC14153/CSR_RWE/REPORT/PGM/eff_pro_evt_ger_subg_i_t.sas OUT=REPORT/OUTPUT/eff_pro_aqlqbw52_ger_acq7_t2_t_x.rtf (29JUN2021 - 17:48)

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

Project Code / Study Number / Analysis: SAR231893 / EFC14153 / CSR_RWE

2 PRO endpoints

2.4 Responder analysis for change from baseline in PAQLQ(S)-IA global score (improvement >= 0.9) at week 52 - ITT type 2 inflammatory asthma phenotype population

2.4.7 By baseline ACQ-7-IA (<=2, >2)

	Baseline ACQ-7-IA			
	<=2		>2	
Type 2 inflammatory asthma phenotype population	**Placebo (N=58)**	**Dupilumab (N=116)**	**Placebo (N=49)**	**Dupilumab (N=95)**
Reversed Risk ratio (95% CI) vs placebo	-	0.78 (0.50 to 1.22)	-	0.82 (0.61 to 1.09)
p-value for Risk Ratio	-	0.272	-	0.169
p-value for heterogeneity of Risk Ratio				0.836
Risk Difference (95% CI) vs placebo	-	14.50 (-6.97 to 35.98)	-	14.74 (-2.28 to 31.76)
p-value for Risk Difference	-	0.184	-	0.089
p-value for heterogeneity of Risk Difference				0.971

[a] Patients who met the corresponding criterion are considered as responders. Patients who did not meet the criterion or had missing value are considered as non-responders.
OR, RR and RD are derived from a logistic regression model with treatment, age, weight group, region, baseline eosinophil level, baseline FeNO level, baseline ICS dose level, and baseline PAQLQ(S)-IA global score as covariates.
Peto OR calculation is based on Yusuf S et al. (Prog Cardiovasc Dis. 1985 Mar-Apr;27(5):335-71) and its p-value is derived using a normal approximation.
p-values for heterogeneity are estimated by using the same logistic model as the one used to estimate OR, RR and RD, with subgroup and treatment-by-subgroup interaction as additional covariates.
p-value for heterogeneity of Peto OR is estimated by using normal approximation.
Only patients of age >=7 years old at randomization are included in the analysis.
PGM=DEVOPS/SAR231893/EFC14153/CSR_RWE/REPORT/PGM/eff_pro_evt_ger_subg_i_t.sas OUT=REPORT/OUTPUT/eff_pro_aqlqbw52_ger_acq7_t2_t_x.rtf (29JUN2021 - 17:48)

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

Project Code / Study Number / Analysis: SAR231893 / EFC14153 / CSR_RWE

2 PRO endpoints

2.4 Responder analysis for change from baseline in PAQLQ(S)-IA global score (improvement >= 0.9) at week 52 - ITT type 2 inflammatory asthma phenotype population

2.4.8 By baseline weight (<=30 kg, >30 kg)

	Baseline weight (kg)			
	<=30		>30	
Type 2 inflammatory asthma phenotype population	**Placebo (N=29)**	**Dupilumab (N=56)**	**Placebo (N=78)**	**Dupilumab (N=155)**
Responder status at Week 52 based on change from baseline in PAQLQ(S)-IA global score >=0.9 [n(%)] [a]				
Responder	14 (48.3%)	34 (60.7%)	42 (53.8%)	98 (63.2%)
Non-responder	15 (51.7%)	22 (39.3%)	36 (46.2%)	57 (36.8%)
Odds Ratio (95% CI) vs placebo	-	1.60 (0.46 to 5.56)	-	2.30 (1.08 to 4.88)
p-value for Odds Ratio	-	0.452	-	0.031
p-value for heterogeneity of Odds Ratio				0.872
Risk Ratio (95% CI) vs placebo	-	1.09 (0.58 to 2.04)	-	1.26 (0.96 to 1.65)

[a] Patients who met the corresponding criterion are considered as responders. Patients who did not meet the criterion or had missing value are considered as non-responders.
OR, RR and RD are derived from a logistic regression model with treatment, age, region, baseline eosinophil level, baseline FeNO level, baseline ICS dose level, and baseline PAQLQ(S)-IA global score as covariates.
Peto OR calculation is based on Yusuf S et al. (Prog Cardiovasc Dis. 1985 Mar-Apr;27(5):335-71) and its p-value is derived using a normal approximation.
p-values for heterogeneity are estimated by using the same logistic model as the one used to estimate OR, RR and RD, with subgroup and treatment-by-subgroup interaction as additional covariates.
p-value for heterogeneity of Peto OR is estimated by using normal approximation.
Only patients of age >=7 years old at randomization are included in the analysis.
PGM=DEVOPS/SAR231893/EFC14153/CSR_RWE/REPORT/PGM/eff_pro_evt_ger_subg_i_t.sas OUT=REPORT/OUTPUT/eff_pro_aqlqbw52_ger_wgt_t2_t_x.rtf (29JUN2021 - 17:48)

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

Project Code / Study Number / Analysis: SAR231893 / EFC14153 / CSR_RWE

2 PRO endpoints

2.4 Responder analysis for change from baseline in PAQLQ(S)-IA global score (improvement >= 0.9) at week 52 - ITT type 2 inflammatory asthma phenotype population

2.4.8 By baseline weight (<=30 kg, >30 kg)

	Baseline weight (kg)			
	<=30		>30	
Type 2 inflammatory asthma phenotype population	**Placebo (N=29)**	**Dupilumab (N=56)**	**Placebo (N=78)**	**Dupilumab (N=155)**
Reversed Risk ratio (95% CI) vs placebo	-	0.92 (0.49 to 1.73)	-	0.80 (0.61 to 1.04)
p-value for Risk Ratio	-	0.794	-	0.097
p-value for heterogeneity of Risk Ratio				0.826
Risk Difference (95% CI) vs placebo	-	10.46 (-15.75 to 36.66)	-	15.83 (0.68 to 30.99)
p-value for Risk Difference	-	0.429	-	0.041
p-value for heterogeneity of Risk Difference				0.907

[a] Patients who met the corresponding criterion are considered as responders. Patients who did not meet the criterion or had missing value are considered as non-responders. OR, RR and RD are derived from a logistic regression model with treatment, age, region, baseline eosinophil level, baseline FeNO level, baseline ICS dose level, and baseline PAQLQ(S)-IA global score as covariates.
Peto OR calculation is based on Yusuf S et al. (Prog Cardiovasc Dis. 1985 Mar-Apr;27(5):335-71) and its p-value is derived using a normal approximation.
p-values for heterogeneity are estimated by using the same logistic model as the one used to estimate OR, RR and RD, with subgroup and treatment-by-subgroup interaction as additional covariates.
p-value for heterogeneity of Peto OR is estimated by using normal approximation.
Only patients of age >=7 years old at randomization are included in the analysis.
PGM=DEVOPS/SAR231893/EFC14153/CSR_RWE/REPORT/PGM/eff_pro_evt_ger_subg_i_t.sas OUT=REPORT/OUTPUT/eff_pro_aqlqbw52_ger_wgt_t2_t_x.rtf (29JUN2021 - 17:48)

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

Project Code / Study Number / Analysis: SAR231893 / EFC14153 / CSR_RWE

2 PRO endpoints

2.4 Responder analysis for change from baseline in PAQLQ(S)-IA global score (improvement >= 0.9) at week 52 - ITT type 2 inflammatory asthma phenotype population

2.4.9 By atopic medical condition (Yes, No)

	Atopic medical condition			
	Yes		**No**	
Type 2 inflammatory asthma phenotype population	**Placebo (N=97)**	**Dupilumab (N=205)**	**Placebo (N=10)**	**Dupilumab (N=6)**
Responder status at Week 52 based on change from baseline in PAQLQ(S)-IA global score >=0.9 [n(%)] [a]				
Responder	49 (50.5%)	128 (62.4%)	7 (70.0%)	4 (66.7%)
Non-responder	48 (49.5%)	77 (37.6%)	3 (30.0%)	2 (33.3%)
Odds Ratio (95% CI) vs placebo	-	2.41 (1.25 to 4.66)	-	0.00 (0.00 to NE)
p-value for Odds Ratio	-	0.009	-	0.989
p-value for heterogeneity of Odds Ratio				0.178
Risk Ratio (95% CI) vs placebo	-	1.30 (1.04 to 1.63)	-	1.35 (0.05 to 40.22)

[a] Patients who met the corresponding criterion are considered as responders. Patients who did not meet the criterion or had missing value are considered as non-responders.
OR, RR and RD are derived from a logistic regression model with treatment, age, weight group, region, baseline eosinophil level, baseline FeNO level, baseline ICS dose level, and baseline PAQLQ(S)-IA global score as covariates.
Peto OR calculation is based on Yusuf S et al. (Prog Cardiovasc Dis. 1985 Mar-Apr;27(5):335-71) and its p-value is derived using a normal approximation.
p-values for heterogeneity are estimated by using the same logistic model as the one used to estimate OR, RR and RD, with subgroup and treatment-by-subgroup interaction as additional covariates.
p-value for heterogeneity of Peto OR is estimated by using normal approximation.
Only patients of age >=7 years old at randomization are included in the analysis.
PGM=DEVOPS/SAR231893/EFC14153/CSR_RWE/REPORT/PGM/eff_pro_evt_ger_subg_i_t.sas OUT=REPORT/OUTPUT/eff_pro_aqlqbw52_ger_amc_t2_t_x.rtf (29JUN2021 - 17:48)

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

Project Code / Study Number / Analysis: SAR231893 / EFC14153 / CSR_RWE

2 PRO endpoints

2.4 Responder analysis for change from baseline in PAQLQ(S)-IA global score (improvement >= 0.9) at week 52 - ITT type 2 inflammatory asthma phenotype population

2.4.9 By atopic medical condition (Yes, No)

	Atopic medical condition			
	Yes		No	
Type 2 inflammatory asthma phenotype population	**Placebo (N=97)**	**Dupilumab (N=205)**	**Placebo (N=10)**	**Dupilumab (N=6)**
Reversed Risk ratio (95% CI) vs placebo	-	0.77 (0.61 to 0.96)	-	0.74 (0.02 to 22.12)
p-value for Risk Ratio	-	0.023	-	0.837
p-value for heterogeneity of Risk Ratio				0.567
Risk Difference (95% CI) vs placebo	-	16.35 (4.37 to 28.34)	-	-0.17 (-363.79 to 363.45)
p-value for Risk Difference	-	0.008	-	0.999
p-value for heterogeneity of Risk Difference				0.409

[a] Patients who met the corresponding criterion are considered as responders. Patients who did not meet the criterion or had missing value are considered as non-responders.
OR, RR and RD are derived from a logistic regression model with treatment, age, weight group, region, baseline eosinophil level, baseline FeNO level, baseline ICS dose level, and baseline PAQLQ(S)-IA global score as covariates.
Peto OR calculation is based on Yusuf S et al. (Prog Cardiovasc Dis. 1985 Mar-Apr;27(5):335-71) and its p-value is derived using a normal approximation.
p-values for heterogeneity are estimated by using the same logistic model as the one used to estimate OR, RR and RD, with subgroup and treatment-by-subgroup interaction as additional covariates.
p-value for heterogeneity of Peto OR is estimated by using normal approximation.
Only patients of age >=7 years old at randomization are included in the analysis.
PGM=DEVOPS/SAR231893/EFC14153/CSR_RWE/REPORT/PGM/eff_pro_evt_ger_subg_i_t.sas OUT=REPORT/OUTPUT/eff_pro_aqlqbw52_ger_amc_t2_t_x.rtf (29JUN2021 - 17:48)

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

Project Code / Study Number / Analysis: SAR231893 / EFC14153 / CSR_RWE

2 PRO endpoints

2.4 Responder analysis for change from baseline in PAQLQ(S)-IA global score (improvement >= 0.9) at week 52 - ITT type 2 inflammatory asthma phenotype population

2.4.10 By baseline total IgE (<median, >= median)

	Baseline Total IgE (IU/mL)			
	<median		>=median	
Type 2 inflammatory asthma phenotype population	**Placebo (N=61)**	**Dupilumab (N=90)**	**Placebo (N=45)**	**Dupilumab (N=116)**
Responder status at Week 52 based on change from baseline in PAQLQ(S)-IA global score >=0.9 [n(%)] [a]				
Responder	36 (59.0%)	60 (66.7%)	19 (42.2%)	70 (60.3%)
Non-responder	25 (41.0%)	30 (33.3%)	26 (57.8%)	46 (39.7%)
Odds Ratio (95% CI) vs placebo	-	2.16 (0.81 to 5.79)	-	2.61 (1.02 to 6.67)
p-value for Odds Ratio	-	0.123	-	0.046
p-value for heterogeneity of Odds Ratio				0.874
Risk Ratio (95% CI) vs placebo	-	1.30 (0.85 to 1.97)	-	1.47 (0.94 to 2.30)

[a] Patients who met the corresponding criterion are considered as responders. Patients who did not meet the criterion or had missing value are considered as non-responders.
OR, RR and RD are derived from a logistic regression model with treatment, age, weight group, region, baseline eosinophil level, baseline FeNO level, baseline ICS dose level, and baseline PAQLQ(S)-IA global score as covariates.
Peto OR calculation is based on Yusuf S et al. (Prog Cardiovasc Dis. 1985 Mar-Apr;27(5):335-71) and its p-value is derived using a normal approximation.
p-values for heterogeneity are estimated by using the same logistic model as the one used to estimate OR, RR and RD, with subgroup and treatment-by-subgroup interaction as additional covariates.
p-value for heterogeneity of Peto OR is estimated by using normal approximation.
Only patients of age >=7 years old at randomization are included in the analysis.
PGM=DEVOPS/SAR231893/EFC14153/CSR_RWE/REPORT/PGM/eff_pro_evt_ger_subg_i_t.sas OUT=REPORT/OUTPUT/eff_pro_aqlqbw52_ger_igem_t2_t_x.rtf (29JUN2021 - 17:49)

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

Project Code / Study Number / Analysis: SAR231893 / EFC14153 / CSR_RWE

2 PRO endpoints

2.4 Responder analysis for change from baseline in PAQLQ(S)-IA global score (improvement >= 0.9) at week 52 - ITT type 2 inflammatory asthma phenotype population

2.4.10 By baseline total IgE (<median, >= median)

	Baseline Total IgE (IU/mL)			
	<median		>=median	
Type 2 inflammatory asthma phenotype population	**Placebo (N=61)**	**Dupilumab (N=90)**	**Placebo (N=45)**	**Dupilumab (N=116)**
Reversed Risk ratio (95% CI) vs placebo	-	0.77 (0.51 to 1.17)	-	0.68 (0.43 to 1.07)
p-value for Risk Ratio	-	0.220	-	0.093
p-value for heterogeneity of Risk Ratio				0.979
Risk Difference (95% CI) vs placebo	-	18.75 (0.12 to 37.39)	-	23.52 (3.60 to 43.44)
p-value for Risk Difference	-	0.049	-	0.021
p-value for heterogeneity of Risk Difference				0.993

[a] Patients who met the corresponding criterion are considered as responders. Patients who did not meet the criterion or had missing value are considered as non-responders. OR, RR and RD are derived from a logistic regression model with treatment, age, weight group, region, baseline eosinophil level, baseline FeNO level, baseline ICS dose level, and baseline PAQLQ(S)-IA global score as covariates.
Peto OR calculation is based on Yusuf S et al. (Prog Cardiovasc Dis. 1985 Mar-Apr;27(5):335-71) and its p-value is derived using a normal approximation.
p-values for heterogeneity are estimated by using the same logistic model as the one used to estimate OR, RR and RD, with subgroup and treatment-by-subgroup interaction as additional covariates.
p-value for heterogeneity of Peto OR is estimated by using normal approximation.
Only patients of age >=7 years old at randomization are included in the analysis.
PGM=DEVOPS/SAR231893/EFC14153/CSR_RWE/REPORT/PGM/eff_pro_evt_ger_subg_i_t.sas OUT=REPORT/OUTPUT/eff_pro_aqlqbw52_ger_igem_t2_t_x.rtf (29JUN2021 - 17:49)

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

Project Code / Study Number / Analysis: SAR231893 / EFC14153 / CSR_RWE

2 PRO endpoints

2.4 Responder analysis for change from baseline in PAQLQ(S)-IA global score (improvement >= 0.9) at week 52 - ITT type 2 inflammatory asthma phenotype population

2.4.11 By baseline total IgE (<100 IU/ml, >= 100 IU/ml)

	Baseline Total IgE (IU/mL)			
	< 100		>= 100	
Type 2 inflammatory asthma phenotype population	**Placebo (N=19)**	**Dupilumab (N=24)**	**Placebo (N=87)**	**Dupilumab (N=182)**
Responder status at Week 52 based on change from baseline in PAQLQ(S)-IA global score >=0.9 [n(%)] [a]				
Responder	13 (68.4%)	16 (66.7%)	42 (48.3%)	114 (62.6%)
Non-responder	6 (31.6%)	8 (33.3%)	45 (51.7%)	68 (37.4%)
Odds Ratio (95% CI) vs placebo	-	1.40 (0.23 to 8.59)	-	2.45 (1.19 to 5.04)
p-value for Odds Ratio	-	0.706	-	0.015
p-value for heterogeneity of Odds Ratio				0.754
Risk Ratio (95% CI) vs placebo	-	1.13 (0.38 to 3.41)	-	1.26 (0.96 to 1.65)

[a] Patients who met the corresponding criterion are considered as responders. Patients who did not meet the criterion or had missing value are considered as non-responders.
OR, RR and RD are derived from a logistic regression model with treatment, age, weight group, region, baseline eosinophil level, baseline FeNO level, baseline ICS dose level, and baseline PAQLQ(S)-IA global score as covariates.
Peto OR calculation is based on Yusuf S et al. (Prog Cardiovasc Dis. 1985 Mar-Apr;27(5):335-71) and its p-value is derived using a normal approximation.
p-values for heterogeneity are estimated by using the same logistic model as the one used to estimate OR, RR and RD, with subgroup and treatment-by-subgroup interaction as additional covariates.
p-value for heterogeneity of Peto OR is estimated by using normal approximation.
Only patients of age >=7 years old at randomization are included in the analysis.
PGM=DEVOPS/SAR231893/EFC14153/CSR_RWE/REPORT/PGM/eff_pro_evt_ger_subg_i_t.sas OUT=REPORT/OUTPUT/eff_pro_aqlqbw52_ger_ige_t2_t_x.rtf (29JUN2021 - 17:49)

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

Project Code / Study Number / Analysis: SAR231893 / EFC14153 / CSR_RWE

2 PRO endpoints

2.4 Responder analysis for change from baseline in PAQLQ(S)-IA global score (improvement >= 0.9) at week 52 - ITT type 2 inflammatory asthma phenotype population

2.4.11 By baseline total IgE (<100 IU/ml, >= 100 IU/ml)

	Baseline Total IgE (IU/mL)			
	< 100		>= 100	
Type 2 inflammatory asthma phenotype population	**Placebo (N=19)**	**Dupilumab (N=24)**	**Placebo (N=87)**	**Dupilumab (N=182)**
Reversed Risk ratio (95% CI) vs placebo	-	0.88 (0.29 to 2.65)	-	0.80 (0.60 to 1.05)
p-value for Risk Ratio	-	0.817	-	0.102
p-value for heterogeneity of Risk Ratio				0.782
Risk Difference (95% CI) vs placebo	-	9.04 (-37.42 to 55.49)	-	16.73 (2.82 to 30.65)
p-value for Risk Difference	-	0.695	-	0.019
p-value for heterogeneity of Risk Difference				0.701

[a] Patients who met the corresponding criterion are considered as responders. Patients who did not meet the criterion or had missing value are considered as non-responders.
OR, RR and RD are derived from a logistic regression model with treatment, age, weight group, region, baseline eosinophil level, baseline FeNO level, baseline ICS dose level, and baseline PAQLQ(S)-IA global score as covariates.
Peto OR calculation is based on Yusuf S et al. (Prog Cardiovasc Dis. 1985 Mar-Apr;27(5):335-71) and its p-value is derived using a normal approximation.
p-values for heterogeneity are estimated by using the same logistic model as the one used to estimate OR, RR and RD, with subgroup and treatment-by-subgroup interaction as additional covariates.
p-value for heterogeneity of Peto OR is estimated by using normal approximation.
Only patients of age >=7 years old at randomization are included in the analysis.
PGM=DEVOPS/SAR231893/EFC14153/CSR_RWE/REPORT/PGM/eff_pro_evt_ger_subg_i_t.sas OUT=REPORT/OUTPUT/eff_pro_aqlqbw52_ger_ige_t2_t_x.rtf (29JUN2021 - 17:49)

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

Project Code / Study Number / Analysis: SAR231893 / EFC14153 / CSR_RWE

2 PRO endpoints

2.4 Responder analysis for change from baseline in PAQLQ(S)-IA global score (improvement >= 0.9) at week 52 - ITT type 2 inflammatory asthma phenotype population

2.4.12 By age at onset of asthma (0-2, 3-5, >=6 years)

	Age of onset of asthma (years)					
	0-2		3-5		>= 6	
Type 2 inflammatory asthma phenotype population	**Placebo (N=36)**	**Dupilumab (N=89)**	**Placebo (N=36)**	**Dupilumab (N=77)**	**Placebo (N=35)**	**Dupilumab (N=45)**
Responder status at Week 52 based on change from baseline in PAQLQ(S)-IA global score >=0.9 [n(%)] [a]						
Responder	12 (33.3%)	57 (64.0%)	22 (61.1%)	41 (53.2%)	22 (62.9%)	34 (75.6%)
Non-responder	24 (66.7%)	32 (36.0%)	14 (38.9%)	36 (46.8%)	13 (37.1%)	11 (24.4%)
Odds Ratio (95% CI) vs placebo	-	4.90 (1.61 to 14.90)	-	1.21 (0.39 to 3.76)	-	1.99 (0.42 to 9.39)
p-value for Odds Ratio	-	0.006	-	0.741	-	0.380
p-value for heterogeneity of Odds Ratio:						
0-2, 3-5						0.047
0-2, >= 6						0.152

[a] Patients who met the corresponding criterion are considered as responders. Patients who did not meet the criterion or had missing value are considered as non-responders.
OR, RR and RD are derived from a logistic regression model with treatment, age, weight group, region, baseline eosinophil level, baseline FeNO level, baseline ICS dose level, and baseline PAQLQ(S)-IA global score as covariates.
Peto OR calculation is based on Yusuf S et al. (Prog Cardiovasc Dis. 1985 Mar-Apr;27(5):335-71) and its p-value is derived using a normal approximation.
p-values for heterogeneity are estimated by using the same logistic model as the one used to estimate OR, RR and RD, with subgroup and treatment-by-subgroup interaction as additional covariates.
p-value for heterogeneity of Peto OR is estimated by using normal approximation.
Only patients of age >=7 years old at randomization are included in the analysis.
PGM=DEVOPS/SAR231893/EFC14153/CSR_RWE/REPORT/PGM/eff_pro_evt_ger_subg_i_t.sas OUT=REPORT/OUTPUT/eff_pro_aqlqbw52_ger_onsa_t2_t_x.rtf (01SEP2021 - 15:27)

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

Project Code / Study Number / Analysis: SAR231893 / EFC14153 / CSR_RWE

2 PRO endpoints

2.4 Responder analysis for change from baseline in PAQLQ(S)-IA global score (improvement >= 0.9) at week 52 - ITT type 2 inflammatory asthma phenotype population

2.4.12 By age at onset of asthma (0-2, 3-5, >=6 years)

	Age of onset of asthma (years)					
	0-2		3-5		>= 6	
Type 2 inflammatory asthma phenotype population	**Placebo (N=36)**	**Dupilumab (N=89)**	**Placebo (N=36)**	**Dupilumab (N=77)**	**Placebo (N=35)**	**Dupilumab (N=45)**
3-5, >= 6						0.656
overall						0.118
Risk Ratio (95% CI) vs placebo	-	1.52 (0.88 to 2.64)	-	1.01 (0.58 to 1.75)	-	1.32 (0.68 to 2.58)
Reversed Risk ratio (95% CI) vs placebo	-	0.66 (0.38 to 1.14)	-	0.99 (0.57 to 1.72)	-	0.76 (0.39 to 1.48)
p-value for Risk Ratio	-	0.135	-	0.972	-	0.410
p-value for heterogeneity of Risk Ratio:						
0-2, 3-5						0.177
0-2, >= 6						0.622
3-5, >= 6						0.398

[a] Patients who met the corresponding criterion are considered as responders. Patients who did not meet the criterion or had missing value are considered as non-responders.
OR, RR and RD are derived from a logistic regression model with treatment, age, weight group, region, baseline eosinophil level, baseline FeNO level, baseline ICS dose level, and baseline PAQLQ(S)-IA global score as covariates.
Peto OR calculation is based on Yusuf S et al. (Prog Cardiovasc Dis. 1985 Mar-Apr;27(5):335-71) and its p-value is derived using a normal approximation.
p-values for heterogeneity are estimated by using the same logistic model as the one used to estimate OR, RR and RD, with subgroup and treatment-by-subgroup interaction as additional covariates.
p-value for heterogeneity of Peto OR is estimated by using normal approximation.
Only patients of age >=7 years old at randomization are included in the analysis.
PGM=DEVOPS/SAR231893/EFC14153/CSR_RWE/REPORT/PGM/eff_pro_evt_ger_subg_i_t.sas OUT=REPORT/OUTPUT/eff_pro_aqlqbw52_ger_onsa_t2_t_x.rtf (01SEP2021 - 15:27)

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

Project Code / Study Number / Analysis: SAR231893 / EFC14153 / CSR_RWE

2 PRO endpoints

2.4 Responder analysis for change from baseline in PAQLQ(S)-IA global score (improvement >= 0.9) at week 52 - ITT type 2 inflammatory asthma phenotype population

2.4.12 By age at onset of asthma (0-2, 3-5, >=6 years)

	Age of onset of asthma (years)					
	0-2		3-5		>= 6	
Type 2 inflammatory asthma phenotype population	**Placebo (N=36)**	**Dupilumab (N=89)**	**Placebo (N=36)**	**Dupilumab (N=77)**	**Placebo (N=35)**	**Dupilumab (N=45)**
overall						0.375
Risk Difference (95% CI) vs placebo	-	25.83 (3.61 to 48.05)	-	5.71 (-19.37 to 30.80)	-	21.50 (-10.62 to 53.62)
p-value for Risk Difference	-	0.023	-	0.652	-	0.186
p-value for heterogeneity of Risk Difference:						
0-2, 3-5						0.253
0-2, >= 6						0.729
3-5, >= 6						0.518
overall						0.513

[a] Patients who met the corresponding criterion are considered as responders. Patients who did not meet the criterion or had missing value are considered as non-responders.
OR, RR and RD are derived from a logistic regression model with treatment, age, weight group, region, baseline eosinophil level, baseline FeNO level, baseline ICS dose level, and baseline PAQLQ(S)-IA global score as covariates.
Peto OR calculation is based on Yusuf S et al. (Prog Cardiovasc Dis. 1985 Mar-Apr;27(5):335-71) and its p-value is derived using a normal approximation.
p-values for heterogeneity are estimated by using the same logistic model as the one used to estimate OR, RR and RD, with subgroup and treatment-by-subgroup interaction as additional covariates.
p-value for heterogeneity of Peto OR is estimated by using normal approximation.
Only patients of age >=7 years old at randomization are included in the analysis.
PGM=DEVOPS/SAR231893/EFC14153/CSR_RWE/REPORT/PGM/eff_pro_evt_ger_subg_i_t.sas OUT=REPORT/OUTPUT/eff_pro_aqlqbw52_ger_onsa_t2_t_x.rtf (01SEP2021 - 15:27)

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

Project Code / Study Number / Analysis: SAR231893 / EFC14153 / CSR_RWE

2 PRO endpoints

2.4 Responder analysis for change from baseline in PAQLQ(S)-IA global score (improvement >= 0.9) at week 52 - ITT type 2 inflammatory asthma phenotype population

2.4.13 By number of severe asthma exacerbation prior to the study (<=1, 2, >2)

	Number of severe asthma exacerbation prior to the study					
	<=1		**2**		**>2**	
Type 2 inflammatory asthma phenotype population	**Placebo (N=43)**	**Dupilumab (N=78)**	**Placebo (N=30)**	**Dupilumab (N=66)**	**Placebo (N=34)**	**Dupilumab (N=67)**
Responder status at Week 52 based on change from baseline in PAQLQ(S)-IA global score >=0.9 [n(%)] [a]						
Responder	23 (53.5%)	46 (59.0%)	14 (46.7%)	41 (62.1%)	19 (55.9%)	45 (67.2%)
Non-responder	20 (46.5%)	32 (41.0%)	16 (53.3%)	25 (37.9%)	15 (44.1%)	22 (32.8%)
Odds Ratio (95% CI) vs placebo	-	2.31 (0.78 to 6.84)	-	2.79 (0.71 to 11.00)	-	1.66 (0.47 to 5.81)
p-value for Odds Ratio	-	0.128	-	0.141	-	0.426
p-value for heterogeneity of Odds Ratio:						
<=1, 2						0.857
<=1, >2						0.679

[a] Patients who met the corresponding criterion are considered as responders. Patients who did not meet the criterion or had missing value are considered as non-responders.
OR, RR and RD are derived from a logistic regression model with treatment, age, weight group, region, baseline eosinophil level, baseline FeNO level, baseline ICS dose level, and baseline PAQLQ(S)-IA global score as covariates.
Peto OR calculation is based on Yusuf S et al. (Prog Cardiovasc Dis. 1985 Mar-Apr;27(5):335-71) and its p-value is derived using a normal approximation.
p-values for heterogeneity are estimated by using the same logistic model as the one used to estimate OR, RR and RD, with subgroup and treatment-by-subgroup interaction as additional covariates.
p-value for heterogeneity of Peto OR is estimated by using normal approximation.
Only patients of age >=7 years old at randomization are included in the analysis.
PGM=DEVOPS/SAR231893/EFC14153/CSR_RWE/REPORT/PGM/eff_pro_evt_ger_subg_i_t.sas OUT=REPORT/OUTPUT/eff_pro_aqlqbw52_ger_exa_t2_t_x.rtf (29JUN2021 - 17:50)

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

Project Code / Study Number / Analysis: SAR231893 / EFC14153 / CSR_RWE

2 PRO endpoints

2.4 Responder analysis for change from baseline in PAQLQ(S)-IA global score (improvement >= 0.9) at week 52 - ITT type 2 inflammatory asthma phenotype population

2.4.13 By number of severe asthma exacerbation prior to the study (<=1, 2, >2)

	Number of severe asthma exacerbation prior to the study					
	<=1		2		>2	
Type 2 inflammatory asthma phenotype population	**Placebo (N=43)**	**Dupilumab (N=78)**	**Placebo (N=30)**	**Dupilumab (N=66)**	**Placebo (N=34)**	**Dupilumab (N=67)**
2, >2						0.822
overall						0.918
Risk Ratio (95% CI) vs placebo	-	1.30 (0.78 to 2.15)	-	1.31 (0.64 to 2.69)	-	1.11 (0.70 to 1.78)
Reversed Risk ratio (95% CI) vs placebo	-	0.77 (0.46 to 1.28)	-	0.76 (0.37 to 1.56)	-	0.90 (0.56 to 1.44)
p-value for Risk Ratio	-	0.312	-	0.450	-	0.654
p-value for heterogeneity of Risk Ratio:						
<=1, 2						0.750
<=1, >2						0.499
2, >2						0.811

[a] Patients who met the corresponding criterion are considered as responders. Patients who did not meet the criterion or had missing value are considered as non-responders.
OR, RR and RD are derived from a logistic regression model with treatment, age, weight group, region, baseline eosinophil level, baseline FeNO level, baseline ICS dose level, and baseline PAQLQ(S)-IA global score as covariates.
Peto OR calculation is based on Yusuf S et al. (Prog Cardiovasc Dis. 1985 Mar-Apr;27(5):335-71) and its p-value is derived using a normal approximation.
p-values for heterogeneity are estimated by using the same logistic model as the one used to estimate OR, RR and RD, with subgroup and treatment-by-subgroup interaction as additional covariates.
p-value for heterogeneity of Peto OR is estimated by using normal approximation.
Only patients of age >=7 years old at randomization are included in the analysis.
PGM=DEVOPS/SAR231893/EFC14153/CSR_RWE/REPORT/PGM/eff_pro_evt_ger_subg_i_t.sas OUT=REPORT/OUTPUT/eff_pro_aqlqbw52_ger_exa_t2_t_x.rtf (29JUN2021 - 17:50)

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

Project Code / Study Number / Analysis: SAR231893 / EFC14153 / CSR_RWE

2 PRO endpoints

2.4 Responder analysis for change from baseline in PAQLQ(S)-IA global score (improvement >= 0.9) at week 52 - ITT type 2 inflammatory asthma phenotype population

2.4.13 By number of severe asthma exacerbation prior to the study (<=1, 2, >2)

	Number of severe asthma exacerbation prior to the study					
	<=1		**2**		**>2**	
Type 2 inflammatory asthma phenotype population	**Placebo (N=43)**	**Dupilumab (N=78)**	**Placebo (N=30)**	**Dupilumab (N=66)**	**Placebo (N=34)**	**Dupilumab (N=67)**
overall						0.794
Risk Difference (95% CI) vs placebo	-	24.32 (1.83 to 46.81)	-	16.98 (-11.97 to 45.92)	-	7.50 (-15.50 to 30.50)
p-value for Risk Difference	-	0.034	-	0.247	-	0.518
p-value for heterogeneity of Risk Difference:						
<=1, 2						0.514
<=1, >2						0.436
2, >2						0.977
overall						0.691

[a] Patients who met the corresponding criterion are considered as responders. Patients who did not meet the criterion or had missing value are considered as non-responders.
OR, RR and RD are derived from a logistic regression model with treatment, age, weight group, region, baseline eosinophil level, baseline FeNO level, baseline ICS dose level, and baseline PAQLQ(S)-IA global score as covariates.
Peto OR calculation is based on Yusuf S et al. (Prog Cardiovasc Dis. 1985 Mar-Apr;27(5):335-71) and its p-value is derived using a normal approximation.
p-values for heterogeneity are estimated by using the same logistic model as the one used to estimate OR, RR and RD, with subgroup and treatment-by-subgroup interaction as additional covariates.
p-value for heterogeneity of Peto OR is estimated by using normal approximation.
Only patients of age >=7 years old at randomization are included in the analysis.
PGM=DEVOPS/SAR231893/EFC14153/CSR_RWE/REPORT/PGM/eff_pro_evt_ger_subg_i_t.sas OUT=REPORT/OUTPUT/eff_pro_aqlqbw52_ger_exa_t2_t_x.rtf (29JUN2021 - 17:50)

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

Project Code / Study Number / Analysis: SAR231893 / EFC14153 / CSR_RWE

2 PRO endpoints

2.5 Responder analysis for change from baseline in AM Asthma symptom score (improvement >= 0.6) at week 52 - ITT type 2 inflammatory asthma phenotype population

Type 2 inflammatory asthma phenotype population	**Placebo (N=114)**	**Dupilumab (N=236)**
Responder status at Week 52 based on change from baseline in AM symptom score <=-0.6 [n(%)] [a]		
Responder	42 (36.8%)	93 (39.4%)
Non-responder	72 (63.2%)	143 (60.6%)
Odds Ratio (95% CI)	-	1.36 (0.71 to 2.59)
p-value for Odds Ratio		0.355
Risk Ratio (95% CI)	-	1.07 (0.76 to 1.50)
Reversed Risk ratio (95% CI)	-	0.94 (0.67 to 1.31)
p-value for Risk Ratio		0.699
Risk Difference (95% CI)	-	1.40 (-10.74 to 13.54)
p-value for Risk Difference		0.821

[a] Patients who met the corresponding criterion are considered as responders. Patients who did not meet the criterion or had missing value are considered as non-responders. OR, RR and RD are derived from a logistic regression model with treatment, age, weight group, region, baseline eosinophil level, baseline FeNO level, baseline ICS dose level, and baseline AM Asthma symptom score as covariates.
Peto OR calculation is based on Yusuf S et al. (Prog Cardiovasc Dis. 1985 Mar-Apr;27(5):335-71) and its p-value is derived using a normal approximation.
PGM=DEVOPS/SAR231893/EFC14153/CSR_RWE/REPORT/PGM/eff_pro_evt_ger_i_t.sas OUT=REPORT/OUTPUT/eff_pro_scamw52_ger_t2_t_x.rtf (30JUN2021 - 8:14)

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

Project Code / Study Number / Analysis: SAR231893 / EFC14153 / CSR_RWE

2 PRO endpoints

2.5 Responder analysis for change from baseline in AM Asthma symptom score (improvement >= 0.6) at week 52 - ITT type 2 inflammatory asthma phenotype population

2.5.1 By gender (Male, Female)

	Gender			
	Male		Female	
Type 2 inflammatory asthma phenotype population	**Placebo (N=78)**	**Dupilumab (N=152)**	**Placebo (N=36)**	**Dupilumab (N=84)**
Responder status at Week 52 based on change from baseline in AM symptom score <=-0.6 [n(%)] [a]				
Responder	27 (34.6%)	57 (37.5%)	15 (41.7%)	36 (42.9%)
Non-responder	51 (65.4%)	95 (62.5%)	21 (58.3%)	48 (57.1%)
Odds Ratio (95% CI) vs placebo	-	1.53 (0.68 to 3.44)	-	1.14 (0.36 to 3.67)
p-value for Odds Ratio	-	0.304	-	0.821
p-value for heterogeneity of Odds Ratio				0.527
Risk Ratio (95% CI) vs placebo	-	1.07 (0.69 to 1.68)	-	0.70 (0.38 to 1.30)
Reversed Risk ratio (95% CI) vs placebo	-	0.93 (0.60 to 1.46)		

[a] Patients who met the corresponding criterion are considered as responders. Patients who did not meet the criterion or had missing value are considered as non-responders.
OR, RR and RD are derived from a logistic regression model with treatment, age, weight group, region, baseline eosinophil level, baseline FeNO level, baseline ICS dose level, and baseline AM Asthma symptom score as covariates.
Peto OR calculation is based on Yusuf S et al. (Prog Cardiovasc Dis. 1985 Mar-Apr;27(5):335-71) and its p-value is derived using a normal approximation.
p-values for heterogeneity are estimated by using the same logistic model as the one used to estimate OR, RR and RD, with subgroup and treatment-by-subgroup interaction as additional covariates.
p-value for heterogeneity of Peto OR is estimated by using normal approximation.
PGM=DEVOPS/SAR231893/EFC14153/CSR_RWE/REPORT/PGM/eff_pro_evt_ger_subg_i_t.sas OUT=REPORT/OUTPUT/eff_pro_scamw52_ger_sex_t2_t_x.rtf (29JUN2021 - 17:50)

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

Project Code / Study Number / Analysis: SAR231893 / EFC14153 / CSR_RWE

2 PRO endpoints

2.5 Responder analysis for change from baseline in AM Asthma symptom score (improvement >= 0.6) at week 52 - ITT type 2 inflammatory asthma phenotype population

2.5.1 By gender (Male, Female)

	Gender			
	Male		Female	
Type 2 inflammatory asthma phenotype population	**Placebo (N=78)**	**Dupilumab (N=152)**	**Placebo (N=36)**	**Dupilumab (N=84)**
p-value for Risk Ratio	-	0.755	-	0.258
p-value for heterogeneity of Risk Ratio				0.039
Risk Difference (95% CI) vs placebo	-	4.83 (-11.66 to 21.33)	-	-5.89 (-30.87 to 19.08)
p-value for Risk Difference	-	0.564	-	0.641
p-value for heterogeneity of Risk Difference				0.255

[a] Patients who met the corresponding criterion are considered as responders. Patients who did not meet the criterion or had missing value are considered as non-responders.
OR, RR and RD are derived from a logistic regression model with treatment, age, weight group, region, baseline eosinophil level, baseline FeNO level, baseline ICS dose level, and baseline AM Asthma symptom score as covariates.
Peto OR calculation is based on Yusuf S et al. (Prog Cardiovasc Dis. 1985 Mar-Apr;27(5):335-71) and its p-value is derived using a normal approximation.
p-values for heterogeneity are estimated by using the same logistic model as the one used to estimate OR, RR and RD, with subgroup and treatment-by-subgroup interaction as additional covariates.
p-value for heterogeneity of Peto OR is estimated by using normal approximation.
PGM=DEVOPS/SAR231893/EFC14153/CSR_RWE/REPORT/PGM/eff_pro_evt_ger_subg_i_t.sas OUT=REPORT/OUTPUT/eff_pro_scamw52_ger_sex_t2_t_x.rtf (29JUN2021 - 17:50)

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

Project Code / Study Number / Analysis: SAR231893 / EFC14153 / CSR_RWE

2 PRO endpoints

2.5 Responder analysis for change from baseline in AM Asthma symptom score (improvement >= 0.6) at week 52 - ITT type 2 inflammatory asthma phenotype population

2.5.2 By region (Latin America, East Europe, Western Countries)

	Region					
	Latin America		East Europe		Western countries	
Type 2 inflammatory asthma phenotype population	**Placebo (N=51)**	**Dupilumab (N=106)**	**Placebo (N=43)**	**Dupilumab (N=78)**	**Placebo (N=20)**	**Dupilumab (N=52)**
Responder status at Week 52 based on change from baseline in AM symptom score <=-0.6 [n(%)] [a]						
Responder	20 (39.2%)	44 (41.5%)	15 (34.9%)	32 (41.0%)	7 (35.0%)	17 (32.7%)
Non-responder	31 (60.8%)	62 (58.5%)	28 (65.1%)	46 (59.0%)	13 (65.0%)	35 (67.3%)
Odds Ratio (95% CI) vs placebo	-	0.86 (0.34 to 2.17)	-	2.11 (0.60 to 7.36)	-	4.94 (0.47 to 51.96)
p-value for Odds Ratio	-	0.752	-	0.239	-	0.180
p-value for heterogeneity of Odds Ratio:						
Latin America, East Europe						0.252
Latin America, Western countries						0.353

[a] Patients who met the corresponding criterion are considered as responders. Patients who did not meet the criterion or had missing value are considered as non-responders.
OR, RR and RD are derived from a logistic regression model with treatment, age, weight group, baseline eosinophil level, baseline FeNO level, baseline ICS dose level, and baseline AM Asthma symptom score as covariates.
Peto OR calculation is based on Yusuf S et al. (Prog Cardiovasc Dis. 1985 Mar-Apr;27(5):335-71) and its p-value is derived using a normal approximation.
p-values for heterogeneity are estimated by using the same logistic model as the one used to estimate OR, RR and RD, with subgroup and treatment-by-subgroup interaction as additional covariates.
p-value for heterogeneity of Peto OR is estimated by using normal approximation.
PGM=DEVOPS/SAR231893/EFC14153/CSR_RWE/REPORT/PGM/eff_pro_evt_ger_subg_i_t.sas OUT=REPORT/OUTPUT/eff_pro_scamw52_ger_cty_t2_t_x.rtf (29JUN2021 - 17:50)

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

Project Code / Study Number / Analysis: SAR231893 / EFC14153 / CSR_RWE

2 PRO endpoints

2.5 Responder analysis for change from baseline in AM Asthma symptom score (improvement >= 0.6) at week 52 - ITT type 2 inflammatory asthma phenotype population

2.5.2 By region (Latin America, East Europe, Western Countries)

	Region					
	Latin America		East Europe		Western countries	
Type 2 inflammatory asthma phenotype population	**Placebo (N=51)**	**Dupilumab (N=106)**	**Placebo (N=43)**	**Dupilumab (N=78)**	**Placebo (N=20)**	**Dupilumab (N=52)**
East Europe, Western countries						0.936
overall						0.439
Risk Ratio (95% CI) vs placebo	-	0.83 (0.55 to 1.27)	-	1.11 (0.57 to 2.14)	-	1.77 (0.38 to 8.29)
Reversed Risk ratio (95% CI) vs placebo			-	0.90 (0.47 to 1.75)	-	0.56 (0.12 to 2.64)
p-value for Risk Ratio	-	0.389	-	0.758	-	0.462
p-value for heterogeneity of Risk Ratio:						
Latin America, East Europe						0.001
Latin America, Western countries						0.468
East Europe, Western countries						0.253

[a] Patients who met the corresponding criterion are considered as responders. Patients who did not meet the criterion or had missing value are considered as non-responders.
OR, RR and RD are derived from a logistic regression model with treatment, age, weight group, baseline eosinophil level, baseline FeNO level, baseline ICS dose level, and baseline AM Asthma symptom score as covariates.
Peto OR calculation is based on Yusuf S et al. (Prog Cardiovasc Dis. 1985 Mar-Apr;27(5):335-71) and its p-value is derived using a normal approximation.
p-values for heterogeneity are estimated by using the same logistic model as the one used to estimate OR, RR and RD, with subgroup and treatment-by-subgroup interaction as additional covariates.
p-value for heterogeneity of Peto OR is estimated by using normal approximation.
PGM=DEVOPS/SAR231893/EFC14153/CSR_RWE/REPORT/PGM/eff_pro_evt_ger_subg_i_t.sas OUT=REPORT/OUTPUT/eff_pro_scamw52_ger_cty_t2_t_x.rtf (29JUN2021 - 17:50)

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

Project Code / Study Number / Analysis: SAR231893 / EFC14153 / CSR_RWE

2 PRO endpoints

2.5 Responder analysis for change from baseline in AM Asthma symptom score (improvement >= 0.6) at week 52 - ITT type 2 inflammatory asthma phenotype population

2.5.2 By region (Latin America, East Europe, Western Countries)

	Region					
	Latin America		East Europe		Western countries	
Type 2 inflammatory asthma phenotype population	**Placebo (N=51)**	**Dupilumab (N=106)**	**Placebo (N=43)**	**Dupilumab (N=78)**	**Placebo (N=20)**	**Dupilumab (N=52)**
overall						0.005
Risk Difference (95% CI) vs placebo	-	-6.88 (-24.92 to 11.16)	-	9.32 (-15.79 to 34.42)	-	12.00 (-33.72 to 57.71)
p-value for Risk Difference	-	0.452	-	0.464	-	0.602
p-value for heterogeneity of Risk Difference:						
Latin America, East Europe						0.087
Latin America, Western countries						0.474
East Europe, Western countries						0.634
overall						0.225

[a] Patients who met the corresponding criterion are considered as responders. Patients who did not meet the criterion or had missing value are considered as non-responders.
OR, RR and RD are derived from a logistic regression model with treatment, age, weight group, baseline eosinophil level, baseline FeNO level, baseline ICS dose level, and baseline AM Asthma symptom score as covariates.
Peto OR calculation is based on Yusuf S et al. (Prog Cardiovasc Dis. 1985 Mar-Apr;27(5):335-71) and its p-value is derived using a normal approximation.
p-values for heterogeneity are estimated by using the same logistic model as the one used to estimate OR, RR and RD, with subgroup and treatment-by-subgroup interaction as additional covariates.
p-value for heterogeneity of Peto OR is estimated by using normal approximation.
PGM=DEVOPS/SAR231893/EFC14153/CSR_RWE/REPORT/PGM/eff_pro_evt_ger_subg_i_t.sas OUT=REPORT/OUTPUT/eff_pro_scamw52_ger_cty_t2_t_x.rtf (29JUN2021 - 17:50)

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

Project Code / Study Number / Analysis: SAR231893 / EFC14153 / CSR_RWE

2 PRO endpoints

2.5 Responder analysis for change from baseline in AM Asthma symptom score (improvement >= 0.6) at week 52 - ITT type 2 inflammatory asthma phenotype population

2.5.3 By race (Caucasian/white, Black/of African descent, Other)

	Race					
	Caucasian/White		Black/of African descent		Other	
Type 2 inflammatory asthma phenotype population	**Placebo (N=102)**	**Dupilumab (N=208)**	**Placebo (N=5)**	**Dupilumab (N=9)**	**Placebo (N=7)**	**Dupilumab (N=19)**
Responder status at Week 52 based on change from baseline in AM symptom score <=-0.6 [n(%)] [a]						
Responder	41 (40.2%)	82 (39.4%)	1 (20.0%)	4 (44.4%)	0	7 (36.8%)
Non-responder	61 (59.8%)	126 (60.6%)	4 (80.0%)	5 (55.6%)	7 (100%)	12 (63.2%)
Odds Ratio (95% CI) vs placebo	-	1.01 (0.51 to 1.99)	-	0.00 (0.00 to NE)	-	6.742E10 (0.00 to NE)
p-value for Odds Ratio	-	0.984	-	0.993	-	0.964
Peto Odds Ratio (95% CI) vs placebo	-	0.97 (0.60 to 1.57)	-	2.69 (0.30 to 24.22)	-	6.05 (0.89 to 41.11)

[a] Patients who met the corresponding criterion are considered as responders. Patients who did not meet the criterion or had missing value are considered as non-responders.
OR, RR and RD are derived from a logistic regression model with treatment, age, weight group, region, baseline eosinophil level, baseline FeNO level, baseline ICS dose level, and baseline AM Asthma symptom score as covariates.
Peto OR calculation is based on Yusuf S et al. (Prog Cardiovasc Dis. 1985 Mar-Apr;27(5):335-71) and its p-value is derived using a normal approximation.
p-values for heterogeneity are estimated by using the same logistic model as the one used to estimate OR, RR and RD, with subgroup and treatment-by-subgroup interaction as additional covariates.
p-value for heterogeneity of Peto OR is estimated by using normal approximation.
PGM=DEVOPS/SAR231893/EFC14153/CSR_RWE/REPORT/PGM/eff_pro_evt_ger_subg_i_t.sas OUT=REPORT/OUTPUT/eff_pro_scamw52_ger_race_t2_t_x.rtf (29JUN2021 - 17:51)

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

Project Code / Study Number / Analysis: SAR231893 / EFC14153 / CSR_RWE

2 PRO endpoints

2.5 Responder analysis for change from baseline in AM Asthma symptom score (improvement >= 0.6) at week 52 - ITT type 2 inflammatory asthma phenotype population

2.5.3 By race (Caucasian/white, Black/of African descent, Other)

	Race					
	Caucasian/White		Black/of African descent		Other	
Type 2 inflammatory asthma phenotype population	**Placebo (N=102)**	**Dupilumab (N=208)**	**Placebo (N=5)**	**Dupilumab (N=9)**	**Placebo (N=7)**	**Dupilumab (N=19)**
Reversed Peto Odds Ratio (95% CI)			-	0.37 (0.04 to 3.33)	-	0.17 (0.02 to 1.12)
p-value for Peto Odds Ratio		0.896		0.378		0.065
p-value for heterogeneity of Peto Odds Ratio:						
Caucasian/White, Black/of African descent						0.374
Caucasian/White, Other						0.069
Black/of African descent, Other						0.585
overall						0.140

[a] Patients who met the corresponding criterion are considered as responders. Patients who did not meet the criterion or had missing value are considered as non-responders.
OR, RR and RD are derived from a logistic regression model with treatment, age, weight group, region, baseline eosinophil level, baseline FeNO level, baseline ICS dose level, and baseline AM Asthma symptom score as covariates.
Peto OR calculation is based on Yusuf S et al. (Prog Cardiovasc Dis. 1985 Mar-Apr;27(5):335-71) and its p-value is derived using a normal approximation.
p-values for heterogeneity are estimated by using the same logistic model as the one used to estimate OR, RR and RD, with subgroup and treatment-by-subgroup interaction as additional covariates.
p-value for heterogeneity of Peto OR is estimated by using normal approximation.
PGM=DEVOPS/SAR231893/EFC14153/CSR_RWE/REPORT/PGM/eff_pro_evt_ger_subg_i_t.sas OUT=REPORT/OUTPUT/eff_pro_scamw52_ger_race_t2_t_x.rtf (29JUN2021 - 17:51)

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

Project Code / Study Number / Analysis: SAR231893 / EFC14153 / CSR_RWE

2 PRO endpoints

2.5 Responder analysis for change from baseline in AM Asthma symptom score (improvement >= 0.6) at week 52 - ITT type 2 inflammatory asthma phenotype population

2.5.3 By race (Caucasian/white, Black/of African descent, Other)

	Race					
	Caucasian/White		Black/of African descent		Other	
Type 2 inflammatory asthma phenotype population	**Placebo (N=102)**	**Dupilumab (N=208)**	**Placebo (N=5)**	**Dupilumab (N=9)**	**Placebo (N=7)**	**Dupilumab (N=19)**
Risk Ratio (95% CI) vs placebo	-	0.98 (0.68 to 1.41)	-	0.47 (0.00 to 160.44)	-	3.87 (0.05 to 276.79)
Reversed Risk ratio (95% CI) vs placebo					-	0.26 (0.00 to 18.50)
p-value for Risk Ratio	-	0.903	-	0.739	-	0.511
p-value for heterogeneity of Risk Ratio:						
Caucasian/White, Black/of African descent						0.713
Caucasian/White, Other						0.990
Black/of African descent, Other						0.990
overall						0.934

[a] Patients who met the corresponding criterion are considered as responders. Patients who did not meet the criterion or had missing value are considered as non-responders.
OR, RR and RD are derived from a logistic regression model with treatment, age, weight group, region, baseline eosinophil level, baseline FeNO level, baseline ICS dose level, and baseline AM Asthma symptom score as covariates.
Peto OR calculation is based on Yusuf S et al. (Prog Cardiovasc Dis. 1985 Mar-Apr;27(5):335-71) and its p-value is derived using a normal approximation.
p-values for heterogeneity are estimated by using the same logistic model as the one used to estimate OR, RR and RD, with subgroup and treatment-by-subgroup interaction as additional covariates.
p-value for heterogeneity of Peto OR is estimated by using normal approximation.
PGM=DEVOPS/SAR231893/EFC14153/CSR_RWE/REPORT/PGM/eff_pro_evt_ger_subg_i_t.sas OUT=REPORT/OUTPUT/eff_pro_scamw52_ger_race_t2_t_x.rtf (29JUN2021 - 17:51)

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

Project Code / Study Number / Analysis: SAR231893 / EFC14153 / CSR_RWE

2 PRO endpoints

2.5 Responder analysis for change from baseline in AM Asthma symptom score (improvement >= 0.6) at week 52 - ITT type 2 inflammatory asthma phenotype population

2.5.3 By race (Caucasian/white, Black/of African descent, Other)

	Race					
	Caucasian/White		Black/of African descent		Other	
Type 2 inflammatory asthma phenotype population	**Placebo (N=102)**	**Dupilumab (N=208)**	**Placebo (N=5)**	**Dupilumab (N=9)**	**Placebo (N=7)**	**Dupilumab (N=19)**
Risk Difference (95% CI) vs placebo	-	-0.77 (-13.67 to 12.13)	-	-16.90 (-307.38 to 273.57)	-	67.71 (-82.08 to 217.50)
p-value for Risk Difference	-	0.907	-	0.879	-	0.352
p-value for heterogeneity of Risk Difference:						
Caucasian/White, Black/of African descent						0.660
Caucasian/White, Other						0.633
Black/of African descent, Other						0.794
overall						0.813

[a] Patients who met the corresponding criterion are considered as responders. Patients who did not meet the criterion or had missing value are considered as non-responders.
OR, RR and RD are derived from a logistic regression model with treatment, age, weight group, region, baseline eosinophil level, baseline FeNO level, baseline ICS dose level, and baseline AM Asthma symptom score as covariates.
Peto OR calculation is based on Yusuf S et al. (Prog Cardiovasc Dis. 1985 Mar-Apr;27(5):335-71) and its p-value is derived using a normal approximation.
p-values for heterogeneity are estimated by using the same logistic model as the one used to estimate OR, RR and RD, with subgroup and treatment-by-subgroup interaction as additional covariates.
p-value for heterogeneity of Peto OR is estimated by using normal approximation.
PGM=DEVOPS/SAR231893/EFC14153/CSR_RWE/REPORT/PGM/eff_pro_evt_ger_subg_i_t.sas OUT=REPORT/OUTPUT/eff_pro_scamw52_ger_race_t2_t_x.rtf (29JUN2021 - 17:51)

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

Project Code / Study Number / Analysis: SAR231893 / EFC14153 / CSR_RWE

2 PRO endpoints

2.5 Responder analysis for change from baseline in AM Asthma symptom score (improvement >= 0.6) at week 52 - ITT type 2 inflammatory asthma phenotype population

2.5.4 By baseline ICS dose level (Medium, High)

	Baseline ICS dose level			
	High		Medium	
Type 2 inflammatory asthma phenotype population	**Placebo (N=50)**	**Dupilumab (N=102)**	**Placebo (N=64)**	**Dupilumab (N=131)**
Responder status at Week 52 based on change from baseline in AM symptom score <=-0.6 [n(%)] [a]				
Responder	21 (42.0%)	43 (42.2%)	21 (32.8%)	50 (38.2%)
Non-responder	29 (58.0%)	59 (57.8%)	43 (67.2%)	81 (61.8%)
Odds Ratio (95% CI) vs placebo	-	1.48 (0.52 to 4.20)	-	1.68 (0.68 to 4.16)
p-value for Odds Ratio	-	0.454	-	0.258
p-value for heterogeneity of Odds Ratio				0.939
Risk Ratio (95% CI) vs placebo	-	0.87 (0.55 to 1.38)	-	1.18 (0.69 to 2.01)
Reversed Risk ratio (95% CI) vs placebo			-	0.85 (0.50 to 1.45)

[a] Patients who met the corresponding criterion are considered as responders. Patients who did not meet the criterion or had missing value are considered as non-responders.
OR, RR and RD are derived from a logistic regression model with treatment, age, weight group, region, baseline eosinophil level, baseline FeNO level and baseline AM Asthma symptom score as covariates.
Peto OR calculation is based on Yusuf S et al. (Prog Cardiovasc Dis. 1985 Mar-Apr;27(5):335-71) and its p-value is derived using a normal approximation.
p-values for heterogeneity are estimated by using the same logistic model as the one used to estimate OR, RR and RD, with subgroup and treatment-by-subgroup interaction as additional covariates.
p-value for heterogeneity of Peto OR is estimated by using normal approximation.
PGM=DEVOPS/SAR231893/EFC14153/CSR_RWE/REPORT/PGM/eff_pro_evt_ger_subg_i_t.sas OUT=REPORT/OUTPUT/eff_pro_scamw52_ger_ics_t2_t_x.rtf (29JUN2021 - 17:51)

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

Project Code / Study Number / Analysis: SAR231893 / EFC14153 / CSR_RWE

2 PRO endpoints

2.5 Responder analysis for change from baseline in AM Asthma symptom score (improvement >= 0.6) at week 52 - ITT type 2 inflammatory asthma phenotype population

2.5.4 By baseline ICS dose level (Medium, High)

	Baseline ICS dose level			
	High		Medium	
Type 2 inflammatory asthma phenotype population	**Placebo (N=50)**	**Dupilumab (N=102)**	**Placebo (N=64)**	**Dupilumab (N=131)**
p-value for Risk Ratio	-	0.550	-	0.547
p-value for heterogeneity of Risk Ratio				0.017
Risk Difference (95% CI) vs placebo	-	-5.80 (-27.41 to 15.80)	-	9.06 (-10.29 to 28.42)
p-value for Risk Difference	-	0.596	-	0.357
p-value for heterogeneity of Risk Difference				0.269

[a] Patients who met the corresponding criterion are considered as responders. Patients who did not meet the criterion or had missing value are considered as non-responders.
OR, RR and RD are derived from a logistic regression model with treatment, age, weight group, region, baseline eosinophil level, baseline FeNO level and baseline AM Asthma symptom score as covariates.
Peto OR calculation is based on Yusuf S et al. (Prog Cardiovasc Dis. 1985 Mar-Apr;27(5):335-71) and its p-value is derived using a normal approximation.
p-values for heterogeneity are estimated by using the same logistic model as the one used to estimate OR, RR and RD, with subgroup and treatment-by-subgroup interaction as additional covariates.
p-value for heterogeneity of Peto OR is estimated by using normal approximation.
PGM=DEVOPS/SAR231893/EFC14153/CSR_RWE/REPORT/PGM/eff_pro_evt_ger_subg_i_t.sas OUT=REPORT/OUTPUT/eff_pro_scamw52_ger_ics_t2_t_x.rtf (29JUN2021 - 17:51)

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

Project Code / Study Number / Analysis: SAR231893 / EFC14153 / CSR_RWE

2 PRO endpoints

2.5 Responder analysis for change from baseline in AM Asthma symptom score (improvement >= 0.6) at week 52 - ITT type 2 inflammatory asthma phenotype population

2.5.5 By baseline ICS dose level 2 (Medium, High)

	Baseline ICS dose level 2			
	High		Medium	
Type 2 inflammatory asthma phenotype population	**Placebo (N=95)**	**Dupilumab (N=200)**	**Placebo (N=19)**	**Dupilumab (N=36)**
Responder status at Week 52 based on change from baseline in AM symptom score <=-0.6 [n(%)] [a]				
Responder	37 (38.9%)	81 (40.5%)	5 (26.3%)	12 (33.3%)
Non-responder	58 (61.1%)	119 (59.5%)	14 (73.7%)	24 (66.7%)
Odds Ratio (95% CI) vs placebo	-	1.23 (0.62 to 2.45)	-	2.05 (0.19 to 22.03)
p-value for Odds Ratio	-	0.545	-	0.545
p-value for heterogeneity of Odds Ratio				0.521
Risk Ratio (95% CI) vs placebo	-	1.07 (0.74 to 1.53)	-	NE (NE to NE)
Reversed Risk ratio (95% CI) vs placebo	-	0.94 (0.65 to 1.35)		

[a] Patients who met the corresponding criterion are considered as responders. Patients who did not meet the criterion or had missing value are considered as non-responders.
OR, RR and RD are derived from a logistic regression model with treatment, age, weight group, region, baseline eosinophil level, baseline FeNO level and baseline AM Asthma symptom score as covariates.
Peto OR calculation is based on Yusuf S et al. (Prog Cardiovasc Dis. 1985 Mar-Apr;27(5):335-71) and its p-value is derived using a normal approximation.
p-values for heterogeneity are estimated by using the same logistic model as the one used to estimate OR, RR and RD, with subgroup and treatment-by-subgroup interaction as additional covariates.
p-value for heterogeneity of Peto OR is estimated by using normal approximation.
PGM=DEVOPS/SAR231893/EFC14153/CSR_RWE/REPORT/PGM/eff_pro_evt_ger_subg_i_t.sas OUT=REPORT/OUTPUT/eff_pro_scamw52_ger_ics2_t2_t_x.rtf (01SEP2021 - 15:27)

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

Project Code / Study Number / Analysis: SAR231893 / EFC14153 / CSR_RWE

2 PRO endpoints

2.5 Responder analysis for change from baseline in AM Asthma symptom score (improvement >= 0.6) at week 52 - ITT type 2 inflammatory asthma phenotype population

2.5.5 By baseline ICS dose level 2 (Medium, High)

	Baseline ICS dose level 2			
	High		Medium	
Type 2 inflammatory asthma phenotype population	**Placebo (N=95)**	**Dupilumab (N=200)**	**Placebo (N=19)**	**Dupilumab (N=36)**
p-value for Risk Ratio	-	0.730	-	<0.001
p-value for heterogeneity of Risk Ratio				0.925
Risk Difference (95% CI) vs placebo	-	0.34 (-12.63 to 13.31)	-	2.95 (-46.84 to 52.75)
p-value for Risk Difference	-	0.959	-	0.905
p-value for heterogeneity of Risk Difference				0.992

[a] Patients who met the corresponding criterion are considered as responders. Patients who did not meet the criterion or had missing value are considered as non-responders.
OR, RR and RD are derived from a logistic regression model with treatment, age, weight group, region, baseline eosinophil level, baseline FeNO level and baseline AM Asthma symptom score as covariates.
Peto OR calculation is based on Yusuf S et al. (Prog Cardiovasc Dis. 1985 Mar-Apr;27(5):335-71) and its p-value is derived using a normal approximation.
p-values for heterogeneity are estimated by using the same logistic model as the one used to estimate OR, RR and RD, with subgroup and treatment-by-subgroup interaction as additional covariates.
p-value for heterogeneity of Peto OR is estimated by using normal approximation.
PGM=DEVOPS/SAR231893/EFC14153/CSR_RWE/REPORT/PGM/eff_pro_evt_ger_subg_i_t.sas OUT=REPORT/OUTPUT/eff_pro_scamw52_ger_ics2_t2_t_x.rtf (01SEP2021 - 15:27)

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

Project Code / Study Number / Analysis: SAR231893 / EFC14153 / CSR_RWE

2 PRO endpoints

2.5 Responder analysis for change from baseline in AM Asthma symptom score (improvement >= 0.6) at week 52 - ITT type 2 inflammatory asthma phenotype population

2.5.6 By baseline predicted FEV1 (<80%, >=80%)

	Baseline Predicted FEV1			
	<80%		>=80%	
Type 2 inflammatory asthma phenotype population	**Placebo (N=59)**	**Dupilumab (N=116)**	**Placebo (N=55)**	**Dupilumab (N=120)**
Responder status at Week 52 based on change from baseline in AM symptom score <=-0.6 [n(%)] [a]				
Responder	21 (35.6%)	46 (39.7%)	21 (38.2%)	47 (39.2%)
Non-responder	38 (64.4%)	70 (60.3%)	34 (61.8%)	73 (60.8%)
Odds Ratio (95% CI) vs placebo	-	1.45 (0.59 to 3.57)	-	1.58 (0.57 to 4.39)
p-value for Odds Ratio	-	0.420	-	0.374
p-value for heterogeneity of Odds Ratio				0.882
Risk Ratio (95% CI) vs placebo	-	0.95 (0.61 to 1.47)	-	0.94 (0.56 to 1.56)
p-value for Risk Ratio	-	0.816	-	0.799

[a] Patients who met the corresponding criterion are considered as responders. Patients who did not meet the criterion or had missing value are considered as non-responders.
OR, RR and RD are derived from a logistic regression model with treatment, age, weight group, region, baseline eosinophil level, baseline FeNO level, baseline ICS dose level, and baseline AM Asthma symptom score as covariates.
Peto OR calculation is based on Yusuf S et al. (Prog Cardiovasc Dis. 1985 Mar-Apr;27(5):335-71) and its p-value is derived using a normal approximation.
p-values for heterogeneity are estimated by using the same logistic model as the one used to estimate OR, RR and RD, with subgroup and treatment-by-subgroup interaction as additional covariates.
p-value for heterogeneity of Peto OR is estimated by using normal approximation.
PGM=DEVOPS/SAR231893/EFC14153/CSR_RWE/REPORT/PGM/eff_pro_evt_ger_subg_i_t.sas OUT=REPORT/OUTPUT/eff_pro_scamw52_ger_pfev1_t2_t_x.rtf (29JUN2021 - 17:51)

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

Project Code / Study Number / Analysis: SAR231893 / EFC14153 / CSR_RWE

2 PRO endpoints

2.5 Responder analysis for change from baseline in AM Asthma symptom score (improvement >= 0.6) at week 52 - ITT type 2 inflammatory asthma phenotype population

2.5.6 By baseline predicted FEV1 (<80%, >=80%)

	Baseline Predicted FEV1			
	<80%		>=80%	
Type 2 inflammatory asthma phenotype population	**Placebo (N=59)**	**Dupilumab (N=116)**	**Placebo (N=55)**	**Dupilumab (N=120)**
p-value for heterogeneity of Risk Ratio				0.105
Risk Difference (95% CI) vs placebo	-	-2.59 (-20.45 to 15.27)	-	4.97 (-15.93 to 25.87)
p-value for Risk Difference	-	0.775	-	0.639
p-value for heterogeneity of Risk Difference				0.375

[a] Patients who met the corresponding criterion are considered as responders. Patients who did not meet the criterion or had missing value are considered as non-responders.
OR, RR and RD are derived from a logistic regression model with treatment, age, weight group, region, baseline eosinophil level, baseline FeNO level, baseline ICS dose level, and baseline AM Asthma symptom score as covariates.
Peto OR calculation is based on Yusuf S et al. (Prog Cardiovasc Dis. 1985 Mar-Apr;27(5):335-71) and its p-value is derived using a normal approximation.
p-values for heterogeneity are estimated by using the same logistic model as the one used to estimate OR, RR and RD, with subgroup and treatment-by-subgroup interaction as additional covariates.
p-value for heterogeneity of Peto OR is estimated by using normal approximation.
PGM=DEVOPS/SAR231893/EFC14153/CSR_RWE/REPORT/PGM/eff_pro_evt_ger_subg_i_t.sas OUT=REPORT/OUTPUT/eff_pro_scamw52_ger_pfev1_t2_t_x.rtf (29JUN2021 - 17:51)

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

Project Code / Study Number / Analysis: SAR231893 / EFC14153 / CSR_RWE

2 PRO endpoints

2.5 Responder analysis for change from baseline in AM Asthma symptom score (improvement >= 0.6) at week 52 - ITT type 2 inflammatory asthma phenotype population

2.5.7 By baseline ACQ-7-IA (<=2, >2)

	Baseline ACQ-7-IA			
	<=2		**>2**	
Type 2 inflammatory asthma phenotype population	**Placebo (N=61)**	**Dupilumab (N=126)**	**Placebo (N=53)**	**Dupilumab (N=110)**
Responder status at Week 52 based on change from baseline in AM symptom score <=-0.6 [n(%)] [a]				
Responder	20 (32.8%)	33 (26.2%)	22 (41.5%)	60 (54.5%)
Non-responder	41 (67.2%)	93 (73.8%)	31 (58.5%)	50 (45.5%)
Odds Ratio (95% CI) vs placebo	-	0.86 (0.32 to 2.29)	-	2.07 (0.83 to 5.20)
p-value for Odds Ratio	-	0.761	-	0.120
p-value for heterogeneity of Odds Ratio				0.149
Risk Ratio (95% CI) vs placebo	-	0.77 (0.43 to 1.36)	-	1.00 (0.67 to 1.50)
Reversed Risk ratio (95% CI) vs placebo			-	1.00 (0.67 to 1.50)

[a] Patients who met the corresponding criterion are considered as responders. Patients who did not meet the criterion or had missing value are considered as non-responders.
OR, RR and RD are derived from a logistic regression model with treatment, age, weight group, region, baseline eosinophil level, baseline FeNO level, baseline ICS dose level, and baseline AM Asthma symptom score as covariates.
Peto OR calculation is based on Yusuf S et al. (Prog Cardiovasc Dis. 1985 Mar-Apr;27(5):335-71) and its p-value is derived using a normal approximation.
p-values for heterogeneity are estimated by using the same logistic model as the one used to estimate OR, RR and RD, with subgroup and treatment-by-subgroup interaction as additional covariates.
p-value for heterogeneity of Peto OR is estimated by using normal approximation.
PGM=DEVOPS/SAR231893/EFC14153/CSR_RWE/REPORT/PGM/eff_pro_evt_ger_subg_i_t.sas OUT=REPORT/OUTPUT/eff_pro_scamw52_ger_acq7_t2_t_x.rtf (29JUN2021 - 17:51)

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

Project Code / Study Number / Analysis: SAR231893 / EFC14153 / CSR_RWE

2 PRO endpoints

2.5 Responder analysis for change from baseline in AM Asthma symptom score (improvement >= 0.6) at week 52 - ITT type 2 inflammatory asthma phenotype population

2.5.7 By baseline ACQ-7-IA (<=2, >2)

	Baseline ACQ-7-IA			
	<=2		>2	
Type 2 inflammatory asthma phenotype population	**Placebo (N=61)**	**Dupilumab (N=126)**	**Placebo (N=53)**	**Dupilumab (N=110)**
p-value for Risk Ratio	-	0.361	-	0.995
p-value for heterogeneity of Risk Ratio				0.376
Risk Difference (95% CI) vs placebo	-	-3.49 (-22.42 to 15.43)	-	2.31 (-15.63 to 20.26)
p-value for Risk Difference	-	0.716	-	0.799
p-value for heterogeneity of Risk Difference				0.924

[a] Patients who met the corresponding criterion are considered as responders. Patients who did not meet the criterion or had missing value are considered as non-responders.
OR, RR and RD are derived from a logistic regression model with treatment, age, weight group, region, baseline eosinophil level, baseline FeNO level, baseline ICS dose level, and baseline AM Asthma symptom score as covariates.
Peto OR calculation is based on Yusuf S et al. (Prog Cardiovasc Dis. 1985 Mar-Apr;27(5):335-71) and its p-value is derived using a normal approximation.
p-values for heterogeneity are estimated by using the same logistic model as the one used to estimate OR, RR and RD, with subgroup and treatment-by-subgroup interaction as additional covariates.
p-value for heterogeneity of Peto OR is estimated by using normal approximation.
PGM=DEVOPS/SAR231893/EFC14153/CSR_RWE/REPORT/PGM/eff_pro_evt_ger_subg_i_t.sas OUT=REPORT/OUTPUT/eff_pro_scamw52_ger_acq7_t2_t_x.rtf (29JUN2021 - 17:51)

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

Project Code / Study Number / Analysis: SAR231893 / EFC14153 / CSR_RWE

2 PRO endpoints

2.5 Responder analysis for change from baseline in AM Asthma symptom score (improvement >= 0.6) at week 52 - ITT type 2 inflammatory asthma phenotype population

2.5.8 By baseline weight (<=30 kg, >30 kg)

	Baseline weight (kg)			
	<=30		>30	
Type 2 inflammatory asthma phenotype population	**Placebo (N=36)**	**Dupilumab (N=76)**	**Placebo (N=78)**	**Dupilumab (N=160)**
Responder status at Week 52 based on change from baseline in AM symptom score <=-0.6 [n(%)] [a]				
Responder	20 (55.6%)	32 (42.1%)	22 (28.2%)	61 (38.1%)
Non-responder	16 (44.4%)	44 (57.9%)	56 (71.8%)	99 (61.9%)
Odds Ratio (95% CI) vs placebo	-	0.58 (0.18 to 1.86)	-	2.11 (0.90 to 4.96)
p-value for Odds Ratio	-	0.355	-	0.087
p-value for heterogeneity of Odds Ratio				0.088
Risk Ratio (95% CI) vs placebo	-	0.60 (0.34 to 1.08)	-	1.05 (0.70 to 1.59)
Reversed Risk ratio (95% CI) vs placebo			-	0.95 (0.63 to 1.43)

[a] Patients who met the corresponding criterion are considered as responders. Patients who did not meet the criterion or had missing value are considered as non-responders.
OR, RR and RD are derived from a logistic regression model with treatment, age, region, baseline eosinophil level, baseline FeNO level, baseline ICS dose level, and baseline AM Asthma symptom score as covariates.
Peto OR calculation is based on Yusuf S et al. (Prog Cardiovasc Dis. 1985 Mar-Apr;27(5):335-71) and its p-value is derived using a normal approximation.
p-values for heterogeneity are estimated by using the same logistic model as the one used to estimate OR, RR and RD, with subgroup and treatment-by-subgroup interaction as additional covariates.
p-value for heterogeneity of Peto OR is estimated by using normal approximation.
PGM=DEVOPS/SAR231893/EFC14153/CSR_RWE/REPORT/PGM/eff_pro_evt_ger_subg_i_t.sas OUT=REPORT/OUTPUT/eff_pro_scamw52_ger_wgt_t2_t_x.rtf (29JUN2021 - 17:51)

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

Project Code / Study Number / Analysis: SAR231893 / EFC14153 / CSR_RWE

2 PRO endpoints

2.5 Responder analysis for change from baseline in AM Asthma symptom score (improvement >= 0.6) at week 52 - ITT type 2 inflammatory asthma phenotype population

2.5.8 By baseline weight (<=30 kg, >30 kg)

	Baseline weight (kg)			
	<=30		>30	
Type 2 inflammatory asthma phenotype population	**Placebo (N=36)**	**Dupilumab (N=76)**	**Placebo (N=78)**	**Dupilumab (N=160)**
p-value for Risk Ratio	-	0.088	-	0.806
p-value for heterogeneity of Risk Ratio				0.003
Risk Difference (95% CI) vs placebo	-	-19.40 (-44.79 to 5.99)	-	8.00 (-7.70 to 23.69)
p-value for Risk Difference	-	0.133	-	0.316
p-value for heterogeneity of Risk Difference				0.018

[a] Patients who met the corresponding criterion are considered as responders. Patients who did not meet the criterion or had missing value are considered as non-responders.
OR, RR and RD are derived from a logistic regression model with treatment, age, region, baseline eosinophil level, baseline FeNO level, baseline ICS dose level, and baseline AM Asthma symptom score as covariates.
Peto OR calculation is based on Yusuf S et al. (Prog Cardiovasc Dis. 1985 Mar-Apr;27(5):335-71) and its p-value is derived using a normal approximation.
p-values for heterogeneity are estimated by using the same logistic model as the one used to estimate OR, RR and RD, with subgroup and treatment-by-subgroup interaction as additional covariates.
p-value for heterogeneity of Peto OR is estimated by using normal approximation.
PGM=DEVOPS/SAR231893/EFC14153/CSR_RWE/REPORT/PGM/eff_pro_evt_ger_subg_i_t.sas OUT=REPORT/OUTPUT/eff_pro_scamw52_ger_wgt_t2_t_x.rtf (29JUN2021 - 17:51)

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

Project Code / Study Number / Analysis: SAR231893 / EFC14153 / CSR_RWE

2 PRO endpoints

2.5 Responder analysis for change from baseline in AM Asthma symptom score (improvement >= 0.6) at week 52 - ITT type 2 inflammatory asthma phenotype population

2.5.9 By atopic medical condition (Yes, No)

	Atopic medical condition			
	Yes		No	
Type 2 inflammatory asthma phenotype population	**Placebo (N=103)**	**Dupilumab (N=227)**	**Placebo (N=11)**	**Dupilumab (N=9)**
Responder status at Week 52 based on change from baseline in AM symptom score <=-0.6 [n(%)] [a]				
Responder	40 (38.8%)	87 (38.3%)	2 (18.2%)	6 (66.7%)
Non-responder	63 (61.2%)	140 (61.7%)	9 (81.8%)	3 (33.3%)
Odds Ratio (95% CI) vs placebo	-	1.28 (0.65 to 2.51)	-	3402787 (0.00 to NE)
p-value for Odds Ratio	-	0.472	-	0.986
p-value for heterogeneity of Odds Ratio				0.400
Risk Ratio (95% CI) vs placebo	-	1.00 (0.71 to 1.41)	-	1.49 (0.02 to 122.90)
Reversed Risk ratio (95% CI) vs placebo			-	0.67 (0.01 to 55.52)

[a] Patients who met the corresponding criterion are considered as responders. Patients who did not meet the criterion or had missing value are considered as non-responders.
OR, RR and RD are derived from a logistic regression model with treatment, age, weight group, region, baseline eosinophil level, baseline FeNO level, baseline ICS dose level, and baseline AM Asthma symptom score as covariates.
Peto OR calculation is based on Yusuf S et al. (Prog Cardiovasc Dis. 1985 Mar-Apr;27(5):335-71) and its p-value is derived using a normal approximation.
p-values for heterogeneity are estimated by using the same logistic model as the one used to estimate OR, RR and RD, with subgroup and treatment-by-subgroup interaction as additional covariates.
p-value for heterogeneity of Peto OR is estimated by using normal approximation.
PGM=DEVOPS/SAR231893/EFC14153/CSR_RWE/REPORT/PGM/eff_pro_evt_ger_subg_i_t.sas OUT=REPORT/OUTPUT/eff_pro_scamw52_ger_amc_t2_t_x.rtf (29JUN2021 - 17:52)

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

Project Code / Study Number / Analysis: SAR231893 / EFC14153 / CSR_RWE

2 PRO endpoints

2.5 Responder analysis for change from baseline in AM Asthma symptom score (improvement >= 0.6) at week 52 - ITT type 2 inflammatory asthma phenotype population

2.5.9 By atopic medical condition (Yes, No)

	Atopic medical condition			
	Yes		No	
Type 2 inflammatory asthma phenotype population	**Placebo (N=103)**	**Dupilumab (N=227)**	**Placebo (N=11)**	**Dupilumab (N=9)**
p-value for Risk Ratio	-	0.980	-	0.845
p-value for heterogeneity of Risk Ratio				0.156
Risk Difference (95% CI) vs placebo	-	0.69 (-12.11 to 13.49)	-	38.17 (-91.61 to 167.95)
p-value for Risk Difference	-	0.916	-	0.527
p-value for heterogeneity of Risk Difference				0.198

[a] Patients who met the corresponding criterion are considered as responders. Patients who did not meet the criterion or had missing value are considered as non-responders.
OR, RR and RD are derived from a logistic regression model with treatment, age, weight group, region, baseline eosinophil level, baseline FeNO level, baseline ICS dose level, and baseline AM Asthma symptom score as covariates.
Peto OR calculation is based on Yusuf S et al. (Prog Cardiovasc Dis. 1985 Mar-Apr;27(5):335-71) and its p-value is derived using a normal approximation.
p-values for heterogeneity are estimated by using the same logistic model as the one used to estimate OR, RR and RD, with subgroup and treatment-by-subgroup interaction as additional covariates.
p-value for heterogeneity of Peto OR is estimated by using normal approximation.
PGM=DEVOPS/SAR231893/EFC14153/CSR_RWE/REPORT/PGM/eff_pro_evt_ger_subg_i_t.sas OUT=REPORT/OUTPUT/eff_pro_scamw52_ger_amc_t2_t_x.rtf (29JUN2021 - 17:52)

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

Project Code / Study Number / Analysis: SAR231893 / EFC14153 / CSR_RWE

2 PRO endpoints

2.5 Responder analysis for change from baseline in AM Asthma symptom score (improvement >= 0.6) at week 52 - ITT type 2 inflammatory asthma phenotype population

2.5.10 By baseline total IgE (<median, >= median)

	Baseline Total IgE (IU/mL)			
	<median		>=median	
Type 2 inflammatory asthma phenotype population	**Placebo (N=66)**	**Dupilumab (N=105)**	**Placebo (N=47)**	**Dupilumab (N=125)**
Responder status at Week 52 based on change from baseline in AM symptom score <=-0.6 [n(%)] [a]				
Responder	24 (36.4%)	36 (34.3%)	17 (36.2%)	55 (44.0%)
Non-responder	42 (63.6%)	69 (65.7%)	30 (63.8%)	70 (56.0%)
Odds Ratio (95% CI) vs placebo	-	0.85 (0.30 to 2.45)	-	2.19 (0.82 to 5.82)
p-value for Odds Ratio	-	0.769	-	0.115
p-value for heterogeneity of Odds Ratio				0.288
Risk Ratio (95% CI) vs placebo	-	0.71 (0.41 to 1.22)	-	1.06 (0.68 to 1.65)
Reversed Risk ratio (95% CI) vs placebo			-	0.94 (0.61 to 1.47)

[a] Patients who met the corresponding criterion are considered as responders. Patients who did not meet the criterion or had missing value are considered as non-responders.
OR, RR and RD are derived from a logistic regression model with treatment, age, weight group, region, baseline eosinophil level, baseline FeNO level, baseline ICS dose level, and baseline AM Asthma symptom score as covariates.
Peto OR calculation is based on Yusuf S et al. (Prog Cardiovasc Dis. 1985 Mar-Apr;27(5):335-71) and its p-value is derived using a normal approximation.
p-values for heterogeneity are estimated by using the same logistic model as the one used to estimate OR, RR and RD, with subgroup and treatment-by-subgroup interaction as additional covariates.
p-value for heterogeneity of Peto OR is estimated by using normal approximation.
PGM=DEVOPS/SAR231893/EFC14153/CSR_RWE/REPORT/PGM/eff_pro_evt_ger_subg_i_t.sas OUT=REPORT/OUTPUT/eff_pro_scamw52_ger_igem_t2_t_x.rtf (29JUN2021 - 17:52)

Project Code / Study Number / Analysis: SAR231893 / EFC14153 / CSR_RWE

2 PRO endpoints

2.5 Responder analysis for change from baseline in AM Asthma symptom score (improvement >= 0.6) at week 52 - ITT type 2 inflammatory asthma phenotype population

2.5.10 By baseline total IgE (<median, >= median)

	Baseline Total IgE (IU/mL)			
	<median		>=median	
Type 2 inflammatory asthma phenotype population	**Placebo (N=66)**	**Dupilumab (N=105)**	**Placebo (N=47)**	**Dupilumab (N=125)**
p-value for Risk Ratio	-	0.209	-	0.797
p-value for heterogeneity of Risk Ratio				0.345
Risk Difference (95% CI) vs placebo	-	-2.43 (-23.82 to 18.96)	-	4.86 (-14.86 to 24.57)
p-value for Risk Difference	-	0.823	-	0.627
p-value for heterogeneity of Risk Difference				0.587

[a] Patients who met the corresponding criterion are considered as responders. Patients who did not meet the criterion or had missing value are considered as non-responders.
OR, RR and RD are derived from a logistic regression model with treatment, age, weight group, region, baseline eosinophil level, baseline FeNO level, baseline ICS dose level, and baseline AM Asthma symptom score as covariates.
Peto OR calculation is based on Yusuf S et al. (Prog Cardiovasc Dis. 1985 Mar-Apr;27(5):335-71) and its p-value is derived using a normal approximation.
p-values for heterogeneity are estimated by using the same logistic model as the one used to estimate OR, RR and RD, with subgroup and treatment-by-subgroup interaction as additional covariates.
p-value for heterogeneity of Peto OR is estimated by using normal approximation.
PGM=DEVOPS/SAR231893/EFC14153/CSR_RWE/REPORT/PGM/eff_pro_evt_ger_subg_i_t.sas OUT=REPORT/OUTPUT/eff_pro_scamw52_ger_igem_t2_t_x.rtf (29JUN2021 - 17:52)

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

Project Code / Study Number / Analysis: SAR231893 / EFC14153 / CSR_RWE

2 PRO endpoints

2.5 Responder analysis for change from baseline in AM Asthma symptom score (improvement >= 0.6) at week 52 - ITT type 2 inflammatory asthma phenotype population

2.5.11 By baseline total IgE (<100 IU/ml, >= 100 IU/ml)

	Baseline Total IgE (IU/mL)			
	< 100		**>= 100**	
Type 2 inflammatory asthma phenotype population	**Placebo (N=22)**	**Dupilumab (N=29)**	**Placebo (N=91)**	**Dupilumab (N=201)**
Responder status at Week 52 based on change from baseline in AM symptom score <=-0.6 [n(%)] [a]				
Responder	6 (27.3%)	10 (34.5%)	35 (38.5%)	81 (40.3%)
Non-responder	16 (72.7%)	19 (65.5%)	56 (61.5%)	120 (59.7%)
Odds Ratio (95% CI) vs placebo	-	0.57 (0.07 to 4.54)	-	1.47 (0.72 to 3.01)
p-value for Odds Ratio	-	0.590	-	0.289
p-value for heterogeneity of Odds Ratio				0.554
Risk Ratio (95% CI) vs placebo	-	0.63 (0.10 to 3.99)	-	1.09 (0.76 to 1.55)
Reversed Risk ratio (95% CI) vs placebo			-	0.92 (0.65 to 1.31)

[a] Patients who met the corresponding criterion are considered as responders. Patients who did not meet the criterion or had missing value are considered as non-responders.
OR, RR and RD are derived from a logistic regression model with treatment, age, weight group, region, baseline eosinophil level, baseline FeNO level, baseline ICS dose level, and baseline AM Asthma symptom score as covariates.
Peto OR calculation is based on Yusuf S et al. (Prog Cardiovasc Dis. 1985 Mar-Apr;27(5):335-71) and its p-value is derived using a normal approximation.
p-values for heterogeneity are estimated by using the same logistic model as the one used to estimate OR, RR and RD, with subgroup and treatment-by-subgroup interaction as additional covariates.
p-value for heterogeneity of Peto OR is estimated by using normal approximation.
PGM=DEVOPS/SAR231893/EFC14153/CSR_RWE/REPORT/PGM/eff_pro_evt_ger_subg_i_t.sas OUT=REPORT/OUTPUT/eff_pro_scamw52_ger_ige_t2_t_x.rtf (29JUN2021 - 17:52)

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

Project Code / Study Number / Analysis: SAR231893 / EFC14153 / CSR_RWE

2 PRO endpoints

2.5 Responder analysis for change from baseline in AM Asthma symptom score (improvement >= 0.6) at week 52 - ITT type 2 inflammatory asthma phenotype population

2.5.11 By baseline total IgE (<100 IU/ml, >= 100 IU/ml)

	Baseline Total IgE (IU/mL)			
	< 100		>= 100	
Type 2 inflammatory asthma phenotype population	**Placebo (N=22)**	**Dupilumab (N=29)**	**Placebo (N=91)**	**Dupilumab (N=201)**
p-value for Risk Ratio	-	0.614	-	0.649
p-value for heterogeneity of Risk Ratio				0.662
Risk Difference (95% CI) vs placebo	-	-13.38 (-60.37 to 33.62)	-	3.28 (-10.39 to 16.96)
p-value for Risk Difference	-	0.568	-	0.637
p-value for heterogeneity of Risk Difference				0.691

[a] Patients who met the corresponding criterion are considered as responders. Patients who did not meet the criterion or had missing value are considered as non-responders. OR, RR and RD are derived from a logistic regression model with treatment, age, weight group, region, baseline eosinophil level, baseline FeNO level, baseline ICS dose level, and baseline AM Asthma symptom score as covariates.
Peto OR calculation is based on Yusuf S et al. (Prog Cardiovasc Dis. 1985 Mar-Apr;27(5):335-71) and its p-value is derived using a normal approximation.
p-values for heterogeneity are estimated by using the same logistic model as the one used to estimate OR, RR and RD, with subgroup and treatment-by-subgroup interaction as additional covariates.
p-value for heterogeneity of Peto OR is estimated by using normal approximation.
PGM=DEVOPS/SAR231893/EFC14153/CSR_RWE/REPORT/PGM/eff_pro_evt_ger_subg_i_t.sas OUT=REPORT/OUTPUT/eff_pro_scamw52_ger_ige_t2_t_x.rtf (29JUN2021 - 17:52)

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

Project Code / Study Number / Analysis: SAR231893 / EFC14153 / CSR_RWE

2 PRO endpoints

2.5 Responder analysis for change from baseline in AM Asthma symptom score (improvement >= 0.6) at week 52 - ITT type 2 inflammatory asthma phenotype population

2.5.12 By age at onset of asthma (0-2, 3-5, >=6 years)

	Age of onset of asthma (years)					
	0-2		3-5		>= 6	
Type 2 inflammatory asthma phenotype population	**Placebo (N=40)**	**Dupilumab (N=105)**	**Placebo (N=39)**	**Dupilumab (N=86)**	**Placebo (N=35)**	**Dupilumab (N=45)**
Responder status at Week 52 based on change from baseline in AM symptom score <=-0.6 [n(%)] [a]						
Responder	13 (32.5%)	39 (37.1%)	22 (56.4%)	36 (41.9%)	7 (20.0%)	18 (40.0%)
Non-responder	27 (67.5%)	66 (62.9%)	17 (43.6%)	50 (58.1%)	28 (80.0%)	27 (60.0%)
Odds Ratio (95% CI) vs placebo	-	1.42 (0.50 to 4.02)	-	0.55 (0.17 to 1.81)	-	5.94 (0.77 to 45.71)
p-value for Odds Ratio	-	0.507	-	0.325	-	0.086
p-value for heterogeneity of Odds Ratio:						
0-2, 3-5						0.194
0-2, >= 6						0.400

[a] Patients who met the corresponding criterion are considered as responders. Patients who did not meet the criterion or had missing value are considered as non-responders. OR, RR and RD are derived from a logistic regression model with treatment, age, weight group, region, baseline eosinophil level, baseline FeNO level, baseline ICS dose level, and baseline AM Asthma symptom score as covariates.
Peto OR calculation is based on Yusuf S et al. (Prog Cardiovasc Dis. 1985 Mar-Apr;27(5):335-71) and its p-value is derived using a normal approximation.
p-values for heterogeneity are estimated by using the same logistic model as the one used to estimate OR, RR and RD, with subgroup and treatment-by-subgroup interaction as additional covariates.
p-value for heterogeneity of Peto OR is estimated by using normal approximation.
PGM=DEVOPS/SAR231893/EFC14153/CSR_RWE/REPORT/PGM/eff_pro_evt_ger_subg_i_t.sas OUT=REPORT/OUTPUT/eff_pro_scamw52_ger_onsa_t2_t_x.rtf (01SEP2021 - 15:27)

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

Project Code / Study Number / Analysis: SAR231893 / EFC14153 / CSR_RWE

2 PRO endpoints

2.5 Responder analysis for change from baseline in AM Asthma symptom score (improvement >= 0.6) at week 52 - ITT type 2 inflammatory asthma phenotype population

2.5.12 By age at onset of asthma (0-2, 3-5, >=6 years)

	Age of onset of asthma (years)					
	0-2		3-5		>= 6	
Type 2 inflammatory asthma phenotype population	**Placebo (N=40)**	**Dupilumab (N=105)**	**Placebo (N=39)**	**Dupilumab (N=86)**	**Placebo (N=35)**	**Dupilumab (N=45)**
3-5, >= 6						0.057
overall						0.139
Risk Ratio (95% CI) vs placebo	-	1.08 (0.60 to 1.92)	-	0.80 (0.45 to 1.39)	-	1.59 (0.47 to 5.38)
Reversed Risk ratio (95% CI) vs placebo	-	0.93 (0.52 to 1.65)			-	0.63 (0.19 to 2.13)
p-value for Risk Ratio	-	0.798	-	0.421	-	0.450
p-value for heterogeneity of Risk Ratio:						
0-2, 3-5						0.234
0-2, >= 6						0.098
3-5, >= 6						0.444

[a] Patients who met the corresponding criterion are considered as responders. Patients who did not meet the criterion or had missing value are considered as non-responders.
OR, RR and RD are derived from a logistic regression model with treatment, age, weight group, region, baseline eosinophil level, baseline FeNO level, baseline ICS dose level, and baseline AM Asthma symptom score as covariates.
Peto OR calculation is based on Yusuf S et al. (Prog Cardiovasc Dis. 1985 Mar-Apr;27(5):335-71) and its p-value is derived using a normal approximation.
p-values for heterogeneity are estimated by using the same logistic model as the one used to estimate OR, RR and RD, with subgroup and treatment-by-subgroup interaction as additional covariates.
p-value for heterogeneity of Peto OR is estimated by using normal approximation.
PGM=DEVOPS/SAR231893/EFC14153/CSR_RWE/REPORT/PGM/eff_pro_evt_ger_subg_i_t.sas OUT=REPORT/OUTPUT/eff_pro_scamw52_ger_onsa_t2_t_x.rtf (01SEP2021 - 15:27)

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

Project Code / Study Number / Analysis: SAR231893 / EFC14153 / CSR_RWE

2 PRO endpoints

2.5 Responder analysis for change from baseline in AM Asthma symptom score (improvement >= 0.6) at week 52 - ITT type 2 inflammatory asthma phenotype population

2.5.12 By age at onset of asthma (0-2, 3-5, >=6 years)

	Age of onset of asthma (years)					
	0-2		3-5		>= 6	
Type 2 inflammatory asthma phenotype population	**Placebo (N=40)**	**Dupilumab (N=105)**	**Placebo (N=39)**	**Dupilumab (N=86)**	**Placebo (N=35)**	**Dupilumab (N=45)**
overall						0.217
Risk Difference (95% CI) vs placebo	-	0.15 (-19.69 to 19.99)	-	-4.45 (-28.95 to 20.04)	-	13.46 (-23.73 to 50.66)
p-value for Risk Difference	-	0.988	-	0.719	-	0.472
p-value for heterogeneity of Risk Difference:						
0-2, 3-5						0.758
0-2, >= 6						0.464
3-5, >= 6						0.617
overall						0.764

[a] Patients who met the corresponding criterion are considered as responders. Patients who did not meet the criterion or had missing value are considered as non-responders.
OR, RR and RD are derived from a logistic regression model with treatment, age, weight group, region, baseline eosinophil level, baseline FeNO level, baseline ICS dose level, and baseline AM Asthma symptom score as covariates.
Peto OR calculation is based on Yusuf S et al. (Prog Cardiovasc Dis. 1985 Mar-Apr;27(5):335-71) and its p-value is derived using a normal approximation.
p-values for heterogeneity are estimated by using the same logistic model as the one used to estimate OR, RR and RD, with subgroup and treatment-by-subgroup interaction as additional covariates.
p-value for heterogeneity of Peto OR is estimated by using normal approximation.
PGM=DEVOPS/SAR231893/EFC14153/CSR_RWE/REPORT/PGM/eff_pro_evt_ger_subg_i_t.sas OUT=REPORT/OUTPUT/eff_pro_scamw52_ger_onsa_t2_t_x.rtf (01SEP2021 - 15:27)

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

Project Code / Study Number / Analysis: SAR231893 / EFC14153 / CSR_RWE

2 PRO endpoints

2.5 Responder analysis for change from baseline in AM Asthma symptom score (improvement >= 0.6) at week 52 - ITT type 2 inflammatory asthma phenotype population

2.5.13 By number of severe asthma exacerbation prior to the study (<=1, 2, >2)

	Number of severe asthma exacerbation prior to the study					
	<=1		**2**		**>2**	
Type 2 inflammatory asthma phenotype population	**Placebo (N=47)**	**Dupilumab (N=85)**	**Placebo (N=32)**	**Dupilumab (N=75)**	**Placebo (N=35)**	**Dupilumab (N=76)**
Responder status at Week 52 based on change from baseline in AM symptom score <=-0.6 [n(%)] [a]						
Responder	17 (36.2%)	32 (37.6%)	12 (37.5%)	30 (40.0%)	13 (37.1%)	31 (40.8%)
Non-responder	30 (63.8%)	53 (62.4%)	20 (62.5%)	45 (60.0%)	22 (62.9%)	45 (59.2%)
Odds Ratio (95% CI) vs placebo	-	1.47 (0.48 to 4.55)	-	0.61 (0.17 to 2.15)	-	5.41 (1.10 to 26.52)
p-value for Odds Ratio	-	0.497	-	0.435	-	0.038
p-value for heterogeneity of Odds Ratio:						
<=1, 2						0.415
<=1, >2						0.376

[a] Patients who met the corresponding criterion are considered as responders. Patients who did not meet the criterion or had missing value are considered as non-responders. OR, RR and RD are derived from a logistic regression model with treatment, age, weight group, region, baseline eosinophil level, baseline FeNO level, baseline ICS dose level, and baseline AM Asthma symptom score as covariates.
Peto OR calculation is based on Yusuf S et al. (Prog Cardiovasc Dis. 1985 Mar-Apr;27(5):335-71) and its p-value is derived using a normal approximation.
p-values for heterogeneity are estimated by using the same logistic model as the one used to estimate OR, RR and RD, with subgroup and treatment-by-subgroup interaction as additional covariates.
p-value for heterogeneity of Peto OR is estimated by using normal approximation.
PGM=DEVOPS/SAR231893/EFC14153/CSR_RWE/REPORT/PGM/eff_pro_evt_ger_subg_i_t.sas OUT=REPORT/OUTPUT/eff_pro_scamw52_ger_exa_t2_t_x.rtf (29JUN2021 - 17:52)

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

Project Code / Study Number / Analysis: SAR231893 / EFC14153 / CSR_RWE

2 PRO endpoints

2.5 Responder analysis for change from baseline in AM Asthma symptom score (improvement >= 0.6) at week 52 - ITT type 2 inflammatory asthma phenotype population

2.5.13 By number of severe asthma exacerbation prior to the study (<=1, 2, >2)

	Number of severe asthma exacerbation prior to the study					
	<=1		2		>2	
Type 2 inflammatory asthma phenotype population	**Placebo (N=47)**	**Dupilumab (N=85)**	**Placebo (N=32)**	**Dupilumab (N=75)**	**Placebo (N=35)**	**Dupilumab (N=76)**
2, >2						0.121
overall						0.299
Risk Ratio (95% CI) vs placebo	-	1.09 (0.57 to 2.08)	-	0.70 (0.34 to 1.42)	-	1.28 (0.52 to 3.11)
Reversed Risk ratio (95% CI) vs placebo	-	0.92 (0.48 to 1.74)			-	0.78 (0.32 to 1.91)
p-value for Risk Ratio	-	0.785	-	0.315	-	0.588
p-value for heterogeneity of Risk Ratio:						
<=1, 2						0.098
<=1, >2						0.106
2, >2						0.003

[a] Patients who met the corresponding criterion are considered as responders. Patients who did not meet the criterion or had missing value are considered as non-responders.
OR, RR and RD are derived from a logistic regression model with treatment, age, weight group, region, baseline eosinophil level, baseline FeNO level, baseline ICS dose level, and baseline AM Asthma symptom score as covariates.
Peto OR calculation is based on Yusuf S et al. (Prog Cardiovasc Dis. 1985 Mar-Apr;27(5):335-71) and its p-value is derived using a normal approximation.
p-values for heterogeneity are estimated by using the same logistic model as the one used to estimate OR, RR and RD, with subgroup and treatment-by-subgroup interaction as additional covariates.
p-value for heterogeneity of Peto OR is estimated by using normal approximation.
PGM=DEVOPS/SAR231893/EFC14153/CSR_RWE/REPORT/PGM/eff_pro_evt_ger_subg_i_t.sas OUT=REPORT/OUTPUT/eff_pro_scamw52_ger_exa_t2_t_x.rtf (29JUN2021 - 17:52)

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

Project Code / Study Number / Analysis: SAR231893 / EFC14153 / CSR_RWE

2 PRO endpoints

2.5 Responder analysis for change from baseline in AM Asthma symptom score (improvement >= 0.6) at week 52 - ITT type 2 inflammatory asthma phenotype population

2.5.13 By number of severe asthma exacerbation prior to the study (<=1, 2, >2)

	Number of severe asthma exacerbation prior to the study					
	<=1		2		>2	
Type 2 inflammatory asthma phenotype population	**Placebo (N=47)**	**Dupilumab (N=85)**	**Placebo (N=32)**	**Dupilumab (N=75)**	**Placebo (N=35)**	**Dupilumab (N=76)**
overall						0.011
Risk Difference (95% CI) vs placebo	-	0.98 (-20.88 to 22.84)	-	-7.23 (-31.44 to 16.98)	-	18.53 (-10.86 to 47.93)
p-value for Risk Difference	-	0.929	-	0.555	-	0.214
p-value for heterogeneity of Risk Difference:						
<=1, 2						0.237
<=1, >2						0.345
2, >2						0.036
overall						0.111

[a] Patients who met the corresponding criterion are considered as responders. Patients who did not meet the criterion or had missing value are considered as non-responders. OR, RR and RD are derived from a logistic regression model with treatment, age, weight group, region, baseline eosinophil level, baseline FeNO level, baseline ICS dose level, and baseline AM Asthma symptom score as covariates.
Peto OR calculation is based on Yusuf S et al. (Prog Cardiovasc Dis. 1985 Mar-Apr;27(5):335-71) and its p-value is derived using a normal approximation.
p-values for heterogeneity are estimated by using the same logistic model as the one used to estimate OR, RR and RD, with subgroup and treatment-by-subgroup interaction as additional covariates.
p-value for heterogeneity of Peto OR is estimated by using normal approximation.
PGM=DEVOPS/SAR231893/EFC14153/CSR_RWE/REPORT/PGM/eff_pro_evt_ger_subg_i_t.sas OUT=REPORT/OUTPUT/eff_pro_scamw52_ger_exa_t2_t_x.rtf (29JUN2021 - 17:52)

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

Project Code / Study Number / Analysis: SAR231893 / EFC14153 / CSR_RWE

2 PRO endpoints

2.6 Responder analysis for change from baseline in PM Asthma symptom score (improvement >= 0.6) at week 52 - ITT type 2 inflammatory asthma phenotype population

Type 2 inflammatory asthma phenotype population	**Placebo (N=114)**	**Dupilumab (N=236)**
Responder status at Week 52 based on change from baseline in PM symptom score <=-0.6 [n(%)] [a]		
Responder	39 (34.2%)	87 (36.9%)
Non-responder	75 (65.8%)	149 (63.1%)
Odds Ratio (95% CI)	-	1.36 (0.74 to 2.51)
p-value for Odds Ratio		0.325
Risk Ratio (95% CI)	-	1.14 (0.82 to 1.60)
Reversed Risk ratio (95% CI)	-	0.87 (0.63 to 1.22)
p-value for Risk Ratio		0.425
Risk Difference (95% CI)	-	2.83 (-9.25 to 14.92)
p-value for Risk Difference		0.645

[a] Patients who met the corresponding criterion are considered as responders. Patients who did not meet the criterion or had missing value are considered as non-responders. OR, RR and RD are derived from a logistic regression model with treatment, age, weight group, region, baseline eosinophil level, baseline FeNO level, baseline ICS dose level, and baseline PM Asthma symptom score as covariates.
Peto OR calculation is based on Yusuf S et al. (Prog Cardiovasc Dis. 1985 Mar-Apr;27(5):335-71) and its p-value is derived using a normal approximation.
PGM=DEVOPS/SAR231893/EFC14153/CSR_RWE/REPORT/PGM/eff_pro_evt_ger_i_t.sas OUT=REPORT/OUTPUT/eff_pro_scpmw52_ger_t2_t_x.rtf (30JUN2021 - 8:14)

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

Project Code / Study Number / Analysis: SAR231893 / EFC14153 / CSR_RWE

2 PRO endpoints

2.6 Responder analysis for change from baseline in PM Asthma symptom score (improvement >= 0.6) at week 52 - ITT type 2 inflammatory asthma phenotype population

2.6.1 By gender (Male, Female)

	Gender			
	Male		Female	
Type 2 inflammatory asthma phenotype population	**Placebo (N=78)**	**Dupilumab (N=152)**	**Placebo (N=36)**	**Dupilumab (N=84)**
Responder status at Week 52 based on change from baseline in PM symptom score <=-0.6 [n(%)] [a]				
Responder	23 (29.5%)	56 (36.8%)	16 (44.4%)	31 (36.9%)
Non-responder	55 (70.5%)	96 (63.2%)	20 (55.6%)	53 (63.1%)
Odds Ratio (95% CI) vs placebo	-	1.74 (0.82 to 3.70)	-	0.78 (0.23 to 2.70)
p-value for Odds Ratio	-	0.150	-	0.695
p-value for heterogeneity of Odds Ratio				0.241
Risk Ratio (95% CI) vs placebo	-	1.14 (0.73 to 1.75)	-	0.80 (0.43 to 1.48)
Reversed Risk ratio (95% CI) vs placebo	-	0.88 (0.57 to 1.36)		

[a] Patients who met the corresponding criterion are considered as responders. Patients who did not meet the criterion or had missing value are considered as non-responders.
OR, RR and RD are derived from a logistic regression model with treatment, age, weight group, region, baseline eosinophil level, baseline FeNO level, baseline ICS dose level, and baseline PM Asthma symptom score as covariates.
Peto OR calculation is based on Yusuf S et al. (Prog Cardiovasc Dis. 1985 Mar-Apr;27(5):335-71) and its p-value is derived using a normal approximation.
p-values for heterogeneity are estimated by using the same logistic model as the one used to estimate OR, RR and RD, with subgroup and treatment-by-subgroup interaction as additional covariates.
p-value for heterogeneity of Peto OR is estimated by using normal approximation.
PGM=DEVOPS/SAR231893/EFC14153/CSR_RWE/REPORT/PGM/eff_pro_evt_ger_subg_i_t.sas OUT=REPORT/OUTPUT/eff_pro_scpmw52_ger_sex_t2_t_x.rtf (29JUN2021 - 17:52)

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

Project Code / Study Number / Analysis: SAR231893 / EFC14153 / CSR_RWE

2 PRO endpoints

2.6 Responder analysis for change from baseline in PM Asthma symptom score (improvement >= 0.6) at week 52 - ITT type 2 inflammatory asthma phenotype population

2.6.1 By gender (Male, Female)

	Gender			
	Male		Female	
Type 2 inflammatory asthma phenotype population	**Placebo (N=78)**	**Dupilumab (N=152)**	**Placebo (N=36)**	**Dupilumab (N=84)**
p-value for Risk Ratio	-	0.566	-	0.471
p-value for heterogeneity of Risk Ratio				0.057
Risk Difference (95% CI) vs placebo	-	6.30 (-8.94 to 21.53)	-	-1.62 (-24.76 to 21.52)
p-value for Risk Difference	-	0.416	-	0.890
p-value for heterogeneity of Risk Difference				0.199

[a] Patients who met the corresponding criterion are considered as responders. Patients who did not meet the criterion or had missing value are considered as non-responders.
OR, RR and RD are derived from a logistic regression model with treatment, age, weight group, region, baseline eosinophil level, baseline FeNO level, baseline ICS dose level, and baseline PM Asthma symptom score as covariates.
Peto OR calculation is based on Yusuf S et al. (Prog Cardiovasc Dis. 1985 Mar-Apr;27(5):335-71) and its p-value is derived using a normal approximation.
p-values for heterogeneity are estimated by using the same logistic model as the one used to estimate OR, RR and RD, with subgroup and treatment-by-subgroup interaction as additional covariates.
p-value for heterogeneity of Peto OR is estimated by using normal approximation.
PGM=DEVOPS/SAR231893/EFC14153/CSR_RWE/REPORT/PGM/eff_pro_evt_ger_subg_i_t.sas OUT=REPORT/OUTPUT/eff_pro_scpmw52_ger_sex_t2_t_x.rtf (29JUN2021 - 17:52)

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

Project Code / Study Number / Analysis: SAR231893 / EFC14153 / CSR_RWE

2 PRO endpoints

2.6 Responder analysis for change from baseline in PM Asthma symptom score (improvement >= 0.6) at week 52 - ITT type 2 inflammatory asthma phenotype population

2.6.2 By region (Latin America, East Europe, Western Countries)

	Region					
	Latin America		East Europe		Western countries	
Type 2 inflammatory asthma phenotype population	**Placebo (N=51)**	**Dupilumab (N=106)**	**Placebo (N=43)**	**Dupilumab (N=78)**	**Placebo (N=20)**	**Dupilumab (N=52)**
Responder status at Week 52 based on change from baseline in PM symptom score <=-0.6 [n(%)] [a]						
Responder	16 (31.4%)	43 (40.6%)	16 (37.2%)	29 (37.2%)	7 (35.0%)	15 (28.8%)
Non-responder	35 (68.6%)	63 (59.4%)	27 (62.8%)	49 (62.8%)	13 (65.0%)	37 (71.2%)
Odds Ratio (95% CI) vs placebo	-	1.25 (0.50 to 3.10)	-	1.21 (0.44 to 3.36)	-	3.91 (0.52 to 29.43)
p-value for Odds Ratio	-	0.635	-	0.706	-	0.182
p-value for heterogeneity of Odds Ratio:						
Latin America, East Europe						0.945
Latin America, Western countries						0.491

[a] Patients who met the corresponding criterion are considered as responders. Patients who did not meet the criterion or had missing value are considered as non-responders. OR, RR and RD are derived from a logistic regression model with treatment, age, weight group, baseline eosinophil level, baseline FeNO level, baseline ICS dose level, and baseline PM Asthma symptom score as covariates.
Peto OR calculation is based on Yusuf S et al. (Prog Cardiovasc Dis. 1985 Mar-Apr;27(5):335-71) and its p-value is derived using a normal approximation.
p-values for heterogeneity are estimated by using the same logistic model as the one used to estimate OR, RR and RD, with subgroup and treatment-by-subgroup interaction as additional covariates.
p-value for heterogeneity of Peto OR is estimated by using normal approximation.
PGM=DEVOPS/SAR231893/EFC14153/CSR_RWE/REPORT/PGM/eff_pro_evt_ger_subg_i_t.sas OUT=REPORT/OUTPUT/eff_pro_scpmw52_ger_cty_t2_t_x.rtf (29JUN2021 - 17:53)

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

Project Code / Study Number / Analysis: SAR231893 / EFC14153 / CSR_RWE

2 PRO endpoints

2.6 Responder analysis for change from baseline in PM Asthma symptom score (improvement >= 0.6) at week 52 - ITT type 2 inflammatory asthma phenotype population

2.6.2 By region (Latin America, East Europe, Western Countries)

	Region					
	Latin America		East Europe		Western countries	
Type 2 inflammatory asthma phenotype population	**Placebo (N=51)**	**Dupilumab (N=106)**	**Placebo (N=43)**	**Dupilumab (N=78)**	**Placebo (N=20)**	**Dupilumab (N=52)**
East Europe, Western countries						0.464
overall						0.746
Risk Ratio (95% CI) vs placebo	-	0.96 (0.61 to 1.51)	-	0.98 (0.56 to 1.73)	-	1.51 (0.36 to 6.32)
Reversed Risk ratio (95% CI) vs placebo					-	0.66 (0.16 to 2.78)
p-value for Risk Ratio	-	0.862	-	0.956	-	0.568
p-value for heterogeneity of Risk Ratio:						
Latin America, East Europe						0.079
Latin America, Western countries						0.471
East Europe, Western countries						0.655
overall						0.212

[a] Patients who met the corresponding criterion are considered as responders. Patients who did not meet the criterion or had missing value are considered as non-responders.
OR, RR and RD are derived from a logistic regression model with treatment, age, weight group, baseline eosinophil level, baseline FeNO level, baseline ICS dose level, and baseline PM Asthma symptom score as covariates.
Peto OR calculation is based on Yusuf S et al. (Prog Cardiovasc Dis. 1985 Mar-Apr;27(5):335-71) and its p-value is derived using a normal approximation.
p-values for heterogeneity are estimated by using the same logistic model as the one used to estimate OR, RR and RD, with subgroup and treatment-by-subgroup interaction as additional covariates.
p-value for heterogeneity of Peto OR is estimated by using normal approximation.
PGM=DEVOPS/SAR231893/EFC14153/CSR_RWE/REPORT/PGM/eff_pro_evt_ger_subg_i_t.sas OUT=REPORT/OUTPUT/eff_pro_scpmw52_ger_cty_t2_t_x.rtf (29JUN2021 - 17:53)

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

Project Code / Study Number / Analysis: SAR231893 / EFC14153 / CSR_RWE

2 PRO endpoints

2.6 Responder analysis for change from baseline in PM Asthma symptom score (improvement >= 0.6) at week 52 - ITT type 2 inflammatory asthma phenotype population

2.6.2 By region (Latin America, East Europe, Western Countries)

	Region					
	Latin America		East Europe		Western countries	
Type 2 inflammatory asthma phenotype population	**Placebo (N=51)**	**Dupilumab (N=106)**	**Placebo (N=43)**	**Dupilumab (N=78)**	**Placebo (N=20)**	**Dupilumab (N=52)**
Risk Difference (95% CI) vs placebo	-	2.21 (-17.45 to 21.86)	-	1.99 (-19.64 to 23.63)	-	12.73 (-21.68 to 47.14)
p-value for Risk Difference	-	0.825	-	0.856	-	0.462
p-value for heterogeneity of Risk Difference:						
Latin America, East Europe						0.582
Latin America, Western countries						0.739
East Europe, Western countries						0.898
overall						0.855

[a] Patients who met the corresponding criterion are considered as responders. Patients who did not meet the criterion or had missing value are considered as non-responders.
OR, RR and RD are derived from a logistic regression model with treatment, age, weight group, baseline eosinophil level, baseline FeNO level, baseline ICS dose level, and baseline PM Asthma symptom score as covariates.
Peto OR calculation is based on Yusuf S et al. (Prog Cardiovasc Dis. 1985 Mar-Apr;27(5):335-71) and its p-value is derived using a normal approximation.
p-values for heterogeneity are estimated by using the same logistic model as the one used to estimate OR, RR and RD, with subgroup and treatment-by-subgroup interaction as additional covariates.
p-value for heterogeneity of Peto OR is estimated by using normal approximation.
PGM=DEVOPS/SAR231893/EFC14153/CSR_RWE/REPORT/PGM/eff_pro_evt_ger_subg_i_t.sas OUT=REPORT/OUTPUT/eff_pro_scpmw52_ger_cty_t2_t_x.rtf (29JUN2021 - 17:53)

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

Project Code / Study Number / Analysis: SAR231893 / EFC14153 / CSR_RWE

2 PRO endpoints

2.6 Responder analysis for change from baseline in PM Asthma symptom score (improvement >= 0.6) at week 52 - ITT type 2 inflammatory asthma phenotype population

2.6.3 By race (Caucasian/white, Black/of African descent, Other)

	Race					
	Caucasian/White		Black/of African descent		Other	
Type 2 inflammatory asthma phenotype population	**Placebo (N=102)**	**Dupilumab (N=208)**	**Placebo (N=5)**	**Dupilumab (N=9)**	**Placebo (N=7)**	**Dupilumab (N=19)**
Responder status at Week 52 based on change from baseline in PM symptom score <=-0.6 [n(%)] [a]						
Responder	38 (37.3%)	77 (37.0%)	1 (20.0%)	4 (44.4%)	0	6 (31.6%)
Non-responder	64 (62.7%)	131 (63.0%)	4 (80.0%)	5 (55.6%)	7 (100%)	13 (68.4%)
Odds Ratio (95% CI) vs placebo	-	1.09 (0.58 to 2.05)	-	0.00 (0.00 to NE)	-	1.324E12 (0.00 to NE)
p-value for Odds Ratio	-	0.793	-	0.991	-	0.995
Peto Odds Ratio (95% CI) vs placebo	-	0.99 (0.61 to 1.62)	-	2.69 (0.30 to 24.22)	-	5.53 (0.74 to 41.57)
Reversed Peto Odds Ratio (95% CI)			-	0.37 (0.04 to 3.33)	-	0.18 (0.02 to 1.35)

[a] Patients who met the corresponding criterion are considered as responders. Patients who did not meet the criterion or had missing value are considered as non-responders.
OR, RR and RD are derived from a logistic regression model with treatment, age, weight group, region, baseline eosinophil level, baseline FeNO level, baseline ICS dose level, and baseline PM Asthma symptom score as covariates.
Peto OR calculation is based on Yusuf S et al. (Prog Cardiovasc Dis. 1985 Mar-Apr;27(5):335-71) and its p-value is derived using a normal approximation.
p-values for heterogeneity are estimated by using the same logistic model as the one used to estimate OR, RR and RD, with subgroup and treatment-by-subgroup interaction as additional covariates.
p-value for heterogeneity of Peto OR is estimated by using normal approximation.
PGM=DEVOPS/SAR231893/EFC14153/CSR_RWE/REPORT/PGM/eff_pro_evt_ger_subg_i_t.sas OUT=REPORT/OUTPUT/eff_pro_scpmw52_ger_race_t2_t_x.rtf (29JUN2021 - 17:53)

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

Project Code / Study Number / Analysis: SAR231893 / EFC14153 / CSR_RWE

2 PRO endpoints

2.6 Responder analysis for change from baseline in PM Asthma symptom score (improvement >= 0.6) at week 52 - ITT type 2 inflammatory asthma phenotype population

2.6.3 By race (Caucasian/white, Black/of African descent, Other)

	Race					
	Caucasian/White		Black/of African descent		Other	
Type 2 inflammatory asthma phenotype population	**Placebo (N=102)**	**Dupilumab (N=208)**	**Placebo (N=5)**	**Dupilumab (N=9)**	**Placebo (N=7)**	**Dupilumab (N=19)**
p-value for Peto Odds Ratio		0.968		0.378		0.096
p-value for heterogeneity of Peto Odds Ratio:						
Caucasian/White, Black/of African descent						0.385
Caucasian/White, Other						0.104
Black/of African descent, Other						0.635
overall						0.196
Risk Ratio (95% CI) vs placebo	-	1.07 (0.75 to 1.51)	-	0.65 (0.00 to 398.00)	-	7.69 (0.02 to 3196.57)
Reversed Risk ratio (95% CI) vs placebo	-	0.94 (0.66 to 1.32)			-	0.13 (0.00 to 54.09)

[a] Patients who met the corresponding criterion are considered as responders. Patients who did not meet the criterion or had missing value are considered as non-responders.
OR, RR and RD are derived from a logistic regression model with treatment, age, weight group, region, baseline eosinophil level, baseline FeNO level, baseline ICS dose level, and baseline PM Asthma symptom score as covariates.
Peto OR calculation is based on Yusuf S et al. (Prog Cardiovasc Dis. 1985 Mar-Apr;27(5):335-71) and its p-value is derived using a normal approximation.
p-values for heterogeneity are estimated by using the same logistic model as the one used to estimate OR, RR and RD, with subgroup and treatment-by-subgroup interaction as additional covariates.
p-value for heterogeneity of Peto OR is estimated by using normal approximation.
PGM=DEVOPS/SAR231893/EFC14153/CSR_RWE/REPORT/PGM/eff_pro_evt_ger_subg_i_t.sas OUT=REPORT/OUTPUT/eff_pro_scpmw52_ger_race_t2_t_x.rtf (29JUN2021 - 17:53)

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

Project Code / Study Number / Analysis: SAR231893 / EFC14153 / CSR_RWE

2 PRO endpoints

2.6 Responder analysis for change from baseline in PM Asthma symptom score (improvement >= 0.6) at week 52 - ITT type 2 inflammatory asthma phenotype population

2.6.3 By race (Caucasian/white, Black/of African descent, Other)

	Race					
	Caucasian/White		Black/of African descent		Other	
Type 2 inflammatory asthma phenotype population	**Placebo (N=102)**	**Dupilumab (N=208)**	**Placebo (N=5)**	**Dupilumab (N=9)**	**Placebo (N=7)**	**Dupilumab (N=19)**
p-value for Risk Ratio	-	0.714	-	0.863	-	0.484
p-value for heterogeneity of Risk Ratio:						
Caucasian/White, Black/of African descent						0.737
Caucasian/White, Other						0.534
Black/of African descent, Other						0.569
overall						0.780
Risk Difference (95% CI) vs placebo	-	-0.08 (-13.00 to 12.84)	-	0.69 (-215.13 to 216.51)	-	84.07 (-183.50 to 351.64)
p-value for Risk Difference	-	0.990	-	0.993	-	0.515

[a] Patients who met the corresponding criterion are considered as responders. Patients who did not meet the criterion or had missing value are considered as non-responders.
OR, RR and RD are derived from a logistic regression model with treatment, age, weight group, region, baseline eosinophil level, baseline FeNO level, baseline ICS dose level, and baseline PM Asthma symptom score as covariates.
Peto OR calculation is based on Yusuf S et al. (Prog Cardiovasc Dis. 1985 Mar-Apr;27(5):335-71) and its p-value is derived using a normal approximation.
p-values for heterogeneity are estimated by using the same logistic model as the one used to estimate OR, RR and RD, with subgroup and treatment-by-subgroup interaction as additional covariates.
p-value for heterogeneity of Peto OR is estimated by using normal approximation.
PGM=DEVOPS/SAR231893/EFC14153/CSR_RWE/REPORT/PGM/eff_pro_evt_ger_subg_i_t.sas OUT=REPORT/OUTPUT/eff_pro_scpmw52_ger_race_t2_t_x.rtf (29JUN2021 - 17:53)

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

Project Code / Study Number / Analysis: SAR231893 / EFC14153 / CSR_RWE

2 PRO endpoints

2.6 Responder analysis for change from baseline in PM Asthma symptom score (improvement >= 0.6) at week 52 - ITT type 2 inflammatory asthma phenotype population

2.6.3 By race (Caucasian/white, Black/of African descent, Other)

	Race					
	Caucasian/White		Black/of African descent		Other	
Type 2 inflammatory asthma phenotype population	**Placebo (N=102)**	**Dupilumab (N=208)**	**Placebo (N=5)**	**Dupilumab (N=9)**	**Placebo (N=7)**	**Dupilumab (N=19)**
p-value for heterogeneity of Risk Difference:						
Caucasian/White, Black/of African descent						0.788
Caucasian/White, Other						0.679
Black/of African descent, Other						0.771
overall						0.887

[a] Patients who met the corresponding criterion are considered as responders. Patients who did not meet the criterion or had missing value are considered as non-responders.
OR, RR and RD are derived from a logistic regression model with treatment, age, weight group, region, baseline eosinophil level, baseline FeNO level, baseline ICS dose level, and baseline PM Asthma symptom score as covariates.
Peto OR calculation is based on Yusuf S et al. (Prog Cardiovasc Dis. 1985 Mar-Apr;27(5):335-71) and its p-value is derived using a normal approximation.
p-values for heterogeneity are estimated by using the same logistic model as the one used to estimate OR, RR and RD, with subgroup and treatment-by-subgroup interaction as additional covariates.
p-value for heterogeneity of Peto OR is estimated by using normal approximation.
PGM=DEVOPS/SAR231893/EFC14153/CSR_RWE/REPORT/PGM/eff_pro_evt_ger_subg_i_t.sas OUT=REPORT/OUTPUT/eff_pro_scpmw52_ger_race_t2_t_x.rtf (29JUN2021 - 17:53)

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

Project Code / Study Number / Analysis: SAR231893 / EFC14153 / CSR_RWE

2 PRO endpoints

2.6 Responder analysis for change from baseline in PM Asthma symptom score (improvement >= 0.6) at week 52 - ITT type 2 inflammatory asthma phenotype population

2.6.4 By baseline ICS dose level (Medium, High)

	Baseline ICS dose level			
	High		Medium	
Type 2 inflammatory asthma phenotype population	**Placebo (N=50)**	**Dupilumab (N=102)**	**Placebo (N=64)**	**Dupilumab (N=131)**
Responder status at Week 52 based on change from baseline in PM symptom score <=-0.6 [n(%)] [a]				
Responder	18 (36.0%)	37 (36.3%)	21 (32.8%)	50 (38.2%)
Non-responder	32 (64.0%)	65 (63.7%)	43 (67.2%)	81 (61.8%)
Odds Ratio (95% CI) vs placebo	-	1.60 (0.61 to 4.22)	-	1.32 (0.58 to 3.04)
p-value for Odds Ratio	-	0.337	-	0.508
p-value for heterogeneity of Odds Ratio				0.695
Risk Ratio (95% CI) vs placebo	-	1.23 (0.74 to 2.04)	-	1.11 (0.71 to 1.74)
Reversed Risk ratio (95% CI) vs placebo	-	0.81 (0.49 to 1.35)	-	0.90 (0.58 to 1.40)

[a] Patients who met the corresponding criterion are considered as responders. Patients who did not meet the criterion or had missing value are considered as non-responders.
OR, RR and RD are derived from a logistic regression model with treatment, age, weight group, region, baseline eosinophil level, baseline FeNO level and baseline PM Asthma symptom score as covariates.
Peto OR calculation is based on Yusuf S et al. (Prog Cardiovasc Dis. 1985 Mar-Apr;27(5):335-71) and its p-value is derived using a normal approximation.
p-values for heterogeneity are estimated by using the same logistic model as the one used to estimate OR, RR and RD, with subgroup and treatment-by-subgroup interaction as additional covariates.
p-value for heterogeneity of Peto OR is estimated by using normal approximation.
PGM=DEVOPS/SAR231893/EFC14153/CSR_RWE/REPORT/PGM/eff_pro_evt_ger_subg_i_t.sas OUT=REPORT/OUTPUT/eff_pro_scpmw52_ger_ics_t2_t_x.rtf (29JUN2021 - 17:53)

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

Project Code / Study Number / Analysis: SAR231893 / EFC14153 / CSR_RWE

2 PRO endpoints

2.6 Responder analysis for change from baseline in PM Asthma symptom score (improvement >= 0.6) at week 52 - ITT type 2 inflammatory asthma phenotype population

2.6.4 By baseline ICS dose level (Medium, High)

	Baseline ICS dose level			
	High		Medium	
Type 2 inflammatory asthma phenotype population	**Placebo (N=50)**	**Dupilumab (N=102)**	**Placebo (N=64)**	**Dupilumab (N=131)**
p-value for Risk Ratio	-	0.424	-	0.639
p-value for heterogeneity of Risk Ratio				0.205
Risk Difference (95% CI) vs placebo	-	2.46 (-16.36 to 21.27)	-	4.98 (-11.84 to 21.80)
p-value for Risk Difference	-	0.796	-	0.560
p-value for heterogeneity of Risk Difference				0.545

[a] Patients who met the corresponding criterion are considered as responders. Patients who did not meet the criterion or had missing value are considered as non-responders.
OR, RR and RD are derived from a logistic regression model with treatment, age, weight group, region, baseline eosinophil level, baseline FeNO level and baseline PM Asthma symptom score as covariates.
Peto OR calculation is based on Yusuf S et al. (Prog Cardiovasc Dis. 1985 Mar-Apr;27(5):335-71) and its p-value is derived using a normal approximation.
p-values for heterogeneity are estimated by using the same logistic model as the one used to estimate OR, RR and RD, with subgroup and treatment-by-subgroup interaction as additional covariates.
p-value for heterogeneity of Peto OR is estimated by using normal approximation.
PGM=DEVOPS/SAR231893/EFC14153/CSR_RWE/REPORT/PGM/eff_pro_evt_ger_subg_i_t.sas OUT=REPORT/OUTPUT/eff_pro_scpmw52_ger_ics_t2_t_x.rtf (29JUN2021 - 17:53)

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

Project Code / Study Number / Analysis: SAR231893 / EFC14153 / CSR_RWE

2 PRO endpoints

2.6 Responder analysis for change from baseline in PM Asthma symptom score (improvement >= 0.6) at week 52 - ITT type 2 inflammatory asthma phenotype population

2.6.5 By baseline ICS dose level 2 (Medium, High)

	Baseline ICS dose level 2			
	High		Medium	
Type 2 inflammatory asthma phenotype population	**Placebo (N=95)**	**Dupilumab (N=200)**	**Placebo (N=19)**	**Dupilumab (N=36)**
Responder status at Week 52 based on change from baseline in PM symptom score <=-0.6 [n(%)] [a]				
Responder	33 (34.7%)	76 (38.0%)	6 (31.6%)	11 (30.6%)
Non-responder	62 (65.3%)	124 (62.0%)	13 (68.4%)	25 (69.4%)
Odds Ratio (95% CI) vs placebo	-	1.39 (0.72 to 2.68)	-	1.25 (0.16 to 9.66)
p-value for Odds Ratio	-	0.322	-	0.827
p-value for heterogeneity of Odds Ratio				0.860
Risk Ratio (95% CI) vs placebo	-	1.18 (0.83 to 1.68)	-	0.84 (0.21 to 3.31)
Reversed Risk ratio (95% CI) vs placebo	-	0.85 (0.60 to 1.20)		

[a] Patients who met the corresponding criterion are considered as responders. Patients who did not meet the criterion or had missing value are considered as non-responders.
OR, RR and RD are derived from a logistic regression model with treatment, age, weight group, region, baseline eosinophil level, baseline FeNO level and baseline PM Asthma symptom score as covariates.
Peto OR calculation is based on Yusuf S et al. (Prog Cardiovasc Dis. 1985 Mar-Apr;27(5):335-71) and its p-value is derived using a normal approximation.
p-values for heterogeneity are estimated by using the same logistic model as the one used to estimate OR, RR and RD, with subgroup and treatment-by-subgroup interaction as additional covariates.
p-value for heterogeneity of Peto OR is estimated by using normal approximation.
PGM=DEVOPS/SAR231893/EFC14153/CSR_RWE/REPORT/PGM/eff_pro_evt_ger_subg_i_t.sas OUT=REPORT/OUTPUT/eff_pro_scpmw52_ger_ics2_t2_t_x.rtf (01SEP2021 - 15:28)

Project Code / Study Number / Analysis: SAR231893 / EFC14153 / CSR_RWE

2 PRO endpoints

2.6 Responder analysis for change from baseline in PM Asthma symptom score (improvement >= 0.6) at week 52 - ITT type 2 inflammatory asthma phenotype population

2.6.5 By baseline ICS dose level 2 (Medium, High)

	Baseline ICS dose level 2			
	High		Medium	
Type 2 inflammatory asthma phenotype population	**Placebo (N=95)**	**Dupilumab (N=200)**	**Placebo (N=19)**	**Dupilumab (N=36)**
p-value for Risk Ratio	-	0.345	-	0.799
p-value for heterogeneity of Risk Ratio				0.672
Risk Difference (95% CI) vs placebo	-	2.68 (-10.23 to 15.58)	-	-0.06 (-48.85 to 48.74)
p-value for Risk Difference	-	0.683	-	0.998
p-value for heterogeneity of Risk Difference				0.983

[a] Patients who met the corresponding criterion are considered as responders. Patients who did not meet the criterion or had missing value are considered as non-responders.
OR, RR and RD are derived from a logistic regression model with treatment, age, weight group, region, baseline eosinophil level, baseline FeNO level and baseline PM Asthma symptom score as covariates.
Peto OR calculation is based on Yusuf S et al. (Prog Cardiovasc Dis. 1985 Mar-Apr;27(5):335-71) and its p-value is derived using a normal approximation.
p-values for heterogeneity are estimated by using the same logistic model as the one used to estimate OR, RR and RD, with subgroup and treatment-by-subgroup interaction as additional covariates.
p-value for heterogeneity of Peto OR is estimated by using normal approximation.
PGM=DEVOPS/SAR231893/EFC14153/CSR_RWE/REPORT/PGM/eff_pro_evt_ger_subg_i_t.sas OUT=REPORT/OUTPUT/eff_pro_scpmw52_ger_ics2_t2_t_x.rtf (01SEP2021 - 15:28)

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

Project Code / Study Number / Analysis: SAR231893 / EFC14153 / CSR_RWE

2 PRO endpoints

2.6 Responder analysis for change from baseline in PM Asthma symptom score (improvement >= 0.6) at week 52 - ITT type 2 inflammatory asthma phenotype population

2.6.6 By baseline predicted FEV1 (<80%, >=80%)

	Baseline Predicted FEV1			
	<80%		>=80%	
Type 2 inflammatory asthma phenotype population	**Placebo (N=59)**	**Dupilumab (N=116)**	**Placebo (N=55)**	**Dupilumab (N=120)**
Responder status at Week 52 based on change from baseline in PM symptom score <=-0.6 [n(%)] [a]				
Responder	19 (32.2%)	43 (37.1%)	20 (36.4%)	44 (36.7%)
Non-responder	40 (67.8%)	73 (62.9%)	35 (63.6%)	76 (63.3%)
Odds Ratio (95% CI) vs placebo	-	1.26 (0.51 to 3.11)	-	1.97 (0.77 to 5.06)
p-value for Odds Ratio	-	0.615	-	0.158
p-value for heterogeneity of Odds Ratio				0.652
Risk Ratio (95% CI) vs placebo	-	1.08 (0.67 to 1.76)	-	1.14 (0.69 to 1.89)
Reversed Risk ratio (95% CI) vs placebo	-	0.92 (0.57 to 1.49)	-	0.87 (0.53 to 1.44)

[a] Patients who met the corresponding criterion are considered as responders. Patients who did not meet the criterion or had missing value are considered as non-responders.
OR, RR and RD are derived from a logistic regression model with treatment, age, weight group, region, baseline eosinophil level, baseline FeNO level, baseline ICS dose level, and baseline PM Asthma symptom score as covariates.
Peto OR calculation is based on Yusuf S et al. (Prog Cardiovasc Dis. 1985 Mar-Apr;27(5):335-71) and its p-value is derived using a normal approximation.
p-values for heterogeneity are estimated by using the same logistic model as the one used to estimate OR, RR and RD, with subgroup and treatment-by-subgroup interaction as additional covariates.
p-value for heterogeneity of Peto OR is estimated by using normal approximation.
PGM=DEVOPS/SAR231893/EFC14153/CSR_RWE/REPORT/PGM/eff_pro_evt_ger_subg_i_t.sas OUT=REPORT/OUTPUT/eff_pro_scpmw52_ger_pfev1_t2_t_x.rtf (29JUN2021 - 17:53)

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

Project Code / Study Number / Analysis: SAR231893 / EFC14153 / CSR_RWE

2 PRO endpoints

2.6 Responder analysis for change from baseline in PM Asthma symptom score (improvement >= 0.6) at week 52 - ITT type 2 inflammatory asthma phenotype population

2.6.6 By baseline predicted FEV1 (<80%, >=80%)

	Baseline Predicted FEV1			
	<80%		>=80%	
Type 2 inflammatory asthma phenotype population	**Placebo (N=59)**	**Dupilumab (N=116)**	**Placebo (N=55)**	**Dupilumab (N=120)**
p-value for Risk Ratio	-	0.741	-	0.595
p-value for heterogeneity of Risk Ratio				0.231
Risk Difference (95% CI) vs placebo	-	0.81 (-17.18 to 18.80)	-	6.03 (-13.62 to 25.68)
p-value for Risk Difference	-	0.929	-	0.545
p-value for heterogeneity of Risk Difference				0.565

[a] Patients who met the corresponding criterion are considered as responders. Patients who did not meet the criterion or had missing value are considered as non-responders.
OR, RR and RD are derived from a logistic regression model with treatment, age, weight group, region, baseline eosinophil level, baseline FeNO level, baseline ICS dose level, and baseline PM Asthma symptom score as covariates.
Peto OR calculation is based on Yusuf S et al. (Prog Cardiovasc Dis. 1985 Mar-Apr;27(5):335-71) and its p-value is derived using a normal approximation.
p-values for heterogeneity are estimated by using the same logistic model as the one used to estimate OR, RR and RD, with subgroup and treatment-by-subgroup interaction as additional covariates.
p-value for heterogeneity of Peto OR is estimated by using normal approximation.
PGM=DEVOPS/SAR231893/EFC14153/CSR_RWE/REPORT/PGM/eff_pro_evt_ger_subg_i_t.sas OUT=REPORT/OUTPUT/eff_pro_scpmw52_ger_pfev1_t2_t_x.rtf (29JUN2021 - 17:53)

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

Project Code / Study Number / Analysis: SAR231893 / EFC14153 / CSR_RWE

2 PRO endpoints

2.6 Responder analysis for change from baseline in PM Asthma symptom score (improvement >= 0.6) at week 52 - ITT type 2 inflammatory asthma phenotype population

2.6.7 By baseline ACQ-7-IA (<=2, >2)

	Baseline ACQ-7-IA			
	<=2		>2	
Type 2 inflammatory asthma phenotype population	**Placebo (N=61)**	**Dupilumab (N=126)**	**Placebo (N=53)**	**Dupilumab (N=110)**
Responder status at Week 52 based on change from baseline in PM symptom score <=-0.6 [n(%)] [a]				
Responder	19 (31.1%)	35 (27.8%)	20 (37.7%)	52 (47.3%)
Non-responder	42 (68.9%)	91 (72.2%)	33 (62.3%)	58 (52.7%)
Odds Ratio (95% CI) vs placebo	-	1.11 (0.43 to 2.86)	-	1.55 (0.65 to 3.68)
p-value for Odds Ratio	-	0.833	-	0.318
p-value for heterogeneity of Odds Ratio				0.388
Risk Ratio (95% CI) vs placebo	-	0.84 (0.48 to 1.46)	-	1.31 (0.84 to 2.07)
Reversed Risk ratio (95% CI) vs placebo			-	0.76 (0.48 to 1.20)

[a] Patients who met the corresponding criterion are considered as responders. Patients who did not meet the criterion or had missing value are considered as non-responders.
OR, RR and RD are derived from a logistic regression model with treatment, age, weight group, region, baseline eosinophil level, baseline FeNO level, baseline ICS dose level, and baseline PM Asthma symptom score as covariates.
Peto OR calculation is based on Yusuf S et al. (Prog Cardiovasc Dis. 1985 Mar-Apr;27(5):335-71) and its p-value is derived using a normal approximation.
p-values for heterogeneity are estimated by using the same logistic model as the one used to estimate OR, RR and RD, with subgroup and treatment-by-subgroup interaction as additional covariates.
p-value for heterogeneity of Peto OR is estimated by using normal approximation.
PGM=DEVOPS/SAR231893/EFC14153/CSR_RWE/REPORT/PGM/eff_pro_evt_ger_subg_i_t.sas OUT=REPORT/OUTPUT/eff_pro_scpmw52_ger_acq7_t2_t_x.rtf (29JUN2021 - 17:53)

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

Project Code / Study Number / Analysis: SAR231893 / EFC14153 / CSR_RWE

2 PRO endpoints

2.6 Responder analysis for change from baseline in PM Asthma symptom score (improvement >= 0.6) at week 52 - ITT type 2 inflammatory asthma phenotype population

2.6.7 By baseline ACQ-7-IA (<=2, >2)

	Baseline ACQ-7-IA			
	<=2		>2	
Type 2 inflammatory asthma phenotype population	**Placebo (N=61)**	**Dupilumab (N=126)**	**Placebo (N=53)**	**Dupilumab (N=110)**
p-value for Risk Ratio	-	0.531	-	0.235
p-value for heterogeneity of Risk Ratio				0.736
Risk Difference (95% CI) vs placebo	-	-3.31 (-23.69 to 17.06)	-	5.44 (-10.35 to 21.24)
p-value for Risk Difference	-	0.749	-	0.497
p-value for heterogeneity of Risk Difference				0.771

[a] Patients who met the corresponding criterion are considered as responders. Patients who did not meet the criterion or had missing value are considered as non-responders.
OR, RR and RD are derived from a logistic regression model with treatment, age, weight group, region, baseline eosinophil level, baseline FeNO level, baseline ICS dose level, and baseline PM Asthma symptom score as covariates.
Peto OR calculation is based on Yusuf S et al. (Prog Cardiovasc Dis. 1985 Mar-Apr;27(5):335-71) and its p-value is derived using a normal approximation.
p-values for heterogeneity are estimated by using the same logistic model as the one used to estimate OR, RR and RD, with subgroup and treatment-by-subgroup interaction as additional covariates.
p-value for heterogeneity of Peto OR is estimated by using normal approximation.
PGM=DEVOPS/SAR231893/EFC14153/CSR_RWE/REPORT/PGM/eff_pro_evt_ger_subg_i_t.sas OUT=REPORT/OUTPUT/eff_pro_scpmw52_ger_acq7_t2_t_x.rtf (29JUN2021 - 17:53)

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

Project Code / Study Number / Analysis: SAR231893 / EFC14153 / CSR_RWE

2 PRO endpoints

2.6 Responder analysis for change from baseline in PM Asthma symptom score (improvement >= 0.6) at week 52 - ITT type 2 inflammatory asthma phenotype population

2.6.8 By baseline weight (<=30 kg, >30 kg)

	Baseline weight (kg)			
	<=30		>30	
Type 2 inflammatory asthma phenotype population	**Placebo (N=36)**	**Dupilumab (N=76)**	**Placebo (N=78)**	**Dupilumab (N=160)**
Responder status at Week 52 based on change from baseline in PM symptom score <=-0.6 [n(%)] [a]				
Responder	15 (41.7%)	28 (36.8%)	24 (30.8%)	59 (36.9%)
Non-responder	21 (58.3%)	48 (63.2%)	54 (69.2%)	101 (63.1%)
Odds Ratio (95% CI) vs placebo	-	0.76 (0.23 to 2.54)	-	1.57 (0.73 to 3.37)
p-value for Odds Ratio	-	0.651	-	0.244
p-value for heterogeneity of Odds Ratio				0.430
Risk Ratio (95% CI) vs placebo	-	0.80 (0.41 to 1.54)	-	1.17 (0.77 to 1.79)
Reversed Risk ratio (95% CI) vs placebo			-	0.85 (0.56 to 1.30)

[a] Patients who met the corresponding criterion are considered as responders. Patients who did not meet the criterion or had missing value are considered as non-responders.
OR, RR and RD are derived from a logistic regression model with treatment, age, region, baseline eosinophil level, baseline FeNO level, baseline ICS dose level, and baseline PM Asthma symptom score as covariates.
Peto OR calculation is based on Yusuf S et al. (Prog Cardiovasc Dis. 1985 Mar-Apr;27(5):335-71) and its p-value is derived using a normal approximation.
p-values for heterogeneity are estimated by using the same logistic model as the one used to estimate OR, RR and RD, with subgroup and treatment-by-subgroup interaction as additional covariates.
p-value for heterogeneity of Peto OR is estimated by using normal approximation.
PGM=DEVOPS/SAR231893/EFC14153/CSR_RWE/REPORT/PGM/eff_pro_evt_ger_subg_i_t.sas OUT=REPORT/OUTPUT/eff_pro_scpmw52_ger_wgt_t2_t_x.rtf (29JUN2021 - 17:54)

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

Project Code / Study Number / Analysis: SAR231893 / EFC14153 / CSR_RWE

2 PRO endpoints

2.6 Responder analysis for change from baseline in PM Asthma symptom score (improvement >= 0.6) at week 52 - ITT type 2 inflammatory asthma phenotype population

2.6.8 By baseline weight (<=30 kg, >30 kg)

	Baseline weight (kg)			
	<=30		>30	
Type 2 inflammatory asthma phenotype population	**Placebo (N=36)**	**Dupilumab (N=76)**	**Placebo (N=78)**	**Dupilumab (N=160)**
p-value for Risk Ratio	-	0.496	-	0.455
p-value for heterogeneity of Risk Ratio				0.023
Risk Difference (95% CI) vs placebo	-	-9.76 (-35.58 to 16.06)	-	5.10 (-8.66 to 18.85)
p-value for Risk Difference	-	0.455	-	0.466
p-value for heterogeneity of Risk Difference				0.186

[a] Patients who met the corresponding criterion are considered as responders. Patients who did not meet the criterion or had missing value are considered as non-responders.
OR, RR and RD are derived from a logistic regression model with treatment, age, region, baseline eosinophil level, baseline FeNO level, baseline ICS dose level, and baseline PM Asthma symptom score as covariates.
Peto OR calculation is based on Yusuf S et al. (Prog Cardiovasc Dis. 1985 Mar-Apr;27(5):335-71) and its p-value is derived using a normal approximation.
p-values for heterogeneity are estimated by using the same logistic model as the one used to estimate OR, RR and RD, with subgroup and treatment-by-subgroup interaction as additional covariates.
p-value for heterogeneity of Peto OR is estimated by using normal approximation.
PGM=DEVOPS/SAR231893/EFC14153/CSR_RWE/REPORT/PGM/eff_pro_evt_ger_subg_i_t.sas OUT=REPORT/OUTPUT/eff_pro_scpmw52_ger_wgt_t2_t_x.rtf (29JUN2021 - 17:54)

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

Project Code / Study Number / Analysis: SAR231893 / EFC14153 / CSR_RWE

2 PRO endpoints

2.6 Responder analysis for change from baseline in PM Asthma symptom score (improvement >= 0.6) at week 52 - ITT type 2 inflammatory asthma phenotype population

2.6.9 By atopic medical condition (Yes, No)

	Atopic medical condition			
	Yes		No	
Type 2 inflammatory asthma phenotype population	**Placebo (N=103)**	**Dupilumab (N=227)**	**Placebo (N=11)**	**Dupilumab (N=9)**
Responder status at Week 52 based on change from baseline in PM symptom score <=-0.6 [n(%)] [a]				
Responder	36 (35.0%)	81 (35.7%)	3 (27.3%)	6 (66.7%)
Non-responder	67 (65.0%)	146 (64.3%)	8 (72.7%)	3 (33.3%)
Odds Ratio (95% CI) vs placebo	-	1.39 (0.72 to 2.66)	-	5.683E21 (0.00 to NE)
p-value for Odds Ratio	-	0.324	-	0.959
p-value for heterogeneity of Odds Ratio				0.505
Risk Ratio (95% CI) vs placebo	-	1.11 (0.78 to 1.58)	-	0.00 (NE to NE)
Reversed Risk ratio (95% CI) vs placebo	-	0.90 (0.63 to 1.29)		

[a] Patients who met the corresponding criterion are considered as responders. Patients who did not meet the criterion or had missing value are considered as non-responders.
OR, RR and RD are derived from a logistic regression model with treatment, age, weight group, region, baseline eosinophil level, baseline FeNO level, baseline ICS dose level, and baseline PM Asthma symptom score as covariates.
Peto OR calculation is based on Yusuf S et al. (Prog Cardiovasc Dis. 1985 Mar-Apr;27(5):335-71) and its p-value is derived using a normal approximation.
p-values for heterogeneity are estimated by using the same logistic model as the one used to estimate OR, RR and RD, with subgroup and treatment-by-subgroup interaction as additional covariates.
p-value for heterogeneity of Peto OR is estimated by using normal approximation.
PGM=DEVOPS/SAR231893/EFC14153/CSR_RWE/REPORT/PGM/eff_pro_evt_ger_subg_i_t.sas OUT=REPORT/OUTPUT/eff_pro_scpmw52_ger_amc_t2_t_x.rtf (29JUN2021 - 17:54)

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

Project Code / Study Number / Analysis: SAR231893 / EFC14153 / CSR_RWE

2 PRO endpoints

2.6 Responder analysis for change from baseline in PM Asthma symptom score (improvement >= 0.6) at week 52 - ITT type 2 inflammatory asthma phenotype population

2.6.9 By atopic medical condition (Yes, No)

	Atopic medical condition			
	Yes		No	
Type 2 inflammatory asthma phenotype population	**Placebo (N=103)**	**Dupilumab (N=227)**	**Placebo (N=11)**	**Dupilumab (N=9)**
p-value for Risk Ratio	-	0.573	-	<0.001
p-value for heterogeneity of Risk Ratio				0.380
Risk Difference (95% CI) vs placebo	-	1.76 (-10.87 to 14.39)	-	46.36 (-213.06 to 305.78)
p-value for Risk Difference	-	0.784	-	0.699
p-value for heterogeneity of Risk Difference				0.290

[a] Patients who met the corresponding criterion are considered as responders. Patients who did not meet the criterion or had missing value are considered as non-responders.
OR, RR and RD are derived from a logistic regression model with treatment, age, weight group, region, baseline eosinophil level, baseline FeNO level, baseline ICS dose level, and baseline PM Asthma symptom score as covariates.
Peto OR calculation is based on Yusuf S et al. (Prog Cardiovasc Dis. 1985 Mar-Apr;27(5):335-71) and its p-value is derived using a normal approximation.
p-values for heterogeneity are estimated by using the same logistic model as the one used to estimate OR, RR and RD, with subgroup and treatment-by-subgroup interaction as additional covariates.
p-value for heterogeneity of Peto OR is estimated by using normal approximation.
PGM=DEVOPS/SAR231893/EFC14153/CSR_RWE/REPORT/PGM/eff_pro_evt_ger_subg_i_t.sas OUT=REPORT/OUTPUT/eff_pro_scpmw52_ger_amc_t2_t_x.rtf (29JUN2021 - 17:54)

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

Project Code / Study Number / Analysis: SAR231893 / EFC14153 / CSR_RWE

2 PRO endpoints

2.6 Responder analysis for change from baseline in PM Asthma symptom score (improvement >= 0.6) at week 52 - ITT type 2 inflammatory asthma phenotype population

2.6.10 By baseline total IgE (<median, >= median)

	Baseline Total IgE (IU/mL)			
	<median		>=median	
Type 2 inflammatory asthma phenotype population	**Placebo (N=66)**	**Dupilumab (N=105)**	**Placebo (N=47)**	**Dupilumab (N=125)**
Responder status at Week 52 based on change from baseline in PM symptom score <=-0.6 [n(%)] [a]				
Responder	25 (37.9%)	35 (33.3%)	13 (27.7%)	50 (40.0%)
Non-responder	41 (62.1%)	70 (66.7%)	34 (72.3%)	75 (60.0%)
Odds Ratio (95% CI) vs placebo	-	0.92 (0.36 to 2.34)	-	2.53 (0.97 to 6.65)
p-value for Odds Ratio	-	0.861	-	0.059
p-value for heterogeneity of Odds Ratio				0.089
Risk Ratio (95% CI) vs placebo	-	0.85 (0.52 to 1.41)	-	1.40 (0.84 to 2.34)
Reversed Risk ratio (95% CI) vs placebo			-	0.71 (0.43 to 1.19)

[a] Patients who met the corresponding criterion are considered as responders. Patients who did not meet the criterion or had missing value are considered as non-responders.
OR, RR and RD are derived from a logistic regression model with treatment, age, weight group, region, baseline eosinophil level, baseline FeNO level, baseline ICS dose level, and baseline PM Asthma symptom score as covariates.
Peto OR calculation is based on Yusuf S et al. (Prog Cardiovasc Dis. 1985 Mar-Apr;27(5):335-71) and its p-value is derived using a normal approximation.
p-values for heterogeneity are estimated by using the same logistic model as the one used to estimate OR, RR and RD, with subgroup and treatment-by-subgroup interaction as additional covariates.
p-value for heterogeneity of Peto OR is estimated by using normal approximation.
PGM=DEVOPS/SAR231893/EFC14153/CSR_RWE/REPORT/PGM/eff_pro_evt_ger_subg_i_t.sas OUT=REPORT/OUTPUT/eff_pro_scpmw52_ger_igem_t2_t_x.rtf (29JUN2021 - 17:54)

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

Project Code / Study Number / Analysis: SAR231893 / EFC14153 / CSR_RWE

2 PRO endpoints

2.6 Responder analysis for change from baseline in PM Asthma symptom score (improvement >= 0.6) at week 52 - ITT type 2 inflammatory asthma phenotype population

2.6.10 By baseline total IgE (<median, >= median)

	Baseline Total IgE (IU/mL)			
	<median		>=median	
Type 2 inflammatory asthma phenotype population	**Placebo (N=66)**	**Dupilumab (N=105)**	**Placebo (N=47)**	**Dupilumab (N=125)**
p-value for Risk Ratio	-	0.537	-	0.196
p-value for heterogeneity of Risk Ratio				0.235
Risk Difference (95% CI) vs placebo	-	1.13 (-18.18 to 20.44)	-	8.21 (-10.48 to 26.90)
p-value for Risk Difference	-	0.908	-	0.387
p-value for heterogeneity of Risk Difference				0.540

[a] Patients who met the corresponding criterion are considered as responders. Patients who did not meet the criterion or had missing value are considered as non-responders.
OR, RR and RD are derived from a logistic regression model with treatment, age, weight group, region, baseline eosinophil level, baseline FeNO level, baseline ICS dose level, and baseline PM Asthma symptom score as covariates.
Peto OR calculation is based on Yusuf S et al. (Prog Cardiovasc Dis. 1985 Mar-Apr;27(5):335-71) and its p-value is derived using a normal approximation.
p-values for heterogeneity are estimated by using the same logistic model as the one used to estimate OR, RR and RD, with subgroup and treatment-by-subgroup interaction as additional covariates.
p-value for heterogeneity of Peto OR is estimated by using normal approximation.
PGM=DEVOPS/SAR231893/EFC14153/CSR_RWE/REPORT/PGM/eff_pro_evt_ger_subg_i_t.sas OUT=REPORT/OUTPUT/eff_pro_scpmw52_ger_igem_t2_t_x.rtf (29JUN2021 - 17:54)

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

Project Code / Study Number / Analysis: SAR231893 / EFC14153 / CSR_RWE

2 PRO endpoints

2.6 Responder analysis for change from baseline in PM Asthma symptom score (improvement >= 0.6) at week 52 - ITT type 2 inflammatory asthma phenotype population

2.6.11 By baseline total IgE (<100 IU/ml, >= 100 IU/ml)

	Baseline Total IgE (IU/mL)			
	< 100		**>= 100**	
Type 2 inflammatory asthma phenotype population	**Placebo (N=22)**	**Dupilumab (N=29)**	**Placebo (N=91)**	**Dupilumab (N=201)**
Responder status at Week 52 based on change from baseline in PM symptom score <=-0.6 [n(%)] [a]				
Responder	6 (27.3%)	10 (34.5%)	32 (35.2%)	75 (37.3%)
Non-responder	16 (72.7%)	19 (65.5%)	59 (64.8%)	126 (62.7%)
Odds Ratio (95% CI) vs placebo	-	0.80 (0.10 to 6.65)	-	1.40 (0.72 to 2.72)
p-value for Odds Ratio	-	0.830	-	0.324
p-value for heterogeneity of Odds Ratio				0.800
Risk Ratio (95% CI) vs placebo	-	0.66 (0.11 to 3.98)	-	1.18 (0.82 to 1.71)
Reversed Risk ratio (95% CI) vs placebo			-	0.85 (0.58 to 1.22)

[a] Patients who met the corresponding criterion are considered as responders. Patients who did not meet the criterion or had missing value are considered as non-responders.
OR, RR and RD are derived from a logistic regression model with treatment, age, weight group, region, baseline eosinophil level, baseline FeNO level, baseline ICS dose level, and baseline PM Asthma symptom score as covariates.
Peto OR calculation is based on Yusuf S et al. (Prog Cardiovasc Dis. 1985 Mar-Apr;27(5):335-71) and its p-value is derived using a normal approximation.
p-values for heterogeneity are estimated by using the same logistic model as the one used to estimate OR, RR and RD, with subgroup and treatment-by-subgroup interaction as additional covariates.
p-value for heterogeneity of Peto OR is estimated by using normal approximation.
PGM=DEVOPS/SAR231893/EFC14153/CSR_RWE/REPORT/PGM/eff_pro_evt_ger_subg_i_t.sas OUT=REPORT/OUTPUT/eff_pro_scpmw52_ger_ige_t2_t_x.rtf (29JUN2021 - 17:54)

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

Project Code / Study Number / Analysis: SAR231893 / EFC14153 / CSR_RWE

2 PRO endpoints

2.6 Responder analysis for change from baseline in PM Asthma symptom score (improvement >= 0.6) at week 52 - ITT type 2 inflammatory asthma phenotype population

2.6.11 By baseline total IgE (<100 IU/ml, >= 100 IU/ml)

	Baseline Total IgE (IU/mL)			
	< 100		**>= 100**	
Type 2 inflammatory asthma phenotype population	**Placebo (N=22)**	**Dupilumab (N=29)**	**Placebo (N=91)**	**Dupilumab (N=201)**
p-value for Risk Ratio	-	0.639	-	0.373
p-value for heterogeneity of Risk Ratio				0.467
Risk Difference (95% CI) vs placebo	-	-6.06 (-56.05 to 43.94)	-	3.11 (-9.95 to 16.17)
p-value for Risk Difference	-	0.808	-	0.640
p-value for heterogeneity of Risk Difference				0.940

[a] Patients who met the corresponding criterion are considered as responders. Patients who did not meet the criterion or had missing value are considered as non-responders.
OR, RR and RD are derived from a logistic regression model with treatment, age, weight group, region, baseline eosinophil level, baseline FeNO level, baseline ICS dose level, and baseline PM Asthma symptom score as covariates.
Peto OR calculation is based on Yusuf S et al. (Prog Cardiovasc Dis. 1985 Mar-Apr;27(5):335-71) and its p-value is derived using a normal approximation.
p-values for heterogeneity are estimated by using the same logistic model as the one used to estimate OR, RR and RD, with subgroup and treatment-by-subgroup interaction as additional covariates.
p-value for heterogeneity of Peto OR is estimated by using normal approximation.
PGM=DEVOPS/SAR231893/EFC14153/CSR_RWE/REPORT/PGM/eff_pro_evt_ger_subg_i_t.sas OUT=REPORT/OUTPUT/eff_pro_scpmw52_ger_ige_t2_t_x.rtf (29JUN2021 - 17:54)

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

Project Code / Study Number / Analysis: SAR231893 / EFC14153 / CSR_RWE

2 PRO endpoints

2.6 Responder analysis for change from baseline in PM Asthma symptom score (improvement >= 0.6) at week 52 - ITT type 2 inflammatory asthma phenotype population

2.6.12 By age at onset of asthma (0-2, 3-5, >=6 years)

	Age of onset of asthma (years)					
	0-2		3-5		>= 6	
Type 2 inflammatory asthma phenotype population	**Placebo (N=40)**	**Dupilumab (N=105)**	**Placebo (N=39)**	**Dupilumab (N=86)**	**Placebo (N=35)**	**Dupilumab (N=45)**
Responder status at Week 52 based on change from baseline in PM symptom score <=-0.6 [n(%)] [a]						
Responder	15 (37.5%)	36 (34.3%)	14 (35.9%)	33 (38.4%)	10 (28.6%)	18 (40.0%)
Non-responder	25 (62.5%)	69 (65.7%)	25 (64.1%)	53 (61.6%)	25 (71.4%)	27 (60.0%)
Odds Ratio (95% CI) vs placebo	-	1.11 (0.42 to 2.91)	-	1.24 (0.42 to 3.65)	-	1.86 (0.39 to 8.87)
p-value for Odds Ratio	-	0.832	-	0.700	-	0.430
p-value for heterogeneity of Odds Ratio:						
0-2, 3-5						0.887
0-2, >= 6						0.797

[a] Patients who met the corresponding criterion are considered as responders. Patients who did not meet the criterion or had missing value are considered as non-responders. OR, RR and RD are derived from a logistic regression model with treatment, age, weight group, region, baseline eosinophil level, baseline FeNO level, baseline ICS dose level, and baseline PM Asthma symptom score as covariates.
Peto OR calculation is based on Yusuf S et al. (Prog Cardiovasc Dis. 1985 Mar-Apr;27(5):335-71) and its p-value is derived using a normal approximation.
p-values for heterogeneity are estimated by using the same logistic model as the one used to estimate OR, RR and RD, with subgroup and treatment-by-subgroup interaction as additional covariates.
p-value for heterogeneity of Peto OR is estimated by using normal approximation.
PGM=DEVOPS/SAR231893/EFC14153/CSR_RWE/REPORT/PGM/eff_pro_evt_ger_subg_i_t.sas OUT=REPORT/OUTPUT/eff_pro_scpmw52_ger_onsa_t2_t_x.rtf (01SEP2021 - 15:28)

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

Project Code / Study Number / Analysis: SAR231893 / EFC14153 / CSR_RWE

2 PRO endpoints

2.6 Responder analysis for change from baseline in PM Asthma symptom score (improvement >= 0.6) at week 52 - ITT type 2 inflammatory asthma phenotype population

2.6.12 By age at onset of asthma (0-2, 3-5, >=6 years)

	Age of onset of asthma (years)					
	0-2		3-5		>= 6	
Type 2 inflammatory asthma phenotype population	**Placebo (N=40)**	**Dupilumab (N=105)**	**Placebo (N=39)**	**Dupilumab (N=86)**	**Placebo (N=35)**	**Dupilumab (N=45)**
3-5, >= 6						0.894
overall						0.967
Risk Ratio (95% CI) vs placebo	-	1.34 (0.70 to 2.57)	-	1.34 (0.66 to 2.71)	-	0.95 (0.35 to 2.56)
Reversed Risk ratio (95% CI) vs placebo	-	0.75 (0.39 to 1.43)	-	0.75 (0.37 to 1.51)		
p-value for Risk Ratio	-	0.374	-	0.413	-	0.914
p-value for heterogeneity of Risk Ratio:						
0-2, 3-5						0.100
0-2, >= 6						0.411
3-5, >= 6						0.526
overall						0.249

[a] Patients who met the corresponding criterion are considered as responders. Patients who did not meet the criterion or had missing value are considered as non-responders.
OR, RR and RD are derived from a logistic regression model with treatment, age, weight group, region, baseline eosinophil level, baseline FeNO level, baseline ICS dose level, and baseline PM Asthma symptom score as covariates.
Peto OR calculation is based on Yusuf S et al. (Prog Cardiovasc Dis. 1985 Mar-Apr;27(5):335-71) and its p-value is derived using a normal approximation.
p-values for heterogeneity are estimated by using the same logistic model as the one used to estimate OR, RR and RD, with subgroup and treatment-by-subgroup interaction as additional covariates.
p-value for heterogeneity of Peto OR is estimated by using normal approximation.
PGM=DEVOPS/SAR231893/EFC14153/CSR_RWE/REPORT/PGM/eff_pro_evt_ger_subg_i_t.sas OUT=REPORT/OUTPUT/eff_pro_scpmw52_ger_onsa_t2_t_x.rtf (01SEP2021 - 15:28)

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

Project Code / Study Number / Analysis: SAR231893 / EFC14153 / CSR_RWE

2 PRO endpoints

2.6 Responder analysis for change from baseline in PM Asthma symptom score (improvement >= 0.6) at week 52 - ITT type 2 inflammatory asthma phenotype population

2.6.12 By age at onset of asthma (0-2, 3-5, >=6 years)

	Age of onset of asthma (years)					
	0-2		3-5		>= 6	
Type 2 inflammatory asthma phenotype population	**Placebo (N=40)**	**Dupilumab (N=105)**	**Placebo (N=39)**	**Dupilumab (N=86)**	**Placebo (N=35)**	**Dupilumab (N=45)**
Risk Difference (95% CI) vs placebo	-	4.63 (-15.44 to 24.70)	-	6.57 (-15.92 to 29.07)	-	6.85 (-25.30 to 39.01)
p-value for Risk Difference	-	0.649	-	0.564	-	0.672
p-value for heterogeneity of Risk Difference:						
0-2, 3-5						0.548
0-2, >= 6						0.572
3-5, >= 6						0.952
overall						0.778

[a] Patients who met the corresponding criterion are considered as responders. Patients who did not meet the criterion or had missing value are considered as non-responders.
OR, RR and RD are derived from a logistic regression model with treatment, age, weight group, region, baseline eosinophil level, baseline FeNO level, baseline ICS dose level, and baseline PM Asthma symptom score as covariates.
Peto OR calculation is based on Yusuf S et al. (Prog Cardiovasc Dis. 1985 Mar-Apr;27(5):335-71) and its p-value is derived using a normal approximation.
p-values for heterogeneity are estimated by using the same logistic model as the one used to estimate OR, RR and RD, with subgroup and treatment-by-subgroup interaction as additional covariates.
p-value for heterogeneity of Peto OR is estimated by using normal approximation.
PGM=DEVOPS/SAR231893/EFC14153/CSR_RWE/REPORT/PGM/eff_pro_evt_ger_subg_i_t.sas OUT=REPORT/OUTPUT/eff_pro_scpmw52_ger_onsa_t2_t_x.rtf (01SEP2021 - 15:28)

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

Project Code / Study Number / Analysis: SAR231893 / EFC14153 / CSR_RWE

2 PRO endpoints

2.6 Responder analysis for change from baseline in PM Asthma symptom score (improvement >= 0.6) at week 52 - ITT type 2 inflammatory asthma phenotype population

2.6.13 By number of severe asthma exacerbation prior to the study (<=1, 2, >2)

	Number of severe asthma exacerbation prior to the study					
	<=1		2		>2	
Type 2 inflammatory asthma phenotype population	**Placebo (N=47)**	**Dupilumab (N=85)**	**Placebo (N=32)**	**Dupilumab (N=75)**	**Placebo (N=35)**	**Dupilumab (N=76)**
Responder status at Week 52 based on change from baseline in PM symptom score <=-0.6 [n(%)] [a]						
Responder	17 (36.2%)	27 (31.8%)	11 (34.4%)	29 (38.7%)	11 (31.4%)	31 (40.8%)
Non-responder	30 (63.8%)	58 (68.2%)	21 (65.6%)	46 (61.3%)	24 (68.6%)	45 (59.2%)
Odds Ratio (95% CI) vs placebo	-	0.87 (0.30 to 2.53)	-	0.65 (0.19 to 2.24)	-	5.65 (1.47 to 21.69)
p-value for Odds Ratio	-	0.803	-	0.487	-	0.012
p-value for heterogeneity of Odds Ratio:						
<=1, 2						0.699
<=1, >2						0.035

[a] Patients who met the corresponding criterion are considered as responders. Patients who did not meet the criterion or had missing value are considered as non-responders. OR, RR and RD are derived from a logistic regression model with treatment, age, weight group, region, baseline eosinophil level, baseline FeNO level, baseline ICS dose level, and baseline PM Asthma symptom score as covariates.
Peto OR calculation is based on Yusuf S et al. (Prog Cardiovasc Dis. 1985 Mar-Apr;27(5):335-71) and its p-value is derived using a normal approximation.
p-values for heterogeneity are estimated by using the same logistic model as the one used to estimate OR, RR and RD, with subgroup and treatment-by-subgroup interaction as additional covariates.
p-value for heterogeneity of Peto OR is estimated by using normal approximation.
PGM=DEVOPS/SAR231893/EFC14153/CSR_RWE/REPORT/PGM/eff_pro_evt_ger_subg_i_t.sas OUT=REPORT/OUTPUT/eff_pro_scpmw52_ger_exa_t2_t_x.rtf (29JUN2021 - 17:55)

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

Project Code / Study Number / Analysis: SAR231893 / EFC14153 / CSR_RWE

2 PRO endpoints

2.6 Responder analysis for change from baseline in PM Asthma symptom score (improvement >= 0.6) at week 52 - ITT type 2 inflammatory asthma phenotype population

2.6.13 By number of severe asthma exacerbation prior to the study (<=1, 2, >2)

	Number of severe asthma exacerbation prior to the study					
	<=1		2		>2	
Type 2 inflammatory asthma phenotype population	**Placebo (N=47)**	**Dupilumab (N=85)**	**Placebo (N=32)**	**Dupilumab (N=75)**	**Placebo (N=35)**	**Dupilumab (N=76)**
2, >2						0.025
overall						0.045
Risk Ratio (95% CI) vs placebo	-	1.12 (0.59 to 2.11)	-	0.80 (0.44 to 1.47)	-	2.15 (0.83 to 5.53)
Reversed Risk ratio (95% CI) vs placebo	-	0.89 (0.47 to 1.69)			-	0.47 (0.18 to 1.20)
p-value for Risk Ratio	-	0.727	-	0.472	-	0.112
p-value for heterogeneity of Risk Ratio:						
<=1, 2						0.252
<=1, >2						0.047
2, >2						0.010

[a] Patients who met the corresponding criterion are considered as responders. Patients who did not meet the criterion or had missing value are considered as non-responders.
OR, RR and RD are derived from a logistic regression model with treatment, age, weight group, region, baseline eosinophil level, baseline FeNO level, baseline ICS dose level, and baseline PM Asthma symptom score as covariates.
Peto OR calculation is based on Yusuf S et al. (Prog Cardiovasc Dis. 1985 Mar-Apr;27(5):335-71) and its p-value is derived using a normal approximation.
p-values for heterogeneity are estimated by using the same logistic model as the one used to estimate OR, RR and RD, with subgroup and treatment-by-subgroup interaction as additional covariates.
p-value for heterogeneity of Peto OR is estimated by using normal approximation.
PGM=DEVOPS/SAR231893/EFC14153/CSR_RWE/REPORT/PGM/eff_pro_evt_ger_subg_i_t.sas OUT=REPORT/OUTPUT/eff_pro_scpmw52_ger_exa_t2_t_x.rtf (29JUN2021 - 17:55)

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

Project Code / Study Number / Analysis: SAR231893 / EFC14153 / CSR_RWE

2 PRO endpoints

2.6 Responder analysis for change from baseline in PM Asthma symptom score (improvement >= 0.6) at week 52 - ITT type 2 inflammatory asthma phenotype population

2.6.13 By number of severe asthma exacerbation prior to the study (<=1, 2, >2)

	Number of severe asthma exacerbation prior to the study					
	<=1		2		>2	
Type 2 inflammatory asthma phenotype population	**Placebo (N=47)**	**Dupilumab (N=85)**	**Placebo (N=32)**	**Dupilumab (N=75)**	**Placebo (N=35)**	**Dupilumab (N=76)**
overall						0.027
Risk Difference (95% CI) vs placebo	-	-2.88 (-25.56 to 19.80)	-	-4.44 (-29.08 to 20.19)	-	23.72 (-2.10 to 49.53)
p-value for Risk Difference	-	0.802	-	0.721	-	0.071
p-value for heterogeneity of Risk Difference:						
<=1, 2						0.610
<=1, >2						0.155
2, >2						0.077
overall						0.165

[a] Patients who met the corresponding criterion are considered as responders. Patients who did not meet the criterion or had missing value are considered as non-responders.
OR, RR and RD are derived from a logistic regression model with treatment, age, weight group, region, baseline eosinophil level, baseline FeNO level, baseline ICS dose level, and baseline PM Asthma symptom score as covariates.
Peto OR calculation is based on Yusuf S et al. (Prog Cardiovasc Dis. 1985 Mar-Apr;27(5):335-71) and its p-value is derived using a normal approximation.
p-values for heterogeneity are estimated by using the same logistic model as the one used to estimate OR, RR and RD, with subgroup and treatment-by-subgroup interaction as additional covariates.
p-value for heterogeneity of Peto OR is estimated by using normal approximation.
PGM=DEVOPS/SAR231893/EFC14153/CSR_RWE/REPORT/PGM/eff_pro_evt_ger_subg_i_t.sas OUT=REPORT/OUTPUT/eff_pro_scpmw52_ger_exa_t2_t_x.rtf (29JUN2021 - 17:55)

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

Project Code / Study Number / Analysis: SAR231893 / EFC14153 / CSR_RWE

2 PRO endpoints

2.7 Responder analysis for change from baseline in EQ-VAS (improvement >= 15) at week 52 - ITT type 2 inflammatory asthma phenotype population

Type 2 inflammatory asthma phenotype population	**Placebo (N=87)**	**Dupilumab (N=181)**
Responder status at Week 52 based on change from baseline in EQ-VAS >=15 [n(%)] [a]		
Responder	30 (34.5%)	85 (47.0%)
Non-responder	57 (65.5%)	96 (53.0%)
Odds Ratio (95% CI)	-	2.23 (1.09 to 4.57)
p-value for Odds Ratio		0.029
Risk Ratio (95% CI)	-	1.38 (0.96 to 1.98)
Reversed Risk ratio (95% CI)	-	0.73 (0.50 to 1.05)
p-value for Risk Ratio		0.085
Risk Difference (95% CI)	-	10.92 (-2.76 to 24.59)
p-value for Risk Difference		0.117

[a] Patients who met the corresponding criterion are considered as responders. Patients who did not meet the criterion or had missing value are considered as non-responders.
OR, RR and RD are derived from a logistic regression model with treatment, age, weight group, region, baseline eosinophil level, baseline FeNO level, baseline ICS dose level, and baseline EQ-VAS as covariates.
Peto OR calculation is based on Yusuf S et al. (Prog Cardiovasc Dis. 1985 Mar-Apr;27(5):335-71) and its p-value is derived using a normal approximation.
Only patients of age >=8 years old at randomization are included in the analysis.
PGM=DEVOPS/SAR231893/EFC14153/CSR_RWE/REPORT/PGM/eff_pro_evt_ger_i_t.sas OUT=REPORT/OUTPUT/eff_pro_eqvasw52_ger_t2_t_x.rtf (30JUN2021 - 8:14)

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

Project Code / Study Number / Analysis: SAR231893 / EFC14153 / CSR_RWE

2 PRO endpoints

2.7 Responder analysis for change from baseline in EQ-VAS (improvement >= 15) at week 52 - ITT type 2 inflammatory asthma phenotype population

2.7.1 By gender (Male, Female)

	Gender			
	Male		Female	
Type 2 inflammatory asthma phenotype population	**Placebo (N=60)**	**Dupilumab (N=119)**	**Placebo (N=27)**	**Dupilumab (N=62)**
Responder status at Week 52 based on change from baseline in EQ-VAS >=15 [n(%)] [a]				
Responder	22 (36.7%)	57 (47.9%)	8 (29.6%)	28 (45.2%)
Non-responder	38 (63.3%)	62 (52.1%)	19 (70.4%)	34 (54.8%)
Odds Ratio (95% CI) vs placebo	-	2.58 (1.02 to 6.53)	-	1.94 (0.53 to 7.06)
p-value for Odds Ratio	-	0.046	-	0.313
p-value for heterogeneity of Odds Ratio				0.869
Risk Ratio (95% CI) vs placebo	-	1.33 (0.83 to 2.12)	-	1.38 (0.54 to 3.51)
Reversed Risk ratio (95% CI) vs placebo	-	0.75 (0.47 to 1.20)	-	0.73 (0.29 to 1.85)

[a] Patients who met the corresponding criterion are considered as responders. Patients who did not meet the criterion or had missing value are considered as non-responders.
OR, RR and RD are derived from a logistic regression model with treatment, age, weight group, region, baseline eosinophil level, baseline FeNO level, baseline ICS dose level, and baseline EQ-VAS as covariates.
Peto OR calculation is based on Yusuf S et al. (Prog Cardiovasc Dis. 1985 Mar-Apr;27(5):335-71) and its p-value is derived using a normal approximation.
p-values for heterogeneity are estimated by using the same logistic model as the one used to estimate OR, RR and RD, with subgroup and treatment-by-subgroup interaction as additional covariates.
p-value for heterogeneity of Peto OR is estimated by using normal approximation.
Only patients of age >=8 years old at randomization are included in the analysis.
PGM=DEVOPS/SAR231893/EFC14153/CSR_RWE/REPORT/PGM/eff_pro_evt_ger_subg_i_t.sas OUT=REPORT/OUTPUT/eff_pro_eqvasw52_ger_sex_t2_t_x.rtf (29JUN2021 - 17:55)

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

Project Code / Study Number / Analysis: SAR231893 / EFC14153 / CSR_RWE

2 PRO endpoints

2.7 Responder analysis for change from baseline in EQ-VAS (improvement >= 15) at week 52 - ITT type 2 inflammatory asthma phenotype population

2.7.1 By gender (Male, Female)

	Gender			
	Male		Female	
Type 2 inflammatory asthma phenotype population	**Placebo (N=60)**	**Dupilumab (N=119)**	**Placebo (N=27)**	**Dupilumab (N=62)**
p-value for Risk Ratio	-	0.234	-	0.500
p-value for heterogeneity of Risk Ratio				0.996
Risk Difference (95% CI) vs placebo	-	12.53 (-6.73 to 31.79)	-	11.31 (-17.07 to 39.68)
p-value for Risk Difference	-	0.201	-	0.430
p-value for heterogeneity of Risk Difference				0.908

[a] Patients who met the corresponding criterion are considered as responders. Patients who did not meet the criterion or had missing value are considered as non-responders.
OR, RR and RD are derived from a logistic regression model with treatment, age, weight group, region, baseline eosinophil level, baseline FeNO level, baseline ICS dose level, and baseline EQ-VAS as covariates.
Peto OR calculation is based on Yusuf S et al. (Prog Cardiovasc Dis. 1985 Mar-Apr;27(5):335-71) and its p-value is derived using a normal approximation.
p-values for heterogeneity are estimated by using the same logistic model as the one used to estimate OR, RR and RD, with subgroup and treatment-by-subgroup interaction as additional covariates.
p-value for heterogeneity of Peto OR is estimated by using normal approximation.
Only patients of age >=8 years old at randomization are included in the analysis.
PGM=DEVOPS/SAR231893/EFC14153/CSR_RWE/REPORT/PGM/eff_pro_evt_ger_subg_i_t.sas OUT=REPORT/OUTPUT/eff_pro_eqvasw52_ger_sex_t2_t_x.rtf (29JUN2021 - 17:55)

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

Project Code / Study Number / Analysis: SAR231893 / EFC14153 / CSR_RWE

2 PRO endpoints

2.7 Responder analysis for change from baseline in EQ-VAS (improvement >= 15) at week 52 - ITT type 2 inflammatory asthma phenotype population

2.7.2 By region (Latin America, East Europe, Western Countries)

	Region					
	Latin America		East Europe		Western countries	
Type 2 inflammatory asthma phenotype population	**Placebo (N=41)**	**Dupilumab (N=82)**	**Placebo (N=31)**	**Dupilumab (N=56)**	**Placebo (N=15)**	**Dupilumab (N=43)**
Responder status at Week 52 based on change from baseline in EQ-VAS >=15 [n(%)] [a]						
Responder	12 (29.3%)	50 (61.0%)	14 (45.2%)	22 (39.3%)	4 (26.7%)	13 (30.2%)
Non-responder	29 (70.7%)	32 (39.0%)	17 (54.8%)	34 (60.7%)	11 (73.3%)	30 (69.8%)
Odds Ratio (95% CI) vs placebo	-	4.62 (1.55 to 13.78)	-	1.36 (0.37 to 4.96)	-	0.73 (0.09 to 5.69)
p-value for Odds Ratio	-	0.007	-	0.634	-	0.761
p-value for heterogeneity of Odds Ratio:						
Latin America, East Europe						0.147
Latin America, Western countries						0.209

[a] Patients who met the corresponding criterion are considered as responders. Patients who did not meet the criterion or had missing value are considered as non-responders.
OR, RR and RD are derived from a logistic regression model with treatment, age, weight group, baseline eosinophil level, baseline FeNO level, baseline ICS dose level, and baseline EQ-VAS as covariates.
Peto OR calculation is based on Yusuf S et al. (Prog Cardiovasc Dis. 1985 Mar-Apr;27(5):335-71) and its p-value is derived using a normal approximation.
p-values for heterogeneity are estimated by using the same logistic model as the one used to estimate OR, RR and RD, with subgroup and treatment-by-subgroup interaction as additional covariates.
p-value for heterogeneity of Peto OR is estimated by using normal approximation.
Only patients of age >=8 years old at randomization are included in the analysis.
PGM=DEVOPS/SAR231893/EFC14153/CSR_RWE/REPORT/PGM/eff_pro_evt_ger_subg_i_t.sas OUT=REPORT/OUTPUT/eff_pro_eqvasw52_ger_cty_t2_t_x.rtf (29JUN2021 - 17:55)

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

Project Code / Study Number / Analysis: SAR231893 / EFC14153 / CSR_RWE

2 PRO endpoints

2.7 Responder analysis for change from baseline in EQ-VAS (improvement >= 15) at week 52 - ITT type 2 inflammatory asthma phenotype population

2.7.2 By region (Latin America, East Europe, Western Countries)

	Region					
	Latin America		East Europe		Western countries	
Type 2 inflammatory asthma phenotype population	**Placebo (N=41)**	**Dupilumab (N=82)**	**Placebo (N=31)**	**Dupilumab (N=56)**	**Placebo (N=15)**	**Dupilumab (N=43)**
East Europe, Western countries						0.849
overall						0.243
Risk Ratio (95% CI) vs placebo	-	1.94 (1.11 to 3.39)	-	1.18 (0.55 to 2.55)	-	0.64 (0.18 to 2.21)
Reversed Risk ratio (95% CI) vs placebo	-	0.52 (0.30 to 0.90)	-	0.84 (0.39 to 1.82)		
p-value for Risk Ratio	-	0.021	-	0.664	-	0.470
p-value for heterogeneity of Risk Ratio:						
Latin America, East Europe						0.119
Latin America, Western countries						0.123
East Europe, Western countries						0.679
overall						0.176

[a] Patients who met the corresponding criterion are considered as responders. Patients who did not meet the criterion or had missing value are considered as non-responders.
OR, RR and RD are derived from a logistic regression model with treatment, age, weight group, baseline eosinophil level, baseline FeNO level, baseline ICS dose level, and baseline EQ-VAS as covariates.
Peto OR calculation is based on Yusuf S et al. (Prog Cardiovasc Dis. 1985 Mar-Apr;27(5):335-71) and its p-value is derived using a normal approximation.
p-values for heterogeneity are estimated by using the same logistic model as the one used to estimate OR, RR and RD, with subgroup and treatment-by-subgroup interaction as additional covariates.
p-value for heterogeneity of Peto OR is estimated by using normal approximation.
Only patients of age >=8 years old at randomization are included in the analysis.
PGM=DEVOPS/SAR231893/EFC14153/CSR_RWE/REPORT/PGM/eff_pro_evt_ger_subg_i_t.sas OUT=REPORT/OUTPUT/eff_pro_eqvasw52_ger_cty_t2_t_x.rtf (29JUN2021 - 17:55)

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

Project Code / Study Number / Analysis: SAR231893 / EFC14153 / CSR_RWE

2 PRO endpoints

2.7 Responder analysis for change from baseline in EQ-VAS (improvement >= 15) at week 52 - ITT type 2 inflammatory asthma phenotype population

2.7.2 By region (Latin America, East Europe, Western Countries)

	Region					
	Latin America		East Europe		Western countries	
Type 2 inflammatory asthma phenotype population	**Placebo (N=41)**	**Dupilumab (N=82)**	**Placebo (N=31)**	**Dupilumab (N=56)**	**Placebo (N=15)**	**Dupilumab (N=43)**
Risk Difference (95% CI) vs placebo	-	25.98 (4.24 to 47.71)	-	4.22 (-25.22 to 33.65)	-	-3.12 (-47.12 to 40.87)
p-value for Risk Difference	-	0.020	-	0.776	-	0.887
p-value for heterogeneity of Risk Difference:						
Latin America, East Europe						0.257
Latin America, Western countries						0.281
East Europe, Western countries						0.776
overall						0.404

[a] Patients who met the corresponding criterion are considered as responders. Patients who did not meet the criterion or had missing value are considered as non-responders.
OR, RR and RD are derived from a logistic regression model with treatment, age, weight group, baseline eosinophil level, baseline FeNO level, baseline ICS dose level, and baseline EQ-VAS as covariates.
Peto OR calculation is based on Yusuf S et al. (Prog Cardiovasc Dis. 1985 Mar-Apr;27(5):335-71) and its p-value is derived using a normal approximation.
p-values for heterogeneity are estimated by using the same logistic model as the one used to estimate OR, RR and RD, with subgroup and treatment-by-subgroup interaction as additional covariates.
p-value for heterogeneity of Peto OR is estimated by using normal approximation.
Only patients of age >=8 years old at randomization are included in the analysis.
PGM=DEVOPS/SAR231893/EFC14153/CSR_RWE/REPORT/PGM/eff_pro_evt_ger_subg_i_t.sas OUT=REPORT/OUTPUT/eff_pro_eqvasw52_ger_cty_t2_t_x.rtf (29JUN2021 - 17:55)

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

Project Code / Study Number / Analysis: SAR231893 / EFC14153 / CSR_RWE

2 PRO endpoints

2.7 Responder analysis for change from baseline in EQ-VAS (improvement >= 15) at week 52 - ITT type 2 inflammatory asthma phenotype population

2.7.3 By race (Caucasian/white, Black/of African descent, Other)

	Race					
	Caucasian/White		Black/of African descent		Other	
Type 2 inflammatory asthma phenotype population	**Placebo (N=78)**	**Dupilumab (N=155)**	**Placebo (N=4)**	**Dupilumab (N=7)**	**Placebo (N=5)**	**Dupilumab (N=19)**
Responder status at Week 52 based on change from baseline in EQ-VAS >=15 [n(%)] [a]						
Responder	29 (37.2%)	75 (48.4%)	0	3 (42.9%)	1 (20.0%)	7 (36.8%)
Non-responder	49 (62.8%)	80 (51.6%)	4 (100%)	4 (57.1%)	4 (80.0%)	12 (63.2%)
Odds Ratio (95% CI) vs placebo	-	1.92 (0.91 to 4.05)	-	779233.9 (NE to NE)	-	75341506 (0.00 to NE)
p-value for Odds Ratio	-	0.086	-	NE	-	0.976
Peto Odds Ratio (95% CI) vs placebo	-	1.57 (0.91 to 2.71)	-	7.13 (0.51 to 98.92)	-	2.07 (0.27 to 15.99)
Reversed Peto Odds Ratio (95% CI)	-	0.64 (0.37 to 1.10)	-	0.14 (0.01 to 1.96)	-	0.48 (0.06 to 3.70)
p-value for Peto Odds Ratio		0.105		0.143		0.487

[a] Patients who met the corresponding criterion are considered as responders. Patients who did not meet the criterion or had missing value are considered as non-responders.
OR, RR and RD are derived from a logistic regression model with treatment, age, weight group, region, baseline eosinophil level, baseline FeNO level, baseline ICS dose level, and baseline EQ-VAS as covariates.
Peto OR calculation is based on Yusuf S et al. (Prog Cardiovasc Dis. 1985 Mar-Apr;27(5):335-71) and its p-value is derived using a normal approximation.
p-values for heterogeneity are estimated by using the same logistic model as the one used to estimate OR, RR and RD, with subgroup and treatment-by-subgroup interaction as additional covariates.
p-value for heterogeneity of Peto OR is estimated by using normal approximation.
Only patients of age >=8 years old at randomization are included in the analysis.
PGM=DEVOPS/SAR231893/EFC14153/CSR_RWE/REPORT/PGM/eff_pro_evt_ger_subg_i_t.sas OUT=REPORT/OUTPUT/eff_pro_eqvasw52_ger_race_t2_t_x.rtf (29JUN2021 - 17:55)

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

Project Code / Study Number / Analysis: SAR231893 / EFC14153 / CSR_RWE

2 PRO endpoints

2.7 Responder analysis for change from baseline in EQ-VAS (improvement >= 15) at week 52 - ITT type 2 inflammatory asthma phenotype population

2.7.3 By race (Caucasian/white, Black/of African descent, Other)

	Race					
	Caucasian/White		Black/of African descent		Other	
Type 2 inflammatory asthma phenotype population	**Placebo (N=78)**	**Dupilumab (N=155)**	**Placebo (N=4)**	**Dupilumab (N=7)**	**Placebo (N=5)**	**Dupilumab (N=19)**
p-value for heterogeneity of Peto Odds Ratio:						
Caucasian/White, Black/of African descent						0.270
Caucasian/White, Other						0.799
Black/of African descent, Other						0.466
overall						0.533
Risk Ratio (95% CI) vs placebo	-	1.31 (0.89 to 1.91)	-	3.36 (NE to NE)	-	1.01 (0.00 to 2865.44)
Reversed Risk ratio (95% CI) vs placebo	-	0.76 (0.52 to 1.12)	-	0.30 (NE to NE)	-	0.99 (0.00 to 2786.02)
p-value for Risk Ratio	-	0.166	-	NE	-	0.997

[a] Patients who met the corresponding criterion are considered as responders. Patients who did not meet the criterion or had missing value are considered as non-responders.
OR, RR and RD are derived from a logistic regression model with treatment, age, weight group, region, baseline eosinophil level, baseline FeNO level, baseline ICS dose level, and baseline EQ-VAS as covariates.
Peto OR calculation is based on Yusuf S et al. (Prog Cardiovasc Dis. 1985 Mar-Apr;27(5):335-71) and its p-value is derived using a normal approximation.
p-values for heterogeneity are estimated by using the same logistic model as the one used to estimate OR, RR and RD, with subgroup and treatment-by-subgroup interaction as additional covariates.
p-value for heterogeneity of Peto OR is estimated by using normal approximation.
Only patients of age >=8 years old at randomization are included in the analysis.
PGM=DEVOPS/SAR231893/EFC14153/CSR_RWE/REPORT/PGM/eff_pro_evt_ger_subg_i_t.sas OUT=REPORT/OUTPUT/eff_pro_eqvasw52_ger_race_t2_t_x.rtf (29JUN2021 - 17:55)

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

Project Code / Study Number / Analysis: SAR231893 / EFC14153 / CSR_RWE

2 PRO endpoints

2.7 Responder analysis for change from baseline in EQ-VAS (improvement >= 15) at week 52 - ITT type 2 inflammatory asthma phenotype population

2.7.3 By race (Caucasian/white, Black/of African descent, Other)

	Race					
	Caucasian/White		Black/of African descent		Other	
Type 2 inflammatory asthma phenotype population	**Placebo (N=78)**	**Dupilumab (N=155)**	**Placebo (N=4)**	**Dupilumab (N=7)**	**Placebo (N=5)**	**Dupilumab (N=19)**
p-value for heterogeneity of Risk Ratio:						
Caucasian/White, Black/of African descent						0.660
Caucasian/White, Other						0.818
Black/of African descent, Other						0.675
overall						0.884
Risk Difference (95% CI) vs placebo	-	9.95 (-4.77 to 24.67)	-	50.00 (NE to NE)	-	18.44 (-183.80 to 220.69)
p-value for Risk Difference	-	0.184	-	NE	-	0.848
p-value for heterogeneity of Risk Difference:						

[a] Patients who met the corresponding criterion are considered as responders. Patients who did not meet the criterion or had missing value are considered as non-responders.
OR, RR and RD are derived from a logistic regression model with treatment, age, weight group, region, baseline eosinophil level, baseline FeNO level, baseline ICS dose level, and baseline EQ-VAS as covariates.
Peto OR calculation is based on Yusuf S et al. (Prog Cardiovasc Dis. 1985 Mar-Apr;27(5):335-71) and its p-value is derived using a normal approximation.
p-values for heterogeneity are estimated by using the same logistic model as the one used to estimate OR, RR and RD, with subgroup and treatment-by-subgroup interaction as additional covariates.
p-value for heterogeneity of Peto OR is estimated by using normal approximation.
Only patients of age >=8 years old at randomization are included in the analysis.
PGM=DEVOPS/SAR231893/EFC14153/CSR_RWE/REPORT/PGM/eff_pro_evt_ger_subg_i_t.sas OUT=REPORT/OUTPUT/eff_pro_eqvasw52_ger_race_t2_t_x.rtf (29JUN2021 - 17:55)

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

Project Code / Study Number / Analysis: SAR231893 / EFC14153 / CSR_RWE

2 PRO endpoints

2.7 Responder analysis for change from baseline in EQ-VAS (improvement >= 15) at week 52 - ITT type 2 inflammatory asthma phenotype population

2.7.3 By race (Caucasian/white, Black/of African descent, Other)

	Race					
	Caucasian/White		Black/of African descent		Other	
Type 2 inflammatory asthma phenotype population	**Placebo (N=78)**	**Dupilumab (N=155)**	**Placebo (N=4)**	**Dupilumab (N=7)**	**Placebo (N=5)**	**Dupilumab (N=19)**
Caucasian/White, Black/of African descent						0.460
Caucasian/White, Other						0.640
Black/of African descent, Other						0.697
overall						0.691

[a] Patients who met the corresponding criterion are considered as responders. Patients who did not meet the criterion or had missing value are considered as non-responders.
OR, RR and RD are derived from a logistic regression model with treatment, age, weight group, region, baseline eosinophil level, baseline FeNO level, baseline ICS dose level, and baseline EQ-VAS as covariates.
Peto OR calculation is based on Yusuf S et al. (Prog Cardiovasc Dis. 1985 Mar-Apr;27(5):335-71) and its p-value is derived using a normal approximation.
p-values for heterogeneity are estimated by using the same logistic model as the one used to estimate OR, RR and RD, with subgroup and treatment-by-subgroup interaction as additional covariates.
p-value for heterogeneity of Peto OR is estimated by using normal approximation.
Only patients of age >=8 years old at randomization are included in the analysis.
PGM=DEVOPS/SAR231893/EFC14153/CSR_RWE/REPORT/PGM/eff_pro_evt_ger_subg_i_t.sas OUT=REPORT/OUTPUT/eff_pro_eqvasw52_ger_race_t2_t_x.rtf (29JUN2021 - 17:55)

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

Project Code / Study Number / Analysis: SAR231893 / EFC14153 / CSR_RWE

2 PRO endpoints

2.7 Responder analysis for change from baseline in EQ-VAS (improvement >= 15) at week 52 - ITT type 2 inflammatory asthma phenotype population

2.7.4 By baseline ICS dose level (Medium, High)

	Baseline ICS dose level			
	High		Medium	
Type 2 inflammatory asthma phenotype population	**Placebo (N=38)**	**Dupilumab (N=81)**	**Placebo (N=49)**	**Dupilumab (N=99)**
Responder status at Week 52 based on change from baseline in EQ-VAS >=15 [n(%)] [a]				
Responder	12 (31.6%)	37 (45.7%)	18 (36.7%)	48 (48.5%)
Non-responder	26 (68.4%)	44 (54.3%)	31 (63.3%)	51 (51.5%)
Odds Ratio (95% CI) vs placebo	-	1.98 (0.69 to 5.74)	-	2.55 (0.87 to 7.51)
p-value for Odds Ratio	-	0.204	-	0.088
p-value for heterogeneity of Odds Ratio				0.962
Risk Ratio (95% CI) vs placebo	-	1.07 (0.63 to 1.81)	-	1.52 (0.83 to 2.78)
Reversed Risk ratio (95% CI) vs placebo	-	0.94 (0.55 to 1.59)	-	0.66 (0.36 to 1.21)

[a] Patients who met the corresponding criterion are considered as responders. Patients who did not meet the criterion or had missing value are considered as non-responders.
OR, RR and RD are derived from a logistic regression model with treatment, age, weight group, region, baseline eosinophil level, baseline FeNO level and baseline EQ-VAS as covariates.
Peto OR calculation is based on Yusuf S et al. (Prog Cardiovasc Dis. 1985 Mar-Apr;27(5):335-71) and its p-value is derived using a normal approximation.
p-values for heterogeneity are estimated by using the same logistic model as the one used to estimate OR, RR and RD, with subgroup and treatment-by-subgroup interaction as additional covariates.
p-value for heterogeneity of Peto OR is estimated by using normal approximation.
Only patients of age >=8 years old at randomization are included in the analysis.
PGM=DEVOPS/SAR231893/EFC14153/CSR_RWE/REPORT/PGM/eff_pro_evt_ger_subg_i_t.sas OUT=REPORT/OUTPUT/eff_pro_eqvasw52_ger_ics_t2_t_x.rtf (29JUN2021 - 17:55)

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

Project Code / Study Number / Analysis: SAR231893 / EFC14153 / CSR_RWE

2 PRO endpoints

2.7 Responder analysis for change from baseline in EQ-VAS (improvement >= 15) at week 52 - ITT type 2 inflammatory asthma phenotype population

2.7.4 By baseline ICS dose level (Medium, High)

	Baseline ICS dose level			
	High		Medium	
Type 2 inflammatory asthma phenotype population	**Placebo (N=38)**	**Dupilumab (N=81)**	**Placebo (N=49)**	**Dupilumab (N=99)**
p-value for Risk Ratio	-	0.810	-	0.174
p-value for heterogeneity of Risk Ratio				0.600
Risk Difference (95% CI) vs placebo	-	9.83 (-12.63 to 32.29)	-	10.41 (-10.62 to 31.43)
p-value for Risk Difference	-	0.388	-	0.329
p-value for heterogeneity of Risk Difference				0.783

[a] Patients who met the corresponding criterion are considered as responders. Patients who did not meet the criterion or had missing value are considered as non-responders.
OR, RR and RD are derived from a logistic regression model with treatment, age, weight group, region, baseline eosinophil level, baseline FeNO level and baseline EQ-VAS as covariates.
Peto OR calculation is based on Yusuf S et al. (Prog Cardiovasc Dis. 1985 Mar-Apr;27(5):335-71) and its p-value is derived using a normal approximation.
p-values for heterogeneity are estimated by using the same logistic model as the one used to estimate OR, RR and RD, with subgroup and treatment-by-subgroup interaction as additional covariates.
p-value for heterogeneity of Peto OR is estimated by using normal approximation.
Only patients of age >=8 years old at randomization are included in the analysis.
PGM=DEVOPS/SAR231893/EFC14153/CSR_RWE/REPORT/PGM/eff_pro_evt_ger_subg_i_t.sas OUT=REPORT/OUTPUT/eff_pro_eqvasw52_ger_ics_t2_t_x.rtf (29JUN2021 - 17:55)

Project Code / Study Number / Analysis: SAR231893 / EFC14153 / CSR_RWE

2 PRO endpoints

2.7 Responder analysis for change from baseline in EQ-VAS (improvement >= 15) at week 52 - ITT type 2 inflammatory asthma phenotype population

2.7.5 By baseline ICS dose level 2 (Medium, High)

	Baseline ICS dose level 2			
	High		Medium	
Type 2 inflammatory asthma phenotype population	**Placebo (N=72)**	**Dupilumab (N=156)**	**Placebo (N=15)**	**Dupilumab (N=25)**
Responder status at Week 52 based on change from baseline in EQ-VAS >=15 [n(%)] [a]				
Responder	26 (36.1%)	75 (48.1%)	4 (26.7%)	10 (40.0%)
Non-responder	46 (63.9%)	81 (51.9%)	11 (73.3%)	15 (60.0%)
Odds Ratio (95% CI) vs placebo	-	2.26 (1.05 to 4.88)	-	6.09 (0.17 to 218.50)
p-value for Odds Ratio	-	0.037	-	0.310
p-value for heterogeneity of Odds Ratio				0.934
Risk Ratio (95% CI) vs placebo	-	1.19 (0.84 to 1.68)	-	2.48 (0.32 to 19.46)
Reversed Risk ratio (95% CI) vs placebo	-	0.84 (0.60 to 1.19)	-	0.40 (0.05 to 3.16)

[a] Patients who met the corresponding criterion are considered as responders. Patients who did not meet the criterion or had missing value are considered as non-responders.
OR, RR and RD are derived from a logistic regression model with treatment, age, weight group, region, baseline eosinophil level, baseline FeNO level and baseline EQ-VAS as covariates.
Peto OR calculation is based on Yusuf S et al. (Prog Cardiovasc Dis. 1985 Mar-Apr;27(5):335-71) and its p-value is derived using a normal approximation.
p-values for heterogeneity are estimated by using the same logistic model as the one used to estimate OR, RR and RD, with subgroup and treatment-by-subgroup interaction as additional covariates.
p-value for heterogeneity of Peto OR is estimated by using normal approximation.
Only patients of age >=8 years old at randomization are included in the analysis.
PGM=DEVOPS/SAR231893/EFC14153/CSR_RWE/REPORT/PGM/eff_pro_evt_ger_subg_i_t.sas OUT=REPORT/OUTPUT/eff_pro_eqvasw52_ger_ics2_t2_t_x.rtf (01SEP2021 - 15:28)

Project Code / Study Number / Analysis: SAR231893 / EFC14153 / CSR_RWE

2 PRO endpoints

2.7 Responder analysis for change from baseline in EQ-VAS (improvement >= 15) at week 52 - ITT type 2 inflammatory asthma phenotype population

2.7.5 By baseline ICS dose level 2 (Medium, High)

	Baseline ICS dose level 2			
	High		Medium	
Type 2 inflammatory asthma phenotype population	**Placebo (N=72)**	**Dupilumab (N=156)**	**Placebo (N=15)**	**Dupilumab (N=25)**
p-value for Risk Ratio	-	0.322	-	0.374
p-value for heterogeneity of Risk Ratio				0.441
Risk Difference (95% CI) vs placebo	-	7.96 (-6.33 to 22.26)	-	35.55 (-31.62 to 102.72)
p-value for Risk Difference	-	0.274	-	0.288
p-value for heterogeneity of Risk Difference				0.644

[a] Patients who met the corresponding criterion are considered as responders. Patients who did not meet the criterion or had missing value are considered as non-responders.
OR, RR and RD are derived from a logistic regression model with treatment, age, weight group, region, baseline eosinophil level, baseline FeNO level and baseline EQ-VAS as covariates.
Peto OR calculation is based on Yusuf S et al. (Prog Cardiovasc Dis. 1985 Mar-Apr;27(5):335-71) and its p-value is derived using a normal approximation.
p-values for heterogeneity are estimated by using the same logistic model as the one used to estimate OR, RR and RD, with subgroup and treatment-by-subgroup interaction as additional covariates.
p-value for heterogeneity of Peto OR is estimated by using normal approximation.
Only patients of age >=8 years old at randomization are included in the analysis.
PGM=DEVOPS/SAR231893/EFC14153/CSR_RWE/REPORT/PGM/eff_pro_evt_ger_subg_i_t.sas OUT=REPORT/OUTPUT/eff_pro_eqvasw52_ger_ics2_t2_t_x.rtf (01SEP2021 - 15:28)

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

Project Code / Study Number / Analysis: SAR231893 / EFC14153 / CSR_RWE

2 PRO endpoints

2.7 Responder analysis for change from baseline in EQ-VAS (improvement >= 15) at week 52 - ITT type 2 inflammatory asthma phenotype population

2.7.6 By baseline predicted FEV1 (<80%, >=80%)

	Baseline Predicted FEV1			
	<80%		>=80%	
Type 2 inflammatory asthma phenotype population	**Placebo (N=48)**	**Dupilumab (N=91)**	**Placebo (N=39)**	**Dupilumab (N=90)**
Responder status at Week 52 based on change from baseline in EQ-VAS >=15 [n(%)] [a]				
Responder	17 (35.4%)	49 (53.8%)	13 (33.3%)	36 (40.0%)
Non-responder	31 (64.6%)	42 (46.2%)	26 (66.7%)	54 (60.0%)
Odds Ratio (95% CI) vs placebo	-	2.70 (0.96 to 7.57)	-	2.71 (0.83 to 8.86)
p-value for Odds Ratio	-	0.059	-	0.099
p-value for heterogeneity of Odds Ratio				0.859
Risk Ratio (95% CI) vs placebo	-	1.40 (0.86 to 2.29)	-	1.44 (0.71 to 2.91)
Reversed Risk ratio (95% CI) vs placebo	-	0.71 (0.44 to 1.17)	-	0.70 (0.34 to 1.41)

[a] Patients who met the corresponding criterion are considered as responders. Patients who did not meet the criterion or had missing value are considered as non-responders.
OR, RR and RD are derived from a logistic regression model with treatment, age, weight group, region, baseline eosinophil level, baseline FeNO level, baseline ICS dose level, and baseline EQ-VAS as covariates.
Peto OR calculation is based on Yusuf S et al. (Prog Cardiovasc Dis. 1985 Mar-Apr;27(5):335-71) and its p-value is derived using a normal approximation.
p-values for heterogeneity are estimated by using the same logistic model as the one used to estimate OR, RR and RD, with subgroup and treatment-by-subgroup interaction as additional covariates.
p-value for heterogeneity of Peto OR is estimated by using normal approximation.
Only patients of age >=8 years old at randomization are included in the analysis.
PGM=DEVOPS/SAR231893/EFC14153/CSR_RWE/REPORT/PGM/eff_pro_evt_ger_subg_i_t.sas OUT=REPORT/OUTPUT/eff_pro_eqvasw52_ger_pfev1_t2_t_x.rtf (29JUN2021 - 17:56)

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

Project Code / Study Number / Analysis: SAR231893 / EFC14153 / CSR_RWE

2 PRO endpoints

2.7 Responder analysis for change from baseline in EQ-VAS (improvement >= 15) at week 52 - ITT type 2 inflammatory asthma phenotype population

2.7.6 By baseline predicted FEV1 (<80%, >=80%)

	Baseline Predicted FEV1			
	<80%		>=80%	
Type 2 inflammatory asthma phenotype population	**Placebo (N=48)**	**Dupilumab (N=91)**	**Placebo (N=39)**	**Dupilumab (N=90)**
p-value for Risk Ratio	-	0.177	-	0.312
p-value for heterogeneity of Risk Ratio				0.720
Risk Difference (95% CI) vs placebo	-	12.84 (-7.91 to 33.59)	-	10.23 (-14.51 to 34.96)
p-value for Risk Difference	-	0.223	-	0.414
p-value for heterogeneity of Risk Difference				0.997

[a] Patients who met the corresponding criterion are considered as responders. Patients who did not meet the criterion or had missing value are considered as non-responders.
OR, RR and RD are derived from a logistic regression model with treatment, age, weight group, region, baseline eosinophil level, baseline FeNO level, baseline ICS dose level, and baseline EQ-VAS as covariates.
Peto OR calculation is based on Yusuf S et al. (Prog Cardiovasc Dis. 1985 Mar-Apr;27(5):335-71) and its p-value is derived using a normal approximation.
p-values for heterogeneity are estimated by using the same logistic model as the one used to estimate OR, RR and RD, with subgroup and treatment-by-subgroup interaction as additional covariates.
p-value for heterogeneity of Peto OR is estimated by using normal approximation.
Only patients of age >=8 years old at randomization are included in the analysis.
PGM=DEVOPS/SAR231893/EFC14153/CSR_RWE/REPORT/PGM/eff_pro_evt_ger_subg_i_t.sas OUT=REPORT/OUTPUT/eff_pro_eqvasw52_ger_pfev1_t2_t_x.rtf (29JUN2021 - 17:56)

Project Code / Study Number / Analysis: SAR231893 / EFC14153 / CSR_RWE

2 PRO endpoints

2.7 Responder analysis for change from baseline in EQ-VAS (improvement >= 15) at week 52 - ITT type 2 inflammatory asthma phenotype population

2.7.7 By baseline ACQ-7-IA (<=2, >2)

	Baseline ACQ-7-IA			
	<=2		>2	
Type 2 inflammatory asthma phenotype population	**Placebo (N=45)**	**Dupilumab (N=100)**	**Placebo (N=42)**	**Dupilumab (N=81)**
Responder status at Week 52 based on change from baseline in EQ-VAS >=15 [n(%)] [a]				
Responder	13 (28.9%)	39 (39.0%)	17 (40.5%)	46 (56.8%)
Non-responder	32 (71.1%)	61 (61.0%)	25 (59.5%)	35 (43.2%)
Odds Ratio (95% CI) vs placebo	-	2.35 (0.75 to 7.37)	-	2.60 (0.92 to 7.33)
p-value for Odds Ratio	-	0.142	-	0.070
p-value for heterogeneity of Odds Ratio				0.560
Risk Ratio (95% CI) vs placebo	-	1.45 (0.73 to 2.88)	-	1.25 (0.77 to 2.02)
Reversed Risk ratio (95% CI) vs placebo	-	0.69 (0.35 to 1.37)	-	0.80 (0.49 to 1.30)

[a] Patients who met the corresponding criterion are considered as responders. Patients who did not meet the criterion or had missing value are considered as non-responders.
OR, RR and RD are derived from a logistic regression model with treatment, age, weight group, region, baseline eosinophil level, baseline FeNO level, baseline ICS dose level, and baseline EQ-VAS as covariates.
Peto OR calculation is based on Yusuf S et al. (Prog Cardiovasc Dis. 1985 Mar-Apr;27(5):335-71) and its p-value is derived using a normal approximation.
p-values for heterogeneity are estimated by using the same logistic model as the one used to estimate OR, RR and RD, with subgroup and treatment-by-subgroup interaction as additional covariates.
p-value for heterogeneity of Peto OR is estimated by using normal approximation.
Only patients of age >=8 years old at randomization are included in the analysis.
PGM=DEVOPS/SAR231893/EFC14153/CSR_RWE/REPORT/PGM/eff_pro_evt_ger_subg_i_t.sas OUT=REPORT/OUTPUT/eff_pro_eqvasw52_ger_acq7_t2_t_x.rtf (29JUN2021 - 17:56)

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

Project Code / Study Number / Analysis: SAR231893 / EFC14153 / CSR_RWE

2 PRO endpoints

2.7 Responder analysis for change from baseline in EQ-VAS (improvement >= 15) at week 52 - ITT type 2 inflammatory asthma phenotype population

2.7.7 By baseline ACQ-7-IA (<=2, >2)

	Baseline ACQ-7-IA			
	<=2		**>2**	
Type 2 inflammatory asthma phenotype population	**Placebo (N=45)**	**Dupilumab (N=100)**	**Placebo (N=42)**	**Dupilumab (N=81)**
p-value for Risk Ratio	-	0.288	-	0.368
p-value for heterogeneity of Risk Ratio				0.639
Risk Difference (95% CI) vs placebo	-	10.52 (-14.71 to 35.74)	-	14.63 (-7.74 to 37.00)
p-value for Risk Difference	-	0.411	-	0.198
p-value for heterogeneity of Risk Difference				0.885

[a] Patients who met the corresponding criterion are considered as responders. Patients who did not meet the criterion or had missing value are considered as non-responders. OR, RR and RD are derived from a logistic regression model with treatment, age, weight group, region, baseline eosinophil level, baseline FeNO level, baseline ICS dose level, and baseline EQ-VAS as covariates.
Peto OR calculation is based on Yusuf S et al. (Prog Cardiovasc Dis. 1985 Mar-Apr;27(5):335-71) and its p-value is derived using a normal approximation.
p-values for heterogeneity are estimated by using the same logistic model as the one used to estimate OR, RR and RD, with subgroup and treatment-by-subgroup interaction as additional covariates.
p-value for heterogeneity of Peto OR is estimated by using normal approximation.
Only patients of age >=8 years old at randomization are included in the analysis.
PGM=DEVOPS/SAR231893/EFC14153/CSR_RWE/REPORT/PGM/eff_pro_evt_ger_subg_i_t.sas OUT=REPORT/OUTPUT/eff_pro_eqvasw52_ger_acq7_t2_t_x.rtf (29JUN2021 - 17:56)

Project Code / Study Number / Analysis: SAR231893 / EFC14153 / CSR_RWE

2 PRO endpoints

2.7 Responder analysis for change from baseline in EQ-VAS (improvement >= 15) at week 52 - ITT type 2 inflammatory asthma phenotype population

2.7.8 By baseline weight (<=30 kg, >30 kg)

	Baseline weight (kg)			
	<=30		>30	
Type 2 inflammatory asthma phenotype population	**Placebo (N=16)**	**Dupilumab (N=38)**	**Placebo (N=71)**	**Dupilumab (N=143)**
Responder status at Week 52 based on change from baseline in EQ-VAS >=15 [n(%)] [a]				
Responder	5 (31.3%)	17 (44.7%)	25 (35.2%)	68 (47.6%)
Non-responder	11 (68.8%)	21 (55.3%)	46 (64.8%)	75 (52.4%)
Odds Ratio (95% CI) vs placebo	-	0.96 (0.11 to 8.37)	-	2.54 (1.14 to 5.66)
p-value for Odds Ratio	-	0.971	-	0.023
p-value for heterogeneity of Odds Ratio				0.493
Risk Ratio (95% CI) vs placebo	-	1.20 (0.39 to 3.70)	-	1.42 (0.95 to 2.14)
Reversed Risk ratio (95% CI) vs placebo	-	0.83 (0.27 to 2.57)	-	0.70 (0.47 to 1.06)

[a] Patients who met the corresponding criterion are considered as responders. Patients who did not meet the criterion or had missing value are considered as non-responders.
OR, RR and RD are derived from a logistic regression model with treatment, age, region, baseline eosinophil level, baseline FeNO level, baseline ICS dose level, and baseline EQ-VAS as covariates.
Peto OR calculation is based on Yusuf S et al. (Prog Cardiovasc Dis. 1985 Mar-Apr;27(5):335-71) and its p-value is derived using a normal approximation.
p-values for heterogeneity are estimated by using the same logistic model as the one used to estimate OR, RR and RD, with subgroup and treatment-by-subgroup interaction as additional covariates.
p-value for heterogeneity of Peto OR is estimated by using normal approximation.
Only patients of age >=8 years old at randomization are included in the analysis.
PGM=DEVOPS/SAR231893/EFC14153/CSR_RWE/REPORT/PGM/eff_pro_evt_ger_subg_i_t.sas OUT=REPORT/OUTPUT/eff_pro_eqvasw52_ger_wgt_t2_t_x.rtf (29JUN2021 - 17:56)

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

Project Code / Study Number / Analysis: SAR231893 / EFC14153 / CSR_RWE

2 PRO endpoints

2.7 Responder analysis for change from baseline in EQ-VAS (improvement >= 15) at week 52 - ITT type 2 inflammatory asthma phenotype population

2.7.8 By baseline weight (<=30 kg, >30 kg)

	Baseline weight (kg)			
	<=30		>30	
Type 2 inflammatory asthma phenotype population	**Placebo (N=16)**	**Dupilumab (N=38)**	**Placebo (N=71)**	**Dupilumab (N=143)**
p-value for Risk Ratio	-	0.746	-	0.089
p-value for heterogeneity of Risk Ratio				0.462
Risk Difference (95% CI) vs placebo	-	5.07 (-37.53 to 47.68)	-	14.45 (-2.10 to 31.00)
p-value for Risk Difference	-	0.811	-	0.087
p-value for heterogeneity of Risk Difference				0.359

[a] Patients who met the corresponding criterion are considered as responders. Patients who did not meet the criterion or had missing value are considered as non-responders. OR, RR and RD are derived from a logistic regression model with treatment, age, region, baseline eosinophil level, baseline FeNO level, baseline ICS dose level, and baseline EQ-VAS as covariates.
Peto OR calculation is based on Yusuf S et al. (Prog Cardiovasc Dis. 1985 Mar-Apr;27(5):335-71) and its p-value is derived using a normal approximation.
p-values for heterogeneity are estimated by using the same logistic model as the one used to estimate OR, RR and RD, with subgroup and treatment-by-subgroup interaction as additional covariates.
p-value for heterogeneity of Peto OR is estimated by using normal approximation.
Only patients of age >=8 years old at randomization are included in the analysis.
PGM=DEVOPS/SAR231893/EFC14153/CSR_RWE/REPORT/PGM/eff_pro_evt_ger_subg_i_t.sas OUT=REPORT/OUTPUT/eff_pro_eqvasw52_ger_wgt_t2_t_x.rtf (29JUN2021 - 17:56)

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

Project Code / Study Number / Analysis: SAR231893 / EFC14153 / CSR_RWE

2 PRO endpoints

2.7 Responder analysis for change from baseline in EQ-VAS (improvement >= 15) at week 52 - ITT type 2 inflammatory asthma phenotype population

2.7.9 By atopic medical condition (Yes, No)

	Atopic medical condition			
	Yes		No	
Type 2 inflammatory asthma phenotype population	**Placebo (N=79)**	**Dupilumab (N=175)**	**Placebo (N=8)**	**Dupilumab (N=6)**
Responder status at Week 52 based on change from baseline in EQ-VAS >=15 [n(%)] [a]				
Responder	27 (34.2%)	83 (47.4%)	3 (37.5%)	2 (33.3%)
Non-responder	52 (65.8%)	92 (52.6%)	5 (62.5%)	4 (66.7%)
Odds Ratio (95% CI) vs placebo	-	2.51 (1.18 to 5.31)	-	0.00 (0.00 to NE)
p-value for Odds Ratio	-	0.017	-	0.994
p-value for heterogeneity of Odds Ratio				0.157
Risk Ratio (95% CI) vs placebo	-	1.42 (0.97 to 2.07)	-	0.70 (0.00 to 2.825E12)
Reversed Risk ratio (95% CI) vs placebo	-	0.71 (0.48 to 1.03)		

[a] Patients who met the corresponding criterion are considered as responders. Patients who did not meet the criterion or had missing value are considered as non-responders.
OR, RR and RD are derived from a logistic regression model with treatment, age, weight group, region, baseline eosinophil level, baseline FeNO level, baseline ICS dose level, and baseline EQ-VAS as covariates.
Peto OR calculation is based on Yusuf S et al. (Prog Cardiovasc Dis. 1985 Mar-Apr;27(5):335-71) and its p-value is derived using a normal approximation.
p-values for heterogeneity are estimated by using the same logistic model as the one used to estimate OR, RR and RD, with subgroup and treatment-by-subgroup interaction as additional covariates.
p-value for heterogeneity of Peto OR is estimated by using normal approximation.
Only patients of age >=8 years old at randomization are included in the analysis.
PGM=DEVOPS/SAR231893/EFC14153/CSR_RWE/REPORT/PGM/eff_pro_evt_ger_subg_i_t.sas OUT=REPORT/OUTPUT/eff_pro_eqvasw52_ger_amc_t2_t_x.rtf (29JUN2021 - 17:56)

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

Project Code / Study Number / Analysis: SAR231893 / EFC14153 / CSR_RWE

2 PRO endpoints

2.7 Responder analysis for change from baseline in EQ-VAS (improvement >= 15) at week 52 - ITT type 2 inflammatory asthma phenotype population

2.7.9 By atopic medical condition (Yes, No)

	Atopic medical condition			
	Yes		**No**	
Type 2 inflammatory asthma phenotype population	**Placebo (N=79)**	**Dupilumab (N=175)**	**Placebo (N=8)**	**Dupilumab (N=6)**
p-value for Risk Ratio	-	0.070	-	0.974
p-value for heterogeneity of Risk Ratio				0.475
Risk Difference (95% CI) vs placebo	-	11.70 (-2.21 to 25.61)	-	-25.24 (-397.49 to 347.02)
p-value for Risk Difference	-	0.099	-	0.860
p-value for heterogeneity of Risk Difference				0.405

[a] Patients who met the corresponding criterion are considered as responders. Patients who did not meet the criterion or had missing value are considered as non-responders.
OR, RR and RD are derived from a logistic regression model with treatment, age, weight group, region, baseline eosinophil level, baseline FeNO level, baseline ICS dose level, and baseline EQ-VAS as covariates.
Peto OR calculation is based on Yusuf S et al. (Prog Cardiovasc Dis. 1985 Mar-Apr;27(5):335-71) and its p-value is derived using a normal approximation.
p-values for heterogeneity are estimated by using the same logistic model as the one used to estimate OR, RR and RD, with subgroup and treatment-by-subgroup interaction as additional covariates.
p-value for heterogeneity of Peto OR is estimated by using normal approximation.
Only patients of age >=8 years old at randomization are included in the analysis.
PGM=DEVOPS/SAR231893/EFC14153/CSR_RWE/REPORT/PGM/eff_pro_evt_ger_subg_i_t.sas OUT=REPORT/OUTPUT/eff_pro_eqvasw52_ger_amc_t2_t_x.rtf (29JUN2021 - 17:56)

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

Project Code / Study Number / Analysis: SAR231893 / EFC14153 / CSR_RWE

2 PRO endpoints

2.7 Responder analysis for change from baseline in EQ-VAS (improvement >= 15) at week 52 - ITT type 2 inflammatory asthma phenotype population

2.7.10 By baseline total IgE (<median, >= median)

	Baseline Total IgE (IU/mL)			
	<median		>=median	
Type 2 inflammatory asthma phenotype population	**Placebo (N=50)**	**Dupilumab (N=77)**	**Placebo (N=36)**	**Dupilumab (N=99)**
Responder status at Week 52 based on change from baseline in EQ-VAS >=15 [n(%)] [a]				
Responder	15 (30.0%)	36 (46.8%)	15 (41.7%)	47 (47.5%)
Non-responder	35 (70.0%)	41 (53.2%)	21 (58.3%)	52 (52.5%)
Odds Ratio (95% CI) vs placebo	-	2.82 (1.03 to 7.76)	-	1.72 (0.57 to 5.19)
p-value for Odds Ratio	-	0.044	-	0.330
p-value for heterogeneity of Odds Ratio				0.382
Risk Ratio (95% CI) vs placebo	-	1.51 (0.86 to 2.66)	-	1.32 (0.77 to 2.26)
Reversed Risk ratio (95% CI) vs placebo	-	0.66 (0.38 to 1.17)	-	0.76 (0.44 to 1.30)

[a] Patients who met the corresponding criterion are considered as responders. Patients who did not meet the criterion or had missing value are considered as non-responders.
OR, RR and RD are derived from a logistic regression model with treatment, age, weight group, region, baseline eosinophil level, baseline FeNO level, baseline ICS dose level, and baseline EQ-VAS as covariates.
Peto OR calculation is based on Yusuf S et al. (Prog Cardiovasc Dis. 1985 Mar-Apr;27(5):335-71) and its p-value is derived using a normal approximation.
p-values for heterogeneity are estimated by using the same logistic model as the one used to estimate OR, RR and RD, with subgroup and treatment-by-subgroup interaction as additional covariates.
p-value for heterogeneity of Peto OR is estimated by using normal approximation.
Only patients of age >=8 years old at randomization are included in the analysis.
PGM=DEVOPS/SAR231893/EFC14153/CSR_RWE/REPORT/PGM/eff_pro_evt_ger_subg_i_t.sas OUT=REPORT/OUTPUT/eff_pro_eqvasw52_ger_igem_t2_t_x.rtf (29JUN2021 - 17:56)

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

Project Code / Study Number / Analysis: SAR231893 / EFC14153 / CSR_RWE

2 PRO endpoints

2.7 Responder analysis for change from baseline in EQ-VAS (improvement >= 15) at week 52 - ITT type 2 inflammatory asthma phenotype population

2.7.10 By baseline total IgE (<median, >= median)

	Baseline Total IgE (IU/mL)			
	<median		>=median	
Type 2 inflammatory asthma phenotype population	**Placebo (N=50)**	**Dupilumab (N=77)**	**Placebo (N=36)**	**Dupilumab (N=99)**
p-value for Risk Ratio	-	0.153	-	0.316
p-value for heterogeneity of Risk Ratio				0.774
Risk Difference (95% CI) vs placebo	-	16.95 (-4.83 to 38.72)	-	5.87 (-16.21 to 27.96)
p-value for Risk Difference	-	0.126	-	0.599
p-value for heterogeneity of Risk Difference				0.338

[a] Patients who met the corresponding criterion are considered as responders. Patients who did not meet the criterion or had missing value are considered as non-responders. OR, RR and RD are derived from a logistic regression model with treatment, age, weight group, region, baseline eosinophil level, baseline FeNO level, baseline ICS dose level, and baseline EQ-VAS as covariates.
Peto OR calculation is based on Yusuf S et al. (Prog Cardiovasc Dis. 1985 Mar-Apr;27(5):335-71) and its p-value is derived using a normal approximation.
p-values for heterogeneity are estimated by using the same logistic model as the one used to estimate OR, RR and RD, with subgroup and treatment-by-subgroup interaction as additional covariates.
p-value for heterogeneity of Peto OR is estimated by using normal approximation.
Only patients of age >=8 years old at randomization are included in the analysis.
PGM=DEVOPS/SAR231893/EFC14153/CSR_RWE/REPORT/PGM/eff_pro_evt_ger_subg_i_t.sas OUT=REPORT/OUTPUT/eff_pro_eqvasw52_ger_igem_t2_t_x.rtf (29JUN2021 - 17:56)

Project Code / Study Number / Analysis: SAR231893 / EFC14153 / CSR_RWE

2 PRO endpoints

2.7 Responder analysis for change from baseline in EQ-VAS (improvement >= 15) at week 52 - ITT type 2 inflammatory asthma phenotype population

2.7.11 By baseline total IgE (<100 IU/ml, >= 100 IU/ml)

	Baseline Total IgE (IU/mL)			
	< 100		**>= 100**	
Type 2 inflammatory asthma phenotype population	**Placebo (N=16)**	**Dupilumab (N=21)**	**Placebo (N=70)**	**Dupilumab (N=155)**
Responder status at Week 52 based on change from baseline in EQ-VAS >=15 [n(%)] [a]				
Responder	6 (37.5%)	6 (28.6%)	24 (34.3%)	77 (49.7%)
Non-responder	10 (62.5%)	15 (71.4%)	46 (65.7%)	78 (50.3%)
Odds Ratio (95% CI) vs placebo	-	0.64 (0.10 to 4.16)	-	2.65 (1.17 to 6.01)
p-value for Odds Ratio	-	0.626	-	0.020
p-value for heterogeneity of Odds Ratio				0.158
Risk Ratio (95% CI) vs placebo	-	0.72 (0.17 to 2.99)	-	1.45 (0.97 to 2.19)
Reversed Risk ratio (95% CI) vs placebo			-	0.69 (0.46 to 1.04)

[a] Patients who met the corresponding criterion are considered as responders. Patients who did not meet the criterion or had missing value are considered as non-responders.
OR, RR and RD are derived from a logistic regression model with treatment, age, weight group, region, baseline eosinophil level, baseline FeNO level, baseline ICS dose level, and baseline EQ-VAS as covariates.
Peto OR calculation is based on Yusuf S et al. (Prog Cardiovasc Dis. 1985 Mar-Apr;27(5):335-71) and its p-value is derived using a normal approximation.
p-values for heterogeneity are estimated by using the same logistic model as the one used to estimate OR, RR and RD, with subgroup and treatment-by-subgroup interaction as additional covariates.
p-value for heterogeneity of Peto OR is estimated by using normal approximation.
Only patients of age >=8 years old at randomization are included in the analysis.
PGM=DEVOPS/SAR231893/EFC14153/CSR_RWE/REPORT/PGM/eff_pro_evt_ger_subg_i_t.sas OUT=REPORT/OUTPUT/eff_pro_eqvasw52_ger_ige_t2_t_x.rtf (29JUN2021 - 17:56)

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

Project Code / Study Number / Analysis: SAR231893 / EFC14153 / CSR_RWE

2 PRO endpoints

2.7 Responder analysis for change from baseline in EQ-VAS (improvement >= 15) at week 52 - ITT type 2 inflammatory asthma phenotype population

2.7.11 By baseline total IgE (<100 IU/ml, >= 100 IU/ml)

	Baseline Total IgE (IU/mL)			
	< 100		**>= 100**	
Type 2 inflammatory asthma phenotype population	**Placebo (N=16)**	**Dupilumab (N=21)**	**Placebo (N=70)**	**Dupilumab (N=155)**
p-value for Risk Ratio	-	0.638	-	0.073
p-value for heterogeneity of Risk Ratio				0.203
Risk Difference (95% CI) vs placebo	-	-6.45 (-47.48 to 34.58)	-	14.19 (-1.35 to 29.73)
p-value for Risk Difference	-	0.750	-	0.073
p-value for heterogeneity of Risk Difference				0.189

[a] Patients who met the corresponding criterion are considered as responders. Patients who did not meet the criterion or had missing value are considered as non-responders. OR, RR and RD are derived from a logistic regression model with treatment, age, weight group, region, baseline eosinophil level, baseline FeNO level, baseline ICS dose level, and baseline EQ-VAS as covariates.
Peto OR calculation is based on Yusuf S et al. (Prog Cardiovasc Dis. 1985 Mar-Apr;27(5):335-71) and its p-value is derived using a normal approximation.
p-values for heterogeneity are estimated by using the same logistic model as the one used to estimate OR, RR and RD, with subgroup and treatment-by-subgroup interaction as additional covariates.
p-value for heterogeneity of Peto OR is estimated by using normal approximation.
Only patients of age >=8 years old at randomization are included in the analysis.
PGM=DEVOPS/SAR231893/EFC14153/CSR_RWE/REPORT/PGM/eff_pro_evt_ger_subg_i_t.sas OUT=REPORT/OUTPUT/eff_pro_eqvasw52_ger_ige_t2_t_x.rtf (29JUN2021 - 17:56)

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

Project Code / Study Number / Analysis: SAR231893 / EFC14153 / CSR_RWE

2 PRO endpoints

2.7 Responder analysis for change from baseline in EQ-VAS (improvement >= 15) at week 52 - ITT type 2 inflammatory asthma phenotype population

2.7.12 By age at onset of asthma (0-2, 3-5, >=6 years)

	Age of onset of asthma (years)					
	0-2		3-5		>= 6	
Type 2 inflammatory asthma phenotype population	**Placebo (N=26)**	**Dupilumab (N=77)**	**Placebo (N=27)**	**Dupilumab (N=62)**	**Placebo (N=34)**	**Dupilumab (N=42)**
Responder status at Week 52 based on change from baseline in EQ-VAS >=15 [n(%)] [a]						
Responder	10 (38.5%)	40 (51.9%)	9 (33.3%)	26 (41.9%)	11 (32.4%)	19 (45.2%)
Non-responder	16 (61.5%)	37 (48.1%)	18 (66.7%)	36 (58.1%)	23 (67.6%)	23 (54.8%)
Odds Ratio (95% CI) vs placebo	-	1.86 (0.49 to 7.04)	-	2.20 (0.57 to 8.46)	-	1.52 (0.37 to 6.22)
p-value for Odds Ratio	-	0.357	-	0.248	-	0.554
p-value for heterogeneity of Odds Ratio:						
0-2, 3-5						0.540
0-2, >= 6						0.654

[a] Patients who met the corresponding criterion are considered as responders. Patients who did not meet the criterion or had missing value are considered as non-responders. OR, RR and RD are derived from a logistic regression model with treatment, age, weight group, region, baseline eosinophil level, baseline FeNO level, baseline ICS dose level, and baseline EQ-VAS as covariates.
Peto OR calculation is based on Yusuf S et al. (Prog Cardiovasc Dis. 1985 Mar-Apr;27(5):335-71) and its p-value is derived using a normal approximation.
p-values for heterogeneity are estimated by using the same logistic model as the one used to estimate OR, RR and RD, with subgroup and treatment-by-subgroup interaction as additional covariates.
p-value for heterogeneity of Peto OR is estimated by using normal approximation.
Only patients of age >=8 years old at randomization are included in the analysis.
PGM=DEVOPS/SAR231893/EFC14153/CSR_RWE/REPORT/PGM/eff_pro_evt_ger_subg_i_t.sas OUT=REPORT/OUTPUT/eff_pro_eqvasw52_ger_onsa_t2_t_x.rtf (01SEP2021 - 15:28)

Project Code / Study Number / Analysis: SAR231893 / EFC14153 / CSR_RWE

2 PRO endpoints

2.7 Responder analysis for change from baseline in EQ-VAS (improvement >= 15) at week 52 - ITT type 2 inflammatory asthma phenotype population

2.7.12 By age at onset of asthma (0-2, 3-5, >=6 years)

	Age of onset of asthma (years)					
	0-2		3-5		>= 6	
Type 2 inflammatory asthma phenotype population	**Placebo (N=26)**	**Dupilumab (N=77)**	**Placebo (N=27)**	**Dupilumab (N=62)**	**Placebo (N=34)**	**Dupilumab (N=42)**
3-5, >= 6						0.293
overall						0.573
Risk Ratio (95% CI) vs placebo	-	1.14 (0.56 to 2.31)	-	1.19 (0.58 to 2.42)	-	1.28 (0.53 to 3.14)
Reversed Risk ratio (95% CI) vs placebo	-	0.88 (0.43 to 1.79)	-	0.84 (0.41 to 1.71)	-	0.78 (0.32 to 1.90)
p-value for Risk Ratio	-	0.719	-	0.628	-	0.578
p-value for heterogeneity of Risk Ratio:						
0-2, 3-5						0.518
0-2, >= 6						0.760
3-5, >= 6						0.816
overall						0.809

[a] Patients who met the corresponding criterion are considered as responders. Patients who did not meet the criterion or had missing value are considered as non-responders.
OR, RR and RD are derived from a logistic regression model with treatment, age, weight group, region, baseline eosinophil level, baseline FeNO level, baseline ICS dose level, and baseline EQ-VAS as covariates.
Peto OR calculation is based on Yusuf S et al. (Prog Cardiovasc Dis. 1985 Mar-Apr;27(5):335-71) and its p-value is derived using a normal approximation.
p-values for heterogeneity are estimated by using the same logistic model as the one used to estimate OR, RR and RD, with subgroup and treatment-by-subgroup interaction as additional covariates.
p-value for heterogeneity of Peto OR is estimated by using normal approximation.
Only patients of age >=8 years old at randomization are included in the analysis.
PGM=DEVOPS/SAR231893/EFC14153/CSR_RWE/REPORT/PGM/eff_pro_evt_ger_subg_i_t.sas OUT=REPORT/OUTPUT/eff_pro_eqvasw52_ger_onsa_t2_t_x.rtf (01SEP2021 - 15:28)

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

Project Code / Study Number / Analysis: SAR231893 / EFC14153 / CSR_RWE

2 PRO endpoints

2.7 Responder analysis for change from baseline in EQ-VAS (improvement >= 15) at week 52 - ITT type 2 inflammatory asthma phenotype population

2.7.12 By age at onset of asthma (0-2, 3-5, >=6 years)

	Age of onset of asthma (years)					
	0-2		3-5		>= 6	
Type 2 inflammatory asthma phenotype population	**Placebo (N=26)**	**Dupilumab (N=77)**	**Placebo (N=27)**	**Dupilumab (N=62)**	**Placebo (N=34)**	**Dupilumab (N=42)**
Risk Difference (95% CI) vs placebo	-	5.67 (-20.82 to 32.15)	-	7.88 (-19.62 to 35.39)	-	7.83 (-22.17 to 37.83)
p-value for Risk Difference	-	0.672	-	0.570	-	0.604
p-value for heterogeneity of Risk Difference:						
0-2, 3-5						0.546
0-2, >= 6						0.910
3-5, >= 6						0.594
overall						0.803

[a] Patients who met the corresponding criterion are considered as responders. Patients who did not meet the criterion or had missing value are considered as non-responders. OR, RR and RD are derived from a logistic regression model with treatment, age, weight group, region, baseline eosinophil level, baseline FeNO level, baseline ICS dose level, and baseline EQ-VAS as covariates.
Peto OR calculation is based on Yusuf S et al. (Prog Cardiovasc Dis. 1985 Mar-Apr;27(5):335-71) and its p-value is derived using a normal approximation.
p-values for heterogeneity are estimated by using the same logistic model as the one used to estimate OR, RR and RD, with subgroup and treatment-by-subgroup interaction as additional covariates.
p-value for heterogeneity of Peto OR is estimated by using normal approximation.
Only patients of age >=8 years old at randomization are included in the analysis.
PGM=DEVOPS/SAR231893/EFC14153/CSR_RWE/REPORT/PGM/eff_pro_evt_ger_subg_i_t.sas OUT=REPORT/OUTPUT/eff_pro_eqvasw52_ger_onsa_t2_t_x.rtf (01SEP2021 - 15:28)

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

Project Code / Study Number / Analysis: SAR231893 / EFC14153 / CSR_RWE

2 PRO endpoints

2.7 Responder analysis for change from baseline in EQ-VAS (improvement >= 15) at week 52 - ITT type 2 inflammatory asthma phenotype population

2.7.13 By number of severe asthma exacerbation prior to the study (<=1, 2, >2)

	Number of severe asthma exacerbation prior to the study					
	<=1		**2**		**>2**	
Type 2 inflammatory asthma phenotype population	**Placebo (N=35)**	**Dupilumab (N=68)**	**Placebo (N=24)**	**Dupilumab (N=59)**	**Placebo (N=28)**	**Dupilumab (N=54)**
Responder status at Week 52 based on change from baseline in EQ-VAS >=15 [n(%)] [a]						
Responder	10 (28.6%)	30 (44.1%)	9 (37.5%)	26 (44.1%)	11 (39.3%)	29 (53.7%)
Non-responder	25 (71.4%)	38 (55.9%)	15 (62.5%)	33 (55.9%)	17 (60.7%)	25 (46.3%)
Odds Ratio (95% CI) vs placebo	-	2.54 (0.67 to 9.58)	-	2.49 (0.51 to 12.07)	-	2.04 (0.51 to 8.06)
p-value for Odds Ratio	-	0.166	-	0.252	-	0.306
p-value for heterogeneity of Odds Ratio:						
<=1, 2						0.966
<=1, >2						0.941

[a] Patients who met the corresponding criterion are considered as responders. Patients who did not meet the criterion or had missing value are considered as non-responders. OR, RR and RD are derived from a logistic regression model with treatment, age, weight group, region, baseline eosinophil level, baseline FeNO level, baseline ICS dose level, and baseline EQ-VAS as covariates.
Peto OR calculation is based on Yusuf S et al. (Prog Cardiovasc Dis. 1985 Mar-Apr;27(5):335-71) and its p-value is derived using a normal approximation.
p-values for heterogeneity are estimated by using the same logistic model as the one used to estimate OR, RR and RD, with subgroup and treatment-by-subgroup interaction as additional covariates.
p-value for heterogeneity of Peto OR is estimated by using normal approximation.
Only patients of age >=8 years old at randomization are included in the analysis.
PGM=DEVOPS/SAR231893/EFC14153/CSR_RWE/REPORT/PGM/eff_pro_evt_ger_subg_i_t.sas OUT=REPORT/OUTPUT/eff_pro_eqvasw52_ger_exa_t2_t_x.rtf (29JUN2021 - 17:57)

Project Code / Study Number / Analysis: SAR231893 / EFC14153 / CSR_RWE

2 PRO endpoints

2.7 Responder analysis for change from baseline in EQ-VAS (improvement >= 15) at week 52 - ITT type 2 inflammatory asthma phenotype population

2.7.13 By number of severe asthma exacerbation prior to the study (<=1, 2, >2)

	Number of severe asthma exacerbation prior to the study					
	<=1		2		>2	
Type 2 inflammatory asthma phenotype population	**Placebo (N=35)**	**Dupilumab (N=68)**	**Placebo (N=24)**	**Dupilumab (N=59)**	**Placebo (N=28)**	**Dupilumab (N=54)**
2, >2						0.976
overall						0.997
Risk Ratio (95% CI) vs placebo	-	1.45 (0.70 to 3.02)	-	0.00 (NE to NE)	-	1.18 (0.65 to 2.13)
Reversed Risk ratio (95% CI) vs placebo	-	0.69 (0.33 to 1.43)			-	0.85 (0.47 to 1.54)
p-value for Risk Ratio	-	0.311	-	<0.001	-	0.586
p-value for heterogeneity of Risk Ratio:						
<=1, 2						0.977
<=1, >2						0.499
2, >2						0.562
overall						0.739

[a] Patients who met the corresponding criterion are considered as responders. Patients who did not meet the criterion or had missing value are considered as non-responders. OR, RR and RD are derived from a logistic regression model with treatment, age, weight group, region, baseline eosinophil level, baseline FeNO level, baseline ICS dose level, and baseline EQ-VAS as covariates.
Peto OR calculation is based on Yusuf S et al. (Prog Cardiovasc Dis. 1985 Mar-Apr;27(5):335-71) and its p-value is derived using a normal approximation.
p-values for heterogeneity are estimated by using the same logistic model as the one used to estimate OR, RR and RD, with subgroup and treatment-by-subgroup interaction as additional covariates.
p-value for heterogeneity of Peto OR is estimated by using normal approximation.
Only patients of age >=8 years old at randomization are included in the analysis.
PGM=DEVOPS/SAR231893/EFC14153/CSR_RWE/REPORT/PGM/eff_pro_evt_ger_subg_i_t.sas OUT=REPORT/OUTPUT/eff_pro_eqvasw52_ger_exa_t2_t_x.rtf (29JUN2021 - 17:57)

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

Project Code / Study Number / Analysis: SAR231893 / EFC14153 / CSR_RWE

2 PRO endpoints

2.7 Responder analysis for change from baseline in EQ-VAS (improvement >= 15) at week 52 - ITT type 2 inflammatory asthma phenotype population

2.7.13 By number of severe asthma exacerbation prior to the study (<=1, 2, >2)

	Number of severe asthma exacerbation prior to the study					
	<=1		**2**		**>2**	
Type 2 inflammatory asthma phenotype population	**Placebo (N=35)**	**Dupilumab (N=68)**	**Placebo (N=24)**	**Dupilumab (N=59)**	**Placebo (N=28)**	**Dupilumab (N=54)**
Risk Difference (95% CI) vs placebo	-	14.43 (-15.22 to 44.08)	-	7.56 (-24.97 to 40.10)	-	9.71 (-17.94 to 37.36)
p-value for Risk Difference	-	0.336	-	0.644	-	0.486
p-value for heterogeneity of Risk Difference:						
<=1, 2						0.985
<=1, >2						0.696
2, >2						0.723
overall						0.908

[a] Patients who met the corresponding criterion are considered as responders. Patients who did not meet the criterion or had missing value are considered as non-responders. OR, RR and RD are derived from a logistic regression model with treatment, age, weight group, region, baseline eosinophil level, baseline FeNO level, baseline ICS dose level, and baseline EQ-VAS as covariates.
Peto OR calculation is based on Yusuf S et al. (Prog Cardiovasc Dis. 1985 Mar-Apr;27(5):335-71) and its p-value is derived using a normal approximation.
p-values for heterogeneity are estimated by using the same logistic model as the one used to estimate OR, RR and RD, with subgroup and treatment-by-subgroup interaction as additional covariates.
p-value for heterogeneity of Peto OR is estimated by using normal approximation.
Only patients of age >=8 years old at randomization are included in the analysis.
PGM=DEVOPS/SAR231893/EFC14153/CSR_RWE/REPORT/PGM/eff_pro_evt_ger_subg_i_t.sas OUT=REPORT/OUTPUT/eff_pro_eqvasw52_ger_exa_t2_t_x.rtf (29JUN2021 - 17:57)

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

Project Code / Study Number / Analysis: SAR231893 / EFC14153 / CSR_RWE

3 Severe exacerbation events

3.1 Patients with at least one severe asthma exacerbation event during the 52-week treatment period - ITT type 2 inflammatory asthma phenotype population

Type 2 inflammatory asthma phenotype population	**Placebo (N=114)**	**Dupilumab (N=236)**
Patients with >=1 severe exacerbation events during the 52-week treatment period [n(%)] [a]		
Yes	46 (40.4%)	54 (22.9%)
No	68 (59.6%)	182 (77.1%)
Odds Ratio (95% CI)	-	0.36 (0.21 to 0.61)
p-value for Odds Ratio		<0.001
Risk Ratio (95% CI)	-	0.48 (0.34 to 0.67)
p-value for Risk Ratio		<0.001
Risk Difference (95% CI)	-	-18.05 (-28.81 to -7.28)
p-value for Risk Difference		0.001

All severe exacerbation events occurred during the 52-week treatment period are included, regardless of whether the patient is on-treatment or not
OR, RR and RD are derived from a logistic regression model with treatment, age, weight group, region, baseline eosinophil level, baseline FeNO level, baseline ICS dose level, and number of severe exacerbation events within 1 year prior to the study as covariates.
Peto OR calculation is based on Yusuf S et al. (Prog Cardiovasc Dis. 1985 Mar-Apr;27(5):335-71) and its p-value is derived using a normal approximation.
PGM=DEVOPS/SAR231893/EFC14153/CSR_RWE/REPORT/PGM/eff_pro_evt_ger_i_t.sas OUT=REPORT/OUTPUT/eff_pro_exaw52_ger_t2_t_x.rtf (30JUN2021 - 8:14)

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

Project Code / Study Number / Analysis: SAR231893 / EFC14153 / CSR_RWE

3 Severe exacerbation events

3.1 Patients with at least one severe asthma exacerbation event during the 52-week treatment period - ITT type 2 inflammatory asthma phenotype population

3.1.1 By gender (Male, Female)

	Gender			
	Male		Female	
Type 2 inflammatory asthma phenotype population	**Placebo (N=78)**	**Dupilumab (N=152)**	**Placebo (N=36)**	**Dupilumab (N=84)**
Patients with >=1 severe exacerbation events during the 52-week treatment period [n(%)]				
Yes	38 (48.7%)	37 (24.3%)	8 (22.2%)	17 (20.2%)
No	40 (51.3%)	115 (75.7%)	28 (77.8%)	67 (79.8%)
Odds Ratio (95% CI) vs placebo	-	0.26 (0.14 to 0.51)	-	0.76 (0.27 to 2.12)
p-value for Odds Ratio	-	<0.001	-	0.593
p-value for heterogeneity of Odds Ratio				0.079
Risk Ratio (95% CI) vs placebo	-	0.43 (0.29 to 0.65)	-	0.76 (0.35 to 1.66)
p-value for Risk Ratio	-	<0.001	-	0.491

All severe exacerbation events occurred during the 52-week treatment period are included, regardless of whether the patient is on-treatment or not
OR, RR and RD are derived from a logistic regression model with treatment, age, weight group, region, baseline eosinophil level, baseline FeNO level, baseline ICS dose level, and number of severe exacerbation events within 1 year prior to the study as covariates.
Peto OR calculation is based on Yusuf S et al. (Prog Cardiovasc Dis. 1985 Mar-Apr;27(5):335-71) and its p-value is derived using a normal approximation.
p-values for heterogeneity are estimated by using the same logistic model as the one used to estimate OR, RR and RD, with subgroup and treatment-by-subgroup interaction as additional covariates.
p-value for heterogeneity of Peto OR is estimated by using normal approximation.
PGM=DEVOPS/SAR231893/EFC14153/CSR_RWE/REPORT/PGM/eff_pro_evt_ger_subg_i_t.sas OUT=REPORT/OUTPUT/eff_pro_exaw52_ger_sex_t2_t_x.rtf (29JUN2021 - 17:57)

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

Project Code / Study Number / Analysis: SAR231893 / EFC14153 / CSR_RWE

3 Severe exacerbation events

3.1 Patients with at least one severe asthma exacerbation event during the 52-week treatment period - ITT type 2 inflammatory asthma phenotype population

3.1.1 By gender (Male, Female)

	Gender			
	Male		Female	
Type 2 inflammatory asthma phenotype population	**Placebo (N=78)**	**Dupilumab (N=152)**	**Placebo (N=36)**	**Dupilumab (N=84)**
p-value for heterogeneity of Risk Ratio				0.153
Risk Difference (95% CI) vs placebo	-	-25.67 (-39.06 to -12.28)	-	-0.60 (-19.73 to 18.52)
p-value for Risk Difference	-	<0.001	-	0.950
p-value for heterogeneity of Risk Difference				0.013

All severe exacerbation events occurred during the 52-week treatment period are included, regardless of whether the patient is on-treatment or not
OR, RR and RD are derived from a logistic regression model with treatment, age, weight group, region, baseline eosinophil level, baseline FeNO level, baseline ICS dose level, and number of severe exacerbation events within 1 year prior to the study as covariates.
Peto OR calculation is based on Yusuf S et al. (Prog Cardiovasc Dis. 1985 Mar-Apr;27(5):335-71) and its p-value is derived using a normal approximation.
p-values for heterogeneity are estimated by using the same logistic model as the one used to estimate OR, RR and RD, with subgroup and treatment-by-subgroup interaction as additional covariates.
p-value for heterogeneity of Peto OR is estimated by using normal approximation.
PGM=DEVOPS/SAR231893/EFC14153/CSR_RWE/REPORT/PGM/eff_pro_evt_ger_subg_i_t.sas OUT=REPORT/OUTPUT/eff_pro_exaw52_ger_sex_t2_t_x.rtf (29JUN2021 - 17:57)

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

Project Code / Study Number / Analysis: SAR231893 / EFC14153 / CSR_RWE

3 Severe exacerbation events

3.1 Patients with at least one severe asthma exacerbation event during the 52-week treatment period - ITT type 2 inflammatory asthma phenotype population

3.1.2 By region (Latin America, East Europe, Western Countries)

	Region					
	Latin America		East Europe		Western countries	
Type 2 inflammatory asthma phenotype population	**Placebo (N=51)**	**Dupilumab (N=106)**	**Placebo (N=43)**	**Dupilumab (N=78)**	**Placebo (N=20)**	**Dupilumab (N=52)**
Patients with >=1 severe exacerbation events during the 52-week treatment period [n(%)]						
Yes	21 (41.2%)	29 (27.4%)	9 (20.9%)	12 (15.4%)	16 (80.0%)	13 (25.0%)
No	30 (58.8%)	77 (72.6%)	34 (79.1%)	66 (84.6%)	4 (20.0%)	39 (75.0%)
Odds Ratio (95% CI) vs placebo	-	0.43 (0.19 to 0.95)	-	0.72 (0.27 to 1.92)	-	0.03 (0.01 to 0.18)
p-value for Odds Ratio	-	0.037	-	0.504	-	<0.001
p-value for heterogeneity of Odds Ratio:						
Latin America, East Europe						0.739

All severe exacerbation events occurred during the 52-week treatment period are included, regardless of whether the patient is on-treatment or not
OR, RR and RD are derived from a logistic regression model with treatment, age, weight group, baseline eosinophil level, baseline FeNO level, baseline ICS dose level, and number of severe exacerbation events within 1 year prior to the study as covariates.
Peto OR calculation is based on Yusuf S et al. (Prog Cardiovasc Dis. 1985 Mar-Apr;27(5):335-71) and its p-value is derived using a normal approximation.
p-values for heterogeneity are estimated by using the same logistic model as the one used to estimate OR, RR and RD, with subgroup and treatment-by-subgroup interaction as additional covariates.
p-value for heterogeneity of Peto OR is estimated by using normal approximation.
PGM=DEVOPS/SAR231893/EFC14153/CSR_RWE/REPORT/PGM/eff_pro_evt_ger_subg_i_t.sas OUT=REPORT/OUTPUT/eff_pro_exaw52_ger_cty_t2_t_x.rtf (29JUN2021 - 17:57)

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

Project Code / Study Number / Analysis: SAR231893 / EFC14153 / CSR_RWE

3 Severe exacerbation events

3.1 Patients with at least one severe asthma exacerbation event during the 52-week treatment period - ITT type 2 inflammatory asthma phenotype population

3.1.2 By region (Latin America, East Europe, Western Countries)

	Region					
	Latin America		East Europe		Western countries	
Type 2 inflammatory asthma phenotype population	**Placebo (N=51)**	**Dupilumab (N=106)**	**Placebo (N=43)**	**Dupilumab (N=78)**	**Placebo (N=20)**	**Dupilumab (N=52)**
Latin America, Western countries						0.004
East Europe, Western countries						0.004
overall						0.009
Risk Ratio (95% CI) vs placebo	-	0.60 (0.36 to 1.02)	-	0.79 (0.36 to 1.74)	-	0.29 (0.10 to 0.84)
p-value for Risk Ratio	-	0.061	-	0.557	-	0.024
p-value for heterogeneity of Risk Ratio:						
Latin America, East Europe						0.928
Latin America, Western countries						0.021

All severe exacerbation events occurred during the 52-week treatment period are included, regardless of whether the patient is on-treatment or not
OR, RR and RD are derived from a logistic regression model with treatment, age, weight group, baseline eosinophil level, baseline FeNO level, baseline ICS dose level, and number of severe exacerbation events within 1 year prior to the study as covariates.
Peto OR calculation is based on Yusuf S et al. (Prog Cardiovasc Dis. 1985 Mar-Apr;27(5):335-71) and its p-value is derived using a normal approximation.
p-values for heterogeneity are estimated by using the same logistic model as the one used to estimate OR, RR and RD, with subgroup and treatment-by-subgroup interaction as additional covariates.
p-value for heterogeneity of Peto OR is estimated by using normal approximation.
PGM=DEVOPS/SAR231893/EFC14153/CSR_RWE/REPORT/PGM/eff_pro_evt_ger_subg_i_t.sas OUT=REPORT/OUTPUT/eff_pro_exaw52_ger_cty_t2_t_x.rtf (29JUN2021 - 17:57)

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

Project Code / Study Number / Analysis: SAR231893 / EFC14153 / CSR_RWE

3 Severe exacerbation events

3.1 Patients with at least one severe asthma exacerbation event during the 52-week treatment period - ITT type 2 inflammatory asthma phenotype population

3.1.2 By region (Latin America, East Europe, Western Countries)

	Region					
	Latin America		East Europe		Western countries	
Type 2 inflammatory asthma phenotype population	**Placebo (N=51)**	**Dupilumab (N=106)**	**Placebo (N=43)**	**Dupilumab (N=78)**	**Placebo (N=20)**	**Dupilumab (N=52)**
East Europe, Western countries						0.066
overall						0.056
Risk Difference (95% CI) vs placebo	-	-19.09 (-35.24 to -2.94)	-	-6.36 (-21.08 to 8.36)	-	-66.95 (-100.07 to -33.83)
p-value for Risk Difference	-	0.021	-	0.394	-	<0.001
p-value for heterogeneity of Risk Difference:						
Latin America, East Europe						0.362
Latin America, Western countries						<0.001
East Europe, Western countries						<0.001

All severe exacerbation events occurred during the 52-week treatment period are included, regardless of whether the patient is on-treatment or not
OR, RR and RD are derived from a logistic regression model with treatment, age, weight group, baseline eosinophil level, baseline FeNO level, baseline ICS dose level, and number of severe exacerbation events within 1 year prior to the study as covariates.
Peto OR calculation is based on Yusuf S et al. (Prog Cardiovasc Dis. 1985 Mar-Apr;27(5):335-71) and its p-value is derived using a normal approximation.
p-values for heterogeneity are estimated by using the same logistic model as the one used to estimate OR, RR and RD, with subgroup and treatment-by-subgroup interaction as additional covariates.
p-value for heterogeneity of Peto OR is estimated by using normal approximation.
PGM=DEVOPS/SAR231893/EFC14153/CSR_RWE/REPORT/PGM/eff_pro_evt_ger_subg_i_t.sas OUT=REPORT/OUTPUT/eff_pro_exaw52_ger_cty_t2_t_x.rtf (29JUN2021 - 17:57)

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

Project Code / Study Number / Analysis: SAR231893 / EFC14153 / CSR_RWE

3 Severe exacerbation events

3.1 Patients with at least one severe asthma exacerbation event during the 52-week treatment period - ITT type 2 inflammatory asthma phenotype population

3.1.2 By region (Latin America, East Europe, Western Countries)

	Region					
	Latin America		East Europe		Western countries	
Type 2 inflammatory asthma phenotype population	**Placebo (N=51)**	**Dupilumab (N=106)**	**Placebo (N=43)**	**Dupilumab (N=78)**	**Placebo (N=20)**	**Dupilumab (N=52)**
overall						<0.001

All severe exacerbation events occurred during the 52-week treatment period are included, regardless of whether the patient is on-treatment or not
OR, RR and RD are derived from a logistic regression model with treatment, age, weight group, baseline eosinophil level, baseline FeNO level, baseline ICS dose level, and number of severe exacerbation events within 1 year prior to the study as covariates.
Peto OR calculation is based on Yusuf S et al. (Prog Cardiovasc Dis. 1985 Mar-Apr;27(5):335-71) and its p-value is derived using a normal approximation.
p-values for heterogeneity are estimated by using the same logistic model as the one used to estimate OR, RR and RD, with subgroup and treatment-by-subgroup interaction as additional covariates.
p-value for heterogeneity of Peto OR is estimated by using normal approximation.
PGM=DEVOPS/SAR231893/EFC14153/CSR_RWE/REPORT/PGM/eff_pro_evt_ger_subg_i_t.sas OUT=REPORT/OUTPUT/eff_pro_exaw52_ger_cty_t2_t_x.rtf (29JUN2021 - 17:57)

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

Project Code / Study Number / Analysis: SAR231893 / EFC14153 / CSR_RWE

3 Severe exacerbation events

3.1 Patients with at least one severe asthma exacerbation event during the 52-week treatment period - ITT type 2 inflammatory asthma phenotype population

3.1.3 By race (Caucasian/white, Black/of African descent, Other)

	Race					
	Caucasian/White		Black/of African descent		Other	
Type 2 inflammatory asthma phenotype population	**Placebo (N=102)**	**Dupilumab (N=208)**	**Placebo (N=5)**	**Dupilumab (N=9)**	**Placebo (N=7)**	**Dupilumab (N=19)**
Patients with >=1 severe exacerbation events during the 52-week treatment period [n(%)]						
Yes	35 (34.3%)	47 (22.6%)	4 (80.0%)	2 (22.2%)	7 (100%)	5 (26.3%)
No	67 (65.7%)	161 (77.4%)	1 (20.0%)	7 (77.8%)	0	14 (73.7%)
Odds Ratio (95% CI) vs placebo	-	0.49 (0.28 to 0.87)	-	0.00 (0.00 to NE)	-	0.00 (0.00 to NE)
p-value for Odds Ratio	-	0.014	-	0.983	-	0.939
Peto Odds Ratio (95% CI) vs placebo	-	0.55 (0.32 to 0.94)	-	0.11 (0.01 to 0.94)	-	0.06 (0.01 to 0.32)

All severe exacerbation events occurred during the 52-week treatment period are included, regardless of whether the patient is on-treatment or not
OR, RR and RD are derived from a logistic regression model with treatment, age, weight group, region, baseline eosinophil level, baseline FeNO level, baseline ICS dose level, and number of severe exacerbation events within 1 year prior to the study as covariates.
Peto OR calculation is based on Yusuf S et al. (Prog Cardiovasc Dis. 1985 Mar-Apr;27(5):335-71) and its p-value is derived using a normal approximation.
p-values for heterogeneity are estimated by using the same logistic model as the one used to estimate OR, RR and RD, with subgroup and treatment-by-subgroup interaction as additional covariates.
p-value for heterogeneity of Peto OR is estimated by using normal approximation.
PGM=DEVOPS/SAR231893/EFC14153/CSR_RWE/REPORT/PGM/eff_pro_evt_ger_subg_i_t.sas OUT=REPORT/OUTPUT/eff_pro_exaw52_ger_race_t2_t_x.rtf (29JUN2021 - 17:57)

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

Project Code / Study Number / Analysis: SAR231893 / EFC14153 / CSR_RWE

3 Severe exacerbation events

3.1 Patients with at least one severe asthma exacerbation event during the 52-week treatment period - ITT type 2 inflammatory asthma phenotype population

3.1.3 By race (Caucasian/white, Black/of African descent, Other)

	Race					
	Caucasian/White		Black/of African descent		Other	
Type 2 inflammatory asthma phenotype population	**Placebo (N=102)**	**Dupilumab (N=208)**	**Placebo (N=5)**	**Dupilumab (N=9)**	**Placebo (N=7)**	**Dupilumab (N=19)**
p-value for Peto Odds Ratio		0.028		0.044		0.001
p-value for heterogeneity of Peto Odds Ratio:						
Caucasian/White, Black/of African descent						0.156
Caucasian/White, Other						0.014
Black/of African descent, Other						0.635
overall						0.022
Risk Ratio (95% CI) vs placebo	-	0.57 (0.38 to 0.84)	-	0.67 (0.00 to 33733202)	-	0.43 (NE to NE)

All severe exacerbation events occurred during the 52-week treatment period are included, regardless of whether the patient is on-treatment or not
OR, RR and RD are derived from a logistic regression model with treatment, age, weight group, region, baseline eosinophil level, baseline FeNO level, baseline ICS dose level, and number of severe exacerbation events within 1 year prior to the study as covariates.
Peto OR calculation is based on Yusuf S et al. (Prog Cardiovasc Dis. 1985 Mar-Apr;27(5):335-71) and its p-value is derived using a normal approximation.
p-values for heterogeneity are estimated by using the same logistic model as the one used to estimate OR, RR and RD, with subgroup and treatment-by-subgroup interaction as additional covariates.
p-value for heterogeneity of Peto OR is estimated by using normal approximation.
PGM=DEVOPS/SAR231893/EFC14153/CSR_RWE/REPORT/PGM/eff_pro_evt_ger_subg_i_t.sas OUT=REPORT/OUTPUT/eff_pro_exaw52_ger_race_t2_t_x.rtf (29JUN2021 - 17:57)

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

Project Code / Study Number / Analysis: SAR231893 / EFC14153 / CSR_RWE

3 Severe exacerbation events

3.1 Patients with at least one severe asthma exacerbation event during the 52-week treatment period - ITT type 2 inflammatory asthma phenotype population

3.1.3 By race (Caucasian/white, Black/of African descent, Other)

	Race					
	Caucasian/White		Black/of African descent		Other	
Type 2 inflammatory asthma phenotype population	**Placebo (N=102)**	**Dupilumab (N=208)**	**Placebo (N=5)**	**Dupilumab (N=9)**	**Placebo (N=7)**	**Dupilumab (N=19)**
p-value for Risk Ratio	-	0.005	-	0.954	-	<0.001
p-value for heterogeneity of Risk Ratio:						
Caucasian/White, Black/of African descent						0.458
Caucasian/White, Other						0.153
Black/of African descent, Other						<0.001
overall						0.153
Risk Difference (95% CI) vs placebo	-	-11.56 (-22.81 to -0.30)	-	-13.21 (-681.76 to 655.35)	-	-88.46 (-391.95 to 215.02)

All severe exacerbation events occurred during the 52-week treatment period are included, regardless of whether the patient is on-treatment or not
OR, RR and RD are derived from a logistic regression model with treatment, age, weight group, region, baseline eosinophil level, baseline FeNO level, baseline ICS dose level, and number of severe exacerbation events within 1 year prior to the study as covariates.
Peto OR calculation is based on Yusuf S et al. (Prog Cardiovasc Dis. 1985 Mar-Apr;27(5):335-71) and its p-value is derived using a normal approximation.
p-values for heterogeneity are estimated by using the same logistic model as the one used to estimate OR, RR and RD, with subgroup and treatment-by-subgroup interaction as additional covariates.
p-value for heterogeneity of Peto OR is estimated by using normal approximation.
PGM=DEVOPS/SAR231893/EFC14153/CSR_RWE/REPORT/PGM/eff_pro_evt_ger_subg_i_t.sas OUT=REPORT/OUTPUT/eff_pro_exaw52_ger_race_t2_t_x.rtf (29JUN2021 - 17:57)

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

Project Code / Study Number / Analysis: SAR231893 / EFC14153 / CSR_RWE

3 Severe exacerbation events

3.1 Patients with at least one severe asthma exacerbation event during the 52-week treatment period - ITT type 2 inflammatory asthma phenotype population

3.1.3 By race (Caucasian/white, Black/of African descent, Other)

	Race					
	Caucasian/White		Black/of African descent		Other	
Type 2 inflammatory asthma phenotype population	**Placebo (N=102)**	**Dupilumab (N=208)**	**Placebo (N=5)**	**Dupilumab (N=9)**	**Placebo (N=7)**	**Dupilumab (N=19)**
p-value for Risk Difference	-	0.044	-	0.959	-	0.545
p-value for heterogeneity of Risk Difference:						
Caucasian/White, Black/of African descent						0.035
Caucasian/White, Other						<0.001
Black/of African descent, Other						<0.001
overall						<0.001

All severe exacerbation events occurred during the 52-week treatment period are included, regardless of whether the patient is on-treatment or not
OR, RR and RD are derived from a logistic regression model with treatment, age, weight group, region, baseline eosinophil level, baseline FeNO level, baseline ICS dose level, and number of severe exacerbation events within 1 year prior to the study as covariates.
Peto OR calculation is based on Yusuf S et al. (Prog Cardiovasc Dis. 1985 Mar-Apr;27(5):335-71) and its p-value is derived using a normal approximation.
p-values for heterogeneity are estimated by using the same logistic model as the one used to estimate OR, RR and RD, with subgroup and treatment-by-subgroup interaction as additional covariates.
p-value for heterogeneity of Peto OR is estimated by using normal approximation.
PGM=DEVOPS/SAR231893/EFC14153/CSR_RWE/REPORT/PGM/eff_pro_evt_ger_subg_i_t.sas OUT=REPORT/OUTPUT/eff_pro_exaw52_ger_race_t2_t_x.rtf (29JUN2021 - 17:57)

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

Project Code / Study Number / Analysis: SAR231893 / EFC14153 / CSR_RWE

3 Severe exacerbation events

3.1 population Patients with at least one severe asthma exacerbation event during the 52-week treatment period - ITT type 2 inflammatory asthma phenotype

3.1.4 By baseline ICS dose level (Medium, High)

	Baseline ICS dose level			
	High		Medium	
Type 2 inflammatory asthma phenotype population	**Placebo (N=50)**	**Dupilumab (N=102)**	**Placebo (N=64)**	**Dupilumab (N=131)**
Patients with >=1 severe exacerbation events during the 52-week treatment period [n(%)]				
Yes	24 (48.0%)	31 (30.4%)	22 (34.4%)	23 (17.6%)
No	26 (52.0%)	71 (69.6%)	42 (65.6%)	108 (82.4%)
Odds Ratio (95% CI) vs placebo	-	0.33 (0.15 to 0.75)	-	0.36 (0.18 to 0.76)
p-value for Odds Ratio	-	0.008	-	0.007
p-value for heterogeneity of Odds Ratio				0.880
Risk Ratio (95% CI) vs placebo	-	0.48 (0.30 to 0.76)	-	0.43 (0.25 to 0.75)
p-value for Risk Ratio	-	0.002	-	0.003

All severe exacerbation events occurred during the 52-week treatment period are included, regardless of whether the patient is on-treatment or not
OR, RR and RD are derived from a logistic regression model with treatment, age, weight group, region, baseline eosinophil level, baseline FeNO level and number of severe exacerbation events within 1 year prior to the study as covariates.
Peto OR calculation is based on Yusuf S et al. (Prog Cardiovasc Dis. 1985 Mar-Apr;27(5):335-71) and its p-value is derived using a normal approximation.
p-values for heterogeneity are estimated by using the same logistic model as the one used to estimate OR, RR and RD, with subgroup and treatment-by-subgroup interaction as additional covariates.
p-value for heterogeneity of Peto OR is estimated by using normal approximation.
PGM=DEVOPS/SAR231893/EFC14153/CSR_RWE/REPORT/PGM/eff_pro_evt_ger_subg_i_t.sas OUT=REPORT/OUTPUT/eff_pro_exaw52_ger_ics_t2_t_x.rtf (29JUN2021 - 17:58)

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

Project Code / Study Number / Analysis: SAR231893 / EFC14153 / CSR_RWE

3 Severe exacerbation events

3.1 Patients with at least one severe asthma exacerbation event during the 52-week treatment period - ITT type 2 inflammatory asthma phenotype population

3.1.4 By baseline ICS dose level (Medium, High)

	Baseline ICS dose level			
	High		Medium	
Type 2 inflammatory asthma phenotype population	**Placebo (N=50)**	**Dupilumab (N=102)**	**Placebo (N=64)**	**Dupilumab (N=131)**
p-value for heterogeneity of Risk Ratio				0.751
Risk Difference (95% CI) vs placebo	-	-22.50 (-39.48 to -5.52)	-	-16.77 (-30.65 to -2.89)
p-value for Risk Difference	-	0.010	-	0.018
p-value for heterogeneity of Risk Difference				0.509

All severe exacerbation events occurred during the 52-week treatment period are included, regardless of whether the patient is on-treatment or not
OR, RR and RD are derived from a logistic regression model with treatment, age, weight group, region, baseline eosinophil level, baseline FeNO level and number of severe exacerbation events within 1 year prior to the study as covariates.
Peto OR calculation is based on Yusuf S et al. (Prog Cardiovasc Dis. 1985 Mar-Apr;27(5):335-71) and its p-value is derived using a normal approximation.
p-values for heterogeneity are estimated by using the same logistic model as the one used to estimate OR, RR and RD, with subgroup and treatment-by-subgroup interaction as additional covariates.
p-value for heterogeneity of Peto OR is estimated by using normal approximation.
PGM=DEVOPS/SAR231893/EFC14153/CSR_RWE/REPORT/PGM/eff_pro_evt_ger_subg_i_t.sas OUT=REPORT/OUTPUT/eff_pro_exaw52_ger_ics_t2_t_x.rtf (29JUN2021 - 17:58)

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

Project Code / Study Number / Analysis: SAR231893 / EFC14153 / CSR_RWE

3 Severe exacerbation events

3.1 Patients with at least one severe asthma exacerbation event during the 52-week treatment period - ITT type 2 inflammatory asthma phenotype population

3.1.5 By baseline ICS dose level 2 (Medium, High)

	Baseline ICS dose level 2			
	High		Medium	
Type 2 inflammatory asthma phenotype population	**Placebo (N=95)**	**Dupilumab (N=200)**	**Placebo (N=19)**	**Dupilumab (N=36)**
Patients with >=1 severe exacerbation events during the 52-week treatment period [n(%)]				
Yes	40 (42.1%)	51 (25.5%)	6 (31.6%)	3 (8.3%)
No	55 (57.9%)	149 (74.5%)	13 (68.4%)	33 (91.7%)
Odds Ratio (95% CI) vs placebo	-	0.37 (0.21 to 0.65)	-	0.17 (0.02 to 1.27)
p-value for Odds Ratio	-	<0.001	-	0.082
p-value for heterogeneity of Odds Ratio				0.519
Risk Ratio (95% CI) vs placebo	-	0.49 (0.35 to 0.69)	-	0.21 (0.02 to 2.32)
p-value for Risk Ratio	-	<0.001	-	0.196

All severe exacerbation events occurred during the 52-week treatment period are included, regardless of whether the patient is on-treatment or not
OR, RR and RD are derived from a logistic regression model with treatment, age, weight group, region, baseline eosinophil level, baseline FeNO level and number of severe exacerbation events within 1 year prior to the study as covariates.
Peto OR calculation is based on Yusuf S et al. (Prog Cardiovasc Dis. 1985 Mar-Apr;27(5):335-71) and its p-value is derived using a normal approximation.
p-values for heterogeneity are estimated by using the same logistic model as the one used to estimate OR, RR and RD, with subgroup and treatment-by-subgroup interaction as additional covariates.
p-value for heterogeneity of Peto OR is estimated by using normal approximation.
PGM=DEVOPS/SAR231893/EFC14153/CSR_RWE/REPORT/PGM/eff_pro_evt_ger_subg_i_t.sas OUT=REPORT/OUTPUT/eff_pro_exaw52_ger_ics2_t2_t_x.rtf (01SEP2021 - 15:28)

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

Project Code / Study Number / Analysis: SAR231893 / EFC14153 / CSR_RWE

3 Severe exacerbation events

3.1 population Patients with at least one severe asthma exacerbation event during the 52-week treatment period - ITT type 2 inflammatory asthma phenotype

3.1.5 By baseline ICS dose level 2 (Medium, High)

	Baseline ICS dose level 2			
	High		Medium	
Type 2 inflammatory asthma phenotype population	**Placebo (N=95)**	**Dupilumab (N=200)**	**Placebo (N=19)**	**Dupilumab (N=36)**
p-value for heterogeneity of Risk Ratio				0.330
Risk Difference (95% CI) vs placebo	-	-18.65 (-30.36 to -6.93)	-	-23.61 (-67.20 to 19.99)
p-value for Risk Difference	-	0.002	-	0.281
p-value for heterogeneity of Risk Difference				0.604

All severe exacerbation events occurred during the 52-week treatment period are included, regardless of whether the patient is on-treatment or not
OR, RR and RD are derived from a logistic regression model with treatment, age, weight group, region, baseline eosinophil level, baseline FeNO level and number of severe exacerbation events within 1 year prior to the study as covariates.
Peto OR calculation is based on Yusuf S et al. (Prog Cardiovasc Dis. 1985 Mar-Apr;27(5):335-71) and its p-value is derived using a normal approximation.
p-values for heterogeneity are estimated by using the same logistic model as the one used to estimate OR, RR and RD, with subgroup and treatment-by-subgroup interaction as additional covariates.
p-value for heterogeneity of Peto OR is estimated by using normal approximation.
PGM=DEVOPS/SAR231893/EFC14153/CSR_RWE/REPORT/PGM/eff_pro_evt_ger_subg_i_t.sas OUT=REPORT/OUTPUT/eff_pro_exaw52_ger_ics2_t2_t_x.rtf (01SEP2021 - 15:28)

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

Project Code / Study Number / Analysis: SAR231893 / EFC14153 / CSR_RWE

3 Severe exacerbation events

3.1 population Patients with at least one severe asthma exacerbation event during the 52-week treatment period - ITT type 2 inflammatory asthma phenotype

3.1.6 By baseline predicted FEV1 (<80%, >=80%)

	Baseline Predicted FEV1			
	<80%		>=80%	
Type 2 inflammatory asthma phenotype population	**Placebo (N=59)**	**Dupilumab (N=116)**	**Placebo (N=55)**	**Dupilumab (N=120)**
Patients with >=1 severe exacerbation events during the 52-week treatment period [n(%)]				
Yes	32 (54.2%)	27 (23.3%)	14 (25.5%)	27 (22.5%)
No	27 (45.8%)	89 (76.7%)	41 (74.5%)	93 (77.5%)
Odds Ratio (95% CI) vs placebo	-	0.21 (0.10 to 0.46)	-	0.63 (0.28 to 1.42)
p-value for Odds Ratio	-	<0.001	-	0.261
p-value for heterogeneity of Odds Ratio				0.102
Risk Ratio (95% CI) vs placebo	-	0.43 (0.27 to 0.69)	-	0.76 (0.43 to 1.36)
p-value for Risk Ratio	-	<0.001	-	0.353

All severe exacerbation events occurred during the 52-week treatment period are included, regardless of whether the patient is on-treatment or not
OR, RR and RD are derived from a logistic regression model with treatment, age, weight group, region, baseline eosinophil level, baseline FeNO level, baseline ICS dose level, and number of severe exacerbation events within 1 year prior to the study as covariates.
Peto OR calculation is based on Yusuf S et al. (Prog Cardiovasc Dis. 1985 Mar-Apr;27(5):335-71) and its p-value is derived using a normal approximation.
p-values for heterogeneity are estimated by using the same logistic model as the one used to estimate OR, RR and RD, with subgroup and treatment-by-subgroup interaction as additional covariates.
p-value for heterogeneity of Peto OR is estimated by using normal approximation.
PGM=DEVOPS/SAR231893/EFC14153/CSR_RWE/REPORT/PGM/eff_pro_evt_ger_subg_i_t.sas OUT=REPORT/OUTPUT/eff_pro_exaw52_ger_pfev1_t2_t_x.rtf (29JUN2021 - 17:58)

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

Project Code / Study Number / Analysis: SAR231893 / EFC14153 / CSR_RWE

3 Severe exacerbation events

3.1 Patients with at least one severe asthma exacerbation event during the 52-week treatment period - ITT type 2 inflammatory asthma phenotype population

3.1.6 By baseline predicted FEV1 (<80%, >=80%)

	Baseline Predicted FEV1			
	<80%		>=80%	
Type 2 inflammatory asthma phenotype population	**Placebo (N=59)**	**Dupilumab (N=116)**	**Placebo (N=55)**	**Dupilumab (N=120)**
p-value for heterogeneity of Risk Ratio				0.295
Risk Difference (95% CI) vs placebo	-	-30.84 (-46.04 to -15.64)	-	-4.76 (-19.04 to 9.52)
p-value for Risk Difference	-	<0.001	-	0.511
p-value for heterogeneity of Risk Difference				0.011

All severe exacerbation events occurred during the 52-week treatment period are included, regardless of whether the patient is on-treatment or not
OR, RR and RD are derived from a logistic regression model with treatment, age, weight group, region, baseline eosinophil level, baseline FeNO level, baseline ICS dose level, and number of severe exacerbation events within 1 year prior to the study as covariates.
Peto OR calculation is based on Yusuf S et al. (Prog Cardiovasc Dis. 1985 Mar-Apr;27(5):335-71) and its p-value is derived using a normal approximation.
p-values for heterogeneity are estimated by using the same logistic model as the one used to estimate OR, RR and RD, with subgroup and treatment-by-subgroup interaction as additional covariates.
p-value for heterogeneity of Peto OR is estimated by using normal approximation.
PGM=DEVOPS/SAR231893/EFC14153/CSR_RWE/REPORT/PGM/eff_pro_evt_ger_subg_i_t.sas OUT=REPORT/OUTPUT/eff_pro_exaw52_ger_pfev1_t2_t_x.rtf (29JUN2021 - 17:58)

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

Project Code / Study Number / Analysis: SAR231893 / EFC14153 / CSR_RWE

3 Severe exacerbation events

3.1 Patients with at least one severe asthma exacerbation event during the 52-week treatment period - ITT type 2 inflammatory asthma phenotype population

3.1.7 By baseline ACQ-7-IA (<=2, >2)

	Baseline ACQ-7-IA			
	<=2		>2	
Type 2 inflammatory asthma phenotype population	**Placebo (N=61)**	**Dupilumab (N=126)**	**Placebo (N=53)**	**Dupilumab (N=110)**
Patients with >=1 severe exacerbation events during the 52-week treatment period [n(%)]				
Yes	19 (31.1%)	26 (20.6%)	27 (50.9%)	28 (25.5%)
No	42 (68.9%)	100 (79.4%)	26 (49.1%)	82 (74.5%)
Odds Ratio (95% CI) vs placebo	-	0.49 (0.23 to 1.05)	-	0.25 (0.12 to 0.55)
p-value for Odds Ratio	-	0.067	-	<0.001
p-value for heterogeneity of Odds Ratio				0.212
Risk Ratio (95% CI) vs placebo	-	0.54 (0.32 to 0.91)	-	0.43 (0.27 to 0.71)
p-value for Risk Ratio	-	0.021	-	<0.001

All severe exacerbation events occurred during the 52-week treatment period are included, regardless of whether the patient is on-treatment or not
OR, RR and RD are derived from a logistic regression model with treatment, age, weight group, region, baseline eosinophil level, baseline FeNO level, baseline ICS dose level, and number of severe exacerbation events within 1 year prior to the study as covariates.
Peto OR calculation is based on Yusuf S et al. (Prog Cardiovasc Dis. 1985 Mar-Apr;27(5):335-71) and its p-value is derived using a normal approximation.
p-values for heterogeneity are estimated by using the same logistic model as the one used to estimate OR, RR and RD, with subgroup and treatment-by-subgroup interaction as additional covariates.
p-value for heterogeneity of Peto OR is estimated by using normal approximation.
PGM=DEVOPS/SAR231893/EFC14153/CSR_RWE/REPORT/PGM/eff_pro_evt_ger_subg_i_t.sas OUT=REPORT/OUTPUT/eff_pro_exaw52_ger_acq7_t2_t_x.rtf (29JUN2021 - 17:58)

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

Project Code / Study Number / Analysis: SAR231893 / EFC14153 / CSR_RWE

3 Severe exacerbation events

3.1 population Patients with at least one severe asthma exacerbation event during the 52-week treatment period - ITT type 2 inflammatory asthma phenotype

3.1.7 By baseline ACQ-7-IA (<=2, >2)

	Baseline ACQ-7-IA			
	<=2		>2	
Type 2 inflammatory asthma phenotype population	**Placebo (N=61)**	**Dupilumab (N=126)**	**Placebo (N=53)**	**Dupilumab (N=110)**
p-value for heterogeneity of Risk Ratio				0.383
Risk Difference (95% CI) vs placebo	-	-10.63 (-24.99 to 3.73)	-	-28.02 (-43.93 to -12.11)
p-value for Risk Difference	-	0.146	-	<0.001
p-value for heterogeneity of Risk Difference				0.047

All severe exacerbation events occurred during the 52-week treatment period are included, regardless of whether the patient is on-treatment or not
OR, RR and RD are derived from a logistic regression model with treatment, age, weight group, region, baseline eosinophil level, baseline FeNO level, baseline ICS dose level, and number of severe exacerbation events within 1 year prior to the study as covariates.
Peto OR calculation is based on Yusuf S et al. (Prog Cardiovasc Dis. 1985 Mar-Apr;27(5):335-71) and its p-value is derived using a normal approximation.
p-values for heterogeneity are estimated by using the same logistic model as the one used to estimate OR, RR and RD, with subgroup and treatment-by-subgroup interaction as additional covariates.
p-value for heterogeneity of Peto OR is estimated by using normal approximation.
PGM=DEVOPS/SAR231893/EFC14153/CSR_RWE/REPORT/PGM/eff_pro_evt_ger_subg_i_t.sas OUT=REPORT/OUTPUT/eff_pro_exaw52_ger_acq7_t2_t_x.rtf (29JUN2021 - 17:58)

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

Project Code / Study Number / Analysis: SAR231893 / EFC14153 / CSR_RWE

3 Severe exacerbation events

3.1 population Patients with at least one severe asthma exacerbation event during the 52-week treatment period - ITT type 2 inflammatory asthma phenotype

3.1.8 By baseline weight (<=30 kg, >30 kg)

	Baseline weight (kg)			
	<=30		>30	
Type 2 inflammatory asthma phenotype population	**Placebo (N=36)**	**Dupilumab (N=76)**	**Placebo (N=78)**	**Dupilumab (N=160)**
Patients with >=1 severe exacerbation events during the 52-week treatment period [n(%)]				
Yes	17 (47.2%)	14 (18.4%)	29 (37.2%)	40 (25.0%)
No	19 (52.8%)	62 (81.6%)	49 (62.8%)	120 (75.0%)
Odds Ratio (95% CI) vs placebo	-	0.21 (0.07 to 0.57)	-	0.45 (0.24 to 0.86)
p-value for Odds Ratio	-	0.003	-	0.015
p-value for heterogeneity of Odds Ratio				0.198
Risk Ratio (95% CI) vs placebo	-	0.33 (0.17 to 0.64)	-	0.53 (0.33 to 0.85)
p-value for Risk Ratio	-	0.001	-	0.009

All severe exacerbation events occurred during the 52-week treatment period are included, regardless of whether the patient is on-treatment or not
OR, RR and RD are derived from a logistic regression model with treatment, age, region, baseline eosinophil level, baseline FeNO level, baseline ICS dose level, and number of severe exacerbation events within 1 year prior to the study as covariates.
Peto OR calculation is based on Yusuf S et al. (Prog Cardiovasc Dis. 1985 Mar-Apr;27(5):335-71) and its p-value is derived using a normal approximation.
p-values for heterogeneity are estimated by using the same logistic model as the one used to estimate OR, RR and RD, with subgroup and treatment-by-subgroup interaction as additional covariates.
p-value for heterogeneity of Peto OR is estimated by using normal approximation.
PGM=DEVOPS/SAR231893/EFC14153/CSR_RWE/REPORT/PGM/eff_pro_evt_ger_subg_i_t.sas OUT=REPORT/OUTPUT/eff_pro_exaw52_ger_wgt_t2_t_x.rtf (29JUN2021 - 17:58)

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

Project Code / Study Number / Analysis: SAR231893 / EFC14153 / CSR_RWE

3 Severe exacerbation events

3.1 population Patients with at least one severe asthma exacerbation event during the 52-week treatment period - ITT type 2 inflammatory asthma phenotype

3.1.8 By baseline weight (<=30 kg, >30 kg)

	Baseline weight (kg)			
	<=30		>30	
Type 2 inflammatory asthma phenotype population	**Placebo (N=36)**	**Dupilumab (N=76)**	**Placebo (N=78)**	**Dupilumab (N=160)**
p-value for heterogeneity of Risk Ratio				0.233
Risk Difference (95% CI) vs placebo	-	-27.03 (-47.99 to -6.07)	-	-14.54 (-27.13 to -1.95)
p-value for Risk Difference	-	0.012	-	0.024
p-value for heterogeneity of Risk Difference				0.328

All severe exacerbation events occurred during the 52-week treatment period are included, regardless of whether the patient is on-treatment or not
OR, RR and RD are derived from a logistic regression model with treatment, age, region, baseline eosinophil level, baseline FeNO level, baseline ICS dose level, and number of severe exacerbation events within 1 year prior to the study as covariates.
Peto OR calculation is based on Yusuf S et al. (Prog Cardiovasc Dis. 1985 Mar-Apr;27(5):335-71) and its p-value is derived using a normal approximation.
p-values for heterogeneity are estimated by using the same logistic model as the one used to estimate OR, RR and RD, with subgroup and treatment-by-subgroup interaction as additional covariates.
p-value for heterogeneity of Peto OR is estimated by using normal approximation.
PGM=DEVOPS/SAR231893/EFC14153/CSR_RWE/REPORT/PGM/eff_pro_evt_ger_subg_i_t.sas OUT=REPORT/OUTPUT/eff_pro_exaw52_ger_wgt_t2_t_x.rtf (29JUN2021 - 17:58)

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

Project Code / Study Number / Analysis: SAR231893 / EFC14153 / CSR_RWE

3 Severe exacerbation events

3.1 Patients with at least one severe asthma exacerbation event during the 52-week treatment period - ITT type 2 inflammatory asthma phenotype population

3.1.9 By atopic medical condition (Yes, No)

	Atopic medical condition			
	Yes		No	
Type 2 inflammatory asthma phenotype population	**Placebo (N=103)**	**Dupilumab (N=227)**	**Placebo (N=11)**	**Dupilumab (N=9)**
Patients with >=1 severe exacerbation events during the 52-week treatment period [n(%)]				
Yes	41 (39.8%)	53 (23.3%)	5 (45.5%)	1 (11.1%)
No	62 (60.2%)	174 (76.7%)	6 (54.5%)	8 (88.9%)
Odds Ratio (95% CI) vs placebo	-	0.38 (0.22 to 0.66)	-	0.00 (0.00 to NE)
p-value for Odds Ratio	-	<0.001	-	0.980
p-value for heterogeneity of Odds Ratio				0.390
Risk Ratio (95% CI) vs placebo	-	0.50 (0.35 to 0.72)	-	0.17 (0.00 to 137.14)
p-value for Risk Ratio	-	<0.001	-	0.564

All severe exacerbation events occurred during the 52-week treatment period are included, regardless of whether the patient is on-treatment or not
OR, RR and RD are derived from a logistic regression model with treatment, age, weight group, region, baseline eosinophil level, baseline FeNO level, baseline ICS dose level, and number of severe exacerbation events within 1 year prior to the study as covariates.
Peto OR calculation is based on Yusuf S et al. (Prog Cardiovasc Dis. 1985 Mar-Apr;27(5):335-71) and its p-value is derived using a normal approximation.
p-values for heterogeneity are estimated by using the same logistic model as the one used to estimate OR, RR and RD, with subgroup and treatment-by-subgroup interaction as additional covariates.
p-value for heterogeneity of Peto OR is estimated by using normal approximation.
PGM=DEVOPS/SAR231893/EFC14153/CSR_RWE/REPORT/PGM/eff_pro_evt_ger_subg_i_t.sas OUT=REPORT/OUTPUT/eff_pro_exaw52_ger_amc_t2_t_x.rtf (29JUN2021 - 17:58)

Project Code / Study Number / Analysis: SAR231893 / EFC14153 / CSR_RWE

3 Severe exacerbation events

3.1 Patients with at least one severe asthma exacerbation event during the 52-week treatment period - ITT type 2 inflammatory asthma phenotype population

3.1.9 By atopic medical condition (Yes, No)

	Atopic medical condition			
	Yes		No	
Type 2 inflammatory asthma phenotype population	**Placebo (N=103)**	**Dupilumab (N=227)**	**Placebo (N=11)**	**Dupilumab (N=9)**
p-value for heterogeneity of Risk Ratio				0.423
Risk Difference (95% CI) vs placebo	-	-16.78 (-28.15 to -5.41)	-	-31.97 (-332.57 to 268.63)
p-value for Risk Difference	-	0.004	-	0.817
p-value for heterogeneity of Risk Difference				0.533

All severe exacerbation events occurred during the 52-week treatment period are included, regardless of whether the patient is on-treatment or not
OR, RR and RD are derived from a logistic regression model with treatment, age, weight group, region, baseline eosinophil level, baseline FeNO level, baseline ICS dose level, and number of severe exacerbation events within 1 year prior to the study as covariates.
Peto OR calculation is based on Yusuf S et al. (Prog Cardiovasc Dis. 1985 Mar-Apr;27(5):335-71) and its p-value is derived using a normal approximation.
p-values for heterogeneity are estimated by using the same logistic model as the one used to estimate OR, RR and RD, with subgroup and treatment-by-subgroup interaction as additional covariates.
p-value for heterogeneity of Peto OR is estimated by using normal approximation.
PGM=DEVOPS/SAR231893/EFC14153/CSR_RWE/REPORT/PGM/eff_pro_evt_ger_subg_i_t.sas OUT=REPORT/OUTPUT/eff_pro_exaw52_ger_amc_t2_t_x.rtf (29JUN2021 - 17:58)

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

Project Code / Study Number / Analysis: SAR231893 / EFC14153 / CSR_RWE

3 Severe exacerbation events

3.1 population Patients with at least one severe asthma exacerbation event during the 52-week treatment period - ITT type 2 inflammatory asthma phenotype

3.1.10 By baseline total IgE (<median, >= median)

	Baseline Total IgE (IU/mL)			
	<median		>=median	
Type 2 inflammatory asthma phenotype population	**Placebo (N=66)**	**Dupilumab (N=105)**	**Placebo (N=47)**	**Dupilumab (N=125)**
Patients with >=1 severe exacerbation events during the 52-week treatment period [n(%)]				
Yes	26 (39.4%)	27 (25.7%)	19 (40.4%)	27 (21.6%)
No	40 (60.6%)	78 (74.3%)	28 (59.6%)	98 (78.4%)
Odds Ratio (95% CI) vs placebo	-	0.44 (0.21 to 0.92)	-	0.31 (0.14 to 0.69)
p-value for Odds Ratio	-	0.030	-	0.004
p-value for heterogeneity of Odds Ratio				0.520
Risk Ratio (95% CI) vs placebo	-	0.56 (0.34 to 0.93)	-	0.46 (0.28 to 0.76)
p-value for Risk Ratio	-	0.025	-	0.003

All severe exacerbation events occurred during the 52-week treatment period are included, regardless of whether the patient is on-treatment or not
OR, RR and RD are derived from a logistic regression model with treatment, age, weight group, region, baseline eosinophil level, baseline FeNO level, baseline ICS dose level, and number of severe exacerbation events within 1 year prior to the study as covariates.
Peto OR calculation is based on Yusuf S et al. (Prog Cardiovasc Dis. 1985 Mar-Apr;27(5):335-71) and its p-value is derived using a normal approximation.
p-values for heterogeneity are estimated by using the same logistic model as the one used to estimate OR, RR and RD, with subgroup and treatment-by-subgroup interaction as additional covariates.
p-value for heterogeneity of Peto OR is estimated by using normal approximation.
PGM=DEVOPS/SAR231893/EFC14153/CSR_RWE/REPORT/PGM/eff_pro_evt_ger_subg_i_t.sas OUT=REPORT/OUTPUT/eff_pro_exaw52_ger_igem_t2_t_x.rtf (29JUN2021 - 17:58)

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

Project Code / Study Number / Analysis: SAR231893 / EFC14153 / CSR_RWE

3 Severe exacerbation events

3.1 population Patients with at least one severe asthma exacerbation event during the 52-week treatment period - ITT type 2 inflammatory asthma phenotype

3.1.10 By baseline total IgE (<median, >= median)

	Baseline Total IgE (IU/mL)			
	<median		>=median	
Type 2 inflammatory asthma phenotype population	**Placebo (N=66)**	**Dupilumab (N=105)**	**Placebo (N=47)**	**Dupilumab (N=125)**
p-value for heterogeneity of Risk Ratio				0.524
Risk Difference (95% CI) vs placebo	-	-15.13 (-29.96 to -0.29)	-	-22.43 (-38.74 to -6.11)
p-value for Risk Difference	-	0.046	-	0.007
p-value for heterogeneity of Risk Difference				0.485

All severe exacerbation events occurred during the 52-week treatment period are included, regardless of whether the patient is on-treatment or not
OR, RR and RD are derived from a logistic regression model with treatment, age, weight group, region, baseline eosinophil level, baseline FeNO level, baseline ICS dose level, and number of severe exacerbation events within 1 year prior to the study as covariates.
Peto OR calculation is based on Yusuf S et al. (Prog Cardiovasc Dis. 1985 Mar-Apr;27(5):335-71) and its p-value is derived using a normal approximation.
p-values for heterogeneity are estimated by using the same logistic model as the one used to estimate OR, RR and RD, with subgroup and treatment-by-subgroup interaction as additional covariates.
p-value for heterogeneity of Peto OR is estimated by using normal approximation.
PGM=DEVOPS/SAR231893/EFC14153/CSR_RWE/REPORT/PGM/eff_pro_evt_ger_subg_i_t.sas OUT=REPORT/OUTPUT/eff_pro_exaw52_ger_igem_t2_t_x.rtf (29JUN2021 - 17:58)

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

Project Code / Study Number / Analysis: SAR231893 / EFC14153 / CSR_RWE

3 Severe exacerbation events

3.1 Patients with at least one severe asthma exacerbation event during the 52-week treatment period - ITT type 2 inflammatory asthma phenotype population

3.1.11 By baseline total IgE (<100 IU/ml, >= 100 IU/ml)

	Baseline Total IgE (IU/mL)			
	< 100		>= 100	
Type 2 inflammatory asthma phenotype population	**Placebo (N=22)**	**Dupilumab (N=29)**	**Placebo (N=91)**	**Dupilumab (N=201)**
Patients with >=1 severe exacerbation events during the 52-week treatment period [n(%)]				
Yes	7 (31.8%)	6 (20.7%)	38 (41.8%)	48 (23.9%)
No	15 (68.2%)	23 (79.3%)	53 (58.2%)	153 (76.1%)
Odds Ratio (95% CI) vs placebo	-	0.13 (0.02 to 1.02)	-	0.38 (0.21 to 0.67)
p-value for Odds Ratio	-	0.053	-	<0.001
p-value for heterogeneity of Odds Ratio				0.965
Risk Ratio (95% CI) vs placebo	-	0.41 (0.10 to 1.76)	-	0.49 (0.34 to 0.71)
p-value for Risk Ratio	-	0.225	-	<0.001

All severe exacerbation events occurred during the 52-week treatment period are included, regardless of whether the patient is on-treatment or not
OR, RR and RD are derived from a logistic regression model with treatment, age, weight group, region, baseline eosinophil level, baseline FeNO level, baseline ICS dose level, and number of severe exacerbation events within 1 year prior to the study as covariates.
Peto OR calculation is based on Yusuf S et al. (Prog Cardiovasc Dis. 1985 Mar-Apr;27(5):335-71) and its p-value is derived using a normal approximation.
p-values for heterogeneity are estimated by using the same logistic model as the one used to estimate OR, RR and RD, with subgroup and treatment-by-subgroup interaction as additional covariates.
p-value for heterogeneity of Peto OR is estimated by using normal approximation.
PGM=DEVOPS/SAR231893/EFC14153/CSR_RWE/REPORT/PGM/eff_pro_evt_ger_subg_i_t.sas OUT=REPORT/OUTPUT/eff_pro_exaw52_ger_ige_t2_t_x.rtf (29JUN2021 - 17:59)

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

Project Code / Study Number / Analysis: SAR231893 / EFC14153 / CSR_RWE

3 Severe exacerbation events

3.1 Patients with at least one severe asthma exacerbation event during the 52-week treatment period - ITT type 2 inflammatory asthma phenotype population

3.1.11 By baseline total IgE (<100 IU/ml, >= 100 IU/ml)

	Baseline Total IgE (IU/mL)			
	< 100		>= 100	
Type 2 inflammatory asthma phenotype population	**Placebo (N=22)**	**Dupilumab (N=29)**	**Placebo (N=91)**	**Dupilumab (N=201)**
p-value for heterogeneity of Risk Ratio				0.959
Risk Difference (95% CI) vs placebo	-	-29.13 (-73.01 to 14.76)	-	-18.09 (-30.30 to -5.87)
p-value for Risk Difference	-	0.187	-	0.004
p-value for heterogeneity of Risk Difference				0.760

All severe exacerbation events occurred during the 52-week treatment period are included, regardless of whether the patient is on-treatment or not
OR, RR and RD are derived from a logistic regression model with treatment, age, weight group, region, baseline eosinophil level, baseline FeNO level, baseline ICS dose level, and number of severe exacerbation events within 1 year prior to the study as covariates.
Peto OR calculation is based on Yusuf S et al. (Prog Cardiovasc Dis. 1985 Mar-Apr;27(5):335-71) and its p-value is derived using a normal approximation.
p-values for heterogeneity are estimated by using the same logistic model as the one used to estimate OR, RR and RD, with subgroup and treatment-by-subgroup interaction as additional covariates.
p-value for heterogeneity of Peto OR is estimated by using normal approximation.
PGM=DEVOPS/SAR231893/EFC14153/CSR_RWE/REPORT/PGM/eff_pro_evt_ger_subg_i_t.sas OUT=REPORT/OUTPUT/eff_pro_exaw52_ger_ige_t2_t_x.rtf (29JUN2021 - 17:59)

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

Project Code / Study Number / Analysis: SAR231893 / EFC14153 / CSR_RWE

3 Severe exacerbation events

3.1 population Patients with at least one severe asthma exacerbation event during the 52-week treatment period - ITT type 2 inflammatory asthma phenotype

3.1.12 By age at onset of asthma (0-2, 3-5, >=6 years)

	Age of onset of asthma (years)					
	0-2		3-5		>= 6	
Type 2 inflammatory asthma phenotype population	**Placebo (N=40)**	**Dupilumab (N=105)**	**Placebo (N=39)**	**Dupilumab (N=86)**	**Placebo (N=35)**	**Dupilumab (N=45)**
Patients with >=1 severe exacerbation events during the 52-week treatment period [n(%)]						
Yes	23 (57.5%)	30 (28.6%)	11 (28.2%)	19 (22.1%)	12 (34.3%)	5 (11.1%)
No	17 (42.5%)	75 (71.4%)	28 (71.8%)	67 (77.9%)	23 (65.7%)	40 (88.9%)
Odds Ratio (95% CI) vs placebo	-	0.23 (0.10 to 0.53)	-	0.64 (0.25 to 1.66)	-	0.26 (0.07 to 1.00)
p-value for Odds Ratio	-	<0.001	-	0.359	-	0.049
p-value for heterogeneity of Odds Ratio:						
0-2, 3-5						0.119
0-2, >= 6						0.909

All severe exacerbation events occurred during the 52-week treatment period are included, regardless of whether the patient is on-treatment or not
OR, RR and RD are derived from a logistic regression model with treatment, age, weight group, region, baseline eosinophil level, baseline FeNO level, baseline ICS dose level, and number of severe exacerbation events within 1 year prior to the study as covariates.
Peto OR calculation is based on Yusuf S et al. (Prog Cardiovasc Dis. 1985 Mar-Apr;27(5):335-71) and its p-value is derived using a normal approximation.
p-values for heterogeneity are estimated by using the same logistic model as the one used to estimate OR, RR and RD, with subgroup and treatment-by-subgroup interaction as additional covariates.
p-value for heterogeneity of Peto OR is estimated by using normal approximation.
PGM=DEVOPS/SAR231893/EFC14153/CSR_RWE/REPORT/PGM/eff_pro_evt_ger_subg_i_t.sas OUT=REPORT/OUTPUT/eff_pro_exaw52_ger_onsa_t2_t_x.rtf (01SEP2021 - 15:29)

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

Project Code / Study Number / Analysis: SAR231893 / EFC14153 / CSR_RWE

3 Severe exacerbation events

3.1 population Patients with at least one severe asthma exacerbation event during the 52-week treatment period - ITT type 2 inflammatory asthma phenotype

3.1.12 By age at onset of asthma (0-2, 3-5, >=6 years)

	Age of onset of asthma (years)					
	0-2		3-5		>= 6	
Type 2 inflammatory asthma phenotype population	**Placebo (N=40)**	**Dupilumab (N=105)**	**Placebo (N=39)**	**Dupilumab (N=86)**	**Placebo (N=35)**	**Dupilumab (N=45)**
3-5, >= 6						0.255
overall						0.262
Risk Ratio (95% CI) vs placebo	-	0.42 (0.27 to 0.64)	-	0.80 (0.41 to 1.54)	-	0.42 (0.14 to 1.22)
p-value for Risk Ratio	-	<0.001	-	0.495	-	0.110
p-value for heterogeneity of Risk Ratio:						
0-2, 3-5						0.175
0-2, >= 6						0.634
3-5, >= 6						0.181
overall						0.290

All severe exacerbation events occurred during the 52-week treatment period are included, regardless of whether the patient is on-treatment or not
OR, RR and RD are derived from a logistic regression model with treatment, age, weight group, region, baseline eosinophil level, baseline FeNO level, baseline ICS dose level, and number of severe exacerbation events within 1 year prior to the study as covariates.
Peto OR calculation is based on Yusuf S et al. (Prog Cardiovasc Dis. 1985 Mar-Apr;27(5):335-71) and its p-value is derived using a normal approximation.
p-values for heterogeneity are estimated by using the same logistic model as the one used to estimate OR, RR and RD, with subgroup and treatment-by-subgroup interaction as additional covariates.
p-value for heterogeneity of Peto OR is estimated by using normal approximation.
PGM=DEVOPS/SAR231893/EFC14153/CSR_RWE/REPORT/PGM/eff_pro_evt_ger_subg_i_t.sas OUT=REPORT/OUTPUT/eff_pro_exaw52_ger_onsa_t2_t_x.rtf (01SEP2021 - 15:29)

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

Project Code / Study Number / Analysis: SAR231893 / EFC14153 / CSR_RWE

3 Severe exacerbation events

3.1 population Patients with at least one severe asthma exacerbation event during the 52-week treatment period - ITT type 2 inflammatory asthma phenotype

3.1.12 By age at onset of asthma (0-2, 3-5, >=6 years)

	Age of onset of asthma (years)					
	0-2		3-5		>= 6	
Type 2 inflammatory asthma phenotype population	**Placebo (N=40)**	**Dupilumab (N=105)**	**Placebo (N=39)**	**Dupilumab (N=86)**	**Placebo (N=35)**	**Dupilumab (N=45)**
Risk Difference (95% CI) vs placebo	-	-32.83 (-51.29 to -14.37)	-	-10.65 (-28.54 to 7.24)	-	-14.90 (-42.60 to 12.80)
p-value for Risk Difference	-	<0.001	-	0.240	-	0.287
p-value for heterogeneity of Risk Difference:						
0-2, 3-5						0.066
0-2, >= 6						0.306
3-5, >= 6						0.489
overall						0.182

All severe exacerbation events occurred during the 52-week treatment period are included, regardless of whether the patient is on-treatment or not
OR, RR and RD are derived from a logistic regression model with treatment, age, weight group, region, baseline eosinophil level, baseline FeNO level, baseline ICS dose level, and number of severe exacerbation events within 1 year prior to the study as covariates.
Peto OR calculation is based on Yusuf S et al. (Prog Cardiovasc Dis. 1985 Mar-Apr;27(5):335-71) and its p-value is derived using a normal approximation.
p-values for heterogeneity are estimated by using the same logistic model as the one used to estimate OR, RR and RD, with subgroup and treatment-by-subgroup interaction as additional covariates.
p-value for heterogeneity of Peto OR is estimated by using normal approximation.
PGM=DEVOPS/SAR231893/EFC14153/CSR_RWE/REPORT/PGM/eff_pro_evt_ger_subg_i_t.sas OUT=REPORT/OUTPUT/eff_pro_exaw52_ger_onsa_t2_t_x.rtf (01SEP2021 - 15:29)

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

Project Code / Study Number / Analysis: SAR231893 / EFC14153 / CSR_RWE

3 Severe exacerbation events

3.1 population Patients with at least one severe asthma exacerbation event during the 52-week treatment period - ITT type 2 inflammatory asthma phenotype

3.1.13 By number of severe asthma exacerbation prior to the study (<=1, 2, >2)

	Number of severe asthma exacerbation prior to the study					
	<=1		**2**		**>2**	
Type 2 inflammatory asthma phenotype population	**Placebo (N=47)**	**Dupilumab (N=85)**	**Placebo (N=32)**	**Dupilumab (N=75)**	**Placebo (N=35)**	**Dupilumab (N=76)**
Patients with >=1 severe exacerbation events during the 52-week treatment period [n(%)]						
Yes	16 (34.0%)	11 (12.9%)	13 (40.6%)	15 (20.0%)	17 (48.6%)	28 (36.8%)
No	31 (66.0%)	74 (87.1%)	19 (59.4%)	60 (80.0%)	18 (51.4%)	48 (63.2%)
Odds Ratio (95% CI) vs placebo	-	0.14 (0.05 to 0.42)	-	0.33 (0.12 to 0.92)	-	0.50 (0.20 to 1.27)
p-value for Odds Ratio	-	<0.001	-	0.035	-	0.142
p-value for heterogeneity of Odds Ratio:						
<=1, 2						0.277
<=1, >2						0.103

All severe exacerbation events occurred during the 52-week treatment period are included, regardless of whether the patient is on-treatment or not
OR, RR and RD are derived from a logistic regression model with treatment, age, weight group, region, baseline eosinophil level, baseline FeNO level and baseline ICS dose level as covariates.
Peto OR calculation is based on Yusuf S et al. (Prog Cardiovasc Dis. 1985 Mar-Apr;27(5):335-71) and its p-value is derived using a normal approximation.
p-values for heterogeneity are estimated by using the same logistic model as the one used to estimate OR, RR and RD, with subgroup and treatment-by-subgroup interaction as additional covariates.
p-value for heterogeneity of Peto OR is estimated by using normal approximation.
PGM=DEVOPS/SAR231893/EFC14153/CSR_RWE/REPORT/PGM/eff_pro_evt_ger_subg_i_t.sas OUT=REPORT/OUTPUT/eff_pro_exaw52_ger_exa_t2_t_x.rtf (29JUN2021 - 17:59)

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

Project Code / Study Number / Analysis: SAR231893 / EFC14153 / CSR_RWE

3 Severe exacerbation events

3.1 Patients with at least one severe asthma exacerbation event during the 52-week treatment period - ITT type 2 inflammatory asthma phenotype population

3.1.13 By number of severe asthma exacerbation prior to the study (<=1, 2, >2)

	Number of severe asthma exacerbation prior to the study					
	<=1		2		>2	
Type 2 inflammatory asthma phenotype population	**Placebo (N=47)**	**Dupilumab (N=85)**	**Placebo (N=32)**	**Dupilumab (N=75)**	**Placebo (N=35)**	**Dupilumab (N=76)**
2, >2						0.633
overall						0.253
Risk Ratio (95% CI) vs placebo	-	0.22 (0.09 to 0.51)	-	0.41 (0.19 to 0.85)	-	0.64 (0.38 to 1.08)
p-value for Risk Ratio	-	<0.001	-	0.018	-	0.094
p-value for heterogeneity of Risk Ratio:						
<=1, 2						0.245
<=1, >2						0.026
2, >2						0.365
overall						0.081

All severe exacerbation events occurred during the 52-week treatment period are included, regardless of whether the patient is on-treatment or not
OR, RR and RD are derived from a logistic regression model with treatment, age, weight group, region, baseline eosinophil level, baseline FeNO level and baseline ICS dose level as covariates.
Peto OR calculation is based on Yusuf S et al. (Prog Cardiovasc Dis. 1985 Mar-Apr;27(5):335-71) and its p-value is derived using a normal approximation.
p-values for heterogeneity are estimated by using the same logistic model as the one used to estimate OR, RR and RD, with subgroup and treatment-by-subgroup interaction as additional covariates.
p-value for heterogeneity of Peto OR is estimated by using normal approximation.
PGM=DEVOPS/SAR231893/EFC14153/CSR_RWE/REPORT/PGM/eff_pro_evt_ger_subg_i_t.sas OUT=REPORT/OUTPUT/eff_pro_exaw52_ger_exa_t2_t_x.rtf (29JUN2021 - 17:59)

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

Project Code / Study Number / Analysis: SAR231893 / EFC14153 / CSR_RWE

3 Severe exacerbation events

3.1 Patients with at least one severe asthma exacerbation event during the 52-week treatment period - ITT type 2 inflammatory asthma phenotype population

3.1.13 By number of severe asthma exacerbation prior to the study (<=1, 2, >2)

	Number of severe asthma exacerbation prior to the study					
	<=1		2		>2	
Type 2 inflammatory asthma phenotype population	**Placebo (N=47)**	**Dupilumab (N=85)**	**Placebo (N=32)**	**Dupilumab (N=75)**	**Placebo (N=35)**	**Dupilumab (N=76)**
Risk Difference (95% CI) vs placebo	-	-25.39 (-44.01 to -6.77)	-	-21.91 (-43.56 to -0.25)	-	-18.74 (-38.20 to 0.72)
p-value for Risk Difference	-	0.008	-	0.047	-	0.059
p-value for heterogeneity of Risk Difference:						
<=1, 2						0.477
<=1, >2						0.448
2, >2						0.944
overall						0.673

All severe exacerbation events occurred during the 52-week treatment period are included, regardless of whether the patient is on-treatment or not
OR, RR and RD are derived from a logistic regression model with treatment, age, weight group, region, baseline eosinophil level, baseline FeNO level and baseline ICS dose level as covariates.
Peto OR calculation is based on Yusuf S et al. (Prog Cardiovasc Dis. 1985 Mar-Apr;27(5):335-71) and its p-value is derived using a normal approximation.
p-values for heterogeneity are estimated by using the same logistic model as the one used to estimate OR, RR and RD, with subgroup and treatment-by-subgroup interaction as additional covariates.
p-value for heterogeneity of Peto OR is estimated by using normal approximation.
PGM=DEVOPS/SAR231893/EFC14153/CSR_RWE/REPORT/PGM/eff_pro_evt_ger_subg_i_t.sas OUT=REPORT/OUTPUT/eff_pro_exaw52_ger_exa_t2_t_x.rtf (29JUN2021 - 17:59)

Subgruppenanalysen: Ereigniszeitanalysen

Project Code / Study Number / Analysis: SAR231893 / EFC14153 / CSR_RWE

2 Severe exacerbation events

2.1 Analysis of time to first severe exacerbation event during the 52-week treatment period - ITT type 2 inflammatory asthma phenotype population

Type 2 inflammatory asthma phenotype population - Severe asthma exacerbation	**Placebo (N=114)**	**Dupilumab (N=236)**
Number of patients who are censored	68 (59.6%)	182 (77.1%)
Number of patients with event	46 (40.4%)	54 (22.9%)
Median time to first event (days) (95% CI) [a]	NE (366.00 to NE)	NE (NE to NE)
Kaplan-Meier estimates for probability of a patient with >=1 event (95% CI) up to [a]		
12 weeks	0.149 (0.091 to 0.221)	0.090 (0.058 to 0.131)
24 weeks	0.281 (0.202 to 0.365)	0.147 (0.105 to 0.195)
36 weeks	0.351 (0.265 to 0.438)	0.195 (0.146 to 0.248)
52 weeks	0.395 (0.305 to 0.483)	0.235 (0.182 to 0.292)
Unstratified Log-Rank test p-value [a]		<0.001
Hazard Ratio (95% CI) [b]	-	0.443 (0.293 to 0.670)
p-value for Hazard Ratio [b]		<0.001

Note: The time-to-event variable is defined as (date of the first event - randomization date +1). For patients who have no event on or before Week 52 or last contact date, the time will be censored at the date of date of visit at Week 52 or the last contact date, whichever happens earlier.

[a] derived from Kaplan-Meier estimates.

[b] derived using Cox regression model including the time to the first event as the dependent variable, and treatment groups, age, baseline weight group, region, baseline eosinophil level, baseline FeNO level, baseline ICS dose level and number of severe exacerbation events within 1 year prior to the study as covariates.

Type 2 inflammatory asthma phenotype population is defined as the randomized patients with baseline blood eosinophils >= 0.15 Giga/L or baseline FeNO >= 20 ppb.

PGM=DEVOPS/SAR231893/EFC14153/CSR_RWE/REPORT/PGM/eff_time2event_ger_i_t.sas OUT=REPORT/OUTPUT/eff_t2evt_eaw52_ger_i_t_x.rtf (29JUN2021 - 17:04)

Project Code / Study Number / Analysis: SAR231893 / EFC14153 / CSR_RWE

2 Severe exacerbation events

2.1 Analysis of time to first severe exacerbation event during the 52-week treatment period - ITT type 2 inflammatory asthma phenotype population

2.1.1 By gender (Male, Female)

	Gender			
	Male		Female	
Type 2 inflammatory asthma phenotype population - Severe asthma exacerbation	**Placebo (N=78)**	**Dupilumab (N=152)**	**Placebo (N=36)**	**Dupilumab (N=84)**
Number of patients who are censored	40 (51.3%)	115 (75.7%)	28 (77.8%)	67 (79.8%)
Number of patients with event	38 (48.7%)	37 (24.3%)	8 (22.2%)	17 (20.2%)
Median time to first event (days) (95% CI) [a]	366.0 (200.00 to NE)	NE (NE to NE)	NE (NE to NE)	NE (NE to NE)
Kaplan-Meier estimates for probability of a patient with >=1 event (95% CI) up to [a]				
12 weeks	0.179 (0.104 to 0.272)	0.086 (0.048 to 0.137)	0.083 (0.021 to 0.201)	0.099 (0.046 to 0.175)
24 weeks	0.333 (0.232 to 0.438)	0.159 (0.106 to 0.222)	0.167 (0.068 to 0.304)	0.123 (0.063 to 0.205)
36 weeks	0.423 (0.313 to 0.529)	0.213 (0.152 to 0.282)	0.194 (0.086 to 0.336)	0.161 (0.091 to 0.249)
52 weeks	0.474 (0.361 to 0.580)	0.248 (0.182 to 0.319)	0.222 (0.105 to 0.367)	0.212 (0.130 to 0.306)

Note: The time-to-event variable is defined as (date of the first event - randomization date +1). For patients who have no event on or before Week 52 or last contact date, the time will be censored at the date of date of visit at Week 52 or the last contact date, whichever happens earlier.
[a] derived from Kaplan-Meier estimates.
[b] derived using Cox regression model including the time to the first event as the dependent variable, and treatment groups, age, baseline weight group, region, baseline eosinophil level, baseline FeNO level, baseline ICS dose level and number of severe exacerbation events within 1 year prior to the study as covariates.
[c] derived using the same Cox regression model as in [b] with subgroup and subgroup-by-treatment interaction as additional covariates.
Type 2 inflammatory asthma phenotype population is defined as the randomized patients with baseline blood eosinophils >= 0.15 Giga/L or baseline FeNO >= 20 ppb.
PGM=DEVOPS/SAR231893/EFC14153/CSR_RWE/REPORT/PGM/eff_time2event_ger_subg_i_t.sas OUT=REPORT/OUTPUT/eff_t2evt_eaw52_ger_sex_t2_t_x.rtf (29JUN2021 - 17:04)

Project Code / Study Number / Analysis: SAR231893 / EFC14153 / CSR_RWE

2 Severe exacerbation events

2.1 Analysis of time to first severe exacerbation event during the 52-week treatment period - ITT type 2 inflammatory asthma phenotype population

2.1.1 By gender (Male, Female)

	Gender			
	Male		Female	
Type 2 inflammatory asthma phenotype population - Severe asthma exacerbation	**Placebo (N=78)**	**Dupilumab (N=152)**	**Placebo (N=36)**	**Dupilumab (N=84)**
Unstratified Log-Rank test p-value [a]		<0.001		0.890
Hazard Ratio (95% CI) [b]	-	0.365 (0.227 to 0.588)	-	0.815 (0.335 to 1.984)
p-value for Hazard Ratio [b]		<0.001		0.653
p-value for heterogeneity of Hazard Ratio [c]				0.096

Note: The time-to-event variable is defined as (date of the first event - randomization date +1). For patients who have no event on or before Week 52 or last contact date, the time will be censored at the date of date of visit at Week 52 or the last contact date, whichever happens earlier.

[a] derived from Kaplan-Meier estimates.

[b] derived using Cox regression model including the time to the first event as the dependent variable, and treatment groups, age, baseline weight group, region, baseline eosinophil level, baseline FeNO level, baseline ICS dose level and number of severe exacerbation events within 1 year prior to the study as covariates.

[c] derived using the same Cox regression model as in [b] with subgroup and subgroup-by-treatment interaction as additional covariates.

Type 2 inflammatory asthma phenotype population is defined as the randomized patients with baseline blood eosinophils >= 0.15 Giga/L or baseline FeNO >= 20 ppb.

PGM=DEVOPS/SAR231893/EFC14153/CSR_RWE/REPORT/PGM/eff_time2event_ger_subg_i_t.sas OUT=REPORT/OUTPUT/eff_t2evt_eaw52_ger_sex_t2_t_x.rtf (29JUN2021 - 17:04)

Project Code / Study Number / Analysis: SAR231893 / EFC14153 / CSR_RWE

2 Severe exacerbation events

2.1 Analysis of time to first severe exacerbation event during the 52-week treatment period - ITT type 2 inflammatory asthma phenotype population

2.1.2 By region (Latin America, East Europe, Western Countries)

	Region					
	Latin America		East Europe		Western countries	
Type 2 inflammatory asthma phenotype population - Severe asthma exacerbation	**Placebo (N=51)**	**Dupilumab (N=106)**	**Placebo (N=43)**	**Dupilumab (N=78)**	**Placebo (N=20)**	**Dupilumab (N=52)**
Number of patients who are censored	30 (58.8%)	77 (72.6%)	34 (79.1%)	66 (84.6%)	4 (20.0%)	39 (75.0%)
Number of patients with event	21 (41.2%)	29 (27.4%)	9 (20.9%)	12 (15.4%)	16 (80.0%)	13 (25.0%)
Median time to first event (days) (95% CI) [a]	366.0 (248.00 to NE)	NE (NE to NE)	NE (NE to NE)	NE (NE to NE)	165.5 (77.00 to 241.00)	NE (NE to NE)
Kaplan-Meier estimates for probability of a patient with >=1 event (95% CI) up to [a]						
12 weeks	0.176 (0.087 to 0.292)	0.095 (0.049 to 0.160)	0.070 (0.018 to 0.171)	0.026 (0.005 to 0.080)	0.250 (0.091 to 0.449)	0.180 (0.089 to 0.297)
24 weeks	0.294 (0.177 to 0.421)	0.181 (0.114 to 0.260)	0.140 (0.057 to 0.259)	0.065 (0.024 to 0.134)	0.550 (0.313 to 0.735)	0.201 (0.104 to 0.321)

Note: The time-to-event variable is defined as (date of the first event - randomization date +1). For patients who have no event on or before Week 52 or last contact date, the time will be censored at the date of date of visit at Week 52 or the last contact date, whichever happens earlier.

[a] derived from Kaplan-Meier estimates.

[b] derived using Cox regression model including the time to the first event as the dependent variable, and treatment groups, age, baseline weight group, baseline eosinophil level, baseline FeNO level, baseline ICS dose level and number of severe exacerbation events within 1 year prior to the study as covariates.

[c] derived using the same Cox regression model as in [b] with subgroup and subgroup-by-treatment interaction as additional covariates.

Type 2 inflammatory asthma phenotype population is defined as the randomized patients with baseline blood eosinophils >= 0.15 Giga/L or baseline FeNO >= 20 ppb.

PGM=DEVOPS/SAR231893/EFC14153/CSR_RWE/REPORT/PGM/eff_time2event_ger_subg_i_t.sas OUT=REPORT/OUTPUT/eff_t2evt_eaw52_ger_cty_t2_t_x.rtf (29JUN2021 - 17:04)

Project Code / Study Number / Analysis: SAR231893 / EFC14153 / CSR_RWE

2 Severe exacerbation events

2.1 Analysis of time to first severe exacerbation event during the 52-week treatment period - ITT type 2 inflammatory asthma phenotype population

2.1.2 By region (Latin America, East Europe, Western Countries)

	Region					
	Latin America		East Europe		Western countries	
Type 2 inflammatory asthma phenotype population - Severe asthma exacerbation	**Placebo (N=51)**	**Dupilumab (N=106)**	**Placebo (N=43)**	**Dupilumab (N=78)**	**Placebo (N=20)**	**Dupilumab (N=52)**
36 weeks	0.353 (0.226 to 0.482)	0.248 (0.170 to 0.334)	0.163 (0.072 to 0.287)	0.104 (0.048 to 0.183)	0.750 (0.500 to 0.887)	0.222 (0.119 to 0.345)
52 weeks	0.392 (0.260 to 0.522)	0.278 (0.196 to 0.366)	0.209 (0.104 to 0.340)	0.156 (0.085 to 0.245)	0.800 (0.551 to 0.920)	0.267 (0.152 to 0.396)
Unstratified Log-Rank test p-value [a]		0.076		0.404		<0.001
Hazard Ratio (95% CI) [b]	-	0.536 (0.288 to 0.995)	-	0.727 (0.305 to 1.734)	-	0.141 (0.059 to 0.337)
p-value for Hazard Ratio [b]		0.048		0.473		<0.001
p-value for heterogeneity of Hazard Ratio [c]:						
Latin America, East Europe						0.960

Note: The time-to-event variable is defined as (date of the first event - randomization date +1). For patients who have no event on or before Week 52 or last contact date, the time will be censored at the date of date of visit at Week 52 or the last contact date, whichever happens earlier.

[a] derived from Kaplan-Meier estimates.

[b] derived using Cox regression model including the time to the first event as the dependent variable, and treatment groups, age, baseline weight group, baseline eosinophil level, baseline FeNO level, baseline ICS dose level and number of severe exacerbation events within 1 year prior to the study as covariates.

[c] derived using the same Cox regression model as in [b] with subgroup and subgroup-by-treatment interaction as additional covariates.

Type 2 inflammatory asthma phenotype population is defined as the randomized patients with baseline blood eosinophils >= 0.15 Giga/L or baseline FeNO >= 20 ppb.

PGM=DEVOPS/SAR231893/EFC14153/CSR_RWE/REPORT/PGM/eff_time2event_ger_subg_i_t.sas OUT=REPORT/OUTPUT/eff_t2evt_eaw52_ger_cty_t2_t_x.rtf (29JUN2021 - 17:04)

Project Code / Study Number / Analysis: SAR231893 / EFC14153 / CSR_RWE

2 Severe exacerbation events

2.1 Analysis of time to first severe exacerbation event during the 52-week treatment period - ITT type 2 inflammatory asthma phenotype population

2.1.2 By region (Latin America, East Europe, Western Countries)

	Region					
	Latin America		East Europe		Western countries	
Type 2 inflammatory asthma phenotype population - Severe asthma exacerbation	**Placebo (N=51)**	**Dupilumab (N=106)**	**Placebo (N=43)**	**Dupilumab (N=78)**	**Placebo (N=20)**	**Dupilumab (N=52)**
Latin America, Western countries						0.029
East Europe, Western countries						0.011
overall						0.024

Note: The time-to-event variable is defined as (date of the first event - randomization date +1). For patients who have no event on or before Week 52 or last contact date, the time will be censored at the date of date of visit at Week 52 or the last contact date, whichever happens earlier.
[a] derived from Kaplan-Meier estimates.
[b] derived using Cox regression model including the time to the first event as the dependent variable, and treatment groups, age, baseline weight group, baseline eosinophil level, baseline FeNO level, baseline ICS dose level and number of severe exacerbation events within 1 year prior to the study as covariates.
[c] derived using the same Cox regression model as in [b] with subgroup and subgroup-by-treatment interaction as additional covariates.
Type 2 inflammatory asthma phenotype population is defined as the randomized patients with baseline blood eosinophils >= 0.15 Giga/L or baseline FeNO >= 20 ppb.
PGM=DEVOPS/SAR231893/EFC14153/CSR_RWE/REPORT/PGM/eff_time2event_ger_subg_i_t.sas OUT=REPORT/OUTPUT/eff_t2evt_eaw52_ger_cty_t2_t_x.rtf (29JUN2021 - 17:04)

Project Code / Study Number / Analysis: SAR231893 / EFC14153 / CSR_RWE

2 Severe exacerbation events

2.1 Analysis of time to first severe exacerbation event during the 52-week treatment period - ITT type 2 inflammatory asthma phenotype population

2.1.3 By race (Caucasian/white, Black/of African descent, Other)

	Race					
	Caucasian/White		Black/of African descent		Other	
Type 2 inflammatory asthma phenotype population - Severe asthma exacerbation	**Placebo (N=102)**	**Dupilumab (N=208)**	**Placebo (N=5)**	**Dupilumab (N=9)**	**Placebo (N=7)**	**Dupilumab (N=19)**
Number of patients who are censored	67 (65.7%)	161 (77.4%)	1 (20.0%)	7 (77.8%)	0 (0.0%)	14 (73.7%)
Number of patients with event	35 (34.3%)	47 (22.6%)	4 (80.0%)	2 (22.2%)	7 (100.0%)	5 (26.3%)
Median time to first event (days) (95% CI) [a]	NE (NE to NE)	NE (NE to NE)	130.0 (0.00 to NE)	NE (13.00 to NE)	77.0 (8.00 to 200.00)	NE (187.00 to NE)
Kaplan-Meier estimates for probability of a patient with >=1 event (95% CI) up to [a]						
12 weeks	0.108 (0.057 to 0.177)	0.082 (0.050 to 0.125)	0.400 (0.052 to 0.753)	0.222 (0.034 to 0.513)	0.571 (0.172 to 0.837)	0.111 (0.019 to 0.298)
24 weeks	0.225 (0.150 to 0.310)	0.141 (0.098 to 0.193)	0.800 (0.204 to 0.969)	0.222 (0.034 to 0.513)	0.714 (0.258 to 0.920)	0.170 (0.042 to 0.373)

Note: The time-to-event variable is defined as (date of the first event - randomization date +1). For patients who have no event on or before Week 52 or last contact date, the time will be censored at the date of date of visit at Week 52 or the last contact date, whichever happens earlier.

[a] derived from Kaplan-Meier estimates.

[b] derived using Cox regression model including the time to the first event as the dependent variable, and treatment groups, age, baseline weight group, region, baseline eosinophil level, baseline FeNO level, baseline ICS dose level and number of severe exacerbation events within 1 year prior to the study as covariates.

[c] derived using the same Cox regression model as in [b] with subgroup and subgroup-by-treatment interaction as additional covariates.

Type 2 inflammatory asthma phenotype population is defined as the randomized patients with baseline blood eosinophils >= 0.15 Giga/L or baseline FeNO >= 20 ppb.

PGM=DEVOPS/SAR231893/EFC14153/CSR_RWE/REPORT/PGM/eff_time2event_ger_subg_i_t.sas OUT=REPORT/OUTPUT/eff_t2evt_eaw52_ger_race_t2_t_x.rtf (29JUN2021 - 17:04)

Project Code / Study Number / Analysis: SAR231893 / EFC14153 / CSR_RWE

2 Severe exacerbation events

2.1 Analysis of time to first severe exacerbation event during the 52-week treatment period - ITT type 2 inflammatory asthma phenotype population

2.1.3 By race (Caucasian/white, Black/of African descent, Other)

Type 2 inflammatory asthma phenotype population - Severe asthma exacerbation	Race					
	Caucasian/White		Black/of African descent		Other	
	Placebo (N=102)	Dupilumab (N=208)	Placebo (N=5)	Dupilumab (N=9)	Placebo (N=7)	Dupilumab (N=19)
36 weeks	0.294 (0.209 to 0.384)	0.191 (0.140 to 0.247)	0.800 (0.204 to 0.969)	0.222 (0.034 to 0.513)	0.857 (0.334 to 0.979)	0.230 (0.071 to 0.441)
52 weeks	0.343 (0.253 to 0.435)	0.231 (0.176 to 0.291)	0.800 (0.204 to 0.969)	0.222 (0.034 to 0.513)	0.857 (0.334 to 0.979)	0.294 (0.106 to 0.512)
Unstratified Log-Rank test p-value [a]		0.034		0.061		<0.001
Hazard Ratio (95% CI) [b]	-	0.581 (0.369 to 0.915)	-	2E-13 (0 to I)	-	0.039 (0.005 to 0.28)
p-value for Hazard Ratio [b]		0.019		1.000		0.001
p-value for heterogeneity of Hazard Ratio [c]:						

Note: The time-to-event variable is defined as (date of the first event - randomization date +1). For patients who have no event on or before Week 52 or last contact date, the time will be censored at the date of date of visit at Week 52 or the last contact date, whichever happens earlier.

[a] derived from Kaplan-Meier estimates.

[b] derived using Cox regression model including the time to the first event as the dependent variable, and treatment groups, age, baseline weight group, region, baseline eosinophil level, baseline FeNO level, baseline ICS dose level and number of severe exacerbation events within 1 year prior to the study as covariates.

[c] derived using the same Cox regression model as in [b] with subgroup and subgroup-by-treatment interaction as additional covariates.

Type 2 inflammatory asthma phenotype population is defined as the randomized patients with baseline blood eosinophils >= 0.15 Giga/L or baseline FeNO >= 20 ppb.

PGM=DEVOPS/SAR231893/EFC14153/CSR_RWE/REPORT/PGM/eff_time2event_ger_subg_i_t.sas OUT=REPORT/OUTPUT/eff_t2evt_eaw52_ger_race_t2_t_x.rtf (29JUN2021 - 17:04)

Project Code / Study Number / Analysis: SAR231893 / EFC14153 / CSR_RWE

2 Severe exacerbation events

2.1 Analysis of time to first severe exacerbation event during the 52-week treatment period - ITT type 2 inflammatory asthma phenotype population

2.1.3 By race (Caucasian/white, Black/of African descent, Other)

	Race					
	Caucasian/White		Black/of African descent		Other	
Type 2 inflammatory asthma phenotype population - Severe asthma exacerbation	**Placebo (N=102)**	**Dupilumab (N=208)**	**Placebo (N=5)**	**Dupilumab (N=9)**	**Placebo (N=7)**	**Dupilumab (N=19)**
Caucasian/White, Black/of African descent						0.160
Caucasian/White, Other						0.527
Black/of African descent, Other						0.003
overall						0.006

Note: The time-to-event variable is defined as (date of the first event - randomization date +1). For patients who have no event on or before Week 52 or last contact date, the time will be censored at the date of date of visit at Week 52 or the last contact date, whichever happens earlier.

[a] derived from Kaplan-Meier estimates.

[b] derived using Cox regression model including the time to the first event as the dependent variable, and treatment groups, age, baseline weight group, region, baseline eosinophil level, baseline FeNO level, baseline ICS dose level and number of severe exacerbation events within 1 year prior to the study as covariates.

[c] derived using the same Cox regression model as in [b] with subgroup and subgroup-by-treatment interaction as additional covariates.

Type 2 inflammatory asthma phenotype population is defined as the randomized patients with baseline blood eosinophils >= 0.15 Giga/L or baseline FeNO >= 20 ppb.

PGM=DEVOPS/SAR231893/EFC14153/CSR_RWE/REPORT/PGM/eff_time2event_ger_subg_i_t.sas OUT=REPORT/OUTPUT/eff_t2evt_eaw52_ger_race_t2_t_x.rtf (29JUN2021 - 17:04)

Project Code / Study Number / Analysis: SAR231893 / EFC14153 / CSR_RWE

2 Severe exacerbation events

2.1 Analysis of time to first severe exacerbation event during the 52-week treatment period - ITT type 2 inflammatory asthma phenotype population

2.1.4 By baseline ICS dose level (Medium, High)

	Baseline ICS dose level			
	High		Medium	
Type 2 inflammatory asthma phenotype population - Severe asthma exacerbation	**Placebo (N=50)**	**Dupilumab (N=102)**	**Placebo (N=64)**	**Dupilumab (N=131)**
Number of patients who are censored	26 (52.0%)	71 (69.6%)	42 (65.6%)	108 (82.4%)
Number of patients with event	24 (48.0%)	31 (30.4%)	22 (34.4%)	23 (17.6%)
Median time to first event (days) (95% CI) [a]	366.0 (181.00 to NE)	NE (NE to NE)	NE (NE to NE)	NE (NE to NE)
Kaplan-Meier estimates for probability of a patient with >=1 event (95% CI) up to [a]				
12 weeks	0.220 (0.118 to 0.342)	0.158 (0.095 to 0.236)	0.094 (0.038 to 0.180)	0.038 (0.014 to 0.082)
24 weeks	0.340 (0.214 to 0.470)	0.228 (0.152 to 0.313)	0.234 (0.140 to 0.343)	0.085 (0.045 to 0.141)
36 weeks	0.440 (0.301 to 0.571)	0.268 (0.186 to 0.357)	0.281 (0.178 to 0.394)	0.140 (0.087 to 0.206)
52 weeks	0.460 (0.319 to 0.590)	0.308 (0.221 to 0.400)	0.344 (0.231 to 0.459)	0.180 (0.119 to 0.252)

Note: The time-to-event variable is defined as (date of the first event - randomization date +1). For patients who have no event on or before Week 52 or last contact date, the time will be censored at the date of date of visit at Week 52 or the last contact date, whichever happens earlier.
[a] derived from Kaplan-Meier estimates.
[b] derived using Cox regression model including the time to the first event as the dependent variable, and treatment groups, age, baseline weight group, region, baseline eosinophil level, baseline FeNO level and number of severe exacerbation events within 1 year prior to the study as covariates.
[c] derived using the same Cox regression model as in [b] with subgroup and subgroup-by-treatment interaction as additional covariates.
Type 2 inflammatory asthma phenotype population is defined as the randomized patients with baseline blood eosinophils >= 0.15 Giga/L or baseline FeNO >= 20 ppb.
PGM=DEVOPS/SAR231893/EFC14153/CSR_RWE/REPORT/PGM/eff_time2event_ger_subg_i_t.sas OUT=REPORT/OUTPUT/eff_t2evt_eaw52_ger_ics_t2_t_x.rtf (29JUN2021 - 17:05)

Project Code / Study Number / Analysis: SAR231893 / EFC14153 / CSR_RWE

2 Severe exacerbation events

2.1 Analysis of time to first severe exacerbation event during the 52-week treatment period - ITT type 2 inflammatory asthma phenotype population

2.1.4 By baseline ICS dose level (Medium, High)

	Baseline ICS dose level			
	High		Medium	
Type 2 inflammatory asthma phenotype population - Severe asthma exacerbation	**Placebo (N=50)**	**Dupilumab (N=102)**	**Placebo (N=64)**	**Dupilumab (N=131)**
Unstratified Log-Rank test p-value [a]		0.038		0.007
Hazard Ratio (95% CI) [b]	-	0.442 (0.247 to 0.792)	-	0.384 (0.205 to 0.718)
p-value for Hazard Ratio [b]		0.006		0.003
p-value for heterogeneity of Hazard Ratio [c]				0.727

Note: The time-to-event variable is defined as (date of the first event - randomization date +1). For patients who have no event on or before Week 52 or last contact date, the time will be censored at the date of date of visit at Week 52 or the last contact date, whichever happens earlier.

[a] derived from Kaplan-Meier estimates.

[b] derived using Cox regression model including the time to the first event as the dependent variable, and treatment groups, age, baseline weight group, region, baseline eosinophil level, baseline FeNO level and number of severe exacerbation events within 1 year prior to the study as covariates.

[c] derived using the same Cox regression model as in [b] with subgroup and subgroup-by-treatment interaction as additional covariates.

Type 2 inflammatory asthma phenotype population is defined as the randomized patients with baseline blood eosinophils >= 0.15 Giga/L or baseline FeNO >= 20 ppb.

PGM=DEVOPS/SAR231893/EFC14153/CSR_RWE/REPORT/PGM/eff_time2event_ger_subg_i_t.sas OUT=REPORT/OUTPUT/eff_t2evt_eaw52_ger_ics_t2_t_x.rtf (29JUN2021 - 17:05)

Project Code / Study Number / Analysis: SAR231893 / EFC14153 / CSR_RWE

2 Severe exacerbation events

2.1 Analysis of time to first severe exacerbation event during the 52-week treatment period - ITT type 2 inflammatory asthma phenotype population

2.1.5 By baseline ICS dose level 2 (Medium, High)

	Baseline ICS dose level 2			
	High		Medium	
Type 2 inflammatory asthma phenotype population - Severe asthma exacerbation	**Placebo (N=95)**	**Dupilumab (N=200)**	**Placebo (N=19)**	**Dupilumab (N=36)**
Number of patients who are censored	55 (57.9%)	149 (74.5%)	13 (68.4%)	33 (91.7%)
Number of patients with event	40 (42.1%)	51 (25.5%)	6 (31.6%)	3 (8.3%)
Median time to first event (days) (95% CI) [a]	NE (306.00 to NE)	NE (NE to NE)	NE (238.00 to NE)	NE (NE to NE)
Kaplan-Meier estimates for probability of a patient with >=1 event (95% CI) up to [a]				
12 weeks	0.158 (0.093 to 0.238)	0.106 (0.068 to 0.153)	0.105 (0.018 to 0.284)	0.000 (0.000 to 0.000)
24 weeks	0.295 (0.207 to 0.388)	0.167 (0.119 to 0.222)	0.211 (0.066 to 0.410)	0.030 (0.002 to 0.134)
36 weeks	0.368 (0.273 to 0.464)	0.213 (0.159 to 0.272)	0.263 (0.096 to 0.468)	0.091 (0.023 to 0.217)
52 weeks	0.411 (0.311 to 0.507)	0.260 (0.201 to 0.323)	0.316 (0.129 to 0.522)	0.091 (0.023 to 0.217)

Note: The time-to-event variable is defined as (date of the first event - randomization date +1). For patients who have no event on or before Week 52 or last contact date, the time will be censored at the date of date of visit at Week 52 or the last contact date, whichever happens earlier.

[a] derived from Kaplan-Meier estimates.

[b] derived using Cox regression model including the time to the first event as the dependent variable, and treatment groups, age, baseline weight group, region, baseline eosinophil level, baseline FeNO level and number of severe exacerbation events within 1 year prior to the study as covariates.

[c] derived using the same Cox regression model as in [b] with subgroup and subgroup-by-treatment interaction as additional covariates.

Type 2 inflammatory asthma phenotype population is defined as the randomized patients with baseline blood eosinophils >= 0.15 Giga/L or baseline FeNO >= 20 ppb.

PGM=DEVOPS/SAR231893/EFC14153/CSR_RWE/REPORT/PGM/eff_time2event_ger_subg_i_t.sas OUT=REPORT/OUTPUT/eff_t2evt_eaw52_ger_ics2_t2_t_x.rtf (01SEP2021 - 15:25)

Project Code / Study Number / Analysis: SAR231893 / EFC14153 / CSR_RWE

2 Severe exacerbation events

2.1 Analysis of time to first severe exacerbation event during the 52-week treatment period - ITT type 2 inflammatory asthma phenotype population

2.1.5 By baseline ICS dose level 2 (Medium, High)

	Baseline ICS dose level 2			
	High		Medium	
Type 2 inflammatory asthma phenotype population - Severe asthma exacerbation	**Placebo (N=95)**	**Dupilumab (N=200)**	**Placebo (N=19)**	**Dupilumab (N=36)**
Unstratified Log-Rank test p-value [a]		0.004		0.031
Hazard Ratio (95% CI) [b]	-	0.449 (0.291 to 0.692)	-	0.161 (0.027 to 0.965)
p-value for Hazard Ratio [b]		<0.001		0.046
p-value for heterogeneity of Hazard Ratio [c]				0.513

Note: The time-to-event variable is defined as (date of the first event - randomization date +1). For patients who have no event on or before Week 52 or last contact date, the time will be censored at the date of date of visit at Week 52 or the last contact date, whichever happens earlier.

[a] derived from Kaplan-Meier estimates.

[b] derived using Cox regression model including the time to the first event as the dependent variable, and treatment groups, age, baseline weight group, region, baseline eosinophil level, baseline FeNO level and number of severe exacerbation events within 1 year prior to the study as covariates.

[c] derived using the same Cox regression model as in [b] with subgroup and subgroup-by-treatment interaction as additional covariates.

Type 2 inflammatory asthma phenotype population is defined as the randomized patients with baseline blood eosinophils >= 0.15 Giga/L or baseline FeNO >= 20 ppb.

PGM=DEVOPS/SAR231893/EFC14153/CSR_RWE/REPORT/PGM/eff_time2event_ger_subg_i_t.sas OUT=REPORT/OUTPUT/eff_t2evt_eaw52_ger_ics2_t2_t_x.rtf (01SEP2021 - 15:25)

Project Code / Study Number / Analysis: SAR231893 / EFC14153 / CSR_RWE

2 Severe exacerbation events

2.1 Analysis of time to first severe exacerbation event during the 52-week treatment period - ITT type 2 inflammatory asthma phenotype population

2.1.6 By baseline predicted FEV1 (<80%, >=80%)

	Baseline Predicted FEV1			
	<80%		>=80%	
Type 2 inflammatory asthma phenotype population - Severe asthma exacerbation	**Placebo (N=59)**	**Dupilumab (N=116)**	**Placebo (N=55)**	**Dupilumab (N=120)**
Number of patients who are censored	27 (45.8%)	89 (76.7%)	41 (74.5%)	93 (77.5%)
Number of patients with event	32 (54.2%)	27 (23.3%)	14 (25.5%)	27 (22.5%)
Median time to first event (days) (95% CI) [a]	265.0 (168.00 to 366.00)	NE (NE to NE)	NE (NE to NE)	NE (NE to NE)
Kaplan-Meier estimates for probability of a patient with >=1 event (95% CI) up to [a]				
12 weeks	0.203 (0.112 to 0.314)	0.087 (0.044 to 0.147)	0.091 (0.033 to 0.184)	0.093 (0.049 to 0.154)
24 weeks	0.373 (0.252 to 0.494)	0.157 (0.097 to 0.229)	0.182 (0.094 to 0.293)	0.136 (0.082 to 0.205)
36 weeks	0.475 (0.344 to 0.595)	0.184 (0.119 to 0.259)	0.218 (0.121 to 0.334)	0.205 (0.138 to 0.283)
52 weeks	0.525 (0.391 to 0.643)	0.237 (0.163 to 0.318)	0.255 (0.149 to 0.374)	0.232 (0.160 to 0.313)

Note: The time-to-event variable is defined as (date of the first event - randomization date +1). For patients who have no event on or before Week 52 or last contact date, the time will be censored at the date of date of visit at Week 52 or the last contact date, whichever happens earlier.

[a] derived from Kaplan-Meier estimates.

[b] derived using Cox regression model including the time to the first event as the dependent variable, and treatment groups, age, baseline weight group, region, baseline eosinophil level, baseline FeNO level, baseline ICS dose level and number of severe exacerbation events within 1 year prior to the study as covariates.

[c] derived using the same Cox regression model as in [b] with subgroup and subgroup-by-treatment interaction as additional covariates.

Type 2 inflammatory asthma phenotype population is defined as the randomized patients with baseline blood eosinophils >= 0.15 Giga/L or baseline FeNO >= 20 ppb.

PGM=DEVOPS/SAR231893/EFC14153/CSR_RWE/REPORT/PGM/eff_time2event_ger_subg_i_t.sas OUT=REPORT/OUTPUT/eff_t2evt_eaw52_ger_pfev1_t2_t_x.rtf (29JUN2021 - 17:05)

Project Code / Study Number / Analysis: SAR231893 / EFC14153 / CSR_RWE

2 Severe exacerbation events

2.1 Analysis of time to first severe exacerbation event during the 52-week treatment period - ITT type 2 inflammatory asthma phenotype population

2.1.6 By baseline predicted FEV1 (<80%, >=80%)

	Baseline Predicted FEV1			
	<80%		>=80%	
Type 2 inflammatory asthma phenotype population - Severe asthma exacerbation	**Placebo (N=59)**	**Dupilumab (N=116)**	**Placebo (N=55)**	**Dupilumab (N=120)**
Unstratified Log-Rank test p-value [a]		<0.001		0.758
Hazard Ratio (95% CI) [b]	-	0.343 (0.203 to 0.581)	-	0.709 (0.359 to 1.4)
p-value for Hazard Ratio [b]		<0.001		0.322
p-value for heterogeneity of Hazard Ratio [c]				0.196

Note: The time-to-event variable is defined as (date of the first event - randomization date +1). For patients who have no event on or before Week 52 or last contact date, the time will be censored at the date of date of visit at Week 52 or the last contact date, whichever happens earlier.

[a] derived from Kaplan-Meier estimates.

[b] derived using Cox regression model including the time to the first event as the dependent variable, and treatment groups, age, baseline weight group, region, baseline eosinophil level, baseline FeNO level, baseline ICS dose level and number of severe exacerbation events within 1 year prior to the study as covariates.

[c] derived using the same Cox regression model as in [b] with subgroup and subgroup-by-treatment interaction as additional covariates.

Type 2 inflammatory asthma phenotype population is defined as the randomized patients with baseline blood eosinophils >= 0.15 Giga/L or baseline FeNO >= 20 ppb.

PGM=DEVOPS/SAR231893/EFC14153/CSR_RWE/REPORT/PGM/eff_time2event_ger_subg_i_t.sas OUT=REPORT/OUTPUT/eff_t2evt_eaw52_ger_pfev1_t2_t_x.rtf (29JUN2021 - 17:05)

Project Code / Study Number / Analysis: SAR231893 / EFC14153 / CSR_RWE

2 Severe exacerbation events

2.1 Analysis of time to first severe exacerbation event during the 52-week treatment period - ITT type 2 inflammatory asthma phenotype population

2.1.7 By baseline ACQ-7-IA (<=2, >2)

	Baseline ACQ-7-IA			
	<=2		**>2**	
Type 2 inflammatory asthma phenotype population - Severe asthma exacerbation	**Placebo (N=61)**	**Dupilumab (N=126)**	**Placebo (N=53)**	**Dupilumab (N=110)**
Number of patients who are censored	42 (68.9%)	100 (79.4%)	26 (49.1%)	82 (74.5%)
Number of patients with event	19 (31.1%)	26 (20.6%)	27 (50.9%)	28 (25.5%)
Median time to first event (days) (95% CI) [a]	NE (366.00 to NE)	NE (NE to NE)	306.0 (155.00 to NE)	NE (NE to NE)
Kaplan-Meier estimates for probability of a patient with >=1 event (95% CI) up to [a]				
12 weeks	0.049 (0.013 to 0.124)	0.064 (0.030 to 0.116)	0.264 (0.155 to 0.387)	0.120 (0.068 to 0.189)
24 weeks	0.180 (0.096 to 0.286)	0.129 (0.077 to 0.194)	0.396 (0.266 to 0.524)	0.167 (0.104 to 0.243)
36 weeks	0.262 (0.160 to 0.376)	0.178 (0.117 to 0.250)	0.453 (0.316 to 0.580)	0.214 (0.142 to 0.295)
52 weeks	0.295 (0.187 to 0.411)	0.212 (0.145 to 0.288)	0.509 (0.369 to 0.634)	0.262 (0.183 to 0.347)

Note: The time-to-event variable is defined as (date of the first event - randomization date +1). For patients who have no event on or before Week 52 or last contact date, the time will be censored at the date of date of visit at Week 52 or the last contact date, whichever happens earlier.

[a] derived from Kaplan-Meier estimates.

[b] derived using Cox regression model including the time to the first event as the dependent variable, and treatment groups, age, baseline weight group, region, baseline eosinophil level, baseline FeNO level, baseline ICS dose level and number of severe exacerbation events within 1 year prior to the study as covariates.

[c] derived using the same Cox regression model as in [b] with subgroup and subgroup-by-treatment interaction as additional covariates.

Type 2 inflammatory asthma phenotype population is defined as the randomized patients with baseline blood eosinophils >= 0.15 Giga/L or baseline FeNO >= 20 ppb.

PGM=DEVOPS/SAR231893/EFC14153/CSR_RWE/REPORT/PGM/eff_time2event_ger_subg_i_t.sas OUT=REPORT/OUTPUT/eff_t2evt_eaw52_ger_acq7_t2_t_x.rtf (29JUN2021 - 17:05)

Project Code / Study Number / Analysis: SAR231893 / EFC14153 / CSR_RWE

2 Severe exacerbation events

2.1 Analysis of time to first severe exacerbation event during the 52-week treatment period - ITT type 2 inflammatory asthma phenotype population

2.1.7 By baseline ACQ-7-IA (<=2, >2)

	Baseline ACQ-7-IA			
	<=2		>2	
Type 2 inflammatory asthma phenotype population - Severe asthma exacerbation	**Placebo (N=61)**	**Dupilumab (N=126)**	**Placebo (N=53)**	**Dupilumab (N=110)**
Unstratified Log-Rank test p-value [a]		0.151		<0.001
Hazard Ratio (95% CI) [b]	-	0.582 (0.31 to 1.094)	-	0.355 (0.202 to 0.625)
p-value for Hazard Ratio [b]		0.093		<0.001
p-value for heterogeneity of Hazard Ratio [c]				0.171

Note: The time-to-event variable is defined as (date of the first event - randomization date +1). For patients who have no event on or before Week 52 or last contact date, the time will be censored at the date of date of visit at Week 52 or the last contact date, whichever happens earlier.

[a] derived from Kaplan-Meier estimates.

[b] derived using Cox regression model including the time to the first event as the dependent variable, and treatment groups, age, baseline weight group, region, baseline eosinophil level, baseline FeNO level, baseline ICS dose level and number of severe exacerbation events within 1 year prior to the study as covariates.

[c] derived using the same Cox regression model as in [b] with subgroup and subgroup-by-treatment interaction as additional covariates.

Type 2 inflammatory asthma phenotype population is defined as the randomized patients with baseline blood eosinophils >= 0.15 Giga/L or baseline FeNO >= 20 ppb.

PGM=DEVOPS/SAR231893/EFC14153/CSR_RWE/REPORT/PGM/eff_time2event_ger_subg_i_t.sas OUT=REPORT/OUTPUT/eff_t2evt_eaw52_ger_acq7_t2_t_x.rtf (29JUN2021 - 17:05)

Project Code / Study Number / Analysis: SAR231893 / EFC14153 / CSR_RWE

2 Severe exacerbation events

2.1 Analysis of time to first severe exacerbation event during the 52-week treatment period - ITT type 2 inflammatory asthma phenotype population

2.1.8 By baseline weight (<=30 kg, >30 kg)

	Baseline weight (kg)			
	<=30		>30	
Type 2 inflammatory asthma phenotype population - Severe asthma exacerbation	**Placebo (N=36)**	**Dupilumab (N=76)**	**Placebo (N=78)**	**Dupilumab (N=160)**
Number of patients who are censored	19 (52.8%)	62 (81.6%)	49 (62.8%)	120 (75.0%)
Number of patients with event	17 (47.2%)	14 (18.4%)	29 (37.2%)	40 (25.0%)
Median time to first event (days) (95% CI) [a]	NE (148.00 to NE)	NE (NE to NE)	NE (366.00 to NE)	NE (NE to NE)
Kaplan-Meier estimates for probability of a patient with >=1 event (95% CI) up to [a]				
12 weeks	0.194 (0.086 to 0.336)	0.095 (0.042 to 0.174)	0.128 (0.066 to 0.212)	0.088 (0.051 to 0.138)
24 weeks	0.389 (0.233 to 0.542)	0.162 (0.089 to 0.254)	0.231 (0.145 to 0.329)	0.139 (0.091 to 0.198)
36 weeks	0.444 (0.280 to 0.596)	0.176 (0.099 to 0.270)	0.308 (0.209 to 0.411)	0.203 (0.145 to 0.269)
52 weeks	0.472 (0.305 to 0.623)	0.190 (0.110 to 0.287)	0.359 (0.255 to 0.464)	0.255 (0.190 to 0.326)

Note: The time-to-event variable is defined as (date of the first event - randomization date +1). For patients who have no event on or before Week 52 or last contact date, the time will be censored at the date of date of visit at Week 52 or the last contact date, whichever happens earlier.

[a] derived from Kaplan-Meier estimates.

[b] derived using Cox regression model including the time to the first event as the dependent variable, and treatment groups, age, region, baseline eosinophil level, baseline FeNO level, baseline ICS dose level and number of severe exacerbation events within 1 year prior to the study as covariates.

[c] derived using the same Cox regression model as in [b] with subgroup and subgroup-by-treatment interaction as additional covariates.

Type 2 inflammatory asthma phenotype population is defined as the randomized patients with baseline blood eosinophils >= 0.15 Giga/L or baseline FeNO >= 20 ppb.

PGM=DEVOPS/SAR231893/EFC14153/CSR_RWE/REPORT/PGM/eff_time2event_ger_subg_i_t.sas OUT=REPORT/OUTPUT/eff_t2evt_eaw52_ger_wgt_t2_t_x.rtf (29JUN2021 - 17:05)

Project Code / Study Number / Analysis: SAR231893 / EFC14153 / CSR_RWE

2 Severe exacerbation events

2.1 Analysis of time to first severe exacerbation event during the 52-week treatment period - ITT type 2 inflammatory asthma phenotype population

2.1.8 By baseline weight (<=30 kg, >30 kg)

	Baseline weight (kg)			
	<=30		>30	
Type 2 inflammatory asthma phenotype population - Severe asthma exacerbation	**Placebo (N=36)**	**Dupilumab (N=76)**	**Placebo (N=78)**	**Dupilumab (N=160)**
Unstratified Log-Rank test p-value [a]		0.002		0.055
Hazard Ratio (95% CI) [b]	-	0.29 (0.132 to 0.639)	-	0.519 (0.313 to 0.859)
p-value for Hazard Ratio [b]		0.002		0.011
p-value for heterogeneity of Hazard Ratio [c]				0.188

Note: The time-to-event variable is defined as (date of the first event - randomization date +1). For patients who have no event on or before Week 52 or last contact date, the time will be censored at the date of date of visit at Week 52 or the last contact date, whichever happens earlier.

[a] derived from Kaplan-Meier estimates.

[b] derived using Cox regression model including the time to the first event as the dependent variable, and treatment groups, age, region, baseline eosinophil level, baseline FeNO level, baseline ICS dose level and number of severe exacerbation events within 1 year prior to the study as covariates.

[c] derived using the same Cox regression model as in [b] with subgroup and subgroup-by-treatment interaction as additional covariates.

Type 2 inflammatory asthma phenotype population is defined as the randomized patients with baseline blood eosinophils >= 0.15 Giga/L or baseline FeNO >= 20 ppb.

PGM=DEVOPS/SAR231893/EFC14153/CSR_RWE/REPORT/PGM/eff_time2event_ger_subg_i_t.sas OUT=REPORT/OUTPUT/eff_t2evt_eaw52_ger_wgt_t2_t_x.rtf (29JUN2021 - 17:05)

Project Code / Study Number / Analysis: SAR231893 / EFC14153 / CSR_RWE

2 Severe exacerbation events

2.1 Analysis of time to first severe exacerbation event during the 52-week treatment period - ITT type 2 inflammatory asthma phenotype population

2.1.9 By atopic medical condition (Yes, No)

	Atopic medical condition			
	Yes		No	
Type 2 inflammatory asthma phenotype population - Severe asthma exacerbation	**Placebo (N=103)**	**Dupilumab (N=227)**	**Placebo (N=11)**	**Dupilumab (N=9)**
Number of patients who are censored	62 (60.2%)	174 (76.7%)	6 (54.5%)	8 (88.9%)
Number of patients with event	41 (39.8%)	53 (23.3%)	5 (45.5%)	1 (11.1%)
Median time to first event (days) (95% CI) [a]	NE (366.00 to NE)	NE (NE to NE)	NE (115.00 to NE)	NE (6.00 to NE)
Kaplan-Meier estimates for probability of a patient with >=1 event (95% CI) up to [a]				
12 weeks	0.155 (0.093 to 0.232)	0.089 (0.057 to 0.131)	0.091 (0.005 to 0.333)	0.111 (0.006 to 0.388)
24 weeks	0.291 (0.207 to 0.381)	0.148 (0.105 to 0.198)	0.182 (0.029 to 0.442)	0.111 (0.006 to 0.388)
36 weeks	0.359 (0.268 to 0.451)	0.198 (0.149 to 0.253)	0.273 (0.065 to 0.539)	0.111 (0.006 to 0.388)
52 weeks	0.388 (0.295 to 0.481)	0.240 (0.186 to 0.298)	0.455 (0.167 to 0.707)	0.111 (0.006 to 0.388)

Note: The time-to-event variable is defined as (date of the first event - randomization date +1). For patients who have no event on or before Week 52 or last contact date, the time will be censored at the date of date of visit at Week 52 or the last contact date, whichever happens earlier.

[a] derived from Kaplan-Meier estimates.

[b] derived using Cox regression model including the time to the first event as the dependent variable, and treatment groups, age, baseline weight group, region, baseline eosinophil level, baseline FeNO level, baseline ICS dose level and number of severe exacerbation events within 1 year prior to the study as covariates.

[c] derived using the same Cox regression model as in [b] with subgroup and subgroup-by-treatment interaction as additional covariates.

Type 2 inflammatory asthma phenotype population is defined as the randomized patients with baseline blood eosinophils >= 0.15 Giga/L or baseline FeNO >= 20 ppb.

PGM=DEVOPS/SAR231893/EFC14153/CSR_RWE/REPORT/PGM/eff_time2event_ger_subg_i_t.sas OUT=REPORT/OUTPUT/eff_t2evt_eaw52_ger_amc_t2_t_x.rtf (29JUN2021 - 17:05)

Project Code / Study Number / Analysis: SAR231893 / EFC14153 / CSR_RWE

2 Severe exacerbation events

2.1 Analysis of time to first severe exacerbation event during the 52-week treatment period - ITT type 2 inflammatory asthma phenotype population

2.1.9 By atopic medical condition (Yes, No)

	Atopic medical condition			
	Yes		No	
Type 2 inflammatory asthma phenotype population - Severe asthma exacerbation	**Placebo (N=103)**	**Dupilumab (N=227)**	**Placebo (N=11)**	**Dupilumab (N=9)**
Unstratified Log-Rank test p-value [a]		0.002		0.136
Hazard Ratio (95% CI) [b]	-	0.45 (0.291 to 0.694)	-	2E-26 (0 to I)
p-value for Hazard Ratio [b]		<0.001		1.000
p-value for heterogeneity of Hazard Ratio [c]				0.489

Note: The time-to-event variable is defined as (date of the first event - randomization date +1). For patients who have no event on or before Week 52 or last contact date, the time will be censored at the date of date of visit at Week 52 or the last contact date, whichever happens earlier.

[a] derived from Kaplan-Meier estimates.

[b] derived using Cox regression model including the time to the first event as the dependent variable, and treatment groups, age, baseline weight group, region, baseline eosinophil level, baseline FeNO level, baseline ICS dose level and number of severe exacerbation events within 1 year prior to the study as covariates.

[c] derived using the same Cox regression model as in [b] with subgroup and subgroup-by-treatment interaction as additional covariates.

Type 2 inflammatory asthma phenotype population is defined as the randomized patients with baseline blood eosinophils >= 0.15 Giga/L or baseline FeNO >= 20 ppb.

PGM=DEVOPS/SAR231893/EFC14153/CSR_RWE/REPORT/PGM/eff_time2event_ger_subg_i_t.sas OUT=REPORT/OUTPUT/eff_t2evt_eaw52_ger_amc_t2_t_x.rtf (29JUN2021 - 17:05)

Project Code / Study Number / Analysis: SAR231893 / EFC14153 / CSR_RWE

2 Severe exacerbation events

2.1 Analysis of time to first severe exacerbation event during the 52-week treatment period - ITT type 2 inflammatory asthma phenotype population

2.1.10 By baseline total IgE (<median, >= median)

	Baseline Total IgE (IU/mL)			
	<median		>=median	
Type 2 inflammatory asthma phenotype population - Severe asthma exacerbation	**Placebo (N=66)**	**Dupilumab (N=105)**	**Placebo (N=47)**	**Dupilumab (N=125)**
Number of patients who are censored	40 (60.6%)	78 (74.3%)	28 (59.6%)	98 (78.4%)
Number of patients with event	26 (39.4%)	27 (25.7%)	19 (40.4%)	27 (21.6%)
Median time to first event (days) (95% CI) [a]	NE (312.00 to NE)	NE (NE to NE)	NE (258.00 to NE)	NE (NE to NE)
Kaplan-Meier estimates for probability of a patient with >=1 event (95% CI) up to [a]				
12 weeks	0.152 (0.078 to 0.248)	0.105 (0.056 to 0.172)	0.128 (0.052 to 0.239)	0.081 (0.041 to 0.137)
24 weeks	0.273 (0.172 to 0.383)	0.172 (0.107 to 0.250)	0.277 (0.159 to 0.408)	0.130 (0.078 to 0.195)
36 weeks	0.348 (0.237 to 0.463)	0.211 (0.139 to 0.294)	0.340 (0.210 to 0.475)	0.187 (0.124 to 0.260)
52 weeks	0.379 (0.263 to 0.494)	0.260 (0.180 to 0.347)	0.404 (0.265 to 0.539)	0.221 (0.152 to 0.298)

Note: The time-to-event variable is defined as (date of the first event - randomization date +1). For patients who have no event on or before Week 52 or last contact date, the time will be censored at the date of date of visit at Week 52 or the last contact date, whichever happens earlier.

[a] derived from Kaplan-Meier estimates.

[b] derived using Cox regression model including the time to the first event as the dependent variable, and treatment groups, age, baseline weight group, region, baseline eosinophil level, baseline FeNO level, baseline ICS dose level and number of severe exacerbation events within 1 year prior to the study as covariates.

[c] derived using the same Cox regression model as in [b] with subgroup and subgroup-by-treatment interaction as additional covariates.

Type 2 inflammatory asthma phenotype population is defined as the randomized patients with baseline blood eosinophils >= 0.15 Giga/L or baseline FeNO >= 20 ppb.

PGM=DEVOPS/SAR231893/EFC14153/CSR_RWE/REPORT/PGM/eff_time2event_ger_subg_i_t.sas OUT=REPORT/OUTPUT/eff_t2evt_eaw52_ger_igem_t2_t_x.rtf (29JUN2021 - 17:05)

Project Code / Study Number / Analysis: SAR231893 / EFC14153 / CSR_RWE

2 Severe exacerbation events

2.1 Analysis of time to first severe exacerbation event during the 52-week treatment period - ITT type 2 inflammatory asthma phenotype population

2.1.10 By baseline total IgE (<median, >= median)

	Baseline Total IgE (IU/mL)			
	<median		>=median	
Type 2 inflammatory asthma phenotype population - Severe asthma exacerbation	**Placebo (N=66)**	**Dupilumab (N=105)**	**Placebo (N=47)**	**Dupilumab (N=125)**
Unstratified Log-Rank test p-value [a]		0.060		0.014
Hazard Ratio (95% CI) [b]	-	0.518 (0.293 to 0.919)	-	0.4 (0.216 to 0.739)
p-value for Hazard Ratio [b]		0.024		0.003
p-value for heterogeneity of Hazard Ratio [c]				0.553

Note: The time-to-event variable is defined as (date of the first event - randomization date +1). For patients who have no event on or before Week 52 or last contact date, the time will be censored at the date of date of visit at Week 52 or the last contact date, whichever happens earlier.

[a] derived from Kaplan-Meier estimates.

[b] derived using Cox regression model including the time to the first event as the dependent variable, and treatment groups, age, baseline weight group, region, baseline eosinophil level, baseline FeNO level, baseline ICS dose level and number of severe exacerbation events within 1 year prior to the study as covariates.

[c] derived using the same Cox regression model as in [b] with subgroup and subgroup-by-treatment interaction as additional covariates.

Type 2 inflammatory asthma phenotype population is defined as the randomized patients with baseline blood eosinophils >= 0.15 Giga/L or baseline FeNO >= 20 ppb.

PGM=DEVOPS/SAR231893/EFC14153/CSR_RWE/REPORT/PGM/eff_time2event_ger_subg_i_t.sas OUT=REPORT/OUTPUT/eff_t2evt_eaw52_ger_igem_t2_t_x.rtf (29JUN2021 - 17:05)

Project Code / Study Number / Analysis: SAR231893 / EFC14153 / CSR_RWE

2 Severe exacerbation events

2.1 Analysis of time to first severe exacerbation event during the 52-week treatment period - ITT type 2 inflammatory asthma phenotype population

2.1.11 By baseline total IgE (<100 IU/ml, >= 100 IU/ml)

	Baseline Total IgE (IU/mL)			
	< 100		**>= 100**	
Type 2 inflammatory asthma phenotype population - Severe asthma exacerbation	**Placebo (N=22)**	**Dupilumab (N=29)**	**Placebo (N=91)**	**Dupilumab (N=201)**
Number of patients who are censored	15 (68.2%)	23 (79.3%)	53 (58.2%)	153 (76.1%)
Number of patients with event	7 (31.8%)	6 (20.7%)	38 (41.8%)	48 (23.9%)
Median time to first event (days) (95% CI) [a]	NE (260.00 to NE)	NE (NE to NE)	366.0 (265.00 to NE)	NE (NE to NE)
Kaplan-Meier estimates for probability of a patient with >=1 event (95% CI) up to [a]				
12 weeks	0.091 (0.016 to 0.251)	0.103 (0.026 to 0.243)	0.154 (0.089 to 0.235)	0.090 (0.055 to 0.135)
24 weeks	0.182 (0.057 to 0.363)	0.172 (0.063 to 0.327)	0.297 (0.207 to 0.392)	0.146 (0.101 to 0.198)
36 weeks	0.227 (0.083 to 0.414)	0.207 (0.084 to 0.367)	0.374 (0.275 to 0.472)	0.197 (0.145 to 0.255)
52 weeks	0.318 (0.142 to 0.511)	0.207 (0.084 to 0.367)	0.407 (0.306 to 0.505)	0.244 (0.186 to 0.306)

Note: The time-to-event variable is defined as (date of the first event - randomization date +1). For patients who have no event on or before Week 52 or last contact date, the time will be censored at the date of date of visit at Week 52 or the last contact date, whichever happens earlier.

[a] derived from Kaplan-Meier estimates.

[b] derived using Cox regression model including the time to the first event as the dependent variable, and treatment groups, age, baseline weight group, region, baseline eosinophil level, baseline FeNO level, baseline ICS dose level and number of severe exacerbation events within 1 year prior to the study as covariates.

[c] derived using the same Cox regression model as in [b] with subgroup and subgroup-by-treatment interaction as additional covariates.

Type 2 inflammatory asthma phenotype population is defined as the randomized patients with baseline blood eosinophils >= 0.15 Giga/L or baseline FeNO >= 20 ppb.

PGM=DEVOPS/SAR231893/EFC14153/CSR_RWE/REPORT/PGM/eff_time2event_ger_subg_i_t.sas OUT=REPORT/OUTPUT/eff_t2evt_eaw52_ger_ige_t2_t_x.rtf (29JUN2021 - 17:06)

Project Code / Study Number / Analysis: SAR231893 / EFC14153 / CSR_RWE

2 Severe exacerbation events

2.1 Analysis of time to first severe exacerbation event during the 52-week treatment period - ITT type 2 inflammatory asthma phenotype population

2.1.11 By baseline total IgE (<100 IU/ml, >= 100 IU/ml)

	Baseline Total IgE (IU/mL)			
	< 100		>= 100	
Type 2 inflammatory asthma phenotype population - Severe asthma exacerbation	**Placebo (N=22)**	**Dupilumab (N=29)**	**Placebo (N=91)**	**Dupilumab (N=201)**
Unstratified Log-Rank test p-value [a]		0.431		0.002
Hazard Ratio (95% CI) [b]	-	0.316 (0.08 to 1.24)	-	0.448 (0.286 to 0.702)
p-value for Hazard Ratio [b]		0.099		<0.001
p-value for heterogeneity of Hazard Ratio [c]				0.957

Note: The time-to-event variable is defined as (date of the first event - randomization date +1). For patients who have no event on or before Week 52 or last contact date, the time will be censored at the date of date of visit at Week 52 or the last contact date, whichever happens earlier.

[a] derived from Kaplan-Meier estimates.

[b] derived using Cox regression model including the time to the first event as the dependent variable, and treatment groups, age, baseline weight group, region, baseline eosinophil level, baseline FeNO level, baseline ICS dose level and number of severe exacerbation events within 1 year prior to the study as covariates.

[c] derived using the same Cox regression model as in [b] with subgroup and subgroup-by-treatment interaction as additional covariates.

Type 2 inflammatory asthma phenotype population is defined as the randomized patients with baseline blood eosinophils >= 0.15 Giga/L or baseline FeNO >= 20 ppb.

PGM=DEVOPS/SAR231893/EFC14153/CSR_RWE/REPORT/PGM/eff_time2event_ger_subg_i_t.sas OUT=REPORT/OUTPUT/eff_t2evt_eaw52_ger_ige_t2_t_x.rtf (29JUN2021 - 17:06)

Project Code / Study Number / Analysis: SAR231893 / EFC14153 / CSR_RWE

2 Severe exacerbation events

2.1 Analysis of time to first severe exacerbation event during the 52-week treatment period - ITT type 2 inflammatory asthma phenotype population

2.1.12 By age at onset of asthma (0-2, 3-5, >=6 years)

	Age of onset of asthma (years)					
	0-2		3-5		>= 6	
Type 2 inflammatory asthma phenotype population - Severe asthma exacerbation	**Placebo (N=40)**	**Dupilumab (N=105)**	**Placebo (N=39)**	**Dupilumab (N=86)**	**Placebo (N=35)**	**Dupilumab (N=45)**
Number of patients who are censored	17 (42.5%)	75 (71.4%)	28 (71.8%)	67 (77.9%)	23 (65.7%)	40 (88.9%)
Number of patients with event	23 (57.5%)	30 (28.6%)	11 (28.2%)	19 (22.1%)	12 (34.3%)	5 (11.1%)
Median time to first event (days) (95% CI) [a]	259.0 (155.00 to NE)	NE (NE to NE)	NE (NE to NE)	NE (NE to NE)	NE (312.00 to NE)	NE (NE to NE)
Kaplan-Meier estimates for probability of a patient with >=1 event (95% CI) up to [a]						
12 weeks	0.175 (0.077 to 0.306)	0.125 (0.070 to 0.196)	0.154 (0.062 to 0.283)	0.071 (0.029 to 0.139)	0.114 (0.036 to 0.242)	0.044 (0.008 to 0.133)
24 weeks	0.375 (0.229 to 0.521)	0.163 (0.100 to 0.241)	0.205 (0.096 to 0.342)	0.168 (0.097 to 0.255)	0.257 (0.128 to 0.408)	0.067 (0.017 to 0.165)

Note: The time-to-event variable is defined as (date of the first event - randomization date +1). For patients who have no event on or before Week 52 or last contact date, the time will be censored at the date of date of visit at Week 52 or the last contact date, whichever happens earlier.

[a] derived from Kaplan-Meier estimates.

[b] derived using Cox regression model including the time to the first event as the dependent variable, and treatment groups, age, baseline weight group, region, baseline eosinophil level, baseline FeNO level, baseline ICS dose level and number of severe exacerbation events within 1 year prior to the study as covariates.

[c] derived using the same Cox regression model as in [b] with subgroup and subgroup-by-treatment interaction as additional covariates.

Type 2 inflammatory asthma phenotype population is defined as the randomized patients with baseline blood eosinophils >= 0.15 Giga/L or baseline FeNO >= 20 ppb.

PGM=DEVOPS/SAR231893/EFC14153/CSR_RWE/REPORT/PGM/eff_time2event_ger_subg_i_t.sas OUT=REPORT/OUTPUT/eff_t2evt_eaw52_ger_onsa_t2_t_x.rtf (10AUG2021 - 16:23)

Project Code / Study Number / Analysis: SAR231893 / EFC14153 / CSR_RWE

2 Severe exacerbation events

2.1 Analysis of time to first severe exacerbation event during the 52-week treatment period - ITT type 2 inflammatory asthma phenotype population

2.1.12 By age at onset of asthma (0-2, 3-5, >=6 years)

	Age of onset of asthma (years)					
	0-2		3-5		>= 6	
Type 2 inflammatory asthma phenotype population - Severe asthma exacerbation	**Placebo (N=40)**	**Dupilumab (N=105)**	**Placebo (N=39)**	**Dupilumab (N=86)**	**Placebo (N=35)**	**Dupilumab (N=45)**
36 weeks	0.475 (0.316 to 0.618)	0.240 (0.163 to 0.326)	0.256 (0.133 to 0.399)	0.192 (0.116 to 0.283)	0.314 (0.171 to 0.468)	0.091 (0.029 to 0.196)
52 weeks	0.550 (0.385 to 0.688)	0.290 (0.206 to 0.380)	0.282 (0.153 to 0.427)	0.230 (0.146 to 0.325)	0.343 (0.193 to 0.498)	0.114 (0.042 to 0.226)
Unstratified Log-Rank test p-value [a]		0.001		0.486		0.013
Hazard Ratio (95% CI) [b]	-	0.337 (0.188 to 0.602)	-	0.746 (0.346 to 1.607)	-	0.341 (0.111 to 1.044)
p-value for Hazard Ratio [b]		<0.001		0.454		0.060
p-value for heterogeneity of Hazard Ratio [c]:						
0-2, 3-5						0.140

Note: The time-to-event variable is defined as (date of the first event - randomization date +1). For patients who have no event on or before Week 52 or last contact date, the time will be censored at the date of date of visit at Week 52 or the last contact date, whichever happens earlier.

[a] derived from Kaplan-Meier estimates.

[b] derived using Cox regression model including the time to the first event as the dependent variable, and treatment groups, age, baseline weight group, region, baseline eosinophil level, baseline FeNO level, baseline ICS dose level and number of severe exacerbation events within 1 year prior to the study as covariates.

[c] derived using the same Cox regression model as in [b] with subgroup and subgroup-by-treatment interaction as additional covariates.

Type 2 inflammatory asthma phenotype population is defined as the randomized patients with baseline blood eosinophils >= 0.15 Giga/L or baseline FeNO >= 20 ppb.

PGM=DEVOPS/SAR231893/EFC14153/CSR_RWE/REPORT/PGM/eff_time2event_ger_subg_i_t.sas OUT=REPORT/OUTPUT/eff_t2evt_eaw52_ger_onsa_t2_t_x.rtf (10AUG2021 - 16:23)

Project Code / Study Number / Analysis: SAR231893 / EFC14153 / CSR_RWE

2 Severe exacerbation events

2.1 Analysis of time to first severe exacerbation event during the 52-week treatment period - ITT type 2 inflammatory asthma phenotype population

2.1.12 By age at onset of asthma (0-2, 3-5, >=6 years)

	Age of onset of asthma (years)					
	0-2		3-5		>= 6	
Type 2 inflammatory asthma phenotype population - Severe asthma exacerbation	**Placebo (N=40)**	**Dupilumab (N=105)**	**Placebo (N=39)**	**Dupilumab (N=86)**	**Placebo (N=35)**	**Dupilumab (N=45)**
0-2, >= 6						0.886
3-5, >= 6						0.231
overall						0.285

Note: The time-to-event variable is defined as (date of the first event - randomization date +1). For patients who have no event on or before Week 52 or last contact date, the time will be censored at the date of date of visit at Week 52 or the last contact date, whichever happens earlier.

[a] derived from Kaplan-Meier estimates.

[b] derived using Cox regression model including the time to the first event as the dependent variable, and treatment groups, age, baseline weight group, region, baseline eosinophil level, baseline FeNO level, baseline ICS dose level and number of severe exacerbation events within 1 year prior to the study as covariates.

[c] derived using the same Cox regression model as in [b] with subgroup and subgroup-by-treatment interaction as additional covariates.

Type 2 inflammatory asthma phenotype population is defined as the randomized patients with baseline blood eosinophils >= 0.15 Giga/L or baseline FeNO >= 20 ppb.

PGM=DEVOPS/SAR231893/EFC14153/CSR_RWE/REPORT/PGM/eff_time2event_ger_subg_i_t.sas OUT=REPORT/OUTPUT/eff_t2evt_eaw52_ger_onsa_t2_t_x.rtf (10AUG2021 - 16:23)

Project Code / Study Number / Analysis: SAR231893 / EFC14153 / CSR_RWE

2 Severe exacerbation events

2.1 Analysis of time to first severe exacerbation event during the 52-week treatment period - ITT type 2 inflammatory asthma phenotype population

2.1.13 By number of severe asthma exacerbation prior to the study (<=1, 2, >2)

	Number of severe asthma exacerbation prior to the study					
	<=1		**2**		**>2**	
Type 2 inflammatory asthma phenotype population - Severe asthma exacerbation	**Placebo (N=47)**	**Dupilumab (N=85)**	**Placebo (N=32)**	**Dupilumab (N=75)**	**Placebo (N=35)**	**Dupilumab (N=76)**
Number of patients who are censored	31 (66.0%)	74 (87.1%)	19 (59.4%)	60 (80.0%)	18 (51.4%)	48 (63.2%)
Number of patients with event	16 (34.0%)	11 (12.9%)	13 (40.6%)	15 (20.0%)	17 (48.6%)	28 (36.8%)
Median time to first event (days) (95% CI) [a]	NE (NE to NE)	NE (NE to NE)	NE (200.00 to NE)	NE (NE to NE)	366.0 (130.00 to 366.00)	NE (338.00 to NE)
Kaplan-Meier estimates for probability of a patient with >=1 event (95% CI) up to [a]						
12 weeks	0.085 (0.027 to 0.186)	0.048 (0.015 to 0.108)	0.156 (0.057 to 0.300)	0.080 (0.033 to 0.155)	0.229 (0.108 to 0.376)	0.148 (0.079 to 0.238)
24 weeks	0.213 (0.110 to 0.338)	0.071 (0.029 to 0.139)	0.281 (0.140 to 0.441)	0.121 (0.059 to 0.206)	0.371 (0.216 to 0.527)	0.258 (0.165 to 0.361)

Note: The time-to-event variable is defined as (date of the first event - randomization date +1). For patients who have no event on or before Week 52 or last contact date, the time will be censored at the date of date of visit at Week 52 or the last contact date, whichever happens earlier.

[a] derived from Kaplan-Meier estimates.

[b] derived using Cox regression model including the time to the first event as the dependent variable, and treatment groups, age, baseline weight group, region, baseline eosinophil level, baseline FeNO level and baseline ICS dose level as covariates.

[c] derived using the same Cox regression model as in [b] with subgroup and subgroup-by-treatment interaction as additional covariates.

Type 2 inflammatory asthma phenotype population is defined as the randomized patients with baseline blood eosinophils >= 0.15 Giga/L or baseline FeNO >= 20 ppb.

PGM=DEVOPS/SAR231893/EFC14153/CSR_RWE/REPORT/PGM/eff_time2event_ger_subg_i_t.sas OUT=REPORT/OUTPUT/eff_t2evt_eaw52_ger_exa_t2_t_x.rtf (29JUN2021 - 17:06)

Project Code / Study Number / Analysis: SAR231893 / EFC14153 / CSR_RWE

2 Severe exacerbation events

2.1 Analysis of time to first severe exacerbation event during the 52-week treatment period - ITT type 2 inflammatory asthma phenotype population

2.1.13 By number of severe asthma exacerbation prior to the study (<=1, 2, >2)

	Number of severe asthma exacerbation prior to the study					
	<=1		2		>2	
Type 2 inflammatory asthma phenotype population - Severe asthma exacerbation	**Placebo (N=47)**	**Dupilumab (N=85)**	**Placebo (N=32)**	**Dupilumab (N=75)**	**Placebo (N=35)**	**Dupilumab (N=76)**
36 weeks	0.319 (0.193 to 0.453)	0.107 (0.053 to 0.184)	0.344 (0.188 to 0.506)	0.176 (0.099 to 0.270)	0.400 (0.240 to 0.555)	0.314 (0.212 to 0.421)
52 weeks	0.340 (0.210 to 0.475)	0.132 (0.070 to 0.213)	0.406 (0.238 to 0.568)	0.204 (0.121 to 0.303)	0.457 (0.289 to 0.610)	0.385 (0.274 to 0.495)
Unstratified Log-Rank test p-value [a]		0.004		0.024		0.244
Hazard Ratio (95% CI) [b]	-	0.218 (0.094 to 0.51)	-	0.378 (0.165 to 0.867)	-	0.588 (0.307 to 1.126)
p-value for Hazard Ratio [b]		<0.001		0.022		0.109
p-value for heterogeneity of Hazard Ratio [c]:						
<=1, 2						0.316
<=1, >2						0.085

Note: The time-to-event variable is defined as (date of the first event - randomization date +1). For patients who have no event on or before Week 52 or last contact date, the time will be censored at the date of date of visit at Week 52 or the last contact date, whichever happens earlier.

[a] derived from Kaplan-Meier estimates.

[b] derived using Cox regression model including the time to the first event as the dependent variable, and treatment groups, age, baseline weight group, region, baseline eosinophil level, baseline FeNO level and baseline ICS dose level as covariates.

[c] derived using the same Cox regression model as in [b] with subgroup and subgroup-by-treatment interaction as additional covariates.

Type 2 inflammatory asthma phenotype population is defined as the randomized patients with baseline blood eosinophils >= 0.15 Giga/L or baseline FeNO >= 20 ppb.

PGM=DEVOPS/SAR231893/EFC14153/CSR_RWE/REPORT/PGM/eff_time2event_ger_subg_i_t.sas OUT=REPORT/OUTPUT/eff_t2evt_eaw52_ger_exa_t2_t_x.rtf (29JUN2021 - 17:06)

Project Code / Study Number / Analysis: SAR231893 / EFC14153 / CSR_RWE

2 Severe exacerbation events

2.1 Analysis of time to first severe exacerbation event during the 52-week treatment period - ITT type 2 inflammatory asthma phenotype population

2.1.13 By number of severe asthma exacerbation prior to the study (<=1, 2, >2)

	Number of severe asthma exacerbation prior to the study					
	<=1		2		>2	
Type 2 inflammatory asthma phenotype population - Severe asthma exacerbation	**Placebo (N=47)**	**Dupilumab (N=85)**	**Placebo (N=32)**	**Dupilumab (N=75)**	**Placebo (N=35)**	**Dupilumab (N=76)**
2, >2						0.531
overall						0.227

Note: The time-to-event variable is defined as (date of the first event - randomization date +1). For patients who have no event on or before Week 52 or last contact date, the time will be censored at the date of date of visit at Week 52 or the last contact date, whichever happens earlier.

[a] derived from Kaplan-Meier estimates.

[b] derived using Cox regression model including the time to the first event as the dependent variable, and treatment groups, age, baseline weight group, region, baseline eosinophil level, baseline FeNO level and baseline ICS dose level as covariates.

[c] derived using the same Cox regression model as in [b] with subgroup and subgroup-by-treatment interaction as additional covariates.

Type 2 inflammatory asthma phenotype population is defined as the randomized patients with baseline blood eosinophils >= 0.15 Giga/L or baseline FeNO >= 20 ppb.

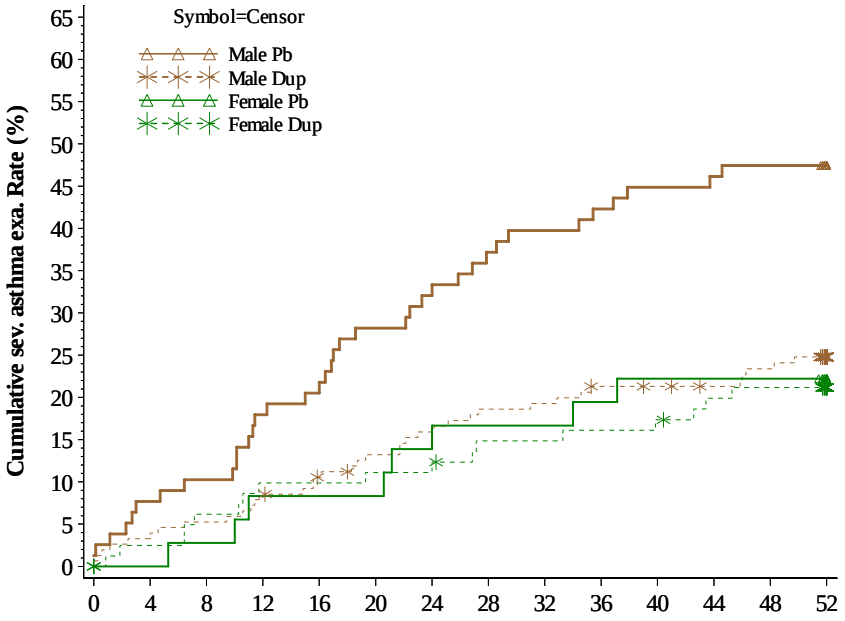
PGM=DEVOPS/SAR231893/EFC14153/CSR_RWE/REPORT/PGM/eff_time2event_ger_subg_i_t.sas OUT=REPORT/OUTPUT/eff_t2evt_eaw52_ger_exa_t2_t_x.rtf (29JUN2021 - 17:06)

Project Code / Study Number / Analysis: SAR231893 / EFC14153 / CSR_RWE

2 Severe exacerbation events

2.2 Kaplan-Meier plot of time to first severe exacerbation event during the 52-week treatment period - ITT type 2 inflammatory asthma phenotype population

2.2.1 By gender (Male, Female)



Number at Risk

Male Pb	78	72	70	64	62	56	53	49	47	45	43	42	41	32
Male Dup	152	147	144	140	134	129	125	121	120	116	115	113	110	81
Female Pb	36	36	35	33	33	33	31	30	30	29	28	28	28	22
Female Dup	84	79	76	73	73	72	72	68	68	67	66	63	62	48

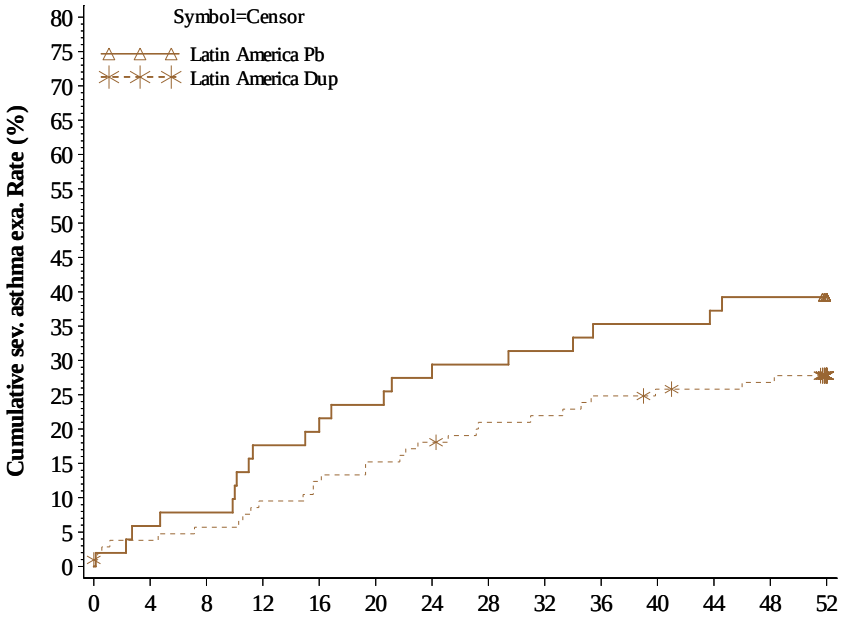
PGM=DEVOPS/SAR231893/EFC14153/CSR_RWE/REPORT/PGM/eff_eventkm_ger_subg_i_g.sas OUT=REPORT/OUTPUT/eff_evtkm_eaw52_ger_sex_t2_g_x.rtf (18JUN2021 - 15:30)

Project Code / Study Number / Analysis: SAR231893 / EFC14153 / CSR_RWE

2 Severe exacerbation events

2.2 Kaplan-Meier plot of time to first severe exacerbation event during the 52-week treatment period - ITT type 2 inflammatory asthma phenotype population

2.2.2 By region (Latin America)



Number at Risk

Latin America Pb	51	48	47	42	41	39	37	36	35	33	33	32	31	26
Latin America Dup	106	101	99	95	92	89	86	82	81	78	76	75	74	54

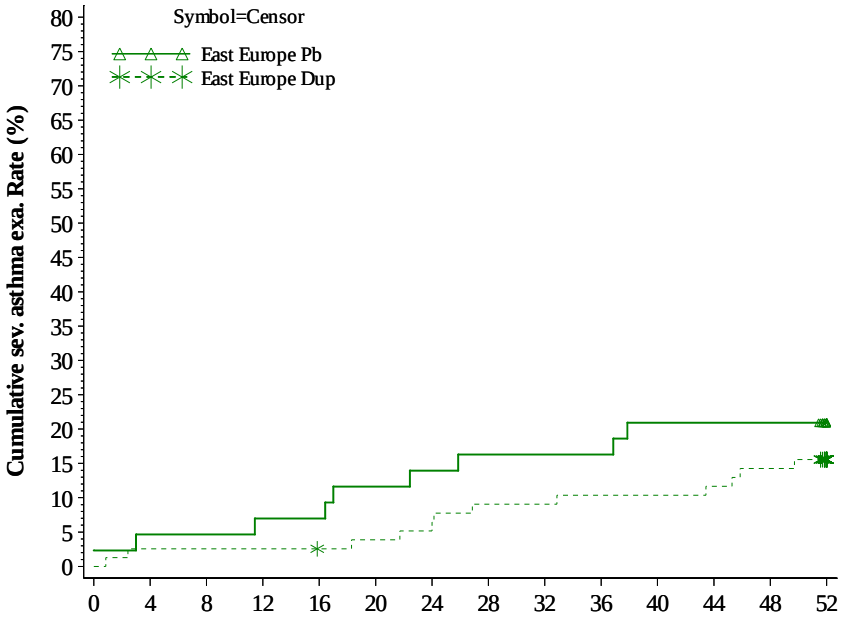
PGM=DEVOPS/SAR231893/EFC14153/CSR_RWE/REPORT/PGM/eff_eventkm_ger_subg_i_g.sas OUT=REPORT/OUTPUT/eff_evtkm_eaw52_ger_cty1_t2_g_x.rtf (18JUN2021 - 15:30)

Project Code / Study Number / Analysis: SAR231893 / EFC14153 / CSR_RWE

2 Severe exacerbation events

2.2 Kaplan-Meier plot of time to first severe exacerbation event during the 52-week treatment period - ITT type 2 inflammatory asthma phenotype population

2.2.3 By region (East Europe)



Number at Risk

East Europe Pb	43	41	41	40	40	38	37	36	36	36	34	34	34	26
East Europe Dup	78	76	76	76	75	74	73	70	70	69	69	68	66	52

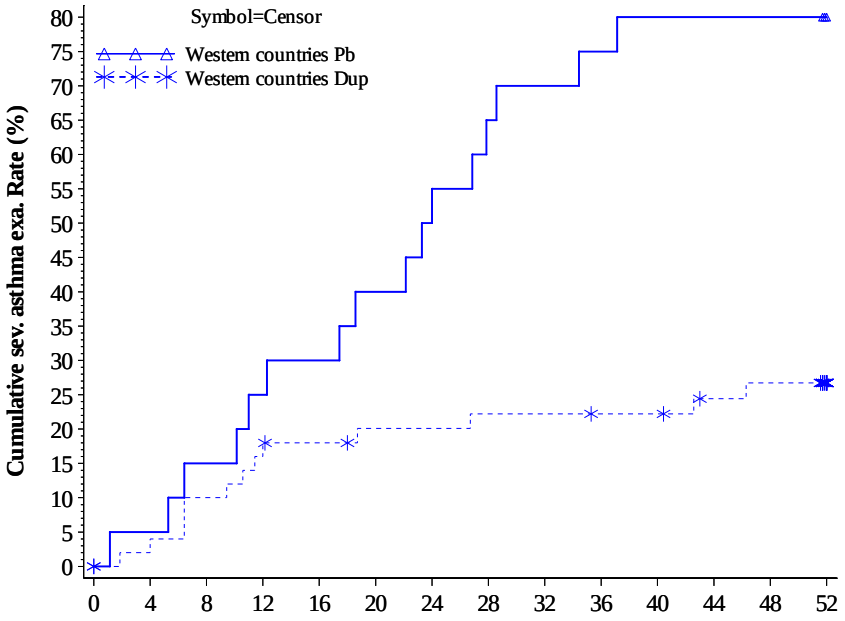
PGM=DEVOPS/SAR231893/EFC14153/CSR_RWE/REPORT/PGM/eff_eventkm_ger_subg_i_g.sas OUT=REPORT/OUTPUT/eff_evtkm_eaw52_ger_cty2_t2_g_x.rtf (18JUN2021 - 15:30)

Project Code / Study Number / Analysis: SAR231893 / EFC14153 / CSR_RWE

2 Severe exacerbation events

2.2 Kaplan-Meier plot of time to first severe exacerbation event during the 52-week treatment period - ITT type 2 inflammatory asthma phenotype population

2.2.4 By region (Western Countries)

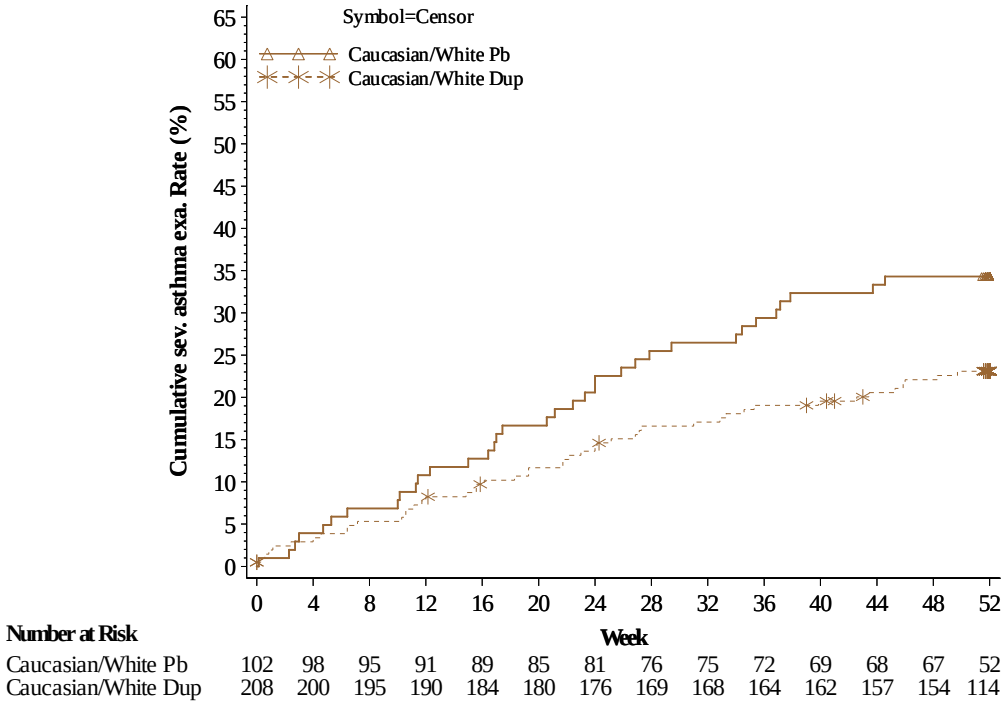


Number at Risk

Western countries Pb	20	19	17	15	14	12	10	7	6	5	4	4	4	2
Western countries Dup	52	49	45	42	40	38	38	37	37	36	36	33	32	23

PGM=DEVOPS/SAR231893/EFC14153/CSR_RWE/REPORT/PGM/eff_eventkm_ger_subg_i_g.sas OUT=REPORT/OUTPUT/eff_evtkm_eaw52_ger_cty3_t2_g_x.rtf (18JUN2021 - 15:30)

Project Code / Study Number / Analysis: SAR231893 / EFC14153 / CSR_RWE
2 Severe exacerbation events
2.2 Kaplan-Meier plot of time to first severe exacerbation event during the 52-week treatment period - ITT type 2 inflammatory asthma phenotype population
2.2.5 By race (Caucasian/white)



Number at Risk

Caucasian/White Pb	102	98	95	91	89	85	81	76	75	72	69	68	67	52
Caucasian/White Dup	208	200	195	190	184	180	176	169	168	164	162	157	154	114

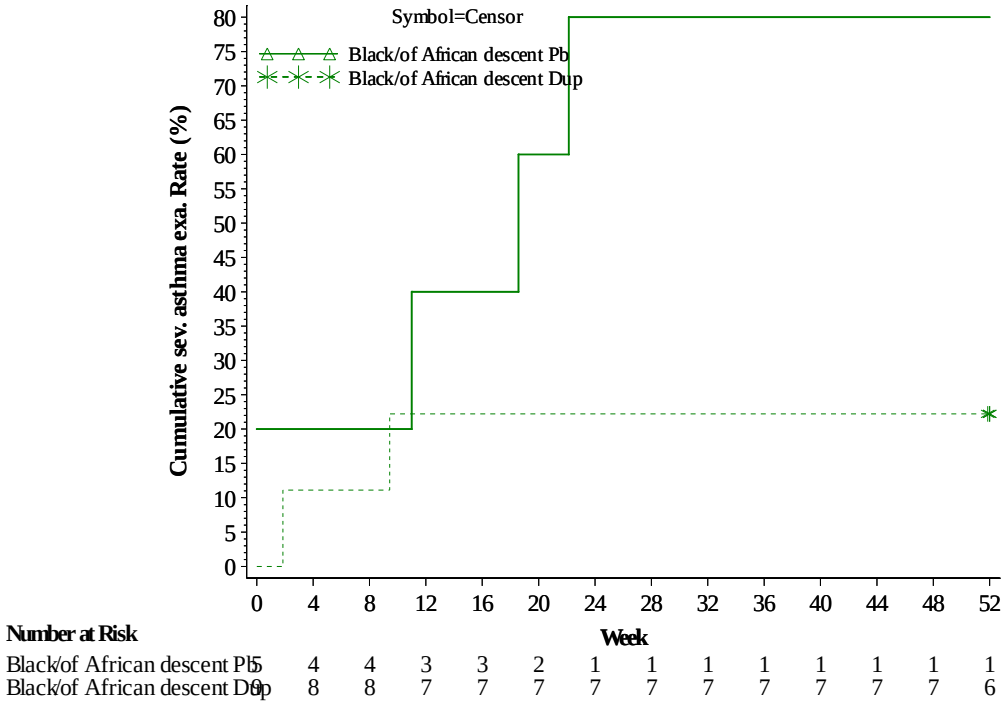
PGM=DEVOPS/SAR231893/EFC14153/CSR_RWE/REPORT/PGM/eff_eventkm_ger_subg_i_g.sas OUT=REPORT/OUTPUT/eff_evtkm_eaw52_ger_race1_t2_g_x.rtf (18JUN2021 - 15:30)

Project Code / Study Number / Analysis: SAR231893 / EFC14153 / CSR_RWE

2 Severe exacerbation events

2.2 Kaplan-Meier plot of time to first severe exacerbation event during the 52-week treatment period - ITT type 2 inflammatory asthma phenotype population

2.2.6 By race (Black/of African descent)



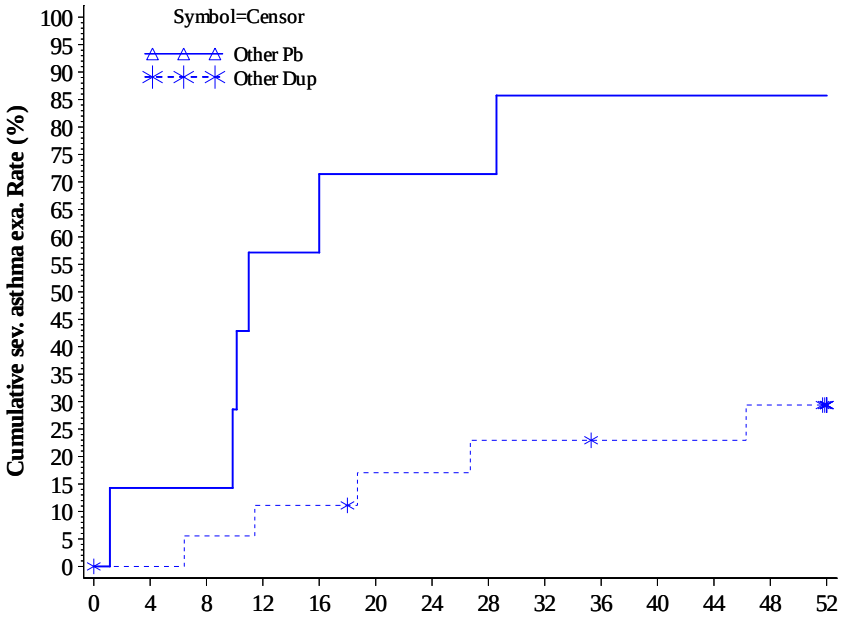
PGM=DEVOPS/SAR231893/EFC14153/CSR_RWE/REPORT/PGM/eff_eventkm_ger_subg_i_g.sas OUT=REPORT/OUTPUT/eff_evtkm_eaw52_ger_race2_t2_g_x.rtf (18JUN2021 - 15:30)

Project Code / Study Number / Analysis: SAR231893 / EFC14153 / CSR_RWE

2 Severe exacerbation events

2.2 Kaplan-Meier plot of time to first severe exacerbation event during the 52-week treatment period - ITT type 2 inflammatory asthma phenotype population

2.2.7 By race (Other)



Number at Risk

Other Pb	7	6	6	3	3	2	2	2	1	1	1	1	1	1
Other Dup	19	18	17	16	16	14	14	13	13	12	12	12	11	9

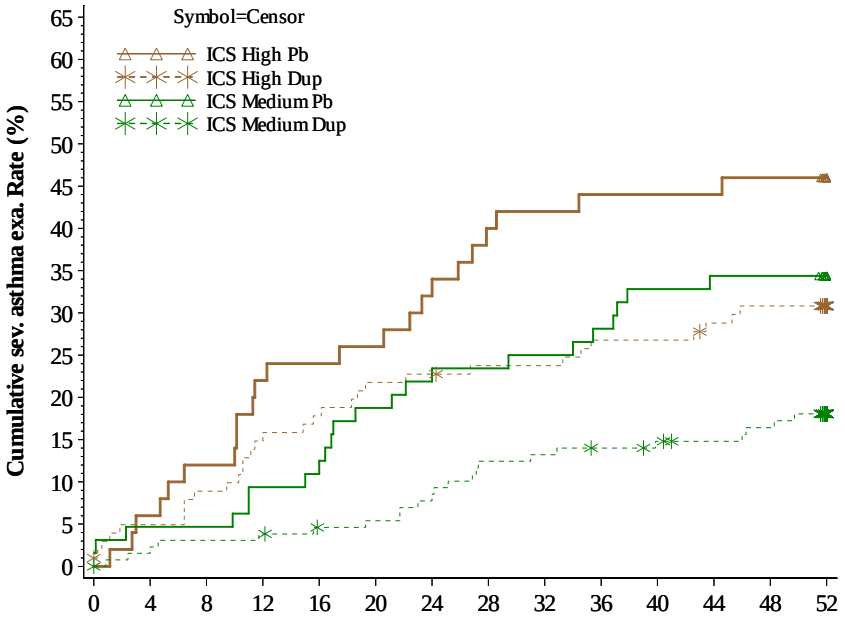
PGM=DEVOPS/SAR231893/EFC14153/CSR_RWE/REPORT/PGM/eff_eventkm_ger_subg_i_g.sas OUT=REPORT/OUTPUT/eff_evtkm_eaw52_ger_race3_t2_g_x.rtf (18JUN2021 - 15:30)

Project Code / Study Number / Analysis: SAR231893 / EFC14153 / CSR_RWE

2 Severe exacerbation events

2.2 Kaplan-Meier plot of time to first severe exacerbation event during the 52-week treatment period - ITT type 2 inflammatory asthma phenotype population

2.2.8 By baseline ICS dose level (Medium, High)



Number at Risk

ICS High Pb	50	47	44	39	38	37	34	30	29	28	28	28	27	20
ICS High Dup	102	96	92	86	83	79	78	76	76	73	73	70	68	51
ICS Medium Pb	64	61	61	58	57	52	50	49	48	46	43	42	42	34
ICS Medium Dup	131	128	126	125	122	121	118	112	111	109	107	105	103	77

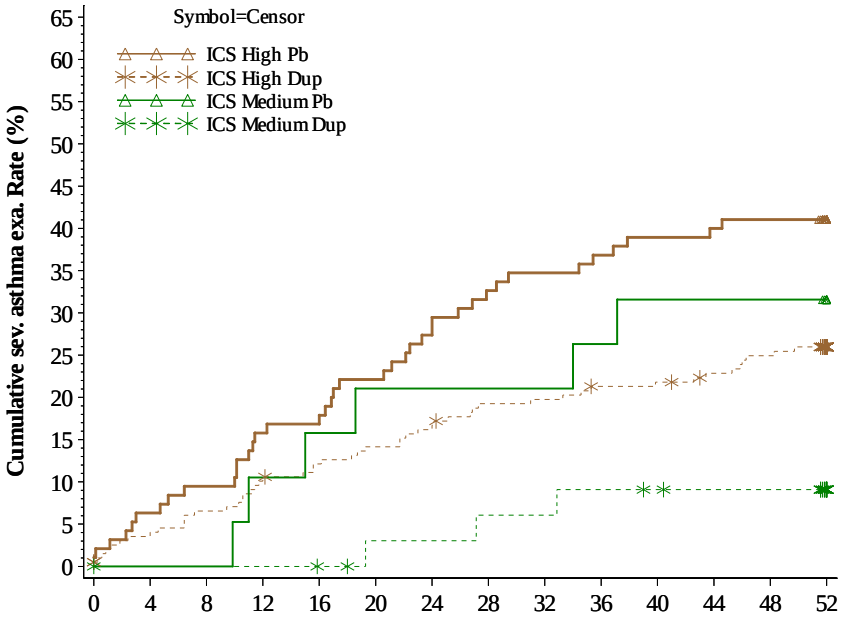
PGM=DEVOPS/SAR231893/EFC14153/CSR_RWE/REPORT/PGM/eff_eventkm_ger_subg_i_g.sas OUT=REPORT/OUTPUT/eff_evtkm_eaw52_ger_ics_t2_g_x.rtf (18JUN2021 - 15:30)

Project Code / Study Number / Analysis: SAR231893 / EFC14153 / CSR_RWE

2 Severe exacerbation events

2.2 Kaplan-Meier plot of time to first severe exacerbation event during the 52-week treatment period - ITT type 2 inflammatory asthma phenotype population

2.2.9 By baseline ICS dose level 2 (Medium, High)



Number at Risk

ICS High Pb	95	89	86	80	79	74	69	64	62	60	58	57	56	43
ICS High Dup	200	191	185	178	173	169	165	158	157	153	152	148	144	110
ICS Medium Pb	19	19	19	17	16	15	15	15	15	14	13	13	13	11
ICS Medium Dup	36	35	35	35	34	32	32	31	31	30	29	28	28	19

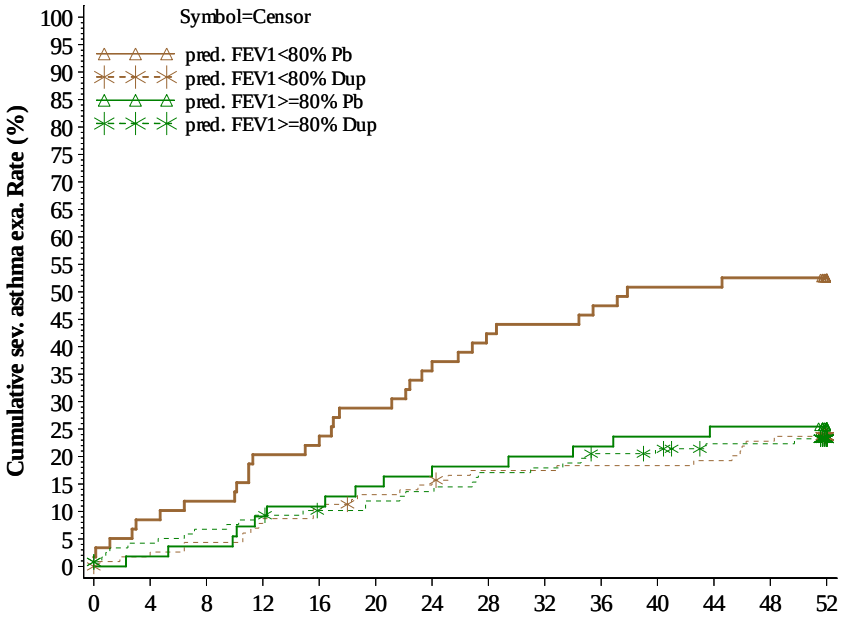
PGM=DEVOPS/SAR231893/EFC14153/CSR_RWE/REPORT/PGM/eff_eventkm_ger_subg_i_g.sas OUT=REPORT/OUTPUT/eff_evtkm_eaw52_ger_ics2_t2_g_x.rtf (01SEP2021 - 15:26)

Project Code / Study Number / Analysis: SAR231893 / EFC14153 / CSR_RWE

2 Severe exacerbation events

2.2 Kaplan-Meier plot of time to first severe exacerbation event during the 52-week treatment period - ITT type 2 inflammatory asthma phenotype population

2.2.10 By baseline predicted FEV1 (<80%, >=80%)



Number at Risk

pred. FEV1<80% Pb	59	54	52	47	46	42	38	34	33	31	29	29	28	20
pred. FEV1<80% Dup	116	113	110	106	103	99	97	93	93	92	92	91	87	66
pred. FEV1>=80% Pb	55	54	53	50	49	47	46	45	44	43	42	41	41	34
pred. FEV1>=80% Dup	120	113	110	107	104	102	100	96	95	91	89	85	85	63

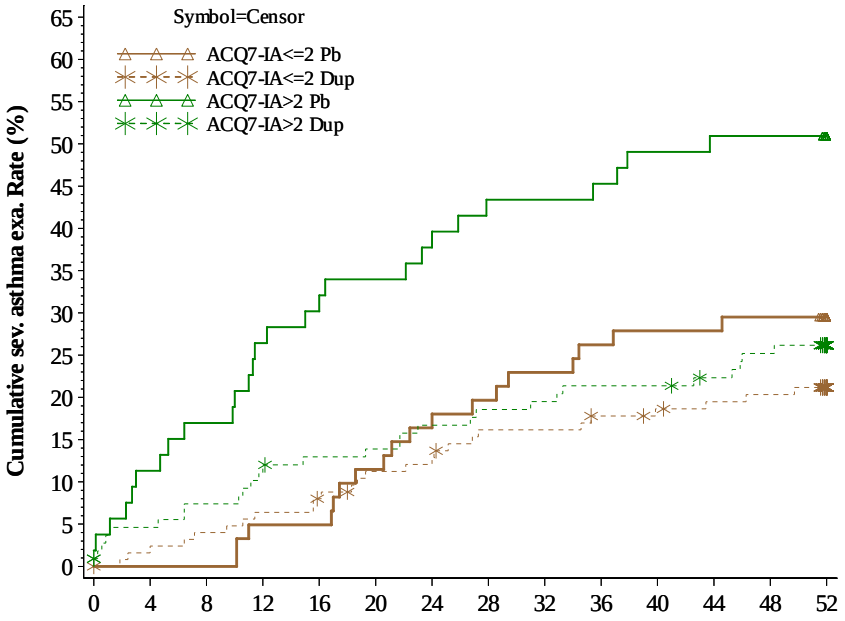
PGM=DEVOPS/SAR231893/EFC14153/CSR_RWE/REPORT/PGM/eff_eventkm_ger_subg_i_g.sas OUT=REPORT/OUTPUT/eff_evtkm_eaw52_ger_pfev1_t2_g_x.rtf (18JUN2021 - 15:30)

Project Code / Study Number / Analysis: SAR231893 / EFC14153 / CSR_RWE

2 Severe exacerbation events

2.2 Kaplan-Meier plot of time to first severe exacerbation event during the 52-week treatment period - ITT type 2 inflammatory asthma phenotype population

2.2.11 By baseline ACQ-7-IA (<=2, >2)



Number at Risk

ACQ7-IA<=2 Pb	61	61	61	58	58	54	51	49	47	45	44	44	43	35
ACQ7-IA<=2 Dup	126	123	120	117	114	109	108	102	102	99	97	95	94	71
ACQ7-IA>2 Pb	53	47	44	39	37	35	33	30	30	29	27	26	26	19
ACQ7-IA>2 Dup	110	103	100	96	93	92	89	87	86	84	84	81	78	58

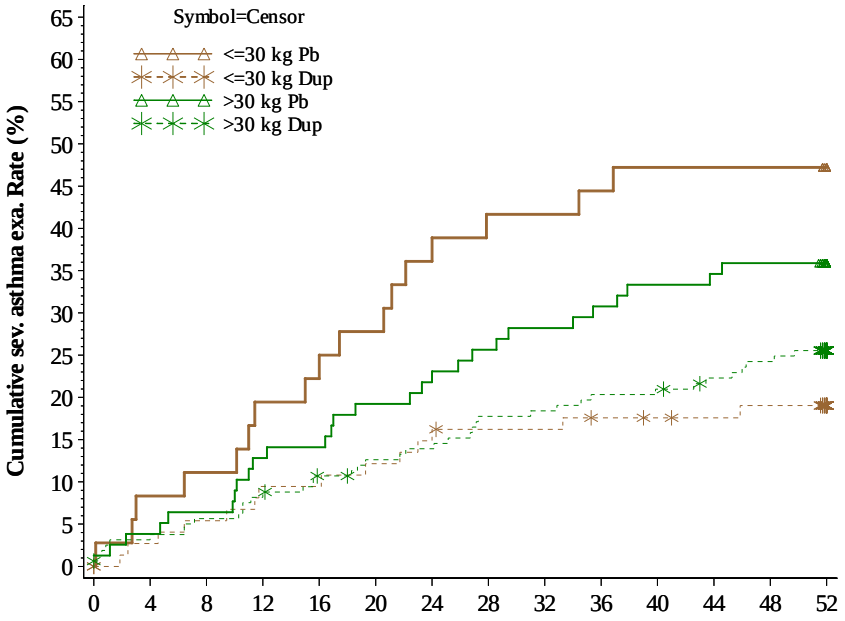
PGM=DEVOPS/SAR231893/EFC14153/CSR_RWE/REPORT/PGM/eff_eventkm_ger_subg_i_g.sas OUT=REPORT/OUTPUT/eff_evtkm_eaw52_ger_acq7_t2_g_x.rtf (18JUN2021 - 15:30)

Project Code / Study Number / Analysis: SAR231893 / EFC14153 / CSR_RWE

2 Severe exacerbation events

2.2 Kaplan-Meier plot of time to first severe exacerbation event during the 52-week treatment period - ITT type 2 inflammatory asthma phenotype population

2.2.12 By baseline weight (<=30 kg, >30 kg)



Number at Risk

<=30 kg Pb	36	33	32	29	28	26	23	21	21	20	19	19	19	15
<=30 kg Dup	76	72	70	67	67	65	63	61	61	59	58	57	56	43
>30 kg Pb	78	75	73	68	67	63	61	58	56	54	52	51	50	39
>30 kg Dup	160	154	150	146	140	136	134	128	127	124	123	119	116	86

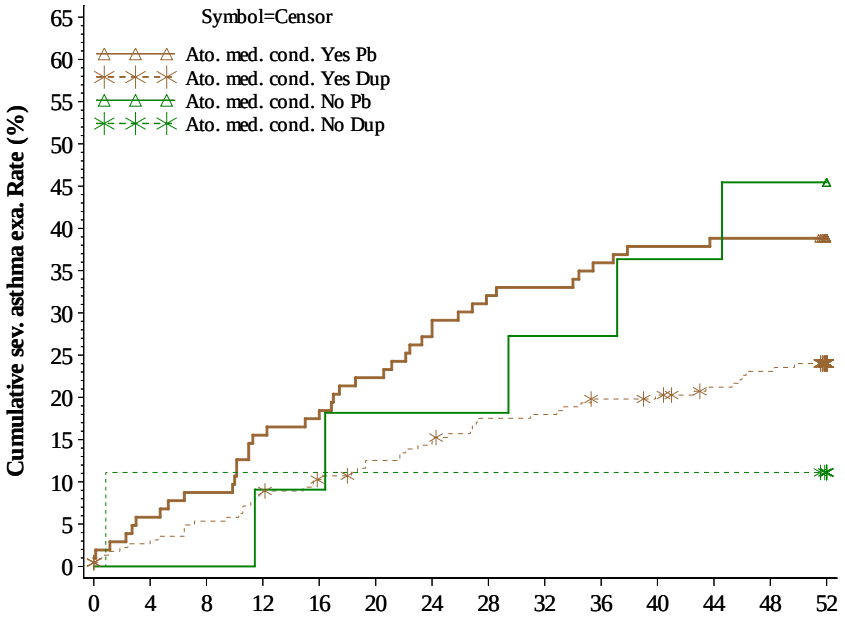
PGM=DEVOPS/SAR231893/EFC14153/CSR_RWE/REPORT/PGM/eff_eventkm_ger_subg_i_g.sas OUT=REPORT/OUTPUT/eff_evtkm_eaw52_ger_wgt_t2_g_x.rtf (18JUN2021 - 15:30)

Project Code / Study Number / Analysis: SAR231893 / EFC14153 / CSR_RWE

2 Severe exacerbation events

2.2 Kaplan-Meier plot of time to first severe exacerbation event during the 52-week treatment period - ITT type 2 inflammatory asthma phenotype population

2.2.13 By atopic medical condition (Yes, No)



Number at Risk

Ato. med. cond. Yes Pb	103	97	94	87	85	80	75	70	69	66	64	63	63	48
Ato. med. cond. Yes Dup	227	218	212	205	199	193	189	181	180	175	173	168	164	123
Ato. med. cond. No Pb	11	11	11	10	10	9	9	9	8	8	7	7	6	6
Ato. med. cond. No Dup	9	8	8	8	8	8	8	8	8	8	8	8	8	6

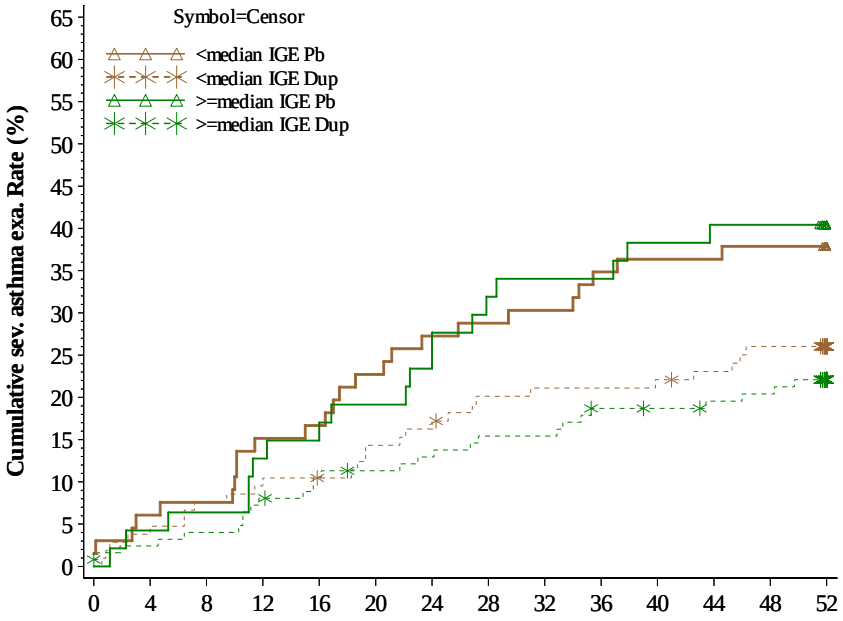
PGM=DEVOPS/SAR231893/EFC14153/CSR_RWE/REPORT/PGM/eff_eventkm_ger_subg_i_g.sas OUT=REPORT/OUTPUT/eff_evtkm_eaw52_ger_amc_t2_g_x.rtf (18JUN2021 - 15:30)

Project Code / Study Number / Analysis: SAR231893 / EFC14153 / CSR_RWE

2 Severe exacerbation events

2.2 Kaplan-Meier plot of time to first severe exacerbation event during the 52-week treatment period - ITT type 2 inflammatory asthma phenotype population

2.2.14 By baseline total IgE (<median, >= median)



Number at Risk

<median IGE Pb	66	62	61	56	55	51	48	47	46	43	42	42	41	35
<median IGE Dup	105	101	97	95	93	89	87	82	81	81	80	78	75	54
>=median IGE Pb	47	45	44	41	40	38	36	32	31	31	29	28	28	19
>=median IGE Dup	125	121	119	114	110	108	106	103	103	98	97	95	94	73

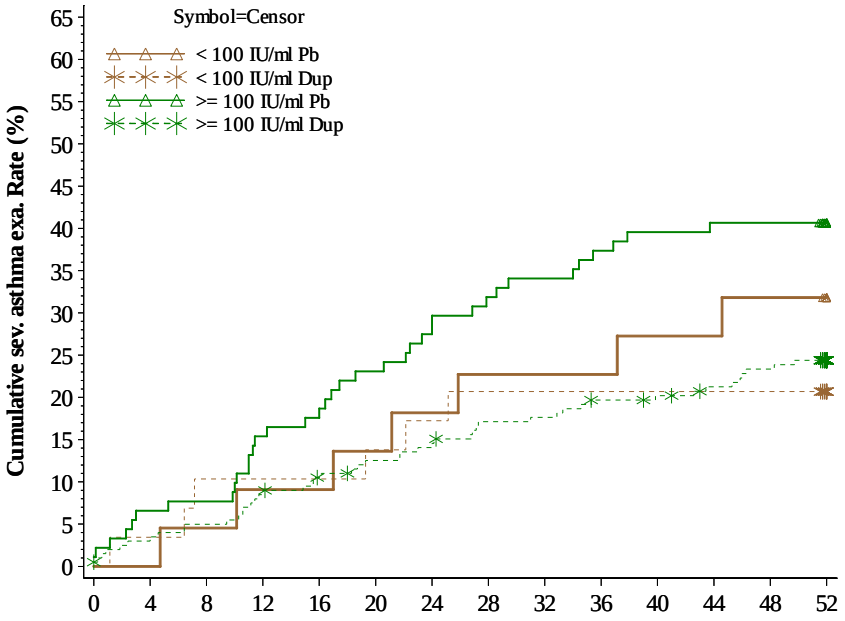
PGM=DEVOPS/SAR231893/EFC14153/CSR_RWE/REPORT/PGM/eff_eventkm_ger_subg_i_g.sas OUT=REPORT/OUTPUT/eff_evtkm_eaw52_ger_igem_t2_g_x.rtf (18JUN2021 - 15:31)

Project Code / Study Number / Analysis: SAR231893 / EFC14153 / CSR_RWE

2 Severe exacerbation events

2.2 Kaplan-Meier plot of time to first severe exacerbation event during the 52-week treatment period - ITT type 2 inflammatory asthma phenotype population

2.2.15 By baseline total IgE (<100 IU/ml, >= 100 IU/ml)



Number at Risk

< 100 IU/ml Pb	22	22	21	20	20	19	18	17	17	17	16	16	15	13
< 100 IU/ml Dup	29	28	26	26	26	25	24	23	23	23	23	23	23	14
>= 100 IU/ml Pb	91	85	84	77	75	70	66	62	60	57	55	54	54	41
>= 100 IU/ml Dup	201	194	190	183	177	172	169	162	161	156	154	150	146	113

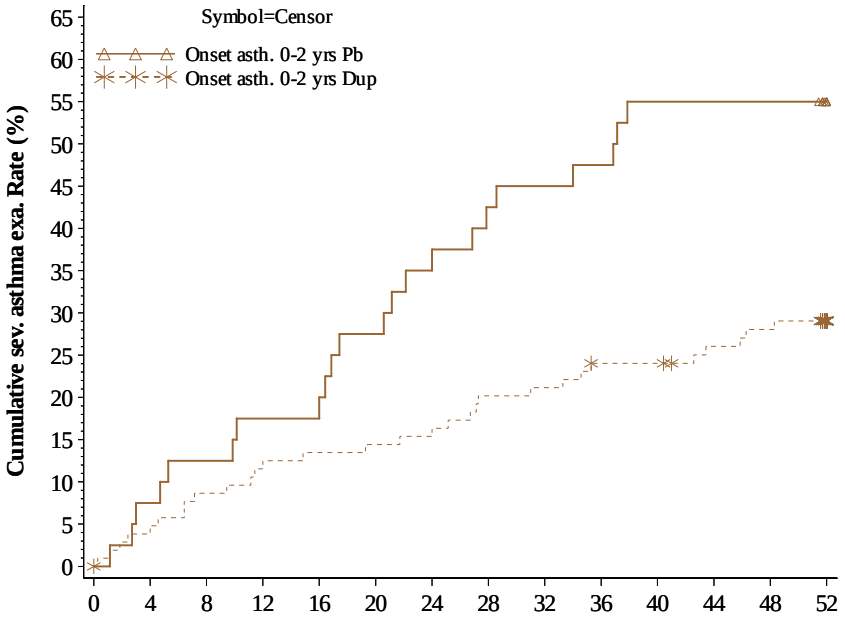
PGM=DEVOPS/SAR231893/EFC14153/CSR_RWE/REPORT/PGM/eff_eventkm_ger_subg_i_g.sas OUT=REPORT/OUTPUT/eff_evtkm_eaw52_ger_ige_t2_g_x.rtf (18JUN2021 - 15:31)

Project Code / Study Number / Analysis: SAR231893 / EFC14153 / CSR_RWE

2 Severe exacerbation events

2.2 Kaplan-Meier plot of time to first severe exacerbation event during the 52-week treatment period - ITT type 2 inflammatory asthma phenotype population

2.2.16 By age at onset of asthma (0-2 years)



Number at Risk

Onset asth. 0-2 yrs Pb	40	37	35	33	33	29	26	23	22	21	18	18	18	13
Onset asth. 0-2 yrs Dup	105	100	95	92	90	89	88	83	82	78	78	74	72	57

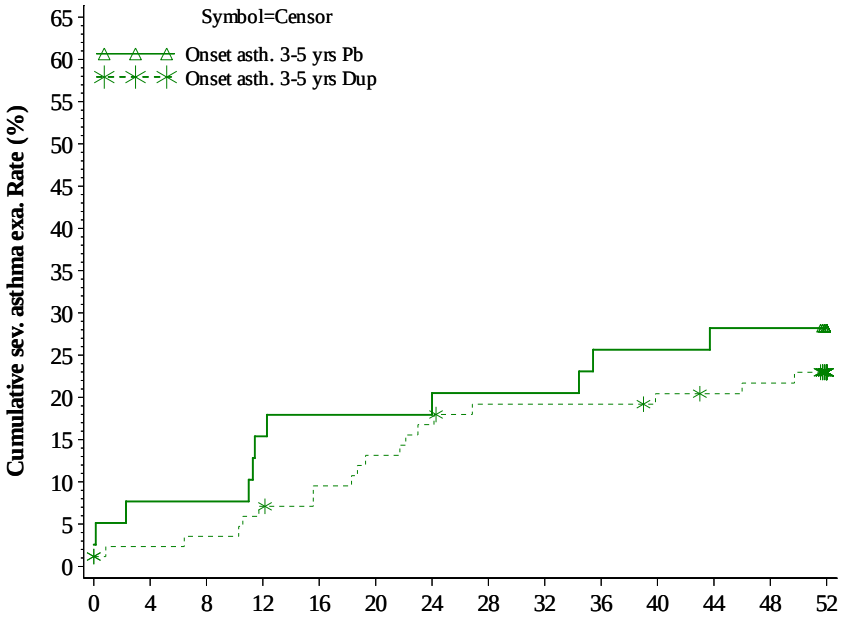
PGM=DEVOPS/SAR231893/EFC14153/CSR_RWE/REPORT/PGM/eff_eventkm_ger_subg_i_g.sas OUT=REPORT/OUTPUT/eff_evtkm_eaw52_ger_onsa1_t2_g_x.rtf (10AUG2021 - 8:09)

Project Code / Study Number / Analysis: SAR231893 / EFC14153 / CSR_RWE

2 Severe exacerbation events

2.2 Kaplan-Meier plot of time to first severe exacerbation event during the 52-week treatment period - ITT type 2 inflammatory asthma phenotype population

2.2.17 By age at onset of asthma (3-5 years)



Number at Risk

Onset asth. 3-5 yrs Pb	39	36	36	33	32	32	32	31	31	29	29	28	28	22
Onset asth. 3-5 yrs Dup	86	82	81	78	75	72	69	66	66	66	64	63	62	48

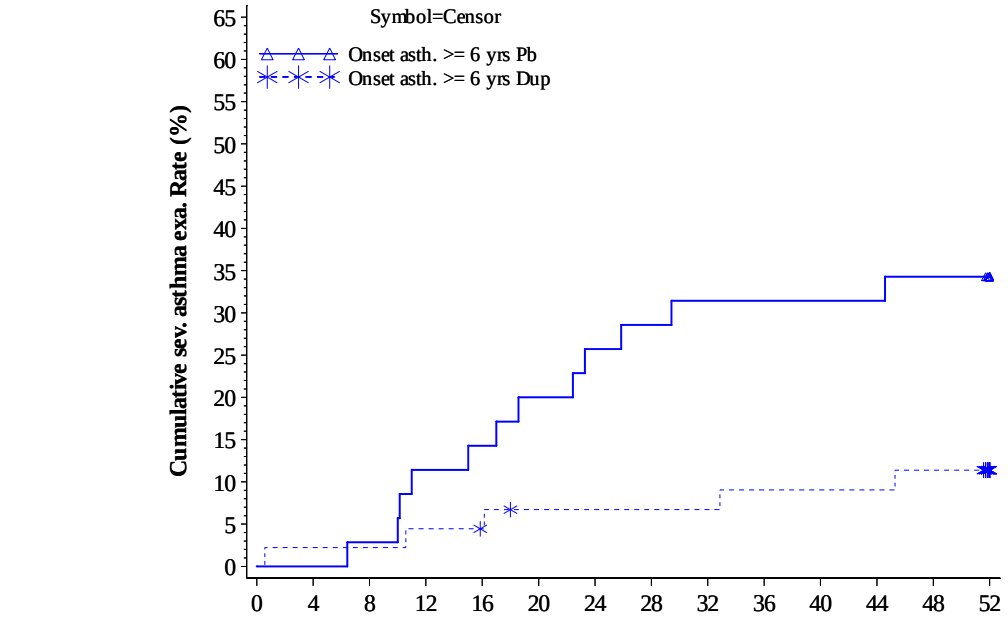
PGM=DEVOPS/SAR231893/EFC14153/CSR_RWE/REPORT/PGM/eff_eventkm_ger_subg_i_g.sas OUT=REPORT/OUTPUT/eff_evtkm_eaw52_ger_onsa2_t2_g_x.rtf (10AUG2021 - 8:09)

Project Code / Study Number / Analysis: SAR231893 / EFC14153 / CSR_RWE

2 Severe exacerbation events

2.2 Kaplan-Meier plot of time to first severe exacerbation event during the 52-week treatment period - ITT type 2 inflammatory asthma phenotype population

2.2.18 By age at onset of asthma (>=6 years)



Number at Risk

Onset asth. >= 6 yrs Pb	35	35	34	31	30	28	26	25	24	24	24	24	23	19
Onset asth. >= 6 yrs Dup	45	44	44	43	42	40	40	40	40	39	39	39	38	24

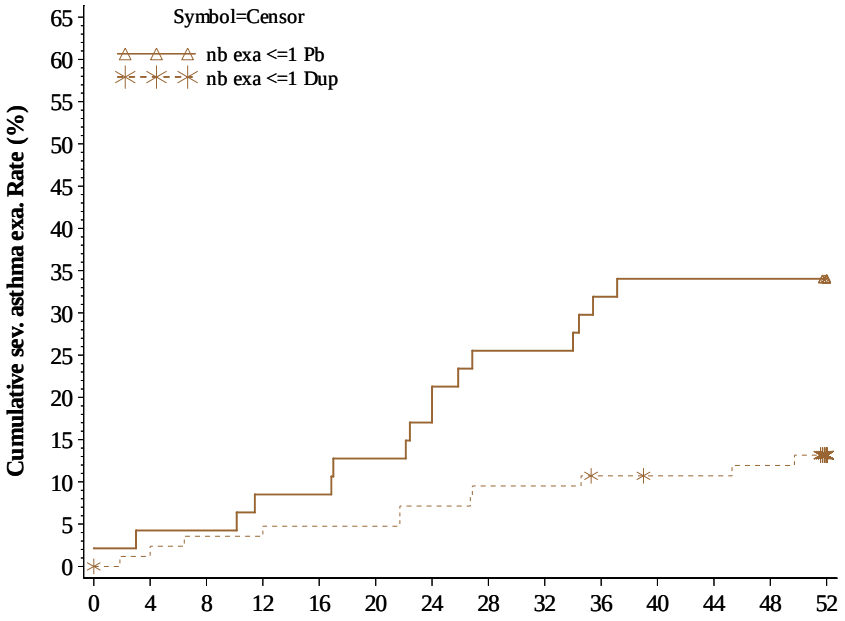
PGM=DEVOPS/SAR231893/EFC14153/CSR_RWE/REPORT/PGM/eff_eventkm_ger_subg_i_g.sas OUT=REPORT/OUTPUT/eff_evtkm_eaw52_ger_onsa3_t2_g_x.rtf (10AUG2021 - 8:09)

Project Code / Study Number / Analysis: SAR231893 / EFC14153 / CSR_RWE

2 Severe exacerbation events

2.2 Kaplan-Meier plot of time to first severe exacerbation event during the 52-week treatment period - ITT type 2 inflammatory asthma phenotype population

2.2.19 By number of severe asthma exacerbation prior to the study (<=1)



Number at Risk

nb exa <=1 Pb	47	45	45	43	43	41	39	35	35	32	31	31	31	27
nb exa <=1 Dup	85	83	81	81	80	80	78	76	76	74	73	73	72	57

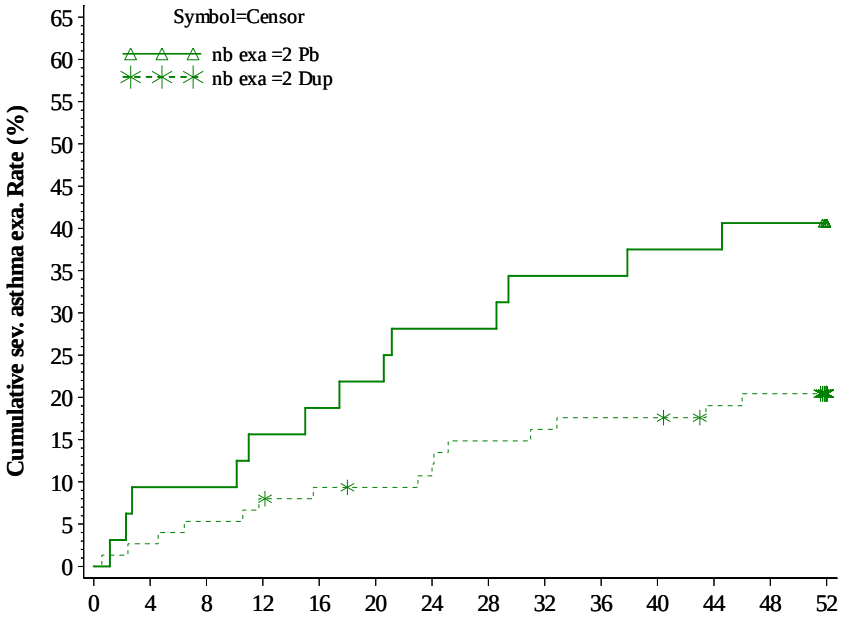
PGM=DEVOPS/SAR231893/EFC14153/CSR_RWE/REPORT/PGM/eff_eventkm_ger_subg_i_g.sas OUT=REPORT/OUTPUT/eff_evtkm_eaw52_ger_exa1_t2_g_x.rtf (18JUN2021 - 15:31)

Project Code / Study Number / Analysis: SAR231893 / EFC14153 / CSR_RWE

2 Severe exacerbation events

2.2 Kaplan-Meier plot of time to first severe exacerbation event during the 52-week treatment period - ITT type 2 inflammatory asthma phenotype population

2.2.20 By number of severe asthma exacerbation prior to the study (2)



Number at Risk

nb exa =2 Pb	32	29	29	27	26	25	23	23	21	21	20	20	19	15
nb exa =2 Dup	75	73	71	69	67	66	65	62	61	60	60	57	56	42

PGM=DEVOPS/SAR231893/EFC14153/CSR_RWE/REPORT/PGM/eff_eventkm_ger_subg_i_g.sas OUT=REPORT/OUTPUT/eff_evtkm_eaw52_ger_exa2_t2_g_x.rtf (18JUN2021 - 15:31)

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen
Project Code / Study Number / Analysis: SAR231893 / EFC14153 / CSR_RWE

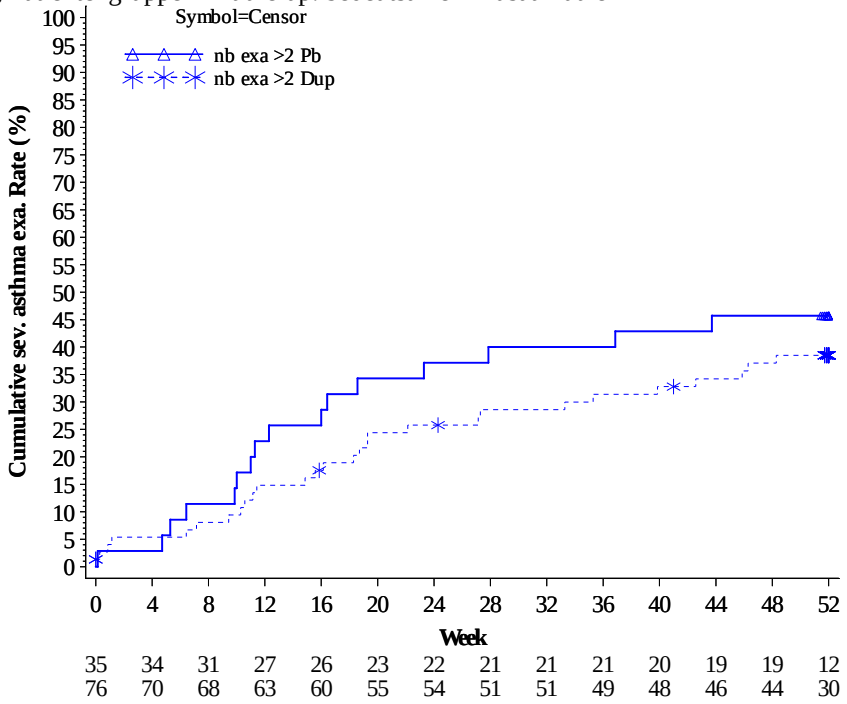
2	Severe exacerbation events
2.2	Kaplan-Meier plot of time to first severe exacerbation event during the 52-week treatment period - ITT type 2 inflammatory asthma phenotype population
2.2.21	By number of severe asthma exacerbation prior to the study (>2)

All severe exacerbation events resulting in hospitalization or emergency room visits occurred during the 52-week treatment period are included, regardless of whether the patient is on-treatment or not

OR, RR and RD are derived from a logistic regression model with treatment, age, weight group, region, baseline eosinophil level, baseline FeNO level, baseline ICS dose level, and number of severe exacerbation events within 1 year prior to the study as covariates.

Peto OR calculation is based on Yusuf S et al. (Prog Cardiovasc Dis. 1985 Mar-Apr;27(5):335-71) and its p-value is derived using a normal approximation.

PGM=DEVOPS/SAR231893/EFC14153/CSR_RWE/REPORT/PGM/eff_pro_evt_ger_i_t.sas OUT=REPORT/OUTPUT/eff_pro_hoerw52_ger_t2_t_x.rtf (30JUN2021 - 8:14)



Number at Risk													
nb exa >2 Pb	35	34	31	27	26	23	22	21	21	21	20	19	19	12
nb exa >2 Dup	76	70	68	63	60	55	54	51	51	49	48	46	44	30

PGM=DEVOPS/SAR231893/EFC14153/CSR_RWE/REPORT/PGM/eff_eventkm_ger_subg_i_g.sas OUT=REPORT/OUTPUT/eff_evtkm_eaw52_ger_exa3_t2_g_x.rtf (18JUN2021 - 15:31)

All severe exacerbation events resulting in hospitalization or emergency room visits occurred during the 52-week treatment period are included, regardless of whether the patient is on-treatment or not

OR, RR and RD are derived from a logistic regression model with treatment, age, weight group, region, baseline eosinophil level, baseline FeNO level, baseline ICS dose level, and number of severe exacerbation events within 1 year prior to the study as covariates.

Peto OR calculation is based on Yusuf S et al. (Prog Cardiovasc Dis. 1985 Mar-Apr;27(5):335-71) and its p-value is derived using a normal approximation.

PGM=DEVOPS/SAR231893/EFC14153/CSR_RWE/REPORT/PGM/eff_pro_evt_ger_i_t.sas OUT=REPORT/OUTPUT/eff_pro_hoerw52_ger_t2_t_x.rtf (30JUN2021 - 8:14)

Subgruppenanalysen: Ereignisraten

Project Code / Study Number / Analysis: SAR231893 / EFC14153 / CSR_RWE

2 Severe exacerbation events

2.1 Annualized event rate of severe asthma exacerbation during the 52-week treatment period - ITT type 2 inflammatory asthma phenotype population

2.1.1 By gender (Male, Female)

	Gender			
	Male		Female	
Severe asthma exacerbation	**Placebo (N=78)**	**Dupilumab (N=152)**	**Placebo (N=36)**	**Dupilumab (N=84)**
Patients with >=1 Severe asthma exacerbation [n(%)]				
Number	78	152	36	84
No	40 (51.3%)	115 (75.7%)	28 (77.8%)	67 (79.8%)
Yes	38 (48.7%)	37 (24.3%)	8 (22.2%)	17 (20.2%)
Number of Severe asthma exacerbation				
0	40 (51.3%)	115 (75.7%)	28 (77.8%)	67 (79.8%)
1	17 (21.8%)	25 (16.4%)	6 (16.7%)	11 (13.1%)
2	14 (17.9%)	9 (5.9%)	1 (2.8%)	2 (2.4%)
3	5 (6.4%)	2 (1.3%)	0	3 (3.6%)
>=4	2 (2.6%)	1 (0.7%)	1 (2.8%)	1 (1.2%)

All severe exacerbation events occurred during the 52-week treatment period are included, regardless of whether the patient is on-treatment or not
[a]The total number of events that occurred during the 52-week treatment period divided by the total number of patient-years followed in the 52-week treatment period.
[b]Derived using negative binomial model with the total number of events onset from randomization up to Week 52 visit or last contact date (whichever comes earlier) as the response variable, with the treatment groups, age, baseline weight group, region, baseline eosinophil level, baseline FeNO level, baseline ICS dose level and number of severe exacerbation events within 1 year prior to the study as covariates, and log-transformed standardized observation duration as an offset variable.
[c]Derived using same negative binomial model as described in [b] with subgroup and subgroup-by-treatment interaction as additional covariates.
[d]Derived using delta method.
PGM=DEVOPS/SAR231893/EFC14153/CSR_RWE/REPORT/PGM/eff_eventsum_ger_subg_i_t.sas OUT=REPORT/OUTPUT/eff_evtsum_eaw52_ger_sex_t2_t_x.rtf (02JUL2021 - 16:21)

Project Code / Study Number / Analysis: SAR231893 / EFC14153 / CSR_RWE

2 Severe exacerbation events

2.1 Annualized event rate of severe asthma exacerbation during the 52-week treatment period - ITT type 2 inflammatory asthma phenotype population

2.1.1 By gender (Male, Female)

	Gender			
	Male		Female	
Severe asthma exacerbation	**Placebo (N=78)**	**Dupilumab (N=152)**	**Placebo (N=36)**	**Dupilumab (N=84)**
Total number of Severe asthma exacerbation	68	54	13	28
Total patient-years followed	77.5	149.1	35.2	80.5
Unadjusted annualized rate of Severe asthma exacerbation[a]	0.88	0.36	0.37	0.35
Adjusted annualized rate of Severe asthma exacerbation				
Estimate (95% CI)[b]	0.95 (0.68 to 1.33)	0.33 (0.23 to 0.48)	0.32 (0.14 to 0.73)	0.23 (0.12 to 0.44)
Risk Ratio (95% CI) vs placebo[b]	-	0.35 (0.23 to 0.54)	-	0.73 (0.29 to 1.85)
p-value for Risk Ratio[b]		<0.001		0.503
p-value for heterogeneity of Risk Ratio[c]				0.086
Risk Difference (95% CI) vs placebo[d]	-	-0.62 (-0.93 to -0.31)	-	-0.09 (-0.36 to 0.19)

All severe exacerbation events occurred during the 52-week treatment period are included, regardless of whether the patient is on-treatment or not
[a]The total number of events that occurred during the 52-week treatment period divided by the total number of patient-years followed in the 52-week treatment period.
[b]Derived using negative binomial model with the total number of events onset from randomization up to Week 52 visit or last contact date (whichever comes earlier) as the response variable, with the treatment groups, age, baseline weight group, region, baseline eosinophil level, baseline FeNO level, baseline ICS dose level and number of severe exacerbation events within 1 year prior to the study as covariates, and log-transformed standardized observation duration as an offset variable.
[c]Derived using same negative binomial model as described in [b] with subgroup and subgroup-by-treatment interaction as additional covariates.
[d]Derived using delta method.
PGM=DEVOPS/SAR231893/EFC14153/CSR_RWE/REPORT/PGM/eff_eventsum_ger_subg_i_t.sas OUT=REPORT/OUTPUT/eff_evtsum_eaw52_ger_sex_t2_t_x.rtf (02JUL2021 - 16:21)

Project Code / Study Number / Analysis: SAR231893 / EFC14153 / CSR_RWE

2 Severe exacerbation events

2.1 Annualized event rate of severe asthma exacerbation during the 52-week treatment period - ITT type 2 inflammatory asthma phenotype population

2.1.2 By region (Latin America, East Europe, Western Countries)

	Region			
	Latin America		East Europe	
Severe asthma exacerbation	**Placebo (N=51)**	**Dupilumab (N=106)**	**Placebo (N=43)**	**Dupilumab (N=78)**
Patients with >=1 Severe asthma exacerbation [n(%)]				
Number	51	106	43	78
No	30 (58.8%)	77 (72.6%)	34 (79.1%)	66 (84.6%)
Yes	21 (41.2%)	29 (27.4%)	9 (20.9%)	12 (15.4%)
Number of Severe asthma exacerbation				
0	30 (58.8%)	77 (72.6%)	34 (79.1%)	66 (84.6%)
1	10 (19.6%)	16 (15.1%)	5 (11.6%)	10 (12.8%)
2	6 (11.8%)	7 (6.6%)	3 (7.0%)	2 (2.6%)
3	3 (5.9%)	5 (4.7%)	1 (2.3%)	0
>=4	2 (3.9%)	1 (0.9%)	0	0

All severe exacerbation events occurred during the 52-week treatment period are included, regardless of whether the patient is on-treatment or not
[a]The total number of events that occurred during the 52-week treatment period divided by the total number of patient-years followed in the 52-week treatment period.
[b]Derived using negative binomial model with the total number of events onset from randomization up to Week 52 visit or last contact date (whichever comes earlier) as the response variable, with the treatment groups, age, baseline weight group, baseline eosinophil level, baseline FeNO level, baseline ICS dose level and number of severe exacerbation events within 1 year prior to the study as covariates, and log-transformed standardized observation duration as an offset variable.
[c]Derived using same negative binomial model as described in [b] with subgroup and subgroup-by-treatment interaction as additional covariates.
[d]Derived using delta method.
PGM=DEVOPS/SAR231893/EFC14153/CSR_RWE/REPORT/PGM/eff_eventsum_ger_subg_i_t.sas OUT=REPORT/OUTPUT/eff_evtsum_eaw52_ger_cty_t2_t_x.rtf (02JUL2021 - 16:21)

Project Code / Study Number / Analysis: SAR231893 / EFC14153 / CSR_RWE

2 Severe exacerbation events

2.1 Annualized event rate of severe asthma exacerbation during the 52-week treatment period - ITT type 2 inflammatory asthma phenotype population

2.1.2 By region (Latin America, East Europe, Western Countries)

	Region			
	Latin America		East Europe	
Severe asthma exacerbation	**Placebo (N=51)**	**Dupilumab (N=106)**	**Placebo (N=43)**	**Dupilumab (N=78)**
Total number of Severe asthma exacerbation	40	50	14	14
Total patient-years followed	51.2	104.1	42.5	77.5
Unadjusted annualized rate of Severe asthma exacerbation[a]	0.78	0.48	0.33	0.18
Adjusted annualized rate of Severe asthma exacerbation				
Estimate (95% CI)[b]	0.87 (0.52 to 1.44)	0.41 (0.26 to 0.64)	0.40 (0.19 to 0.83)	0.23 (0.12 to 0.44)
Risk Ratio (95% CI) vs placebo[b]	-	0.47 (0.26 to 0.87)	-	0.56 (0.23 to 1.37)
p-value for Risk Ratio[b]		0.017		0.204
p-value for heterogeneity of Risk Ratio[c]:				
Latin America, East Europe				
Latin America, Western countries				
East Europe, Western countries				

All severe exacerbation events occurred during the 52-week treatment period are included, regardless of whether the patient is on-treatment or not
[a]The total number of events that occurred during the 52-week treatment period divided by the total number of patient-years followed in the 52-week treatment period.
[b]Derived using negative binomial model with the total number of events onset from randomization up to Week 52 visit or last contact date (whichever comes earlier) as the response variable, with the treatment groups, age, baseline weight group, baseline eosinophil level, baseline FeNO level, baseline ICS dose level and number of severe exacerbation events within 1 year prior to the study as covariates, and log-transformed standardized observation duration as an offset variable.
[c]Derived using same negative binomial model as described in [b] with subgroup and subgroup-by-treatment interaction as additional covariates.
[d]Derived using delta method.
PGM=DEVOPS/SAR231893/EFC14153/CSR_RWE/REPORT/PGM/eff_eventsum_ger_subg_i_t.sas OUT=REPORT/OUTPUT/eff_evtsum_eaw52_ger_cty_t2_t_x.rtf (02JUL2021 - 16:21)

Project Code / Study Number / Analysis: SAR231893 / EFC14153 / CSR_RWE

2 Severe exacerbation events

2.1 Annualized event rate of severe asthma exacerbation during the 52-week treatment period - ITT type 2 inflammatory asthma phenotype population

2.1.2 By region (Latin America, East Europe, Western Countries)

	Region			
	Latin America		East Europe	
Severe asthma exacerbation	**Placebo (N=51)**	**Dupilumab (N=106)**	**Placebo (N=43)**	**Dupilumab (N=78)**
overall				
Risk Difference (95% CI) vs placebo[d]	-	-0.46 (-0.91 to -0.01)	-	-0.18 (-0.48 to 0.13)

All severe exacerbation events occurred during the 52-week treatment period are included, regardless of whether the patient is on-treatment or not

[a]The total number of events that occurred during the 52-week treatment period divided by the total number of patient-years followed in the 52-week treatment period.

[b]Derived using negative binomial model with the total number of events onset from randomization up to Week 52 visit or last contact date (whichever comes earlier) as the response variable, with the treatment groups, age, baseline weight group, baseline eosinophil level, baseline FeNO level, baseline ICS dose level and number of severe exacerbation events within 1 year prior to the study as covariates, and log-transformed standardized observation duration as an offset variable.

[c]Derived using same negative binomial model as described in [b] with subgroup and subgroup-by-treatment interaction as additional covariates.

[d]Derived using delta method.

PGM=DEVOPS/SAR231893/EFC14153/CSR_RWE/REPORT/PGM/eff_eventsum_ger_subg_i_t.sas OUT=REPORT/OUTPUT/eff_evtsum_eaw52_ger_cty_t2_t_x.rtf (02JUL2021 - 16:21)

Project Code / Study Number / Analysis: SAR231893 / EFC14153 / CSR_RWE

2 Severe exacerbation events

2.1 Annualized event rate of severe asthma exacerbation during the 52-week treatment period - ITT type 2 inflammatory asthma phenotype population

2.1.2 By region (Latin America, East Europe, Western Countries)

	Region	
	Western countries	
Severe asthma exacerbation	**Placebo (N=20)**	**Dupilumab (N=52)**
Patients with >=1 Severe asthma exacerbation [n(%)]		
Number	20	52
No	4 (20.0%)	39 (75.0%)
Yes	16 (80.0%)	13 (25.0%)
Number of Severe asthma exacerbation		
0	4 (20.0%)	39 (75.0%)
1	8 (40.0%)	10 (19.2%)
2	6 (30.0%)	2 (3.8%)
3	1 (5.0%)	0
>=4	1 (5.0%)	1 (1.9%)

All severe exacerbation events occurred during the 52-week treatment period are included, regardless of whether the patient is on-treatment or not
[a]The total number of events that occurred during the 52-week treatment period divided by the total number of patient-years followed in the 52-week treatment period.
[b]Derived using negative binomial model with the total number of events onset from randomization up to Week 52 visit or last contact date (whichever comes earlier) as the response variable, with the treatment groups, age, baseline weight group, baseline eosinophil level, baseline FeNO level, baseline ICS dose level and number of severe exacerbation events within 1 year prior to the study as covariates, and log-transformed standardized observation duration as an offset variable.
[c]Derived using same negative binomial model as described in [b] with subgroup and subgroup-by-treatment interaction as additional covariates.
[d]Derived using delta method.
PGM=DEVOPS/SAR231893/EFC14153/CSR_RWE/REPORT/PGM/eff_eventsum_ger_subg_i_t.sas OUT=REPORT/OUTPUT/eff_evtsum_eaw52_ger_cty_t2_t_x.rtf (02JUL2021 - 16:21)

Project Code / Study Number / Analysis: SAR231893 / EFC14153 / CSR_RWE

2 Severe exacerbation events

2.1 Annualized event rate of severe asthma exacerbation during the 52-week treatment period - ITT type 2 inflammatory asthma phenotype population

2.1.2 By region (Latin America, East Europe, Western Countries)

	Region	
	Western countries	
Severe asthma exacerbation	**Placebo (N=20)**	**Dupilumab (N=52)**
Total number of Severe asthma exacerbation	27	18
Total patient-years followed	19.0	48.0
Unadjusted annualized rate of Severe asthma exacerbation[a]	1.42	0.38
Adjusted annualized rate of Severe asthma exacerbation		
Estimate (95% CI)[b]	1.19 (0.63 to 2.24)	0.28 (0.14 to 0.56)
Risk Ratio (95% CI) vs placebo[b]	-	0.23 (0.12 to 0.45)
p-value for Risk Ratio[b]		<0.001
p-value for heterogeneity of Risk Ratio[c]:		
Latin America, East Europe		0.997
Latin America, Western countries		0.070

All severe exacerbation events occurred during the 52-week treatment period are included, regardless of whether the patient is on-treatment or not
[a]The total number of events that occurred during the 52-week treatment period divided by the total number of patient-years followed in the 52-week treatment period.
[b]Derived using negative binomial model with the total number of events onset from randomization up to Week 52 visit or last contact date (whichever comes earlier) as the response variable, with the treatment groups, age, baseline weight group, baseline eosinophil level, baseline FeNO level, baseline ICS dose level and number of severe exacerbation events within 1 year prior to the study as covariates, and log-transformed standardized observation duration as an offset variable.
[c]Derived using same negative binomial model as described in [b] with subgroup and subgroup-by-treatment interaction as additional covariates.
[d]Derived using delta method.
PGM=DEVOPS/SAR231893/EFC14153/CSR_RWE/REPORT/PGM/eff_eventsum_ger_subg_i_t.sas OUT=REPORT/OUTPUT/eff_evtsum_eaw52_ger_cty_t2_t_x.rtf (02JUL2021 - 16:21)

Project Code / Study Number / Analysis: SAR231893 / EFC14153 / CSR_RWE

2 Severe exacerbation events

2.1 Annualized event rate of severe asthma exacerbation during the 52-week treatment period - ITT type 2 inflammatory asthma phenotype population

2.1.2 By region (Latin America, East Europe, Western Countries)

	Region	
	Western countries	
Severe asthma exacerbation	**Placebo (N=20)**	**Dupilumab (N=52)**
East Europe, Western countries		0.029
overall		0.074
Risk Difference (95% CI) vs placebo[d]	-	-0.91 (-1.59 to -0.24)

All severe exacerbation events occurred during the 52-week treatment period are included, regardless of whether the patient is on-treatment or not
[a]The total number of events that occurred during the 52-week treatment period divided by the total number of patient-years followed in the 52-week treatment period.
[b]Derived using negative binomial model with the total number of events onset from randomization up to Week 52 visit or last contact date (whichever comes earlier) as the response variable, with the treatment groups, age, baseline weight group, baseline eosinophil level, baseline FeNO level, baseline ICS dose level and number of severe exacerbation events within 1 year prior to the study as covariates, and log-transformed standardized observation duration as an offset variable.
[c]Derived using same negative binomial model as described in [b] with subgroup and subgroup-by-treatment interaction as additional covariates.
[d]Derived using delta method.
PGM=DEVOPS/SAR231893/EFC14153/CSR_RWE/REPORT/PGM/eff_eventsum_ger_subg_i_t.sas OUT=REPORT/OUTPUT/eff_evtsum_eaw52_ger_cty_t2_t_x.rtf (02JUL2021 - 16:21)

Project Code / Study Number / Analysis: SAR231893 / EFC14153 / CSR_RWE

2 Severe exacerbation events

2.1 Annualized event rate of severe asthma exacerbation during the 52-week treatment period - ITT type 2 inflammatory asthma phenotype population

2.1.3 By race (Caucasian/white, Black/of African descent, Other)

	Race			
	Caucasian/White		Black/of African descent	
Severe asthma exacerbation	**Placebo (N=102)**	**Dupilumab (N=208)**	**Placebo (N=5)**	**Dupilumab (N=9)**
Patients with >=1 Severe asthma exacerbation [n(%)]				
Number	102	208	5	9
No	67 (65.7%)	161 (77.4%)	1 (20.0%)	7 (77.8%)
Yes	35 (34.3%)	47 (22.6%)	4 (80.0%)	2 (22.2%)
Number of Severe asthma exacerbation				
0	67 (65.7%)	161 (77.4%)	1 (20.0%)	7 (77.8%)
1	19 (18.6%)	31 (14.9%)	3 (60.0%)	2 (22.2%)
2	8 (7.8%)	10 (4.8%)	1 (20.0%)	0
3	5 (4.9%)	5 (2.4%)	0	0
>=4	3 (2.9%)	1 (0.5%)	0	0

All severe exacerbation events occurred during the 52-week treatment period are included, regardless of whether the patient is on-treatment or not
[a]The total number of events that occurred during the 52-week treatment period divided by the total number of patient-years followed in the 52-week treatment period.
[b]Derived using negative binomial model with the total number of events onset from randomization up to Week 52 visit or last contact date (whichever comes earlier) as the response variable, with the treatment groups, age, baseline weight group, region, baseline eosinophil level, baseline FeNO level, baseline ICS dose level and number of severe exacerbation events within 1 year prior to the study as covariates, and log-transformed standardized observation duration as an offset variable.
[c]Derived using same negative binomial model as described in [b] with subgroup and subgroup-by-treatment interaction as additional covariates.
[d]Derived using delta method.
PGM=DEVOPS/SAR231893/EFC14153/CSR_RWE/REPORT/PGM/eff_eventsum_ger_subg_i_t.sas OUT=REPORT/OUTPUT/eff_evtsum_eaw52_ger_race_t2_t_x.rtf (02JUL2021 - 16:21)

Project Code / Study Number / Analysis: SAR231893 / EFC14153 / CSR_RWE

2 Severe exacerbation events

2.1 Annualized event rate of severe asthma exacerbation during the 52-week treatment period - ITT type 2 inflammatory asthma phenotype population

2.1.3 By race (Caucasian/white, Black/of African descent, Other)

	Race			
	Caucasian/White		Black/of African descent	
Severe asthma exacerbation	**Placebo (N=102)**	**Dupilumab (N=208)**	**Placebo (N=5)**	**Dupilumab (N=9)**
Total number of Severe asthma exacerbation	63	71	5	2
Total patient-years followed	101.4	203.5	4.2	9.1
Unadjusted annualized rate of Severe asthma exacerbation[a]	0.62	0.35	1.18	0.22
Adjusted annualized rate of Severe asthma exacerbation				
Estimate (95% CI)[b]	0.65 (0.44 to 0.96)	0.32 (0.22 to 0.46)	0.20 (0.00 to 900.09)	0.07 (0.00 to 186.14)
Risk Ratio (95% CI) vs placebo[b]	-	0.49 (0.31 to 0.77)	-	0.37 (0.01 to 19.70)
p-value for Risk Ratio[b]		0.002		0.524
p-value for heterogeneity of Risk Ratio[c]:				
Caucasian/White, Black/of African descent				
Caucasian/White, Other				
Black/of African descent, Other				

All severe exacerbation events occurred during the 52-week treatment period are included, regardless of whether the patient is on-treatment or not
[a]The total number of events that occurred during the 52-week treatment period divided by the total number of patient-years followed in the 52-week treatment period.
[b]Derived using negative binomial model with the total number of events onset from randomization up to Week 52 visit or last contact date (whichever comes earlier) as the response variable, with the treatment groups, age, baseline weight group, region, baseline eosinophil level, baseline FeNO level, baseline ICS dose level and number of severe exacerbation events within 1 year prior to the study as covariates, and log-transformed standardized observation duration as an offset variable.
[c]Derived using same negative binomial model as described in [b] with subgroup and subgroup-by-treatment interaction as additional covariates.
[d]Derived using delta method.
PGM=DEVOPS/SAR231893/EFC14153/CSR_RWE/REPORT/PGM/eff_eventsum_ger_subg_i_t.sas OUT=REPORT/OUTPUT/eff_evtsum_eaw52_ger_race_t2_t_x.rtf (02JUL2021 - 16:21)

Project Code / Study Number / Analysis: SAR231893 / EFC14153 / CSR_RWE

2 Severe exacerbation events

2.1 Annualized event rate of severe asthma exacerbation during the 52-week treatment period - ITT type 2 inflammatory asthma phenotype population

2.1.3 By race (Caucasian/white, Black/of African descent, Other)

	Race			
	Caucasian/White		Black/of African descent	
Severe asthma exacerbation	**Placebo (N=102)**	**Dupilumab (N=208)**	**Placebo (N=5)**	**Dupilumab (N=9)**
overall				
Risk Difference (95% CI) vs placebo[d]	-	-0.33 (-0.58 to -0.08)	-	-0.12 (-1.31 to 1.06)

All severe exacerbation events occurred during the 52-week treatment period are included, regardless of whether the patient is on-treatment or not

[a]The total number of events that occurred during the 52-week treatment period divided by the total number of patient-years followed in the 52-week treatment period.

[b]Derived using negative binomial model with the total number of events onset from randomization up to Week 52 visit or last contact date (whichever comes earlier) as the response variable, with the treatment groups, age, baseline weight group, region, baseline eosinophil level, baseline FeNO level, baseline ICS dose level and number of severe exacerbation events within 1 year prior to the study as covariates, and log-transformed standardized observation duration as an offset variable.

[c]Derived using same negative binomial model as described in [b] with subgroup and subgroup-by-treatment interaction as additional covariates.

[d]Derived using delta method.

PGM=DEVOPS/SAR231893/EFC14153/CSR_RWE/REPORT/PGM/eff_eventsum_ger_subg_i_t.sas OUT=REPORT/OUTPUT/eff_evtsum_eaw52_ger_race_t2_t_x.rtf (02JUL2021 - 16:21)

Project Code / Study Number / Analysis: SAR231893 / EFC14153 / CSR_RWE

2 Severe exacerbation events

2.1 Annualized event rate of severe asthma exacerbation during the 52-week treatment period - ITT type 2 inflammatory asthma phenotype population

2.1.3 By race (Caucasian/white, Black/of African descent, Other)

	Race	
	Other	
Severe asthma exacerbation	**Placebo (N=7)**	**Dupilumab (N=19)**
Patients with >=1 Severe asthma exacerbation [n(%)]		
Number	7	19
No	0	14 (73.7%)
Yes	7 (100%)	5 (26.3%)
Number of Severe asthma exacerbation		
0	0	14 (73.7%)
1	1 (14.3%)	3 (15.8%)
2	6 (85.7%)	1 (5.3%)
3	0	0
>=4	0	1 (5.3%)

All severe exacerbation events occurred during the 52-week treatment period are included, regardless of whether the patient is on-treatment or not
[a]The total number of events that occurred during the 52-week treatment period divided by the total number of patient-years followed in the 52-week treatment period.
[b]Derived using negative binomial model with the total number of events onset from randomization up to Week 52 visit or last contact date (whichever comes earlier) as the response variable, with the treatment groups, age, baseline weight group, region, baseline eosinophil level, baseline FeNO level, baseline ICS dose level and number of severe exacerbation events within 1 year prior to the study as covariates, and log-transformed standardized observation duration as an offset variable.
[c]Derived using same negative binomial model as described in [b] with subgroup and subgroup-by-treatment interaction as additional covariates.
[d]Derived using delta method.
PGM=DEVOPS/SAR231893/EFC14153/CSR_RWE/REPORT/PGM/eff_eventsum_ger_subg_i_t.sas OUT=REPORT/OUTPUT/eff_evtsum_eaw52_ger_race_t2_t_x.rtf (02JUL2021 - 16:21)

Project Code / Study Number / Analysis: SAR231893 / EFC14153 / CSR_RWE

2 Severe exacerbation events

2.1 Annualized event rate of severe asthma exacerbation during the 52-week treatment period - ITT type 2 inflammatory asthma phenotype population

2.1.3 By race (Caucasian/white, Black/of African descent, Other)

	Race	
	Other	
Severe asthma exacerbation	**Placebo (N=7)**	**Dupilumab (N=19)**
Total number of Severe asthma exacerbation	13	9
Total patient-years followed	7.1	17.0
Unadjusted annualized rate of Severe asthma exacerbation[a]	1.83	0.53
Adjusted annualized rate of Severe asthma exacerbation		
Estimate (95% CI)[b]	2.29 (0.78 to 6.67)	0.26 (0.07 to 0.89)
Risk Ratio (95% CI) vs placebo[b]	-	0.11 (0.02 to 0.51)
p-value for Risk Ratio[b]		0.007
p-value for heterogeneity of Risk Ratio[c]:		
Caucasian/White, Black/of African descent		0.185
Caucasian/White, Other		0.875

All severe exacerbation events occurred during the 52-week treatment period are included, regardless of whether the patient is on-treatment or not
[a]The total number of events that occurred during the 52-week treatment period divided by the total number of patient-years followed in the 52-week treatment period.
[b]Derived using negative binomial model with the total number of events onset from randomization up to Week 52 visit or last contact date (whichever comes earlier) as the response variable, with the treatment groups, age, baseline weight group, region, baseline eosinophil level, baseline FeNO level, baseline ICS dose level and number of severe exacerbation events within 1 year prior to the study as covariates, and log-transformed standardized observation duration as an offset variable.
[c]Derived using same negative binomial model as described in [b] with subgroup and subgroup-by-treatment interaction as additional covariates.
[d]Derived using delta method.
PGM=DEVOPS/SAR231893/EFC14153/CSR_RWE/REPORT/PGM/eff_eventsum_ger_subg_i_t.sas OUT=REPORT/OUTPUT/eff_evtsum_eaw52_ger_race_t2_t_x.rtf (02JUL2021 - 16:21)

Project Code / Study Number / Analysis: SAR231893 / EFC14153 / CSR_RWE

2 Severe exacerbation events

2.1 Annualized event rate of severe asthma exacerbation during the 52-week treatment period - ITT type 2 inflammatory asthma phenotype population

2.1.3 By race (Caucasian/white, Black/of African descent, Other)

	Race	
	Other	
Severe asthma exacerbation	**Placebo (N=7)**	**Dupilumab (N=19)**
Black/of African descent, Other		0.086
overall		0.110
Risk Difference (95% CI) vs placebo[d]	-	-2.03 (-4.45 to 0.39)

All severe exacerbation events occurred during the 52-week treatment period are included, regardless of whether the patient is on-treatment or not

[a]The total number of events that occurred during the 52-week treatment period divided by the total number of patient-years followed in the 52-week treatment period.

[b]Derived using negative binomial model with the total number of events onset from randomization up to Week 52 visit or last contact date (whichever comes earlier) as the response variable, with the treatment groups, age, baseline weight group, region, baseline eosinophil level, baseline FeNO level, baseline ICS dose level and number of severe exacerbation events within 1 year prior to the study as covariates, and log-transformed standardized observation duration as an offset variable.

[c]Derived using same negative binomial model as described in [b] with subgroup and subgroup-by-treatment interaction as additional covariates.

[d]Derived using delta method.

PGM=DEVOPS/SAR231893/EFC14153/CSR_RWE/REPORT/PGM/eff_eventsum_ger_subg_i_t.sas OUT=REPORT/OUTPUT/eff_evtsum_eaw52_ger_race_t2_t_x.rtf (02JUL2021 - 16:21)

Project Code / Study Number / Analysis: SAR231893 / EFC14153 / CSR_RWE

2 Severe exacerbation events

2.1 Annualized event rate of severe asthma exacerbation during the 52-week treatment period - ITT type 2 inflammatory asthma phenotype population

2.1.4 By baseline ICS dose level (Medium, High)

	Baseline ICS dose level			
	High		Medium	
Severe asthma exacerbation	**Placebo (N=50)**	**Dupilumab (N=102)**	**Placebo (N=64)**	**Dupilumab (N=131)**
Patients with >=1 Severe asthma exacerbation [n(%)]				
Number	50	102	64	131
No	26 (52.0%)	71 (69.6%)	42 (65.6%)	108 (82.4%)
Yes	24 (48.0%)	31 (30.4%)	22 (34.4%)	23 (17.6%)
Number of Severe asthma exacerbation				
0	26 (52.0%)	71 (69.6%)	42 (65.6%)	108 (82.4%)
1	11 (22.0%)	18 (17.6%)	12 (18.8%)	18 (13.7%)
2	7 (14.0%)	8 (7.8%)	8 (12.5%)	3 (2.3%)
3	3 (6.0%)	3 (2.9%)	2 (3.1%)	2 (1.5%)
>=4	3 (6.0%)	2 (2.0%)	0	0

All severe exacerbation events occurred during the 52-week treatment period are included, regardless of whether the patient is on-treatment or not
[a]The total number of events that occurred during the 52-week treatment period divided by the total number of patient-years followed in the 52-week treatment period.
[b]Derived using negative binomial model with the total number of events onset from randomization up to Week 52 visit or last contact date (whichever comes earlier) as the response variable, with the treatment groups, age, baseline weight group, region, baseline eosinophil level, baseline FeNO level and number of severe exacerbation events within 1 year prior to the study as covariates, and log-transformed standardized observation duration as an offset variable.
[c]Derived using same negative binomial model as described in [b] with subgroup and subgroup-by-treatment interaction as additional covariates.
[d]Derived using delta method.
PGM=DEVOPS/SAR231893/EFC14153/CSR_RWE/REPORT/PGM/eff_eventsum_ger_subg_i_t.sas OUT=REPORT/OUTPUT/eff_evtsum_eaw52_ger_ics_t2_t_x.rtf (02JUL2021 - 16:22)

Project Code / Study Number / Analysis: SAR231893 / EFC14153 / CSR_RWE

2 Severe exacerbation events

2.1 Annualized event rate of severe asthma exacerbation during the 52-week treatment period - ITT type 2 inflammatory asthma phenotype population

2.1.4 By baseline ICS dose level (Medium, High)

	Baseline ICS dose level			
	High		Medium	
Severe asthma exacerbation	**Placebo (N=50)**	**Dupilumab (N=102)**	**Placebo (N=64)**	**Dupilumab (N=131)**
Total number of Severe asthma exacerbation	47	52	34	30
Total patient-years followed	49.3	100.6	63.4	127.6
Unadjusted annualized rate of Severe asthma exacerbation[a]	0.95	0.52	0.54	0.24
Adjusted annualized rate of Severe asthma exacerbation				
Estimate (95% CI)[b]	1.14 (0.74 to 1.78)	0.42 (0.28 to 0.63)	0.48 (0.29 to 0.79)	0.20 (0.12 to 0.33)
Risk Ratio (95% CI) vs placebo[b]	-	0.37 (0.21 to 0.64)	-	0.41 (0.23 to 0.73)
p-value for Risk Ratio[b]		<0.001		0.003
p-value for heterogeneity of Risk Ratio[c]				0.900
Risk Difference (95% CI) vs placebo[d]	-	-0.72 (-1.23 to -0.22)	-	-0.28 (-0.51 to -0.05)

All severe exacerbation events occurred during the 52-week treatment period are included, regardless of whether the patient is on-treatment or not
[a]The total number of events that occurred during the 52-week treatment period divided by the total number of patient-years followed in the 52-week treatment period.
[b]Derived using negative binomial model with the total number of events onset from randomization up to Week 52 visit or last contact date (whichever comes earlier) as the response variable, with the treatment groups, age, baseline weight group, region, baseline eosinophil level, baseline FeNO level and number of severe exacerbation events within 1 year prior to the study as covariates, and log-transformed standardized observation duration as an offset variable.
[c]Derived using same negative binomial model as described in [b] with subgroup and subgroup-by-treatment interaction as additional covariates.
[d]Derived using delta method.
PGM=DEVOPS/SAR231893/EFC14153/CSR_RWE/REPORT/PGM/eff_eventsum_ger_subg_i_t.sas OUT=REPORT/OUTPUT/eff_evtsum_eaw52_ger_ics_t2_t_x.rtf (02JUL2021 - 16:22)

Project Code / Study Number / Analysis: SAR231893 / EFC14153 / CSR_RWE

2 Severe exacerbation events

2.1 Annualized event rate of severe asthma exacerbation during the 52-week treatment period - ITT type 2 inflammatory asthma phenotype population

2.1.5 By baseline ICS dose level 2 (Medium, High)

	Baseline ICS dose level 2			
	High		Medium	
Severe asthma exacerbation	**Placebo (N=95)**	**Dupilumab (N=200)**	**Placebo (N=19)**	**Dupilumab (N=36)**
Patients with >=1 Severe asthma exacerbation [n(%)]				
Number	95	200	19	36
No	55 (57.9%)	149 (74.5%)	13 (68.4%)	33 (91.7%)
Yes	40 (42.1%)	51 (25.5%)	6 (31.6%)	3 (8.3%)
Number of Severe asthma exacerbation				
0	55 (57.9%)	149 (74.5%)	13 (68.4%)	33 (91.7%)
1	20 (21.1%)	34 (17.0%)	3 (15.8%)	2 (5.6%)
2	12 (12.6%)	10 (5.0%)	3 (15.8%)	1 (2.8%)
3	5 (5.3%)	5 (2.5%)	0	0
>=4	3 (3.2%)	2 (1.0%)	0	0

All severe exacerbation events occurred during the 52-week treatment period are included, regardless of whether the patient is on-treatment or not
[a]The total number of events that occurred during the 52-week treatment period divided by the total number of patient-years followed in the 52-week treatment period.
[b]Derived using negative binomial model with the total number of events onset from randomization up to Week 52 visit or last contact date (whichever comes earlier) as the response variable, with the treatment groups, age, baseline weight group, region, baseline eosinophil level, baseline FeNO level and number of severe exacerbation events within 1 year prior to the study as covariates, and log-transformed standardized observation duration as an offset variable.
[c]Derived using same negative binomial model as described in [b] with subgroup and subgroup-by-treatment interaction as additional covariates.
[d]Derived using delta method.
PGM=DEVOPS/SAR231893/EFC14153/CSR_RWE/REPORT/PGM/eff_eventsum_ger_subg_i_t.sas OUT=REPORT/OUTPUT/eff_evtsum_eaw52_ger_ics2_t2_t_x.rtf (01SEP2021 - 15:25)

Project Code / Study Number / Analysis: SAR231893 / EFC14153 / CSR_RWE

2 Severe exacerbation events

2.1 Annualized event rate of severe asthma exacerbation during the 52-week treatment period - ITT type 2 inflammatory asthma phenotype population

2.1.5 By baseline ICS dose level 2 (Medium, High)

	Baseline ICS dose level 2			
	High		Medium	
Severe asthma exacerbation	**Placebo (N=95)**	**Dupilumab (N=200)**	**Placebo (N=19)**	**Dupilumab (N=36)**
Total number of Severe asthma exacerbation	72	78	9	4
Total patient-years followed	93.7	196.4	19.0	33.2
Unadjusted annualized rate of Severe asthma exacerbation[a]	0.77	0.40	0.47	0.12
Adjusted annualized rate of Severe asthma exacerbation				
Estimate (95% CI)[b]	0.85 (0.60 to 1.20)	0.35 (0.26 to 0.49)	0.26 (0.08 to 0.90)	0.08 (0.02 to 0.36)
Risk Ratio (95% CI) vs placebo[b]	-	0.41 (0.27 to 0.63)	-	0.32 (0.08 to 1.31)
p-value for Risk Ratio[b]		<0.001		0.111
p-value for heterogeneity of Risk Ratio[c]				0.621
Risk Difference (95% CI) vs placebo[d]	-	-0.50 (-0.79 to -0.21)	-	-0.18 (-0.46 to 0.11)

All severe exacerbation events occurred during the 52-week treatment period are included, regardless of whether the patient is on-treatment or not
[a]The total number of events that occurred during the 52-week treatment period divided by the total number of patient-years followed in the 52-week treatment period.
[b]Derived using negative binomial model with the total number of events onset from randomization up to Week 52 visit or last contact date (whichever comes earlier) as the response variable, with the treatment groups, age, baseline weight group, region, baseline eosinophil level, baseline FeNO level and number of severe exacerbation events within 1 year prior to the study as covariates, and log-transformed standardized observation duration as an offset variable.
[c]Derived using same negative binomial model as described in [b] with subgroup and subgroup-by-treatment interaction as additional covariates.
[d]Derived using delta method.
PGM=DEVOPS/SAR231893/EFC14153/CSR_RWE/REPORT/PGM/eff_eventsum_ger_subg_i_t.sas OUT=REPORT/OUTPUT/eff_evtsum_eaw52_ger_ics2_t2_t_x.rtf (01SEP2021 - 15:25)

Project Code / Study Number / Analysis: SAR231893 / EFC14153 / CSR_RWE

2 Severe exacerbation events

2.1 Annualized event rate of severe asthma exacerbation during the 52-week treatment period - ITT type 2 inflammatory asthma phenotype population

2.1.6 By baseline predicted FEV1 (<80%, >=80%)

	Baseline Predicted FEV1			
	<80%		>=80%	
Severe asthma exacerbation	**Placebo (N=59)**	**Dupilumab (N=116)**	**Placebo (N=55)**	**Dupilumab (N=120)**
Patients with >=1 Severe asthma exacerbation [n(%)]				
Number	59	116	55	120
No	27 (45.8%)	89 (76.7%)	41 (74.5%)	93 (77.5%)
Yes	32 (54.2%)	27 (23.3%)	14 (25.5%)	27 (22.5%)
Number of Severe asthma exacerbation				
0	27 (45.8%)	89 (76.7%)	41 (74.5%)	93 (77.5%)
1	18 (30.5%)	19 (16.4%)	5 (9.1%)	17 (14.2%)
2	8 (13.6%)	5 (4.3%)	7 (12.7%)	6 (5.0%)
3	3 (5.1%)	2 (1.7%)	2 (3.6%)	3 (2.5%)
>=4	3 (5.1%)	1 (0.9%)	0	1 (0.8%)

All severe exacerbation events occurred during the 52-week treatment period are included, regardless of whether the patient is on-treatment or not
[a]The total number of events that occurred during the 52-week treatment period divided by the total number of patient-years followed in the 52-week treatment period.
[b]Derived using negative binomial model with the total number of events onset from randomization up to Week 52 visit or last contact date (whichever comes earlier) as the response variable, with the treatment groups, age, baseline weight group, region, baseline eosinophil level, baseline FeNO level, baseline ICS dose level and number of severe exacerbation events within 1 year prior to the study as covariates, and log-transformed standardized observation duration as an offset variable.
[c]Derived using same negative binomial model as described in [b] with subgroup and subgroup-by-treatment interaction as additional covariates.
[d]Derived using delta method.
PGM=DEVOPS/SAR231893/EFC14153/CSR_RWE/REPORT/PGM/eff_eventsum_ger_subg_i_t.sas OUT=REPORT/OUTPUT/eff_evtsum_eaw52_ger_pfev1_t2_t_x.rtf (02JUL2021 - 16:22)

Project Code / Study Number / Analysis: SAR231893 / EFC14153 / CSR_RWE

2 Severe exacerbation events

2.1 Annualized event rate of severe asthma exacerbation during the 52-week treatment period - ITT type 2 inflammatory asthma phenotype population

2.1.6 By baseline predicted FEV1 (<80%, >=80%)

	Baseline Predicted FEV1			
	<80%		>=80%	
Severe asthma exacerbation	**Placebo (N=59)**	**Dupilumab (N=116)**	**Placebo (N=55)**	**Dupilumab (N=120)**
Total number of Severe asthma exacerbation	56	39	25	43
Total patient-years followed	58.4	114.1	54.3	115.5
Unadjusted annualized rate of Severe asthma exacerbation[a]	0.96	0.34	0.46	0.37
Adjusted annualized rate of Severe asthma exacerbation				
Estimate (95% CI)[b]	0.91 (0.62 to 1.33)	0.30 (0.19 to 0.45)	0.49 (0.27 to 0.87)	0.27 (0.16 to 0.44)
Risk Ratio (95% CI) vs placebo[b]	-	0.32 (0.20 to 0.52)	-	0.55 (0.28 to 1.09)
p-value for Risk Ratio[b]		<0.001		0.088
p-value for heterogeneity of Risk Ratio[c]				0.168
Risk Difference (95% CI) vs placebo[d]	-	-0.61 (-0.94 to -0.29)	-	-0.22 (-0.51 to 0.07)

All severe exacerbation events occurred during the 52-week treatment period are included, regardless of whether the patient is on-treatment or not
[a]The total number of events that occurred during the 52-week treatment period divided by the total number of patient-years followed in the 52-week treatment period.
[b]Derived using negative binomial model with the total number of events onset from randomization up to Week 52 visit or last contact date (whichever comes earlier) as the response variable, with the treatment groups, age, baseline weight group, region, baseline eosinophil level, baseline FeNO level, baseline ICS dose level and number of severe exacerbation events within 1 year prior to the study as covariates, and log-transformed standardized observation duration as an offset variable.
[c]Derived using same negative binomial model as described in [b] with subgroup and subgroup-by-treatment interaction as additional covariates.
[d]Derived using delta method.
PGM=DEVOPS/SAR231893/EFC14153/CSR_RWE/REPORT/PGM/eff_eventsum_ger_subg_i_t.sas OUT=REPORT/OUTPUT/eff_evtsum_eaw52_ger_pfev1_t2_t_x.rtf (02JUL2021 - 16:22)

Project Code / Study Number / Analysis: SAR231893 / EFC14153 / CSR_RWE

2 Severe exacerbation events

2.1 Annualized event rate of severe asthma exacerbation during the 52-week treatment period - ITT type 2 inflammatory asthma phenotype population

2.1.7 By baseline ACQ-7-IA (<=2, >2)

	Baseline ACQ-7-IA			
	<=2		>2	
Severe asthma exacerbation	**Placebo (N=61)**	**Dupilumab (N=126)**	**Placebo (N=53)**	**Dupilumab (N=110)**
Patients with >=1 Severe asthma exacerbation [n(%)]				
Number	61	126	53	110
No	42 (68.9%)	100 (79.4%)	26 (49.1%)	82 (74.5%)
Yes	19 (31.1%)	26 (20.6%)	27 (50.9%)	28 (25.5%)
Number of Severe asthma exacerbation				
0	42 (68.9%)	100 (79.4%)	26 (49.1%)	82 (74.5%)
1	13 (21.3%)	19 (15.1%)	10 (18.9%)	17 (15.5%)
2	4 (6.6%)	5 (4.0%)	11 (20.8%)	6 (5.5%)
3	2 (3.3%)	2 (1.6%)	3 (5.7%)	3 (2.7%)
>=4	0	0	3 (5.7%)	2 (1.8%)

All severe exacerbation events occurred during the 52-week treatment period are included, regardless of whether the patient is on-treatment or not
[a]The total number of events that occurred during the 52-week treatment period divided by the total number of patient-years followed in the 52-week treatment period.
[b]Derived using negative binomial model with the total number of events onset from randomization up to Week 52 visit or last contact date (whichever comes earlier) as the response variable, with the treatment groups, age, baseline weight group, region, baseline eosinophil level, baseline FeNO level, baseline ICS dose level and number of severe exacerbation events within 1 year prior to the study as covariates, and log-transformed standardized observation duration as an offset variable.
[c]Derived using same negative binomial model as described in [b] with subgroup and subgroup-by-treatment interaction as additional covariates.
[d]Derived using delta method.
PGM=DEVOPS/SAR231893/EFC14153/CSR_RWE/REPORT/PGM/eff_eventsum_ger_subg_i_t.sas OUT=REPORT/OUTPUT/eff_evtsum_eaw52_ger_acq7_t2_t_x.rtf (02JUL2021 - 16:22)

Project Code / Study Number / Analysis: SAR231893 / EFC14153 / CSR_RWE

2 Severe exacerbation events

2.1 Annualized event rate of severe asthma exacerbation during the 52-week treatment period - ITT type 2 inflammatory asthma phenotype population

2.1.7 By baseline ACQ-7-IA (<=2, >2)

	Baseline ACQ-7-IA			
	<=2		>2	
Severe asthma exacerbation	**Placebo (N=61)**	**Dupilumab (N=126)**	**Placebo (N=53)**	**Dupilumab (N=110)**
Total number of Severe asthma exacerbation	27	35	54	47
Total patient-years followed	61.1	122.6	51.6	107.0
Unadjusted annualized rate of Severe asthma exacerbation[a]	0.44	0.29	1.05	0.44
Adjusted annualized rate of Severe asthma exacerbation				
Estimate (95% CI)[b]	0.48 (0.29 to 0.77)	0.28 (0.18 to 0.43)	1.06 (0.70 to 1.62)	0.33 (0.21 to 0.51)
Risk Ratio (95% CI) vs placebo[b]	-	0.58 (0.32 to 1.05)	-	0.31 (0.18 to 0.52)
p-value for Risk Ratio[b]		0.073		<0.001
p-value for heterogeneity of Risk Ratio[c]				0.123
Risk Difference (95% CI) vs placebo[d]	-	-0.20 (-0.44 to 0.04)	-	-0.74 (-1.17 to -0.30)

All severe exacerbation events occurred during the 52-week treatment period are included, regardless of whether the patient is on-treatment or not
[a]The total number of events that occurred during the 52-week treatment period divided by the total number of patient-years followed in the 52-week treatment period.
[b]Derived using negative binomial model with the total number of events onset from randomization up to Week 52 visit or last contact date (whichever comes earlier) as the response variable, with the treatment groups, age, baseline weight group, region, baseline eosinophil level, baseline FeNO level, baseline ICS dose level and number of severe exacerbation events within 1 year prior to the study as covariates, and log-transformed standardized observation duration as an offset variable.
[c]Derived using same negative binomial model as described in [b] with subgroup and subgroup-by-treatment interaction as additional covariates.
[d]Derived using delta method.
PGM=DEVOPS/SAR231893/EFC14153/CSR_RWE/REPORT/PGM/eff_eventsum_ger_subg_i_t.sas OUT=REPORT/OUTPUT/eff_evtsum_eaw52_ger_acq7_t2_t_x.rtf (02JUL2021 - 16:22)

Project Code / Study Number / Analysis: SAR231893 / EFC14153 / CSR_RWE

2 Severe exacerbation events

2.1 Annualized event rate of severe asthma exacerbation during the 52-week treatment period - ITT type 2 inflammatory asthma phenotype population

2.1.8 By baseline weight (<=30 kg, >30 kg)

	Baseline weight (kg)			
	<=30		>30	
Severe asthma exacerbation	**Placebo (N=36)**	**Dupilumab (N=76)**	**Placebo (N=78)**	**Dupilumab (N=160)**
Patients with >=1 Severe asthma exacerbation [n(%)]				
Number	36	76	78	160
No	19 (52.8%)	62 (81.6%)	49 (62.8%)	120 (75.0%)
Yes	17 (47.2%)	14 (18.4%)	29 (37.2%)	40 (25.0%)
Number of Severe asthma exacerbation				
0	19 (52.8%)	62 (81.6%)	49 (62.8%)	120 (75.0%)
1	10 (27.8%)	10 (13.2%)	13 (16.7%)	26 (16.3%)
2	4 (11.1%)	3 (3.9%)	11 (14.1%)	8 (5.0%)
3	3 (8.3%)	1 (1.3%)	2 (2.6%)	4 (2.5%)
>=4	0	0	3 (3.8%)	2 (1.3%)

All severe exacerbation events occurred during the 52-week treatment period are included, regardless of whether the patient is on-treatment or not
[a]The total number of events that occurred during the 52-week treatment period divided by the total number of patient-years followed in the 52-week treatment period.
[b]Derived using negative binomial model with the total number of events onset from randomization up to Week 52 visit or last contact date (whichever comes earlier) as the response variable, with the treatment groups, age, region, baseline eosinophil level, baseline FeNO level, baseline ICS dose level and number of severe exacerbation events within 1 year prior to the study as covariates, and log-transformed standardized observation duration as an offset variable.
[c]Derived using same negative binomial model as described in [b] with subgroup and subgroup-by-treatment interaction as additional covariates.
[d]Derived using delta method.
PGM=DEVOPS/SAR231893/EFC14153/CSR_RWE/REPORT/PGM/eff_eventsum_ger_subg_i_t.sas OUT=REPORT/OUTPUT/eff_evtsum_eaw52_ger_wgt_t2_t_x.rtf (02JUL2021 - 16:22)

Project Code / Study Number / Analysis: SAR231893 / EFC14153 / CSR_RWE

2 Severe exacerbation events

2.1 Annualized event rate of severe asthma exacerbation during the 52-week treatment period - ITT type 2 inflammatory asthma phenotype population

2.1.8 By baseline weight (<=30 kg, >30 kg)

	Baseline weight (kg)			
	<=30		>30	
Severe asthma exacerbation	**Placebo (N=36)**	**Dupilumab (N=76)**	**Placebo (N=78)**	**Dupilumab (N=160)**
Total number of Severe asthma exacerbation	27	19	54	63
Total patient-years followed	35.9	72.9	76.8	156.7
Unadjusted annualized rate of Severe asthma exacerbation[a]	0.75	0.26	0.70	0.40
Adjusted annualized rate of Severe asthma exacerbation				
Estimate (95% CI)[b]	0.62 (0.36 to 1.08)	0.20 (0.11 to 0.36)	0.77 (0.52 to 1.13)	0.34 (0.24 to 0.49)
Risk Ratio (95% CI) vs placebo[b]	-	0.32 (0.16 to 0.64)	-	0.45 (0.28 to 0.72)
p-value for Risk Ratio[b]		0.002		0.001
p-value for heterogeneity of Risk Ratio[c]				0.327
Risk Difference (95% CI) vs placebo[d]	-	-0.42 (-0.75 to -0.09)	-	-0.42 (-0.72 to -0.12)

All severe exacerbation events occurred during the 52-week treatment period are included, regardless of whether the patient is on-treatment or not
[a]The total number of events that occurred during the 52-week treatment period divided by the total number of patient-years followed in the 52-week treatment period.
[b]Derived using negative binomial model with the total number of events onset from randomization up to Week 52 visit or last contact date (whichever comes earlier) as the response variable, with the treatment groups, age, region, baseline eosinophil level, baseline FeNO level, baseline ICS dose level and number of severe exacerbation events within 1 year prior to the study as covariates, and log-transformed standardized observation duration as an offset variable.
[c]Derived using same negative binomial model as described in [b] with subgroup and subgroup-by-treatment interaction as additional covariates.
[d]Derived using delta method.
PGM=DEVOPS/SAR231893/EFC14153/CSR_RWE/REPORT/PGM/eff_eventsum_ger_subg_i_t.sas OUT=REPORT/OUTPUT/eff_evtsum_eaw52_ger_wgt_t2_t_x.rtf (02JUL2021 - 16:22)

Project Code / Study Number / Analysis: SAR231893 / EFC14153 / CSR_RWE

2 Severe exacerbation events

2.1 Annualized event rate of severe asthma exacerbation during the 52-week treatment period - ITT type 2 inflammatory asthma phenotype population

2.1.9 By atopic medical condition (Yes, No)

	Atopic medical condition			
	Yes		No	
Severe asthma exacerbation	**Placebo (N=103)**	**Dupilumab (N=227)**	**Placebo (N=11)**	**Dupilumab (N=9)**
Patients with >=1 Severe asthma exacerbation [n(%)]				
Number	103	227	11	9
No	62 (60.2%)	174 (76.7%)	6 (54.5%)	8 (88.9%)
Yes	41 (39.8%)	53 (23.3%)	5 (45.5%)	1 (11.1%)
Number of Severe asthma exacerbation				
0	62 (60.2%)	174 (76.7%)	6 (54.5%)	8 (88.9%)
1	21 (20.4%)	35 (15.4%)	2 (18.2%)	1 (11.1%)
2	13 (12.6%)	11 (4.8%)	2 (18.2%)	0
3	4 (3.9%)	5 (2.2%)	1 (9.1%)	0
>=4	3 (2.9%)	2 (0.9%)	0	0

All severe exacerbation events occurred during the 52-week treatment period are included, regardless of whether the patient is on-treatment or not

[a]The total number of events that occurred during the 52-week treatment period divided by the total number of patient-years followed in the 52-week treatment period.

[b]Derived using negative binomial model with the total number of events onset from randomization up to Week 52 visit or last contact date (whichever comes earlier) as the response variable, with the treatment groups, age, baseline weight group, region, baseline eosinophil level, baseline FeNO level, baseline ICS dose level and number of severe exacerbation events within 1 year prior to the study as covariates, and log-transformed standardized observation duration as an offset variable.

[c]Derived using same negative binomial model as described in [b] with subgroup and subgroup-by-treatment interaction as additional covariates.

[d]Derived using delta method.

PGM=DEVOPS/SAR231893/EFC14153/CSR_RWE/REPORT/PGM/eff_eventsum_ger_subg_i_t.sas OUT=REPORT/OUTPUT/eff_evtsum_eaw52_ger_amc_t2_t_x.rtf (02JUL2021 - 16:23)

Project Code / Study Number / Analysis: SAR231893 / EFC14153 / CSR_RWE

2 Severe exacerbation events

2.1 Annualized event rate of severe asthma exacerbation during the 52-week treatment period - ITT type 2 inflammatory asthma phenotype population

2.1.9 By atopic medical condition (Yes, No)

	Atopic medical condition			
	Yes		No	
Severe asthma exacerbation	**Placebo (N=103)**	**Dupilumab (N=227)**	**Placebo (N=11)**	**Dupilumab (N=9)**
Total number of Severe asthma exacerbation	72	81	9	1
Total patient-years followed	101.7	220.6	11.0	9.0
Unadjusted annualized rate of Severe asthma exacerbation[a]	0.71	0.37	0.82	0.11
Adjusted annualized rate of Severe asthma exacerbation				
Estimate (95% CI)[b]	0.71 (0.50 to 1.01)	0.30 (0.22 to 0.42)	0.52 (0.10 to 2.73)	0.07 (0.00 to 1.90)
Risk Ratio (95% CI) vs placebo[b]	-	0.43 (0.28 to 0.64)	-	0.14 (0.01 to 2.27)
p-value for Risk Ratio[b]		<0.001		0.146
p-value for heterogeneity of Risk Ratio[c]				0.247
Risk Difference (95% CI) vs placebo[d]	-	-0.41 (-0.65 to -0.17)	-	-0.44 (-1.21 to 0.32)

All severe exacerbation events occurred during the 52-week treatment period are included, regardless of whether the patient is on-treatment or not
[a]The total number of events that occurred during the 52-week treatment period divided by the total number of patient-years followed in the 52-week treatment period.
[b]Derived using negative binomial model with the total number of events onset from randomization up to Week 52 visit or last contact date (whichever comes earlier) as the response variable, with the treatment groups, age, baseline weight group, region, baseline eosinophil level, baseline FeNO level, baseline ICS dose level and number of severe exacerbation events within 1 year prior to the study as covariates, and log-transformed standardized observation duration as an offset variable.
[c]Derived using same negative binomial model as described in [b] with subgroup and subgroup-by-treatment interaction as additional covariates.
[d]Derived using delta method.
PGM=DEVOPS/SAR231893/EFC14153/CSR_RWE/REPORT/PGM/eff_eventsum_ger_subg_i_t.sas OUT=REPORT/OUTPUT/eff_evtsum_eaw52_ger_amc_t2_t_x.rtf (02JUL2021 - 16:23)

Project Code / Study Number / Analysis: SAR231893 / EFC14153 / CSR_RWE

2 Severe exacerbation events

2.1 Annualized event rate of severe asthma exacerbation during the 52-week treatment period - ITT type 2 inflammatory asthma phenotype population

2.1.10 By baseline total IgE (<median, >= median)

	Baseline Total IgE (IU/mL)			
	<median		>=median	
Severe asthma exacerbation	**Placebo (N=66)**	**Dupilumab (N=105)**	**Placebo (N=47)**	**Dupilumab (N=125)**
Patients with >=1 Severe asthma exacerbation [n(%)]				
Number	66	105	47	125
No	40 (60.6%)	78 (74.3%)	28 (59.6%)	98 (78.4%)
Yes	26 (39.4%)	27 (25.7%)	19 (40.4%)	27 (21.6%)
Number of Severe asthma exacerbation				
0	40 (60.6%)	78 (74.3%)	28 (59.6%)	98 (78.4%)
1	13 (19.7%)	18 (17.1%)	10 (21.3%)	18 (14.4%)
2	8 (12.1%)	7 (6.7%)	6 (12.8%)	4 (3.2%)
3	3 (4.5%)	1 (1.0%)	2 (4.3%)	4 (3.2%)
>=4	2 (3.0%)	1 (1.0%)	1 (2.1%)	1 (0.8%)

All severe exacerbation events occurred during the 52-week treatment period are included, regardless of whether the patient is on-treatment or not

[a]The total number of events that occurred during the 52-week treatment period divided by the total number of patient-years followed in the 52-week treatment period.

[b]Derived using negative binomial model with the total number of events onset from randomization up to Week 52 visit or last contact date (whichever comes earlier) as the response variable, with the treatment groups, age, baseline weight group, region, baseline eosinophil level, baseline FeNO level, baseline ICS dose level and number of severe exacerbation events within 1 year prior to the study as covariates, and log-transformed standardized observation duration as an offset variable.

[c]Derived using same negative binomial model as described in [b] with subgroup and subgroup-by-treatment interaction as additional covariates.

[d]Derived using delta method.

PGM=DEVOPS/SAR231893/EFC14153/CSR_RWE/REPORT/PGM/eff_eventsum_ger_subg_i_t.sas OUT=REPORT/OUTPUT/eff_evtsum_eaw52_ger_igem_t2_t_x.rtf (02JUL2021 - 16:23)

Project Code / Study Number / Analysis: SAR231893 / EFC14153 / CSR_RWE

2 Severe exacerbation events

2.1 Annualized event rate of severe asthma exacerbation during the 52-week treatment period - ITT type 2 inflammatory asthma phenotype population

2.1.10 By baseline total IgE (<median, >= median)

	Baseline Total IgE (IU/mL)			
	<median		>=median	
Severe asthma exacerbation	**Placebo (N=66)**	**Dupilumab (N=105)**	**Placebo (N=47)**	**Dupilumab (N=125)**
Total number of Severe asthma exacerbation	47	40	32	42
Total patient-years followed	65.7	103.7	46.0	122.1
Unadjusted annualized rate of Severe asthma exacerbation[a]	0.72	0.39	0.70	0.34
Adjusted annualized rate of Severe asthma exacerbation				
Estimate (95% CI)[b]	0.82 (0.54 to 1.25)	0.35 (0.23 to 0.53)	0.54 (0.29 to 1.00)	0.21 (0.12 to 0.37)
Risk Ratio (95% CI) vs placebo[b]	-	0.42 (0.24 to 0.74)	-	0.39 (0.22 to 0.70)
p-value for Risk Ratio[b]		0.002		0.002
p-value for heterogeneity of Risk Ratio[c]				0.779
Risk Difference (95% CI) vs placebo[d]	-	-0.47 (-0.83 to -0.12)	-	-0.32 (-0.61 to -0.04)

All severe exacerbation events occurred during the 52-week treatment period are included, regardless of whether the patient is on-treatment or not
[a]The total number of events that occurred during the 52-week treatment period divided by the total number of patient-years followed in the 52-week treatment period.
[b]Derived using negative binomial model with the total number of events onset from randomization up to Week 52 visit or last contact date (whichever comes earlier) as the response variable, with the treatment groups, age, baseline weight group, region, baseline eosinophil level, baseline FeNO level, baseline ICS dose level and number of severe exacerbation events within 1 year prior to the study as covariates, and log-transformed standardized observation duration as an offset variable.
[c]Derived using same negative binomial model as described in [b] with subgroup and subgroup-by-treatment interaction as additional covariates.
[d]Derived using delta method.
PGM=DEVOPS/SAR231893/EFC14153/CSR_RWE/REPORT/PGM/eff_eventsum_ger_subg_i_t.sas OUT=REPORT/OUTPUT/eff_evtsum_eaw52_ger_igem_t2_t_x.rtf (02JUL2021 - 16:23)

Project Code / Study Number / Analysis: SAR231893 / EFC14153 / CSR_RWE

2 Severe exacerbation events

2.1 Annualized event rate of severe asthma exacerbation during the 52-week treatment period - ITT type 2 inflammatory asthma phenotype population

2.1.11 By baseline total IgE (<100 IU/ml, >= 100 IU/ml)

	Baseline Total IgE (IU/mL)			
	< 100		>= 100	
Severe asthma exacerbation	**Placebo (N=22)**	**Dupilumab (N=29)**	**Placebo (N=91)**	**Dupilumab (N=201)**
Patients with >=1 Severe asthma exacerbation [n(%)]				
Number	22	29	91	201
No	15 (68.2%)	23 (79.3%)	53 (58.2%)	153 (76.1%)
Yes	7 (31.8%)	6 (20.7%)	38 (41.8%)	48 (23.9%)
Number of Severe asthma exacerbation				
0	15 (68.2%)	23 (79.3%)	53 (58.2%)	153 (76.1%)
1	5 (22.7%)	1 (3.4%)	18 (19.8%)	35 (17.4%)
2	1 (4.5%)	3 (10.3%)	13 (14.3%)	8 (4.0%)
3	1 (4.5%)	1 (3.4%)	4 (4.4%)	4 (2.0%)
>=4	0	1 (3.4%)	3 (3.3%)	1 (0.5%)

All severe exacerbation events occurred during the 52-week treatment period are included, regardless of whether the patient is on-treatment or not
[a]The total number of events that occurred during the 52-week treatment period divided by the total number of patient-years followed in the 52-week treatment period.
[b]Derived using negative binomial model with the total number of events onset from randomization up to Week 52 visit or last contact date (whichever comes earlier) as the response variable, with the treatment groups, age, baseline weight group, region, baseline eosinophil level, baseline FeNO level, baseline ICS dose level and number of severe exacerbation events within 1 year prior to the study as covariates, and log-transformed standardized observation duration as an offset variable.
[c]Derived using same negative binomial model as described in [b] with subgroup and subgroup-by-treatment interaction as additional covariates.
[d]Derived using delta method.
PGM=DEVOPS/SAR231893/EFC14153/CSR_RWE/REPORT/PGM/eff_eventsum_ger_subg_i_t.sas OUT=REPORT/OUTPUT/eff_evtsum_eaw52_ger_ige_t2_t_x.rtf (02JUL2021 - 16:23)

Project Code / Study Number / Analysis: SAR231893 / EFC14153 / CSR_RWE

2 Severe exacerbation events

2.1 Annualized event rate of severe asthma exacerbation during the 52-week treatment period - ITT type 2 inflammatory asthma phenotype population

2.1.11 By baseline total IgE (<100 IU/ml, >= 100 IU/ml)

	Baseline Total IgE (IU/mL)			
	< 100		**>= 100**	
Severe asthma exacerbation	**Placebo (N=22)**	**Dupilumab (N=29)**	**Placebo (N=91)**	**Dupilumab (N=201)**
Total number of Severe asthma exacerbation	10	15	69	67
Total patient-years followed	22.0	29.0	89.7	196.8
Unadjusted annualized rate of Severe asthma exacerbation[a]	0.45	0.52	0.77	0.34
Adjusted annualized rate of Severe asthma exacerbation				
Estimate (95% CI)[b]	0.26 (0.08 to 0.84)	0.14 (0.04 to 0.51)	0.76 (0.52 to 1.10)	0.29 (0.21 to 0.41)
Risk Ratio (95% CI) vs placebo[b]	-	0.55 (0.21 to 1.43)	-	0.39 (0.25 to 0.59)
p-value for Risk Ratio[b]		0.213		<0.001
p-value for heterogeneity of Risk Ratio[c]				0.267
Risk Difference (95% CI) vs placebo[d]	-	-0.12 (-0.34 to 0.10)	-	-0.46 (-0.73 to -0.20)

All severe exacerbation events occurred during the 52-week treatment period are included, regardless of whether the patient is on-treatment or not
[a]The total number of events that occurred during the 52-week treatment period divided by the total number of patient-years followed in the 52-week treatment period.
[b]Derived using negative binomial model with the total number of events onset from randomization up to Week 52 visit or last contact date (whichever comes earlier) as the response variable, with the treatment groups, age, baseline weight group, region, baseline eosinophil level, baseline FeNO level, baseline ICS dose level and number of severe exacerbation events within 1 year prior to the study as covariates, and log-transformed standardized observation duration as an offset variable.
[c]Derived using same negative binomial model as described in [b] with subgroup and subgroup-by-treatment interaction as additional covariates.
[d]Derived using delta method.
PGM=DEVOPS/SAR231893/EFC14153/CSR_RWE/REPORT/PGM/eff_eventsum_ger_subg_i_t.sas OUT=REPORT/OUTPUT/eff_evtsum_eaw52_ger_ige_t2_t_x.rtf (02JUL2021 - 16:23)

Project Code / Study Number / Analysis: SAR231893 / EFC14153 / CSR_RWE

2 Severe exacerbation events

2.1 Annualized event rate of severe asthma exacerbation during the 52-week treatment period - ITT type 2 inflammatory asthma phenotype population

2.1.12 By age at onset of asthma (0-2, 3-5, >=6 years)

	Age of onset of asthma (years)			
	0-2		3-5	
Severe asthma exacerbation	**Placebo (N=40)**	**Dupilumab (N=105)**	**Placebo (N=39)**	**Dupilumab (N=86)**
Patients with >=1 Severe asthma exacerbation [n(%)]				
Number	40	105	39	86
No	17 (42.5%)	75 (71.4%)	28 (71.8%)	67 (77.9%)
Yes	23 (57.5%)	30 (28.6%)	11 (28.2%)	19 (22.1%)
Number of Severe asthma exacerbation				
0	17 (42.5%)	75 (71.4%)	28 (71.8%)	67 (77.9%)
1	14 (35.0%)	23 (21.9%)	5 (12.8%)	8 (9.3%)
2	7 (17.5%)	4 (3.8%)	4 (10.3%)	7 (8.1%)
3	2 (5.0%)	1 (1.0%)	1 (2.6%)	4 (4.7%)
>=4	0	2 (1.9%)	1 (2.6%)	0

All severe exacerbation events occurred during the 52-week treatment period are included, regardless of whether the patient is on-treatment or not
[a]The total number of events that occurred during the 52-week treatment period divided by the total number of patient-years followed in the 52-week treatment period.
[b]Derived using negative binomial model with the total number of events onset from randomization up to Week 52 visit or last contact date (whichever comes earlier) as the response variable, with the treatment groups, age, baseline weight group, region, baseline eosinophil level, baseline FeNO level, baseline ICS dose level and number of severe exacerbation events within 1 year prior to the study as covariates, and log-transformed standardized observation duration as an offset variable.
[c]Derived using same negative binomial model as described in [b] with subgroup and subgroup-by-treatment interaction as additional covariates.
[d]Derived using delta method.
PGM=DEVOPS/SAR231893/EFC14153/CSR_RWE/REPORT/PGM/eff_eventsum_ger_subg_i_t.sas OUT=REPORT/OUTPUT/eff_evtsum_eaw52_ger_onsa_t2_t_x.rtf (10AUG2021 - 8:10)

Project Code / Study Number / Analysis: SAR231893 / EFC14153 / CSR_RWE

2 Severe exacerbation events

2.1 Annualized event rate of severe asthma exacerbation during the 52-week treatment period - ITT type 2 inflammatory asthma phenotype population

2.1.12 By age at onset of asthma (0-2, 3-5, >=6 years)

	Age of onset of asthma (years)			
	0-2		3-5	
Severe asthma exacerbation	**Placebo (N=40)**	**Dupilumab (N=105)**	**Placebo (N=39)**	**Dupilumab (N=86)**
Total number of Severe asthma exacerbation	34	43	20	34
Total patient-years followed	39.1	103.5	38.5	82.3
Unadjusted annualized rate of Severe asthma exacerbation[a]	0.87	0.42	0.52	0.41
Adjusted annualized rate of Severe asthma exacerbation				
Estimate (95% CI)[b]	1.10 (0.71 to 1.71)	0.40 (0.27 to 0.60)	0.39 (0.19 to 0.80)	0.27 (0.15 to 0.49)
Risk Ratio (95% CI) vs placebo[b]	-	0.36 (0.21 to 0.62)	-	0.70 (0.32 to 1.53)
p-value for Risk Ratio[b]		<0.001		0.364
p-value for heterogeneity of Risk Ratio[c]:				
0-2, 3-5				
0-2, >= 6				
3-5, >= 6				

All severe exacerbation events occurred during the 52-week treatment period are included, regardless of whether the patient is on-treatment or not
[a]The total number of events that occurred during the 52-week treatment period divided by the total number of patient-years followed in the 52-week treatment period.
[b]Derived using negative binomial model with the total number of events onset from randomization up to Week 52 visit or last contact date (whichever comes earlier) as the response variable, with the treatment groups, age, baseline weight group, region, baseline eosinophil level, baseline FeNO level, baseline ICS dose level and number of severe exacerbation events within 1 year prior to the study as covariates, and log-transformed standardized observation duration as an offset variable.
[c]Derived using same negative binomial model as described in [b] with subgroup and subgroup-by-treatment interaction as additional covariates.
[d]Derived using delta method.
PGM=DEVOPS/SAR231893/EFC14153/CSR_RWE/REPORT/PGM/eff_eventsum_ger_subg_i_t.sas OUT=REPORT/OUTPUT/eff_evtsum_eaw52_ger_onsa_t2_t_x.rtf (10AUG2021 - 8:10)

Project Code / Study Number / Analysis: SAR231893 / EFC14153 / CSR_RWE

2 Severe exacerbation events

2.1 Annualized event rate of severe asthma exacerbation during the 52-week treatment period - ITT type 2 inflammatory asthma phenotype population

2.1.12 By age at onset of asthma (0-2, 3-5, >=6 years)

	Age of onset of asthma (years)			
	0-2		3-5	
Severe asthma exacerbation	**Placebo (N=40)**	**Dupilumab (N=105)**	**Placebo (N=39)**	**Dupilumab (N=86)**
overall				
Risk Difference (95% CI) vs placebo[d]	-	-0.70 (-1.18 to -0.22)	-	-0.12 (-0.39 to 0.16)

All severe exacerbation events occurred during the 52-week treatment period are included, regardless of whether the patient is on-treatment or not
[a]The total number of events that occurred during the 52-week treatment period divided by the total number of patient-years followed in the 52-week treatment period.
[b]Derived using negative binomial model with the total number of events onset from randomization up to Week 52 visit or last contact date (whichever comes earlier) as the response variable, with the treatment groups, age, baseline weight group, region, baseline eosinophil level, baseline FeNO level, baseline ICS dose level and number of severe exacerbation events within 1 year prior to the study as covariates, and log-transformed standardized observation duration as an offset variable.
[c]Derived using same negative binomial model as described in [b] with subgroup and subgroup-by-treatment interaction as additional covariates.
[d]Derived using delta method.
PGM=DEVOPS/SAR231893/EFC14153/CSR_RWE/REPORT/PGM/eff_eventsum_ger_subg_i_t.sas OUT=REPORT/OUTPUT/eff_evtsum_eaw52_ger_onsa_t2_t_x.rtf (10AUG2021 - 8:10)

Project Code / Study Number / Analysis: SAR231893 / EFC14153 / CSR_RWE

2 Severe exacerbation events

2.1 Annualized event rate of severe asthma exacerbation during the 52-week treatment period - ITT type 2 inflammatory asthma phenotype population

2.1.12 By age at onset of asthma (0-2, 3-5, >=6 years)

	Age of onset of asthma (years)	
	>= 6	
Severe asthma exacerbation	**Placebo (N=35)**	**Dupilumab (N=45)**
Patients with >=1 Severe asthma exacerbation [n(%)]		
Number	35	45
No	23 (65.7%)	40 (88.9%)
Yes	12 (34.3%)	5 (11.1%)
Number of Severe asthma exacerbation		
0	23 (65.7%)	40 (88.9%)
1	4 (11.4%)	5 (11.1%)
2	4 (11.4%)	0
3	2 (5.7%)	0
>=4	2 (5.7%)	0

All severe exacerbation events occurred during the 52-week treatment period are included, regardless of whether the patient is on-treatment or not
[a]The total number of events that occurred during the 52-week treatment period divided by the total number of patient-years followed in the 52-week treatment period.
[b]Derived using negative binomial model with the total number of events onset from randomization up to Week 52 visit or last contact date (whichever comes earlier) as the response variable, with the treatment groups, age, baseline weight group, region, baseline eosinophil level, baseline FeNO level, baseline ICS dose level and number of severe exacerbation events within 1 year prior to the study as covariates, and log-transformed standardized observation duration as an offset variable.
[c]Derived using same negative binomial model as described in [b] with subgroup and subgroup-by-treatment interaction as additional covariates.
[d]Derived using delta method.
PGM=DEVOPS/SAR231893/EFC14153/CSR_RWE/REPORT/PGM/eff_eventsum_ger_subg_i_t.sas OUT=REPORT/OUTPUT/eff_evtsum_eaw52_ger_onsa_t2_t_x.rtf (10AUG2021 - 8:10)

Project Code / Study Number / Analysis: SAR231893 / EFC14153 / CSR_RWE

2 Severe exacerbation events

2.1 Annualized event rate of severe asthma exacerbation during the 52-week treatment period - ITT type 2 inflammatory asthma phenotype population

2.1.12 By age at onset of asthma (0-2, 3-5, >=6 years)

	Age of onset of asthma (years)	
	>= 6	
Severe asthma exacerbation	**Placebo (N=35)**	**Dupilumab (N=45)**
Total number of Severe asthma exacerbation	27	5
Total patient-years followed	35.1	43.7
Unadjusted annualized rate of Severe asthma exacerbation[a]	0.77	0.11
Adjusted annualized rate of Severe asthma exacerbation		
Estimate (95% CI)[b]	0.59 (0.28 to 1.25)	0.12 (0.04 to 0.35)
Risk Ratio (95% CI) vs placebo[b]	-	0.20 (0.07 to 0.60)
p-value for Risk Ratio[b]		0.005
p-value for heterogeneity of Risk Ratio[c]:		
0-2, 3-5		0.090
0-2, >= 6		0.274

All severe exacerbation events occurred during the 52-week treatment period are included, regardless of whether the patient is on-treatment or not
[a]The total number of events that occurred during the 52-week treatment period divided by the total number of patient-years followed in the 52-week treatment period.
[b]Derived using negative binomial model with the total number of events onset from randomization up to Week 52 visit or last contact date (whichever comes earlier) as the response variable, with the treatment groups, age, baseline weight group, region, baseline eosinophil level, baseline FeNO level, baseline ICS dose level and number of severe exacerbation events within 1 year prior to the study as covariates, and log-transformed standardized observation duration as an offset variable.
[c]Derived using same negative binomial model as described in [b] with subgroup and subgroup-by-treatment interaction as additional covariates.
[d]Derived using delta method.
PGM=DEVOPS/SAR231893/EFC14153/CSR_RWE/REPORT/PGM/eff_eventsum_ger_subg_i_t.sas OUT=REPORT/OUTPUT/eff_evtsum_eaw52_ger_onsa_t2_t_x.rtf (10AUG2021 - 8:10)

Project Code / Study Number / Analysis: SAR231893 / EFC14153 / CSR_RWE

2 Severe exacerbation events

2.1 Annualized event rate of severe asthma exacerbation during the 52-week treatment period - ITT type 2 inflammatory asthma phenotype population

2.1.12 By age at onset of asthma (0-2, 3-5, >=6 years)

	Age of onset of asthma (years)	
	>= 6	
Severe asthma exacerbation	**Placebo (N=35)**	**Dupilumab (N=45)**
3-5, >= 6		0.024
overall		0.054
Risk Difference (95% CI) vs placebo[d]	-	-0.47 (-0.89 to -0.05)

All severe exacerbation events occurred during the 52-week treatment period are included, regardless of whether the patient is on-treatment or not

[a]The total number of events that occurred during the 52-week treatment period divided by the total number of patient-years followed in the 52-week treatment period.

[b]Derived using negative binomial model with the total number of events onset from randomization up to Week 52 visit or last contact date (whichever comes earlier) as the response variable, with the treatment groups, age, baseline weight group, region, baseline eosinophil level, baseline FeNO level, baseline ICS dose level and number of severe exacerbation events within 1 year prior to the study as covariates, and log-transformed standardized observation duration as an offset variable.

[c]Derived using same negative binomial model as described in [b] with subgroup and subgroup-by-treatment interaction as additional covariates.

[d]Derived using delta method.

PGM=DEVOPS/SAR231893/EFC14153/CSR_RWE/REPORT/PGM/eff_eventsum_ger_subg_i_t.sas OUT=REPORT/OUTPUT/eff_evtsum_eaw52_ger_onsa_t2_t_x.rtf (10AUG2021 - 8:10)

Project Code / Study Number / Analysis: SAR231893 / EFC14153 / CSR_RWE

2 Severe exacerbation events

2.1 Annualized event rate of severe asthma exacerbation during the 52-week treatment period - ITT type 2 inflammatory asthma phenotype population

2.1.13 By number of severe asthma exacerbation prior to the study (<=1, 2, >2)

	Number of severe asthma exacerbation prior to the study			
	<=1		2	
Severe asthma exacerbation	**Placebo (N=47)**	**Dupilumab (N=85)**	**Placebo (N=32)**	**Dupilumab (N=75)**
Patients with >=1 Severe asthma exacerbation [n(%)]				
Number	47	85	32	75
No	31 (66.0%)	74 (87.1%)	19 (59.4%)	60 (80.0%)
Yes	16 (34.0%)	11 (12.9%)	13 (40.6%)	15 (20.0%)
Number of Severe asthma exacerbation				
0	31 (66.0%)	74 (87.1%)	19 (59.4%)	60 (80.0%)
1	10 (21.3%)	10 (11.8%)	7 (21.9%)	11 (14.7%)
2	4 (8.5%)	1 (1.2%)	4 (12.5%)	2 (2.7%)
3	2 (4.3%)	0	2 (6.3%)	2 (2.7%)
>=4	0	0	0	0

All severe exacerbation events occurred during the 52-week treatment period are included, regardless of whether the patient is on-treatment or not
[a]The total number of events that occurred during the 52-week treatment period divided by the total number of patient-years followed in the 52-week treatment period.
[b]Derived using negative binomial model with the total number of events onset from randomization up to Week 52 visit or last contact date (whichever comes earlier) as the response variable, with the treatment groups, age, baseline weight group, region, baseline eosinophil level, baseline FeNO level and baseline ICS dose level as covariates, and log-transformed standardized observation duration as an offset variable.
[c]Derived using same negative binomial model as described in [b] with subgroup and subgroup-by-treatment interaction as additional covariates.
[d]Derived using delta method.
PGM=DEVOPS/SAR231893/EFC14153/CSR_RWE/REPORT/PGM/eff_eventsum_ger_subg_i_t.sas OUT=REPORT/OUTPUT/eff_evtsum_eaw52_ger_exa_t2_t_x.rtf (02JUL2021 - 16:24)

Project Code / Study Number / Analysis: SAR231893 / EFC14153 / CSR_RWE

2 Severe exacerbation events

2.1 Annualized event rate of severe asthma exacerbation during the 52-week treatment period - ITT type 2 inflammatory asthma phenotype population

2.1.13 By number of severe asthma exacerbation prior to the study (<=1, 2, >2)

	Number of severe asthma exacerbation prior to the study			
	<=1		**2**	
Severe asthma exacerbation	**Placebo (N=47)**	**Dupilumab (N=85)**	**Placebo (N=32)**	**Dupilumab (N=75)**
Total number of Severe asthma exacerbation	24	12	21	21
Total patient-years followed	46.4	83.8	32.0	73.2
Unadjusted annualized rate of Severe asthma exacerbation[a]	0.52	0.14	0.66	0.29
Adjusted annualized rate of Severe asthma exacerbation				
Estimate (95% CI)[b]	0.57 (0.35 to 0.93)	0.12 (0.06 to 0.24)	0.63 (0.33 to 1.21)	0.24 (0.12 to 0.47)
Risk Ratio (95% CI) vs placebo[b]	-	0.21 (0.10 to 0.47)	-	0.37 (0.16 to 0.85)
p-value for Risk Ratio[b]		<0.001		0.019
p-value for heterogeneity of Risk Ratio[c]:				
<=1, 2				
<=1, >2				
2, >2				

All severe exacerbation events occurred during the 52-week treatment period are included, regardless of whether the patient is on-treatment or not
[a]The total number of events that occurred during the 52-week treatment period divided by the total number of patient-years followed in the 52-week treatment period.
[b]Derived using negative binomial model with the total number of events onset from randomization up to Week 52 visit or last contact date (whichever comes earlier) as the response variable, with the treatment groups, age, baseline weight group, region, baseline eosinophil level, baseline FeNO level and baseline ICS dose level as covariates, and log-transformed standardized observation duration as an offset variable.
[c]Derived using same negative binomial model as described in [b] with subgroup and subgroup-by-treatment interaction as additional covariates.
[d]Derived using delta method.
PGM=DEVOPS/SAR231893/EFC14153/CSR_RWE/REPORT/PGM/eff_eventsum_ger_subg_i_t.sas OUT=REPORT/OUTPUT/eff_evtsum_eaw52_ger_exa_t2_t_x.rtf (02JUL2021 - 16:24)

Project Code / Study Number / Analysis: SAR231893 / EFC14153 / CSR_RWE

2 Severe exacerbation events

2.1 Annualized event rate of severe asthma exacerbation during the 52-week treatment period - ITT type 2 inflammatory asthma phenotype population

2.1.13 By number of severe asthma exacerbation prior to the study (<=1, 2, >2)

	Number of severe asthma exacerbation prior to the study			
	<=1		2	
Severe asthma exacerbation	**Placebo (N=47)**	**Dupilumab (N=85)**	**Placebo (N=32)**	**Dupilumab (N=75)**
overall				
Risk Difference (95% CI) vs placebo[d]	-	-0.45 (-0.72 to -0.17)	-	-0.40 (-0.80 to 0.01)

All severe exacerbation events occurred during the 52-week treatment period are included, regardless of whether the patient is on-treatment or not
[a]The total number of events that occurred during the 52-week treatment period divided by the total number of patient-years followed in the 52-week treatment period.
[b]Derived using negative binomial model with the total number of events onset from randomization up to Week 52 visit or last contact date (whichever comes earlier) as the response variable, with the treatment groups, age, baseline weight group, region, baseline eosinophil level, baseline FeNO level and baseline ICS dose level as covariates, and log-transformed standardized observation duration as an offset variable.
[c]Derived using same negative binomial model as described in [b] with subgroup and subgroup-by-treatment interaction as additional covariates.
[d]Derived using delta method.
PGM=DEVOPS/SAR231893/EFC14153/CSR_RWE/REPORT/PGM/eff_eventsum_ger_subg_i_t.sas OUT=REPORT/OUTPUT/eff_evtsum_eaw52_ger_exa_t2_t_x.rtf (02JUL2021 - 16:24)

Project Code / Study Number / Analysis: SAR231893 / EFC14153 / CSR_RWE

2 Severe exacerbation events

2.1 Annualized event rate of severe asthma exacerbation during the 52-week treatment period - ITT type 2 inflammatory asthma phenotype population

2.1.13 By number of severe asthma exacerbation prior to the study (<=1, 2, >2)

	Number of severe asthma exacerbation prior to the study	
	>2	
Severe asthma exacerbation	**Placebo (N=35)**	**Dupilumab (N=76)**
Patients with >=1 Severe asthma exacerbation [n(%)]		
Number	35	76
No	18 (51.4%)	48 (63.2%)
Yes	17 (48.6%)	28 (36.8%)
Number of Severe asthma exacerbation		
0	18 (51.4%)	48 (63.2%)
1	6 (17.1%)	15 (19.7%)
2	7 (20.0%)	8 (10.5%)
3	1 (2.9%)	3 (3.9%)
>=4	3 (8.6%)	2 (2.6%)

All severe exacerbation events occurred during the 52-week treatment period are included, regardless of whether the patient is on-treatment or not
[a]The total number of events that occurred during the 52-week treatment period divided by the total number of patient-years followed in the 52-week treatment period.
[b]Derived using negative binomial model with the total number of events onset from randomization up to Week 52 visit or last contact date (whichever comes earlier) as the response variable, with the treatment groups, age, baseline weight group, region, baseline eosinophil level, baseline FeNO level and baseline ICS dose level as covariates, and log-transformed standardized observation duration as an offset variable.
[c]Derived using same negative binomial model as described in [b] with subgroup and subgroup-by-treatment interaction as additional covariates.
[d]Derived using delta method.
PGM=DEVOPS/SAR231893/EFC14153/CSR_RWE/REPORT/PGM/eff_eventsum_ger_subg_i_t.sas OUT=REPORT/OUTPUT/eff_evtsum_eaw52_ger_exa_t2_t_x.rtf (02JUL2021 - 16:24)

Project Code / Study Number / Analysis: SAR231893 / EFC14153 / CSR_RWE

2 Severe exacerbation events

2.1 Annualized event rate of severe asthma exacerbation during the 52-week treatment period - ITT type 2 inflammatory asthma phenotype population

2.1.13 By number of severe asthma exacerbation prior to the study (<=1, 2, >2)

	Number of severe asthma exacerbation prior to the study	
	>2	
Severe asthma exacerbation	**Placebo (N=35)**	**Dupilumab (N=76)**
Total number of Severe asthma exacerbation	36	49
Total patient-years followed	34.3	72.6
Unadjusted annualized rate of Severe asthma exacerbation[a]	1.05	0.67
Adjusted annualized rate of Severe asthma exacerbation		
Estimate (95% CI)[b]	0.96 (0.55 to 1.69)	0.47 (0.29 to 0.76)
Risk Ratio (95% CI) vs placebo[b]	-	0.49 (0.27 to 0.87)
p-value for Risk Ratio[b]		0.016
p-value for heterogeneity of Risk Ratio[c]:		
<=1, 2		0.137
<=1, >2		0.078

All severe exacerbation events occurred during the 52-week treatment period are included, regardless of whether the patient is on-treatment or not
[a]The total number of events that occurred during the 52-week treatment period divided by the total number of patient-years followed in the 52-week treatment period.
[b]Derived using negative binomial model with the total number of events onset from randomization up to Week 52 visit or last contact date (whichever comes earlier) as the response variable, with the treatment groups, age, baseline weight group, region, baseline eosinophil level, baseline FeNO level and baseline ICS dose level as covariates, and log-transformed standardized observation duration as an offset variable.
[c]Derived using same negative binomial model as described in [b] with subgroup and subgroup-by-treatment interaction as additional covariates.
[d]Derived using delta method.
PGM=DEVOPS/SAR231893/EFC14153/CSR_RWE/REPORT/PGM/eff_eventsum_ger_subg_i_t.sas OUT=REPORT/OUTPUT/eff_evtsum_eaw52_ger_exa_t2_t_x.rtf (02JUL2021 - 16:24)

Project Code / Study Number / Analysis: SAR231893 / EFC14153 / CSR_RWE

2 Severe exacerbation events

2.1 Annualized event rate of severe asthma exacerbation during the 52-week treatment period - ITT type 2 inflammatory asthma phenotype population

2.1.13 By number of severe asthma exacerbation prior to the study (<=1, 2, >2)

	Number of severe asthma exacerbation prior to the study	
	>2	
Severe asthma exacerbation	**Placebo (N=35)**	**Dupilumab (N=76)**
2, >2		0.906
overall		0.181
Risk Difference (95% CI) vs placebo[d]	-	-0.49 (-0.99 to 0.01)

All severe exacerbation events occurred during the 52-week treatment period are included, regardless of whether the patient is on-treatment or not

[a]The total number of events that occurred during the 52-week treatment period divided by the total number of patient-years followed in the 52-week treatment period.

[b]Derived using negative binomial model with the total number of events onset from randomization up to Week 52 visit or last contact date (whichever comes earlier) as the response variable, with the treatment groups, age, baseline weight group, region, baseline eosinophil level, baseline FeNO level and baseline ICS dose level as covariates, and log-transformed standardized observation duration as an offset variable.

[c]Derived using same negative binomial model as described in [b] with subgroup and subgroup-by-treatment interaction as additional covariates.

[d]Derived using delta method.

PGM=DEVOPS/SAR231893/EFC14153/CSR_RWE/REPORT/PGM/eff_eventsum_ger_subg_i_t.sas OUT=REPORT/OUTPUT/eff_evtsum_eaw52_ger_exa_t2_t_x.rtf (02JUL2021 - 16:24)

Subgruppenanalysen: kontinuierliche Endpunkte

Project Code / Study Number / Analysis: SAR231893 / EFC14153 / CSR_RWE

2 Pre-bronchodilator % predicted FEV1 - ITT type 2 inflammatory asthma phenotype population

2.1 Summary of treatment effect on change from baseline at Week 52

Pre-bronchodilator % predicted FEV1	Placebo (N=114)	Dupilumab (N=236)
Baseline		
Value		
Number	114	236
Mean (SD)	78.36 (14.51)	77.66 (14.38)
Median	79.00	80.00
Q1 : Q3	71.00 : 87.00	69.00 : 88.00
Min : Max	31.0 : 110.0	30.0 : 112.0
Week 52		
Value		
Number	106	215
Mean (SD)	83.08 (16.08)	89.61 (15.69)
Median	84.00	90.00
Q1 : Q3	75.00 : 92.00	81.00 : 97.00
Min : Max	32.0 : 118.0	37.0 : 179.0
Change from baseline		
Number	106	215
LS Mean (SE)[a]	4.36 (1.50)	12.15 (1.10)

[a]Derived from MMRM model with change from baseline in pre-bronchodilator % predicted FEV1 values up to Week 52 as the response variable, and treatment, baseline weight group, region, ethnicity, baseline eosinophil level, baseline FeNO level, baseline ICS dose level, visit, treatment by-visit interaction, baseline pre-bronchodilator % Predicted FEV1 value and baseline-by-visit interaction as covariates.

Type 2 inflammatory asthma phenotype population is defined as the randomized patients with baseline blood eosinophils >= 0.15 Giga/L or baseline FeNO >= 20 ppb.

PGM=DEVOPS/SAR231893/EFC14153/CSR_RWE/REPORT/PGM/eff_mmrm_ger_i_t.sas OUT=REPORT/OUTPUT/eff_mmrm_ppfev1_ger_i_t_x.rtf (22JUL2021 - 7:44)

Project Code / Study Number / Analysis: SAR231893 / EFC14153 / CSR_RWE

2 Pre-bronchodilator % predicted FEV1 - ITT type 2 inflammatory asthma phenotype population

2.1 Summary of treatment effect on change from baseline at Week 52

Pre-bronchodilator % predicted FEV1	**Placebo (N=114)**	**Dupilumab (N=236)**
LS Mean Diff (95% CI)[a]	-	7.79 (4.36 to 11.22)
Hedges'g (95% CI)	-	0.529 (0.296 to 0.761)
p-value[a]		<0.001

[a]Derived from MMRM model with change from baseline in pre-bronchodilator % predicted FEV1 values up to Week 52 as the response variable, and treatment, baseline weight group, region, ethnicity, baseline eosinophil level, baseline FeNO level, baseline ICS dose level, visit, treatment by-visit interaction, baseline pre-bronchodilator % Predicted FEV1 value and baseline-by-visit interaction as covariates.

Type 2 inflammatory asthma phenotype population is defined as the randomized patients with baseline blood eosinophils >= 0.15 Giga/L or baseline FeNO >= 20 ppb.

PGM=DEVOPS/SAR231893/EFC14153/CSR_RWE/REPORT/PGM/eff_mmrm_ger_i_t.sas OUT=REPORT/OUTPUT/eff_mmrm_ppfev1_ger_i_t_x.rtf (22JUL2021 - 7:44)

Project Code / Study Number / Analysis: SAR231893 / EFC14153 / CSR_RWE

2 Pre-bronchodilator % predicted FEV1 - ITT type 2 inflammatory asthma phenotype population

2.1 Summary of treatment effect on change from baseline at Week 52

2.1.1 By gender (Male, Female)

	Gender			
	Male		Female	
Pre-bronchodilator % predicted FEV1	**Placebo (N=78)**	**Dupilumab (N=152)**	**Placebo (N=36)**	**Dupilumab (N=84)**
Baseline				
Value				
Number	78	152	36	84
Mean (SD)	77.32 (15.78)	76.82 (14.73)	80.61 (11.17)	79.19 (13.67)
Median	78.00	79.00	80.00	82.50
Q1 : Q3	69.00 : 87.00	66.50 : 88.00	73.00 : 87.50	72.50 : 88.50
Min : Max	31.0 : 110.0	30.0 : 112.0	54.0 : 106.0	43.0 : 108.0

[a]Derived from MMRM model with change from baseline in pre-bronchodilator % predicted FEV1 values up to Week 52 as the response variable, and treatment, baseline weight group, region, ethnicity, baseline eosinophil level, baseline FeNO level, baseline ICS dose level, visit, treatment by-visit interaction, baseline pre-bronchodilator % Predicted FEV1 value and baseline-by-visit interaction as covariates.
[b]Similar model as that mentioned in the footnote [a] with subgroup and subgroup-by-treatment interaction as additional covariates.
Type 2 inflammatory asthma phenotype population is defined as the randomized patients with baseline blood eosinophils >= 0.15 Giga/L or baseline FeNO >= 20 ppb.
PGM=DEVOPS/SAR231893/EFC14153/CSR_RWE/REPORT/PGM/eff_mmrm_ger_subg_i_t.sas OUT=REPORT/OUTPUT/eff_mmrm_ppfev1_ger_sex_i_t_x.rtf (21JUL2021 - 8:43)

Project Code / Study Number / Analysis: SAR231893 / EFC14153 / CSR_RWE

2 Pre-bronchodilator % predicted FEV1 - ITT type 2 inflammatory asthma phenotype population

2.1 Summary of treatment effect on change from baseline at Week 52

2.1.1 By gender (Male, Female)

	Gender			
	Male		Female	
Pre-bronchodilator % predicted FEV1	**Placebo (N=78)**	**Dupilumab (N=152)**	**Placebo (N=36)**	**Dupilumab (N=84)**
Week 52				
Value				
Number	73	138	33	77
Mean (SD)	82.78 (16.69)	88.93 (15.70)	83.73 (14.86)	90.84 (15.71)
Median	84.00	90.50	85.00	90.00
Q1 : Q3	74.00 : 92.00	81.00 : 96.00	79.00 : 92.00	82.00 : 98.00
Min : Max	35.0 : 118.0	37.0 : 179.0	32.0 : 111.0	60.0 : 156.0
Change from baseline				
Number	73	138	33	77
LS Mean (SE)[a]	5.35 (1.87)	12.34 (1.42)	1.81 (2.55)	11.57 (1.79)
LS Mean Diff (95% CI)[a]	-	6.99 (2.65 to 11.32)	-	9.76 (4.04 to 15.48)
p-value[a]		0.002		<0.001
Hedges'g (95% CI)	-	0.461 (0.175 to 0.747)	-	0.692 (0.286 to 1.097)
p-value for heterogeneity[b]				0.543

[a]Derived from MMRM model with change from baseline in pre-bronchodilator % predicted FEV1 values up to Week 52 as the response variable, and treatment, baseline weight group, region, ethnicity, baseline eosinophil level, baseline FeNO level, baseline ICS dose level, visit, treatment by-visit interaction, baseline pre-bronchodilator % Predicted FEV1 value and baseline-by-visit interaction as covariates.
[b]Similar model as that mentioned in the footnote [a] with subgroup and subgroup-by-treatment interaction as additional covariates.
Type 2 inflammatory asthma phenotype population is defined as the randomized patients with baseline blood eosinophils >= 0.15 Giga/L or baseline FeNO >= 20 ppb.
PGM=DEVOPS/SAR231893/EFC14153/CSR_RWE/REPORT/PGM/eff_mmrm_ger_subg_i_t.sas OUT=REPORT/OUTPUT/eff_mmrm_ppfev1_ger_sex_i_t_x.rtf (21JUL2021 - 8:43)

Project Code / Study Number / Analysis: SAR231893 / EFC14153 / CSR_RWE

2 Pre-bronchodilator % predicted FEV1 - ITT type 2 inflammatory asthma phenotype population

2.1 Summary of treatment effect on change from baseline at Week 52

2.1.2 By region (Latin America, East Europe, Western Countries)

	Region					
	Latin America		East Europe		Western countries	
Pre-bronchodilator % predicted FEV1	**Placebo (N=51)**	**Dupilumab (N=106)**	**Placebo (N=43)**	**Dupilumab (N=78)**	**Placebo (N=20)**	**Dupilumab (N=52)**
Baseline						
Value						
Number	51	106	43	78	20	52
Mean (SD)	77.04 (14.33)	77.76 (14.47)	80.72 (15.33)	77.01 (14.22)	76.65 (13.12)	78.42 (14.67)
Median	75.00	80.00	81.00	79.50	77.00	80.50
Q1 : Q3	66.00 : 87.00	71.00 : 88.00	73.00 : 89.00	66.00 : 88.00	71.50 : 83.00	74.00 : 85.50
Min : Max	39.0 : 109.0	34.0 : 108.0	31.0 : 110.0	44.0 : 100.0	48.0 : 108.0	30.0 : 112.0

[a]Derived from MMRM model with change from baseline in pre-bronchodilator % predicted FEV1 values up to Week 52 as the response variable, and treatment, baseline weight group, ethnicity, baseline eosinophil level, baseline FeNO level, baseline ICS dose level, visit, treatment by-visit interaction, baseline pre-bronchodilator % Predicted FEV1 value and baseline-by-visit interaction as covariates.
[b]Similar model as that mentioned in the footnote [a] with subgroup and subgroup-by-treatment interaction as additional covariates.
Type 2 inflammatory asthma phenotype population is defined as the randomized patients with baseline blood eosinophils >= 0.15 Giga/L or baseline FeNO >= 20 ppb.
PGM=DEVOPS/SAR231893/EFC14153/CSR_RWE/REPORT/PGM/eff_mmrm_ger_subg_i_t.sas OUT=REPORT/OUTPUT/eff_mmrm_ppfev1_ger_cty_i_t_x.rtf (21JUL2021 - 9:02)

Project Code / Study Number / Analysis: SAR231893 / EFC14153 / CSR_RWE

2 Pre-bronchodilator % predicted FEV1 - ITT type 2 inflammatory asthma phenotype population

2.1 Summary of treatment effect on change from baseline at Week 52

2.1.2 By region (Latin America, East Europe, Western Countries)

	Region					
	Latin America		East Europe		Western countries	
Pre-bronchodilator % predicted FEV1	**Placebo (N=51)**	**Dupilumab (N=106)**	**Placebo (N=43)**	**Dupilumab (N=78)**	**Placebo (N=20)**	**Dupilumab (N=52)**
Week 52						
Value						
Number	48	100	42	76	16	39
Mean (SD)	80.44 (17.46)	91.07 (18.02)	88.48 (11.98)	89.92 (14.16)	76.81 (17.77)	85.28 (10.95)
Median	84.00	92.50	86.00	92.00	73.50	86.00
Q1 : Q3	72.50 : 90.50	81.00 : 99.00	82.00 : 96.00	83.50 : 97.50	65.00 : 83.50	79.00 : 92.00
Min : Max	32.0 : 111.0	37.0 : 179.0	63.0 : 118.0	51.0 : 156.0	43.0 : 111.0	59.0 : 113.0
Change from baseline						
Number	48	100	42	76	16	39
LS Mean (SE)[a]	1.81 (2.78)	12.92 (2.00)	3.07 (5.07)	6.17 (5.15)	6.78 (3.43)	10.52 (2.25)
LS Mean Diff (95% CI)[a]	-	11.11 (5.18 to 17.04)	-	3.10 (-1.72 to 7.92)	-	3.73 (-3.49 to 10.95)
p-value[a]		<0.001		0.205		0.304

[a]Derived from MMRM model with change from baseline in pre-bronchodilator % predicted FEV1 values up to Week 52 as the response variable, and treatment, baseline weight group, ethnicity, baseline eosinophil level, baseline FeNO level, baseline ICS dose level, visit, treatment by-visit interaction, baseline pre-bronchodilator % Predicted FEV1 value and baseline-by-visit interaction as covariates.
[b]Similar model as that mentioned in the footnote [a] with subgroup and subgroup-by-treatment interaction as additional covariates.
Type 2 inflammatory asthma phenotype population is defined as the randomized patients with baseline blood eosinophils >= 0.15 Giga/L or baseline FeNO >= 20 ppb.
PGM=DEVOPS/SAR231893/EFC14153/CSR_RWE/REPORT/PGM/eff_mmrm_ger_subg_i_t.sas OUT=REPORT/OUTPUT/eff_mmrm_ppfev1_ger_cty_i_t_x.rtf (21JUL2021 - 9:02)

Project Code / Study Number / Analysis: SAR231893 / EFC14153 / CSR_RWE

2 Pre-bronchodilator % predicted FEV1 - ITT type 2 inflammatory asthma phenotype population

2.1 Summary of treatment effect on change from baseline at Week 52

2.1.2 By region (Latin America, East Europe, Western Countries)

	Region					
	Latin America		East Europe		Western countries	
Pre-bronchodilator % predicted FEV1	**Placebo (N=51)**	**Dupilumab (N=106)**	**Placebo (N=43)**	**Dupilumab (N=78)**	**Placebo (N=20)**	**Dupilumab (N=52)**
Hedges'g (95% CI)	-	0.655 (0.305 to 1.004)	-	0.248 (-0.137 to 0.634)	-	0.313 (-0.292 to 0.918)
p-value for heterogeneity[b]:						
Latin America, East Europe						0.031
Latin America, Western countries						0.375
East Europe, Western countries						0.448
overall						0.097

[a]Derived from MMRM model with change from baseline in pre-bronchodilator % predicted FEV1 values up to Week 52 as the response variable, and treatment, baseline weight group, ethnicity, baseline eosinophil level, baseline FeNO level, baseline ICS dose level, visit, treatment by-visit interaction, baseline pre-bronchodilator % Predicted FEV1 value and baseline-by-visit interaction as covariates.
[b]Similar model as that mentioned in the footnote [a] with subgroup and subgroup-by-treatment interaction as additional covariates.
Type 2 inflammatory asthma phenotype population is defined as the randomized patients with baseline blood eosinophils >= 0.15 Giga/L or baseline FeNO >= 20 ppb.
PGM=DEVOPS/SAR231893/EFC14153/CSR_RWE/REPORT/PGM/eff_mmrm_ger_subg_i_t.sas OUT=REPORT/OUTPUT/eff_mmrm_ppfev1_ger_cty_i_t_x.rtf (21JUL2021 - 9:02)

Project Code / Study Number / Analysis: SAR231893 / EFC14153 / CSR_RWE

2 Pre-bronchodilator % predicted FEV1 - ITT type 2 inflammatory asthma phenotype population

2.1 Summary of treatment effect on change from baseline at Week 52

2.1.3 By race (Caucasian/white, Black/of African descent, Other)

	Race					
	Caucasian/White		Black/of African descent		Other	
Pre-bronchodilator % predicted FEV1	**Placebo (N=102)**	**Dupilumab (N=208)**	**Placebo (N=5)**	**Dupilumab (N=9)**	**Placebo (N=7)**	**Dupilumab (N=19)**
Baseline						
Value						
Number	102	208	5	9	7	19
Mean (SD)	78.96 (13.84)	78.33 (14.58)	69.00 (22.80)	68.00 (15.12)	76.29 (17.68)	74.95 (9.58)
Median	79.50	80.00	79.00	66.00	74.00	77.00
Q1 : Q3	71.00 : 87.00	70.50 : 88.00	65.00 : 83.00	56.00 : 81.00	63.00 : 90.00	70.00 : 83.00
Min : Max	39.0 : 110.0	30.0 : 112.0	31.0 : 87.0	43.0 : 87.0	57.0 : 108.0	53.0 : 88.0

[a]Derived from MMRM model with change from baseline in pre-bronchodilator % predicted FEV1 values up to Week 52 as the response variable, and treatment, baseline weight group, region, ethnicity, baseline eosinophil level, baseline FeNO level, baseline ICS dose level, visit, treatment by-visit interaction, baseline pre-bronchodilator % Predicted FEV1 value and baseline-by-visit interaction as covariates.

[b]Similar model as that mentioned in the footnote [a] with subgroup and subgroup-by-treatment interaction as additional covariates.

Type 2 inflammatory asthma phenotype population is defined as the randomized patients with baseline blood eosinophils >= 0.15 Giga/L or baseline FeNO >= 20 ppb.

PGM=DEVOPS/SAR231893/EFC14153/CSR_RWE/REPORT/PGM/eff_mmrm_ger_subg_i_t.sas OUT=REPORT/OUTPUT/eff_mmrm_ppfev1_ger_race_i_t_x.rtf (21JUL2021 - 9:21)

Project Code / Study Number / Analysis: SAR231893 / EFC14153 / CSR_RWE

2 Pre-bronchodilator % predicted FEV1 - ITT type 2 inflammatory asthma phenotype population

2.1 Summary of treatment effect on change from baseline at Week 52

2.1.3 By race (Caucasian/white, Black/of African descent, Other)

	Race					
	Caucasian/White		Black/of African descent		Other	
Pre-bronchodilator % predicted FEV1	**Placebo (N=102)**	**Dupilumab (N=208)**	**Placebo (N=5)**	**Dupilumab (N=9)**	**Placebo (N=7)**	**Dupilumab (N=19)**
Week 52						
Value						
Number	99	193	2	6	5	16
Mean (SD)	83.41 (15.99)	90.62 (15.95)	60.50 (3.54)	79.83 (10.19)	85.40 (16.01)	81.13 (9.69)
Median	85.00	92.00	60.50	79.00	84.00	81.50
Q1 : Q3	76.00 : 93.00	83.00 : 98.00	58.00 : 63.00	79.00 : 82.00	83.00 : 87.00	77.50 : 88.00
Min : Max	32.0 : 118.0	37.0 : 179.0	58.0 : 63.0	64.0 : 96.0	64.0 : 109.0	59.0 : 95.0
Change from baseline						
Number	99	193	2	6	5	16
LS Mean (SE)[a]	4.63 (1.63)	12.29 (1.22)			5.74 (3.65)	3.64 (2.62)
LS Mean Diff (95% CI)[a]	-	7.66 (3.97 to 11.35)	-	-9.89 (-49.08 to 29.30)	-	-2.10 (-10.37 to 6.18)
p-value[a]		<0.001		0.610		0.602

[a]Derived from MMRM model with change from baseline in pre-bronchodilator % predicted FEV1 values up to Week 52 as the response variable, and treatment, baseline weight group, region, ethnicity, baseline eosinophil level, baseline FeNO level, baseline ICS dose level, visit, treatment by-visit interaction, baseline pre-bronchodilator % Predicted FEV1 value and baseline-by-visit interaction as covariates.
[b]Similar model as that mentioned in the footnote [a] with subgroup and subgroup-by-treatment interaction as additional covariates.
Type 2 inflammatory asthma phenotype population is defined as the randomized patients with baseline blood eosinophils >= 0.15 Giga/L or baseline FeNO >= 20 ppb.
PGM=DEVOPS/SAR231893/EFC14153/CSR_RWE/REPORT/PGM/eff_mmrm_ger_subg_i_t.sas OUT=REPORT/OUTPUT/eff_mmrm_ppfev1_ger_race_i_t_x.rtf (21JUL2021 - 9:21)

Project Code / Study Number / Analysis: SAR231893 / EFC14153 / CSR_RWE

2 Pre-bronchodilator % predicted FEV1 - ITT type 2 inflammatory asthma phenotype population

2.1 Summary of treatment effect on change from baseline at Week 52

2.1.3 By race (Caucasian/white, Black/of African descent, Other)

	Race					
	Caucasian/White		Black/of African descent		Other	
Pre-bronchodilator % predicted FEV1	**Placebo (N=102)**	**Dupilumab (N=208)**	**Placebo (N=5)**	**Dupilumab (N=9)**	**Placebo (N=7)**	**Dupilumab (N=19)**
Hedges'g (95% CI)	-	0.507 (0.263 to 0.751)	-	. (. to .)	-	-0.200 (-0.991 to 0.590)
p-value for heterogeneity[b]:						
Caucasian/White, Black/of African descent						0.099
Caucasian/White, Other						0.069
Black/of African descent, Other						0.456
overall						0.182

[a]Derived from MMRM model with change from baseline in pre-bronchodilator % predicted FEV1 values up to Week 52 as the response variable, and treatment, baseline weight group, region, ethnicity, baseline eosinophil level, baseline FeNO level, baseline ICS dose level, visit, treatment by-visit interaction, baseline pre-bronchodilator % Predicted FEV1 value and baseline-by-visit interaction as covariates.
[b]Similar model as that mentioned in the footnote [a] with subgroup and subgroup-by-treatment interaction as additional covariates.
Type 2 inflammatory asthma phenotype population is defined as the randomized patients with baseline blood eosinophils >= 0.15 Giga/L or baseline FeNO >= 20 ppb.
PGM=DEVOPS/SAR231893/EFC14153/CSR_RWE/REPORT/PGM/eff_mmrm_ger_subg_i_t.sas OUT=REPORT/OUTPUT/eff_mmrm_ppfev1_ger_race_i_t_x.rtf (21JUL2021 - 9:21)

Project Code / Study Number / Analysis: SAR231893 / EFC14153 / CSR_RWE

2 Pre-bronchodilator % predicted FEV1 - ITT type 2 inflammatory asthma phenotype population

2.1 Summary of treatment effect on change from baseline at Week 52

2.1.4 By baseline ICS dose level (Medium, High)

	Baseline ICS dose level			
	High		Medium	
Pre-bronchodilator % predicted FEV1	**Placebo (N=50)**	**Dupilumab (N=102)**	**Placebo (N=64)**	**Dupilumab (N=131)**
Baseline				
Value				
Number	50	102	64	131
Mean (SD)	75.80 (12.76)	77.93 (12.99)	80.36 (15.55)	77.27 (15.33)
Median	76.00	78.00	80.50	81.00
Q1 : Q3	70.00 : 85.00	70.00 : 87.00	72.00 : 89.50	67.00 : 88.00
Min : Max	41.0 : 108.0	44.0 : 112.0	31.0 : 110.0	30.0 : 108.0

[a]Derived from MMRM model with change from baseline in pre-bronchodilator % predicted FEV1 values up to Week 52 as the response variable, and treatment, baseline weight group, region, ethnicity, baseline eosinophil level, baseline FeNO level, visit, treatment by-visit interaction, baseline pre-bronchodilator % Predicted FEV1 value and baseline-by-visit interaction as covariates.

[b]Similar model as that mentioned in the footnote [a] with subgroup and subgroup-by-treatment interaction as additional covariates.

Type 2 inflammatory asthma phenotype population is defined as the randomized patients with baseline blood eosinophils >= 0.15 Giga/L or baseline FeNO >= 20 ppb.

PGM=DEVOPS/SAR231893/EFC14153/CSR_RWE/REPORT/PGM/eff_mmrm_ger_subg_i_t.sas OUT=REPORT/OUTPUT/eff_mmrm_ppfev1_ger_ics_i_t_x.rtf (21JUL2021 - 9:35)

Project Code / Study Number / Analysis: SAR231893 / EFC14153 / CSR_RWE

2 Pre-bronchodilator % predicted FEV1 - ITT type 2 inflammatory asthma phenotype population

2.1 Summary of treatment effect on change from baseline at Week 52

2.1.4 By baseline ICS dose level (Medium, High)

	Baseline ICS dose level			
	High		Medium	
Pre-bronchodilator % predicted FEV1	**Placebo (N=50)**	**Dupilumab (N=102)**	**Placebo (N=64)**	**Dupilumab (N=131)**
Week 52				
Value				
Number	46	93	60	122
Mean (SD)	81.24 (16.84)	86.65 (13.29)	84.48 (15.46)	91.88 (17.01)
Median	83.00	87.00	85.00	92.00
Q1 : Q3	72.00 : 93.00	79.00 : 95.00	76.50 : 92.00	85.00 : 98.00
Min : Max	32.0 : 111.0	37.0 : 121.0	35.0 : 118.0	46.0 : 179.0
Change from baseline				
Number	46	93	60	122
LS Mean (SE)[a]	4.84 (2.06)	10.54 (1.52)	4.42 (2.19)	13.77 (1.62)
LS Mean Diff (95% CI)[a]	-	5.70 (0.99 to 10.40)	-	9.35 (4.38 to 14.33)
p-value[a]		0.018		<0.001
Hedges'g (95% CI)	-	0.429 (0.075 to 0.783)	-	0.591 (0.277 to 0.905)
p-value for heterogeneity[b]				0.238

[a]Derived from MMRM model with change from baseline in pre-bronchodilator % predicted FEV1 values up to Week 52 as the response variable, and treatment, baseline weight group, region, ethnicity, baseline eosinophil level, baseline FeNO level, visit, treatment by-visit interaction, baseline pre-bronchodilator % Predicted FEV1 value and baseline-by-visit interaction as covariates.

[b]Similar model as that mentioned in the footnote [a] with subgroup and subgroup-by-treatment interaction as additional covariates.

Type 2 inflammatory asthma phenotype population is defined as the randomized patients with baseline blood eosinophils >= 0.15 Giga/L or baseline FeNO >= 20 ppb.

PGM=DEVOPS/SAR231893/EFC14153/CSR_RWE/REPORT/PGM/eff_mmrm_ger_subg_i_t.sas OUT=REPORT/OUTPUT/eff_mmrm_ppfev1_ger_ics_i_t_x.rtf (21JUL2021 - 9:35)

Project Code / Study Number / Analysis: SAR231893 / EFC14153 / CSR_RWE

2 Pre-bronchodilator % predicted FEV1 - ITT type 2 inflammatory asthma phenotype population

2.1 Summary of treatment effect on change from baseline at Week 52

2.1.5 By baseline ICS dose level 2 (Medium, High)

	Baseline ICS dose level 2			
	High		Medium	
Pre-bronchodilator % predicted FEV1	**Placebo (N=95)**	**Dupilumab (N=200)**	**Placebo (N=19)**	**Dupilumab (N=36)**
Baseline				
Value				
Number	95	200	19	36
Mean (SD)	78.36 (13.88)	77.35 (13.49)	78.37 (17.79)	79.39 (18.68)
Median	78.00	79.00	83.00	84.00
Q1 : Q3	71.00 : 87.00	68.50 : 87.50	66.00 : 90.00	74.00 : 89.50
Min : Max	31.0 : 110.0	43.0 : 112.0	39.0 : 106.0	30.0 : 108.0

[a]Derived from MMRM model with change from baseline in pre-bronchodilator % predicted FEV1 values up to Week 52 as the response variable, and treatment, baseline weight group, region, ethnicity, baseline eosinophil level, baseline FeNO level, visit, treatment by-visit interaction, baseline pre-bronchodilator % Predicted FEV1 value and baseline-by-visit interaction as covariates.

[b]Similar model as that mentioned in the footnote [a] with subgroup and subgroup-by-treatment interaction as additional covariates.

Type 2 inflammatory asthma phenotype population is defined as the randomized patients with baseline blood eosinophils >= 0.15 Giga/L or baseline FeNO >= 20 ppb.

PGM=DEVOPS/SAR231893/EFC14153/CSR_RWE/REPORT/PGM/eff_mmrm_ger_subg_i_t.sas OUT=REPORT/OUTPUT/eff_mmrm_ppfev1_ger_ics2_i_t_x.rtf (01SEP2021 - 16:21)

Project Code / Study Number / Analysis: SAR231893 / EFC14153 / CSR_RWE

2 Pre-bronchodilator % predicted FEV1 - ITT type 2 inflammatory asthma phenotype population

2.1 Summary of treatment effect on change from baseline at Week 52

2.1.5 By baseline ICS dose level 2 (Medium, High)

	Baseline ICS dose level 2			
	High		Medium	
Pre-bronchodilator % predicted FEV1	**Placebo (N=95)**	**Dupilumab (N=200)**	**Placebo (N=19)**	**Dupilumab (N=36)**
Week 52				
Value				
Number	88	187	18	28
Mean (SD)	83.44 (15.70)	88.59 (13.77)	81.28 (18.21)	96.43 (24.30)
Median	84.50	89.00	83.00	95.00
Q1 : Q3	77.00 : 92.00	80.00 : 96.00	69.00 : 93.00	85.50 : 101.00
Min : Max	32.0 : 118.0	37.0 : 156.0	35.0 : 111.0	46.0 : 179.0
Change from baseline				
Number	88	187	18	28
LS Mean (SE)[a]	4.67 (1.48)	11.65 (1.09)	1.32 (5.73)	18.54 (4.35)
LS Mean Diff (95% CI)[a]	-	6.98 (3.65 to 10.30)	-	17.22 (3.38 to 31.06)
p-value[a]		<0.001		0.016
Hedges'g (95% CI)	-	0.532 (0.278 to 0.785)	-	0.766 (0.150 to 1.381)
p-value for heterogeneity[b]				0.119

[a]Derived from MMRM model with change from baseline in pre-bronchodilator % predicted FEV1 values up to Week 52 as the response variable, and treatment, baseline weight group, region, ethnicity, baseline eosinophil level, baseline FeNO level, visit, treatment by-visit interaction, baseline pre-bronchodilator % Predicted FEV1 value and baseline-by-visit interaction as covariates.

[b]Similar model as that mentioned in the footnote [a] with subgroup and subgroup-by-treatment interaction as additional covariates.

Type 2 inflammatory asthma phenotype population is defined as the randomized patients with baseline blood eosinophils >= 0.15 Giga/L or baseline FeNO >= 20 ppb.

PGM=DEVOPS/SAR231893/EFC14153/CSR_RWE/REPORT/PGM/eff_mmrm_ger_subg_i_t.sas OUT=REPORT/OUTPUT/eff_mmrm_ppfev1_ger_ics2_i_t_x.rtf (01SEP2021 - 16:21)

Project Code / Study Number / Analysis: SAR231893 / EFC14153 / CSR_RWE

2 Pre-bronchodilator % predicted FEV1 - ITT type 2 inflammatory asthma phenotype population

2.1 Summary of treatment effect on change from baseline at Week 52

2.1.6 By baseline predicted FEV1 (<80%, >=80%)

	Baseline Predicted FEV1			
	<80%		>=80%	
Pre-bronchodilator % predicted FEV1	**Placebo (N=59)**	**Dupilumab (N=116)**	**Placebo (N=55)**	**Dupilumab (N=120)**
Baseline				
Value				
Number	59	116	55	120
Mean (SD)	67.83 (10.54)	66.32 (11.06)	89.65 (8.38)	88.63 (6.59)
Median	71.00	69.00	87.00	88.00
Q1 : Q3	65.00 : 75.00	59.00 : 76.00	84.00 : 95.00	83.50 : 92.00
Min : Max	31.0 : 79.0	30.0 : 79.0	80.0 : 110.0	80.0 : 112.0

[a]Derived from MMRM model with change from baseline in pre-bronchodilator % predicted FEV1 values up to Week 52 as the response variable, and treatment, baseline weight group, region, ethnicity, baseline eosinophil level, baseline FeNO level, baseline ICS dose level, visit, treatment by-visit interaction, baseline pre-bronchodilator % Predicted FEV1 value and baseline-by-visit interaction as covariates.
[b]Similar model as that mentioned in the footnote [a] with subgroup and subgroup-by-treatment interaction as additional covariates.
Type 2 inflammatory asthma phenotype population is defined as the randomized patients with baseline blood eosinophils >= 0.15 Giga/L or baseline FeNO >= 20 ppb.
PGM=DEVOPS/SAR231893/EFC14153/CSR_RWE/REPORT/PGM/eff_mmrm_ger_subg_i_t.sas OUT=REPORT/OUTPUT/eff_mmrm_ppfev1_ger_pfev1_i_t_x.rtf (21JUL2021 - 9:50)

Project Code / Study Number / Analysis: SAR231893 / EFC14153 / CSR_RWE

2 Pre-bronchodilator % predicted FEV1 - ITT type 2 inflammatory asthma phenotype population

2.1 Summary of treatment effect on change from baseline at Week 52

2.1.6 By baseline predicted FEV1 (<80%, >=80%)

	Baseline Predicted FEV1			
	<80%		>=80%	
Pre-bronchodilator % predicted FEV1	**Placebo (N=59)**	**Dupilumab (N=116)**	**Placebo (N=55)**	**Dupilumab (N=120)**
Week 52				
Value				
Number	52	109	54	106
Mean (SD)	76.29 (16.33)	85.89 (16.04)	89.61 (12.91)	93.44 (14.42)
Median	79.50	85.00	88.50	93.50
Q1 : Q3	68.50 : 85.00	78.00 : 94.00	83.00 : 98.00	87.00 : 99.00
Min : Max	32.0 : 111.0	37.0 : 179.0	58.0 : 118.0	46.0 : 156.0
Change from baseline				
Number	52	109	54	106
LS Mean (SE)[a]	9.38 (2.32)	19.61 (1.74)	-0.49 (1.92)	4.73 (1.41)
LS Mean Diff (95% CI)[a]	-	10.23 (4.97 to 15.48)	-	5.22 (0.80 to 9.64)
p-value[a]		<0.001		0.021
Hedges'g (95% CI)	-	0.640 (0.311 to 0.969)	-	0.394 (0.060 to 0.728)
p-value for heterogeneity[b]				0.119

[a]Derived from MMRM model with change from baseline in pre-bronchodilator % predicted FEV1 values up to Week 52 as the response variable, and treatment, baseline weight group, region, ethnicity, baseline eosinophil level, baseline FeNO level, baseline ICS dose level, visit, treatment by-visit interaction, baseline pre-bronchodilator % Predicted FEV1 value and baseline-by-visit interaction as covariates.
[b]Similar model as that mentioned in the footnote [a] with subgroup and subgroup-by-treatment interaction as additional covariates.
Type 2 inflammatory asthma phenotype population is defined as the randomized patients with baseline blood eosinophils >= 0.15 Giga/L or baseline FeNO >= 20 ppb.
PGM=DEVOPS/SAR231893/EFC14153/CSR_RWE/REPORT/PGM/eff_mmrm_ger_subg_i_t.sas OUT=REPORT/OUTPUT/eff_mmrm_ppfev1_ger_pfev1_i_t_x.rtf (21JUL2021 - 9:50)

Project Code / Study Number / Analysis: SAR231893 / EFC14153 / CSR_RWE

2 Pre-bronchodilator % predicted FEV1 - ITT type 2 inflammatory asthma phenotype population

2.1 Summary of treatment effect on change from baseline at Week 52

2.1.7 By baseline ACQ-7-IA (<=2, >2)

	Baseline ACQ-7-IA			
	<=2		>2	
Pre-bronchodilator % predicted FEV1	**Placebo (N=61)**	**Dupilumab (N=126)**	**Placebo (N=53)**	**Dupilumab (N=110)**
Baseline				
Value				
Number	61	126	53	110
Mean (SD)	82.31 (12.86)	82.65 (10.86)	73.81 (15.08)	71.95 (15.77)
Median	81.00	84.00	75.00	74.00
Q1 : Q3	74.00 : 90.00	77.00 : 89.00	66.00 : 84.00	61.00 : 83.00
Min : Max	50.0 : 109.0	43.0 : 108.0	31.0 : 110.0	30.0 : 112.0

[a]Derived from MMRM model with change from baseline in pre-bronchodilator % predicted FEV1 values up to Week 52 as the response variable, and treatment, baseline weight group, region, ethnicity, baseline eosinophil level, baseline FeNO level, baseline ICS dose level, visit, treatment by-visit interaction, baseline pre-bronchodilator % Predicted FEV1 value and baseline-by-visit interaction as covariates.
[b]Similar model as that mentioned in the footnote [a] with subgroup and subgroup-by-treatment interaction as additional covariates.
Type 2 inflammatory asthma phenotype population is defined as the randomized patients with baseline blood eosinophils >= 0.15 Giga/L or baseline FeNO >= 20 ppb.
PGM=DEVOPS/SAR231893/EFC14153/CSR_RWE/REPORT/PGM/eff_mmrm_ger_subg_i_t.sas OUT=REPORT/OUTPUT/eff_mmrm_ppfev1_ger_acq7_i_t_x.rtf (21JUL2021 - 10:04)

Project Code / Study Number / Analysis: SAR231893 / EFC14153 / CSR_RWE

2 Pre-bronchodilator % predicted FEV1 - ITT type 2 inflammatory asthma phenotype population

2.1 Summary of treatment effect on change from baseline at Week 52

2.1.7 By baseline ACQ-7-IA (<=2, >2)

	Baseline ACQ-7-IA			
	<=2		>2	
Pre-bronchodilator % predicted FEV1	**Placebo (N=61)**	**Dupilumab (N=126)**	**Placebo (N=53)**	**Dupilumab (N=110)**
Week 52				
Value				
Number	58	113	48	102
Mean (SD)	83.29 (14.67)	91.38 (12.83)	82.81 (17.79)	87.66 (18.21)
Median	85.00	92.00	83.50	87.00
Q1 : Q3	77.00 : 92.00	83.00 : 97.00	72.00 : 93.00	78.00 : 97.00
Min : Max	38.0 : 111.0	60.0 : 156.0	32.0 : 118.0	37.0 : 179.0
Change from baseline				
Number	58	113	48	102
LS Mean (SE)[a]	0.11 (1.62)	8.76 (1.22)	10.08 (2.75)	16.73 (1.99)
LS Mean Diff (95% CI)[a]	-	8.65 (4.90 to 12.40)	-	6.66 (0.45 to 12.86)
p-value[a]		<0.001		0.036
Hedges'g (95% CI)	-	0.730 (0.414 to 1.047)	-	0.373 (0.025 to 0.720)
p-value for heterogeneity[b]				0.653

[a]Derived from MMRM model with change from baseline in pre-bronchodilator % predicted FEV1 values up to Week 52 as the response variable, and treatment, baseline weight group, region, ethnicity, baseline eosinophil level, baseline FeNO level, baseline ICS dose level, visit, treatment by-visit interaction, baseline pre-bronchodilator % Predicted FEV1 value and baseline-by-visit interaction as covariates.
[b]Similar model as that mentioned in the footnote [a] with subgroup and subgroup-by-treatment interaction as additional covariates.
Type 2 inflammatory asthma phenotype population is defined as the randomized patients with baseline blood eosinophils >= 0.15 Giga/L or baseline FeNO >= 20 ppb.
PGM=DEVOPS/SAR231893/EFC14153/CSR_RWE/REPORT/PGM/eff_mmrm_ger_subg_i_t.sas OUT=REPORT/OUTPUT/eff_mmrm_ppfev1_ger_acq7_i_t_x.rtf (21JUL2021 - 10:04)

Project Code / Study Number / Analysis: SAR231893 / EFC14153 / CSR_RWE

2 Pre-bronchodilator % predicted FEV1 - ITT type 2 inflammatory asthma phenotype population

2.1 Summary of treatment effect on change from baseline at Week 52

2.1.8 By baseline weight (<=30 kg, >30 kg)

	Baseline weight (kg)			
	<=30		>30	
Pre-bronchodilator % predicted FEV1	**Placebo (N=36)**	**Dupilumab (N=76)**	**Placebo (N=78)**	**Dupilumab (N=160)**
Baseline				
Value				
Number	36	76	78	160
Mean (SD)	77.22 (13.60)	78.11 (15.41)	78.88 (14.97)	77.45 (13.91)
Median	79.00	80.50	78.00	80.00
Q1 : Q3	71.50 : 86.00	71.00 : 88.50	71.00 : 88.00	67.50 : 88.00
Min : Max	39.0 : 99.0	30.0 : 108.0	31.0 : 110.0	34.0 : 112.0

[a]Derived from MMRM model with change from baseline in pre-bronchodilator % predicted FEV1 values up to Week 52 as the response variable, and treatment, region, ethnicity, baseline eosinophil level, baseline FeNO level, baseline ICS dose level, visit, treatment by-visit interaction, baseline pre-bronchodilator % Predicted FEV1 value and baseline-by-visit interaction as covariates.

[b]Similar model as that mentioned in the footnote [a] with subgroup and subgroup-by-treatment interaction as additional covariates.

Type 2 inflammatory asthma phenotype population is defined as the randomized patients with baseline blood eosinophils >= 0.15 Giga/L or baseline FeNO >= 20 ppb.

PGM=DEVOPS/SAR231893/EFC14153/CSR_RWE/REPORT/PGM/eff_mmrm_ger_subg_i_t.sas OUT=REPORT/OUTPUT/eff_mmrm_ppfev1_ger_wgt_i_t_x.rtf (21JUL2021 - 10:18)

Project Code / Study Number / Analysis: SAR231893 / EFC14153 / CSR_RWE

2 Pre-bronchodilator % predicted FEV1 - ITT type 2 inflammatory asthma phenotype population

2.1 Summary of treatment effect on change from baseline at Week 52

2.1.8 By baseline weight (<=30 kg, >30 kg)

	Baseline weight (kg)			
	<=30		>30	
Pre-bronchodilator % predicted FEV1	**Placebo (N=36)**	**Dupilumab (N=76)**	**Placebo (N=78)**	**Dupilumab (N=160)**
Week 52				
Value				
Number	32	64	74	151
Mean (SD)	83.72 (15.61)	90.72 (17.34)	82.80 (16.37)	89.15 (14.97)
Median	85.00	92.00	83.00	90.00
Q1 : Q3	77.50 : 93.00	81.50 : 100.50	72.00 : 92.00	81.00 : 96.00
Min : Max	35.0 : 104.0	46.0 : 156.0	32.0 : 118.0	37.0 : 179.0
Change from baseline				
Number	32	64	74	151
LS Mean (SE)[a]	6.11 (2.86)	13.15 (2.05)	3.30 (1.78)	11.29 (1.30)
LS Mean Diff (95% CI)[a]	-	7.04 (0.37 to 13.70)	-	7.99 (3.96 to 12.03)
p-value[a]		0.039		<0.001
Hedges'g (95% CI)	-	0.450 (0.024 to 0.876)	-	0.557 (0.276 to 0.838)
p-value for heterogeneity[b]				0.807

[a]Derived from MMRM model with change from baseline in pre-bronchodilator % predicted FEV1 values up to Week 52 as the response variable, and treatment, region, ethnicity, baseline eosinophil level, baseline FeNO level, baseline ICS dose level, visit, treatment by-visit interaction, baseline pre-bronchodilator % Predicted FEV1 value and baseline-by-visit interaction as covariates.
[b]Similar model as that mentioned in the footnote [a] with subgroup and subgroup-by-treatment interaction as additional covariates.
Type 2 inflammatory asthma phenotype population is defined as the randomized patients with baseline blood eosinophils >= 0.15 Giga/L or baseline FeNO >= 20 ppb.
PGM=DEVOPS/SAR231893/EFC14153/CSR_RWE/REPORT/PGM/eff_mmrm_ger_subg_i_t.sas OUT=REPORT/OUTPUT/eff_mmrm_ppfev1_ger_wgt_i_t_x.rtf (21JUL2021 - 10:18)

Project Code / Study Number / Analysis: SAR231893 / EFC14153 / CSR_RWE

2 Pre-bronchodilator % predicted FEV1 - ITT type 2 inflammatory asthma phenotype population

2.1 Summary of treatment effect on change from baseline at Week 52

2.1.9 By atopic medical condition (Yes, No)

	Atopic medical condition			
	Yes		No	
Pre-bronchodilator % predicted FEV1	**Placebo (N=103)**	**Dupilumab (N=227)**	**Placebo (N=11)**	**Dupilumab (N=9)**
Baseline				
Value				
Number	103	227	11	9
Mean (SD)	78.26 (14.60)	77.75 (14.43)	79.27 (14.26)	75.33 (13.56)
Median	79.00	80.00	77.00	79.00
Q1 : Q3	71.00 : 87.00	69.00 : 88.00	72.00 : 87.00	73.00 : 83.00
Min : Max	31.0 : 110.0	30.0 : 112.0	54.0 : 110.0	50.0 : 94.0

[a]Derived from MMRM model with change from baseline in pre-bronchodilator % predicted FEV1 values up to Week 52 as the response variable, and treatment, baseline weight group, region, ethnicity, baseline eosinophil level, baseline FeNO level, baseline ICS dose level, visit, treatment by-visit interaction, baseline pre-bronchodilator % Predicted FEV1 value and baseline-by-visit interaction as covariates.
[b]Similar model as that mentioned in the footnote [a] with subgroup and subgroup-by-treatment interaction as additional covariates.
Type 2 inflammatory asthma phenotype population is defined as the randomized patients with baseline blood eosinophils >= 0.15 Giga/L or baseline FeNO >= 20 ppb.
PGM=DEVOPS/SAR231893/EFC14153/CSR_RWE/REPORT/PGM/eff_mmrm_ger_subg_i_t.sas OUT=REPORT/OUTPUT/eff_mmrm_ppfev1_ger_amc_i_t_x.rtf (21JUL2021 - 10:32)

Project Code / Study Number / Analysis: SAR231893 / EFC14153 / CSR_RWE

2 Pre-bronchodilator % predicted FEV1 - ITT type 2 inflammatory asthma phenotype population

2.1 Summary of treatment effect on change from baseline at Week 52

2.1.9 By atopic medical condition (Yes, No)

	Atopic medical condition			
	Yes		No	
Pre-bronchodilator % predicted FEV1	**Placebo (N=103)**	**Dupilumab (N=227)**	**Placebo (N=11)**	**Dupilumab (N=9)**
Week 52				
Value				
Number	95	206	11	9
Mean (SD)	82.11 (16.15)	89.66 (15.85)	91.45 (13.32)	88.67 (12.05)
Median	84.00	90.00	92.00	87.00
Q1 : Q3	72.00 : 92.00	81.00 : 97.00	77.00 : 102.00	83.00 : 99.00
Min : Max	32.0 : 118.0	37.0 : 179.0	75.0 : 114.0	70.0 : 105.0
Change from baseline				
Number	95	206	11	9
LS Mean (SE)[a]	3.66 (1.61)	12.39 (1.15)	12.78 (3.98)	0.93 (5.12)
LS Mean Diff (95% CI)[a]	-	8.73 (5.10 to 12.35)	-	-11.85 (-22.09 to -1.61)
p-value[a]		<0.001		0.027
Hedges'g (95% CI)	-	0.586 (0.342 to 0.829)	-	-0.780 (-1.454 to -0.106)
p-value for heterogeneity[b]				0.114

[a]Derived from MMRM model with change from baseline in pre-bronchodilator % predicted FEV1 values up to Week 52 as the response variable, and treatment, baseline weight group, region, ethnicity, baseline eosinophil level, baseline FeNO level, baseline ICS dose level, visit, treatment by-visit interaction, baseline pre-bronchodilator % Predicted FEV1 value and baseline-by-visit interaction as covariates.
[b]Similar model as that mentioned in the footnote [a] with subgroup and subgroup-by-treatment interaction as additional covariates.
Type 2 inflammatory asthma phenotype population is defined as the randomized patients with baseline blood eosinophils >= 0.15 Giga/L or baseline FeNO >= 20 ppb.
PGM=DEVOPS/SAR231893/EFC14153/CSR_RWE/REPORT/PGM/eff_mmrm_ger_subg_i_t.sas OUT=REPORT/OUTPUT/eff_mmrm_ppfev1_ger_amc_i_t_x.rtf (21JUL2021 - 10:32)

Project Code / Study Number / Analysis: SAR231893 / EFC14153 / CSR_RWE

2 Pre-bronchodilator % predicted FEV1 - ITT type 2 inflammatory asthma phenotype population

2.1 Summary of treatment effect on change from baseline at Week 52

2.1.10 By baseline total IgE (<median, >= median)

	Baseline Total IgE (IU/mL)			
	<median		>=median	
Pre-bronchodilator % predicted FEV1	**Placebo (N=66)**	**Dupilumab (N=105)**	**Placebo (N=47)**	**Dupilumab (N=125)**
Baseline				
Value				
Number	66	105	47	125
Mean (SD)	77.86 (16.12)	78.11 (11.69)	79.70 (11.31)	76.91 (16.24)
Median	77.50	79.00	80.00	80.00
Q1 : Q3	72.00 : 87.00	72.00 : 86.00	71.00 : 88.00	66.00 : 88.00
Min : Max	31.0 : 110.0	44.0 : 100.0	57.0 : 99.0	30.0 : 112.0

[a]Derived from MMRM model with change from baseline in pre-bronchodilator % predicted FEV1 values up to Week 52 as the response variable, and treatment, baseline weight group, region, ethnicity, baseline eosinophil level, baseline FeNO level, baseline ICS dose level, visit, treatment by-visit interaction, baseline pre-bronchodilator % Predicted FEV1 value and baseline-by-visit interaction as covariates.

[b]Similar model as that mentioned in the footnote [a] with subgroup and subgroup-by-treatment interaction as additional covariates.

Type 2 inflammatory asthma phenotype population is defined as the randomized patients with baseline blood eosinophils >= 0.15 Giga/L or baseline FeNO >= 20 ppb.

PGM=DEVOPS/SAR231893/EFC14153/CSR_RWE/REPORT/PGM/eff_mmrm_ger_subg_i_t.sas OUT=REPORT/OUTPUT/eff_mmrm_ppfev1_ger_igem_i_t_x.rtf (21JUL2021 - 10:46)

Project Code / Study Number / Analysis: SAR231893 / EFC14153 / CSR_RWE

2 Pre-bronchodilator % predicted FEV1 - ITT type 2 inflammatory asthma phenotype population

2.1 Summary of treatment effect on change from baseline at Week 52

2.1.10 By baseline total IgE (<median, >= median)

	Baseline Total IgE (IU/mL)			
	<median		>=median	
Pre-bronchodilator % predicted FEV1	**Placebo (N=66)**	**Dupilumab (N=105)**	**Placebo (N=47)**	**Dupilumab (N=125)**
Week 52				
Value				
Number	62	99	43	113
Mean (SD)	85.50 (17.71)	89.45 (14.73)	80.51 (11.70)	89.58 (16.71)
Median	85.50	91.00	83.00	89.00
Q1 : Q3	78.00 : 98.00	81.00 : 97.00	71.00 : 91.00	80.00 : 97.00
Min : Max	32.0 : 118.0	46.0 : 153.0	51.0 : 101.0	37.0 : 179.0
Change from baseline				
Number	62	99	43	113
LS Mean (SE)[a]	7.04 (1.99)	11.95 (1.60)	2.55 (2.43)	12.38 (1.64)
LS Mean Diff (95% CI)[a]	-	4.91 (0.19 to 9.63)	-	9.83 (4.75 to 14.91)
p-value[a]		0.042		<0.001
Hedges'g (95% CI)	-	0.332 (0.013 to 0.651)	-	0.680 (0.328 to 1.031)
p-value for heterogeneity[b]				0.109

[a]Derived from MMRM model with change from baseline in pre-bronchodilator % predicted FEV1 values up to Week 52 as the response variable, and treatment, baseline weight group, region, ethnicity, baseline eosinophil level, baseline FeNO level, baseline ICS dose level, visit, treatment by-visit interaction, baseline pre-bronchodilator % Predicted FEV1 value and baseline-by-visit interaction as covariates.
[b]Similar model as that mentioned in the footnote [a] with subgroup and subgroup-by-treatment interaction as additional covariates.
Type 2 inflammatory asthma phenotype population is defined as the randomized patients with baseline blood eosinophils >= 0.15 Giga/L or baseline FeNO >= 20 ppb.
PGM=DEVOPS/SAR231893/EFC14153/CSR_RWE/REPORT/PGM/eff_mmrm_ger_subg_i_t.sas OUT=REPORT/OUTPUT/eff_mmrm_ppfev1_ger_igem_i_t_x.rtf (21JUL2021 - 10:46)

Project Code / Study Number / Analysis: SAR231893 / EFC14153 / CSR_RWE

2 Pre-bronchodilator % predicted FEV1 - ITT type 2 inflammatory asthma phenotype population

2.1 Summary of treatment effect on change from baseline at Week 52

2.1.11 By baseline total IgE (<100 IU/ml, >= 100 IU/ml)

	Baseline Total IgE (IU/mL)			
	< 100		>= 100	
Pre-bronchodilator % predicted FEV1	**Placebo (N=22)**	**Dupilumab (N=29)**	**Placebo (N=91)**	**Dupilumab (N=201)**
Baseline				
Value				
Number	22	29	91	201
Mean (SD)	75.09 (10.65)	80.79 (12.79)	79.48 (14.96)	76.98 (14.50)
Median	75.00	83.00	80.00	79.00
Q1 : Q3	69.00 : 81.00	77.00 : 90.00	71.00 : 88.00	67.00 : 88.00
Min : Max	50.0 : 92.0	48.0 : 98.0	31.0 : 110.0	30.0 : 112.0

[a]Derived from MMRM model with change from baseline in pre-bronchodilator % predicted FEV1 values up to Week 52 as the response variable, and treatment, baseline weight group, region, ethnicity, baseline eosinophil level, baseline FeNO level, baseline ICS dose level, visit, treatment by-visit interaction, baseline pre-bronchodilator % Predicted FEV1 value and baseline-by-visit interaction as covariates.
[b]Similar model as that mentioned in the footnote [a] with subgroup and subgroup-by-treatment interaction as additional covariates.
Type 2 inflammatory asthma phenotype population is defined as the randomized patients with baseline blood eosinophils >= 0.15 Giga/L or baseline FeNO >= 20 ppb.
PGM=DEVOPS/SAR231893/EFC14153/CSR_RWE/REPORT/PGM/eff_mmrm_ger_subg_i_t.sas OUT=REPORT/OUTPUT/eff_mmrm_ppfev1_ger_ige_i_t_x.rtf (21JUL2021 - 11:00)

Project Code / Study Number / Analysis: SAR231893 / EFC14153 / CSR_RWE

2 Pre-bronchodilator % predicted FEV1 - ITT type 2 inflammatory asthma phenotype population

2.1 Summary of treatment effect on change from baseline at Week 52

2.1.11 By baseline total IgE (<100 IU/ml, >= 100 IU/ml)

	Baseline Total IgE (IU/mL)			
	< 100		>= 100	
Pre-bronchodilator % predicted FEV1	**Placebo (N=22)**	**Dupilumab (N=29)**	**Placebo (N=91)**	**Dupilumab (N=201)**
Week 52				
Value				
Number	22	28	83	184
Mean (SD)	83.50 (15.49)	89.11 (12.38)	83.45 (15.81)	89.59 (16.26)
Median	84.00	92.00	84.00	90.00
Q1 : Q3	77.00 : 93.00	77.50 : 97.00	74.00 : 92.00	81.00 : 97.00
Min : Max	38.0 : 102.0	62.0 : 112.0	32.0 : 118.0	37.0 : 179.0
Change from baseline				
Number	22	28	83	184
LS Mean (SE)[a]	6.12 (3.19)	12.41 (3.06)	4.26 (1.78)	12.23 (1.25)
LS Mean Diff (95% CI)[a]	-	6.28 (-0.55 to 13.11)	-	7.98 (4.04 to 11.91)
p-value[a]		0.071		<0.001
Hedges'g (95% CI)	-	0.557 (-0.049 to 1.162)	-	0.528 (0.267 to 0.788)
p-value for heterogeneity[b]				0.358

[a]Derived from MMRM model with change from baseline in pre-bronchodilator % predicted FEV1 values up to Week 52 as the response variable, and treatment, baseline weight group, region, ethnicity, baseline eosinophil level, baseline FeNO level, baseline ICS dose level, visit, treatment by-visit interaction, baseline pre-bronchodilator % Predicted FEV1 value and baseline-by-visit interaction as covariates.
[b]Similar model as that mentioned in the footnote [a] with subgroup and subgroup-by-treatment interaction as additional covariates.
Type 2 inflammatory asthma phenotype population is defined as the randomized patients with baseline blood eosinophils >= 0.15 Giga/L or baseline FeNO >= 20 ppb.
PGM=DEVOPS/SAR231893/EFC14153/CSR_RWE/REPORT/PGM/eff_mmrm_ger_subg_i_t.sas OUT=REPORT/OUTPUT/eff_mmrm_ppfev1_ger_ige_i_t_x.rtf (21JUL2021 - 11:00)

Project Code / Study Number / Analysis: SAR231893 / EFC14153 / CSR_RWE

2 Pre-bronchodilator % predicted FEV1 - ITT type 2 inflammatory asthma phenotype population

2.1 Summary of treatment effect on change from baseline at Week 52

2.1.12 By age at onset of asthma (0-2, 3-5, >=6 years)

	Age of onset of asthma (years)					
	0-2		3-5		>= 6	
Pre-bronchodilator % predicted FEV1	**Placebo (N=40)**	**Dupilumab (N=105)**	**Placebo (N=39)**	**Dupilumab (N=86)**	**Placebo (N=35)**	**Dupilumab (N=45)**
Baseline						
Value						
Number	40	105	39	86	35	45
Mean (SD)	79.63 (14.95)	77.38 (12.05)	79.33 (14.57)	78.87 (16.94)	75.83 (14.03)	76.00 (14.18)
Median	79.50	79.00	80.00	81.50	77.00	79.00
Q1 : Q3	70.00 : 89.50	71.00 : 86.00	74.00 : 87.00	70.00 : 90.00	68.00 : 85.00	65.00 : 88.00
Min : Max	49.0 : 110.0	43.0 : 101.0	31.0 : 110.0	30.0 : 112.0	41.0 : 109.0	48.0 : 100.0

[a]Derived from MMRM model with change from baseline in pre-bronchodilator % predicted FEV1 values up to Week 52 as the response variable, and treatment, baseline weight group, region, ethnicity, baseline eosinophil level, baseline FeNO level, baseline ICS dose level, visit, treatment by-visit interaction, baseline pre-bronchodilator % Predicted FEV1 value and baseline-by-visit interaction as covariates.
[b]Similar model as that mentioned in the footnote [a] with subgroup and subgroup-by-treatment interaction as additional covariates.
Type 2 inflammatory asthma phenotype population is defined as the randomized patients with baseline blood eosinophils >= 0.15 Giga/L or baseline FeNO >= 20 ppb.
PGM=DEVOPS/SAR231893/EFC14153/CSR_RWE/REPORT/PGM/eff_mmrm_ger_subg_i_t.sas OUT=REPORT/OUTPUT/eff_mmrm_ppfev1_ger_onsa_i_t_x.rtf (10AUG2021 - 8:36)

Project Code / Study Number / Analysis: SAR231893 / EFC14153 / CSR_RWE

2 Pre-bronchodilator % predicted FEV1 - ITT type 2 inflammatory asthma phenotype population

2.1 Summary of treatment effect on change from baseline at Week 52

2.1.12 By age at onset of asthma (0-2, 3-5, >=6 years)

	Age of onset of asthma (years)					
	0-2		3-5		>= 6	
Pre-bronchodilator % predicted FEV1	**Placebo (N=40)**	**Dupilumab (N=105)**	**Placebo (N=39)**	**Dupilumab (N=86)**	**Placebo (N=35)**	**Dupilumab (N=45)**
Week 52						
Value						
Number	36	95	36	78	34	42
Mean (SD)	84.39 (16.58)	89.21 (13.79)	85.08 (15.95)	91.81 (18.61)	79.56 (15.55)	86.45 (13.35)
Median	85.00	90.00	85.00	92.50	82.50	87.50
Q1 : Q3	76.50 : 96.00	80.00 : 97.00	75.50 : 95.50	83.00 : 98.00	69.00 : 89.00	77.00 : 95.00
Min : Max	32.0 : 114.0	51.0 : 156.0	35.0 : 118.0	37.0 : 179.0	38.0 : 111.0	46.0 : 111.0
Change from baseline						
Number	36	95	36	78	34	42
LS Mean (SE)[a]	5.76 (2.34)	12.16 (1.55)	6.29 (3.00)	14.02 (2.13)	1.57 (2.62)	9.00 (2.45)
LS Mean Diff (95% CI)[a]	-	6.41 (1.29 to 11.52)	-	7.73 (0.95 to 14.51)	-	7.44 (1.38 to 13.50)
p-value[a]		0.015		0.026		0.017

[a]Derived from MMRM model with change from baseline in pre-bronchodilator % predicted FEV1 values up to Week 52 as the response variable, and treatment, baseline weight group, region, ethnicity, baseline eosinophil level, baseline FeNO level, baseline ICS dose level, visit, treatment by-visit interaction, baseline pre-bronchodilator % Predicted FEV1 value and baseline-by-visit interaction as covariates.
[b]Similar model as that mentioned in the footnote [a] with subgroup and subgroup-by-treatment interaction as additional covariates.
Type 2 inflammatory asthma phenotype population is defined as the randomized patients with baseline blood eosinophils >= 0.15 Giga/L or baseline FeNO >= 20 ppb.
PGM=DEVOPS/SAR231893/EFC14153/CSR_RWE/REPORT/PGM/eff_mmrm_ger_subg_i_t.sas OUT=REPORT/OUTPUT/eff_mmrm_ppfev1_ger_onsa_i_t_x.rtf (10AUG2021 - 8:36)

Project Code / Study Number / Analysis: SAR231893 / EFC14153 / CSR_RWE

2 Pre-bronchodilator % predicted FEV1 - ITT type 2 inflammatory asthma phenotype population

2.1 Summary of treatment effect on change from baseline at Week 52

2.1.12 By age at onset of asthma (0-2, 3-5, >=6 years)

	Age of onset of asthma (years)					
	0-2		3-5		>= 6	
Pre-bronchodilator % predicted FEV1	**Placebo (N=40)**	**Dupilumab (N=105)**	**Placebo (N=39)**	**Dupilumab (N=86)**	**Placebo (N=35)**	**Dupilumab (N=45)**
Hedges'g (95% CI)	-	0.482 (0.097 to 0.867)	-	0.448 (0.055 to 0.841)	-	0.575 (0.106 to 1.043)
p-value for heterogeneity[b]:						
0-2, 3-5						0.758
0-2, >= 6						0.794
3-5, >= 6						0.984
overall						0.944

[a]Derived from MMRM model with change from baseline in pre-bronchodilator % predicted FEV1 values up to Week 52 as the response variable, and treatment, baseline weight group, region, ethnicity, baseline eosinophil level, baseline FeNO level, baseline ICS dose level, visit, treatment by-visit interaction, baseline pre-bronchodilator % Predicted FEV1 value and baseline-by-visit interaction as covariates.
[b]Similar model as that mentioned in the footnote [a] with subgroup and subgroup-by-treatment interaction as additional covariates.
Type 2 inflammatory asthma phenotype population is defined as the randomized patients with baseline blood eosinophils >= 0.15 Giga/L or baseline FeNO >= 20 ppb.
PGM=DEVOPS/SAR231893/EFC14153/CSR_RWE/REPORT/PGM/eff_mmrm_ger_subg_i_t.sas OUT=REPORT/OUTPUT/eff_mmrm_ppfev1_ger_onsa_i_t_x.rtf (10AUG2021 - 8:36)

Project Code / Study Number / Analysis: SAR231893 / EFC14153 / CSR_RWE

2 Pre-bronchodilator % predicted FEV1 - ITT type 2 inflammatory asthma phenotype population

2.1 Summary of treatment effect on change from baseline at Week 52

2.1.13 By number of severe asthma exacerbation prior to the study (<=1, 2, >2)

	Number of severe asthma exacerbation prior to the study					
	<=1		2		>2	
Pre-bronchodilator % predicted FEV1	**Placebo (N=47)**	**Dupilumab (N=85)**	**Placebo (N=32)**	**Dupilumab (N=75)**	**Placebo (N=35)**	**Dupilumab (N=76)**
Baseline						
Value						
Number	47	85	32	75	35	76
Mean (SD)	80.32 (13.84)	78.38 (13.59)	77.50 (13.70)	76.81 (16.11)	76.51 (16.12)	77.70 (13.54)
Median	80.00	80.00	76.00	80.00	79.00	79.00
Q1 : Q3	73.00 : 86.00	69.00 : 88.00	71.00 : 87.50	64.00 : 89.00	66.00 : 87.00	72.50 : 86.00
Min : Max	31.0 : 110.0	44.0 : 107.0	49.0 : 108.0	34.0 : 112.0	39.0 : 110.0	30.0 : 108.0

[a]Derived from MMRM model with change from baseline in pre-bronchodilator % predicted FEV1 values up to Week 52 as the response variable, and treatment, baseline weight group, region, ethnicity, baseline eosinophil level, baseline FeNO level, baseline ICS dose level, visit, treatment by-visit interaction, baseline pre-bronchodilator % Predicted FEV1 value and baseline-by-visit interaction as covariates.

[b]Similar model as that mentioned in the footnote [a] with subgroup and subgroup-by-treatment interaction as additional covariates.

Type 2 inflammatory asthma phenotype population is defined as the randomized patients with baseline blood eosinophils >= 0.15 Giga/L or baseline FeNO >= 20 ppb.

PGM=DEVOPS/SAR231893/EFC14153/CSR_RWE/REPORT/PGM/eff_mmrm_ger_subg_i_t.sas OUT=REPORT/OUTPUT/eff_mmrm_ppfev1_ger_exa_i_t_x.rtf (21JUL2021 - 11:38)

Project Code / Study Number / Analysis: SAR231893 / EFC14153 / CSR_RWE

2 Pre-bronchodilator % predicted FEV1 - ITT type 2 inflammatory asthma phenotype population

2.1 Summary of treatment effect on change from baseline at Week 52

2.1.13 By number of severe asthma exacerbation prior to the study (<=1, 2, >2)

	Number of severe asthma exacerbation prior to the study					
	<=1		2		>2	
Pre-bronchodilator % predicted FEV1	**Placebo (N=47)**	**Dupilumab (N=85)**	**Placebo (N=32)**	**Dupilumab (N=75)**	**Placebo (N=35)**	**Dupilumab (N=76)**
Week 52						
Value						
Number	44	76	32	70	30	69
Mean (SD)	84.39 (16.77)	88.39 (14.28)	83.72 (13.92)	93.06 (17.93)	80.47 (17.37)	87.46 (14.32)
Median	85.00	88.50	84.00	93.00	84.00	88.00
Q1 : Q3	78.00 : 94.50	80.50 : 96.00	77.00 : 92.50	85.00 : 99.00	72.00 : 89.00	81.00 : 96.00
Min : Max	32.0 : 118.0	37.0 : 156.0	38.0 : 109.0	60.0 : 179.0	35.0 : 114.0	46.0 : 121.0
Change from baseline						
Number	44	76	32	70	30	69
LS Mean (SE)[a]	2.91 (2.07)	9.74 (1.61)	6.89 (3.20)	17.45 (2.38)	2.46 (2.91)	10.25 (2.06)
LS Mean Diff (95% CI)[a]	-	6.84 (2.00 to 11.68)	-	10.56 (3.18 to 17.94)	-	7.79 (1.69 to 13.90)
p-value[a]		0.006		0.005		0.013

[a]Derived from MMRM model with change from baseline in pre-bronchodilator % predicted FEV1 values up to Week 52 as the response variable, and treatment, baseline weight group, region, ethnicity, baseline eosinophil level, baseline FeNO level, baseline ICS dose level, visit, treatment by-visit interaction, baseline pre-bronchodilator % Predicted FEV1 value and baseline-by-visit interaction as covariates.
[b]Similar model as that mentioned in the footnote [a] with subgroup and subgroup-by-treatment interaction as additional covariates.
Type 2 inflammatory asthma phenotype population is defined as the randomized patients with baseline blood eosinophils >= 0.15 Giga/L or baseline FeNO >= 20 ppb.
PGM=DEVOPS/SAR231893/EFC14153/CSR_RWE/REPORT/PGM/eff_mmrm_ger_subg_i_t.sas OUT=REPORT/OUTPUT/eff_mmrm_ppfev1_ger_exa_i_t_x.rtf (21JUL2021 - 11:38)

Project Code / Study Number / Analysis: SAR231893 / EFC14153 / CSR_RWE

2 Pre-bronchodilator % predicted FEV1 - ITT type 2 inflammatory asthma phenotype population

2.1 Summary of treatment effect on change from baseline at Week 52

2.1.13 By number of severe asthma exacerbation prior to the study (<=1, 2, >2)

	Number of severe asthma exacerbation prior to the study					
	<=1		2		>2	
Pre-bronchodilator % predicted FEV1	**Placebo (N=47)**	**Dupilumab (N=85)**	**Placebo (N=32)**	**Dupilumab (N=75)**	**Placebo (N=35)**	**Dupilumab (N=76)**
Hedges'g (95% CI)	-	0.532 (0.155 to 0.908)	-	0.621 (0.187 to 1.055)	-	0.554 (0.120 to 0.988)
p-value for heterogeneity[b]:						
<=1, 2						0.339
<=1, >2						0.669
2, >2						0.620
overall						0.633

[a]Derived from MMRM model with change from baseline in pre-bronchodilator % predicted FEV1 values up to Week 52 as the response variable, and treatment, baseline weight group, region, ethnicity, baseline eosinophil level, baseline FeNO level, baseline ICS dose level, visit, treatment by-visit interaction, baseline pre-bronchodilator % Predicted FEV1 value and baseline-by-visit interaction as covariates.

[b]Similar model as that mentioned in the footnote [a] with subgroup and subgroup-by-treatment interaction as additional covariates.

Type 2 inflammatory asthma phenotype population is defined as the randomized patients with baseline blood eosinophils >= 0.15 Giga/L or baseline FeNO >= 20 ppb.

PGM=DEVOPS/SAR231893/EFC14153/CSR_RWE/REPORT/PGM/eff_mmrm_ger_subg_i_t.sas OUT=REPORT/OUTPUT/eff_mmrm_ppfev1_ger_exa_i_t_x.rtf (21JUL2021 - 11:38)

Project Code / Study Number / Analysis: SAR231893 / EFC14153 / CSR_RWE

3 ACQ-5-IA - ITT type 2 inflammatory asthma phenotype population

3.1 Summary of treatment effect on change from baseline at Week 52

ACQ-5-IA	Placebo (N=114)	Dupilumab (N=236)
Baseline		
Value		
Number	114	236
Mean (SD)	2.15 (0.84)	2.18 (0.79)
Median	2.20	2.00
Q1 : Q3	1.60 : 2.60	1.80 : 2.60
Min : Max	0.0 : 5.0	0.0 : 5.6
Week 52		
Value		
Number	110	222
Mean (SD)	0.83 (0.94)	0.40 (0.64)
Median	0.60	0.00
Q1 : Q3	0.00 : 1.20	0.00 : 0.60
Min : Max	0.0 : 4.8	0.0 : 4.0
Change from baseline		
Number	110	222
LS Mean (SE)[a]	-1.30 (0.07)	-1.70 (0.05)

[a]Derived from MMRM model with change from baseline in ACQ-5-IA values up to Week 52 as the response variable, and treatment, baseline weight group, region, age, baseline eosinophil level, baseline FeNO level, baseline ICS dose level, visit, treatment by-visit interaction, baseline ACQ-5-IA value and baseline-by-visit interaction as covariates.

Type 2 inflammatory asthma phenotype population is defined as the randomized patients with baseline blood eosinophils >= 0.15 Giga/L or baseline FeNO >= 20 ppb.

PGM=DEVOPS/SAR231893/EFC14153/CSR_RWE/REPORT/PGM/eff_mmrm_ger_i_t.sas OUT=REPORT/OUTPUT/eff_mmrm_acq5_ger_i_t_x.rtf (22JUL2021 - 7:48)

Project Code / Study Number / Analysis: SAR231893 / EFC14153 / CSR_RWE

3 ACQ-5-IA - ITT type 2 inflammatory asthma phenotype population

3.1 Summary of treatment effect on change from baseline at Week 52

ACQ-5-IA	Placebo (N=114)	Dupilumab (N=236)
LS Mean Diff (95% CI)[a]	-	-0.39 (-0.55 to -0.23)
Hedges'g (95% CI)	-	-0.571 (-0.803 to -0.339)
p-value[a]		<0.001

[a]Derived from MMRM model with change from baseline in ACQ-5-IA values up to Week 52 as the response variable, and treatment, baseline weight group, region, age, baseline eosinophil level, baseline FeNO level, baseline ICS dose level, visit, treatment by-visit interaction, baseline ACQ-5-IA value and baseline-by-visit interaction as covariates.

Type 2 inflammatory asthma phenotype population is defined as the randomized patients with baseline blood eosinophils >= 0.15 Giga/L or baseline FeNO >= 20 ppb.

PGM=DEVOPS/SAR231893/EFC14153/CSR_RWE/REPORT/PGM/eff_mmrm_ger_i_t.sas OUT=REPORT/OUTPUT/eff_mmrm_acq5_ger_i_t_x.rtf (22JUL2021 - 7:48)

Project Code / Study Number / Analysis: SAR231893 / EFC14153 / CSR_RWE

3 ACQ-5-IA - ITT type 2 inflammatory asthma phenotype population

3.1 Summary of treatment effect on change from baseline at Week 52

3.1.1 By gender (Male, Female)

	Gender			
	Male		Female	
ACQ-5-IA	**Placebo (N=78)**	**Dupilumab (N=152)**	**Placebo (N=36)**	**Dupilumab (N=84)**
Baseline				
Value				
Number	78	152	36	84
Mean (SD)	2.17 (0.89)	2.20 (0.82)	2.10 (0.73)	2.13 (0.73)
Median	2.20	2.10	2.10	2.00
Q1 : Q3	1.60 : 2.60	1.80 : 2.70	1.60 : 2.50	1.60 : 2.60
Min : Max	0.0 : 5.0	0.0 : 5.6	0.4 : 4.0	0.6 : 4.8

[a]Derived from MMRM model with change from baseline in ACQ-5-IA values up to Week 52 as the response variable, and treatment, baseline weight group, region, age, baseline eosinophil level, baseline FeNO level, baseline ICS dose level, visit, treatment by-visit interaction, baseline ACQ-5-IA value and baseline-by-visit interaction as covariates.

[b]Similar model as that mentioned in the footnote [a] with subgroup and subgroup-by-treatment interaction as additional covariates.

Type 2 inflammatory asthma phenotype population is defined as the randomized patients with baseline blood eosinophils >= 0.15 Giga/L or baseline FeNO >= 20 ppb.

PGM=DEVOPS/SAR231893/EFC14153/CSR_RWE/REPORT/PGM/eff_mmrm_ger_subg_i_t.sas OUT=REPORT/OUTPUT/eff_mmrm_acq5_ger_sex_i_t_x.rtf (21JUL2021 - 8:43)

Project Code / Study Number / Analysis: SAR231893 / EFC14153 / CSR_RWE

3 ACQ-5-IA - ITT type 2 inflammatory asthma phenotype population

3.1 Summary of treatment effect on change from baseline at Week 52

3.1.1 By gender (Male, Female)

	Gender			
	Male		Female	
ACQ-5-IA	**Placebo (N=78)**	**Dupilumab (N=152)**	**Placebo (N=36)**	**Dupilumab (N=84)**
Week 52				
Value				
Number	76	143	34	79
Mean (SD)	0.94 (0.98)	0.34 (0.52)	0.56 (0.82)	0.50 (0.81)
Median	0.70	0.00	0.20	0.20
Q1 : Q3	0.20 : 1.40	0.00 : 0.40	0.00 : 1.00	0.00 : 0.60
Min : Max	0.0 : 4.8	0.0 : 2.2	0.0 : 3.6	0.0 : 4.0
Change from baseline				
Number	76	143	34	79
LS Mean (SE)[a]	-1.24 (0.08)	-1.76 (0.06)	-1.41 (0.13)	-1.56 (0.09)
LS Mean Diff (95% CI)[a]	-	-0.52 (-0.70 to -0.33)	-	-0.15 (-0.45 to 0.15)
p-value[a]		<0.001		0.328
Hedges'g (95% CI)	-	-0.794 (-1.080 to -0.508)	-	-0.200 (-0.604 to 0.204)
p-value for heterogeneity[b]				0.036

[a]Derived from MMRM model with change from baseline in ACQ-5-IA values up to Week 52 as the response variable, and treatment, baseline weight group, region, age, baseline eosinophil level, baseline FeNO level, baseline ICS dose level, visit, treatment by-visit interaction, baseline ACQ-5-IA value and baseline-by-visit interaction as covariates.

[b]Similar model as that mentioned in the footnote [a] with subgroup and subgroup-by-treatment interaction as additional covariates.

Type 2 inflammatory asthma phenotype population is defined as the randomized patients with baseline blood eosinophils >= 0.15 Giga/L or baseline FeNO >= 20 ppb.

PGM=DEVOPS/SAR231893/EFC14153/CSR_RWE/REPORT/PGM/eff_mmrm_ger_subg_i_t.sas OUT=REPORT/OUTPUT/eff_mmrm_acq5_ger_sex_i_t_x.rtf (21JUL2021 - 8:43)

Project Code / Study Number / Analysis: SAR231893 / EFC14153 / CSR_RWE

3 ACQ-5-IA - ITT type 2 inflammatory asthma phenotype population

3.1 Summary of treatment effect on change from baseline at Week 52

3.1.2 By region (Latin America, East Europe, Western Countries)

	Region					
	Latin America		East Europe		Western countries	
ACQ-5-IA	**Placebo (N=51)**	**Dupilumab (N=106)**	**Placebo (N=43)**	**Dupilumab (N=78)**	**Placebo (N=20)**	**Dupilumab (N=52)**
Baseline						
Value						
Number	51	106	43	78	20	52
Mean (SD)	2.24 (0.78)	2.15 (0.74)	2.11 (0.73)	2.24 (0.58)	1.98 (1.17)	2.15 (1.12)
Median	2.20	2.00	2.20	2.20	1.80	2.20
Q1 : Q3	1.60 : 2.60	1.60 : 2.60	1.80 : 2.40	1.80 : 2.60	1.00 : 3.00	1.40 : 2.70
Min : Max	0.6 : 5.0	0.0 : 4.4	0.0 : 4.4	0.8 : 3.8	0.2 : 4.0	0.4 : 5.6

[a]Derived from MMRM model with change from baseline in ACQ-5-IA values up to Week 52 as the response variable, and treatment, baseline weight group, age, baseline eosinophil level, baseline FeNO level, baseline ICS dose level, visit, treatment by-visit interaction, baseline ACQ-5-IA value and baseline-by-visit interaction as covariates.

[b]Similar model as that mentioned in the footnote [a] with subgroup and subgroup-by-treatment interaction as additional covariates.

Type 2 inflammatory asthma phenotype population is defined as the randomized patients with baseline blood eosinophils >= 0.15 Giga/L or baseline FeNO >= 20 ppb.

PGM=DEVOPS/SAR231893/EFC14153/CSR_RWE/REPORT/PGM/eff_mmrm_ger_subg_i_t.sas OUT=REPORT/OUTPUT/eff_mmrm_acq5_ger_cty_i_t_x.rtf (21JUL2021 - 9:01)

Project Code / Study Number / Analysis: SAR231893 / EFC14153 / CSR_RWE

3 ACQ-5-IA - ITT type 2 inflammatory asthma phenotype population

3.1 Summary of treatment effect on change from baseline at Week 52

3.1.2 By region (Latin America, East Europe, Western Countries)

	Region					
	Latin America		East Europe		Western countries	
ACQ-5-IA	**Placebo (N=51)**	**Dupilumab (N=106)**	**Placebo (N=43)**	**Dupilumab (N=78)**	**Placebo (N=20)**	**Dupilumab (N=52)**
Week 52						
Value						
Number	51	102	42	77	17	43
Mean (SD)	0.71 (1.04)	0.21 (0.39)	0.84 (0.71)	0.54 (0.71)	1.15 (1.12)	0.60 (0.85)
Median	0.40	0.00	0.80	0.20	0.80	0.40
Q1 : Q3	0.00 : 0.80	0.00 : 0.40	0.20 : 1.60	0.00 : 0.80	0.40 : 1.40	0.00 : 0.80
Min : Max	0.0 : 4.6	0.0 : 2.0	0.0 : 2.4	0.0 : 2.4	0.0 : 4.8	0.0 : 4.0
Change from baseline						
Number	51	102	42	77	17	43
LS Mean (SE)[a]	-1.55 (0.09)	-1.90 (0.06)	-1.32 (0.12)	-1.61 (0.09)	-0.52 (0.26)	-1.48 (0.17)
LS Mean Diff (95% CI)[a]	-	-0.36 (-0.55 to -0.16)	-	-0.29 (-0.56 to -0.02)	-	-0.96 (-1.53 to -0.40)
p-value[a]		<0.001		0.034		0.001

[a]Derived from MMRM model with change from baseline in ACQ-5-IA values up to Week 52 as the response variable, and treatment, baseline weight group, age, baseline eosinophil level, baseline FeNO level, baseline ICS dose level, visit, treatment by-visit interaction, baseline ACQ-5-IA value and baseline-by-visit interaction as covariates.
[b]Similar model as that mentioned in the footnote [a] with subgroup and subgroup-by-treatment interaction as additional covariates.
Type 2 inflammatory asthma phenotype population is defined as the randomized patients with baseline blood eosinophils >= 0.15 Giga/L or baseline FeNO >= 20 ppb.
PGM=DEVOPS/SAR231893/EFC14153/CSR_RWE/REPORT/PGM/eff_mmrm_ger_subg_i_t.sas OUT=REPORT/OUTPUT/eff_mmrm_acq5_ger_cty_i_t_x.rtf (21JUL2021 - 9:01)

Project Code / Study Number / Analysis: SAR231893 / EFC14153 / CSR_RWE

3 ACQ-5-IA - ITT type 2 inflammatory asthma phenotype population

3.1 Summary of treatment effect on change from baseline at Week 52

3.1.2 By region (Latin America, East Europe, Western Countries)

	Region					
	Latin America		East Europe		Western countries	
ACQ-5-IA	**Placebo (N=51)**	**Dupilumab (N=106)**	**Placebo (N=43)**	**Dupilumab (N=78)**	**Placebo (N=20)**	**Dupilumab (N=52)**
Hedges'g (95% CI)	-	-0.631 (-0.978 to -0.283)	-	-0.412 (-0.791 to -0.032)	-	-0.966 (-1.535 to -0.397)
p-value for heterogeneity[b]:						
Latin America, East Europe						0.780
Latin America, Western countries						0.115
East Europe, Western countries						0.163
overall						0.268

[a]Derived from MMRM model with change from baseline in ACQ-5-IA values up to Week 52 as the response variable, and treatment, baseline weight group, age, baseline eosinophil level, baseline FeNO level, baseline ICS dose level, visit, treatment by-visit interaction, baseline ACQ-5-IA value and baseline-by-visit interaction as covariates.

[b]Similar model as that mentioned in the footnote [a] with subgroup and subgroup-by-treatment interaction as additional covariates.

Type 2 inflammatory asthma phenotype population is defined as the randomized patients with baseline blood eosinophils >= 0.15 Giga/L or baseline FeNO >= 20 ppb.

PGM=DEVOPS/SAR231893/EFC14153/CSR_RWE/REPORT/PGM/eff_mmrm_ger_subg_i_t.sas OUT=REPORT/OUTPUT/eff_mmrm_acq5_ger_cty_i_t_x.rtf (21JUL2021 - 9:01)

Project Code / Study Number / Analysis: SAR231893 / EFC14153 / CSR_RWE

3 ACQ-5-IA - ITT type 2 inflammatory asthma phenotype population

3.1 Summary of treatment effect on change from baseline at Week 52

3.1.3 By race (Caucasian/white, Black/of African descent, Other)

	Race					
	Caucasian/White		Black/of African descent		Other	
ACQ-5-IA	**Placebo (N=102)**	**Dupilumab (N=208)**	**Placebo (N=5)**	**Dupilumab (N=9)**	**Placebo (N=7)**	**Dupilumab (N=19)**
Baseline						
Value						
Number	102	208	5	9	7	19
Mean (SD)	2.18 (0.84)	2.20 (0.70)	1.60 (1.02)	2.29 (1.49)	2.00 (0.67)	1.90 (1.19)
Median	2.20	2.10	1.40	1.80	2.20	2.00
Q1 : Q3	1.60 : 2.60	1.80 : 2.60	1.00 : 2.20	1.40 : 2.60	1.40 : 2.60	1.00 : 2.40
Min : Max	0.0 : 5.0	0.0 : 4.4	0.4 : 3.0	0.6 : 4.8	1.0 : 2.8	0.4 : 5.6

[a]Derived from MMRM model with change from baseline in ACQ-5-IA values up to Week 52 as the response variable, and treatment, baseline weight group, region, age, baseline eosinophil level, baseline FeNO level, baseline ICS dose level, visit, treatment by-visit interaction, baseline ACQ-5-IA value and baseline-by-visit interaction as covariates.

[b]Similar model as that mentioned in the footnote [a] with subgroup and subgroup-by-treatment interaction as additional covariates.

Type 2 inflammatory asthma phenotype population is defined as the randomized patients with baseline blood eosinophils >= 0.15 Giga/L or baseline FeNO >= 20 ppb.

PGM=DEVOPS/SAR231893/EFC14153/CSR_RWE/REPORT/PGM/eff_mmrm_ger_subg_i_t.sas OUT=REPORT/OUTPUT/eff_mmrm_acq5_ger_race_i_t_x.rtf (21JUL2021 - 9:20)

Project Code / Study Number / Analysis: SAR231893 / EFC14153 / CSR_RWE

3 ACQ-5-IA - ITT type 2 inflammatory asthma phenotype population

3.1 Summary of treatment effect on change from baseline at Week 52

3.1.3 By race (Caucasian/white, Black/of African descent, Other)

	Race					
	Caucasian/White		Black/of African descent		Other	
ACQ-5-IA	**Placebo (N=102)**	**Dupilumab (N=208)**	**Placebo (N=5)**	**Dupilumab (N=9)**	**Placebo (N=7)**	**Dupilumab (N=19)**
Week 52						
Value						
Number	101	199	2	7	7	16
Mean (SD)	0.75 (0.85)	0.37 (0.63)	1.70 (0.71)	1.03 (1.05)	1.74 (1.64)	0.39 (0.46)
Median	0.60	0.00	1.70	1.00	1.40	0.30
Q1 : Q3	0.00 : 1.00	0.00 : 0.40	1.20 : 2.20	0.20 : 1.20	0.40 : 3.40	0.00 : 0.60
Min : Max	0.0 : 4.8	0.0 : 4.0	1.2 : 2.2	0.0 : 3.2	0.4 : 4.6	0.0 : 1.6
Change from baseline						
Number	101	199	2	7	7	16
LS Mean (SE)[a]	-1.39 (0.07)	-1.71 (0.06)	-0.20 (0.80)	-1.28 (0.49)	-0.90 (0.30)	-1.74 (0.22)
LS Mean Diff (95% CI)[a]	-	-0.32 (-0.48 to -0.16)	-	-1.08 (-2.65 to 0.49)	-	-0.84 (-1.55 to -0.13)
p-value[a]		<0.001		0.172		0.024

[a]Derived from MMRM model with change from baseline in ACQ-5-IA values up to Week 52 as the response variable, and treatment, baseline weight group, region, age, baseline eosinophil level, baseline FeNO level, baseline ICS dose level, visit, treatment by-visit interaction, baseline ACQ-5-IA value and baseline-by-visit interaction as covariates.

[b]Similar model as that mentioned in the footnote [a] with subgroup and subgroup-by-treatment interaction as additional covariates.

Type 2 inflammatory asthma phenotype population is defined as the randomized patients with baseline blood eosinophils >= 0.15 Giga/L or baseline FeNO >= 20 ppb.

PGM=DEVOPS/SAR231893/EFC14153/CSR_RWE/REPORT/PGM/eff_mmrm_ger_subg_i_t.sas OUT=REPORT/OUTPUT/eff_mmrm_acq5_ger_race_i_t_x.rtf (21JUL2021 - 9:20)

Project Code / Study Number / Analysis: SAR231893 / EFC14153 / CSR_RWE

3 ACQ-5-IA - ITT type 2 inflammatory asthma phenotype population

3.1 Summary of treatment effect on change from baseline at Week 52

3.1.3 By race (Caucasian/white, Black/of African descent, Other)

	Race					
	Caucasian/White		Black/of African descent		Other	
ACQ-5-IA	**Placebo (N=102)**	**Dupilumab (N=208)**	**Placebo (N=5)**	**Dupilumab (N=9)**	**Placebo (N=7)**	**Dupilumab (N=19)**
Hedges'g (95% CI)	-	-0.482 (-0.726 to -0.238)	-	-0.835 (-2.048 to 0.379)	-	-0.934 (-1.727 to -0.142)
p-value for heterogeneity[b]:						
Caucasian/White, Black/of African descent						0.275
Caucasian/White, Other						0.756
Black/of African descent, Other						0.031
overall						0.058

[a]Derived from MMRM model with change from baseline in ACQ-5-IA values up to Week 52 as the response variable, and treatment, baseline weight group, region, age, baseline eosinophil level, baseline FeNO level, baseline ICS dose level, visit, treatment by-visit interaction, baseline ACQ-5-IA value and baseline-by-visit interaction as covariates.

[b]Similar model as that mentioned in the footnote [a] with subgroup and subgroup-by-treatment interaction as additional covariates.

Type 2 inflammatory asthma phenotype population is defined as the randomized patients with baseline blood eosinophils >= 0.15 Giga/L or baseline FeNO >= 20 ppb.

PGM=DEVOPS/SAR231893/EFC14153/CSR_RWE/REPORT/PGM/eff_mmrm_ger_subg_i_t.sas OUT=REPORT/OUTPUT/eff_mmrm_acq5_ger_race_i_t_x.rtf (21JUL2021 - 9:20)

Project Code / Study Number / Analysis: SAR231893 / EFC14153 / CSR_RWE

3 ACQ-5-IA - ITT type 2 inflammatory asthma phenotype population

3.1 Summary of treatment effect on change from baseline at Week 52

3.1.4 By baseline ICS dose level (Medium, High)

	Baseline ICS dose level			
	High		Medium	
ACQ-5-IA	**Placebo (N=50)**	**Dupilumab (N=102)**	**Placebo (N=64)**	**Dupilumab (N=131)**
Baseline				
Value				
Number	50	102	64	131
Mean (SD)	2.02 (0.72)	2.19 (0.90)	2.24 (0.92)	2.18 (0.69)
Median	2.00	2.20	2.20	2.00
Q1 : Q3	1.60 : 2.40	1.60 : 2.80	1.60 : 2.70	1.80 : 2.60
Min : Max	0.2 : 3.6	0.0 : 5.6	0.0 : 5.0	0.6 : 4.8
Week 52				
Value				
Number	49	98	61	123
Mean (SD)	1.00 (1.05)	0.44 (0.63)	0.69 (0.83)	0.36 (0.65)
Median	0.80	0.20	0.40	0.00
Q1 : Q3	0.40 : 1.40	0.00 : 0.60	0.00 : 1.00	0.00 : 0.40
Min : Max	0.0 : 4.8	0.0 : 2.4	0.0 : 3.4	0.0 : 4.0

[a]Derived from MMRM model with change from baseline in ACQ-5-IA values up to Week 52 as the response variable, and treatment, baseline weight group, region, age, baseline eosinophil level, baseline FeNO level, visit, treatment by-visit interaction, baseline ACQ-5-IA value and baseline-by-visit interaction as covariates.
[b]Similar model as that mentioned in the footnote [a] with subgroup and subgroup-by-treatment interaction as additional covariates.
Type 2 inflammatory asthma phenotype population is defined as the randomized patients with baseline blood eosinophils >= 0.15 Giga/L or baseline FeNO >= 20 ppb.
PGM=DEVOPS/SAR231893/EFC14153/CSR_RWE/REPORT/PGM/eff_mmrm_ger_subg_i_t.sas OUT=REPORT/OUTPUT/eff_mmrm_acq5_ger_ics_i_t_x.rtf (21JUL2021 - 9:34)

Project Code / Study Number / Analysis: SAR231893 / EFC14153 / CSR_RWE

3 ACQ-5-IA - ITT type 2 inflammatory asthma phenotype population

3.1 Summary of treatment effect on change from baseline at Week 52

3.1.4 By baseline ICS dose level (Medium, High)

	Baseline ICS dose level			
	High		Medium	
ACQ-5-IA	**Placebo (N=50)**	**Dupilumab (N=102)**	**Placebo (N=64)**	**Dupilumab (N=131)**
Change from baseline				
Number	49	98	61	123
LS Mean (SE)[a]	-1.14 (0.11)	-1.68 (0.08)	-1.39 (0.10)	-1.70 (0.07)
LS Mean Diff (95% CI)[a]	-	-0.54 (-0.78 to -0.29)	-	-0.31 (-0.53 to -0.10)
p-value[a]		<0.001		0.005
Hedges'g (95% CI)	-	-0.770 (-1.124 to -0.417)	-	-0.451 (-0.764 to -0.139)
p-value for heterogeneity[b]				0.184

[a]Derived from MMRM model with change from baseline in ACQ-5-IA values up to Week 52 as the response variable, and treatment, baseline weight group, region, age, baseline eosinophil level, baseline FeNO level, visit, treatment by-visit interaction, baseline ACQ-5-IA value and baseline-by-visit interaction as covariates.
[b]Similar model as that mentioned in the footnote [a] with subgroup and subgroup-by-treatment interaction as additional covariates.
Type 2 inflammatory asthma phenotype population is defined as the randomized patients with baseline blood eosinophils >= 0.15 Giga/L or baseline FeNO >= 20 ppb.
PGM=DEVOPS/SAR231893/EFC14153/CSR_RWE/REPORT/PGM/eff_mmrm_ger_subg_i_t.sas OUT=REPORT/OUTPUT/eff_mmrm_acq5_ger_ics_i_t_x.rtf (21JUL2021 - 9:34)

Project Code / Study Number / Analysis: SAR231893 / EFC14153 / CSR_RWE

3 ACQ-5-IA - ITT type 2 inflammatory asthma phenotype population

3.1 Summary of treatment effect on change from baseline at Week 52

3.1.5 By baseline ICS dose level 2 (Medium, High)

	Baseline ICS dose level 2			
	High		Medium	
ACQ-5-IA	**Placebo (N=95)**	**Dupilumab (N=200)**	**Placebo (N=19)**	**Dupilumab (N=36)**
Baseline				
Value				
Number	95	200	19	36
Mean (SD)	2.13 (0.70)	2.21 (0.81)	2.21 (1.36)	2.02 (0.68)
Median	2.20	2.00	2.00	2.10
Q1 : Q3	1.60 : 2.60	1.60 : 2.60	1.40 : 3.40	1.80 : 2.40
Min : Max	0.0 : 4.4	0.0 : 5.6	0.2 : 5.0	0.4 : 3.4
Week 52				
Value				
Number	92	192	18	30
Mean (SD)	0.87 (0.97)	0.40 (0.65)	0.63 (0.83)	0.40 (0.55)
Median	0.60	0.00	0.40	0.10
Q1 : Q3	0.20 : 1.30	0.00 : 0.50	0.00 : 1.00	0.00 : 0.60
Min : Max	0.0 : 4.8	0.0 : 4.0	0.0 : 2.4	0.0 : 1.6

[a]Derived from MMRM model with change from baseline in ACQ-5-IA values up to Week 52 as the response variable, and treatment, baseline weight group, region, age, baseline eosinophil level, baseline FeNO level, visit, treatment by-visit interaction, baseline ACQ-5-IA value and baseline-by-visit interaction as covariates.
[b]Similar model as that mentioned in the footnote [a] with subgroup and subgroup-by-treatment interaction as additional covariates.
Type 2 inflammatory asthma phenotype population is defined as the randomized patients with baseline blood eosinophils >= 0.15 Giga/L or baseline FeNO >= 20 ppb.
PGM=DEVOPS/SAR231893/EFC14153/CSR_RWE/REPORT/PGM/eff_mmrm_ger_subg_i_t.sas OUT=REPORT/OUTPUT/eff_mmrm_acq5_ger_ics2_i_t_x.rtf (01SEP2021 - 16:35)

Project Code / Study Number / Analysis: SAR231893 / EFC14153 / CSR_RWE

3 ACQ-5-IA - ITT type 2 inflammatory asthma phenotype population

3.1 Summary of treatment effect on change from baseline at Week 52

3.1.5 By baseline ICS dose level 2 (Medium, High)

	Baseline ICS dose level 2			
	High		Medium	
ACQ-5-IA	**Placebo (N=95)**	**Dupilumab (N=200)**	**Placebo (N=19)**	**Dupilumab (N=36)**
Change from baseline				
Number	92	192	18	30
LS Mean (SE)[a]	-1.24 (0.08)	-1.71 (0.06)	-1.41 (0.16)	-1.61 (0.13)
LS Mean Diff (95% CI)[a]	-	-0.47 (-0.65 to -0.30)	-	-0.20 (-0.57 to 0.17)
p-value[a]		<0.001		0.291
Hedges'g (95% CI)	-	-0.673 (-0.925 to -0.422)	-	-0.348 (-1.005 to 0.309)
p-value for heterogeneity[b]				0.080

[a]Derived from MMRM model with change from baseline in ACQ-5-IA values up to Week 52 as the response variable, and treatment, baseline weight group, region, age, baseline eosinophil level, baseline FeNO level, visit, treatment by-visit interaction, baseline ACQ-5-IA value and baseline-by-visit interaction as covariates.
[b]Similar model as that mentioned in the footnote [a] with subgroup and subgroup-by-treatment interaction as additional covariates.
Type 2 inflammatory asthma phenotype population is defined as the randomized patients with baseline blood eosinophils >= 0.15 Giga/L or baseline FeNO >= 20 ppb.
PGM=DEVOPS/SAR231893/EFC14153/CSR_RWE/REPORT/PGM/eff_mmrm_ger_subg_i_t.sas OUT=REPORT/OUTPUT/eff_mmrm_acq5_ger_ics2_i_t_x.rtf (01SEP2021 - 16:35)

Project Code / Study Number / Analysis: SAR231893 / EFC14153 / CSR_RWE

3 ACQ-5-IA - ITT type 2 inflammatory asthma phenotype population

3.1 Summary of treatment effect on change from baseline at Week 52

3.1.6 By baseline predicted FEV1 (<80%, >=80%)

	Baseline Predicted FEV1			
	<80%		>=80%	
ACQ-5-IA	**Placebo (N=59)**	**Dupilumab (N=116)**	**Placebo (N=55)**	**Dupilumab (N=120)**
Baseline				
Value				
Number	59	116	55	120
Mean (SD)	2.14 (0.92)	2.19 (0.77)	2.15 (0.76)	2.16 (0.81)
Median	2.20	2.20	2.20	2.00
Q1 : Q3	1.60 : 2.60	1.80 : 2.60	1.60 : 2.60	1.70 : 2.60
Min : Max	0.0 : 5.0	0.4 : 4.8	0.2 : 4.4	0.0 : 5.6

[a]Derived from MMRM model with change from baseline in ACQ-5-IA values up to Week 52 as the response variable, and treatment, baseline weight group, region, age, baseline eosinophil level, baseline FeNO level, baseline ICS dose level, visit, treatment by-visit interaction, baseline ACQ-5-IA value and baseline-by-visit interaction as covariates.
[b]Similar model as that mentioned in the footnote [a] with subgroup and subgroup-by-treatment interaction as additional covariates.
Type 2 inflammatory asthma phenotype population is defined as the randomized patients with baseline blood eosinophils >= 0.15 Giga/L or baseline FeNO >= 20 ppb.
PGM=DEVOPS/SAR231893/EFC14153/CSR_RWE/REPORT/PGM/eff_mmrm_ger_subg_i_t.sas OUT=REPORT/OUTPUT/eff_mmrm_acq5_ger_pfev1_i_t_x.rtf (21JUL2021 - 9:48)

Project Code / Study Number / Analysis: SAR231893 / EFC14153 / CSR_RWE

3 ACQ-5-IA - ITT type 2 inflammatory asthma phenotype population

3.1 Summary of treatment effect on change from baseline at Week 52

3.1.6 By baseline predicted FEV1 (<80%, >=80%)

	Baseline Predicted FEV1			
	<80%		>=80%	
ACQ-5-IA	**Placebo (N=59)**	**Dupilumab (N=116)**	**Placebo (N=55)**	**Dupilumab (N=120)**
Week 52				
Value				
Number	56	113	54	109
Mean (SD)	0.89 (0.95)	0.41 (0.61)	0.76 (0.94)	0.38 (0.68)
Median	0.80	0.20	0.40	0.00
Q1 : Q3	0.20 : 1.30	0.00 : 0.60	0.00 : 1.00	0.00 : 0.40
Min : Max	0.0 : 4.6	0.0 : 3.2	0.0 : 4.8	0.0 : 4.0
Change from baseline				
Number	56	113	54	109
LS Mean (SE)[a]	-1.30 (0.09)	-1.78 (0.07)	-1.30 (0.11)	-1.66 (0.08)
LS Mean Diff (95% CI)[a]	-	-0.47 (-0.68 to -0.27)	-	-0.36 (-0.60 to -0.11)
p-value[a]		<0.001		0.005
Hedges'g (95% CI)	-	-0.744 (-1.073 to -0.416)	-	-0.484 (-0.816 to -0.152)
p-value for heterogeneity[b]				0.489

[a]Derived from MMRM model with change from baseline in ACQ-5-IA values up to Week 52 as the response variable, and treatment, baseline weight group, region, age, baseline eosinophil level, baseline FeNO level, baseline ICS dose level, visit, treatment by-visit interaction, baseline ACQ-5-IA value and baseline-by-visit interaction as covariates.

[b]Similar model as that mentioned in the footnote [a] with subgroup and subgroup-by-treatment interaction as additional covariates.

Type 2 inflammatory asthma phenotype population is defined as the randomized patients with baseline blood eosinophils >= 0.15 Giga/L or baseline FeNO >= 20 ppb.

PGM=DEVOPS/SAR231893/EFC14153/CSR_RWE/REPORT/PGM/eff_mmrm_ger_subg_i_t.sas OUT=REPORT/OUTPUT/eff_mmrm_acq5_ger_pfev1_i_t_x.rtf (21JUL2021 - 9:48)

Project Code / Study Number / Analysis: SAR231893 / EFC14153 / CSR_RWE

3 ACQ-5-IA - ITT type 2 inflammatory asthma phenotype population

3.1 Summary of treatment effect on change from baseline at Week 52

3.1.7 By baseline ACQ-7-IA (<=2, >2)

	Baseline ACQ-7-IA			
	<=2		>2	
ACQ-5-IA	**Placebo (N=61)**	**Dupilumab (N=126)**	**Placebo (N=53)**	**Dupilumab (N=110)**
Baseline				
Value				
Number	61	126	53	110
Mean (SD)	1.61 (0.59)	1.66 (0.48)	2.76 (0.64)	2.77 (0.65)
Median	1.60	1.80	2.60	2.60
Q1 : Q3	1.40 : 2.00	1.40 : 2.00	2.40 : 3.00	2.20 : 3.00
Min : Max	0.0 : 2.6	0.0 : 2.6	1.6 : 5.0	1.6 : 5.6

[a]Derived from MMRM model with change from baseline in ACQ-5-IA values up to Week 52 as the response variable, and treatment, baseline weight group, region, age, baseline eosinophil level, baseline FeNO level, baseline ICS dose level, visit, treatment by-visit interaction, baseline ACQ-5-IA value and baseline-by-visit interaction as covariates.
[b]Similar model as that mentioned in the footnote [a] with subgroup and subgroup-by-treatment interaction as additional covariates.
Type 2 inflammatory asthma phenotype population is defined as the randomized patients with baseline blood eosinophils >= 0.15 Giga/L or baseline FeNO >= 20 ppb.
PGM=DEVOPS/SAR231893/EFC14153/CSR_RWE/REPORT/PGM/eff_mmrm_ger_subg_i_t.sas OUT=REPORT/OUTPUT/eff_mmrm_acq5_ger_acq7_i_t_x.rtf (21JUL2021 - 10:01)

Project Code / Study Number / Analysis: SAR231893 / EFC14153 / CSR_RWE

3 ACQ-5-IA - ITT type 2 inflammatory asthma phenotype population

3.1 Summary of treatment effect on change from baseline at Week 52

3.1.7 By baseline ACQ-7-IA (<=2, >2)

	Baseline ACQ-7-IA			
	<=2		>2	
ACQ-5-IA	**Placebo (N=61)**	**Dupilumab (N=126)**	**Placebo (N=53)**	**Dupilumab (N=110)**
Week 52				
Value				
Number	60	117	50	105
Mean (SD)	0.73 (0.86)	0.36 (0.63)	0.95 (1.03)	0.44 (0.65)
Median	0.40	0.00	0.80	0.20
Q1 : Q3	0.00 : 1.00	0.00 : 0.40	0.20 : 1.60	0.00 : 0.60
Min : Max	0.0 : 4.6	0.0 : 4.0	0.0 : 4.8	0.0 : 3.2
Change from baseline				
Number	60	117	50	105
LS Mean (SE)[a]	-0.91 (0.09)	-1.21 (0.06)	-1.76 (0.12)	-2.26 (0.09)
LS Mean Diff (95% CI)[a]	-	-0.30 (-0.50 to -0.11)	-	-0.50 (-0.76 to -0.23)
p-value[a]		0.003		<0.001
Hedges'g (95% CI)	-	-0.487 (-0.803 to -0.170)	-	-0.651 (-0.997 to -0.305)
p-value for heterogeneity[b]				0.181

[a]Derived from MMRM model with change from baseline in ACQ-5-IA values up to Week 52 as the response variable, and treatment, baseline weight group, region, age, baseline eosinophil level, baseline FeNO level, baseline ICS dose level, visit, treatment by-visit interaction, baseline ACQ-5-IA value and baseline-by-visit interaction as covariates.

[b]Similar model as that mentioned in the footnote [a] with subgroup and subgroup-by-treatment interaction as additional covariates.

Type 2 inflammatory asthma phenotype population is defined as the randomized patients with baseline blood eosinophils >= 0.15 Giga/L or baseline FeNO >= 20 ppb.

PGM=DEVOPS/SAR231893/EFC14153/CSR_RWE/REPORT/PGM/eff_mmrm_ger_subg_i_t.sas OUT=REPORT/OUTPUT/eff_mmrm_acq5_ger_acq7_i_t_x.rtf (21JUL2021 - 10:01)

Project Code / Study Number / Analysis: SAR231893 / EFC14153 / CSR_RWE

3 ACQ-5-IA - ITT type 2 inflammatory asthma phenotype population

3.1 Summary of treatment effect on change from baseline at Week 52

3.1.8 By baseline weight (<=30 kg, >30 kg)

	Baseline weight (kg)			
	<=30		>30	
ACQ-5-IA	**Placebo (N=36)**	**Dupilumab (N=76)**	**Placebo (N=78)**	**Dupilumab (N=160)**
Baseline				
Value				
Number	36	76	78	160
Mean (SD)	2.13 (0.88)	2.17 (0.79)	2.15 (0.83)	2.18 (0.80)
Median	2.20	2.10	2.20	2.00
Q1 : Q3	1.60 : 2.70	1.60 : 2.60	1.60 : 2.60	1.80 : 2.60
Min : Max	0.2 : 3.8	0.6 : 4.8	0.0 : 5.0	0.0 : 5.6
Week 52				
Value				
Number	34	69	76	153
Mean (SD)	0.78 (0.79)	0.34 (0.58)	0.85 (1.01)	0.42 (0.67)
Median	0.60	0.00	0.60	0.00
Q1 : Q3	0.20 : 1.00	0.00 : 0.40	0.00 : 1.30	0.00 : 0.60
Min : Max	0.0 : 3.4	0.0 : 3.2	0.0 : 4.8	0.0 : 4.0

[a]Derived from MMRM model with change from baseline in ACQ-5-IA values up to Week 52 as the response variable, and treatment, region, age, baseline eosinophil level, baseline FeNO level, baseline ICS dose level, visit, treatment by-visit interaction, baseline ACQ-5-IA value and baseline-by-visit interaction as covariates.
[b]Similar model as that mentioned in the footnote [a] with subgroup and subgroup-by-treatment interaction as additional covariates.
Type 2 inflammatory asthma phenotype population is defined as the randomized patients with baseline blood eosinophils >= 0.15 Giga/L or baseline FeNO >= 20 ppb.
PGM=DEVOPS/SAR231893/EFC14153/CSR_RWE/REPORT/PGM/eff_mmrm_ger_subg_i_t.sas OUT=REPORT/OUTPUT/eff_mmrm_acq5_ger_wgt_i_t_x.rtf (21JUL2021 - 10:15)

Project Code / Study Number / Analysis: SAR231893 / EFC14153 / CSR_RWE

3 ACQ-5-IA - ITT type 2 inflammatory asthma phenotype population

3.1 Summary of treatment effect on change from baseline at Week 52

3.1.8 By baseline weight (<=30 kg, >30 kg)

	Baseline weight (kg)			
	<=30		>30	
ACQ-5-IA	**Placebo (N=36)**	**Dupilumab (N=76)**	**Placebo (N=78)**	**Dupilumab (N=160)**
Change from baseline				
Number	34	69	76	153
LS Mean (SE)[a]	-1.39 (0.12)	-1.80 (0.08)	-1.28 (0.09)	-1.66 (0.06)
LS Mean Diff (95% CI)[a]	-	-0.40 (-0.67 to -0.14)	-	-0.38 (-0.58 to -0.18)
p-value[a]		0.003		<0.001
Hedges'g (95% CI)	-	-0.635 (-1.055 to -0.215)	-	-0.530 (-0.810 to -0.249)
p-value for heterogeneity[b]				0.854

[a]Derived from MMRM model with change from baseline in ACQ-5-IA values up to Week 52 as the response variable, and treatment, region, age, baseline eosinophil level, baseline FeNO level, baseline ICS dose level, visit, treatment by-visit interaction, baseline ACQ-5-IA value and baseline-by-visit interaction as covariates.
[b]Similar model as that mentioned in the footnote [a] with subgroup and subgroup-by-treatment interaction as additional covariates.
Type 2 inflammatory asthma phenotype population is defined as the randomized patients with baseline blood eosinophils >= 0.15 Giga/L or baseline FeNO >= 20 ppb.
PGM=DEVOPS/SAR231893/EFC14153/CSR_RWE/REPORT/PGM/eff_mmrm_ger_subg_i_t.sas OUT=REPORT/OUTPUT/eff_mmrm_acq5_ger_wgt_i_t_x.rtf (21JUL2021 - 10:15)

Project Code / Study Number / Analysis: SAR231893 / EFC14153 / CSR_RWE

3 ACQ-5-IA - ITT type 2 inflammatory asthma phenotype population

3.1 Summary of treatment effect on change from baseline at Week 52

3.1.9 By atopic medical condition (Yes, No)

	Atopic medical condition			
	Yes		No	
ACQ-5-IA	**Placebo (N=103)**	**Dupilumab (N=227)**	**Placebo (N=11)**	**Dupilumab (N=9)**
Baseline				
Value				
Number	103	227	11	9
Mean (SD)	2.14 (0.82)	2.18 (0.80)	2.24 (1.08)	2.18 (0.41)
Median	2.20	2.00	2.20	2.00
Q1 : Q3	1.60 : 2.60	1.60 : 2.60	1.40 : 2.40	1.80 : 2.40
Min : Max	0.0 : 5.0	0.0 : 5.6	1.0 : 4.4	1.8 : 2.8

[a]Derived from MMRM model with change from baseline in ACQ-5-IA values up to Week 52 as the response variable, and treatment, baseline weight group, region, age, baseline eosinophil level, baseline FeNO level, baseline ICS dose level, visit, treatment by-visit interaction, baseline ACQ-5-IA value and baseline-by-visit interaction as covariates.
[b]Similar model as that mentioned in the footnote [a] with subgroup and subgroup-by-treatment interaction as additional covariates.
Type 2 inflammatory asthma phenotype population is defined as the randomized patients with baseline blood eosinophils >= 0.15 Giga/L or baseline FeNO >= 20 ppb.
PGM=DEVOPS/SAR231893/EFC14153/CSR_RWE/REPORT/PGM/eff_mmrm_ger_subg_i_t.sas OUT=REPORT/OUTPUT/eff_mmrm_acq5_ger_amc_i_t_x.rtf (21JUL2021 - 10:29)

Project Code / Study Number / Analysis: SAR231893 / EFC14153 / CSR_RWE

3 ACQ-5-IA - ITT type 2 inflammatory asthma phenotype population

3.1 Summary of treatment effect on change from baseline at Week 52

3.1.9 By atopic medical condition (Yes, No)

	Atopic medical condition			
	Yes		No	
ACQ-5-IA	**Placebo (N=103)**	**Dupilumab (N=227)**	**Placebo (N=11)**	**Dupilumab (N=9)**
Week 52				
Value				
Number	99	213	11	9
Mean (SD)	0.86 (0.95)	0.41 (0.65)	0.56 (0.91)	0.02 (0.07)
Median	0.60	0.00	0.00	0.00
Q1 : Q3	0.20 : 1.20	0.00 : 0.60	0.00 : 1.60	0.00 : 0.00
Min : Max	0.0 : 4.8	0.0 : 4.0	0.0 : 2.4	0.0 : 0.2
Change from baseline				
Number	99	213	11	9
LS Mean (SE)[a]	-1.27 (0.07)	-1.68 (0.05)	-1.98 (0.26)	-2.54 (0.27)
LS Mean Diff (95% CI)[a]	-	-0.41 (-0.58 to -0.24)	-	-0.56 (-1.24 to 0.11)
p-value[a]		<0.001		0.096
Hedges'g (95% CI)	-	-0.598 (-0.840 to -0.355)	-	-0.648 (-1.423 to 0.127)
p-value for heterogeneity[b]				0.947

[a]Derived from MMRM model with change from baseline in ACQ-5-IA values up to Week 52 as the response variable, and treatment, baseline weight group, region, age, baseline eosinophil level, baseline FeNO level, baseline ICS dose level, visit, treatment by-visit interaction, baseline ACQ-5-IA value and baseline-by-visit interaction as covariates.

[b]Similar model as that mentioned in the footnote [a] with subgroup and subgroup-by-treatment interaction as additional covariates.

Type 2 inflammatory asthma phenotype population is defined as the randomized patients with baseline blood eosinophils >= 0.15 Giga/L or baseline FeNO >= 20 ppb.

PGM=DEVOPS/SAR231893/EFC14153/CSR_RWE/REPORT/PGM/eff_mmrm_ger_subg_i_t.sas OUT=REPORT/OUTPUT/eff_mmrm_acq5_ger_amc_i_t_x.rtf (21JUL2021 - 10:29)

Project Code / Study Number / Analysis: SAR231893 / EFC14153 / CSR_RWE

3 ACQ-5-IA - ITT type 2 inflammatory asthma phenotype population

3.1 Summary of treatment effect on change from baseline at Week 52

3.1.10 By baseline total IgE (<median, >= median)

	Baseline Total IgE (IU/mL)			
	<median		>=median	
ACQ-5-IA	**Placebo (N=66)**	**Dupilumab (N=105)**	**Placebo (N=47)**	**Dupilumab (N=125)**
Baseline				
Value				
Number	66	105	47	125
Mean (SD)	2.08 (0.82)	2.10 (0.63)	2.21 (0.86)	2.25 (0.91)
Median	2.20	2.00	2.20	2.20
Q1 : Q3	1.60 : 2.60	1.80 : 2.40	1.80 : 2.60	1.60 : 2.80
Min : Max	0.0 : 4.4	0.6 : 3.8	0.2 : 5.0	0.0 : 5.6

[a]Derived from MMRM model with change from baseline in ACQ-5-IA values up to Week 52 as the response variable, and treatment, baseline weight group, region, age, baseline eosinophil level, baseline FeNO level, baseline ICS dose level, visit, treatment by-visit interaction, baseline ACQ-5-IA value and baseline-by-visit interaction as covariates.

[b]Similar model as that mentioned in the footnote [a] with subgroup and subgroup-by-treatment interaction as additional covariates.

Type 2 inflammatory asthma phenotype population is defined as the randomized patients with baseline blood eosinophils >= 0.15 Giga/L or baseline FeNO >= 20 ppb.

PGM=DEVOPS/SAR231893/EFC14153/CSR_RWE/REPORT/PGM/eff_mmrm_ger_subg_i_t.sas OUT=REPORT/OUTPUT/eff_mmrm_acq5_ger_igem_i_t_x.rtf (21JUL2021 - 10:43)

Project Code / Study Number / Analysis: SAR231893 / EFC14153 / CSR_RWE

3 ACQ-5-IA - ITT type 2 inflammatory asthma phenotype population

3.1 Summary of treatment effect on change from baseline at Week 52

3.1.10 By baseline total IgE (<median, >= median)

	Baseline Total IgE (IU/mL)			
	<median		>=median	
ACQ-5-IA	**Placebo (N=66)**	**Dupilumab (N=105)**	**Placebo (N=47)**	**Dupilumab (N=125)**
Week 52				
Value				
Number	65	101	44	118
Mean (SD)	0.79 (0.93)	0.39 (0.64)	0.86 (0.98)	0.41 (0.65)
Median	0.40	0.00	0.60	0.00
Q1 : Q3	0.00 : 1.00	0.00 : 0.60	0.20 : 1.20	0.00 : 0.40
Min : Max	0.0 : 4.6	0.0 : 4.0	0.0 : 4.8	0.0 : 3.2
Change from baseline				
Number	65	101	44	118
LS Mean (SE)[a]	-1.31 (0.09)	-1.62 (0.08)	-1.24 (0.12)	-1.71 (0.09)
LS Mean Diff (95% CI)[a]	-	-0.31 (-0.53 to -0.09)	-	-0.47 (-0.72 to -0.22)
p-value[a]		0.005		<0.001
Hedges'g (95% CI)	-	-0.457 (-0.776 to -0.138)	-	-0.657 (-1.006 to -0.308)
p-value for heterogeneity[b]				0.500

[a]Derived from MMRM model with change from baseline in ACQ-5-IA values up to Week 52 as the response variable, and treatment, baseline weight group, region, age, baseline eosinophil level, baseline FeNO level, baseline ICS dose level, visit, treatment by-visit interaction, baseline ACQ-5-IA value and baseline-by-visit interaction as covariates.

[b]Similar model as that mentioned in the footnote [a] with subgroup and subgroup-by-treatment interaction as additional covariates.

Type 2 inflammatory asthma phenotype population is defined as the randomized patients with baseline blood eosinophils >= 0.15 Giga/L or baseline FeNO >= 20 ppb.

PGM=DEVOPS/SAR231893/EFC14153/CSR_RWE/REPORT/PGM/eff_mmrm_ger_subg_i_t.sas OUT=REPORT/OUTPUT/eff_mmrm_acq5_ger_igem_i_t_x.rtf (21JUL2021 - 10:43)

Project Code / Study Number / Analysis: SAR231893 / EFC14153 / CSR_RWE

3 ACQ-5-IA - ITT type 2 inflammatory asthma phenotype population

3.1 Summary of treatment effect on change from baseline at Week 52

3.1.11 By baseline total IgE (<100 IU/ml, >= 100 IU/ml)

	Baseline Total IgE (IU/mL)			
	< 100		>= 100	
ACQ-5-IA	**Placebo (N=22)**	**Dupilumab (N=29)**	**Placebo (N=91)**	**Dupilumab (N=201)**
Baseline				
Value				
Number	22	29	91	201
Mean (SD)	1.98 (0.82)	2.12 (0.45)	2.17 (0.84)	2.19 (0.83)
Median	2.00	2.00	2.20	2.20
Q1 : Q3	1.40 : 2.40	1.80 : 2.40	1.60 : 2.60	1.60 : 2.60
Min : Max	0.0 : 4.0	1.2 : 3.0	0.2 : 5.0	0.0 : 5.6

[a]Derived from MMRM model with change from baseline in ACQ-5-IA values up to Week 52 as the response variable, and treatment, baseline weight group, region, age, baseline eosinophil level, baseline FeNO level, baseline ICS dose level, visit, treatment by-visit interaction, baseline ACQ-5-IA value and baseline-by-visit interaction as covariates.

[b]Similar model as that mentioned in the footnote [a] with subgroup and subgroup-by-treatment interaction as additional covariates.

Type 2 inflammatory asthma phenotype population is defined as the randomized patients with baseline blood eosinophils >= 0.15 Giga/L or baseline FeNO >= 20 ppb.

PGM=DEVOPS/SAR231893/EFC14153/CSR_RWE/REPORT/PGM/eff_mmrm_ger_subg_i_t.sas OUT=REPORT/OUTPUT/eff_mmrm_acq5_ger_ige_i_t_x.rtf (21JUL2021 - 10:57)

Project Code / Study Number / Analysis: SAR231893 / EFC14153 / CSR_RWE

3 ACQ-5-IA - ITT type 2 inflammatory asthma phenotype population

3.1 Summary of treatment effect on change from baseline at Week 52

3.1.11 By baseline total IgE (<100 IU/ml, >= 100 IU/ml)

	Baseline Total IgE (IU/mL)			
	< 100		>= 100	
ACQ-5-IA	**Placebo (N=22)**	**Dupilumab (N=29)**	**Placebo (N=91)**	**Dupilumab (N=201)**
Week 52				
Value				
Number	22	29	87	190
Mean (SD)	0.69 (0.68)	0.51 (0.90)	0.85 (1.00)	0.38 (0.60)
Median	0.70	0.00	0.60	0.00
Q1 : Q3	0.00 : 1.00	0.00 : 0.60	0.20 : 1.20	0.00 : 0.40
Min : Max	0.0 : 2.0	0.0 : 4.0	0.0 : 4.8	0.0 : 3.2
Change from baseline				
Number	22	29	87	190
LS Mean (SE)[a]	-1.23 (0.21)	-1.26 (0.21)	-1.34 (0.08)	-1.77 (0.06)
LS Mean Diff (95% CI)[a]	-	-0.02 (-0.49 to 0.45)	-	-0.43 (-0.60 to -0.26)
p-value[a]		0.924		<0.001
Hedges'g (95% CI)	-	-0.028 (-0.622 to 0.565)	-	-0.641 (-0.899 to -0.383)
p-value for heterogeneity[b]				0.181

[a]Derived from MMRM model with change from baseline in ACQ-5-IA values up to Week 52 as the response variable, and treatment, baseline weight group, region, age, baseline eosinophil level, baseline FeNO level, baseline ICS dose level, visit, treatment by-visit interaction, baseline ACQ-5-IA value and baseline-by-visit interaction as covariates.

[b]Similar model as that mentioned in the footnote [a] with subgroup and subgroup-by-treatment interaction as additional covariates.

Type 2 inflammatory asthma phenotype population is defined as the randomized patients with baseline blood eosinophils >= 0.15 Giga/L or baseline FeNO >= 20 ppb.

PGM=DEVOPS/SAR231893/EFC14153/CSR_RWE/REPORT/PGM/eff_mmrm_ger_subg_i_t.sas OUT=REPORT/OUTPUT/eff_mmrm_acq5_ger_ige_i_t_x.rtf (21JUL2021 - 10:57)

Project Code / Study Number / Analysis: SAR231893 / EFC14153 / CSR_RWE

3 ACQ-5-IA - ITT type 2 inflammatory asthma phenotype population

3.1 Summary of treatment effect on change from baseline at Week 52

3.1.12 By age at onset of asthma (0-2, 3-5, >=6 years)

	Age of onset of asthma (years)					
	0-2		3-5		>= 6	
ACQ-5-IA	Placebo (N=40)	Dupilumab (N=105)	Placebo (N=39)	Dupilumab (N=86)	Placebo (N=35)	Dupilumab (N=45)
Baseline						
Value						
Number	40	105	39	86	35	45
Mean (SD)	2.20 (0.83)	2.20 (0.81)	2.17 (0.77)	2.17 (0.80)	2.06 (0.95)	2.12 (0.75)
Median	2.20	2.20	2.40	2.00	1.80	2.20
Q1 : Q3	1.60 : 2.60	1.80 : 2.60	1.80 : 2.80	1.60 : 2.80	1.60 : 2.40	1.60 : 2.60
Min : Max	0.2 : 4.4	0.6 : 5.6	0.2 : 3.4	0.0 : 4.8	0.0 : 5.0	0.4 : 3.8

[a]Derived from MMRM model with change from baseline in ACQ-5-IA values up to Week 52 as the response variable, and treatment, baseline weight group, region, age, baseline eosinophil level, baseline FeNO level, baseline ICS dose level, visit, treatment by-visit interaction, baseline ACQ-5-IA value and baseline-by-visit interaction as covariates.

[b]Similar model as that mentioned in the footnote [a] with subgroup and subgroup-by-treatment interaction as additional covariates.

Type 2 inflammatory asthma phenotype population is defined as the randomized patients with baseline blood eosinophils >= 0.15 Giga/L or baseline FeNO >= 20 ppb.

PGM=DEVOPS/SAR231893/EFC14153/CSR_RWE/REPORT/PGM/eff_mmrm_ger_subg_i_t.sas OUT=REPORT/OUTPUT/eff_mmrm_acq5_ger_onsa_i_t_x.rtf (10AUG2021 - 8:54)

Project Code / Study Number / Analysis: SAR231893 / EFC14153 / CSR_RWE

3 ACQ-5-IA - ITT type 2 inflammatory asthma phenotype population

3.1 Summary of treatment effect on change from baseline at Week 52

3.1.12 By age at onset of asthma (0-2, 3-5, >=6 years)

	Age of onset of asthma (years)					
	0-2		3-5		>= 6	
ACQ-5-IA	**Placebo (N=40)**	**Dupilumab (N=105)**	**Placebo (N=39)**	**Dupilumab (N=86)**	**Placebo (N=35)**	**Dupilumab (N=45)**
Week 52						
Value						
Number	38	99	37	80	35	43
Mean (SD)	0.92 (1.02)	0.37 (0.50)	0.65 (0.87)	0.48 (0.83)	0.91 (0.94)	0.30 (0.50)
Median	0.60	0.20	0.60	0.00	0.60	0.00
Q1 : Q3	0.20 : 1.40	0.00 : 0.60	0.00 : 0.80	0.00 : 0.60	0.00 : 1.60	0.00 : 0.40
Min : Max	0.0 : 4.6	0.0 : 2.0	0.0 : 4.8	0.0 : 4.0	0.0 : 3.6	0.0 : 1.6
Change from baseline						
Number	38	99	37	80	35	43
LS Mean (SE)[a]	-1.26 (0.10)	-1.72 (0.07)	-1.33 (0.13)	-1.50 (0.09)	-1.24 (0.15)	-1.78 (0.14)
LS Mean Diff (95% CI)[a]	-	-0.46 (-0.68 to -0.24)	-	-0.17 (-0.46 to 0.12)	-	-0.54 (-0.88 to -0.19)
p-value[a]		<0.001		0.256		0.003

[a]Derived from MMRM model with change from baseline in ACQ-5-IA values up to Week 52 as the response variable, and treatment, baseline weight group, region, age, baseline eosinophil level, baseline FeNO level, baseline ICS dose level, visit, treatment by-visit interaction, baseline ACQ-5-IA value and baseline-by-visit interaction as covariates.

[b]Similar model as that mentioned in the footnote [a] with subgroup and subgroup-by-treatment interaction as additional covariates.

Type 2 inflammatory asthma phenotype population is defined as the randomized patients with baseline blood eosinophils >= 0.15 Giga/L or baseline FeNO >= 20 ppb.

PGM=DEVOPS/SAR231893/EFC14153/CSR_RWE/REPORT/PGM/eff_mmrm_ger_subg_i_t.sas OUT=REPORT/OUTPUT/eff_mmrm_acq5_ger_onsa_i_t_x.rtf (10AUG2021 - 8:54)

Project Code / Study Number / Analysis: SAR231893 / EFC14153 / CSR_RWE

3 ACQ-5-IA - ITT type 2 inflammatory asthma phenotype population

3.1 Summary of treatment effect on change from baseline at Week 52

3.1.12 By age at onset of asthma (0-2, 3-5, >=6 years)

	Age of onset of asthma (years)					
	0-2		3-5		>= 6	
ACQ-5-IA	**Placebo (N=40)**	**Dupilumab (N=105)**	**Placebo (N=39)**	**Dupilumab (N=86)**	**Placebo (N=35)**	**Dupilumab (N=45)**
Hedges'g (95% CI)	-	-0.790 (-1.171 to -0.408)	-	-0.227 (-0.621 to 0.167)	-	-0.729 (-1.196 to -0.263)
p-value for heterogeneity[b]:						
0-2, 3-5						0.075
0-2, >= 6						0.773
3-5, >= 6						0.059
overall						0.101

[a]Derived from MMRM model with change from baseline in ACQ-5-IA values up to Week 52 as the response variable, and treatment, baseline weight group, region, age, baseline eosinophil level, baseline FeNO level, baseline ICS dose level, visit, treatment by-visit interaction, baseline ACQ-5-IA value and baseline-by-visit interaction as covariates.

[b]Similar model as that mentioned in the footnote [a] with subgroup and subgroup-by-treatment interaction as additional covariates.

Type 2 inflammatory asthma phenotype population is defined as the randomized patients with baseline blood eosinophils >= 0.15 Giga/L or baseline FeNO >= 20 ppb.

PGM=DEVOPS/SAR231893/EFC14153/CSR_RWE/REPORT/PGM/eff_mmrm_ger_subg_i_t.sas OUT=REPORT/OUTPUT/eff_mmrm_acq5_ger_onsa_i_t_x.rtf (10AUG2021 - 8:54)

Project Code / Study Number / Analysis: SAR231893 / EFC14153 / CSR_RWE

3 ACQ-5-IA - ITT type 2 inflammatory asthma phenotype population

3.1 Summary of treatment effect on change from baseline at Week 52

3.1.13 By number of severe asthma exacerbation prior to the study (<=1, 2, >2)

	Number of severe asthma exacerbation prior to the study					
	<=1		2		>2	
ACQ-5-IA	**Placebo (N=47)**	**Dupilumab (N=85)**	**Placebo (N=32)**	**Dupilumab (N=75)**	**Placebo (N=35)**	**Dupilumab (N=76)**
Baseline						
Value						
Number	47	85	32	75	35	76
Mean (SD)	2.08 (0.78)	2.08 (0.78)	2.03 (0.90)	2.21 (0.79)	2.34 (0.86)	2.25 (0.81)
Median	2.20	2.00	2.00	2.00	2.40	2.20
Q1 : Q3	1.60 : 2.60	1.60 : 2.44	1.40 : 2.40	1.80 : 2.80	1.80 : 2.80	1.80 : 2.80
Min : Max	0.0 : 4.0	0.0 : 4.8	0.2 : 5.0	0.4 : 4.4	0.4 : 4.4	0.6 : 5.6

[a]Derived from MMRM model with change from baseline in ACQ-5-IA values up to Week 52 as the response variable, and treatment, baseline weight group, region, age, baseline eosinophil level, baseline FeNO level, baseline ICS dose level, visit, treatment by-visit interaction, baseline ACQ-5-IA value and baseline-by-visit interaction as covariates.
[b]Similar model as that mentioned in the footnote [a] with subgroup and subgroup-by-treatment interaction as additional covariates.
Type 2 inflammatory asthma phenotype population is defined as the randomized patients with baseline blood eosinophils >= 0.15 Giga/L or baseline FeNO >= 20 ppb.
PGM=DEVOPS/SAR231893/EFC14153/CSR_RWE/REPORT/PGM/eff_mmrm_ger_subg_i_t.sas OUT=REPORT/OUTPUT/eff_mmrm_acq5_ger_exa_i_t_x.rtf (21JUL2021 - 11:35)

Project Code / Study Number / Analysis: SAR231893 / EFC14153 / CSR_RWE

3 ACQ-5-IA - ITT type 2 inflammatory asthma phenotype population

3.1 Summary of treatment effect on change from baseline at Week 52

3.1.13 By number of severe asthma exacerbation prior to the study (<=1, 2, >2)

	Number of severe asthma exacerbation prior to the study					
	<=1		2		>2	
ACQ-5-IA	**Placebo (N=47)**	**Dupilumab (N=85)**	**Placebo (N=32)**	**Dupilumab (N=75)**	**Placebo (N=35)**	**Dupilumab (N=76)**
Week 52						
Value						
Number	45	81	32	71	33	70
Mean (SD)	0.60 (0.68)	0.46 (0.67)	0.74 (0.74)	0.31 (0.55)	1.22 (1.27)	0.41 (0.69)
Median	0.40	0.20	0.60	0.00	0.80	0.10
Q1 : Q3	0.00 : 0.80	0.00 : 0.60	0.00 : 1.20	0.00 : 0.40	0.40 : 1.60	0.00 : 0.60
Min : Max	0.0 : 2.4	0.0 : 3.2	0.0 : 2.4	0.0 : 2.0	0.0 : 4.8	0.0 : 4.0
Change from baseline						
Number	45	81	32	71	33	70
LS Mean (SE)[a]	-1.43 (0.11)	-1.68 (0.08)	-1.34 (0.11)	-1.62 (0.09)	-1.18 (0.16)	-1.81 (0.12)
LS Mean Diff (95% CI)[a]	-	-0.25 (-0.49 to -0.01)	-	-0.28 (-0.53 to -0.03)	-	-0.62 (-0.98 to -0.27)
p-value[a]		0.043		0.030		<0.001

[a]Derived from MMRM model with change from baseline in ACQ-5-IA values up to Week 52 as the response variable, and treatment, baseline weight group, region, age, baseline eosinophil level, baseline FeNO level, baseline ICS dose level, visit, treatment by-visit interaction, baseline ACQ-5-IA value and baseline-by-visit interaction as covariates.
[b]Similar model as that mentioned in the footnote [a] with subgroup and subgroup-by-treatment interaction as additional covariates.
Type 2 inflammatory asthma phenotype population is defined as the randomized patients with baseline blood eosinophils >= 0.15 Giga/L or baseline FeNO >= 20 ppb.
PGM=DEVOPS/SAR231893/EFC14153/CSR_RWE/REPORT/PGM/eff_mmrm_ger_subg_i_t.sas OUT=REPORT/OUTPUT/eff_mmrm_acq5_ger_exa_i_t_x.rtf (21JUL2021 - 11:35)

Project Code / Study Number / Analysis: SAR231893 / EFC14153 / CSR_RWE

3 ACQ-5-IA - ITT type 2 inflammatory asthma phenotype population

3.1 Summary of treatment effect on change from baseline at Week 52

3.1.13 By number of severe asthma exacerbation prior to the study (<=1, 2, >2)

	Number of severe asthma exacerbation prior to the study					
	<=1		2		>2	
ACQ-5-IA	**Placebo (N=47)**	**Dupilumab (N=85)**	**Placebo (N=32)**	**Dupilumab (N=75)**	**Placebo (N=35)**	**Dupilumab (N=76)**
Hedges'g (95% CI)	-	-0.386 (-0.759 to -0.012)	-	-0.490 (-0.931 to -0.050)	-	-0.750 (-1.180 to -0.320)
p-value for heterogeneity[b]:						
<=1, 2						0.458
<=1, >2						0.057
2, >2						0.280
overall						0.162

[a]Derived from MMRM model with change from baseline in ACQ-5-IA values up to Week 52 as the response variable, and treatment, baseline weight group, region, age, baseline eosinophil level, baseline FeNO level, baseline ICS dose level, visit, treatment by-visit interaction, baseline ACQ-5-IA value and baseline-by-visit interaction as covariates.

[b]Similar model as that mentioned in the footnote [a] with subgroup and subgroup-by-treatment interaction as additional covariates.

Type 2 inflammatory asthma phenotype population is defined as the randomized patients with baseline blood eosinophils >= 0.15 Giga/L or baseline FeNO >= 20 ppb.

PGM=DEVOPS/SAR231893/EFC14153/CSR_RWE/REPORT/PGM/eff_mmrm_ger_subg_i_t.sas OUT=REPORT/OUTPUT/eff_mmrm_acq5_ger_exa_i_t_x.rtf (21JUL2021 - 11:35)

Project Code / Study Number / Analysis: SAR231893 / EFC14153 / CSR_RWE

4 AM Asthma symptom score - ITT type 2 inflammatory asthma phenotype population

4.1 Summary of treatment effect on change from baseline at Week 52

AM symptom score	Placebo (N=114)	Dupilumab (N=236)
Baseline		
Value		
Number	114	236
Mean (SD)	0.90 (0.72)	0.90 (0.78)
Median	0.86	0.86
Q1 : Q3	0.29 : 1.43	0.17 : 1.33
Min : Max	0.0 : 2.7	0.0 : 3.0
Week 52		
Value		
Number	111	222
Mean (SD)	0.40 (0.58)	0.30 (0.55)
Median	0.05	0.00
Q1 : Q3	0.00 : 0.87	0.00 : 0.41
Min : Max	0.0 : 3.0	0.0 : 3.0
Change from baseline		
Number	111	222
LS Mean (SE)[a]	-0.50 (0.05)	-0.61 (0.04)

[a]Derived from MMRM model with change from baseline in AM Asthma symptom score values up to Week 52 as the response variable, and treatment, baseline weight group, region, age, baseline eosinophil level, baseline FeNO level, baseline ICS dose level, visit, treatment by-visit interaction, baseline AM Asthma symptom score value and baseline-by-visit interaction as covariates.

Type 2 inflammatory asthma phenotype population is defined as the randomized patients with baseline blood eosinophils >= 0.15 Giga/L or baseline FeNO >= 20 ppb.

PGM=DEVOPS/SAR231893/EFC14153/CSR_RWE/REPORT/PGM/eff_mmrm_ger_i_t.sas OUT=REPORT/OUTPUT/eff_mmrm_scam_ger_i_t_x.rtf (22JUL2021 - 7:51)

Project Code / Study Number / Analysis: SAR231893 / EFC14153 / CSR_RWE

4 AM Asthma symptom score - ITT type 2 inflammatory asthma phenotype population

4.1 Summary of treatment effect on change from baseline at Week 52

AM symptom score	**Placebo (N=114)**	**Dupilumab (N=236)**
LS Mean Diff (95% CI)[a]	-	-0.12 (-0.23 to 0.00)
Hedges'g (95% CI)	-	-0.223 (-0.453 to 0.008)
p-value[a]		0.058

[a]Derived from MMRM model with change from baseline in AM Asthma symptom score values up to Week 52 as the response variable, and treatment, baseline weight group, region, age, baseline eosinophil level, baseline FeNO level, baseline ICS dose level, visit, treatment by-visit interaction, baseline AM Asthma symptom score value and baseline-by-visit interaction as covariates.

Type 2 inflammatory asthma phenotype population is defined as the randomized patients with baseline blood eosinophils >= 0.15 Giga/L or baseline FeNO >= 20 ppb.

PGM=DEVOPS/SAR231893/EFC14153/CSR_RWE/REPORT/PGM/eff_mmrm_ger_i_t.sas OUT=REPORT/OUTPUT/eff_mmrm_scam_ger_i_t_x.rtf (22JUL2021 - 7:51)

Project Code / Study Number / Analysis: SAR231893 / EFC14153 / CSR_RWE

4 AM Asthma symptom score - ITT type 2 inflammatory asthma phenotype population

4.1 Summary of treatment effect on change from baseline at Week 52

4.1.1 By gender (Male, Female)

	Gender			
	Male		Female	
AM symptom score	**Placebo (N=78)**	**Dupilumab (N=152)**	**Placebo (N=36)**	**Dupilumab (N=84)**
Baseline				
Value				
Number	78	152	36	84
Mean (SD)	0.93 (0.73)	0.89 (0.78)	0.84 (0.70)	0.90 (0.79)
Median	0.93	0.86	0.69	0.86
Q1 : Q3	0.29 : 1.57	0.17 : 1.33	0.23 : 1.38	0.17 : 1.29
Min : Max	0.0 : 2.7	0.0 : 3.0	0.0 : 2.3	0.0 : 3.0

[a]Derived from MMRM model with change from baseline in AM Asthma symptom score values up to Week 52 as the response variable, and treatment, baseline weight group, region, age, baseline eosinophil level, baseline FeNO level, baseline ICS dose level, visit, treatment by-visit interaction, baseline AM Asthma symptom score value and baseline-by-visit interaction as covariates.

[b]Similar model as that mentioned in the footnote [a] with subgroup and subgroup-by-treatment interaction as additional covariates.

Type 2 inflammatory asthma phenotype population is defined as the randomized patients with baseline blood eosinophils >= 0.15 Giga/L or baseline FeNO >= 20 ppb.

PGM=DEVOPS/SAR231893/EFC14153/CSR_RWE/REPORT/PGM/eff_mmrm_ger_subg_i_t.sas OUT=REPORT/OUTPUT/eff_mmrm_scam_ger_sex_i_t_x.rtf (21JUL2021 - 8:43)

Project Code / Study Number / Analysis: SAR231893 / EFC14153 / CSR_RWE

4 AM Asthma symptom score - ITT type 2 inflammatory asthma phenotype population

4.1 Summary of treatment effect on change from baseline at Week 52

4.1.1 By gender (Male, Female)

	Gender			
	Male		Female	
AM symptom score	**Placebo (N=78)**	**Dupilumab (N=152)**	**Placebo (N=36)**	**Dupilumab (N=84)**
Week 52				
Value				
Number	76	143	35	79
Mean (SD)	0.49 (0.63)	0.29 (0.52)	0.20 (0.39)	0.32 (0.59)
Median	0.19	0.00	0.00	0.00
Q1 : Q3	0.00 : 1.00	0.00 : 0.38	0.00 : 0.18	0.00 : 0.46
Min : Max	0.0 : 3.0	0.0 : 2.0	0.0 : 1.4	0.0 : 3.0
Change from baseline				
Number	76	143	35	79
LS Mean (SE)[a]	-0.43 (0.06)	-0.62 (0.05)	-0.66 (0.09)	-0.58 (0.07)
LS Mean Diff (95% CI)[a]	-	-0.19 (-0.33 to -0.05)	-	0.08 (-0.13 to 0.30)
p-value[a]		0.008		0.460
Hedges'g (95% CI)	-	-0.388 (-0.673 to -0.104)	-	0.150 (-0.250 to 0.550)
p-value for heterogeneity[b]				0.039

[a]Derived from MMRM model with change from baseline in AM Asthma symptom score values up to Week 52 as the response variable, and treatment, baseline weight group, region, age, baseline eosinophil level, baseline FeNO level, baseline ICS dose level, visit, treatment by-visit interaction, baseline AM Asthma symptom score value and baseline-by-visit interaction as covariates.

[b]Similar model as that mentioned in the footnote [a] with subgroup and subgroup-by-treatment interaction as additional covariates.

Type 2 inflammatory asthma phenotype population is defined as the randomized patients with baseline blood eosinophils >= 0.15 Giga/L or baseline FeNO >= 20 ppb.

PGM=DEVOPS/SAR231893/EFC14153/CSR_RWE/REPORT/PGM/eff_mmrm_ger_subg_i_t.sas OUT=REPORT/OUTPUT/eff_mmrm_scam_ger_sex_i_t_x.rtf (21JUL2021 - 8:43)

Project Code / Study Number / Analysis: SAR231893 / EFC14153 / CSR_RWE

4 AM Asthma symptom score - ITT type 2 inflammatory asthma phenotype population

4.1 Summary of treatment effect on change from baseline at Week 52

4.1.2 By region (Latin America, East Europe, Western Countries)

	Region					
	Latin America		East Europe		Western countries	
AM symptom score	**Placebo (N=51)**	**Dupilumab (N=106)**	**Placebo (N=43)**	**Dupilumab (N=78)**	**Placebo (N=20)**	**Dupilumab (N=52)**
Baseline						
Value						
Number	51	106	43	78	20	52
Mean (SD)	0.82 (0.65)	0.93 (0.84)	0.99 (0.75)	0.93 (0.79)	0.93 (0.86)	0.76 (0.65)
Median	0.71	0.93	1.00	0.86	0.83	0.73
Q1 : Q3	0.17 : 1.29	0.17 : 1.29	0.40 : 1.67	0.29 : 1.43	0.15 : 1.63	0.17 : 1.21
Min : Max	0.0 : 2.0	0.0 : 3.0	0.0 : 2.6	0.0 : 3.0	0.0 : 2.7	0.0 : 2.2

[a]Derived from MMRM model with change from baseline in AM Asthma symptom score values up to Week 52 as the response variable, and treatment, baseline weight group, age, baseline eosinophil level, baseline FeNO level, baseline ICS dose level, visit, treatment by-visit interaction, baseline AM Asthma symptom score value and baseline-by-visit interaction as covariates.
[b]Similar model as that mentioned in the footnote [a] with subgroup and subgroup-by-treatment interaction as additional covariates.
Type 2 inflammatory asthma phenotype population is defined as the randomized patients with baseline blood eosinophils >= 0.15 Giga/L or baseline FeNO >= 20 ppb.
PGM=DEVOPS/SAR231893/EFC14153/CSR_RWE/REPORT/PGM/eff_mmrm_ger_subg_i_t.sas OUT=REPORT/OUTPUT/eff_mmrm_scam_ger_cty_i_t_x.rtf (21JUL2021 - 9:02)

Project Code / Study Number / Analysis: SAR231893 / EFC14153 / CSR_RWE

4 AM Asthma symptom score - ITT type 2 inflammatory asthma phenotype population

4.1 Summary of treatment effect on change from baseline at Week 52

4.1.2 By region (Latin America, East Europe, Western Countries)

	Region					
	Latin America		East Europe		Western countries	
AM symptom score	**Placebo (N=51)**	**Dupilumab (N=106)**	**Placebo (N=43)**	**Dupilumab (N=78)**	**Placebo (N=20)**	**Dupilumab (N=52)**
Week 52						
Value						
Number	51	102	42	77	18	43
Mean (SD)	0.33 (0.48)	0.30 (0.57)	0.53 (0.71)	0.36 (0.51)	0.32 (0.44)	0.19 (0.55)
Median	0.00	0.00	0.18	0.04	0.07	0.00
Q1 : Q3	0.00 : 0.86	0.00 : 0.38	0.00 : 1.00	0.00 : 0.85	0.00 : 0.65	0.00 : 0.00
Min : Max	0.0 : 2.0	0.0 : 3.0	0.0 : 3.0	0.0 : 2.0	0.0 : 1.2	0.0 : 3.0
Change from baseline						
Number	51	102	42	77	18	43
LS Mean (SE)[a]	-0.58 (0.07)	-0.62 (0.05)	-0.42 (0.09)	-0.56 (0.07)	-0.41 (0.15)	-0.63 (0.09)
LS Mean Diff (95% CI)[a]	-	-0.03 (-0.20 to 0.13)	-	-0.14 (-0.34 to 0.06)	-	-0.22 (-0.54 to 0.11)
p-value[a]		0.682		0.169		0.190

[a]Derived from MMRM model with change from baseline in AM Asthma symptom score values up to Week 52 as the response variable, and treatment, baseline weight group, age, baseline eosinophil level, baseline FeNO level, baseline ICS dose level, visit, treatment by-visit interaction, baseline AM Asthma symptom score value and baseline-by-visit interaction as covariates.

[b]Similar model as that mentioned in the footnote [a] with subgroup and subgroup-by-treatment interaction as additional covariates.

Type 2 inflammatory asthma phenotype population is defined as the randomized patients with baseline blood eosinophils >= 0.15 Giga/L or baseline FeNO >= 20 ppb.

PGM=DEVOPS/SAR231893/EFC14153/CSR_RWE/REPORT/PGM/eff_mmrm_ger_subg_i_t.sas OUT=REPORT/OUTPUT/eff_mmrm_scam_ger_cty_i_t_x.rtf (21JUL2021 - 9:02)

Project Code / Study Number / Analysis: SAR231893 / EFC14153 / CSR_RWE

4 AM Asthma symptom score - ITT type 2 inflammatory asthma phenotype population

4.1 Summary of treatment effect on change from baseline at Week 52

4.1.2 By region (Latin America, East Europe, Western Countries)

	Region					
	Latin America		East Europe		Western countries	
AM symptom score	**Placebo (N=51)**	**Dupilumab (N=106)**	**Placebo (N=43)**	**Dupilumab (N=78)**	**Placebo (N=20)**	**Dupilumab (N=52)**
Hedges'g (95% CI)	-	-0.072 (-0.419 to 0.275)	-	-0.264 (-0.641 to 0.114)	-	-0.368 (-0.924 to 0.188)
p-value for heterogeneity[b]:						
Latin America, East Europe						0.440
Latin America, Western countries						0.707
East Europe, Western countries						0.321
overall						0.554

[a]Derived from MMRM model with change from baseline in AM Asthma symptom score values up to Week 52 as the response variable, and treatment, baseline weight group, age, baseline eosinophil level, baseline FeNO level, baseline ICS dose level, visit, treatment by-visit interaction, baseline AM Asthma symptom score value and baseline-by-visit interaction as covariates.

[b]Similar model as that mentioned in the footnote [a] with subgroup and subgroup-by-treatment interaction as additional covariates.

Type 2 inflammatory asthma phenotype population is defined as the randomized patients with baseline blood eosinophils >= 0.15 Giga/L or baseline FeNO >= 20 ppb.

PGM=DEVOPS/SAR231893/EFC14153/CSR_RWE/REPORT/PGM/eff_mmrm_ger_subg_i_t.sas OUT=REPORT/OUTPUT/eff_mmrm_scam_ger_cty_i_t_x.rtf (21JUL2021 - 9:02)

Project Code / Study Number / Analysis: SAR231893 / EFC14153 / CSR_RWE

4 AM Asthma symptom score - ITT type 2 inflammatory asthma phenotype population

4.1 Summary of treatment effect on change from baseline at Week 52

4.1.3 By race (Caucasian/white, Black/of African descent, Other)

	Race					
	Caucasian/White		Black/of African descent		Other	
AM symptom score	**Placebo (N=102)**	**Dupilumab (N=208)**	**Placebo (N=5)**	**Dupilumab (N=9)**	**Placebo (N=7)**	**Dupilumab (N=19)**
Baseline						
Value						
Number	102	208	5	9	7	19
Mean (SD)	0.92 (0.72)	0.92 (0.80)	0.98 (1.11)	1.18 (0.81)	0.62 (0.32)	0.52 (0.46)
Median	0.93	0.86	0.57	1.14	0.71	0.57
Q1 : Q3	0.29 : 1.50	0.17 : 1.38	0.00 : 2.00	0.43 : 2.00	0.29 : 0.86	0.00 : 1.00
Min : Max	0.0 : 2.7	0.0 : 3.0	0.0 : 2.3	0.0 : 2.2	0.1 : 1.0	0.0 : 1.3

[a]Derived from MMRM model with change from baseline in AM Asthma symptom score values up to Week 52 as the response variable, and treatment, baseline weight group, region, age, baseline eosinophil level, baseline FeNO level, baseline ICS dose level, visit, treatment by-visit interaction, baseline AM Asthma symptom score value and baseline-by-visit interaction as covariates.

[b]Similar model as that mentioned in the footnote [a] with subgroup and subgroup-by-treatment interaction as additional covariates.

Type 2 inflammatory asthma phenotype population is defined as the randomized patients with baseline blood eosinophils >= 0.15 Giga/L or baseline FeNO >= 20 ppb.

PGM=DEVOPS/SAR231893/EFC14153/CSR_RWE/REPORT/PGM/eff_mmrm_ger_subg_i_t.sas OUT=REPORT/OUTPUT/eff_mmrm_scam_ger_race_i_t_x.rtf (21JUL2021 - 9:22)

Project Code / Study Number / Analysis: SAR231893 / EFC14153 / CSR_RWE

4 AM Asthma symptom score - ITT type 2 inflammatory asthma phenotype population

4.1 Summary of treatment effect on change from baseline at Week 52

4.1.3 By race (Caucasian/white, Black/of African descent, Other)

	Race					
	Caucasian/White		Black/of African descent		Other	
AM symptom score	**Placebo (N=102)**	**Dupilumab (N=208)**	**Placebo (N=5)**	**Dupilumab (N=9)**	**Placebo (N=7)**	**Dupilumab (N=19)**
Week 52						
Value						
Number	101	198	3	8	7	16
Mean (SD)	0.40 (0.59)	0.32 (0.56)	0.02 (0.04)	0.31 (0.56)	0.64 (0.50)	0.03 (0.09)
Median	0.04	0.00	0.00	0.07	0.67	0.00
Q1 : Q3	0.00 : 0.86	0.00 : 0.46	0.00 : 0.06	0.00 : 0.34	0.00 : 1.08	0.00 : 0.00
Min : Max	0.0 : 3.0	0.0 : 3.0	0.0 : 0.1	0.0 : 1.6	0.0 : 1.2	0.0 : 0.3
Change from baseline						
Number	101	198	3	8	7	16
LS Mean (SE)[a]	-0.55 (0.06)	-0.63 (0.04)	-1.00 (0.56)	-0.93 (0.46)	0.27 (0.05)	-0.55 (0.05)
LS Mean Diff (95% CI)[a]	-	-0.09 (-0.21 to 0.04)	-	0.07 (-0.94 to 1.08)	-	-0.81 (-0.94 to -0.68)
p-value[a]		0.195		0.864		<0.001

[a]Derived from MMRM model with change from baseline in AM Asthma symptom score values up to Week 52 as the response variable, and treatment, baseline weight group, region, age, baseline eosinophil level, baseline FeNO level, baseline ICS dose level, visit, treatment by-visit interaction, baseline AM Asthma symptom score value and baseline-by-visit interaction as covariates.
[b]Similar model as that mentioned in the footnote [a] with subgroup and subgroup-by-treatment interaction as additional covariates.
Type 2 inflammatory asthma phenotype population is defined as the randomized patients with baseline blood eosinophils >= 0.15 Giga/L or baseline FeNO >= 20 ppb.
PGM=DEVOPS/SAR231893/EFC14153/CSR_RWE/REPORT/PGM/eff_mmrm_ger_subg_i_t.sas OUT=REPORT/OUTPUT/eff_mmrm_scam_ger_race_i_t_x.rtf (21JUL2021 - 9:22)

Project Code / Study Number / Analysis: SAR231893 / EFC14153 / CSR_RWE

4 AM Asthma symptom score - ITT type 2 inflammatory asthma phenotype population

4.1 Summary of treatment effect on change from baseline at Week 52

4.1.3 By race (Caucasian/white, Black/of African descent, Other)

	Race					
	Caucasian/White		Black/of African descent		Other	
AM symptom score	**Placebo (N=102)**	**Dupilumab (N=208)**	**Placebo (N=5)**	**Dupilumab (N=9)**	**Placebo (N=7)**	**Dupilumab (N=19)**
Hedges'g (95% CI)	-	-0.160 (-0.404 to 0.083)	-	0.052 (-0.659 to 0.764)	-	-4.575 (-5.302 to -3.849)
p-value for heterogeneity[b]:						
Caucasian/White, Black/of African descent						0.934
Caucasian/White, Other						0.184
Black/of African descent, Other						0.047
overall						0.136

[a]Derived from MMRM model with change from baseline in AM Asthma symptom score values up to Week 52 as the response variable, and treatment, baseline weight group, region, age, baseline eosinophil level, baseline FeNO level, baseline ICS dose level, visit, treatment by-visit interaction, baseline AM Asthma symptom score value and baseline-by-visit interaction as covariates.

[b]Similar model as that mentioned in the footnote [a] with subgroup and subgroup-by-treatment interaction as additional covariates.

Type 2 inflammatory asthma phenotype population is defined as the randomized patients with baseline blood eosinophils >= 0.15 Giga/L or baseline FeNO >= 20 ppb.

PGM=DEVOPS/SAR231893/EFC14153/CSR_RWE/REPORT/PGM/eff_mmrm_ger_subg_i_t.sas OUT=REPORT/OUTPUT/eff_mmrm_scam_ger_race_i_t_x.rtf (21JUL2021 - 9:22)

Project Code / Study Number / Analysis: SAR231893 / EFC14153 / CSR_RWE

4 AM Asthma symptom score - ITT type 2 inflammatory asthma phenotype population

4.1 Summary of treatment effect on change from baseline at Week 52

4.1.4 By baseline ICS dose level (Medium, High)

	Baseline ICS dose level			
	High		Medium	
AM symptom score	**Placebo (N=50)**	**Dupilumab (N=102)**	**Placebo (N=64)**	**Dupilumab (N=131)**
Baseline				
Value				
Number	50	102	64	131
Mean (SD)	0.98 (0.76)	0.90 (0.82)	0.84 (0.69)	0.90 (0.75)
Median	0.86	0.86	0.71	0.86
Q1 : Q3	0.29 : 1.67	0.14 : 1.43	0.24 : 1.23	0.29 : 1.29
Min : Max	0.0 : 2.7	0.0 : 3.0	0.0 : 2.6	0.0 : 3.0

[a]Derived from MMRM model with change from baseline in AM Asthma symptom score values up to Week 52 as the response variable, and treatment, baseline weight group, region, age, baseline eosinophil level, baseline FeNO level, visit, treatment by-visit interaction, baseline AM Asthma symptom score value and baseline-by-visit interaction as covariates.

[b]Similar model as that mentioned in the footnote [a] with subgroup and subgroup-by-treatment interaction as additional covariates.

Type 2 inflammatory asthma phenotype population is defined as the randomized patients with baseline blood eosinophils >= 0.15 Giga/L or baseline FeNO >= 20 ppb.

PGM=DEVOPS/SAR231893/EFC14153/CSR_RWE/REPORT/PGM/eff_mmrm_ger_subg_i_t.sas OUT=REPORT/OUTPUT/eff_mmrm_scam_ger_ics_i_t_x.rtf (21JUL2021 - 9:36)

Project Code / Study Number / Analysis: SAR231893 / EFC14153 / CSR_RWE

4 AM Asthma symptom score - ITT type 2 inflammatory asthma phenotype population

4.1 Summary of treatment effect on change from baseline at Week 52

4.1.4 By baseline ICS dose level (Medium, High)

	Baseline ICS dose level			
	High		Medium	
AM symptom score	**Placebo (N=50)**	**Dupilumab (N=102)**	**Placebo (N=64)**	**Dupilumab (N=131)**
Week 52				
Value				
Number	49	97	62	124
Mean (SD)	0.43 (0.51)	0.30 (0.58)	0.38 (0.63)	0.29 (0.50)
Median	0.07	0.00	0.04	0.00
Q1 : Q3	0.00 : 1.00	0.00 : 0.24	0.00 : 0.86	0.00 : 0.45
Min : Max	0.0 : 2.0	0.0 : 3.0	0.0 : 3.0	0.0 : 3.0
Change from baseline				
Number	49	97	62	124
LS Mean (SE)[a]	-0.46 (0.08)	-0.61 (0.06)	-0.50 (0.07)	-0.62 (0.05)
LS Mean Diff (95% CI)[a]	-	-0.15 (-0.33 to 0.03)	-	-0.12 (-0.28 to 0.04)
p-value[a]		0.100		0.148
Hedges'g (95% CI)	-	-0.294 (-0.645 to 0.057)	-	-0.228 (-0.538 to 0.081)
p-value for heterogeneity[b]				0.831

[a]Derived from MMRM model with change from baseline in AM Asthma symptom score values up to Week 52 as the response variable, and treatment, baseline weight group, region, age, baseline eosinophil level, baseline FeNO level, visit, treatment by-visit interaction, baseline AM Asthma symptom score value and baseline-by-visit interaction as covariates.

[b]Similar model as that mentioned in the footnote [a] with subgroup and subgroup-by-treatment interaction as additional covariates.

Type 2 inflammatory asthma phenotype population is defined as the randomized patients with baseline blood eosinophils >= 0.15 Giga/L or baseline FeNO >= 20 ppb.

PGM=DEVOPS/SAR231893/EFC14153/CSR_RWE/REPORT/PGM/eff_mmrm_ger_subg_i_t.sas OUT=REPORT/OUTPUT/eff_mmrm_scam_ger_ics_i_t_x.rtf (21JUL2021 - 9:36)

Project Code / Study Number / Analysis: SAR231893 / EFC14153 / CSR_RWE

4 AM Asthma symptom score - ITT type 2 inflammatory asthma phenotype population

4.1 Summary of treatment effect on change from baseline at Week 52

4.1.5 By baseline ICS dose level 2 (Medium, High)

	Baseline ICS dose level 2			
	High		Medium	
AM symptom score	**Placebo (N=95)**	**Dupilumab (N=200)**	**Placebo (N=19)**	**Dupilumab (N=36)**
Baseline				
Value				
Number	95	200	19	36
Mean (SD)	0.92 (0.71)	0.93 (0.80)	0.80 (0.78)	0.72 (0.69)
Median	0.86	0.86	0.71	0.54
Q1 : Q3	0.33 : 1.43	0.17 : 1.33	0.00 : 1.50	0.08 : 1.00
Min : Max	0.0 : 2.7	0.0 : 3.0	0.0 : 2.3	0.0 : 2.7

[a]Derived from MMRM model with change from baseline in AM Asthma symptom score values up to Week 52 as the response variable, and treatment, baseline weight group, region, age, baseline eosinophil level, baseline FeNO level, visit, treatment by-visit interaction, baseline AM Asthma symptom score value and baseline-by-visit interaction as covariates.

[b]Similar model as that mentioned in the footnote [a] with subgroup and subgroup-by-treatment interaction as additional covariates.

Type 2 inflammatory asthma phenotype population is defined as the randomized patients with baseline blood eosinophils >= 0.15 Giga/L or baseline FeNO >= 20 ppb.

PGM=DEVOPS/SAR231893/EFC14153/CSR_RWE/REPORT/PGM/eff_mmrm_ger_subg_i_t.sas OUT=REPORT/OUTPUT/eff_mmrm_scam_ger_ics2_i_t_x.rtf (01SEP2021 - 16:50)

Project Code / Study Number / Analysis: SAR231893 / EFC14153 / CSR_RWE

4 AM Asthma symptom score - ITT type 2 inflammatory asthma phenotype population

4.1 Summary of treatment effect on change from baseline at Week 52

4.1.5 By baseline ICS dose level 2 (Medium, High)

	Baseline ICS dose level 2			
	High		Medium	
AM symptom score	**Placebo (N=95)**	**Dupilumab (N=200)**	**Placebo (N=19)**	**Dupilumab (N=36)**
Week 52				
Value				
Number	92	191	19	31
Mean (SD)	0.42 (0.58)	0.32 (0.56)	0.33 (0.58)	0.18 (0.45)
Median	0.10	0.00	0.00	0.00
Q1 : Q3	0.00 : 0.86	0.00 : 0.46	0.00 : 0.92	0.00 : 0.08
Min : Max	0.0 : 3.0	0.0 : 3.0	0.0 : 2.0	0.0 : 2.0
Change from baseline				
Number	92	191	19	31
LS Mean (SE)[a]	-0.47 (0.06)	-0.60 (0.04)	-0.52 (0.13)	-0.69 (0.10)
LS Mean Diff (95% CI)[a]	-	-0.13 (-0.26 to 0.00)	-	-0.16 (-0.47 to 0.15)
p-value[a]		0.051		0.293
Hedges'g (95% CI)	-	-0.249 (-0.500 to 0.001)	-	-0.320 (-0.928 to 0.287)

[a]Derived from MMRM model with change from baseline in AM Asthma symptom score values up to Week 52 as the response variable, and treatment, baseline weight group, region, age, baseline eosinophil level, baseline FeNO level, visit, treatment by-visit interaction, baseline AM Asthma symptom score value and baseline-by-visit interaction as covariates.

[b]Similar model as that mentioned in the footnote [a] with subgroup and subgroup-by-treatment interaction as additional covariates.

Type 2 inflammatory asthma phenotype population is defined as the randomized patients with baseline blood eosinophils >= 0.15 Giga/L or baseline FeNO >= 20 ppb.

PGM=DEVOPS/SAR231893/EFC14153/CSR_RWE/REPORT/PGM/eff_mmrm_ger_subg_i_t.sas OUT=REPORT/OUTPUT/eff_mmrm_scam_ger_ics2_i_t_x.rtf (01SEP2021 - 16:50)

Project Code / Study Number / Analysis: SAR231893 / EFC14153 / CSR_RWE

4 AM Asthma symptom score - ITT type 2 inflammatory asthma phenotype population

4.1 Summary of treatment effect on change from baseline at Week 52

4.1.5 By baseline ICS dose level 2 (Medium, High)

	Baseline ICS dose level 2			
	High		Medium	
AM symptom score	**Placebo (N=95)**	**Dupilumab (N=200)**	**Placebo (N=19)**	**Dupilumab (N=36)**
p-value for heterogeneity[b]				0.676

[a]Derived from MMRM model with change from baseline in AM Asthma symptom score values up to Week 52 as the response variable, and treatment, baseline weight group, region, age, baseline eosinophil level, baseline FeNO level, visit, treatment by-visit interaction, baseline AM Asthma symptom score value and baseline-by-visit interaction as covariates.

[b]Similar model as that mentioned in the footnote [a] with subgroup and subgroup-by-treatment interaction as additional covariates.

Type 2 inflammatory asthma phenotype population is defined as the randomized patients with baseline blood eosinophils >= 0.15 Giga/L or baseline FeNO >= 20 ppb.

PGM=DEVOPS/SAR231893/EFC14153/CSR_RWE/REPORT/PGM/eff_mmrm_ger_subg_i_t.sas OUT=REPORT/OUTPUT/eff_mmrm_scam_ger_ics2_i_t_x.rtf (01SEP2021 - 16:50)

Project Code / Study Number / Analysis: SAR231893 / EFC14153 / CSR_RWE

4 AM Asthma symptom score - ITT type 2 inflammatory asthma phenotype population

4.1 Summary of treatment effect on change from baseline at Week 52

4.1.6 By baseline predicted FEV1 (<80%, >=80%)

	Baseline Predicted FEV1			
	<80%		>=80%	
AM symptom score	**Placebo (N=59)**	**Dupilumab (N=116)**	**Placebo (N=55)**	**Dupilumab (N=120)**
Baseline				
Value				
Number	59	116	55	120
Mean (SD)	0.89 (0.73)	0.92 (0.76)	0.91 (0.72)	0.87 (0.80)
Median	0.86	1.00	0.86	0.83
Q1 : Q3	0.17 : 1.43	0.23 : 1.38	0.29 : 1.57	0.17 : 1.29
Min : Max	0.0 : 2.7	0.0 : 3.0	0.0 : 2.6	0.0 : 3.0

[a]Derived from MMRM model with change from baseline in AM Asthma symptom score values up to Week 52 as the response variable, and treatment, baseline weight group, region, age, baseline eosinophil level, baseline FeNO level, baseline ICS dose level, visit, treatment by-visit interaction, baseline AM Asthma symptom score value and baseline-by-visit interaction as covariates.

[b]Similar model as that mentioned in the footnote [a] with subgroup and subgroup-by-treatment interaction as additional covariates.

Type 2 inflammatory asthma phenotype population is defined as the randomized patients with baseline blood eosinophils >= 0.15 Giga/L or baseline FeNO >= 20 ppb.

PGM=DEVOPS/SAR231893/EFC14153/CSR_RWE/REPORT/PGM/eff_mmrm_ger_subg_i_t.sas OUT=REPORT/OUTPUT/eff_mmrm_scam_ger_pfev1_i_t_x.rtf (21JUL2021 - 9:50)

Project Code / Study Number / Analysis: SAR231893 / EFC14153 / CSR_RWE

4 AM Asthma symptom score - ITT type 2 inflammatory asthma phenotype population

4.1 Summary of treatment effect on change from baseline at Week 52

4.1.6 By baseline predicted FEV1 (<80%, >=80%)

	Baseline Predicted FEV1			
	<80%		>=80%	
AM symptom score	**Placebo (N=59)**	**Dupilumab (N=116)**	**Placebo (N=55)**	**Dupilumab (N=120)**
Week 52				
Value				
Number	57	112	54	110
Mean (SD)	0.31 (0.48)	0.36 (0.57)	0.50 (0.65)	0.24 (0.52)
Median	0.04	0.00	0.07	0.00
Q1 : Q3	0.00 : 0.52	0.00 : 0.84	0.00 : 1.00	0.00 : 0.12
Min : Max	0.0 : 2.0	0.0 : 3.0	0.0 : 3.0	0.0 : 3.0
Change from baseline				
Number	57	112	54	110
LS Mean (SE)[a]	-0.59 (0.07)	-0.57 (0.06)	-0.38 (0.08)	-0.63 (0.05)
LS Mean Diff (95% CI)[a]	-	0.02 (-0.15 to 0.18)	-	-0.25 (-0.43 to -0.08)
p-value[a]		0.845		0.005
Hedges'g (95% CI)	-	0.032 (-0.293 to 0.358)	-	-0.481 (-0.811 to -0.151)
p-value for heterogeneity[b]				0.026

[a]Derived from MMRM model with change from baseline in AM Asthma symptom score values up to Week 52 as the response variable, and treatment, baseline weight group, region, age, baseline eosinophil level, baseline FeNO level, baseline ICS dose level, visit, treatment by-visit interaction, baseline AM Asthma symptom score value and baseline-by-visit interaction as covariates.

[b]Similar model as that mentioned in the footnote [a] with subgroup and subgroup-by-treatment interaction as additional covariates.

Type 2 inflammatory asthma phenotype population is defined as the randomized patients with baseline blood eosinophils >= 0.15 Giga/L or baseline FeNO >= 20 ppb.

PGM=DEVOPS/SAR231893/EFC14153/CSR_RWE/REPORT/PGM/eff_mmrm_ger_subg_i_t.sas OUT=REPORT/OUTPUT/eff_mmrm_scam_ger_pfev1_i_t_x.rtf (21JUL2021 - 9:50)

Project Code / Study Number / Analysis: SAR231893 / EFC14153 / CSR_RWE

4 AM Asthma symptom score - ITT type 2 inflammatory asthma phenotype population

4.1 Summary of treatment effect on change from baseline at Week 52

4.1.7 By baseline ACQ-7-IA (<=2, >2)

	Baseline ACQ-7-IA			
	<=2		>2	
AM symptom score	**Placebo (N=61)**	**Dupilumab (N=126)**	**Placebo (N=53)**	**Dupilumab (N=110)**
Baseline				
Value				
Number	61	126	53	110
Mean (SD)	0.76 (0.74)	0.67 (0.71)	1.07 (0.68)	1.16 (0.79)
Median	0.57	0.50	1.00	1.00
Q1 : Q3	0.00 : 1.17	0.00 : 1.00	0.57 : 1.57	0.50 : 1.71
Min : Max	0.0 : 2.6	0.0 : 3.0	0.0 : 2.7	0.0 : 3.0

[a]Derived from MMRM model with change from baseline in AM Asthma symptom score values up to Week 52 as the response variable, and treatment, baseline weight group, region, age, baseline eosinophil level, baseline FeNO level, baseline ICS dose level, visit, treatment by-visit interaction, baseline AM Asthma symptom score value and baseline-by-visit interaction as covariates.
[b]Similar model as that mentioned in the footnote [a] with subgroup and subgroup-by-treatment interaction as additional covariates.
Type 2 inflammatory asthma phenotype population is defined as the randomized patients with baseline blood eosinophils >= 0.15 Giga/L or baseline FeNO >= 20 ppb.
PGM=DEVOPS/SAR231893/EFC14153/CSR_RWE/REPORT/PGM/eff_mmrm_ger_subg_i_t.sas OUT=REPORT/OUTPUT/eff_mmrm_scam_ger_acq7_i_t_x.rtf (21JUL2021 - 10:05)

Project Code / Study Number / Analysis: SAR231893 / EFC14153 / CSR_RWE

4 AM Asthma symptom score - ITT type 2 inflammatory asthma phenotype population

4.1 Summary of treatment effect on change from baseline at Week 52

4.1.7 By baseline ACQ-7-IA (<=2, >2)

	Baseline ACQ-7-IA			
	<=2		>2	
AM symptom score	**Placebo (N=61)**	**Dupilumab (N=126)**	**Placebo (N=53)**	**Dupilumab (N=110)**
Week 52				
Value				
Number	61	117	50	105
Mean (SD)	0.36 (0.60)	0.25 (0.53)	0.45 (0.55)	0.35 (0.57)
Median	0.00	0.00	0.15	0.00
Q1 : Q3	0.00 : 0.52	0.00 : 0.09	0.00 : 0.96	0.00 : 0.57
Min : Max	0.0 : 3.0	0.0 : 3.0	0.0 : 2.0	0.0 : 3.0
Change from baseline				
Number	61	117	50	105
LS Mean (SE)[a]	-0.37 (0.07)	-0.45 (0.05)	-0.67 (0.08)	-0.80 (0.06)
LS Mean Diff (95% CI)[a]	-	-0.08 (-0.24 to 0.07)	-	-0.13 (-0.32 to 0.06)
p-value[a]		0.303		0.164
Hedges'g (95% CI)	-	-0.164 (-0.477 to 0.149)	-	-0.243 (-0.588 to 0.101)
p-value for heterogeneity[b]				0.620

[a]Derived from MMRM model with change from baseline in AM Asthma symptom score values up to Week 52 as the response variable, and treatment, baseline weight group, region, age, baseline eosinophil level, baseline FeNO level, baseline ICS dose level, visit, treatment by-visit interaction, baseline AM Asthma symptom score value and baseline-by-visit interaction as covariates.

[b]Similar model as that mentioned in the footnote [a] with subgroup and subgroup-by-treatment interaction as additional covariates.

Type 2 inflammatory asthma phenotype population is defined as the randomized patients with baseline blood eosinophils >= 0.15 Giga/L or baseline FeNO >= 20 ppb.

PGM=DEVOPS/SAR231893/EFC14153/CSR_RWE/REPORT/PGM/eff_mmrm_ger_subg_i_t.sas OUT=REPORT/OUTPUT/eff_mmrm_scam_ger_acq7_i_t_x.rtf (21JUL2021 - 10:05)

Project Code / Study Number / Analysis: SAR231893 / EFC14153 / CSR_RWE

4 AM Asthma symptom score - ITT type 2 inflammatory asthma phenotype population

4.1 Summary of treatment effect on change from baseline at Week 52

4.1.8 By baseline weight (<=30 kg, >30 kg)

	Baseline weight (kg)			
	<=30		>30	
AM symptom score	**Placebo (N=36)**	**Dupilumab (N=76)**	**Placebo (N=78)**	**Dupilumab (N=160)**
Baseline				
Value				
Number	36	76	78	160
Mean (SD)	1.16 (0.79)	0.95 (0.79)	0.79 (0.66)	0.87 (0.78)
Median	1.00	1.00	0.69	0.86
Q1 : Q3	0.53 : 1.86	0.29 : 1.38	0.17 : 1.20	0.17 : 1.29
Min : Max	0.0 : 2.7	0.0 : 3.0	0.0 : 2.6	0.0 : 3.0

[a]Derived from MMRM model with change from baseline in AM Asthma symptom score values up to Week 52 as the response variable, and treatment, region, age, baseline eosinophil level, baseline FeNO level, baseline ICS dose level, visit, treatment by-visit interaction, baseline AM Asthma symptom score value and baseline-by-visit interaction as covariates.

[b]Similar model as that mentioned in the footnote [a] with subgroup and subgroup-by-treatment interaction as additional covariates.

Type 2 inflammatory asthma phenotype population is defined as the randomized patients with baseline blood eosinophils >= 0.15 Giga/L or baseline FeNO >= 20 ppb.

PGM=DEVOPS/SAR231893/EFC14153/CSR_RWE/REPORT/PGM/eff_mmrm_ger_subg_i_t.sas OUT=REPORT/OUTPUT/eff_mmrm_scam_ger_wgt_i_t_x.rtf (21JUL2021 - 10:19)

Project Code / Study Number / Analysis: SAR231893 / EFC14153 / CSR_RWE

4 AM Asthma symptom score - ITT type 2 inflammatory asthma phenotype population

4.1 Summary of treatment effect on change from baseline at Week 52

4.1.8 By baseline weight (<=30 kg, >30 kg)

	Baseline weight (kg)			
	<=30		>30	
AM symptom score	**Placebo (N=36)**	**Dupilumab (N=76)**	**Placebo (N=78)**	**Dupilumab (N=160)**
Week 52				
Value				
Number	35	69	76	153
Mean (SD)	0.43 (0.53)	0.30 (0.59)	0.39 (0.60)	0.30 (0.53)
Median	0.05	0.00	0.05	0.00
Q1 : Q3	0.00 : 1.00	0.00 : 0.33	0.00 : 0.67	0.00 : 0.43
Min : Max	0.0 : 1.8	0.0 : 3.0	0.0 : 3.0	0.0 : 3.0
Change from baseline				
Number	35	69	76	153
LS Mean (SE)[a]	-0.65 (0.10)	-0.73 (0.07)	-0.43 (0.06)	-0.56 (0.04)
LS Mean Diff (95% CI)[a]	-	-0.08 (-0.31 to 0.15)	-	-0.12 (-0.27 to 0.02)
p-value[a]		0.472		0.080
Hedges'g (95% CI)	-	-0.151 (-0.565 to 0.263)	-	-0.249 (-0.529 to 0.031)
p-value for heterogeneity[b]				0.791

[a]Derived from MMRM model with change from baseline in AM Asthma symptom score values up to Week 52 as the response variable, and treatment, region, age, baseline eosinophil level, baseline FeNO level, baseline ICS dose level, visit, treatment by-visit interaction, baseline AM Asthma symptom score value and baseline-by-visit interaction as covariates.
[b]Similar model as that mentioned in the footnote [a] with subgroup and subgroup-by-treatment interaction as additional covariates.
Type 2 inflammatory asthma phenotype population is defined as the randomized patients with baseline blood eosinophils >= 0.15 Giga/L or baseline FeNO >= 20 ppb.
PGM=DEVOPS/SAR231893/EFC14153/CSR_RWE/REPORT/PGM/eff_mmrm_ger_subg_i_t.sas OUT=REPORT/OUTPUT/eff_mmrm_scam_ger_wgt_i_t_x.rtf (21JUL2021 - 10:19)

Project Code / Study Number / Analysis: SAR231893 / EFC14153 / CSR_RWE

4 AM Asthma symptom score - ITT type 2 inflammatory asthma phenotype population

4.1 Summary of treatment effect on change from baseline at Week 52

4.1.9 By atopic medical condition (Yes, No)

	Atopic medical condition			
	Yes		No	
AM symptom score	**Placebo (N=103)**	**Dupilumab (N=227)**	**Placebo (N=11)**	**Dupilumab (N=9)**
Baseline				
Value				
Number	103	227	11	9
Mean (SD)	0.95 (0.73)	0.89 (0.79)	0.49 (0.54)	1.01 (0.54)
Median	1.00	0.86	0.43	1.14
Q1 : Q3	0.29 : 1.57	0.17 : 1.33	0.00 : 0.71	0.67 : 1.33
Min : Max	0.0 : 2.7	0.0 : 3.0	0.0 : 1.6	0.0 : 1.7

[a]Derived from MMRM model with change from baseline in AM Asthma symptom score values up to Week 52 as the response variable, and treatment, baseline weight group, region, age, baseline eosinophil level, baseline FeNO level, baseline ICS dose level, visit, treatment by-visit interaction, baseline AM Asthma symptom score value and baseline-by-visit interaction as covariates.
[b]Similar model as that mentioned in the footnote [a] with subgroup and subgroup-by-treatment interaction as additional covariates.
Type 2 inflammatory asthma phenotype population is defined as the randomized patients with baseline blood eosinophils >= 0.15 Giga/L or baseline FeNO >= 20 ppb.
PGM=DEVOPS/SAR231893/EFC14153/CSR_RWE/REPORT/PGM/eff_mmrm_ger_subg_i_t.sas OUT=REPORT/OUTPUT/eff_mmrm_scam_ger_amc_i_t_x.rtf (21JUL2021 - 10:33)

Project Code / Study Number / Analysis: SAR231893 / EFC14153 / CSR_RWE

4 AM Asthma symptom score - ITT type 2 inflammatory asthma phenotype population

4.1 Summary of treatment effect on change from baseline at Week 52

4.1.9 By atopic medical condition (Yes, No)

	Atopic medical condition			
	Yes		No	
AM symptom score	**Placebo (N=103)**	**Dupilumab (N=227)**	**Placebo (N=11)**	**Dupilumab (N=9)**
Week 52				
Value				
Number	100	213	11	9
Mean (SD)	0.42 (0.59)	0.30 (0.55)	0.20 (0.38)	0.24 (0.43)
Median	0.07	0.00	0.00	0.00
Q1 : Q3	0.00 : 0.92	0.00 : 0.41	0.00 : 0.36	0.00 : 0.11
Min : Max	0.0 : 3.0	0.0 : 3.0	0.0 : 1.1	0.0 : 1.0
Change from baseline				
Number	100	213	11	9
LS Mean (SE)[a]	-0.49 (0.06)	-0.62 (0.04)	-0.31 (0.16)	-0.52 (0.17)
LS Mean Diff (95% CI)[a]	-	-0.13 (-0.26 to -0.00)	-	-0.21 (-0.66 to 0.23)
p-value[a]		0.048		0.331
Hedges'g (95% CI)	-	-0.243 (-0.484 to -0.003)	-	-0.383 (-1.187 to 0.420)
p-value for heterogeneity[b]				0.847

[a]Derived from MMRM model with change from baseline in AM Asthma symptom score values up to Week 52 as the response variable, and treatment, baseline weight group, region, age, baseline eosinophil level, baseline FeNO level, baseline ICS dose level, visit, treatment by-visit interaction, baseline AM Asthma symptom score value and baseline-by-visit interaction as covariates.

[b]Similar model as that mentioned in the footnote [a] with subgroup and subgroup-by-treatment interaction as additional covariates.

Type 2 inflammatory asthma phenotype population is defined as the randomized patients with baseline blood eosinophils >= 0.15 Giga/L or baseline FeNO >= 20 ppb.

PGM=DEVOPS/SAR231893/EFC14153/CSR_RWE/REPORT/PGM/eff_mmrm_ger_subg_i_t.sas OUT=REPORT/OUTPUT/eff_mmrm_scam_ger_amc_i_t_x.rtf (21JUL2021 - 10:33)

Project Code / Study Number / Analysis: SAR231893 / EFC14153 / CSR_RWE

4 AM Asthma symptom score - ITT type 2 inflammatory asthma phenotype population

4.1 Summary of treatment effect on change from baseline at Week 52

4.1.10 By baseline total IgE (<median, >= median)

	Baseline Total IgE (IU/mL)			
	<median		>=median	
AM symptom score	**Placebo (N=66)**	**Dupilumab (N=105)**	**Placebo (N=47)**	**Dupilumab (N=125)**
Baseline				
Value				
Number	66	105	47	125
Mean (SD)	0.82 (0.69)	0.83 (0.78)	0.97 (0.73)	0.96 (0.77)
Median	0.71	0.80	0.86	0.86
Q1 : Q3	0.14 : 1.29	0.14 : 1.17	0.40 : 1.71	0.29 : 1.43
Min : Max	0.0 : 2.3	0.0 : 3.0	0.0 : 2.6	0.0 : 3.0

[a]Derived from MMRM model with change from baseline in AM Asthma symptom score values up to Week 52 as the response variable, and treatment, baseline weight group, region, age, baseline eosinophil level, baseline FeNO level, baseline ICS dose level, visit, treatment by-visit interaction, baseline AM Asthma symptom score value and baseline-by-visit interaction as covariates.

[b]Similar model as that mentioned in the footnote [a] with subgroup and subgroup-by-treatment interaction as additional covariates.

Type 2 inflammatory asthma phenotype population is defined as the randomized patients with baseline blood eosinophils >= 0.15 Giga/L or baseline FeNO >= 20 ppb.

PGM=DEVOPS/SAR231893/EFC14153/CSR_RWE/REPORT/PGM/eff_mmrm_ger_subg_i_t.sas OUT=REPORT/OUTPUT/eff_mmrm_scam_ger_igem_i_t_x.rtf (21JUL2021 - 10:47)

Project Code / Study Number / Analysis: SAR231893 / EFC14153 / CSR_RWE

4 AM Asthma symptom score - ITT type 2 inflammatory asthma phenotype population

4.1 Summary of treatment effect on change from baseline at Week 52

4.1.10 By baseline total IgE (<median, >= median)

	Baseline Total IgE (IU/mL)			
	<median		>=median	
AM symptom score	**Placebo (N=66)**	**Dupilumab (N=105)**	**Placebo (N=47)**	**Dupilumab (N=125)**
Week 52				
Value				
Number	65	101	45	118
Mean (SD)	0.34 (0.51)	0.31 (0.54)	0.50 (0.66)	0.30 (0.56)
Median	0.00	0.00	0.17	0.00
Q1 : Q3	0.00 : 0.76	0.00 : 0.46	0.00 : 1.00	0.00 : 0.38
Min : Max	0.0 : 2.0	0.0 : 3.0	0.0 : 3.0	0.0 : 3.0
Change from baseline				
Number	65	101	45	118
LS Mean (SE)[a]	-0.48 (0.07)	-0.52 (0.05)	-0.39 (0.09)	-0.61 (0.06)
LS Mean Diff (95% CI)[a]	-	-0.04 (-0.20 to 0.12)	-	-0.22 (-0.40 to -0.04)
p-value[a]		0.594		0.017
Hedges'g (95% CI)	-	-0.086 (-0.403 to 0.231)	-	-0.421 (-0.766 to -0.075)
p-value for heterogeneity[b]				0.145

[a]Derived from MMRM model with change from baseline in AM Asthma symptom score values up to Week 52 as the response variable, and treatment, baseline weight group, region, age, baseline eosinophil level, baseline FeNO level, baseline ICS dose level, visit, treatment by-visit interaction, baseline AM Asthma symptom score value and baseline-by-visit interaction as covariates.

[b]Similar model as that mentioned in the footnote [a] with subgroup and subgroup-by-treatment interaction as additional covariates.

Type 2 inflammatory asthma phenotype population is defined as the randomized patients with baseline blood eosinophils >= 0.15 Giga/L or baseline FeNO >= 20 ppb.

PGM=DEVOPS/SAR231893/EFC14153/CSR_RWE/REPORT/PGM/eff_mmrm_ger_subg_i_t.sas OUT=REPORT/OUTPUT/eff_mmrm_scam_ger_igem_i_t_x.rtf (21JUL2021 - 10:47)

Project Code / Study Number / Analysis: SAR231893 / EFC14153 / CSR_RWE

4 AM Asthma symptom score - ITT type 2 inflammatory asthma phenotype population

4.1 Summary of treatment effect on change from baseline at Week 52

4.1.11 By baseline total IgE (<100 IU/ml, >= 100 IU/ml)

	Baseline Total IgE (IU/mL)			
	< 100		>= 100	
AM symptom score	**Placebo (N=22)**	**Dupilumab (N=29)**	**Placebo (N=91)**	**Dupilumab (N=201)**
Baseline				
Value				
Number	22	29	91	201
Mean (SD)	0.63 (0.74)	0.94 (0.67)	0.95 (0.69)	0.89 (0.79)
Median	0.43	1.00	1.00	0.86
Q1 : Q3	0.00 : 1.00	0.50 : 1.29	0.33 : 1.57	0.17 : 1.33
Min : Max	0.0 : 2.3	0.0 : 3.0	0.0 : 2.6	0.0 : 3.0

[a]Derived from MMRM model with change from baseline in AM Asthma symptom score values up to Week 52 as the response variable, and treatment, baseline weight group, region, age, baseline eosinophil level, baseline FeNO level, baseline ICS dose level, visit, treatment by-visit interaction, baseline AM Asthma symptom score value and baseline-by-visit interaction as covariates.

[b]Similar model as that mentioned in the footnote [a] with subgroup and subgroup-by-treatment interaction as additional covariates.

Type 2 inflammatory asthma phenotype population is defined as the randomized patients with baseline blood eosinophils >= 0.15 Giga/L or baseline FeNO >= 20 ppb.

PGM=DEVOPS/SAR231893/EFC14153/CSR_RWE/REPORT/PGM/eff_mmrm_ger_subg_i_t.sas OUT=REPORT/OUTPUT/eff_mmrm_scam_ger_ige_i_t_x.rtf (21JUL2021 - 11:01)

Project Code / Study Number / Analysis: SAR231893 / EFC14153 / CSR_RWE

4 AM Asthma symptom score - ITT type 2 inflammatory asthma phenotype population

4.1 Summary of treatment effect on change from baseline at Week 52

4.1.11 By baseline total IgE (<100 IU/ml, >= 100 IU/ml)

	Baseline Total IgE (IU/mL)			
	< 100		>= 100	
AM symptom score	**Placebo (N=22)**	**Dupilumab (N=29)**	**Placebo (N=91)**	**Dupilumab (N=201)**
Week 52				
Value				
Number	22	29	88	190
Mean (SD)	0.36 (0.49)	0.51 (0.73)	0.42 (0.60)	0.27 (0.51)
Median	0.00	0.04	0.06	0.00
Q1 : Q3	0.00 : 0.87	0.00 : 1.00	0.00 : 0.89	0.00 : 0.33
Min : Max	0.0 : 1.4	0.0 : 3.0	0.0 : 3.0	0.0 : 3.0
Change from baseline				
Number	22	29	88	190
LS Mean (SE)[a]	-0.37 (0.14)	-0.31 (0.14)	-0.49 (0.06)	-0.63 (0.04)
LS Mean Diff (95% CI)[a]	-	0.06 (-0.30 to 0.43)	-	-0.14 (-0.27 to -0.01)
p-value[a]		0.732		0.030
Hedges'g (95% CI)	-	0.104 (-0.503 to 0.711)	-	-0.283 (-0.539 to -0.028)
p-value for heterogeneity[b]				0.218

[a]Derived from MMRM model with change from baseline in AM Asthma symptom score values up to Week 52 as the response variable, and treatment, baseline weight group, region, age, baseline eosinophil level, baseline FeNO level, baseline ICS dose level, visit, treatment by-visit interaction, baseline AM Asthma symptom score value and baseline-by-visit interaction as covariates.
[b]Similar model as that mentioned in the footnote [a] with subgroup and subgroup-by-treatment interaction as additional covariates.
Type 2 inflammatory asthma phenotype population is defined as the randomized patients with baseline blood eosinophils >= 0.15 Giga/L or baseline FeNO >= 20 ppb.
PGM=DEVOPS/SAR231893/EFC14153/CSR_RWE/REPORT/PGM/eff_mmrm_ger_subg_i_t.sas OUT=REPORT/OUTPUT/eff_mmrm_scam_ger_ige_i_t_x.rtf (21JUL2021 - 11:01)

Project Code / Study Number / Analysis: SAR231893 / EFC14153 / CSR_RWE

4 AM Asthma symptom score - ITT type 2 inflammatory asthma phenotype population

4.1 Summary of treatment effect on change from baseline at Week 52

4.1.12 By age at onset of asthma (0-2, 3-5, >=6 years)

	Age of onset of asthma (years)					
	0-2		3-5		>= 6	
AM symptom score	**Placebo (N=40)**	**Dupilumab (N=105)**	**Placebo (N=39)**	**Dupilumab (N=86)**	**Placebo (N=35)**	**Dupilumab (N=45)**
Baseline						
Value						
Number	40	105	39	86	35	45
Mean (SD)	0.90 (0.70)	0.88 (0.74)	1.02 (0.73)	0.92 (0.77)	0.77 (0.75)	0.89 (0.91)
Median	0.71	0.86	1.00	0.86	0.57	0.50
Q1 : Q3	0.41 : 1.48	0.17 : 1.25	0.29 : 1.57	0.29 : 1.43	0.14 : 1.20	0.00 : 1.43
Min : Max	0.0 : 2.3	0.0 : 3.0	0.0 : 2.6	0.0 : 3.0	0.0 : 2.7	0.0 : 3.0

[a]Derived from MMRM model with change from baseline in AM Asthma symptom score values up to Week 52 as the response variable, and treatment, baseline weight group, region, age, baseline eosinophil level, baseline FeNO level, baseline ICS dose level, visit, treatment by-visit interaction, baseline AM Asthma symptom score value and baseline-by-visit interaction as covariates.

[b]Similar model as that mentioned in the footnote [a] with subgroup and subgroup-by-treatment interaction as additional covariates.

Type 2 inflammatory asthma phenotype population is defined as the randomized patients with baseline blood eosinophils >= 0.15 Giga/L or baseline FeNO >= 20 ppb.

PGM=DEVOPS/SAR231893/EFC14153/CSR_RWE/REPORT/PGM/eff_mmrm_ger_subg_i_t.sas OUT=REPORT/OUTPUT/eff_mmrm_scam_ger_onsa_i_t_x.rtf (10AUG2021 - 9:14)

Project Code / Study Number / Analysis: SAR231893 / EFC14153 / CSR_RWE

4 AM Asthma symptom score - ITT type 2 inflammatory asthma phenotype population

4.1 Summary of treatment effect on change from baseline at Week 52

4.1.12 By age at onset of asthma (0-2, 3-5, >=6 years)

	Age of onset of asthma (years)					
	0-2		3-5		>= 6	
AM symptom score	**Placebo (N=40)**	**Dupilumab (N=105)**	**Placebo (N=39)**	**Dupilumab (N=86)**	**Placebo (N=35)**	**Dupilumab (N=45)**
Week 52						
Value						
Number	38	100	38	79	35	43
Mean (SD)	0.44 (0.56)	0.30 (0.56)	0.37 (0.61)	0.29 (0.55)	0.39 (0.57)	0.33 (0.53)
Median	0.19	0.00	0.00	0.00	0.04	0.00
Q1 : Q3	0.00 : 1.00	0.00 : 0.36	0.00 : 0.86	0.00 : 0.33	0.00 : 0.92	0.00 : 0.65
Min : Max	0.0 : 2.0	0.0 : 3.0	0.0 : 3.0	0.0 : 3.0	0.0 : 2.0	0.0 : 2.0
Change from baseline						
Number	38	100	38	79	35	43
LS Mean (SE)[a]	-0.38 (0.09)	-0.56 (0.06)	-0.64 (0.09)	-0.70 (0.07)	-0.58 (0.10)	-0.67 (0.09)
LS Mean Diff (95% CI)[a]	-	-0.18 (-0.38 to 0.02)	-	-0.06 (-0.28 to 0.16)	-	-0.10 (-0.32 to 0.12)
p-value[a]		0.077		0.581		0.387

[a]Derived from MMRM model with change from baseline in AM Asthma symptom score values up to Week 52 as the response variable, and treatment, baseline weight group, region, age, baseline eosinophil level, baseline FeNO level, baseline ICS dose level, visit, treatment by-visit interaction, baseline AM Asthma symptom score value and baseline-by-visit interaction as covariates.

[b]Similar model as that mentioned in the footnote [a] with subgroup and subgroup-by-treatment interaction as additional covariates.

Type 2 inflammatory asthma phenotype population is defined as the randomized patients with baseline blood eosinophils >= 0.15 Giga/L or baseline FeNO >= 20 ppb.

PGM=DEVOPS/SAR231893/EFC14153/CSR_RWE/REPORT/PGM/eff_mmrm_ger_subg_i_t.sas OUT=REPORT/OUTPUT/eff_mmrm_scam_ger_onsa_i_t_x.rtf (10AUG2021 - 9:14)

Project Code / Study Number / Analysis: SAR231893 / EFC14153 / CSR_RWE

4 AM Asthma symptom score - ITT type 2 inflammatory asthma phenotype population

4.1 Summary of treatment effect on change from baseline at Week 52

4.1.12 By age at onset of asthma (0-2, 3-5, >=6 years)

	Age of onset of asthma (years)					
	0-2		3-5		>= 6	
AM symptom score	**Placebo (N=40)**	**Dupilumab (N=105)**	**Placebo (N=39)**	**Dupilumab (N=86)**	**Placebo (N=35)**	**Dupilumab (N=45)**
Hedges'g (95% CI)	-	-0.340 (-0.716 to 0.037)	-	-0.109 (-0.500 to 0.281)	-	-0.203 (-0.670 to 0.263)
p-value for heterogeneity[b]:						
0-2, 3-5						0.332
0-2, >= 6						0.499
3-5, >= 6						0.836
overall						0.600

[a]Derived from MMRM model with change from baseline in AM Asthma symptom score values up to Week 52 as the response variable, and treatment, baseline weight group, region, age, baseline eosinophil level, baseline FeNO level, baseline ICS dose level, visit, treatment by-visit interaction, baseline AM Asthma symptom score value and baseline-by-visit interaction as covariates.

[b]Similar model as that mentioned in the footnote [a] with subgroup and subgroup-by-treatment interaction as additional covariates.

Type 2 inflammatory asthma phenotype population is defined as the randomized patients with baseline blood eosinophils >= 0.15 Giga/L or baseline FeNO >= 20 ppb.

PGM=DEVOPS/SAR231893/EFC14153/CSR_RWE/REPORT/PGM/eff_mmrm_ger_subg_i_t.sas OUT=REPORT/OUTPUT/eff_mmrm_scam_ger_onsa_i_t_x.rtf (10AUG2021 - 9:14)

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

Project Code / Study Number / Analysis: SAR231893 / EFC14153 / CSR_RWE

4 AM Asthma symptom score - ITT type 2 inflammatory asthma phenotype population

4.1 Summary of treatment effect on change from baseline at Week 52

4.1.13 By number of severe asthma exacerbation prior to the study (<=1, 2, >2)

	Number of severe asthma exacerbation prior to the study					
	<=1		2		>2	
AM symptom score	**Placebo (N=47)**	**Dupilumab (N=85)**	**Placebo (N=32)**	**Dupilumab (N=75)**	**Placebo (N=35)**	**Dupilumab (N=76)**
Baseline						
Value						
Number	47	85	32	75	35	76
Mean (SD)	0.82 (0.69)	0.80 (0.67)	0.90 (0.74)	1.16 (0.93)	1.02 (0.76)	0.75 (0.68)
Median	0.83	0.80	0.86	1.00	1.00	0.63
Q1 : Q3	0.17 : 1.20	0.17 : 1.25	0.14 : 1.58	0.43 : 1.71	0.43 : 1.57	0.00 : 1.14
Min : Max	0.0 : 2.0	0.0 : 2.3	0.0 : 2.3	0.0 : 3.0	0.0 : 2.7	0.0 : 2.4

[a]Derived from MMRM model with change from baseline in AM Asthma symptom score values up to Week 52 as the response variable, and treatment, baseline weight group, region, age, baseline eosinophil level, baseline FeNO level, baseline ICS dose level, visit, treatment by-visit interaction, baseline AM Asthma symptom score value and baseline-by-visit interaction as covariates.

[b]Similar model as that mentioned in the footnote [a] with subgroup and subgroup-by-treatment interaction as additional covariates.

Type 2 inflammatory asthma phenotype population is defined as the randomized patients with baseline blood eosinophils >= 0.15 Giga/L or baseline FeNO >= 20 ppb.

PGM=DEVOPS/SAR231893/EFC14153/CSR_RWE/REPORT/PGM/eff_mmrm_ger_subg_i_t.sas OUT=REPORT/OUTPUT/eff_mmrm_scam_ger_exa_i_t_x.rtf (21JUL2021 - 11:41)

Project Code / Study Number / Analysis: SAR231893 / EFC14153 / CSR_RWE

4 AM Asthma symptom score - ITT type 2 inflammatory asthma phenotype population

4.1 Summary of treatment effect on change from baseline at Week 52

4.1.13 By number of severe asthma exacerbation prior to the study (<=1, 2, >2)

	Number of severe asthma exacerbation prior to the study					
	<=1		2		>2	
AM symptom score	**Placebo (N=47)**	**Dupilumab (N=85)**	**Placebo (N=32)**	**Dupilumab (N=75)**	**Placebo (N=35)**	**Dupilumab (N=76)**
Week 52						
Value						
Number	45	82	32	71	34	69
Mean (SD)	0.32 (0.49)	0.29 (0.49)	0.41 (0.53)	0.42 (0.63)	0.51 (0.72)	0.18 (0.49)
Median	0.00	0.00	0.06	0.00	0.10	0.00
Q1 : Q3	0.00 : 0.48	0.00 : 0.43	0.00 : 0.86	0.00 : 1.00	0.00 : 1.00	0.00 : 0.06
Min : Max	0.0 : 2.0	0.0 : 2.0	0.0 : 2.0	0.0 : 3.0	0.0 : 3.0	0.0 : 3.0
Change from baseline						
Number	45	82	32	71	34	69
LS Mean (SE)[a]	-0.50 (0.07)	-0.55 (0.05)	-0.70 (0.11)	-0.74 (0.08)	-0.29 (0.11)	-0.64 (0.08)
LS Mean Diff (95% CI)[a]	-	-0.05 (-0.21 to 0.12)	-	-0.04 (-0.30 to 0.21)	-	-0.35 (-0.60 to -0.11)
p-value[a]		0.564		0.731		0.004

[a]Derived from MMRM model with change from baseline in AM Asthma symptom score values up to Week 52 as the response variable, and treatment, baseline weight group, region, age, baseline eosinophil level, baseline FeNO level, baseline ICS dose level, visit, treatment by-visit interaction, baseline AM Asthma symptom score value and baseline-by-visit interaction as covariates.
[b]Similar model as that mentioned in the footnote [a] with subgroup and subgroup-by-treatment interaction as additional covariates.
Type 2 inflammatory asthma phenotype population is defined as the randomized patients with baseline blood eosinophils >= 0.15 Giga/L or baseline FeNO >= 20 ppb.
PGM=DEVOPS/SAR231893/EFC14153/CSR_RWE/REPORT/PGM/eff_mmrm_ger_subg_i_t.sas OUT=REPORT/OUTPUT/eff_mmrm_scam_ger_exa_i_t_x.rtf (21JUL2021 - 11:41)

Project Code / Study Number / Analysis: SAR231893 / EFC14153 / CSR_RWE

4 AM Asthma symptom score - ITT type 2 inflammatory asthma phenotype population

4.1 Summary of treatment effect on change from baseline at Week 52

4.1.13 By number of severe asthma exacerbation prior to the study (<=1, 2, >2)

	Number of severe asthma exacerbation prior to the study					
	<=1		2		>2	
AM symptom score	**Placebo (N=47)**	**Dupilumab (N=85)**	**Placebo (N=32)**	**Dupilumab (N=75)**	**Placebo (N=35)**	**Dupilumab (N=76)**
Hedges'g (95% CI)	-	-0.108 (-0.476 to 0.261)	-	-0.076 (-0.516 to 0.363)	-	-0.638 (-1.070 to -0.206)
p-value for heterogeneity[b]:						
<=1, 2						0.853
<=1, >2						0.062
2, >2						0.121
overall						0.141

[a]Derived from MMRM model with change from baseline in AM Asthma symptom score values up to Week 52 as the response variable, and treatment, baseline weight group, region, age, baseline eosinophil level, baseline FeNO level, baseline ICS dose level, visit, treatment by-visit interaction, baseline AM Asthma symptom score value and baseline-by-visit interaction as covariates.

[b]Similar model as that mentioned in the footnote [a] with subgroup and subgroup-by-treatment interaction as additional covariates.

Type 2 inflammatory asthma phenotype population is defined as the randomized patients with baseline blood eosinophils >= 0.15 Giga/L or baseline FeNO >= 20 ppb.

PGM=DEVOPS/SAR231893/EFC14153/CSR_RWE/REPORT/PGM/eff_mmrm_ger_subg_i_t.sas OUT=REPORT/OUTPUT/eff_mmrm_scam_ger_exa_i_t_x.rtf (21JUL2021 - 11:41)

Project Code / Study Number / Analysis: SAR231893 / EFC14153 / CSR_RWE

5 PM Asthma symptom score - ITT type 2 inflammatory asthma phenotype population

5.1 Summary of treatment effect on change from baseline at Week 52

PM symptom score	Placebo (N=114)	Dupilumab (N=236)
Baseline		
Value		
Number	114	236
Mean (SD)	0.92 (0.72)	0.92 (0.77)
Median	0.93	1.00
Q1 : Q3	0.29 : 1.43	0.29 : 1.29
Min : Max	0.0 : 2.6	0.0 : 3.0
Week 52		
Value		
Number	111	222
Mean (SD)	0.42 (0.60)	0.34 (0.61)
Median	0.00	0.00
Q1 : Q3	0.00 : 0.96	0.00 : 0.46
Min : Max	0.0 : 3.0	0.0 : 3.5
Change from baseline		
Number	111	222
LS Mean (SE)[a]	-0.50 (0.06)	-0.59 (0.04)

[a]Derived from MMRM model with change from baseline in PM Asthma symptom score values up to Week 52 as the response variable, and treatment, baseline weight group, region, age, baseline eosinophil level, baseline FeNO level, baseline ICS dose level, visit, treatment by-visit interaction, baseline PM Asthma symptom score value and baseline-by-visit interaction as covariates.

Type 2 inflammatory asthma phenotype population is defined as the randomized patients with baseline blood eosinophils >= 0.15 Giga/L or baseline FeNO >= 20 ppb.

PGM=DEVOPS/SAR231893/EFC14153/CSR_RWE/REPORT/PGM/eff_mmrm_ger_i_t.sas OUT=REPORT/OUTPUT/eff_mmrm_scpm_ger_i_t_x.rtf (22JUL2021 - 7:55)

Project Code / Study Number / Analysis: SAR231893 / EFC14153 / CSR_RWE

5 PM Asthma symptom score - ITT type 2 inflammatory asthma phenotype population

5.1 Summary of treatment effect on change from baseline at Week 52

PM symptom score	Placebo (N=114)	Dupilumab (N=236)
LS Mean Diff (95% CI)[a]	-	-0.09 (-0.22 to 0.03)
Hedges'g (95% CI)	-	-0.171 (-0.401 to 0.060)
p-value[a]		0.146

[a]Derived from MMRM model with change from baseline in PM Asthma symptom score values up to Week 52 as the response variable, and treatment, baseline weight group, region, age, baseline eosinophil level, baseline FeNO level, baseline ICS dose level, visit, treatment by-visit interaction, baseline PM Asthma symptom score value and baseline-by-visit interaction as covariates.

Type 2 inflammatory asthma phenotype population is defined as the randomized patients with baseline blood eosinophils >= 0.15 Giga/L or baseline FeNO >= 20 ppb.

PGM=DEVOPS/SAR231893/EFC14153/CSR_RWE/REPORT/PGM/eff_mmrm_ger_i_t.sas OUT=REPORT/OUTPUT/eff_mmrm_scpm_ger_i_t_x.rtf (22JUL2021 - 7:55)

Project Code / Study Number / Analysis: SAR231893 / EFC14153 / CSR_RWE

5 PM Asthma symptom score - ITT type 2 inflammatory asthma phenotype population

5.1 Summary of treatment effect on change from baseline at Week 52

5.1.1 By gender (Male, Female)

	Gender			
	Male		Female	
PM symptom score	**Placebo (N=78)**	**Dupilumab (N=152)**	**Placebo (N=36)**	**Dupilumab (N=84)**
Baseline				
Value				
Number	78	152	36	84
Mean (SD)	0.91 (0.71)	0.94 (0.76)	0.95 (0.74)	0.89 (0.78)
Median	0.86	1.00	1.00	0.77
Q1 : Q3	0.29 : 1.43	0.29 : 1.33	0.23 : 1.43	0.29 : 1.17
Min : Max	0.0 : 2.6	0.0 : 3.0	0.0 : 2.4	0.0 : 3.0

[a]Derived from MMRM model with change from baseline in PM Asthma symptom score values up to Week 52 as the response variable, and treatment, baseline weight group, region, age, baseline eosinophil level, baseline FeNO level, baseline ICS dose level, visit, treatment by-visit interaction, baseline PM Asthma symptom score value and baseline-by-visit interaction as covariates.
[b]Similar model as that mentioned in the footnote [a] with subgroup and subgroup-by-treatment interaction as additional covariates.
Type 2 inflammatory asthma phenotype population is defined as the randomized patients with baseline blood eosinophils >= 0.15 Giga/L or baseline FeNO >= 20 ppb.
PGM=DEVOPS/SAR231893/EFC14153/CSR_RWE/REPORT/PGM/eff_mmrm_ger_subg_i_t.sas OUT=REPORT/OUTPUT/eff_mmrm_scpm_ger_sex_i_t_x.rtf (21JUL2021 - 8:44)

Project Code / Study Number / Analysis: SAR231893 / EFC14153 / CSR_RWE

5 PM Asthma symptom score - ITT type 2 inflammatory asthma phenotype population

5.1 Summary of treatment effect on change from baseline at Week 52

5.1.1 By gender (Male, Female)

	Gender			
	Male		Female	
PM symptom score	**Placebo (N=78)**	**Dupilumab (N=152)**	**Placebo (N=36)**	**Dupilumab (N=84)**
Week 52				
Value				
Number	76	143	35	79
Mean (SD)	0.51 (0.64)	0.33 (0.59)	0.22 (0.45)	0.37 (0.66)
Median	0.21	0.00	0.00	0.00
Q1 : Q3	0.00 : 1.00	0.00 : 0.37	0.00 : 0.00	0.00 : 0.56
Min : Max	0.0 : 3.0	0.0 : 3.0	0.0 : 1.8	0.0 : 3.5
Change from baseline				
Number	76	143	35	79
LS Mean (SE)[a]	-0.43 (0.06)	-0.63 (0.05)	-0.67 (0.10)	-0.54 (0.07)
LS Mean Diff (95% CI)[a]	-	-0.20 (-0.34 to -0.05)	-	0.14 (-0.09 to 0.37)
p-value[a]		0.008		0.243
Hedges'g (95% CI)	-	-0.384 (-0.668 to -0.100)	-	0.236 (-0.163 to 0.636)
p-value for heterogeneity[b]				0.016

[a]Derived from MMRM model with change from baseline in PM Asthma symptom score values up to Week 52 as the response variable, and treatment, baseline weight group, region, age, baseline eosinophil level, baseline FeNO level, baseline ICS dose level, visit, treatment by-visit interaction, baseline PM Asthma symptom score value and baseline-by-visit interaction as covariates.
[b]Similar model as that mentioned in the footnote [a] with subgroup and subgroup-by-treatment interaction as additional covariates.
Type 2 inflammatory asthma phenotype population is defined as the randomized patients with baseline blood eosinophils >= 0.15 Giga/L or baseline FeNO >= 20 ppb.
PGM=DEVOPS/SAR231893/EFC14153/CSR_RWE/REPORT/PGM/eff_mmrm_ger_subg_i_t.sas OUT=REPORT/OUTPUT/eff_mmrm_scpm_ger_sex_i_t_x.rtf (21JUL2021 - 8:44)

Project Code / Study Number / Analysis: SAR231893 / EFC14153 / CSR_RWE

5 PM Asthma symptom score - ITT type 2 inflammatory asthma phenotype population

5.1 Summary of treatment effect on change from baseline at Week 52

5.1.2 By region (Latin America, East Europe, Western Countries)

	Region					
	Latin America		East Europe		Western countries	
PM symptom score	**Placebo (N=51)**	**Dupilumab (N=106)**	**Placebo (N=43)**	**Dupilumab (N=78)**	**Placebo (N=20)**	**Dupilumab (N=52)**
Baseline						
Value						
Number	51	106	43	78	20	52
Mean (SD)	0.83 (0.67)	0.99 (0.85)	0.99 (0.71)	0.93 (0.65)	1.04 (0.86)	0.77 (0.75)
Median	0.86	1.00	1.00	1.00	0.93	0.54
Q1 : Q3	0.17 : 1.29	0.29 : 1.43	0.43 : 1.57	0.43 : 1.43	0.18 : 1.93	0.17 : 1.14
Min : Max	0.0 : 2.4	0.0 : 3.0	0.0 : 2.3	0.0 : 3.0	0.0 : 2.6	0.0 : 3.0

[a]Derived from MMRM model with change from baseline in PM Asthma symptom score values up to Week 52 as the response variable, and treatment, baseline weight group, age, baseline eosinophil level, baseline FeNO level, baseline ICS dose level, visit, treatment by-visit interaction, baseline PM Asthma symptom score value and baseline-by-visit interaction as covariates.

[b]Similar model as that mentioned in the footnote [a] with subgroup and subgroup-by-treatment interaction as additional covariates.

Type 2 inflammatory asthma phenotype population is defined as the randomized patients with baseline blood eosinophils >= 0.15 Giga/L or baseline FeNO >= 20 ppb.

PGM=DEVOPS/SAR231893/EFC14153/CSR_RWE/REPORT/PGM/eff_mmrm_ger_subg_i_t.sas OUT=REPORT/OUTPUT/eff_mmrm_scpm_ger_cty_i_t_x.rtf (21JUL2021 - 9:04)

Project Code / Study Number / Analysis: SAR231893 / EFC14153 / CSR_RWE

5 PM Asthma symptom score - ITT type 2 inflammatory asthma phenotype population

5.1 Summary of treatment effect on change from baseline at Week 52

5.1.2 By region (Latin America, East Europe, Western Countries)

	Region					
	Latin America		East Europe		Western countries	
PM symptom score	**Placebo (N=51)**	**Dupilumab (N=106)**	**Placebo (N=43)**	**Dupilumab (N=78)**	**Placebo (N=20)**	**Dupilumab (N=52)**
Week 52						
Value						
Number	51	102	42	77	18	43
Mean (SD)	0.36 (0.50)	0.35 (0.66)	0.55 (0.73)	0.38 (0.51)	0.29 (0.44)	0.24 (0.66)
Median	0.00	0.00	0.17	0.06	0.00	0.00
Q1 : Q3	0.00 : 0.92	0.00 : 0.33	0.00 : 1.05	0.00 : 0.89	0.00 : 0.45	0.00 : 0.00
Min : Max	0.0 : 2.0	0.0 : 3.0	0.0 : 3.0	0.0 : 2.0	0.0 : 1.4	0.0 : 3.5
Change from baseline						
Number	51	102	42	77	18	43
LS Mean (SE)[a]	-0.55 (0.08)	-0.61 (0.06)	-0.42 (0.09)	-0.56 (0.07)	-0.50 (0.15)	-0.56 (0.10)
LS Mean Diff (95% CI)[a]	-	-0.06 (-0.25 to 0.12)	-	-0.14 (-0.35 to 0.06)	-	-0.06 (-0.40 to 0.28)
p-value[a]		0.507		0.174		0.717

[a]Derived from MMRM model with change from baseline in PM Asthma symptom score values up to Week 52 as the response variable, and treatment, baseline weight group, age, baseline eosinophil level, baseline FeNO level, baseline ICS dose level, visit, treatment by-visit interaction, baseline PM Asthma symptom score value and baseline-by-visit interaction as covariates.

[b]Similar model as that mentioned in the footnote [a] with subgroup and subgroup-by-treatment interaction as additional covariates.

Type 2 inflammatory asthma phenotype population is defined as the randomized patients with baseline blood eosinophils >= 0.15 Giga/L or baseline FeNO >= 20 ppb.

PGM=DEVOPS/SAR231893/EFC14153/CSR_RWE/REPORT/PGM/eff_mmrm_ger_subg_i_t.sas OUT=REPORT/OUTPUT/eff_mmrm_scpm_ger_cty_i_t_x.rtf (21JUL2021 - 9:04)

Project Code / Study Number / Analysis: SAR231893 / EFC14153 / CSR_RWE

5 PM Asthma symptom score - ITT type 2 inflammatory asthma phenotype population

5.1 Summary of treatment effect on change from baseline at Week 52

5.1.2 By region (Latin America, East Europe, Western Countries)

	Region					
	Latin America		East Europe		Western countries	
PM symptom score	**Placebo (N=51)**	**Dupilumab (N=106)**	**Placebo (N=43)**	**Dupilumab (N=78)**	**Placebo (N=20)**	**Dupilumab (N=52)**
Hedges'g (95% CI)	-	-0.117 (-0.464 to 0.230)	-	-0.261 (-0.639 to 0.117)	-	-0.102 (-0.663 to 0.458)
p-value for heterogeneity[b]:						
Latin America, East Europe						0.528
Latin America, Western countries						0.680
East Europe, Western countries						0.942
overall						0.808

[a]Derived from MMRM model with change from baseline in PM Asthma symptom score values up to Week 52 as the response variable, and treatment, baseline weight group, age, baseline eosinophil level, baseline FeNO level, baseline ICS dose level, visit, treatment by-visit interaction, baseline PM Asthma symptom score value and baseline-by-visit interaction as covariates.

[b]Similar model as that mentioned in the footnote [a] with subgroup and subgroup-by-treatment interaction as additional covariates.

Type 2 inflammatory asthma phenotype population is defined as the randomized patients with baseline blood eosinophils >= 0.15 Giga/L or baseline FeNO >= 20 ppb.

PGM=DEVOPS/SAR231893/EFC14153/CSR_RWE/REPORT/PGM/eff_mmrm_ger_subg_i_t.sas OUT=REPORT/OUTPUT/eff_mmrm_scpm_ger_cty_i_t_x.rtf (21JUL2021 - 9:04)

Project Code / Study Number / Analysis: SAR231893 / EFC14153 / CSR_RWE

5 PM Asthma symptom score - ITT type 2 inflammatory asthma phenotype population

5.1 Summary of treatment effect on change from baseline at Week 52

5.1.3 By race (Caucasian/white, Black/of African descent, Other)

	Race					
	Caucasian/White		Black/of African descent		Other	
PM symptom score	**Placebo (N=102)**	**Dupilumab (N=208)**	**Placebo (N=5)**	**Dupilumab (N=9)**	**Placebo (N=7)**	**Dupilumab (N=19)**
Baseline						
Value						
Number	102	208	5	9	7	19
Mean (SD)	0.95 (0.73)	0.94 (0.76)	0.83 (0.85)	1.24 (1.13)	0.59 (0.38)	0.50 (0.43)
Median	1.00	1.00	0.57	1.14	0.71	0.43
Q1 : Q3	0.29 : 1.43	0.29 : 1.38	0.17 : 1.43	0.29 : 1.86	0.14 : 0.86	0.00 : 1.00
Min : Max	0.0 : 2.6	0.0 : 3.0	0.0 : 2.0	0.0 : 3.0	0.0 : 1.0	0.0 : 1.1

[a]Derived from MMRM model with change from baseline in PM Asthma symptom score values up to Week 52 as the response variable, and treatment, baseline weight group, region, age, baseline eosinophil level, baseline FeNO level, baseline ICS dose level, visit, treatment by-visit interaction, baseline PM Asthma symptom score value and baseline-by-visit interaction as covariates.

[b]Similar model as that mentioned in the footnote [a] with subgroup and subgroup-by-treatment interaction as additional covariates.

Type 2 inflammatory asthma phenotype population is defined as the randomized patients with baseline blood eosinophils >= 0.15 Giga/L or baseline FeNO >= 20 ppb.

PGM=DEVOPS/SAR231893/EFC14153/CSR_RWE/REPORT/PGM/eff_mmrm_ger_subg_i_t.sas OUT=REPORT/OUTPUT/eff_mmrm_scpm_ger_race_i_t_x.rtf (21JUL2021 - 9:24)

Project Code / Study Number / Analysis: SAR231893 / EFC14153 / CSR_RWE

5 PM Asthma symptom score - ITT type 2 inflammatory asthma phenotype population

5.1 Summary of treatment effect on change from baseline at Week 52

5.1.3 By race (Caucasian/white, Black/of African descent, Other)

	Race					
	Caucasian/White		Black/of African descent		Other	
PM symptom score	**Placebo (N=102)**	**Dupilumab (N=208)**	**Placebo (N=5)**	**Dupilumab (N=9)**	**Placebo (N=7)**	**Dupilumab (N=19)**
Week 52						
Value						
Number	101	198	3	8	7	16
Mean (SD)	0.42 (0.61)	0.36 (0.62)	0.07 (0.12)	0.43 (0.76)	0.59 (0.52)	0.05 (0.20)
Median	0.00	0.00	0.00	0.00	0.45	0.00
Q1 : Q3	0.00 : 0.95	0.00 : 0.56	0.00 : 0.20	0.00 : 0.67	0.00 : 1.08	0.00 : 0.00
Min : Max	0.0 : 3.0	0.0 : 3.5	0.0 : 0.2	0.0 : 2.1	0.0 : 1.2	0.0 : 0.8
Change from baseline						
Number	101	198	3	8	7	16
LS Mean (SE)[a]	-0.55 (0.06)	-0.62 (0.05)	-1.25 (0.51)	-1.05 (0.39)	0.13 (0.08)	-0.55 (0.05)
LS Mean Diff (95% CI)[a]	-	-0.07 (-0.21 to 0.06)	-	0.21 (-0.68 to 1.09)	-	-0.68 (-0.87 to -0.49)
p-value[a]		0.292		0.605		<0.001

[a]Derived from MMRM model with change from baseline in PM Asthma symptom score values up to Week 52 as the response variable, and treatment, baseline weight group, region, age, baseline eosinophil level, baseline FeNO level, baseline ICS dose level, visit, treatment by-visit interaction, baseline PM Asthma symptom score value and baseline-by-visit interaction as covariates.
[b]Similar model as that mentioned in the footnote [a] with subgroup and subgroup-by-treatment interaction as additional covariates.
Type 2 inflammatory asthma phenotype population is defined as the randomized patients with baseline blood eosinophils >= 0.15 Giga/L or baseline FeNO >= 20 ppb.
PGM=DEVOPS/SAR231893/EFC14153/CSR_RWE/REPORT/PGM/eff_mmrm_ger_subg_i_t.sas OUT=REPORT/OUTPUT/eff_mmrm_scpm_ger_race_i_t_x.rtf (21JUL2021 - 9:24)

Project Code / Study Number / Analysis: SAR231893 / EFC14153 / CSR_RWE

5 PM Asthma symptom score - ITT type 2 inflammatory asthma phenotype population

5.1 Summary of treatment effect on change from baseline at Week 52

5.1.3 By race (Caucasian/white, Black/of African descent, Other)

	Race					
	Caucasian/White		Black/of African descent		Other	
PM symptom score	**Placebo (N=102)**	**Dupilumab (N=208)**	**Placebo (N=5)**	**Dupilumab (N=9)**	**Placebo (N=7)**	**Dupilumab (N=19)**
Hedges'g (95% CI)	-	-0.130 (-0.374 to 0.113)	-	0.178 (-0.580 to 0.935)	-	-3.141 (-4.030 to -2.253)
p-value for heterogeneity[b]:						
Caucasian/White, Black/of African descent						0.647
Caucasian/White, Other						0.182
Black/of African descent, Other						0.127
overall						0.270

[a]Derived from MMRM model with change from baseline in PM Asthma symptom score values up to Week 52 as the response variable, and treatment, baseline weight group, region, age, baseline eosinophil level, baseline FeNO level, baseline ICS dose level, visit, treatment by-visit interaction, baseline PM Asthma symptom score value and baseline-by-visit interaction as covariates.

[b]Similar model as that mentioned in the footnote [a] with subgroup and subgroup-by-treatment interaction as additional covariates.

Type 2 inflammatory asthma phenotype population is defined as the randomized patients with baseline blood eosinophils >= 0.15 Giga/L or baseline FeNO >= 20 ppb.

PGM=DEVOPS/SAR231893/EFC14153/CSR_RWE/REPORT/PGM/eff_mmrm_ger_subg_i_t.sas OUT=REPORT/OUTPUT/eff_mmrm_scpm_ger_race_i_t_x.rtf (21JUL2021 - 9:24)

Project Code / Study Number / Analysis: SAR231893 / EFC14153 / CSR_RWE

5 PM Asthma symptom score - ITT type 2 inflammatory asthma phenotype population

5.1 Summary of treatment effect on change from baseline at Week 52

5.1.4 By baseline ICS dose level (Medium, High)

	Baseline ICS dose level			
	High		Medium	
PM symptom score	**Placebo (N=50)**	**Dupilumab (N=102)**	**Placebo (N=64)**	**Dupilumab (N=131)**
Baseline				
Value				
Number	50	102	64	131
Mean (SD)	1.02 (0.76)	0.90 (0.81)	0.85 (0.68)	0.94 (0.73)
Median	1.00	0.71	0.85	1.00
Q1 : Q3	0.29 : 1.67	0.20 : 1.43	0.29 : 1.29	0.33 : 1.29
Min : Max	0.0 : 2.6	0.0 : 3.0	0.0 : 2.4	0.0 : 3.0

[a]Derived from MMRM model with change from baseline in PM Asthma symptom score values up to Week 52 as the response variable, and treatment, baseline weight group, region, age, baseline eosinophil level, baseline FeNO level, visit, treatment by-visit interaction, baseline PM Asthma symptom score value and baseline-by-visit interaction as covariates.

[b]Similar model as that mentioned in the footnote [a] with subgroup and subgroup-by-treatment interaction as additional covariates.

Type 2 inflammatory asthma phenotype population is defined as the randomized patients with baseline blood eosinophils >= 0.15 Giga/L or baseline FeNO >= 20 ppb.

PGM=DEVOPS/SAR231893/EFC14153/CSR_RWE/REPORT/PGM/eff_mmrm_ger_subg_i_t.sas OUT=REPORT/OUTPUT/eff_mmrm_scpm_ger_ics_i_t_x.rtf (21JUL2021 - 9:39)

Project Code / Study Number / Analysis: SAR231893 / EFC14153 / CSR_RWE

5 PM Asthma symptom score - ITT type 2 inflammatory asthma phenotype population

5.1 Summary of treatment effect on change from baseline at Week 52

5.1.4 By baseline ICS dose level (Medium, High)

	Baseline ICS dose level			
	High		Medium	
PM symptom score	**Placebo (N=50)**	**Dupilumab (N=102)**	**Placebo (N=64)**	**Dupilumab (N=131)**
Week 52				
Value				
Number	49	97	62	124
Mean (SD)	0.45 (0.54)	0.33 (0.63)	0.40 (0.64)	0.34 (0.58)
Median	0.20	0.00	0.00	0.00
Q1 : Q3	0.00 : 1.00	0.00 : 0.33	0.00 : 0.92	0.00 : 0.53
Min : Max	0.0 : 2.0	0.0 : 3.0	0.0 : 3.0	0.0 : 3.5
Change from baseline				
Number	49	97	62	124
LS Mean (SE)[a]	-0.46 (0.08)	-0.58 (0.06)	-0.48 (0.08)	-0.60 (0.06)
LS Mean Diff (95% CI)[a]	-	-0.12 (-0.30 to 0.07)	-	-0.12 (-0.29 to 0.05)
p-value[a]		0.231		0.169
Hedges'g (95% CI)	-	-0.214 (-0.565 to 0.137)	-	-0.217 (-0.528 to 0.093)
p-value for heterogeneity[b]				0.958

[a]Derived from MMRM model with change from baseline in PM Asthma symptom score values up to Week 52 as the response variable, and treatment, baseline weight group, region, age, baseline eosinophil level, baseline FeNO level, visit, treatment by-visit interaction, baseline PM Asthma symptom score value and baseline-by-visit interaction as covariates.

[b]Similar model as that mentioned in the footnote [a] with subgroup and subgroup-by-treatment interaction as additional covariates.

Type 2 inflammatory asthma phenotype population is defined as the randomized patients with baseline blood eosinophils >= 0.15 Giga/L or baseline FeNO >= 20 ppb.

PGM=DEVOPS/SAR231893/EFC14153/CSR_RWE/REPORT/PGM/eff_mmrm_ger_subg_i_t.sas OUT=REPORT/OUTPUT/eff_mmrm_scpm_ger_ics_i_t_x.rtf (21JUL2021 - 9:39)

Project Code / Study Number / Analysis: SAR231893 / EFC14153 / CSR_RWE

5 PM Asthma symptom score - ITT type 2 inflammatory asthma phenotype population

5.1 Summary of treatment effect on change from baseline at Week 52

5.1.5 By baseline ICS dose level 2 (Medium, High)

	Baseline ICS dose level 2			
	High		Medium	
PM symptom score	**Placebo (N=95)**	**Dupilumab (N=200)**	**Placebo (N=19)**	**Dupilumab (N=36)**
Baseline				
Value				
Number	95	200	19	36
Mean (SD)	0.94 (0.72)	0.96 (0.77)	0.86 (0.76)	0.68 (0.68)
Median	0.86	1.00	1.00	0.57
Q1 : Q3	0.33 : 1.43	0.29 : 1.43	0.17 : 1.33	0.00 : 1.00
Min : Max	0.0 : 2.6	0.0 : 3.0	0.0 : 2.4	0.0 : 2.7

[a]Derived from MMRM model with change from baseline in PM Asthma symptom score values up to Week 52 as the response variable, and treatment, baseline weight group, region, age, baseline eosinophil level, baseline FeNO level, visit, treatment by-visit interaction, baseline PM Asthma symptom score value and baseline-by-visit interaction as covariates.

[b]Similar model as that mentioned in the footnote [a] with subgroup and subgroup-by-treatment interaction as additional covariates.

Type 2 inflammatory asthma phenotype population is defined as the randomized patients with baseline blood eosinophils >= 0.15 Giga/L or baseline FeNO >= 20 ppb.

PGM=DEVOPS/SAR231893/EFC14153/CSR_RWE/REPORT/PGM/eff_mmrm_ger_subg_i_t.sas OUT=REPORT/OUTPUT/eff_mmrm_scpm_ger_ics2_i_t_x.rtf (01SEP2021 - 17:05)

Project Code / Study Number / Analysis: SAR231893 / EFC14153 / CSR_RWE

5 PM Asthma symptom score - ITT type 2 inflammatory asthma phenotype population

5.1 Summary of treatment effect on change from baseline at Week 52

5.1.5 By baseline ICS dose level 2 (Medium, High)

	Baseline ICS dose level 2			
	High		Medium	
PM symptom score	**Placebo (N=95)**	**Dupilumab (N=200)**	**Placebo (N=19)**	**Dupilumab (N=36)**
Week 52				
Value				
Number	92	191	19	31
Mean (SD)	0.43 (0.60)	0.36 (0.63)	0.36 (0.60)	0.21 (0.45)
Median	0.02	0.00	0.00	0.00
Q1 : Q3	0.00 : 0.98	0.00 : 0.56	0.00 : 0.92	0.00 : 0.20
Min : Max	0.0 : 3.0	0.0 : 3.5	0.0 : 2.0	0.0 : 2.0
Change from baseline				
Number	92	191	19	31
LS Mean (SE)[a]	-0.48 (0.06)	-0.59 (0.05)	-0.50 (0.13)	-0.64 (0.10)
LS Mean Diff (95% CI)[a]	-	-0.11 (-0.25 to 0.03)	-	-0.14 (-0.44 to 0.17)
p-value[a]		0.131		0.363
Hedges'g (95% CI)	-	-0.193 (-0.443 to 0.058)	-	-0.280 (-0.894 to 0.335)
p-value for heterogeneity[b]				0.706

[a]Derived from MMRM model with change from baseline in PM Asthma symptom score values up to Week 52 as the response variable, and treatment, baseline weight group, region, age, baseline eosinophil level, baseline FeNO level, visit, treatment by-visit interaction, baseline PM Asthma symptom score value and baseline-by-visit interaction as covariates.

[b]Similar model as that mentioned in the footnote [a] with subgroup and subgroup-by-treatment interaction as additional covariates.

Type 2 inflammatory asthma phenotype population is defined as the randomized patients with baseline blood eosinophils >= 0.15 Giga/L or baseline FeNO >= 20 ppb.

PGM=DEVOPS/SAR231893/EFC14153/CSR_RWE/REPORT/PGM/eff_mmrm_ger_subg_i_t.sas OUT=REPORT/OUTPUT/eff_mmrm_scpm_ger_ics2_i_t_x.rtf (01SEP2021 - 17:05)

Project Code / Study Number / Analysis: SAR231893 / EFC14153 / CSR_RWE

5 PM Asthma symptom score - ITT type 2 inflammatory asthma phenotype population

5.1 Summary of treatment effect on change from baseline at Week 52

5.1.6 By baseline predicted FEV1 (<80%, >=80%)

	Baseline Predicted FEV1			
	<80%		>=80%	
PM symptom score	**Placebo (N=59)**	**Dupilumab (N=116)**	**Placebo (N=55)**	**Dupilumab (N=120)**
Baseline				
Value				
Number	59	116	55	120
Mean (SD)	0.88 (0.75)	0.97 (0.78)	0.97 (0.70)	0.87 (0.75)
Median	0.86	1.00	1.00	0.79
Q1 : Q3	0.20 : 1.43	0.29 : 1.43	0.40 : 1.43	0.29 : 1.14
Min : Max	0.0 : 2.6	0.0 : 3.0	0.0 : 2.4	0.0 : 3.0
Week 52				
Value				
Number	57	112	54	110
Mean (SD)	0.31 (0.49)	0.42 (0.63)	0.54 (0.68)	0.26 (0.58)
Median	0.00	0.00	0.17	0.00
Q1 : Q3	0.00 : 0.57	0.00 : 0.98	0.00 : 1.05	0.00 : 0.31
Min : Max	0.0 : 2.0	0.0 : 3.0	0.0 : 3.0	0.0 : 3.5

[a]Derived from MMRM model with change from baseline in PM Asthma symptom score values up to Week 52 as the response variable, and treatment, baseline weight group, region, age, baseline eosinophil level, baseline FeNO level, baseline ICS dose level, visit, treatment by-visit interaction, baseline PM Asthma symptom score value and baseline-by-visit interaction as covariates.

[b]Similar model as that mentioned in the footnote [a] with subgroup and subgroup-by-treatment interaction as additional covariates.

Type 2 inflammatory asthma phenotype population is defined as the randomized patients with baseline blood eosinophils >= 0.15 Giga/L or baseline FeNO >= 20 ppb.

PGM=DEVOPS/SAR231893/EFC14153/CSR_RWE/REPORT/PGM/eff_mmrm_ger_subg_i_t.sas OUT=REPORT/OUTPUT/eff_mmrm_scpm_ger_pfev1_i_t_x.rtf (21JUL2021 - 9:54)

Project Code / Study Number / Analysis: SAR231893 / EFC14153 / CSR_RWE

5 PM Asthma symptom score - ITT type 2 inflammatory asthma phenotype population

5.1 Summary of treatment effect on change from baseline at Week 52

5.1.6 By baseline predicted FEV1 (<80%, >=80%)

	Baseline Predicted FEV1			
	<80%		>=80%	
PM symptom score	**Placebo (N=59)**	**Dupilumab (N=116)**	**Placebo (N=55)**	**Dupilumab (N=120)**
Change from baseline				
Number	57	112	54	110
LS Mean (SE)[a]	-0.62 (0.08)	-0.57 (0.06)	-0.37 (0.08)	-0.61 (0.06)
LS Mean Diff (95% CI)[a]	-	0.05 (-0.13 to 0.22)	-	-0.24 (-0.42 to -0.06)
p-value[a]		0.578		0.010
Hedges'g (95% CI)	-	0.092 (-0.234 to 0.418)	-	-0.437 (-0.768 to -0.107)
p-value for heterogeneity[b]				0.022

[a]Derived from MMRM model with change from baseline in PM Asthma symptom score values up to Week 52 as the response variable, and treatment, baseline weight group, region, age, baseline eosinophil level, baseline FeNO level, baseline ICS dose level, visit, treatment by-visit interaction, baseline PM Asthma symptom score value and baseline-by-visit interaction as covariates.

[b]Similar model as that mentioned in the footnote [a] with subgroup and subgroup-by-treatment interaction as additional covariates.

Type 2 inflammatory asthma phenotype population is defined as the randomized patients with baseline blood eosinophils >= 0.15 Giga/L or baseline FeNO >= 20 ppb.

PGM=DEVOPS/SAR231893/EFC14153/CSR_RWE/REPORT/PGM/eff_mmrm_ger_subg_i_t.sas OUT=REPORT/OUTPUT/eff_mmrm_scpm_ger_pfev1_i_t_x.rtf (21JUL2021 - 9:54)

Project Code / Study Number / Analysis: SAR231893 / EFC14153 / CSR_RWE

5 PM Asthma symptom score - ITT type 2 inflammatory asthma phenotype population

5.1 Summary of treatment effect on change from baseline at Week 52

5.1.7 By baseline ACQ-7-IA (<=2, >2)

	Baseline ACQ-7-IA			
	<=2		>2	
PM symptom score	**Placebo (N=61)**	**Dupilumab (N=126)**	**Placebo (N=53)**	**Dupilumab (N=110)**
Baseline				
Value				
Number	61	126	53	110
Mean (SD)	0.75 (0.68)	0.68 (0.64)	1.13 (0.72)	1.19 (0.81)
Median	0.57	0.57	1.00	1.00
Q1 : Q3	0.14 : 1.29	0.00 : 1.00	0.57 : 1.71	0.57 : 1.86
Min : Max	0.0 : 2.1	0.0 : 3.0	0.0 : 2.6	0.0 : 3.0
Week 52				
Value				
Number	61	117	50	105
Mean (SD)	0.37 (0.60)	0.27 (0.55)	0.48 (0.59)	0.42 (0.67)
Median	0.00	0.00	0.04	0.04
Q1 : Q3	0.00 : 0.58	0.00 : 0.31	0.00 : 1.00	0.00 : 0.89
Min : Max	0.0 : 3.0	0.0 : 3.5	0.0 : 2.0	0.0 : 3.0

[a]Derived from MMRM model with change from baseline in PM Asthma symptom score values up to Week 52 as the response variable, and treatment, baseline weight group, region, age, baseline eosinophil level, baseline FeNO level, baseline ICS dose level, visit, treatment by-visit interaction, baseline PM Asthma symptom score value and baseline-by-visit interaction as covariates.

[b]Similar model as that mentioned in the footnote [a] with subgroup and subgroup-by-treatment interaction as additional covariates.

Type 2 inflammatory asthma phenotype population is defined as the randomized patients with baseline blood eosinophils >= 0.15 Giga/L or baseline FeNO >= 20 ppb.

PGM=DEVOPS/SAR231893/EFC14153/CSR_RWE/REPORT/PGM/eff_mmrm_ger_subg_i_t.sas OUT=REPORT/OUTPUT/eff_mmrm_scpm_ger_acq7_i_t_x.rtf (21JUL2021 - 10:09)

Project Code / Study Number / Analysis: SAR231893 / EFC14153 / CSR_RWE

5 PM Asthma symptom score - ITT type 2 inflammatory asthma phenotype population

5.1 Summary of treatment effect on change from baseline at Week 52

5.1.7 By baseline ACQ-7-IA (<=2, >2)

	Baseline ACQ-7-IA			
	<=2		**>2**	
PM symptom score	**Placebo (N=61)**	**Dupilumab (N=126)**	**Placebo (N=53)**	**Dupilumab (N=110)**
Change from baseline				
Number	61	117	50	105
LS Mean (SE)[a]	-0.35 (0.07)	-0.42 (0.05)	-0.70 (0.09)	-0.82 (0.07)
LS Mean Diff (95% CI)[a]	-	-0.07 (-0.23 to 0.09)	-	-0.11 (-0.32 to 0.09)
p-value[a]		0.394		0.275
Hedges'g (95% CI)	-	-0.136 (-0.449 to 0.178)	-	-0.191 (-0.535 to 0.153)
p-value for heterogeneity[b]				0.702

[a]Derived from MMRM model with change from baseline in PM Asthma symptom score values up to Week 52 as the response variable, and treatment, baseline weight group, region, age, baseline eosinophil level, baseline FeNO level, baseline ICS dose level, visit, treatment by-visit interaction, baseline PM Asthma symptom score value and baseline-by-visit interaction as covariates.

[b]Similar model as that mentioned in the footnote [a] with subgroup and subgroup-by-treatment interaction as additional covariates.

Type 2 inflammatory asthma phenotype population is defined as the randomized patients with baseline blood eosinophils >= 0.15 Giga/L or baseline FeNO >= 20 ppb.

PGM=DEVOPS/SAR231893/EFC14153/CSR_RWE/REPORT/PGM/eff_mmrm_ger_subg_i_t.sas OUT=REPORT/OUTPUT/eff_mmrm_scpm_ger_acq7_i_t_x.rtf (21JUL2021 - 10:09)

Project Code / Study Number / Analysis: SAR231893 / EFC14153 / CSR_RWE

5 PM Asthma symptom score - ITT type 2 inflammatory asthma phenotype population

5.1 Summary of treatment effect on change from baseline at Week 52

5.1.8 By baseline weight (<=30 kg, >30 kg)

	Baseline weight (kg)			
	<=30		>30	
PM symptom score	**Placebo (N=36)**	**Dupilumab (N=76)**	**Placebo (N=78)**	**Dupilumab (N=160)**
Baseline				
Value				
Number	36	76	78	160
Mean (SD)	1.07 (0.73)	0.95 (0.74)	0.86 (0.71)	0.90 (0.78)
Median	1.07	1.00	0.71	0.86
Q1 : Q3	0.41 : 1.64	0.38 : 1.36	0.17 : 1.29	0.29 : 1.29
Min : Max	0.0 : 2.6	0.0 : 3.0	0.0 : 2.4	0.0 : 3.0

[a]Derived from MMRM model with change from baseline in PM Asthma symptom score values up to Week 52 as the response variable, and treatment, region, age, baseline eosinophil level, baseline FeNO level, baseline ICS dose level, visit, treatment by-visit interaction, baseline PM Asthma symptom score value and baseline-by-visit interaction as covariates.
[b]Similar model as that mentioned in the footnote [a] with subgroup and subgroup-by-treatment interaction as additional covariates.
Type 2 inflammatory asthma phenotype population is defined as the randomized patients with baseline blood eosinophils >= 0.15 Giga/L or baseline FeNO >= 20 ppb.
PGM=DEVOPS/SAR231893/EFC14153/CSR_RWE/REPORT/PGM/eff_mmrm_ger_subg_i_t.sas OUT=REPORT/OUTPUT/eff_mmrm_scpm_ger_wgt_i_t_x.rtf (21JUL2021 - 10:24)

Project Code / Study Number / Analysis: SAR231893 / EFC14153 / CSR_RWE

5 PM Asthma symptom score - ITT type 2 inflammatory asthma phenotype population

5.1 Summary of treatment effect on change from baseline at Week 52

5.1.8 By baseline weight (<=30 kg, >30 kg)

	Baseline weight (kg)			
	<=30		>30	
PM symptom score	**Placebo (N=36)**	**Dupilumab (N=76)**	**Placebo (N=78)**	**Dupilumab (N=160)**
Week 52				
Value				
Number	35	69	76	153
Mean (SD)	0.43 (0.57)	0.33 (0.62)	0.42 (0.61)	0.35 (0.61)
Median	0.00	0.00	0.02	0.00
Q1 : Q3	0.00 : 1.00	0.00 : 0.37	0.00 : 0.85	0.00 : 0.46
Min : Max	0.0 : 1.8	0.0 : 3.0	0.0 : 3.0	0.0 : 3.5
Change from baseline				
Number	35	69	76	153
LS Mean (SE)[a]	-0.62 (0.10)	-0.67 (0.07)	-0.44 (0.07)	-0.54 (0.05)
LS Mean Diff (95% CI)[a]	-	-0.05 (-0.28 to 0.18)	-	-0.10 (-0.25 to 0.05)
p-value[a]		0.654		0.201
Hedges'g (95% CI)	-	-0.094 (-0.507 to 0.320)	-	-0.182 (-0.461 to 0.098)
p-value for heterogeneity[b]				0.819

[a]Derived from MMRM model with change from baseline in PM Asthma symptom score values up to Week 52 as the response variable, and treatment, region, age, baseline eosinophil level, baseline FeNO level, baseline ICS dose level, visit, treatment by-visit interaction, baseline PM Asthma symptom score value and baseline-by-visit interaction as covariates.
[b]Similar model as that mentioned in the footnote [a] with subgroup and subgroup-by-treatment interaction as additional covariates.
Type 2 inflammatory asthma phenotype population is defined as the randomized patients with baseline blood eosinophils >= 0.15 Giga/L or baseline FeNO >= 20 ppb.
PGM=DEVOPS/SAR231893/EFC14153/CSR_RWE/REPORT/PGM/eff_mmrm_ger_subg_i_t.sas OUT=REPORT/OUTPUT/eff_mmrm_scpm_ger_wgt_i_t_x.rtf (21JUL2021 - 10:24)

Project Code / Study Number / Analysis: SAR231893 / EFC14153 / CSR_RWE

5 PM Asthma symptom score - ITT type 2 inflammatory asthma phenotype population

5.1 Summary of treatment effect on change from baseline at Week 52

5.1.9 By atopic medical condition (Yes, No)

	Atopic medical condition			
	Yes		No	
PM symptom score	**Placebo (N=103)**	**Dupilumab (N=227)**	**Placebo (N=11)**	**Dupilumab (N=9)**
Baseline				
Value				
Number	103	227	11	9
Mean (SD)	0.96 (0.73)	0.92 (0.78)	0.60 (0.56)	1.00 (0.43)
Median	1.00	0.86	0.43	1.00
Q1 : Q3	0.29 : 1.43	0.29 : 1.33	0.00 : 1.14	1.00 : 1.14
Min : Max	0.0 : 2.6	0.0 : 3.0	0.0 : 1.4	0.0 : 1.6

[a]Derived from MMRM model with change from baseline in PM Asthma symptom score values up to Week 52 as the response variable, and treatment, baseline weight group, region, age, baseline eosinophil level, baseline FeNO level, baseline ICS dose level, visit, treatment by-visit interaction, baseline PM Asthma symptom score value and baseline-by-visit interaction as covariates.
[b]Similar model as that mentioned in the footnote [a] with subgroup and subgroup-by-treatment interaction as additional covariates.
Type 2 inflammatory asthma phenotype population is defined as the randomized patients with baseline blood eosinophils >= 0.15 Giga/L or baseline FeNO >= 20 ppb.
PGM=DEVOPS/SAR231893/EFC14153/CSR_RWE/REPORT/PGM/eff_mmrm_ger_subg_i_t.sas OUT=REPORT/OUTPUT/eff_mmrm_scpm_ger_amc_i_t_x.rtf (21JUL2021 - 10:39)

Project Code / Study Number / Analysis: SAR231893 / EFC14153 / CSR_RWE

5 PM Asthma symptom score - ITT type 2 inflammatory asthma phenotype population

5.1 Summary of treatment effect on change from baseline at Week 52

5.1.9 By atopic medical condition (Yes, No)

	Atopic medical condition			
	Yes		No	
PM symptom score	**Placebo (N=103)**	**Dupilumab (N=227)**	**Placebo (N=11)**	**Dupilumab (N=9)**
Week 52				
Value				
Number	100	213	11	9
Mean (SD)	0.44 (0.61)	0.35 (0.62)	0.23 (0.42)	0.23 (0.44)
Median	0.02	0.00	0.00	0.00
Q1 : Q3	0.00 : 0.98	0.00 : 0.46	0.00 : 0.39	0.00 : 0.07
Min : Max	0.0 : 3.0	0.0 : 3.5	0.0 : 1.1	0.0 : 1.0
Change from baseline				
Number	100	213	11	9
LS Mean (SE)[a]	-0.49 (0.06)	-0.60 (0.04)	-0.38 (0.15)	-0.86 (0.19)
LS Mean Diff (95% CI)[a]	-	-0.11 (-0.24 to 0.03)	-	-0.48 (-0.92 to -0.05)
p-value[a]		0.118		0.031
Hedges'g (95% CI)	-	-0.192 (-0.433 to 0.049)	-	-0.870 (-1.651 to -0.089)
p-value for heterogeneity[b]				0.951

[a]Derived from MMRM model with change from baseline in PM Asthma symptom score values up to Week 52 as the response variable, and treatment, baseline weight group, region, age, baseline eosinophil level, baseline FeNO level, baseline ICS dose level, visit, treatment by-visit interaction, baseline PM Asthma symptom score value and baseline-by-visit interaction as covariates.

[b]Similar model as that mentioned in the footnote [a] with subgroup and subgroup-by-treatment interaction as additional covariates.

Type 2 inflammatory asthma phenotype population is defined as the randomized patients with baseline blood eosinophils >= 0.15 Giga/L or baseline FeNO >= 20 ppb.

PGM=DEVOPS/SAR231893/EFC14153/CSR_RWE/REPORT/PGM/eff_mmrm_ger_subg_i_t.sas OUT=REPORT/OUTPUT/eff_mmrm_scpm_ger_amc_i_t_x.rtf (21JUL2021 - 10:39)

Project Code / Study Number / Analysis: SAR231893 / EFC14153 / CSR_RWE

5 PM Asthma symptom score - ITT type 2 inflammatory asthma phenotype population

5.1 Summary of treatment effect on change from baseline at Week 52

5.1.10 By baseline total IgE (<median, >= median)

	Baseline Total IgE (IU/mL)			
	<median		>=median	
PM symptom score	**Placebo (N=66)**	**Dupilumab (N=105)**	**Placebo (N=47)**	**Dupilumab (N=125)**
Baseline				
Value				
Number	66	105	47	125
Mean (SD)	0.88 (0.68)	0.87 (0.74)	0.96 (0.77)	0.96 (0.78)
Median	0.93	0.86	0.86	1.00
Q1 : Q3	0.29 : 1.43	0.29 : 1.20	0.29 : 1.43	0.29 : 1.43
Min : Max	0.0 : 2.3	0.0 : 3.0	0.0 : 2.6	0.0 : 3.0

[a]Derived from MMRM model with change from baseline in PM Asthma symptom score values up to Week 52 as the response variable, and treatment, baseline weight group, region, age, baseline eosinophil level, baseline FeNO level, baseline ICS dose level, visit, treatment by-visit interaction, baseline PM Asthma symptom score value and baseline-by-visit interaction as covariates.
[b]Similar model as that mentioned in the footnote [a] with subgroup and subgroup-by-treatment interaction as additional covariates.
Type 2 inflammatory asthma phenotype population is defined as the randomized patients with baseline blood eosinophils >= 0.15 Giga/L or baseline FeNO >= 20 ppb.
PGM=DEVOPS/SAR231893/EFC14153/CSR_RWE/REPORT/PGM/eff_mmrm_ger_subg_i_t.sas OUT=REPORT/OUTPUT/eff_mmrm_scpm_ger_igem_i_t_x.rtf (21JUL2021 - 10:54)

Project Code / Study Number / Analysis: SAR231893 / EFC14153 / CSR_RWE

5 PM Asthma symptom score - ITT type 2 inflammatory asthma phenotype population

5.1 Summary of treatment effect on change from baseline at Week 52

5.1.10 By baseline total IgE (<median, >= median)

	Baseline Total IgE (IU/mL)			
	<median		>=median	
PM symptom score	**Placebo (N=66)**	**Dupilumab (N=105)**	**Placebo (N=47)**	**Dupilumab (N=125)**
Week 52				
Value				
Number	65	101	45	118
Mean (SD)	0.36 (0.53)	0.35 (0.62)	0.53 (0.68)	0.35 (0.61)
Median	0.00	0.00	0.20	0.00
Q1 : Q3	0.00 : 0.70	0.00 : 0.67	0.00 : 1.00	0.00 : 0.33
Min : Max	0.0 : 2.0	0.0 : 3.5	0.0 : 3.0	0.0 : 3.0
Change from baseline				
Number	65	101	45	118
LS Mean (SE)[a]	-0.49 (0.07)	-0.52 (0.06)	-0.36 (0.09)	-0.56 (0.06)
LS Mean Diff (95% CI)[a]	-	-0.03 (-0.20 to 0.14)	-	-0.20 (-0.39 to -0.01)
p-value[a]		0.758		0.038
Hedges'g (95% CI)	-	-0.050 (-0.367 to 0.268)	-	-0.367 (-0.712 to -0.021)
p-value for heterogeneity[b]				0.148

[a]Derived from MMRM model with change from baseline in PM Asthma symptom score values up to Week 52 as the response variable, and treatment, baseline weight group, region, age, baseline eosinophil level, baseline FeNO level, baseline ICS dose level, visit, treatment by-visit interaction, baseline PM Asthma symptom score value and baseline-by-visit interaction as covariates.

[b]Similar model as that mentioned in the footnote [a] with subgroup and subgroup-by-treatment interaction as additional covariates.

Type 2 inflammatory asthma phenotype population is defined as the randomized patients with baseline blood eosinophils >= 0.15 Giga/L or baseline FeNO >= 20 ppb.

PGM=DEVOPS/SAR231893/EFC14153/CSR_RWE/REPORT/PGM/eff_mmrm_ger_subg_i_t.sas OUT=REPORT/OUTPUT/eff_mmrm_scpm_ger_igem_i_t_x.rtf (21JUL2021 - 10:54)

Project Code / Study Number / Analysis: SAR231893 / EFC14153 / CSR_RWE

5 PM Asthma symptom score - ITT type 2 inflammatory asthma phenotype population

5.1 Summary of treatment effect on change from baseline at Week 52

5.1.11 By baseline total IgE (<100 IU/ml, >= 100 IU/ml)

	Baseline Total IgE (IU/mL)			
	< 100		>= 100	
PM symptom score	**Placebo (N=22)**	**Dupilumab (N=29)**	**Placebo (N=91)**	**Dupilumab (N=201)**
Baseline				
Value				
Number	22	29	91	201
Mean (SD)	0.70 (0.69)	0.88 (0.57)	0.97 (0.72)	0.92 (0.78)
Median	0.43	1.00	1.00	0.86
Q1 : Q3	0.00 : 1.33	0.33 : 1.14	0.40 : 1.43	0.29 : 1.43
Min : Max	0.0 : 2.0	0.0 : 2.1	0.0 : 2.6	0.0 : 3.0

[a]Derived from MMRM model with change from baseline in PM Asthma symptom score values up to Week 52 as the response variable, and treatment, baseline weight group, region, age, baseline eosinophil level, baseline FeNO level, baseline ICS dose level, visit, treatment by-visit interaction, baseline PM Asthma symptom score value and baseline-by-visit interaction as covariates.
[b]Similar model as that mentioned in the footnote [a] with subgroup and subgroup-by-treatment interaction as additional covariates.
Type 2 inflammatory asthma phenotype population is defined as the randomized patients with baseline blood eosinophils >= 0.15 Giga/L or baseline FeNO >= 20 ppb.
PGM=DEVOPS/SAR231893/EFC14153/CSR_RWE/REPORT/PGM/eff_mmrm_ger_subg_i_t.sas OUT=REPORT/OUTPUT/eff_mmrm_scpm_ger_ige_i_t_x.rtf (21JUL2021 - 11:08)

Project Code / Study Number / Analysis: SAR231893 / EFC14153 / CSR_RWE

5 PM Asthma symptom score - ITT type 2 inflammatory asthma phenotype population

5.1 Summary of treatment effect on change from baseline at Week 52

5.1.11 By baseline total IgE (<100 IU/ml, >= 100 IU/ml)

	Baseline Total IgE (IU/mL)			
	< 100		>= 100	
PM symptom score	**Placebo (N=22)**	**Dupilumab (N=29)**	**Placebo (N=91)**	**Dupilumab (N=201)**
Week 52				
Value				
Number	22	29	88	190
Mean (SD)	0.37 (0.53)	0.51 (0.79)	0.44 (0.62)	0.32 (0.58)
Median	0.00	0.00	0.04	0.00
Q1 : Q3	0.00 : 0.95	0.00 : 1.00	0.00 : 0.98	0.00 : 0.33
Min : Max	0.0 : 1.8	0.0 : 3.5	0.0 : 3.0	0.0 : 3.0
Change from baseline				
Number	22	29	88	190
LS Mean (SE)[a]	-0.30 (0.16)	-0.15 (0.15)	-0.50 (0.06)	-0.62 (0.04)
LS Mean Diff (95% CI)[a]	-	0.15 (-0.25 to 0.55)	-	-0.12 (-0.26 to 0.01)
p-value[a]		0.450		0.073
Hedges'g (95% CI)	-	0.221 (-0.365 to 0.807)	-	-0.234 (-0.490 to 0.022)
p-value for heterogeneity[b]				0.208

[a]Derived from MMRM model with change from baseline in PM Asthma symptom score values up to Week 52 as the response variable, and treatment, baseline weight group, region, age, baseline eosinophil level, baseline FeNO level, baseline ICS dose level, visit, treatment by-visit interaction, baseline PM Asthma symptom score value and baseline-by-visit interaction as covariates.
[b]Similar model as that mentioned in the footnote [a] with subgroup and subgroup-by-treatment interaction as additional covariates.
Type 2 inflammatory asthma phenotype population is defined as the randomized patients with baseline blood eosinophils >= 0.15 Giga/L or baseline FeNO >= 20 ppb.
PGM=DEVOPS/SAR231893/EFC14153/CSR_RWE/REPORT/PGM/eff_mmrm_ger_subg_i_t.sas OUT=REPORT/OUTPUT/eff_mmrm_scpm_ger_ige_i_t_x.rtf (21JUL2021 - 11:08)

Project Code / Study Number / Analysis: SAR231893 / EFC14153 / CSR_RWE

5 PM Asthma symptom score - ITT type 2 inflammatory asthma phenotype population

5.1 Summary of treatment effect on change from baseline at Week 52

5.1.12 By age at onset of asthma (0-2, 3-5, >=6 years)

	Age of onset of asthma (years)					
	0-2		3-5		>= 6	
PM symptom score	**Placebo (N=40)**	**Dupilumab (N=105)**	**Placebo (N=39)**	**Dupilumab (N=86)**	**Placebo (N=35)**	**Dupilumab (N=45)**
Baseline						
Value						
Number	40	105	39	86	35	45
Mean (SD)	1.02 (0.72)	0.88 (0.71)	0.92 (0.67)	0.93 (0.76)	0.83 (0.78)	0.99 (0.91)
Median	0.86	1.00	1.00	1.00	0.57	0.86
Q1 : Q3	0.45 : 1.50	0.29 : 1.14	0.43 : 1.43	0.29 : 1.43	0.00 : 1.43	0.17 : 1.57
Min : Max	0.0 : 2.6	0.0 : 3.0	0.0 : 2.4	0.0 : 2.8	0.0 : 2.3	0.0 : 3.0

[a]Derived from MMRM model with change from baseline in PM Asthma symptom score values up to Week 52 as the response variable, and treatment, baseline weight group, region, age, baseline eosinophil level, baseline FeNO level, baseline ICS dose level, visit, treatment by-visit interaction, baseline PM Asthma symptom score value and baseline-by-visit interaction as covariates.
[b]Similar model as that mentioned in the footnote [a] with subgroup and subgroup-by-treatment interaction as additional covariates.
Type 2 inflammatory asthma phenotype population is defined as the randomized patients with baseline blood eosinophils >= 0.15 Giga/L or baseline FeNO >= 20 ppb.
PGM=DEVOPS/SAR231893/EFC14153/CSR_RWE/REPORT/PGM/eff_mmrm_ger_subg_i_t.sas OUT=REPORT/OUTPUT/eff_mmrm_scpm_ger_onsa_i_t_x.rtf (10AUG2021 - 9:34)

Project Code / Study Number / Analysis: SAR231893 / EFC14153 / CSR_RWE

5 PM Asthma symptom score - ITT type 2 inflammatory asthma phenotype population

5.1 Summary of treatment effect on change from baseline at Week 52

5.1.12 By age at onset of asthma (0-2, 3-5, >=6 years)

	Age of onset of asthma (years)					
	0-2		3-5		>= 6	
PM symptom score	**Placebo (N=40)**	**Dupilumab (N=105)**	**Placebo (N=39)**	**Dupilumab (N=86)**	**Placebo (N=35)**	**Dupilumab (N=45)**
Week 52						
Value						
Number	38	100	38	79	35	43
Mean (SD)	0.44 (0.59)	0.33 (0.59)	0.42 (0.64)	0.33 (0.62)	0.41 (0.57)	0.39 (0.66)
Median	0.02	0.00	0.00	0.00	0.00	0.00
Q1 : Q3	0.00 : 1.00	0.00 : 0.50	0.00 : 0.95	0.00 : 0.33	0.00 : 0.92	0.00 : 0.62
Min : Max	0.0 : 1.9	0.0 : 3.0	0.0 : 3.0	0.0 : 3.5	0.0 : 2.0	0.0 : 3.0
Change from baseline						
Number	38	100	38	79	35	43
LS Mean (SE)[a]	-0.45 (0.09)	-0.52 (0.06)	-0.53 (0.10)	-0.62 (0.07)	-0.65 (0.10)	-0.73 (0.10)
LS Mean Diff (95% CI)[a]	-	-0.08 (-0.28 to 0.12)	-	-0.09 (-0.33 to 0.14)	-	-0.08 (-0.32 to 0.15)
p-value[a]		0.446		0.435		0.483

[a]Derived from MMRM model with change from baseline in PM Asthma symptom score values up to Week 52 as the response variable, and treatment, baseline weight group, region, age, baseline eosinophil level, baseline FeNO level, baseline ICS dose level, visit, treatment by-visit interaction, baseline PM Asthma symptom score value and baseline-by-visit interaction as covariates.
[b]Similar model as that mentioned in the footnote [a] with subgroup and subgroup-by-treatment interaction as additional covariates.
Type 2 inflammatory asthma phenotype population is defined as the randomized patients with baseline blood eosinophils >= 0.15 Giga/L or baseline FeNO >= 20 ppb.
PGM=DEVOPS/SAR231893/EFC14153/CSR_RWE/REPORT/PGM/eff_mmrm_ger_subg_i_t.sas OUT=REPORT/OUTPUT/eff_mmrm_scpm_ger_onsa_i_t_x.rtf (10AUG2021 - 9:34)

Project Code / Study Number / Analysis: SAR231893 / EFC14153 / CSR_RWE

5 PM Asthma symptom score - ITT type 2 inflammatory asthma phenotype population

5.1 Summary of treatment effect on change from baseline at Week 52

5.1.12 By age at onset of asthma (0-2, 3-5, >=6 years)

	Age of onset of asthma (years)					
	0-2		3-5		>= 6	
PM symptom score	**Placebo (N=40)**	**Dupilumab (N=105)**	**Placebo (N=39)**	**Dupilumab (N=86)**	**Placebo (N=35)**	**Dupilumab (N=45)**
Hedges'g (95% CI)	-	-0.146 (-0.524 to 0.232)	-	-0.155 (-0.546 to 0.236)	-	-0.165 (-0.632 to 0.302)
p-value for heterogeneity[b]:						
0-2, 3-5						0.967
0-2, >= 6						0.901
3-5, >= 6						0.931
overall						0.992

[a]Derived from MMRM model with change from baseline in PM Asthma symptom score values up to Week 52 as the response variable, and treatment, baseline weight group, region, age, baseline eosinophil level, baseline FeNO level, baseline ICS dose level, visit, treatment by-visit interaction, baseline PM Asthma symptom score value and baseline-by-visit interaction as covariates.

[b]Similar model as that mentioned in the footnote [a] with subgroup and subgroup-by-treatment interaction as additional covariates.

Type 2 inflammatory asthma phenotype population is defined as the randomized patients with baseline blood eosinophils >= 0.15 Giga/L or baseline FeNO >= 20 ppb.

PGM=DEVOPS/SAR231893/EFC14153/CSR_RWE/REPORT/PGM/eff_mmrm_ger_subg_i_t.sas OUT=REPORT/OUTPUT/eff_mmrm_scpm_ger_onsa_i_t_x.rtf (10AUG2021 - 9:34)

Project Code / Study Number / Analysis: SAR231893 / EFC14153 / CSR_RWE

5 PM Asthma symptom score - ITT type 2 inflammatory asthma phenotype population

5.1 Summary of treatment effect on change from baseline at Week 52

5.1.13 By number of severe asthma exacerbation prior to the study (<=1, 2, >2)

	Number of severe asthma exacerbation prior to the study					
	<=1		2		>2	
PM symptom score	**Placebo (N=47)**	**Dupilumab (N=85)**	**Placebo (N=32)**	**Dupilumab (N=75)**	**Placebo (N=35)**	**Dupilumab (N=76)**
Baseline						
Value						
Number	47	85	32	75	35	76
Mean (SD)	0.83 (0.70)	0.84 (0.69)	0.88 (0.75)	1.15 (0.88)	1.10 (0.71)	0.78 (0.68)
Median	0.71	0.71	0.79	1.00	1.00	0.71
Q1 : Q3	0.14 : 1.29	0.29 : 1.29	0.21 : 1.50	0.43 : 1.86	0.57 : 1.43	0.18 : 1.14
Min : Max	0.0 : 2.1	0.0 : 3.0	0.0 : 2.4	0.0 : 3.0	0.0 : 2.6	0.0 : 2.5

[a]Derived from MMRM model with change from baseline in PM Asthma symptom score values up to Week 52 as the response variable, and treatment, baseline weight group, region, age, baseline eosinophil level, baseline FeNO level, baseline ICS dose level, visit, treatment by-visit interaction, baseline PM Asthma symptom score value and baseline-by-visit interaction as covariates.
[b]Similar model as that mentioned in the footnote [a] with subgroup and subgroup-by-treatment interaction as additional covariates.
Type 2 inflammatory asthma phenotype population is defined as the randomized patients with baseline blood eosinophils >= 0.15 Giga/L or baseline FeNO >= 20 ppb.
PGM=DEVOPS/SAR231893/EFC14153/CSR_RWE/REPORT/PGM/eff_mmrm_ger_subg_i_t.sas OUT=REPORT/OUTPUT/eff_mmrm_scpm_ger_exa_i_t_x.rtf (21JUL2021 - 11:49)

Project Code / Study Number / Analysis: SAR231893 / EFC14153 / CSR_RWE

5 PM Asthma symptom score - ITT type 2 inflammatory asthma phenotype population

5.1 Summary of treatment effect on change from baseline at Week 52

5.1.13 By number of severe asthma exacerbation prior to the study (<=1, 2, >2)

	Number of severe asthma exacerbation prior to the study					
	<=1		2		>2	
PM symptom score	**Placebo (N=47)**	**Dupilumab (N=85)**	**Placebo (N=32)**	**Dupilumab (N=75)**	**Placebo (N=35)**	**Dupilumab (N=76)**
Week 52						
Value						
Number	45	82	32	71	34	69
Mean (SD)	0.33 (0.52)	0.35 (0.54)	0.38 (0.54)	0.47 (0.71)	0.59 (0.71)	0.20 (0.55)
Median	0.00	0.00	0.00	0.00	0.35	0.00
Q1 : Q3	0.00 : 0.58	0.00 : 0.67	0.00 : 0.94	0.00 : 1.00	0.00 : 1.00	0.00 : 0.06
Min : Max	0.0 : 1.9	0.0 : 2.1	0.0 : 2.0	0.0 : 3.0	0.0 : 3.0	0.0 : 3.5
Change from baseline						
Number	45	82	32	71	34	69
LS Mean (SE)[a]	-0.51 (0.08)	-0.54 (0.06)	-0.70 (0.11)	-0.67 (0.08)	-0.30 (0.12)	-0.65 (0.08)
LS Mean Diff (95% CI)[a]	-	-0.03 (-0.21 to 0.15)	-	0.03 (-0.24 to 0.29)	-	-0.35 (-0.60 to -0.10)
p-value[a]		0.749		0.824		0.007

[a]Derived from MMRM model with change from baseline in PM Asthma symptom score values up to Week 52 as the response variable, and treatment, baseline weight group, region, age, baseline eosinophil level, baseline FeNO level, baseline ICS dose level, visit, treatment by-visit interaction, baseline PM Asthma symptom score value and baseline-by-visit interaction as covariates.
[b]Similar model as that mentioned in the footnote [a] with subgroup and subgroup-by-treatment interaction as additional covariates.
Type 2 inflammatory asthma phenotype population is defined as the randomized patients with baseline blood eosinophils >= 0.15 Giga/L or baseline FeNO >= 20 ppb.
PGM=DEVOPS/SAR231893/EFC14153/CSR_RWE/REPORT/PGM/eff_mmrm_ger_subg_i_t.sas OUT=REPORT/OUTPUT/eff_mmrm_scpm_ger_exa_i_t_x.rtf (21JUL2021 - 11:49)

Project Code / Study Number / Analysis: SAR231893 / EFC14153 / CSR_RWE

5 PM Asthma symptom score - ITT type 2 inflammatory asthma phenotype population

5.1 Summary of treatment effect on change from baseline at Week 52

5.1.13 By number of severe asthma exacerbation prior to the study (<=1, 2, >2)

	Number of severe asthma exacerbation prior to the study					
	<=1		**2**		**>2**	
PM symptom score	**Placebo (N=47)**	**Dupilumab (N=85)**	**Placebo (N=32)**	**Dupilumab (N=75)**	**Placebo (N=35)**	**Dupilumab (N=76)**
Hedges'g (95% CI)	-	-0.060 (-0.429 to 0.310)	-	0.049 (-0.390 to 0.489)	-	-0.601 (-1.035 to -0.167)
p-value for heterogeneity[b]:						
<=1, 2						0.950
<=1, >2						0.029
2, >2						0.050
overall						0.059

[a]Derived from MMRM model with change from baseline in PM Asthma symptom score values up to Week 52 as the response variable, and treatment, baseline weight group, region, age, baseline eosinophil level, baseline FeNO level, baseline ICS dose level, visit, treatment by-visit interaction, baseline PM Asthma symptom score value and baseline-by-visit interaction as covariates.

[b]Similar model as that mentioned in the footnote [a] with subgroup and subgroup-by-treatment interaction as additional covariates.

Type 2 inflammatory asthma phenotype population is defined as the randomized patients with baseline blood eosinophils >= 0.15 Giga/L or baseline FeNO >= 20 ppb.

PGM=DEVOPS/SAR231893/EFC14153/CSR_RWE/REPORT/PGM/eff_mmrm_ger_subg_i_t.sas OUT=REPORT/OUTPUT/eff_mmrm_scpm_ger_exa_i_t_x.rtf (21JUL2021 - 11:49)

Project Code / Study Number / Analysis: SAR231893 / EFC14153 / CSR_RWE

6 Number of nocturnal awakenings - ITT type 2 inflammatory asthma phenotype population

6.1 Summary of treatment effect on change from baseline at Week 52

Number of nocturnal awakenings	**Placebo (N=114)**	**Dupilumab (N=236)**
Baseline		
Value		
Number	114	236
Mean (SD)	0.32 (0.45)	0.39 (0.68)
Median	0.14	0.14
Q1 : Q3	0.00 : 0.50	0.00 : 0.43
Min : Max	0.0 : 2.5	0.0 : 4.4
Week 52		
Value		
Number	111	222
Mean (SD)	0.11 (0.31)	0.07 (0.26)
Median	0.00	0.00
Q1 : Q3	0.00 : 0.04	0.00 : 0.00
Min : Max	0.0 : 2.1	0.0 : 2.0
Change from baseline		
Number	111	222
LS Mean (SE)[a]	-0.26 (0.03)	-0.32 (0.02)

[a]Derived from MMRM model with change from baseline in Number of nocturnal awakenings values up to Week 52 as the response variable, and treatment, baseline weight group, region, age, baseline eosinophil level, baseline FeNO level, baseline ICS dose level, visit, treatment by-visit interaction, baseline Number of nocturnal awakenings value and baseline-by-visit interaction as covariates.
Type 2 inflammatory asthma phenotype population is defined as the randomized patients with baseline blood eosinophils >= 0.15 Giga/L or baseline FeNO >= 20 ppb.
PGM=DEVOPS/SAR231893/EFC14153/CSR_RWE/REPORT/PGM/eff_mmrm_ger_i_t.sas OUT=REPORT/OUTPUT/eff_mmrm_awak_ger_i_t_x.rtf (22JUL2021 - 7:59)

Project Code / Study Number / Analysis: SAR231893 / EFC14153 / CSR_RWE

6 Number of nocturnal awakenings - ITT type 2 inflammatory asthma phenotype population

6.1 Summary of treatment effect on change from baseline at Week 52

Number of nocturnal awakenings	**Placebo (N=114)**	**Dupilumab (N=236)**
LS Mean Diff (95% CI)[a]	-	-0.06 (-0.12 to -0.00)
Hedges'g (95% CI)	-	-0.237 (-0.469 to -0.006)
p-value[a]		0.044

[a]Derived from MMRM model with change from baseline in Number of nocturnal awakenings values up to Week 52 as the response variable, and treatment, baseline weight group, region, age, baseline eosinophil level, baseline FeNO level, baseline ICS dose level, visit, treatment by-visit interaction, baseline Number of nocturnal awakenings value and baseline-by-visit interaction as covariates.
Type 2 inflammatory asthma phenotype population is defined as the randomized patients with baseline blood eosinophils >= 0.15 Giga/L or baseline FeNO >= 20 ppb.
PGM=DEVOPS/SAR231893/EFC14153/CSR_RWE/REPORT/PGM/eff_mmrm_ger_i_t.sas OUT=REPORT/OUTPUT/eff_mmrm_awak_ger_i_t_x.rtf (22JUL2021 - 7:59)

Project Code / Study Number / Analysis: SAR231893 / EFC14153 / CSR_RWE

6 Number of nocturnal awakenings - ITT type 2 inflammatory asthma phenotype population

6.1 Summary of treatment effect on change from baseline at Week 52

6.1.1 By gender (Male, Female)

	Gender			
	Male		Female	
Number of nocturnal awakenings	**Placebo (N=78)**	**Dupilumab (N=152)**	**Placebo (N=36)**	**Dupilumab (N=84)**
Baseline				
Value				
Number	78	152	36	84
Mean (SD)	0.34 (0.49)	0.37 (0.65)	0.29 (0.36)	0.42 (0.74)
Median	0.14	0.14	0.17	0.14
Q1 : Q3	0.00 : 0.57	0.00 : 0.46	0.00 : 0.50	0.00 : 0.43
Min : Max	0.0 : 2.5	0.0 : 4.4	0.0 : 1.3	0.0 : 3.9

[a]Derived from MMRM model with change from baseline in Number of nocturnal awakenings values up to Week 52 as the response variable, and treatment, baseline weight group, region, age, baseline eosinophil level, baseline FeNO level, baseline ICS dose level, visit, treatment by-visit interaction, baseline Number of nocturnal awakenings value and baseline-by-visit interaction as covariates.
[b]Similar model as that mentioned in the footnote [a] with subgroup and subgroup-by-treatment interaction as additional covariates.
Type 2 inflammatory asthma phenotype population is defined as the randomized patients with baseline blood eosinophils >= 0.15 Giga/L or baseline FeNO >= 20 ppb.
PGM=DEVOPS/SAR231893/EFC14153/CSR_RWE/REPORT/PGM/eff_mmrm_ger_subg_i_t.sas OUT=REPORT/OUTPUT/eff_mmrm_awak_ger_sex_i_t_x.rtf (21JUL2021 - 8:44)

Project Code / Study Number / Analysis: SAR231893 / EFC14153 / CSR_RWE

6 Number of nocturnal awakenings - ITT type 2 inflammatory asthma phenotype population

6.1 Summary of treatment effect on change from baseline at Week 52

6.1.1 By gender (Male, Female)

	Gender			
	Male		Female	
Number of nocturnal awakenings	**Placebo (N=78)**	**Dupilumab (N=152)**	**Placebo (N=36)**	**Dupilumab (N=84)**
Week 52				
Value				
Number	76	143	35	79
Mean (SD)	0.14 (0.36)	0.06 (0.21)	0.03 (0.12)	0.08 (0.33)
Median	0.00	0.00	0.00	0.00
Q1 : Q3	0.00 : 0.08	0.00 : 0.00	0.00 : 0.00	0.00 : 0.00
Min : Max	0.0 : 2.1	0.0 : 1.0	0.0 : 0.7	0.0 : 2.0
Change from baseline				
Number	76	143	35	79
LS Mean (SE)[a]	-0.23 (0.03)	-0.33 (0.02)	-0.34 (0.05)	-0.31 (0.03)
LS Mean Diff (95% CI)[a]	-	-0.10 (-0.17 to -0.03)	-	0.03 (-0.08 to 0.14)
p-value[a]		0.008		0.537
Hedges'g (95% CI)	-	-0.387 (-0.672 to -0.102)	-	0.125 (-0.276 to 0.526)
p-value for heterogeneity[b]				0.059

[a]Derived from MMRM model with change from baseline in Number of nocturnal awakenings values up to Week 52 as the response variable, and treatment, baseline weight group, region, age, baseline eosinophil level, baseline FeNO level, baseline ICS dose level, visit, treatment by-visit interaction, baseline Number of nocturnal awakenings value and baseline-by-visit interaction as covariates.
[b]Similar model as that mentioned in the footnote [a] with subgroup and subgroup-by-treatment interaction as additional covariates.
Type 2 inflammatory asthma phenotype population is defined as the randomized patients with baseline blood eosinophils >= 0.15 Giga/L or baseline FeNO >= 20 ppb.
PGM=DEVOPS/SAR231893/EFC14153/CSR_RWE/REPORT/PGM/eff_mmrm_ger_subg_i_t.sas OUT=REPORT/OUTPUT/eff_mmrm_awak_ger_sex_i_t_x.rtf (21JUL2021 - 8:44)

Project Code / Study Number / Analysis: SAR231893 / EFC14153 / CSR_RWE

6 Number of nocturnal awakenings - ITT type 2 inflammatory asthma phenotype population

6.1 Summary of treatment effect on change from baseline at Week 52

6.1.2 By region (Latin America, East Europe, Western Countries)

	Region					
	Latin America		East Europe		Western countries	
Number of nocturnal awakenings	**Placebo (N=51)**	**Dupilumab (N=106)**	**Placebo (N=43)**	**Dupilumab (N=78)**	**Placebo (N=20)**	**Dupilumab (N=52)**
Baseline						
Value						
Number	51	106	43	78	20	52
Mean (SD)	0.24 (0.33)	0.42 (0.81)	0.37 (0.45)	0.39 (0.64)	0.43 (0.67)	0.33 (0.42)
Median	0.00	0.00	0.20	0.14	0.15	0.14
Q1 : Q3	0.00 : 0.43	0.00 : 0.33	0.00 : 0.71	0.00 : 0.43	0.00 : 0.75	0.00 : 0.54
Min : Max	0.0 : 1.0	0.0 : 4.4	0.0 : 1.6	0.0 : 3.9	0.0 : 2.5	0.0 : 1.7

[a]Derived from MMRM model with change from baseline in Number of nocturnal awakenings values up to Week 52 as the response variable, and treatment, baseline weight group, age, baseline eosinophil level, baseline FeNO level, baseline ICS dose level, visit, treatment by-visit interaction, baseline Number of nocturnal awakenings value and baseline-by-visit interaction as covariates.
[b]Similar model as that mentioned in the footnote [a] with subgroup and subgroup-by-treatment interaction as additional covariates.
Type 2 inflammatory asthma phenotype population is defined as the randomized patients with baseline blood eosinophils >= 0.15 Giga/L or baseline FeNO >= 20 ppb.
PGM=DEVOPS/SAR231893/EFC14153/CSR_RWE/REPORT/PGM/eff_mmrm_ger_subg_i_t.sas OUT=REPORT/OUTPUT/eff_mmrm_awak_ger_cty_i_t_x.rtf (21JUL2021 - 9:03)

Project Code / Study Number / Analysis: SAR231893 / EFC14153 / CSR_RWE

6 Number of nocturnal awakenings - ITT type 2 inflammatory asthma phenotype population

6.1 Summary of treatment effect on change from baseline at Week 52

6.1.2 By region (Latin America, East Europe, Western Countries)

	Region					
	Latin America		East Europe		Western countries	
Number of nocturnal awakenings	**Placebo (N=51)**	**Dupilumab (N=106)**	**Placebo (N=43)**	**Dupilumab (N=78)**	**Placebo (N=20)**	**Dupilumab (N=52)**
Week 52						
Value						
Number	51	102	42	77	18	43
Mean (SD)	0.07 (0.21)	0.06 (0.28)	0.16 (0.43)	0.07 (0.20)	0.07 (0.17)	0.07 (0.32)
Median	0.00	0.00	0.00	0.00	0.00	0.00
Q1 : Q3	0.00 : 0.00	0.00 : 0.00	0.00 : 0.05	0.00 : 0.00	0.00 : 0.07	0.00 : 0.00
Min : Max	0.0 : 1.0	0.0 : 2.0	0.0 : 2.1	0.0 : 1.0	0.0 : 0.7	0.0 : 2.0
Change from baseline						
Number	51	102	42	77	18	43
LS Mean (SE)[a]	-0.27 (0.04)	-0.30 (0.03)	-0.21 (0.04)	-0.30 (0.04)	-0.25 (0.07)	-0.31 (0.05)
LS Mean Diff (95% CI)[a]	-	-0.04 (-0.12 to 0.04)	-	-0.09 (-0.20 to 0.01)	-	-0.06 (-0.22 to 0.11)
p-value[a]		0.367		0.090		0.509

[a]Derived from MMRM model with change from baseline in Number of nocturnal awakenings values up to Week 52 as the response variable, and treatment, baseline weight group, age, baseline eosinophil level, baseline FeNO level, baseline ICS dose level, visit, treatment by-visit interaction, baseline Number of nocturnal awakenings value and baseline-by-visit interaction as covariates.
[b]Similar model as that mentioned in the footnote [a] with subgroup and subgroup-by-treatment interaction as additional covariates.
Type 2 inflammatory asthma phenotype population is defined as the randomized patients with baseline blood eosinophils >= 0.15 Giga/L or baseline FeNO >= 20 ppb.
PGM=DEVOPS/SAR231893/EFC14153/CSR_RWE/REPORT/PGM/eff_mmrm_ger_subg_i_t.sas OUT=REPORT/OUTPUT/eff_mmrm_awak_ger_cty_i_t_x.rtf (21JUL2021 - 9:03)

Project Code / Study Number / Analysis: SAR231893 / EFC14153 / CSR_RWE

6 Number of nocturnal awakenings - ITT type 2 inflammatory asthma phenotype population

6.1 Summary of treatment effect on change from baseline at Week 52

6.1.2 By region (Latin America, East Europe, Western Countries)

	Region					
	Latin America		East Europe		Western countries	
Number of nocturnal awakenings	Placebo (N=51)	Dupilumab (N=106)	Placebo (N=43)	Dupilumab (N=78)	Placebo (N=20)	Dupilumab (N=52)
Hedges'g (95% CI)	-	-0.160 (-0.508 to 0.189)	-	-0.326 (-0.703 to 0.051)	-	-0.184 (-0.740 to 0.371)
p-value for heterogeneity[b]:						
Latin America, East Europe						0.442
Latin America, Western countries						0.575
East Europe, Western countries						0.980
overall						0.718

[a]Derived from MMRM model with change from baseline in Number of nocturnal awakenings values up to Week 52 as the response variable, and treatment, baseline weight group, age, baseline eosinophil level, baseline FeNO level, baseline ICS dose level, visit, treatment by-visit interaction, baseline Number of nocturnal awakenings value and baseline-by-visit interaction as covariates.
[b]Similar model as that mentioned in the footnote [a] with subgroup and subgroup-by-treatment interaction as additional covariates.
Type 2 inflammatory asthma phenotype population is defined as the randomized patients with baseline blood eosinophils >= 0.15 Giga/L or baseline FeNO >= 20 ppb.
PGM=DEVOPS/SAR231893/EFC14153/CSR_RWE/REPORT/PGM/eff_mmrm_ger_subg_i_t.sas OUT=REPORT/OUTPUT/eff_mmrm_awak_ger_cty_i_t_x.rtf (21JUL2021 - 9:03)

Project Code / Study Number / Analysis: SAR231893 / EFC14153 / CSR_RWE

6 Number of nocturnal awakenings - ITT type 2 inflammatory asthma phenotype population

6.1 Summary of treatment effect on change from baseline at Week 52

6.1.3 By race (Caucasian/white, Black/of African descent, Other)

	Race					
	Caucasian/White		Black/of African descent		Other	
Number of nocturnal awakenings	**Placebo (N=102)**	**Dupilumab (N=208)**	**Placebo (N=5)**	**Dupilumab (N=9)**	**Placebo (N=7)**	**Dupilumab (N=19)**
Baseline						
Value						
Number	102	208	5	9	7	19
Mean (SD)	0.33 (0.45)	0.40 (0.71)	0.47 (0.65)	0.65 (0.51)	0.15 (0.17)	0.18 (0.24)
Median	0.14	0.14	0.00	0.57	0.14	0.14
Q1 : Q3	0.00 : 0.57	0.00 : 0.43	0.00 : 1.00	0.17 : 1.00	0.00 : 0.29	0.00 : 0.29
Min : Max	0.0 : 2.5	0.0 : 4.4	0.0 : 1.3	0.0 : 1.3	0.0 : 0.4	0.0 : 0.8

[a]Derived from MMRM model with change from baseline in Number of nocturnal awakenings values up to Week 52 as the response variable, and treatment, baseline weight group, region, age, baseline eosinophil level, baseline FeNO level, baseline ICS dose level, visit, treatment by-visit interaction, baseline Number of nocturnal awakenings value and baseline-by-visit interaction as covariates.
[b]Similar model as that mentioned in the footnote [a] with subgroup and subgroup-by-treatment interaction as additional covariates.
Type 2 inflammatory asthma phenotype population is defined as the randomized patients with baseline blood eosinophils >= 0.15 Giga/L or baseline FeNO >= 20 ppb.
PGM=DEVOPS/SAR231893/EFC14153/CSR_RWE/REPORT/PGM/eff_mmrm_ger_subg_i_t.sas OUT=REPORT/OUTPUT/eff_mmrm_awak_ger_race_i_t_x.rtf (21JUL2021 - 9:23)

Project Code / Study Number / Analysis: SAR231893 / EFC14153 / CSR_RWE

6 Number of nocturnal awakenings - ITT type 2 inflammatory asthma phenotype population

6.1 Summary of treatment effect on change from baseline at Week 52

6.1.3 By race (Caucasian/white, Black/of African descent, Other)

	Race					
	Caucasian/White		Black/of African descent		Other	
Number of nocturnal awakenings	**Placebo (N=102)**	**Dupilumab (N=208)**	**Placebo (N=5)**	**Dupilumab (N=9)**	**Placebo (N=7)**	**Dupilumab (N=19)**
Week 52						
Value						
Number	101	198	3	8	7	16
Mean (SD)	0.11 (0.32)	0.07 (0.27)	0.00 (0.00)	0.10 (0.25)	0.10 (0.18)	0.00 (0.00)
Median	0.00	0.00	0.00	0.00	0.00	0.00
Q1 : Q3	0.00 : 0.04	0.00 : 0.00	0.00 : 0.00	0.00 : 0.06	0.00 : 0.23	0.00 : 0.00
Min : Max	0.0 : 2.1	0.0 : 2.0	0.0 : 0.0	0.0 : 0.7	0.0 : 0.5	0.0 : 0.0
Change from baseline						
Number	101	198	3	8	7	16
LS Mean (SE)[a]	-0.27 (0.03)	-0.33 (0.02)	-0.70 (0.33)	-0.58 (0.26)	-0.09 (0.10)	-0.22 (0.06)
LS Mean Diff (95% CI)[a]	-	-0.06 (-0.13 to 0.01)	-	0.12 (-0.45 to 0.68)	-	-0.14 (-0.37 to 0.09)
p-value[a]		0.084		0.651		0.246

[a]Derived from MMRM model with change from baseline in Number of nocturnal awakenings values up to Week 52 as the response variable, and treatment, baseline weight group, region, age, baseline eosinophil level, baseline FeNO level, baseline ICS dose level, visit, treatment by-visit interaction, baseline Number of nocturnal awakenings value and baseline-by-visit interaction as covariates.
[b]Similar model as that mentioned in the footnote [a] with subgroup and subgroup-by-treatment interaction as additional covariates.
Type 2 inflammatory asthma phenotype population is defined as the randomized patients with baseline blood eosinophils >= 0.15 Giga/L or baseline FeNO >= 20 ppb.
PGM=DEVOPS/SAR231893/EFC14153/CSR_RWE/REPORT/PGM/eff_mmrm_ger_subg_i_t.sas OUT=REPORT/OUTPUT/eff_mmrm_awak_ger_race_i_t_x.rtf (21JUL2021 - 9:23)

Project Code / Study Number / Analysis: SAR231893 / EFC14153 / CSR_RWE

6 Number of nocturnal awakenings - ITT type 2 inflammatory asthma phenotype population

6.1 Summary of treatment effect on change from baseline at Week 52

6.1.3 By race (Caucasian/white, Black/of African descent, Other)

	Race					
	Caucasian/White		Black/of African descent		Other	
Number of nocturnal awakenings	**Placebo (N=102)**	**Dupilumab (N=208)**	**Placebo (N=5)**	**Dupilumab (N=9)**	**Placebo (N=7)**	**Dupilumab (N=19)**
Hedges'g (95% CI)	-	-0.215 (-0.459 to 0.029)	-	0.146 (-0.572 to 0.865)	-	-0.532 (-1.433 to 0.369)
p-value for heterogeneity[b]:						
Caucasian/White, Black/of African descent						0.548
Caucasian/White, Other						0.512
Black/of African descent, Other						0.788
overall						0.798

[a]Derived from MMRM model with change from baseline in Number of nocturnal awakenings values up to Week 52 as the response variable, and treatment, baseline weight group, region, age, baseline eosinophil level, baseline FeNO level, baseline ICS dose level, visit, treatment by-visit interaction, baseline Number of nocturnal awakenings value and baseline-by-visit interaction as covariates.
[b]Similar model as that mentioned in the footnote [a] with subgroup and subgroup-by-treatment interaction as additional covariates.
Type 2 inflammatory asthma phenotype population is defined as the randomized patients with baseline blood eosinophils >= 0.15 Giga/L or baseline FeNO >= 20 ppb.
PGM=DEVOPS/SAR231893/EFC14153/CSR_RWE/REPORT/PGM/eff_mmrm_ger_subg_i_t.sas OUT=REPORT/OUTPUT/eff_mmrm_awak_ger_race_i_t_x.rtf (21JUL2021 - 9:23)

Project Code / Study Number / Analysis: SAR231893 / EFC14153 / CSR_RWE

6 Number of nocturnal awakenings - ITT type 2 inflammatory asthma phenotype population

6.1 Summary of treatment effect on change from baseline at Week 52

6.1.4 By baseline ICS dose level (Medium, High)

	Baseline ICS dose level			
	High		Medium	
Number of nocturnal awakenings	**Placebo (N=50)**	**Dupilumab (N=102)**	**Placebo (N=64)**	**Dupilumab (N=131)**
Baseline				
Value				
Number	50	102	64	131
Mean (SD)	0.39 (0.52)	0.42 (0.67)	0.27 (0.39)	0.37 (0.70)
Median	0.17	0.14	0.07	0.14
Q1 : Q3	0.00 : 0.71	0.00 : 0.57	0.00 : 0.42	0.00 : 0.33
Min : Max	0.0 : 2.5	0.0 : 3.3	0.0 : 1.6	0.0 : 4.4

[a]Derived from MMRM model with change from baseline in Number of nocturnal awakenings values up to Week 52 as the response variable, and treatment, baseline weight group, region, age, baseline eosinophil level, baseline FeNO level, visit, treatment by-visit interaction, baseline Number of nocturnal awakenings value and baseline-by-visit interaction as covariates.
[b]Similar model as that mentioned in the footnote [a] with subgroup and subgroup-by-treatment interaction as additional covariates.
Type 2 inflammatory asthma phenotype population is defined as the randomized patients with baseline blood eosinophils >= 0.15 Giga/L or baseline FeNO >= 20 ppb.
PGM=DEVOPS/SAR231893/EFC14153/CSR_RWE/REPORT/PGM/eff_mmrm_ger_subg_i_t.sas OUT=REPORT/OUTPUT/eff_mmrm_awak_ger_ics_i_t_x.rtf (21JUL2021 - 9:37)

Project Code / Study Number / Analysis: SAR231893 / EFC14153 / CSR_RWE

6 Number of nocturnal awakenings - ITT type 2 inflammatory asthma phenotype population

6.1 Summary of treatment effect on change from baseline at Week 52

6.1.4 By baseline ICS dose level (Medium, High)

	Baseline ICS dose level			
	High		Medium	
Number of nocturnal awakenings	**Placebo (N=50)**	**Dupilumab (N=102)**	**Placebo (N=64)**	**Dupilumab (N=131)**
Week 52				
Value				
Number	49	97	62	124
Mean (SD)	0.07 (0.20)	0.09 (0.29)	0.13 (0.37)	0.04 (0.22)
Median	0.00	0.00	0.00	0.00
Q1 : Q3	0.00 : 0.04	0.00 : 0.00	0.00 : 0.04	0.00 : 0.00
Min : Max	0.0 : 1.0	0.0 : 2.0	0.0 : 2.1	0.0 : 2.0
Change from baseline				
Number	49	97	62	124
LS Mean (SE)[a]	-0.33 (0.04)	-0.34 (0.03)	-0.20 (0.04)	-0.32 (0.03)
LS Mean Diff (95% CI)[a]	-	-0.01 (-0.10 to 0.08)	-	-0.12 (-0.21 to -0.04)
p-value[a]		0.823		0.005
Hedges'g (95% CI)	-	-0.040 (-0.393 to 0.313)	-	-0.450 (-0.761 to -0.140)
p-value for heterogeneity[b]				0.062

[a]Derived from MMRM model with change from baseline in Number of nocturnal awakenings values up to Week 52 as the response variable, and treatment, baseline weight group, region, age, baseline eosinophil level, baseline FeNO level, visit, treatment by-visit interaction, baseline Number of nocturnal awakenings value and baseline-by-visit interaction as covariates.
[b]Similar model as that mentioned in the footnote [a] with subgroup and subgroup-by-treatment interaction as additional covariates.
Type 2 inflammatory asthma phenotype population is defined as the randomized patients with baseline blood eosinophils >= 0.15 Giga/L or baseline FeNO >= 20 ppb.
PGM=DEVOPS/SAR231893/EFC14153/CSR_RWE/REPORT/PGM/eff_mmrm_ger_subg_i_t.sas OUT=REPORT/OUTPUT/eff_mmrm_awak_ger_ics_i_t_x.rtf (21JUL2021 - 9:37)

Project Code / Study Number / Analysis: SAR231893 / EFC14153 / CSR_RWE

6 Number of nocturnal awakenings - ITT type 2 inflammatory asthma phenotype population

6.1 Summary of treatment effect on change from baseline at Week 52

6.1.5 By baseline ICS dose level 2 (Medium, High)

	Baseline ICS dose level 2			
	High		Medium	
Number of nocturnal awakenings	**Placebo (N=95)**	**Dupilumab (N=200)**	**Placebo (N=19)**	**Dupilumab (N=36)**
Baseline				
Value				
Number	95	200	19	36
Mean (SD)	0.33 (0.46)	0.41 (0.71)	0.30 (0.42)	0.29 (0.50)
Median	0.14	0.14	0.00	0.14
Q1 : Q3	0.00 : 0.57	0.00 : 0.50	0.00 : 0.50	0.00 : 0.31
Min : Max	0.0 : 2.5	0.0 : 4.4	0.0 : 1.3	0.0 : 2.3

[a]Derived from MMRM model with change from baseline in Number of nocturnal awakenings values up to Week 52 as the response variable, and treatment, baseline weight group, region, age, baseline eosinophil level, baseline FeNO level, visit, treatment by-visit interaction, baseline Number of nocturnal awakenings value and baseline-by-visit interaction as covariates.
[b]Similar model as that mentioned in the footnote [a] with subgroup and subgroup-by-treatment interaction as additional covariates.
Type 2 inflammatory asthma phenotype population is defined as the randomized patients with baseline blood eosinophils >= 0.15 Giga/L or baseline FeNO >= 20 ppb.
PGM=DEVOPS/SAR231893/EFC14153/CSR_RWE/REPORT/PGM/eff_mmrm_ger_subg_i_t.sas OUT=REPORT/OUTPUT/eff_mmrm_awak_ger_ics2_i_t_x.rtf (01SEP2021 - 17:20)

Project Code / Study Number / Analysis: SAR231893 / EFC14153 / CSR_RWE

6 Number of nocturnal awakenings - ITT type 2 inflammatory asthma phenotype population

6.1 Summary of treatment effect on change from baseline at Week 52

6.1.5 By baseline ICS dose level 2 (Medium, High)

	Baseline ICS dose level 2			
	High		Medium	
Number of nocturnal awakenings	**Placebo (N=95)**	**Dupilumab (N=200)**	**Placebo (N=19)**	**Dupilumab (N=36)**
Week 52				
Value				
Number	92	191	19	31
Mean (SD)	0.11 (0.32)	0.07 (0.27)	0.07 (0.23)	0.04 (0.18)
Median	0.00	0.00	0.00	0.00
Q1 : Q3	0.00 : 0.05	0.00 : 0.00	0.00 : 0.00	0.00 : 0.00
Min : Max	0.0 : 2.1	0.0 : 2.0	0.0 : 1.0	0.0 : 1.0
Change from baseline				
Number	92	191	19	31
LS Mean (SE)[a]	-0.25 (0.03)	-0.33 (0.02)	-0.23 (0.06)	-0.29 (0.04)
LS Mean Diff (95% CI)[a]	-	-0.07 (-0.14 to -0.00)	-	-0.06 (-0.19 to 0.06)
p-value[a]		0.041		0.319
Hedges'g (95% CI)	-	-0.263 (-0.515 to -0.011)	-	-0.315 (-0.944 to 0.315)
p-value for heterogeneity[b]				0.628

[a]Derived from MMRM model with change from baseline in Number of nocturnal awakenings values up to Week 52 as the response variable, and treatment, baseline weight group, region, age, baseline eosinophil level, baseline FeNO level, visit, treatment by-visit interaction, baseline Number of nocturnal awakenings value and baseline-by-visit interaction as covariates.
[b]Similar model as that mentioned in the footnote [a] with subgroup and subgroup-by-treatment interaction as additional covariates.
Type 2 inflammatory asthma phenotype population is defined as the randomized patients with baseline blood eosinophils >= 0.15 Giga/L or baseline FeNO >= 20 ppb.
PGM=DEVOPS/SAR231893/EFC14153/CSR_RWE/REPORT/PGM/eff_mmrm_ger_subg_i_t.sas OUT=REPORT/OUTPUT/eff_mmrm_awak_ger_ics2_i_t_x.rtf (01SEP2021 - 17:20)

Project Code / Study Number / Analysis: SAR231893 / EFC14153 / CSR_RWE

6 Number of nocturnal awakenings - ITT type 2 inflammatory asthma phenotype population

6.1 Summary of treatment effect on change from baseline at Week 52

6.1.6 By baseline predicted FEV1 (<80%, >=80%)

	Baseline Predicted FEV1			
	<80%		>=80%	
Number of nocturnal awakenings	**Placebo (N=59)**	**Dupilumab (N=116)**	**Placebo (N=55)**	**Dupilumab (N=120)**
Baseline				
Value				
Number	59	116	55	120
Mean (SD)	0.32 (0.49)	0.40 (0.60)	0.33 (0.41)	0.39 (0.76)
Median	0.14	0.14	0.17	0.00
Q1 : Q3	0.00 : 0.50	0.00 : 0.59	0.00 : 0.57	0.00 : 0.43
Min : Max	0.0 : 2.5	0.0 : 3.3	0.0 : 1.6	0.0 : 4.4

[a]Derived from MMRM model with change from baseline in Number of nocturnal awakenings values up to Week 52 as the response variable, and treatment, baseline weight group, region, age, baseline eosinophil level, baseline FeNO level, baseline ICS dose level, visit, treatment by-visit interaction, baseline Number of nocturnal awakenings value and baseline-by-visit interaction as covariates.
[b]Similar model as that mentioned in the footnote [a] with subgroup and subgroup-by-treatment interaction as additional covariates.
Type 2 inflammatory asthma phenotype population is defined as the randomized patients with baseline blood eosinophils >= 0.15 Giga/L or baseline FeNO >= 20 ppb.
PGM=DEVOPS/SAR231893/EFC14153/CSR_RWE/REPORT/PGM/eff_mmrm_ger_subg_i_t.sas OUT=REPORT/OUTPUT/eff_mmrm_awak_ger_pfev1_i_t_x.rtf (21JUL2021 - 9:52)

Project Code / Study Number / Analysis: SAR231893 / EFC14153 / CSR_RWE

6 Number of nocturnal awakenings - ITT type 2 inflammatory asthma phenotype population

6.1 Summary of treatment effect on change from baseline at Week 52

6.1.6 By baseline predicted FEV1 (<80%, >=80%)

	Baseline Predicted FEV1			
	<80%		>=80%	
Number of nocturnal awakenings	**Placebo (N=59)**	**Dupilumab (N=116)**	**Placebo (N=55)**	**Dupilumab (N=120)**
Week 52				
Value				
Number	57	112	54	110
Mean (SD)	0.06 (0.20)	0.07 (0.26)	0.15 (0.39)	0.06 (0.26)
Median	0.00	0.00	0.00	0.00
Q1 : Q3	0.00 : 0.00	0.00 : 0.00	0.00 : 0.05	0.00 : 0.00
Min : Max	0.0 : 1.0	0.0 : 2.0	0.0 : 2.1	0.0 : 2.0
Change from baseline				
Number	57	112	54	110
LS Mean (SE)[a]	-0.32 (0.03)	-0.34 (0.03)	-0.22 (0.04)	-0.32 (0.03)
LS Mean Diff (95% CI)[a]	-	-0.02 (-0.09 to 0.06)	-	-0.10 (-0.20 to -0.00)
p-value[a]		0.640		0.041
Hedges'g (95% CI)	-	-0.078 (-0.406 to 0.250)	-	-0.345 (-0.676 to -0.014)
p-value for heterogeneity[b]				0.108

[a]Derived from MMRM model with change from baseline in Number of nocturnal awakenings values up to Week 52 as the response variable, and treatment, baseline weight group, region, age, baseline eosinophil level, baseline FeNO level, baseline ICS dose level, visit, treatment by-visit interaction, baseline Number of nocturnal awakenings value and baseline-by-visit interaction as covariates.
[b]Similar model as that mentioned in the footnote [a] with subgroup and subgroup-by-treatment interaction as additional covariates.
Type 2 inflammatory asthma phenotype population is defined as the randomized patients with baseline blood eosinophils >= 0.15 Giga/L or baseline FeNO >= 20 ppb.
PGM=DEVOPS/SAR231893/EFC14153/CSR_RWE/REPORT/PGM/eff_mmrm_ger_subg_i_t.sas OUT=REPORT/OUTPUT/eff_mmrm_awak_ger_pfev1_i_t_x.rtf (21JUL2021 - 9:52)

Project Code / Study Number / Analysis: SAR231893 / EFC14153 / CSR_RWE

6 Number of nocturnal awakenings - ITT type 2 inflammatory asthma phenotype population

6.1 Summary of treatment effect on change from baseline at Week 52

6.1.7 By baseline ACQ-7-IA (<=2, >2)

	Baseline ACQ-7-IA			
	<=2		>2	
Number of nocturnal awakenings	**Placebo (N=61)**	**Dupilumab (N=126)**	**Placebo (N=53)**	**Dupilumab (N=110)**
Baseline				
Value				
Number	61	126	53	110
Mean (SD)	0.27 (0.41)	0.23 (0.51)	0.38 (0.49)	0.57 (0.81)
Median	0.00	0.00	0.17	0.29
Q1 : Q3	0.00 : 0.43	0.00 : 0.29	0.00 : 0.71	0.00 : 0.83
Min : Max	0.0 : 1.6	0.0 : 3.3	0.0 : 2.5	0.0 : 4.4

[a]Derived from MMRM model with change from baseline in Number of nocturnal awakenings values up to Week 52 as the response variable, and treatment, baseline weight group, region, age, baseline eosinophil level, baseline FeNO level, baseline ICS dose level, visit, treatment by-visit interaction, baseline Number of nocturnal awakenings value and baseline-by-visit interaction as covariates.
[b]Similar model as that mentioned in the footnote [a] with subgroup and subgroup-by-treatment interaction as additional covariates.
Type 2 inflammatory asthma phenotype population is defined as the randomized patients with baseline blood eosinophils >= 0.15 Giga/L or baseline FeNO >= 20 ppb.
PGM=DEVOPS/SAR231893/EFC14153/CSR_RWE/REPORT/PGM/eff_mmrm_ger_subg_i_t.sas OUT=REPORT/OUTPUT/eff_mmrm_awak_ger_acq7_i_t_x.rtf (21JUL2021 - 10:06)

Project Code / Study Number / Analysis: SAR231893 / EFC14153 / CSR_RWE

6 Number of nocturnal awakenings - ITT type 2 inflammatory asthma phenotype population

6.1 Summary of treatment effect on change from baseline at Week 52

6.1.7 By baseline ACQ-7-IA (<=2, >2)

	Baseline ACQ-7-IA			
	<=2		>2	
Number of nocturnal awakenings	**Placebo (N=61)**	**Dupilumab (N=126)**	**Placebo (N=53)**	**Dupilumab (N=110)**
Week 52				
Value				
Number	61	117	50	105
Mean (SD)	0.10 (0.33)	0.05 (0.25)	0.11 (0.27)	0.08 (0.27)
Median	0.00	0.00	0.00	0.00
Q1 : Q3	0.00 : 0.04	0.00 : 0.00	0.00 : 0.05	0.00 : 0.00
Min : Max	0.0 : 2.1	0.0 : 2.0	0.0 : 1.0	0.0 : 2.0
Change from baseline				
Number	61	117	50	105
LS Mean (SE)[a]	-0.16 (0.04)	-0.20 (0.03)	-0.39 (0.04)	-0.47 (0.03)
LS Mean Diff (95% CI)[a]	-	-0.04 (-0.12 to 0.05)	-	-0.08 (-0.17 to 0.01)
p-value[a]		0.362		0.078
Hedges'g (95% CI)	-	-0.145 (-0.458 to 0.168)	-	-0.313 (-0.661 to 0.036)
p-value for heterogeneity[b]				0.481

[a]Derived from MMRM model with change from baseline in Number of nocturnal awakenings values up to Week 52 as the response variable, and treatment, baseline weight group, region, age, baseline eosinophil level, baseline FeNO level, baseline ICS dose level, visit, treatment by-visit interaction, baseline Number of nocturnal awakenings value and baseline-by-visit interaction as covariates.
[b]Similar model as that mentioned in the footnote [a] with subgroup and subgroup-by-treatment interaction as additional covariates.
Type 2 inflammatory asthma phenotype population is defined as the randomized patients with baseline blood eosinophils >= 0.15 Giga/L or baseline FeNO >= 20 ppb.
PGM=DEVOPS/SAR231893/EFC14153/CSR_RWE/REPORT/PGM/eff_mmrm_ger_subg_i_t.sas OUT=REPORT/OUTPUT/eff_mmrm_awak_ger_acq7_i_t_x.rtf (21JUL2021 - 10:06)

Project Code / Study Number / Analysis: SAR231893 / EFC14153 / CSR_RWE

6 Number of nocturnal awakenings - ITT type 2 inflammatory asthma phenotype population

6.1 Summary of treatment effect on change from baseline at Week 52

6.1.8 By baseline weight (<=30 kg, >30 kg)

	Baseline weight (kg)			
	<=30		>30	
Number of nocturnal awakenings	**Placebo (N=36)**	**Dupilumab (N=76)**	**Placebo (N=78)**	**Dupilumab (N=160)**
Baseline				
Value				
Number	36	76	78	160
Mean (SD)	0.49 (0.57)	0.45 (0.85)	0.25 (0.36)	0.36 (0.59)
Median	0.31	0.14	0.07	0.14
Q1 : Q3	0.00 : 0.86	0.00 : 0.54	0.00 : 0.33	0.00 : 0.43
Min : Max	0.0 : 2.5	0.0 : 4.4	0.0 : 1.6	0.0 : 3.3

[a]Derived from MMRM model with change from baseline in Number of nocturnal awakenings values up to Week 52 as the response variable, and treatment, region, age, baseline eosinophil level, baseline FeNO level, baseline ICS dose level, visit, treatment by-visit interaction, baseline Number of nocturnal awakenings value and baseline-by-visit interaction as covariates.

[b]Similar model as that mentioned in the footnote [a] with subgroup and subgroup-by-treatment interaction as additional covariates.

Type 2 inflammatory asthma phenotype population is defined as the randomized patients with baseline blood eosinophils >= 0.15 Giga/L or baseline FeNO >= 20 ppb.

PGM=DEVOPS/SAR231893/EFC14153/CSR_RWE/REPORT/PGM/eff_mmrm_ger_subg_i_t.sas OUT=REPORT/OUTPUT/eff_mmrm_awak_ger_wgt_i_t_x.rtf (21JUL2021 - 10:21)

Project Code / Study Number / Analysis: SAR231893 / EFC14153 / CSR_RWE

6 Number of nocturnal awakenings - ITT type 2 inflammatory asthma phenotype population

6.1 Summary of treatment effect on change from baseline at Week 52

6.1.8 By baseline weight (<=30 kg, >30 kg)

	Baseline weight (kg)			
	<=30		>30	
Number of nocturnal awakenings	**Placebo (N=36)**	**Dupilumab (N=76)**	**Placebo (N=78)**	**Dupilumab (N=160)**
Week 52				
Value				
Number	35	69	76	153
Mean (SD)	0.09 (0.24)	0.08 (0.31)	0.12 (0.33)	0.06 (0.24)
Median	0.00	0.00	0.00	0.00
Q1 : Q3	0.00 : 0.04	0.00 : 0.00	0.00 : 0.04	0.00 : 0.00
Min : Max	0.0 : 1.2	0.0 : 2.0	0.0 : 2.1	0.0 : 2.0
Change from baseline				
Number	35	69	76	153
LS Mean (SE)[a]	-0.39 (0.05)	-0.39 (0.04)	-0.20 (0.03)	-0.28 (0.02)
LS Mean Diff (95% CI)[a]	-	-0.01 (-0.13 to 0.11)	-	-0.08 (-0.15 to -0.01)
p-value[a]		0.892		0.024
Hedges'g (95% CI)	-	-0.028 (-0.441 to 0.384)	-	-0.324 (-0.606 to -0.043)
p-value for heterogeneity[b]				0.356

[a]Derived from MMRM model with change from baseline in Number of nocturnal awakenings values up to Week 52 as the response variable, and treatment, region, age, baseline eosinophil level, baseline FeNO level, baseline ICS dose level, visit, treatment by-visit interaction, baseline Number of nocturnal awakenings value and baseline-by-visit interaction as covariates.
[b]Similar model as that mentioned in the footnote [a] with subgroup and subgroup-by-treatment interaction as additional covariates.
Type 2 inflammatory asthma phenotype population is defined as the randomized patients with baseline blood eosinophils >= 0.15 Giga/L or baseline FeNO >= 20 ppb.
PGM=DEVOPS/SAR231893/EFC14153/CSR_RWE/REPORT/PGM/eff_mmrm_ger_subg_i_t.sas OUT=REPORT/OUTPUT/eff_mmrm_awak_ger_wgt_i_t_x.rtf (21JUL2021 - 10:21)

Project Code / Study Number / Analysis: SAR231893 / EFC14153 / CSR_RWE

6 Number of nocturnal awakenings - ITT type 2 inflammatory asthma phenotype population

6.1 Summary of treatment effect on change from baseline at Week 52

6.1.9 By atopic medical condition (Yes, No)

	Atopic medical condition			
	Yes		No	
Number of nocturnal awakenings	**Placebo (N=103)**	**Dupilumab (N=227)**	**Placebo (N=11)**	**Dupilumab (N=9)**
Baseline				
Value				
Number	103	227	11	9
Mean (SD)	0.34 (0.47)	0.40 (0.70)	0.14 (0.19)	0.26 (0.26)
Median	0.14	0.14	0.00	0.14
Q1 : Q3	0.00 : 0.67	0.00 : 0.43	0.00 : 0.29	0.00 : 0.43
Min : Max	0.0 : 2.5	0.0 : 4.4	0.0 : 0.6	0.0 : 0.7

[a]Derived from MMRM model with change from baseline in Number of nocturnal awakenings values up to Week 52 as the response variable, and treatment, baseline weight group, region, age, baseline eosinophil level, baseline FeNO level, baseline ICS dose level, visit, treatment by-visit interaction, baseline Number of nocturnal awakenings value and baseline-by-visit interaction as covariates.
[b]Similar model as that mentioned in the footnote [a] with subgroup and subgroup-by-treatment interaction as additional covariates.
Type 2 inflammatory asthma phenotype population is defined as the randomized patients with baseline blood eosinophils >= 0.15 Giga/L or baseline FeNO >= 20 ppb.
PGM=DEVOPS/SAR231893/EFC14153/CSR_RWE/REPORT/PGM/eff_mmrm_ger_subg_i_t.sas OUT=REPORT/OUTPUT/eff_mmrm_awak_ger_amc_i_t_x.rtf (21JUL2021 - 10:35)

Project Code / Study Number / Analysis: SAR231893 / EFC14153 / CSR_RWE

6 Number of nocturnal awakenings - ITT type 2 inflammatory asthma phenotype population

6.1 Summary of treatment effect on change from baseline at Week 52

6.1.9 By atopic medical condition (Yes, No)

	Atopic medical condition			
	Yes		No	
Number of nocturnal awakenings	**Placebo (N=103)**	**Dupilumab (N=227)**	**Placebo (N=11)**	**Dupilumab (N=9)**
Week 52				
Value				
Number	100	213	11	9
Mean (SD)	0.11 (0.32)	0.07 (0.26)	0.04 (0.11)	0.01 (0.02)
Median	0.00	0.00	0.00	0.00
Q1 : Q3	0.00 : 0.04	0.00 : 0.00	0.00 : 0.00	0.00 : 0.00
Min : Max	0.0 : 2.1	0.0 : 2.0	0.0 : 0.4	0.0 : 0.0
Change from baseline				
Number	100	213	11	9
LS Mean (SE)[a]	-0.26 (0.03)	-0.33 (0.02)	-0.17 (0.09)	-0.21 (0.10)
LS Mean Diff (95% CI)[a]	-	-0.07 (-0.13 to -0.00)	-	-0.05 (-0.29 to 0.19)
p-value[a]		0.039		0.690
Hedges'g (95% CI)	-	-0.254 (-0.496 to -0.013)	-	-0.154 (-0.941 to 0.633)
p-value for heterogeneity[b]				0.870

[a]Derived from MMRM model with change from baseline in Number of nocturnal awakenings values up to Week 52 as the response variable, and treatment, baseline weight group, region, age, baseline eosinophil level, baseline FeNO level, baseline ICS dose level, visit, treatment by-visit interaction, baseline Number of nocturnal awakenings value and baseline-by-visit interaction as covariates.
[b]Similar model as that mentioned in the footnote [a] with subgroup and subgroup-by-treatment interaction as additional covariates.
Type 2 inflammatory asthma phenotype population is defined as the randomized patients with baseline blood eosinophils >= 0.15 Giga/L or baseline FeNO >= 20 ppb.
PGM=DEVOPS/SAR231893/EFC14153/CSR_RWE/REPORT/PGM/eff_mmrm_ger_subg_i_t.sas OUT=REPORT/OUTPUT/eff_mmrm_awak_ger_amc_i_t_x.rtf (21JUL2021 - 10:35)

Project Code / Study Number / Analysis: SAR231893 / EFC14153 / CSR_RWE

6 Number of nocturnal awakenings - ITT type 2 inflammatory asthma phenotype population

6.1 Summary of treatment effect on change from baseline at Week 52

6.1.10 By baseline total IgE (<median, >= median)

	Baseline Total IgE (IU/mL)			
	<median		>=median	
Number of nocturnal awakenings	**Placebo (N=66)**	**Dupilumab (N=105)**	**Placebo (N=47)**	**Dupilumab (N=125)**
Baseline				
Value				
Number	66	105	47	125
Mean (SD)	0.26 (0.38)	0.31 (0.55)	0.37 (0.43)	0.44 (0.73)
Median	0.00	0.00	0.17	0.14
Q1 : Q3	0.00 : 0.29	0.00 : 0.33	0.00 : 0.71	0.00 : 0.57
Min : Max	0.0 : 1.4	0.0 : 2.5	0.0 : 1.6	0.0 : 4.4

[a]Derived from MMRM model with change from baseline in Number of nocturnal awakenings values up to Week 52 as the response variable, and treatment, baseline weight group, region, age, baseline eosinophil level, baseline FeNO level, baseline ICS dose level, visit, treatment by-visit interaction, baseline Number of nocturnal awakenings value and baseline-by-visit interaction as covariates.
[b]Similar model as that mentioned in the footnote [a] with subgroup and subgroup-by-treatment interaction as additional covariates.
Type 2 inflammatory asthma phenotype population is defined as the randomized patients with baseline blood eosinophils >= 0.15 Giga/L or baseline FeNO >= 20 ppb.
PGM=DEVOPS/SAR231893/EFC14153/CSR_RWE/REPORT/PGM/eff_mmrm_ger_subg_i_t.sas OUT=REPORT/OUTPUT/eff_mmrm_awak_ger_igem_i_t_x.rtf (21JUL2021 - 10:50)

Project Code / Study Number / Analysis: SAR231893 / EFC14153 / CSR_RWE

6 Number of nocturnal awakenings - ITT type 2 inflammatory asthma phenotype population

6.1 Summary of treatment effect on change from baseline at Week 52

6.1.10 By baseline total IgE (<median, >= median)

	Baseline Total IgE (IU/mL)			
	<median		>=median	
Number of nocturnal awakenings	**Placebo (N=66)**	**Dupilumab (N=105)**	**Placebo (N=47)**	**Dupilumab (N=125)**
Week 52				
Value				
Number	65	101	45	118
Mean (SD)	0.06 (0.20)	0.06 (0.25)	0.17 (0.41)	0.08 (0.27)
Median	0.00	0.00	0.00	0.00
Q1 : Q3	0.00 : 0.00	0.00 : 0.00	0.00 : 0.09	0.00 : 0.00
Min : Max	0.0 : 1.0	0.0 : 2.0	0.0 : 2.1	0.0 : 2.0
Change from baseline				
Number	65	101	45	118
LS Mean (SE)[a]	-0.23 (0.03)	-0.24 (0.02)	-0.20 (0.05)	-0.33 (0.04)
LS Mean Diff (95% CI)[a]	-	-0.02 (-0.09 to 0.05)	-	-0.13 (-0.24 to -0.03)
p-value[a]		0.637		0.011
Hedges'g (95% CI)	-	-0.076 (-0.393 to 0.241)	-	-0.454 (-0.801 to -0.108)
p-value for heterogeneity[b]				0.077

[a]Derived from MMRM model with change from baseline in Number of nocturnal awakenings values up to Week 52 as the response variable, and treatment, baseline weight group, region, age, baseline eosinophil level, baseline FeNO level, baseline ICS dose level, visit, treatment by-visit interaction, baseline Number of nocturnal awakenings value and baseline-by-visit interaction as covariates.
[b]Similar model as that mentioned in the footnote [a] with subgroup and subgroup-by-treatment interaction as additional covariates.
Type 2 inflammatory asthma phenotype population is defined as the randomized patients with baseline blood eosinophils >= 0.15 Giga/L or baseline FeNO >= 20 ppb.
PGM=DEVOPS/SAR231893/EFC14153/CSR_RWE/REPORT/PGM/eff_mmrm_ger_subg_i_t.sas OUT=REPORT/OUTPUT/eff_mmrm_awak_ger_igem_i_t_x.rtf (21JUL2021 - 10:50)

Project Code / Study Number / Analysis: SAR231893 / EFC14153 / CSR_RWE

6 Number of nocturnal awakenings - ITT type 2 inflammatory asthma phenotype population

6.1 Summary of treatment effect on change from baseline at Week 52

6.1.11 By baseline total IgE (<100 IU/ml, >= 100 IU/ml)

	Baseline Total IgE (IU/mL)			
	< 100		>= 100	
Number of nocturnal awakenings	**Placebo (N=22)**	**Dupilumab (N=29)**	**Placebo (N=91)**	**Dupilumab (N=201)**
Baseline				
Value				
Number	22	29	91	201
Mean (SD)	0.22 (0.41)	0.27 (0.46)	0.33 (0.40)	0.40 (0.68)
Median	0.00	0.14	0.14	0.14
Q1 : Q3	0.00 : 0.29	0.00 : 0.29	0.00 : 0.57	0.00 : 0.50
Min : Max	0.0 : 1.4	0.0 : 2.3	0.0 : 1.6	0.0 : 4.4

[a]Derived from MMRM model with change from baseline in Number of nocturnal awakenings values up to Week 52 as the response variable, and treatment, baseline weight group, region, age, baseline eosinophil level, baseline FeNO level, baseline ICS dose level, visit, treatment by-visit interaction, baseline Number of nocturnal awakenings value and baseline-by-visit interaction as covariates.
[b]Similar model as that mentioned in the footnote [a] with subgroup and subgroup-by-treatment interaction as additional covariates.
Type 2 inflammatory asthma phenotype population is defined as the randomized patients with baseline blood eosinophils >= 0.15 Giga/L or baseline FeNO >= 20 ppb.
PGM=DEVOPS/SAR231893/EFC14153/CSR_RWE/REPORT/PGM/eff_mmrm_ger_subg_i_t.sas OUT=REPORT/OUTPUT/eff_mmrm_awak_ger_ige_i_t_x.rtf (21JUL2021 - 11:04)

Project Code / Study Number / Analysis: SAR231893 / EFC14153 / CSR_RWE

6 Number of nocturnal awakenings - ITT type 2 inflammatory asthma phenotype population

6.1 Summary of treatment effect on change from baseline at Week 52

6.1.11 By baseline total IgE (<100 IU/ml, >= 100 IU/ml)

	Baseline Total IgE (IU/mL)			
	< 100		>= 100	
Number of nocturnal awakenings	**Placebo (N=22)**	**Dupilumab (N=29)**	**Placebo (N=91)**	**Dupilumab (N=201)**
Week 52				
Value				
Number	22	29	88	190
Mean (SD)	0.04 (0.14)	0.12 (0.41)	0.12 (0.33)	0.06 (0.23)
Median	0.00	0.00	0.00	0.00
Q1 : Q3	0.00 : 0.00	0.00 : 0.00	0.00 : 0.06	0.00 : 0.00
Min : Max	0.0 : 0.7	0.0 : 2.0	0.0 : 2.1	0.0 : 2.0
Change from baseline				
Number	22	29	88	190
LS Mean (SE)[a]	-0.22 (0.08)	-0.13 (0.07)	-0.23 (0.03)	-0.32 (0.02)
LS Mean Diff (95% CI)[a]	-	0.09 (-0.10 to 0.29)	-	-0.09 (-0.16 to -0.03)
p-value[a]		0.329		0.005
Hedges'g (95% CI)	-	0.282 (-0.293 to 0.856)	-	-0.373 (-0.630 to -0.116)
p-value for heterogeneity[b]				0.044

[a]Derived from MMRM model with change from baseline in Number of nocturnal awakenings values up to Week 52 as the response variable, and treatment, baseline weight group, region, age, baseline eosinophil level, baseline FeNO level, baseline ICS dose level, visit, treatment by-visit interaction, baseline Number of nocturnal awakenings value and baseline-by-visit interaction as covariates.
[b]Similar model as that mentioned in the footnote [a] with subgroup and subgroup-by-treatment interaction as additional covariates.
Type 2 inflammatory asthma phenotype population is defined as the randomized patients with baseline blood eosinophils >= 0.15 Giga/L or baseline FeNO >= 20 ppb.
PGM=DEVOPS/SAR231893/EFC14153/CSR_RWE/REPORT/PGM/eff_mmrm_ger_subg_i_t.sas OUT=REPORT/OUTPUT/eff_mmrm_awak_ger_ige_i_t_x.rtf (21JUL2021 - 11:04)

Project Code / Study Number / Analysis: SAR231893 / EFC14153 / CSR_RWE

6 Number of nocturnal awakenings - ITT type 2 inflammatory asthma phenotype population

6.1 Summary of treatment effect on change from baseline at Week 52

6.1.12 By age at onset of asthma (0-2, 3-5, >=6 years)

	Age of onset of asthma (years)					
	0-2		3-5		>= 6	
Number of nocturnal awakenings	**Placebo (N=40)**	**Dupilumab (N=105)**	**Placebo (N=39)**	**Dupilumab (N=86)**	**Placebo (N=35)**	**Dupilumab (N=45)**
Baseline						
Value						
Number	40	105	39	86	35	45
Mean (SD)	0.32 (0.40)	0.37 (0.68)	0.37 (0.43)	0.40 (0.67)	0.28 (0.53)	0.42 (0.74)
Median	0.15	0.14	0.17	0.14	0.00	0.14
Q1 : Q3	0.00 : 0.58	0.00 : 0.43	0.00 : 0.71	0.00 : 0.50	0.00 : 0.29	0.00 : 0.50
Min : Max	0.0 : 1.3	0.0 : 4.4	0.0 : 1.6	0.0 : 3.9	0.0 : 2.5	0.0 : 3.3

[a]Derived from MMRM model with change from baseline in Number of nocturnal awakenings values up to Week 52 as the response variable, and treatment, baseline weight group, region, age, baseline eosinophil level, baseline FeNO level, baseline ICS dose level, visit, treatment by-visit interaction, baseline Number of nocturnal awakenings value and baseline-by-visit interaction as covariates.
[b]Similar model as that mentioned in the footnote [a] with subgroup and subgroup-by-treatment interaction as additional covariates.
Type 2 inflammatory asthma phenotype population is defined as the randomized patients with baseline blood eosinophils >= 0.15 Giga/L or baseline FeNO >= 20 ppb.
PGM=DEVOPS/SAR231893/EFC14153/CSR_RWE/REPORT/PGM/eff_mmrm_ger_subg_i_t.sas OUT=REPORT/OUTPUT/eff_mmrm_awak_ger_onsa_i_t_x.rtf (10AUG2021 - 9:54)

Project Code / Study Number / Analysis: SAR231893 / EFC14153 / CSR_RWE

6 Number of nocturnal awakenings - ITT type 2 inflammatory asthma phenotype population

6.1 Summary of treatment effect on change from baseline at Week 52

6.1.12 By age at onset of asthma (0-2, 3-5, >=6 years)

	Age of onset of asthma (years)					
	0-2		3-5		>= 6	
Number of nocturnal awakenings	**Placebo (N=40)**	**Dupilumab (N=105)**	**Placebo (N=39)**	**Dupilumab (N=86)**	**Placebo (N=35)**	**Dupilumab (N=45)**
Week 52						
Value						
Number	38	100	38	79	35	43
Mean (SD)	0.12 (0.27)	0.07 (0.27)	0.11 (0.39)	0.06 (0.27)	0.09 (0.24)	0.06 (0.21)
Median	0.00	0.00	0.00	0.00	0.00	0.00
Q1 : Q3	0.00 : 0.10	0.00 : 0.00	0.00 : 0.00	0.00 : 0.00	0.00 : 0.06	0.00 : 0.00
Min : Max	0.0 : 1.2	0.0 : 2.0	0.0 : 2.1	0.0 : 2.0	0.0 : 1.0	0.0 : 1.0
Change from baseline						
Number	38	100	38	79	35	43
LS Mean (SE)[a]	-0.21 (0.04)	-0.28 (0.03)	-0.33 (0.05)	-0.38 (0.04)	-0.29 (0.04)	-0.35 (0.04)
LS Mean Diff (95% CI)[a]	-	-0.07 (-0.17 to 0.03)	-	-0.05 (-0.17 to 0.07)	-	-0.06 (-0.16 to 0.03)
p-value[a]		0.146		0.407		0.174

[a]Derived from MMRM model with change from baseline in Number of nocturnal awakenings values up to Week 52 as the response variable, and treatment, baseline weight group, region, age, baseline eosinophil level, baseline FeNO level, baseline ICS dose level, visit, treatment by-visit interaction, baseline Number of nocturnal awakenings value and baseline-by-visit interaction as covariates.
[b]Similar model as that mentioned in the footnote [a] with subgroup and subgroup-by-treatment interaction as additional covariates.
Type 2 inflammatory asthma phenotype population is defined as the randomized patients with baseline blood eosinophils >= 0.15 Giga/L or baseline FeNO >= 20 ppb.
PGM=DEVOPS/SAR231893/EFC14153/CSR_RWE/REPORT/PGM/eff_mmrm_ger_subg_i_t.sas OUT=REPORT/OUTPUT/eff_mmrm_awak_ger_onsa_i_t_x.rtf (10AUG2021 - 9:54)

Project Code / Study Number / Analysis: SAR231893 / EFC14153 / CSR_RWE

6 Number of nocturnal awakenings - ITT type 2 inflammatory asthma phenotype population

6.1 Summary of treatment effect on change from baseline at Week 52

6.1.12 By age at onset of asthma (0-2, 3-5, >=6 years)

	Age of onset of asthma (years)					
	0-2		3-5		>= 6	
Number of nocturnal awakenings	**Placebo (N=40)**	**Dupilumab (N=105)**	**Placebo (N=39)**	**Dupilumab (N=86)**	**Placebo (N=35)**	**Dupilumab (N=45)**
Hedges'g (95% CI)	-	-0.280 (-0.659 to 0.098)	-	-0.164 (-0.556 to 0.227)	-	-0.323 (-0.792 to 0.146)
p-value for heterogeneity[b]:						
0-2, 3-5						0.729
0-2, >= 6						0.898
3-5, >= 6						0.852
overall						0.941

[a]Derived from MMRM model with change from baseline in Number of nocturnal awakenings values up to Week 52 as the response variable, and treatment, baseline weight group, region, age, baseline eosinophil level, baseline FeNO level, baseline ICS dose level, visit, treatment by-visit interaction, baseline Number of nocturnal awakenings value and baseline-by-visit interaction as covariates.
[b]Similar model as that mentioned in the footnote [a] with subgroup and subgroup-by-treatment interaction as additional covariates.
Type 2 inflammatory asthma phenotype population is defined as the randomized patients with baseline blood eosinophils >= 0.15 Giga/L or baseline FeNO >= 20 ppb.
PGM=DEVOPS/SAR231893/EFC14153/CSR_RWE/REPORT/PGM/eff_mmrm_ger_subg_i_t.sas OUT=REPORT/OUTPUT/eff_mmrm_awak_ger_onsa_i_t_x.rtf (10AUG2021 - 9:54)

Project Code / Study Number / Analysis: SAR231893 / EFC14153 / CSR_RWE

6 Number of nocturnal awakenings - ITT type 2 inflammatory asthma phenotype population

6.1 Summary of treatment effect on change from baseline at Week 52

6.1.13 By number of severe asthma exacerbation prior to the study (<=1, 2, >2)

	Number of severe asthma exacerbation prior to the study					
	<=1		2		>2	
Number of nocturnal awakenings	**Placebo (N=47)**	**Dupilumab (N=85)**	**Placebo (N=32)**	**Dupilumab (N=75)**	**Placebo (N=35)**	**Dupilumab (N=76)**
Baseline						
Value						
Number	47	85	32	75	35	76
Mean (SD)	0.26 (0.35)	0.29 (0.37)	0.32 (0.39)	0.65 (1.02)	0.41 (0.60)	0.25 (0.43)
Median	0.14	0.14	0.15	0.14	0.17	0.00
Q1 : Q3	0.00 : 0.33	0.00 : 0.43	0.00 : 0.62	0.00 : 0.86	0.00 : 0.71	0.00 : 0.31
Min : Max	0.0 : 1.0	0.0 : 1.3	0.0 : 1.3	0.0 : 4.4	0.0 : 2.5	0.0 : 1.9

[a]Derived from MMRM model with change from baseline in Number of nocturnal awakenings values up to Week 52 as the response variable, and treatment, baseline weight group, region, age, baseline eosinophil level, baseline FeNO level, baseline ICS dose level, visit, treatment by-visit interaction, baseline Number of nocturnal awakenings value and baseline-by-visit interaction as covariates.
[b]Similar model as that mentioned in the footnote [a] with subgroup and subgroup-by-treatment interaction as additional covariates.
Type 2 inflammatory asthma phenotype population is defined as the randomized patients with baseline blood eosinophils >= 0.15 Giga/L or baseline FeNO >= 20 ppb.
PGM=DEVOPS/SAR231893/EFC14153/CSR_RWE/REPORT/PGM/eff_mmrm_ger_subg_i_t.sas OUT=REPORT/OUTPUT/eff_mmrm_awak_ger_exa_i_t_x.rtf (21JUL2021 - 11:44)

Project Code / Study Number / Analysis: SAR231893 / EFC14153 / CSR_RWE

6 Number of nocturnal awakenings - ITT type 2 inflammatory asthma phenotype population

6.1 Summary of treatment effect on change from baseline at Week 52

6.1.13 By number of severe asthma exacerbation prior to the study (<=1, 2, >2)

	Number of severe asthma exacerbation prior to the study					
	<=1		2		>2	
Number of nocturnal awakenings	**Placebo (N=47)**	**Dupilumab (N=85)**	**Placebo (N=32)**	**Dupilumab (N=75)**	**Placebo (N=35)**	**Dupilumab (N=76)**
Week 52						
Value						
Number	45	82	32	71	34	69
Mean (SD)	0.06 (0.18)	0.06 (0.20)	0.10 (0.25)	0.08 (0.31)	0.18 (0.45)	0.06 (0.28)
Median	0.00	0.00	0.00	0.00	0.00	0.00
Q1 : Q3	0.00 : 0.00	0.00 : 0.00	0.00 : 0.05	0.00 : 0.00	0.00 : 0.07	0.00 : 0.00
Min : Max	0.0 : 1.0	0.0 : 1.0	0.0 : 1.0	0.0 : 2.0	0.0 : 2.1	0.0 : 2.0
Change from baseline						
Number	45	82	32	71	34	69
LS Mean (SE)[a]	-0.23 (0.03)	-0.25 (0.02)	-0.43 (0.05)	-0.50 (0.04)	-0.10 (0.06)	-0.24 (0.05)
LS Mean Diff (95% CI)[a]	-	-0.02 (-0.08 to 0.05)	-	-0.06 (-0.19 to 0.06)	-	-0.14 (-0.28 to 0.00)
p-value[a]		0.584		0.305		0.052

[a]Derived from MMRM model with change from baseline in Number of nocturnal awakenings values up to Week 52 as the response variable, and treatment, baseline weight group, region, age, baseline eosinophil level, baseline FeNO level, baseline ICS dose level, visit, treatment by-visit interaction, baseline Number of nocturnal awakenings value and baseline-by-visit interaction as covariates.
[b]Similar model as that mentioned in the footnote [a] with subgroup and subgroup-by-treatment interaction as additional covariates.
Type 2 inflammatory asthma phenotype population is defined as the randomized patients with baseline blood eosinophils >= 0.15 Giga/L or baseline FeNO >= 20 ppb.
PGM=DEVOPS/SAR231893/EFC14153/CSR_RWE/REPORT/PGM/eff_mmrm_ger_subg_i_t.sas OUT=REPORT/OUTPUT/eff_mmrm_awak_ger_exa_i_t_x.rtf (21JUL2021 - 11:44)

Project Code / Study Number / Analysis: SAR231893 / EFC14153 / CSR_RWE

6 Number of nocturnal awakenings - ITT type 2 inflammatory asthma phenotype population

6.1 Summary of treatment effect on change from baseline at Week 52

6.1.13 By number of severe asthma exacerbation prior to the study (<=1, 2, >2)

	Number of severe asthma exacerbation prior to the study					
	<=1		2		>2	
Number of nocturnal awakenings	**Placebo (N=47)**	**Dupilumab (N=85)**	**Placebo (N=32)**	**Dupilumab (N=75)**	**Placebo (N=35)**	**Dupilumab (N=76)**
Hedges'g (95% CI)	-	-0.102 (-0.472 to 0.267)	-	-0.229 (-0.671 to 0.212)	-	-0.426 (-0.855 to 0.003)
p-value for heterogeneity[b]:						
<=1, 2						0.332
<=1, >2						0.086
2, >2						0.497
overall						0.221

[a]Derived from MMRM model with change from baseline in Number of nocturnal awakenings values up to Week 52 as the response variable, and treatment, baseline weight group, region, age, baseline eosinophil level, baseline FeNO level, baseline ICS dose level, visit, treatment by-visit interaction, baseline Number of nocturnal awakenings value and baseline-by-visit interaction as covariates.
[b]Similar model as that mentioned in the footnote [a] with subgroup and subgroup-by-treatment interaction as additional covariates.
Type 2 inflammatory asthma phenotype population is defined as the randomized patients with baseline blood eosinophils >= 0.15 Giga/L or baseline FeNO >= 20 ppb.
PGM=DEVOPS/SAR231893/EFC14153/CSR_RWE/REPORT/PGM/eff_mmrm_ger_subg_i_t.sas OUT=REPORT/OUTPUT/eff_mmrm_awak_ger_exa_i_t_x.rtf (21JUL2021 - 11:44)

Project Code / Study Number / Analysis: SAR231893 / EFC14153 / CSR_RWE

7 PAQLQ(S)-IA global score - ITT type 2 inflammatory asthma phenotype population

7.1 Summary of treatment effect on change from baseline at Week 52

PAQLQ(S)-IA global score	Placebo (N=107)	Dupilumab (N=211)
Baseline		
Value		
Number	104	203
Mean (SD)	4.92 (1.13)	4.95 (1.08)
Median	5.11	5.13
Q1 : Q3	4.20 : 5.89	4.26 : 5.70
Min : Max	1.8 : 6.9	1.3 : 6.8
Week 52		
Value		
Number	103	191
Mean (SD)	6.18 (0.94)	6.54 (0.66)
Median	6.57	6.78
Q1 : Q3	5.87 : 6.87	6.35 : 6.96
Min : Max	3.1 : 7.0	3.3 : 7.0

[a]Derived from MMRM model with change from baseline in PAQLQ(S)-IA global score values up to Week 52 as the response variable, and treatment, baseline weight group, region, age, baseline eosinophil level, baseline FeNO level, baseline ICS dose level, visit, treatment by-visit interaction, baseline PAQLQ(S)-IA global score value and baseline-by-visit interaction as covariates.

Type 2 inflammatory asthma phenotype population is defined as the randomized patients with baseline blood eosinophils >= 0.15 Giga/L or baseline FeNO >= 20 ppb. Only patients of age >=7 years old at randomization are included in the analysis.

PGM=DEVOPS/SAR231893/EFC14153/CSR_RWE/REPORT/PGM/eff_mmrm_ger_i_t.sas OUT=REPORT/OUTPUT/eff_mmrm_aqlq_ger_i_t_x.rtf (22JUL2021 - 7:59)

Project Code / Study Number / Analysis: SAR231893 / EFC14153 / CSR_RWE

7 PAQLQ(S)-IA global score - ITT type 2 inflammatory asthma phenotype population

7.1 Summary of treatment effect on change from baseline at Week 52

PAQLQ(S)-IA global score	Placebo (N=107)	Dupilumab (N=211)
Change from baseline		
Number	101	184
LS Mean (SE)[a]	1.19 (0.08)	1.53 (0.06)
LS Mean Diff (95% CI)[a]	-	0.34 (0.16 to 0.52)
Hedges'g (95% CI)	-	0.471 (0.225 to 0.716)
p-value[a]		<0.001

[a]Derived from MMRM model with change from baseline in PAQLQ(S)-IA global score values up to Week 52 as the response variable, and treatment, baseline weight group, region, age, baseline eosinophil level, baseline FeNO level, baseline ICS dose level, visit, treatment by-visit interaction, baseline PAQLQ(S)-IA global score value and baseline-by-visit interaction as covariates.
Type 2 inflammatory asthma phenotype population is defined as the randomized patients with baseline blood eosinophils >= 0.15 Giga/L or baseline FeNO >= 20 ppb.
Only patients of age >=7 years old at randomization are included in the analysis.
PGM=DEVOPS/SAR231893/EFC14153/CSR_RWE/REPORT/PGM/eff_mmrm_ger_i_t.sas OUT=REPORT/OUTPUT/eff_mmrm_aqlq_ger_i_t_x.rtf (22JUL2021 - 7:59)

Project Code / Study Number / Analysis: SAR231893 / EFC14153 / CSR_RWE

7 PAQLQ(S)-IA global score - ITT type 2 inflammatory asthma phenotype population

7.1 Summary of treatment effect on change from baseline at Week 52

7.1.1 By gender (Male, Female)

	Gender			
	Male		Female	
PAQLQ(S)-IA global score	**Placebo (N=72)**	**Dupilumab (N=134)**	**Placebo (N=35)**	**Dupilumab (N=77)**
Baseline				
Value				
Number	70	128	34	75
Mean (SD)	4.84 (1.19)	4.98 (1.00)	5.08 (1.00)	4.90 (1.21)
Median	5.07	5.17	5.15	5.00
Q1 : Q3	3.83 : 5.87	4.33 : 5.67	4.35 : 5.91	4.09 : 5.91
Min : Max	1.8 : 6.9	1.3 : 6.8	2.7 : 6.7	1.3 : 6.8

[a]Derived from MMRM model with change from baseline in PAQLQ(S)-IA global score values up to Week 52 as the response variable, and treatment, baseline weight group, region, age, baseline eosinophil level, baseline FeNO level, baseline ICS dose level, visit, treatment by-visit interaction, baseline PAQLQ(S)-IA global score value and baseline-by-visit interaction as covariates.

[b]Similar model as that mentioned in the footnote [a] with subgroup and subgroup-by-treatment interaction as additional covariates.

Type 2 inflammatory asthma phenotype population is defined as the randomized patients with baseline blood eosinophils >= 0.15 Giga/L or baseline FeNO >= 20 ppb.

Only patients of age >=7 years old at randomization are included in the analysis.

PGM=DEVOPS/SAR231893/EFC14153/CSR_RWE/REPORT/PGM/eff_mmrm_ger_subg_i_t.sas OUT=REPORT/OUTPUT/eff_mmrm_aqlq_ger_sex_i_t_x.rtf (21JUL2021 - 8:29)

Project Code / Study Number / Analysis: SAR231893 / EFC14153 / CSR_RWE

7 PAQLQ(S)-IA global score - ITT type 2 inflammatory asthma phenotype population

7.1 Summary of treatment effect on change from baseline at Week 52

7.1.1 By gender (Male, Female)

	Gender			
	Male		Female	
PAQLQ(S)-IA global score	**Placebo (N=72)**	**Dupilumab (N=134)**	**Placebo (N=35)**	**Dupilumab (N=77)**
Week 52				
Value				
Number	70	120	33	71
Mean (SD)	6.08 (0.94)	6.56 (0.60)	6.40 (0.91)	6.50 (0.75)
Median	6.35	6.78	6.78	6.78
Q1 : Q3	5.74 : 6.74	6.37 : 6.96	6.48 : 6.91	6.35 : 6.96
Min : Max	3.1 : 7.0	3.7 : 7.0	3.3 : 7.0	3.3 : 7.0
Change from baseline				
Number	69	115	32	69
LS Mean (SE)[a]	1.19 (0.10)	1.61 (0.08)	1.26 (0.14)	1.50 (0.10)
LS Mean Diff (95% CI)[a]	-	0.42 (0.20 to 0.64)	-	0.23 (-0.08 to 0.55)
p-value[a]		<0.001		0.142
Hedges'g (95% CI)	-	0.575 (0.269 to 0.880)	-	0.316 (-0.108 to 0.741)

[a]Derived from MMRM model with change from baseline in PAQLQ(S)-IA global score values up to Week 52 as the response variable, and treatment, baseline weight group, region, age, baseline eosinophil level, baseline FeNO level, baseline ICS dose level, visit, treatment by-visit interaction, baseline PAQLQ(S)-IA global score value and baseline-by-visit interaction as covariates.
[b]Similar model as that mentioned in the footnote [a] with subgroup and subgroup-by-treatment interaction as additional covariates.
Type 2 inflammatory asthma phenotype population is defined as the randomized patients with baseline blood eosinophils >= 0.15 Giga/L or baseline FeNO >= 20 ppb.
Only patients of age >=7 years old at randomization are included in the analysis.
PGM=DEVOPS/SAR231893/EFC14153/CSR_RWE/REPORT/PGM/eff_mmrm_ger_subg_i_t.sas OUT=REPORT/OUTPUT/eff_mmrm_aqlq_ger_sex_i_t_x.rtf (21JUL2021 - 8:29)

Project Code / Study Number / Analysis: SAR231893 / EFC14153 / CSR_RWE

7 PAQLQ(S)-IA global score - ITT type 2 inflammatory asthma phenotype population

7.1 Summary of treatment effect on change from baseline at Week 52

7.1.1 By gender (Male, Female)

	Gender			
	Male		Female	
PAQLQ(S)-IA global score	**Placebo (N=72)**	**Dupilumab (N=134)**	**Placebo (N=35)**	**Dupilumab (N=77)**
p-value for heterogeneity[b]				0.235

[a]Derived from MMRM model with change from baseline in PAQLQ(S)-IA global score values up to Week 52 as the response variable, and treatment, baseline weight group, region, age, baseline eosinophil level, baseline FeNO level, baseline ICS dose level, visit, treatment by-visit interaction, baseline PAQLQ(S)-IA global score value and baseline-by-visit interaction as covariates.

[b]Similar model as that mentioned in the footnote [a] with subgroup and subgroup-by-treatment interaction as additional covariates.

Type 2 inflammatory asthma phenotype population is defined as the randomized patients with baseline blood eosinophils >= 0.15 Giga/L or baseline FeNO >= 20 ppb.

Only patients of age >=7 years old at randomization are included in the analysis.

PGM=DEVOPS/SAR231893/EFC14153/CSR_RWE/REPORT/PGM/eff_mmrm_ger_subg_i_t.sas OUT=REPORT/OUTPUT/eff_mmrm_aqlq_ger_sex_i_t_x.rtf (21JUL2021 - 8:29)

Project Code / Study Number / Analysis: SAR231893 / EFC14153 / CSR_RWE

7 PAQLQ(S)-IA global score - ITT type 2 inflammatory asthma phenotype population

7.1 Summary of treatment effect on change from baseline at Week 52

7.1.2 By region (Latin America, East Europe, Western Countries)

	Region					
	Latin America		East Europe		Western countries	
PAQLQ(S)-IA global score	**Placebo (N=50)**	**Dupilumab (N=94)**	**Placebo (N=37)**	**Dupilumab (N=68)**	**Placebo (N=20)**	**Dupilumab (N=49)**
Baseline						
Value						
Number	48	89	36	67	20	47
Mean (SD)	4.89 (1.24)	4.99 (0.98)	4.93 (0.93)	5.05 (0.93)	4.97 (1.22)	4.74 (1.41)
Median	5.09	5.04	4.98	5.39	5.39	4.70
Q1 : Q3	4.04 : 6.00	4.30 : 5.91	4.48 : 5.57	4.43 : 5.65	3.54 : 6.00	3.91 : 6.04
Min : Max	1.8 : 6.7	3.1 : 6.8	2.7 : 6.8	2.2 : 6.6	3.0 : 6.9	1.3 : 6.7

[a]Derived from MMRM model with change from baseline in PAQLQ(S)-IA global score values up to Week 52 as the response variable, and treatment, baseline weight group, age, baseline eosinophil level, baseline FeNO level, baseline ICS dose level, visit, treatment by-visit interaction, baseline PAQLQ(S)-IA global score value and baseline-by-visit interaction as covariates.
[b]Similar model as that mentioned in the footnote [a] with subgroup and subgroup-by-treatment interaction as additional covariates.
Type 2 inflammatory asthma phenotype population is defined as the randomized patients with baseline blood eosinophils >= 0.15 Giga/L or baseline FeNO >= 20 ppb.
Only patients of age >=7 years old at randomization are included in the analysis.
PGM=DEVOPS/SAR231893/EFC14153/CSR_RWE/REPORT/PGM/eff_mmrm_ger_subg_i_t.sas OUT=REPORT/OUTPUT/eff_mmrm_aqlq_ger_cty_i_t_x.rtf (21JUL2021 - 8:45)

Project Code / Study Number / Analysis: SAR231893 / EFC14153 / CSR_RWE

7 PAQLQ(S)-IA global score - ITT type 2 inflammatory asthma phenotype population

7.1 Summary of treatment effect on change from baseline at Week 52

7.1.2 By region (Latin America, East Europe, Western Countries)

	Region					
	Latin America		East Europe		Western countries	
PAQLQ(S)-IA global score	**Placebo (N=50)**	**Dupilumab (N=94)**	**Placebo (N=37)**	**Dupilumab (N=68)**	**Placebo (N=20)**	**Dupilumab (N=49)**
Week 52						
Value						
Number	50	89	36	65	17	37
Mean (SD)	6.33 (0.94)	6.70 (0.48)	6.14 (0.78)	6.41 (0.65)	5.83 (1.16)	6.37 (0.93)
Median	6.67	6.87	6.33	6.57	6.48	6.70
Q1 : Q3	6.26 : 6.91	6.74 : 6.96	5.80 : 6.67	6.17 : 6.91	5.13 : 6.78	6.30 : 6.91
Min : Max	3.1 : 7.0	4.7 : 7.0	3.3 : 7.0	4.2 : 7.0	3.6 : 7.0	3.3 : 7.0
Change from baseline						
Number	48	84	36	64	17	36
LS Mean (SE)[a]	1.42 (0.11)	1.73 (0.08)	1.11 (0.13)	1.36 (0.10)	0.89 (0.30)	1.54 (0.21)
LS Mean Diff (95% CI)[a]	-	0.31 (0.07 to 0.55)	-	0.25 (-0.03 to 0.52)	-	0.65 (0.01 to 1.28)
p-value[a]		0.012		0.078		0.046

[a]Derived from MMRM model with change from baseline in PAQLQ(S)-IA global score values up to Week 52 as the response variable, and treatment, baseline weight group, age, baseline eosinophil level, baseline FeNO level, baseline ICS dose level, visit, treatment by-visit interaction, baseline PAQLQ(S)-IA global score value and baseline-by-visit interaction as covariates.

[b]Similar model as that mentioned in the footnote [a] with subgroup and subgroup-by-treatment interaction as additional covariates.

Type 2 inflammatory asthma phenotype population is defined as the randomized patients with baseline blood eosinophils >= 0.15 Giga/L or baseline FeNO >= 20 ppb.

Only patients of age >=7 years old at randomization are included in the analysis.

PGM=DEVOPS/SAR231893/EFC14153/CSR_RWE/REPORT/PGM/eff_mmrm_ger_subg_i_t.sas OUT=REPORT/OUTPUT/eff_mmrm_aqlq_ger_cty_i_t_x.rtf (21JUL2021 - 8:45)

Project Code / Study Number / Analysis: SAR231893 / EFC14153 / CSR_RWE

7 PAQLQ(S)-IA global score - ITT type 2 inflammatory asthma phenotype population

7.1 Summary of treatment effect on change from baseline at Week 52

7.1.2 By region (Latin America, East Europe, Western Countries)

	Region					
	Latin America		East Europe		Western countries	
PAQLQ(S)-IA global score	**Placebo (N=50)**	**Dupilumab (N=94)**	**Placebo (N=37)**	**Dupilumab (N=68)**	**Placebo (N=20)**	**Dupilumab (N=49)**
Hedges'g (95% CI)	-	0.474 (0.107 to 0.841)	-	0.370 (-0.043 to 0.783)	-	0.597 (0.012 to 1.182)
p-value for heterogeneity[b]:						
Latin America, East Europe						0.774
Latin America, Western countries						0.137
East Europe, Western countries						0.188
overall						0.305

[a]Derived from MMRM model with change from baseline in PAQLQ(S)-IA global score values up to Week 52 as the response variable, and treatment, baseline weight group, age, baseline eosinophil level, baseline FeNO level, baseline ICS dose level, visit, treatment by-visit interaction, baseline PAQLQ(S)-IA global score value and baseline-by-visit interaction as covariates.

[b]Similar model as that mentioned in the footnote [a] with subgroup and subgroup-by-treatment interaction as additional covariates.

Type 2 inflammatory asthma phenotype population is defined as the randomized patients with baseline blood eosinophils >= 0.15 Giga/L or baseline FeNO >= 20 ppb. Only patients of age >=7 years old at randomization are included in the analysis.

PGM=DEVOPS/SAR231893/EFC14153/CSR_RWE/REPORT/PGM/eff_mmrm_ger_subg_i_t.sas OUT=REPORT/OUTPUT/eff_mmrm_aqlq_ger_cty_i_t_x.rtf (21JUL2021 - 8:45)

Project Code / Study Number / Analysis: SAR231893 / EFC14153 / CSR_RWE

7 PAQLQ(S)-IA global score - ITT type 2 inflammatory asthma phenotype population

7.1 Summary of treatment effect on change from baseline at Week 52

7.1.3 By race (Caucasian/white, Black/of African descent, Other)

	Race					
	Caucasian/White		Black/of African descent		Other	
PAQLQ(S)-IA global score	**Placebo (N=95)**	**Dupilumab (N=183)**	**Placebo (N=5)**	**Dupilumab (N=9)**	**Placebo (N=7)**	**Dupilumab (N=19)**
Baseline						
Value						
Number	93	175	4	9	7	19
Mean (SD)	4.90 (1.14)	4.97 (0.97)	5.36 (1.22)	4.44 (1.70)	4.94 (1.09)	5.07 (1.58)
Median	5.04	5.09	5.87	5.22	5.52	5.26
Q1 : Q3	4.22 : 5.87	4.30 : 5.65	4.59 : 6.13	3.35 : 5.52	3.83 : 5.87	4.09 : 6.26
Min : Max	1.8 : 6.9	2.1 : 6.8	3.6 : 6.1	1.3 : 6.5	3.3 : 6.0	1.3 : 6.8

[a]Derived from MMRM model with change from baseline in PAQLQ(S)-IA global score values up to Week 52 as the response variable, and treatment, baseline weight group, region, age, baseline eosinophil level, baseline FeNO level, baseline ICS dose level, visit, treatment by-visit interaction, baseline PAQLQ(S)-IA global score value and baseline-by-visit interaction as covariates.
[b]Similar model as that mentioned in the footnote [a] with subgroup and subgroup-by-treatment interaction as additional covariates.
Type 2 inflammatory asthma phenotype population is defined as the randomized patients with baseline blood eosinophils >= 0.15 Giga/L or baseline FeNO >= 20 ppb.
Only patients of age >=7 years old at randomization are included in the analysis.
PGM=DEVOPS/SAR231893/EFC14153/CSR_RWE/REPORT/PGM/eff_mmrm_ger_subg_i_t.sas OUT=REPORT/OUTPUT/eff_mmrm_aqlq_ger_race_i_t_x.rtf (21JUL2021 - 8:30)

Project Code / Study Number / Analysis: SAR231893 / EFC14153 / CSR_RWE

7 PAQLQ(S)-IA global score - ITT type 2 inflammatory asthma phenotype population

7.1 Summary of treatment effect on change from baseline at Week 52

7.1.3 By race (Caucasian/white, Black/of African descent, Other)

	Race					
	Caucasian/White		Black/of African descent		Other	
PAQLQ(S)-IA global score	**Placebo (N=95)**	**Dupilumab (N=183)**	**Placebo (N=5)**	**Dupilumab (N=9)**	**Placebo (N=7)**	**Dupilumab (N=19)**
Week 52						
Value						
Number	94	170	2	7	7	14
Mean (SD)	6.29 (0.83)	6.56 (0.64)	5.04 (0.86)	6.16 (0.84)	5.06 (1.45)	6.44 (0.73)
Median	6.57	6.83	5.04	6.26	5.13	6.67
Q1 : Q3	6.00 : 6.91	6.43 : 6.96	4.43 : 5.65	5.91 : 6.87	3.61 : 6.48	6.30 : 6.87
Min : Max	3.3 : 7.0	3.3 : 7.0	4.4 : 5.7	4.4 : 6.9	3.1 : 6.6	4.2 : 7.0
Change from baseline						
Number	92	163	2	7	7	14
LS Mean (SE)[a]	1.33 (0.08)	1.58 (0.07)	-0.75 (1.18)	0.81 (0.72)	0.54 (0.50)	1.72 (0.37)
LS Mean Diff (95% CI)[a]	-	0.24 (0.07 to 0.42)	-	1.56 (-0.57 to 3.69)	-	1.18 (-0.13 to 2.49)
p-value[a]		0.006		0.134		0.072

[a]Derived from MMRM model with change from baseline in PAQLQ(S)-IA global score values up to Week 52 as the response variable, and treatment, baseline weight group, region, age, baseline eosinophil level, baseline FeNO level, baseline ICS dose level, visit, treatment by-visit interaction, baseline PAQLQ(S)-IA global score value and baseline-by-visit interaction as covariates.

[b]Similar model as that mentioned in the footnote [a] with subgroup and subgroup-by-treatment interaction as additional covariates.

Type 2 inflammatory asthma phenotype population is defined as the randomized patients with baseline blood eosinophils >= 0.15 Giga/L or baseline FeNO >= 20 ppb. Only patients of age >=7 years old at randomization are included in the analysis.

PGM=DEVOPS/SAR231893/EFC14153/CSR_RWE/REPORT/PGM/eff_mmrm_ger_subg_i_t.sas OUT=REPORT/OUTPUT/eff_mmrm_aqlq_ger_race_i_t_x.rtf (21JUL2021 - 8:30)

Project Code / Study Number / Analysis: SAR231893 / EFC14153 / CSR_RWE

7 PAQLQ(S)-IA global score - ITT type 2 inflammatory asthma phenotype population

7.1 Summary of treatment effect on change from baseline at Week 52

7.1.3 By race (Caucasian/white, Black/of African descent, Other)

	Race					
	Caucasian/White		Black/of African descent		Other	
PAQLQ(S)-IA global score	**Placebo (N=95)**	**Dupilumab (N=183)**	**Placebo (N=5)**	**Dupilumab (N=9)**	**Placebo (N=7)**	**Dupilumab (N=19)**
Hedges'g (95% CI)	-	0.364 (0.105 to 0.623)	-	0.769 (-0.282 to 1.819)	-	0.942 (-0.103 to 1.987)
p-value for heterogeneity[b]:						
Caucasian/White, Black/of African descent						0.045
Caucasian/White, Other						0.894
Black/of African descent, Other						0.006
overall						0.004

[a]Derived from MMRM model with change from baseline in PAQLQ(S)-IA global score values up to Week 52 as the response variable, and treatment, baseline weight group, region, age, baseline eosinophil level, baseline FeNO level, baseline ICS dose level, visit, treatment by-visit interaction, baseline PAQLQ(S)-IA global score value and baseline-by-visit interaction as covariates.

[b]Similar model as that mentioned in the footnote [a] with subgroup and subgroup-by-treatment interaction as additional covariates.

Type 2 inflammatory asthma phenotype population is defined as the randomized patients with baseline blood eosinophils >= 0.15 Giga/L or baseline FeNO >= 20 ppb.

Only patients of age >=7 years old at randomization are included in the analysis.

PGM=DEVOPS/SAR231893/EFC14153/CSR_RWE/REPORT/PGM/eff_mmrm_ger_subg_i_t.sas OUT=REPORT/OUTPUT/eff_mmrm_aqlq_ger_race_i_t_x.rtf (21JUL2021 - 8:30)

Project Code / Study Number / Analysis: SAR231893 / EFC14153 / CSR_RWE

7 PAQLQ(S)-IA global score - ITT type 2 inflammatory asthma phenotype population

7.1 Summary of treatment effect on change from baseline at Week 52

7.1.4 By baseline ICS dose level (Medium, High)

	Baseline ICS dose level			
	High		Medium	
PAQLQ(S)-IA global score	**Placebo (N=45)**	**Dupilumab (N=92)**	**Placebo (N=62)**	**Dupilumab (N=118)**
Baseline				
Value				
Number	44	87	60	115
Mean (SD)	4.87 (1.18)	4.74 (1.19)	4.96 (1.10)	5.10 (0.96)
Median	5.24	4.96	5.07	5.26
Q1 : Q3	3.54 : 5.87	4.04 : 5.57	4.28 : 5.91	4.43 : 5.87
Min : Max	2.7 : 6.9	1.3 : 6.7	1.8 : 6.8	1.3 : 6.8

[a]Derived from MMRM model with change from baseline in PAQLQ(S)-IA global score values up to Week 52 as the response variable, and treatment, baseline weight group, region, age, baseline eosinophil level, baseline FeNO level, visit, treatment by-visit interaction, baseline PAQLQ(S)-IA global score value and baseline-by-visit interaction as covariates.

[b]Similar model as that mentioned in the footnote [a] with subgroup and subgroup-by-treatment interaction as additional covariates.

Type 2 inflammatory asthma phenotype population is defined as the randomized patients with baseline blood eosinophils >= 0.15 Giga/L or baseline FeNO >= 20 ppb.

Only patients of age >=7 years old at randomization are included in the analysis.

PGM=DEVOPS/SAR231893/EFC14153/CSR_RWE/REPORT/PGM/eff_mmrm_ger_subg_i_t.sas OUT=REPORT/OUTPUT/eff_mmrm_aqlq_ger_ics_i_t_x.rtf (21JUL2021 - 8:30)

Project Code / Study Number / Analysis: SAR231893 / EFC14153 / CSR_RWE

7 PAQLQ(S)-IA global score - ITT type 2 inflammatory asthma phenotype population

7.1 Summary of treatment effect on change from baseline at Week 52

7.1.4 By baseline ICS dose level (Medium, High)

	Baseline ICS dose level			
	High		Medium	
PAQLQ(S)-IA global score	**Placebo (N=45)**	**Dupilumab (N=92)**	**Placebo (N=62)**	**Dupilumab (N=118)**
Week 52				
Value				
Number	44	82	59	109
Mean (SD)	6.03 (1.05)	6.44 (0.69)	6.29 (0.84)	6.61 (0.63)
Median	6.46	6.74	6.61	6.83
Q1 : Q3	5.35 : 6.80	6.13 : 6.91	5.91 : 6.91	6.57 : 6.96
Min : Max	3.3 : 7.0	3.7 : 7.0	3.1 : 7.0	3.3 : 7.0
Change from baseline				
Number	43	78	58	106
LS Mean (SE)[a]	1.19 (0.14)	1.61 (0.10)	1.15 (0.10)	1.48 (0.08)
LS Mean Diff (95% CI)[a]	-	0.42 (0.12 to 0.72)	-	0.32 (0.09 to 0.56)
p-value[a]		0.006		0.007
Hedges'g (95% CI)	-	0.540 (0.159 to 0.921)	-	0.456 (0.129 to 0.783)

[a]Derived from MMRM model with change from baseline in PAQLQ(S)-IA global score values up to Week 52 as the response variable, and treatment, baseline weight group, region, age, baseline eosinophil level, baseline FeNO level, visit, treatment by-visit interaction, baseline PAQLQ(S)-IA global score value and baseline-by-visit interaction as covariates.
[b]Similar model as that mentioned in the footnote [a] with subgroup and subgroup-by-treatment interaction as additional covariates.
Type 2 inflammatory asthma phenotype population is defined as the randomized patients with baseline blood eosinophils >= 0.15 Giga/L or baseline FeNO >= 20 ppb.
Only patients of age >=7 years old at randomization are included in the analysis.
PGM=DEVOPS/SAR231893/EFC14153/CSR_RWE/REPORT/PGM/eff_mmrm_ger_subg_i_t.sas OUT=REPORT/OUTPUT/eff_mmrm_aqlq_ger_ics_i_t_x.rtf (21JUL2021 - 8:30)

Project Code / Study Number / Analysis: SAR231893 / EFC14153 / CSR_RWE

7 PAQLQ(S)-IA global score - ITT type 2 inflammatory asthma phenotype population

7.1 Summary of treatment effect on change from baseline at Week 52

7.1.4 By baseline ICS dose level (Medium, High)

	Baseline ICS dose level			
	High		Medium	
PAQLQ(S)-IA global score	**Placebo (N=45)**	**Dupilumab (N=92)**	**Placebo (N=62)**	**Dupilumab (N=118)**
p-value for heterogeneity[b]				0.632

[a]Derived from MMRM model with change from baseline in PAQLQ(S)-IA global score values up to Week 52 as the response variable, and treatment, baseline weight group, region, age, baseline eosinophil level, baseline FeNO level, visit, treatment by-visit interaction, baseline PAQLQ(S)-IA global score value and baseline-by-visit interaction as covariates.

[b]Similar model as that mentioned in the footnote [a] with subgroup and subgroup-by-treatment interaction as additional covariates.

Type 2 inflammatory asthma phenotype population is defined as the randomized patients with baseline blood eosinophils >= 0.15 Giga/L or baseline FeNO >= 20 ppb. Only patients of age >=7 years old at randomization are included in the analysis.

PGM=DEVOPS/SAR231893/EFC14153/CSR_RWE/REPORT/PGM/eff_mmrm_ger_subg_i_t.sas OUT=REPORT/OUTPUT/eff_mmrm_aqlq_ger_ics_i_t_x.rtf (21JUL2021 - 8:30)

Project Code / Study Number / Analysis: SAR231893 / EFC14153 / CSR_RWE

7 PAQLQ(S)-IA global score - ITT type 2 inflammatory asthma phenotype population

7.1 Summary of treatment effect on change from baseline at Week 52

7.1.5 By baseline ICS dose level 2 (Medium, High)

	Baseline ICS dose level 2			
	High		Medium	
PAQLQ(S)-IA global score	**Placebo (N=88)**	**Dupilumab (N=182)**	**Placebo (N=19)**	**Dupilumab (N=29)**
Baseline				
Value				
Number	86	175	18	28
Mean (SD)	4.90 (1.14)	4.91 (1.11)	5.01 (1.09)	5.21 (0.86)
Median	5.07	5.09	5.15	5.15
Q1 : Q3	4.17 : 5.87	4.13 : 5.70	4.30 : 6.00	4.63 : 5.91
Min : Max	1.8 : 6.9	1.3 : 6.8	2.3 : 6.7	3.1 : 6.8

[a]Derived from MMRM model with change from baseline in PAQLQ(S)-IA global score values up to Week 52 as the response variable, and treatment, baseline weight group, region, age, baseline eosinophil level, baseline FeNO level, visit, treatment by-visit interaction, baseline PAQLQ(S)-IA global score value and baseline-by-visit interaction as covariates.
[b]Similar model as that mentioned in the footnote [a] with subgroup and subgroup-by-treatment interaction as additional covariates.
Type 2 inflammatory asthma phenotype population is defined as the randomized patients with baseline blood eosinophils >= 0.15 Giga/L or baseline FeNO >= 20 ppb.
Only patients of age >=7 years old at randomization are included in the analysis.
PGM=DEVOPS/SAR231893/EFC14153/CSR_RWE/REPORT/PGM/eff_mmrm_ger_subg_i_t.sas OUT=REPORT/OUTPUT/eff_mmrm_aqlq_ger_ics2_i_t_x.rtf (01SEP2021 - 17:20)

Project Code / Study Number / Analysis: SAR231893 / EFC14153 / CSR_RWE

7 PAQLQ(S)-IA global score - ITT type 2 inflammatory asthma phenotype population

7.1 Summary of treatment effect on change from baseline at Week 52

7.1.5 By baseline ICS dose level 2 (Medium, High)

	Baseline ICS dose level 2			
	High		Medium	
PAQLQ(S)-IA global score	**Placebo (N=88)**	**Dupilumab (N=182)**	**Placebo (N=19)**	**Dupilumab (N=29)**
Week 52				
Value				
Number	85	168	18	23
Mean (SD)	6.11 (0.98)	6.51 (0.69)	6.50 (0.60)	6.76 (0.26)
Median	6.52	6.78	6.72	6.83
Q1 : Q3	5.83 : 6.78	6.30 : 6.96	6.00 : 7.00	6.70 : 6.96
Min : Max	3.1 : 7.0	3.3 : 7.0	4.9 : 7.0	5.9 : 7.0
Change from baseline				
Number	84	162	17	22
LS Mean (SE)[a]	1.14 (0.09)	1.53 (0.07)	1.37 (0.11)	1.58 (0.09)
LS Mean Diff (95% CI)[a]	-	0.40 (0.19 to 0.60)	-	0.21 (-0.04 to 0.45)
p-value[a]		<0.001		0.097
Hedges'g (95% CI)	-	0.521 (0.254 to 0.787)	-	0.600 (-0.115 to 1.315)

[a]Derived from MMRM model with change from baseline in PAQLQ(S)-IA global score values up to Week 52 as the response variable, and treatment, baseline weight group, region, age, baseline eosinophil level, baseline FeNO level, visit, treatment by-visit interaction, baseline PAQLQ(S)-IA global score value and baseline-by-visit interaction as covariates.
[b]Similar model as that mentioned in the footnote [a] with subgroup and subgroup-by-treatment interaction as additional covariates.
Type 2 inflammatory asthma phenotype population is defined as the randomized patients with baseline blood eosinophils >= 0.15 Giga/L or baseline FeNO >= 20 ppb.
Only patients of age >=7 years old at randomization are included in the analysis.
PGM=DEVOPS/SAR231893/EFC14153/CSR_RWE/REPORT/PGM/eff_mmrm_ger_subg_i_t.sas OUT=REPORT/OUTPUT/eff_mmrm_aqlq_ger_ics2_i_t_x.rtf (01SEP2021 - 17:20)

Project Code / Study Number / Analysis: SAR231893 / EFC14153 / CSR_RWE

7 PAQLQ(S)-IA global score - ITT type 2 inflammatory asthma phenotype population

7.1 Summary of treatment effect on change from baseline at Week 52

7.1.5 By baseline ICS dose level 2 (Medium, High)

	Baseline ICS dose level 2			
	High		Medium	
PAQLQ(S)-IA global score	**Placebo (N=88)**	**Dupilumab (N=182)**	**Placebo (N=19)**	**Dupilumab (N=29)**
p-value for heterogeneity[b]				0.344

[a]Derived from MMRM model with change from baseline in PAQLQ(S)-IA global score values up to Week 52 as the response variable, and treatment, baseline weight group, region, age, baseline eosinophil level, baseline FeNO level, visit, treatment by-visit interaction, baseline PAQLQ(S)-IA global score value and baseline-by-visit interaction as covariates.

[b]Similar model as that mentioned in the footnote [a] with subgroup and subgroup-by-treatment interaction as additional covariates.

Type 2 inflammatory asthma phenotype population is defined as the randomized patients with baseline blood eosinophils >= 0.15 Giga/L or baseline FeNO >= 20 ppb. Only patients of age >=7 years old at randomization are included in the analysis.

PGM=DEVOPS/SAR231893/EFC14153/CSR_RWE/REPORT/PGM/eff_mmrm_ger_subg_i_t.sas OUT=REPORT/OUTPUT/eff_mmrm_aqlq_ger_ics2_i_t_x.rtf (01SEP2021 - 17:20)

Project Code / Study Number / Analysis: SAR231893 / EFC14153 / CSR_RWE

7 PAQLQ(S)-IA global score - ITT type 2 inflammatory asthma phenotype population

7.1 Summary of treatment effect on change from baseline at Week 52

7.1.6 By baseline predicted FEV1 (<80%, >=80%)

	Baseline Predicted FEV1			
	<80%		>=80%	
PAQLQ(S)-IA global score	**Placebo (N=59)**	**Dupilumab (N=98)**	**Placebo (N=48)**	**Dupilumab (N=113)**
Baseline				
Value				
Number	57	95	47	108
Mean (SD)	4.76 (1.26)	4.90 (1.00)	5.11 (0.93)	5.00 (1.15)
Median	4.91	5.00	5.17	5.28
Q1 : Q3	3.65 : 5.87	4.26 : 5.48	4.39 : 5.91	4.24 : 5.91
Min : Max	1.8 : 6.9	1.3 : 6.8	3.0 : 6.7	1.3 : 6.8

[a]Derived from MMRM model with change from baseline in PAQLQ(S)-IA global score values up to Week 52 as the response variable, and treatment, baseline weight group, region, age, baseline eosinophil level, baseline FeNO level, baseline ICS dose level, visit, treatment by-visit interaction, baseline PAQLQ(S)-IA global score value and baseline-by-visit interaction as covariates.

[b]Similar model as that mentioned in the footnote [a] with subgroup and subgroup-by-treatment interaction as additional covariates.

Type 2 inflammatory asthma phenotype population is defined as the randomized patients with baseline blood eosinophils >= 0.15 Giga/L or baseline FeNO >= 20 ppb.

Only patients of age >=7 years old at randomization are included in the analysis.

PGM=DEVOPS/SAR231893/EFC14153/CSR_RWE/REPORT/PGM/eff_mmrm_ger_subg_i_t.sas OUT=REPORT/OUTPUT/eff_mmrm_aqlq_ger_pfev1_i_t_x.rtf (21JUL2021 - 8:30)

Project Code / Study Number / Analysis: SAR231893 / EFC14153 / CSR_RWE

7 PAQLQ(S)-IA global score - ITT type 2 inflammatory asthma phenotype population

7.1 Summary of treatment effect on change from baseline at Week 52

7.1.6 By baseline predicted FEV1 (<80%, >=80%)

	Baseline Predicted FEV1			
	<80%		>=80%	
PAQLQ(S)-IA global score	**Placebo (N=59)**	**Dupilumab (N=98)**	**Placebo (N=48)**	**Dupilumab (N=113)**
Week 52				
Value				
Number	56	92	47	99
Mean (SD)	6.12 (0.99)	6.50 (0.65)	6.25 (0.88)	6.57 (0.66)
Median	6.54	6.74	6.61	6.83
Q1 : Q3	5.83 : 6.80	6.30 : 6.91	5.91 : 6.91	6.48 : 6.96
Min : Max	3.1 : 7.0	3.7 : 7.0	3.5 : 7.0	3.3 : 7.0
Change from baseline				
Number	55	89	46	95
LS Mean (SE)[a]	1.29 (0.11)	1.66 (0.10)	1.11 (0.12)	1.43 (0.08)
LS Mean Diff (95% CI)[a]	-	0.38 (0.12 to 0.63)	-	0.32 (0.07 to 0.58)
p-value[a]		0.004		0.014
Hedges'g (95% CI)	-	0.516 (0.166 to 0.867)	-	0.452 (0.094 to 0.810)

[a]Derived from MMRM model with change from baseline in PAQLQ(S)-IA global score values up to Week 52 as the response variable, and treatment, baseline weight group, region, age, baseline eosinophil level, baseline FeNO level, baseline ICS dose level, visit, treatment by-visit interaction, baseline PAQLQ(S)-IA global score value and baseline-by-visit interaction as covariates.
[b]Similar model as that mentioned in the footnote [a] with subgroup and subgroup-by-treatment interaction as additional covariates.
Type 2 inflammatory asthma phenotype population is defined as the randomized patients with baseline blood eosinophils >= 0.15 Giga/L or baseline FeNO >= 20 ppb.
Only patients of age >=7 years old at randomization are included in the analysis.
PGM=DEVOPS/SAR231893/EFC14153/CSR_RWE/REPORT/PGM/eff_mmrm_ger_subg_i_t.sas OUT=REPORT/OUTPUT/eff_mmrm_aqlq_ger_pfev1_i_t_x.rtf (21JUL2021 - 8:30)

Project Code / Study Number / Analysis: SAR231893 / EFC14153 / CSR_RWE

7 PAQLQ(S)-IA global score - ITT type 2 inflammatory asthma phenotype population

7.1 Summary of treatment effect on change from baseline at Week 52

7.1.6 By baseline predicted FEV1 (<80%, >=80%)

	Baseline Predicted FEV1			
	<80%		>=80%	
PAQLQ(S)-IA global score	**Placebo (N=59)**	**Dupilumab (N=98)**	**Placebo (N=48)**	**Dupilumab (N=113)**
p-value for heterogeneity[b]				0.677

[a]Derived from MMRM model with change from baseline in PAQLQ(S)-IA global score values up to Week 52 as the response variable, and treatment, baseline weight group, region, age, baseline eosinophil level, baseline FeNO level, baseline ICS dose level, visit, treatment by-visit interaction, baseline PAQLQ(S)-IA global score value and baseline-by-visit interaction as covariates.

[b]Similar model as that mentioned in the footnote [a] with subgroup and subgroup-by-treatment interaction as additional covariates.

Type 2 inflammatory asthma phenotype population is defined as the randomized patients with baseline blood eosinophils >= 0.15 Giga/L or baseline FeNO >= 20 ppb.

Only patients of age >=7 years old at randomization are included in the analysis.

PGM=DEVOPS/SAR231893/EFC14153/CSR_RWE/REPORT/PGM/eff_mmrm_ger_subg_i_t.sas OUT=REPORT/OUTPUT/eff_mmrm_aqlq_ger_pfev1_i_t_x.rtf (21JUL2021 - 8:30)

Project Code / Study Number / Analysis: SAR231893 / EFC14153 / CSR_RWE

7 PAQLQ(S)-IA global score - ITT type 2 inflammatory asthma phenotype population

7.1 Summary of treatment effect on change from baseline at Week 52

7.1.7 By baseline ACQ-7-IA (<=2, >2)

	Baseline ACQ-7-IA			
	<=2		>2	
PAQLQ(S)-IA global score	**Placebo (N=58)**	**Dupilumab (N=116)**	**Placebo (N=49)**	**Dupilumab (N=95)**
Baseline				
Value				
Number	58	113	46	90
Mean (SD)	5.41 (1.01)	5.38 (0.90)	4.30 (0.96)	4.42 (1.05)
Median	5.61	5.52	4.33	4.43
Q1 : Q3	5.04 : 6.13	4.78 : 6.04	3.57 : 5.00	3.65 : 5.17
Min : Max	1.8 : 6.9	2.2 : 6.8	2.3 : 6.2	1.3 : 6.8

[a]Derived from MMRM model with change from baseline in PAQLQ(S)-IA global score values up to Week 52 as the response variable, and treatment, baseline weight group, region, age, baseline eosinophil level, baseline FeNO level, baseline ICS dose level, visit, treatment by-visit interaction, baseline PAQLQ(S)-IA global score value and baseline-by-visit interaction as covariates.

[b]Similar model as that mentioned in the footnote [a] with subgroup and subgroup-by-treatment interaction as additional covariates.

Type 2 inflammatory asthma phenotype population is defined as the randomized patients with baseline blood eosinophils >= 0.15 Giga/L or baseline FeNO >= 20 ppb.

Only patients of age >=7 years old at randomization are included in the analysis.

PGM=DEVOPS/SAR231893/EFC14153/CSR_RWE/REPORT/PGM/eff_mmrm_ger_subg_i_t.sas OUT=REPORT/OUTPUT/eff_mmrm_aqlq_ger_acq7_i_t_x.rtf (21JUL2021 - 8:30)

Project Code / Study Number / Analysis: SAR231893 / EFC14153 / CSR_RWE

7 PAQLQ(S)-IA global score - ITT type 2 inflammatory asthma phenotype population

7.1 Summary of treatment effect on change from baseline at Week 52

7.1.7 By baseline ACQ-7-IA (<=2, >2)

	Baseline ACQ-7-IA			
	<=2		>2	
PAQLQ(S)-IA global score	**Placebo (N=58)**	**Dupilumab (N=116)**	**Placebo (N=49)**	**Dupilumab (N=95)**
Week 52				
Value				
Number	57	104	46	87
Mean (SD)	6.34 (0.77)	6.57 (0.68)	5.99 (1.09)	6.50 (0.63)
Median	6.61	6.80	6.37	6.74
Q1 : Q3	6.09 : 6.87	6.54 : 6.96	5.48 : 6.78	6.26 : 6.96
Min : Max	3.5 : 7.0	3.3 : 7.0	3.1 : 7.0	4.2 : 7.0
Change from baseline				
Number	57	101	44	83
LS Mean (SE)[a]	0.90 (0.10)	1.09 (0.08)	1.59 (0.14)	2.15 (0.11)
LS Mean Diff (95% CI)[a]	-	0.19 (-0.03 to 0.41)	-	0.55 (0.26 to 0.85)
p-value[a]		0.094		<0.001
Hedges'g (95% CI)	-	0.281 (-0.049 to 0.610)	-	0.699 (0.324 to 1.074)
p-value for heterogeneity[b]				0.046

[a]Derived from MMRM model with change from baseline in PAQLQ(S)-IA global score values up to Week 52 as the response variable, and treatment, baseline weight group, region, age, baseline eosinophil level, baseline FeNO level, baseline ICS dose level, visit, treatment by-visit interaction, baseline PAQLQ(S)-IA global score value and baseline-by-visit interaction as covariates.

[b]Similar model as that mentioned in the footnote [a] with subgroup and subgroup-by-treatment interaction as additional covariates.

Type 2 inflammatory asthma phenotype population is defined as the randomized patients with baseline blood eosinophils >= 0.15 Giga/L or baseline FeNO >= 20 ppb.

Only patients of age >=7 years old at randomization are included in the analysis.

PGM=DEVOPS/SAR231893/EFC14153/CSR_RWE/REPORT/PGM/eff_mmrm_ger_subg_i_t.sas OUT=REPORT/OUTPUT/eff_mmrm_aqlq_ger_acq7_i_t_x.rtf (21JUL2021 - 8:30)

Project Code / Study Number / Analysis: SAR231893 / EFC14153 / CSR_RWE

7 PAQLQ(S)-IA global score - ITT type 2 inflammatory asthma phenotype population

7.1 Summary of treatment effect on change from baseline at Week 52

7.1.8 By baseline weight (<=30 kg, >30 kg)

	Baseline weight (kg)			
	<=30		>30	
PAQLQ(S)-IA global score	**Placebo (N=29)**	**Dupilumab (N=56)**	**Placebo (N=78)**	**Dupilumab (N=155)**
Baseline				
Value				
Number	29	56	75	147
Mean (SD)	5.15 (1.07)	5.11 (1.14)	4.83 (1.15)	4.89 (1.05)
Median	5.52	5.33	5.04	5.00
Q1 : Q3	4.52 : 6.04	4.50 : 5.98	4.17 : 5.78	4.13 : 5.65
Min : Max	3.0 : 6.9	1.3 : 6.8	1.8 : 6.8	1.3 : 6.7

[a]Derived from MMRM model with change from baseline in PAQLQ(S)-IA global score values up to Week 52 as the response variable, and treatment, region, age, baseline eosinophil level, baseline FeNO level, baseline ICS dose level, visit, treatment by-visit interaction, baseline PAQLQ(S)-IA global score value and baseline-by-visit interaction as covariates.

[b]Similar model as that mentioned in the footnote [a] with subgroup and subgroup-by-treatment interaction as additional covariates.

Type 2 inflammatory asthma phenotype population is defined as the randomized patients with baseline blood eosinophils >= 0.15 Giga/L or baseline FeNO >= 20 ppb.

Only patients of age >=7 years old at randomization are included in the analysis.

PGM=DEVOPS/SAR231893/EFC14153/CSR_RWE/REPORT/PGM/eff_mmrm_ger_subg_i_t.sas OUT=REPORT/OUTPUT/eff_mmrm_aqlq_ger_wgt_i_t_x.rtf (21JUL2021 - 8:31)

Project Code / Study Number / Analysis: SAR231893 / EFC14153 / CSR_RWE

7 PAQLQ(S)-IA global score - ITT type 2 inflammatory asthma phenotype population

7.1 Summary of treatment effect on change from baseline at Week 52

7.1.8 By baseline weight (<=30 kg, >30 kg)

	Baseline weight (kg)			
	<=30		>30	
PAQLQ(S)-IA global score	**Placebo (N=29)**	**Dupilumab (N=56)**	**Placebo (N=78)**	**Dupilumab (N=155)**
Week 52				
Value				
Number	27	48	76	143
Mean (SD)	6.18 (1.00)	6.66 (0.45)	6.18 (0.92)	6.49 (0.71)
Median	6.57	6.80	6.52	6.78
Q1 : Q3	5.87 : 6.91	6.50 : 6.96	5.85 : 6.80	6.30 : 6.96
Min : Max	3.1 : 7.0	4.4 : 7.0	3.3 : 7.0	3.3 : 7.0
Change from baseline				
Number	27	48	74	136
LS Mean (SE)[a]	1.04 (0.16)	1.52 (0.12)	1.25 (0.09)	1.54 (0.07)
LS Mean Diff (95% CI)[a]	-	0.48 (0.12 to 0.84)	-	0.29 (0.08 to 0.50)
p-value[a]		0.011		0.007
Hedges'g (95% CI)	-	0.641 (0.155 to 1.126)	-	0.400 (0.112 to 0.687)

[a]Derived from MMRM model with change from baseline in PAQLQ(S)-IA global score values up to Week 52 as the response variable, and treatment, region, age, baseline eosinophil level, baseline FeNO level, baseline ICS dose level, visit, treatment by-visit interaction, baseline PAQLQ(S)-IA global score value and baseline-by-visit interaction as covariates.
[b]Similar model as that mentioned in the footnote [a] with subgroup and subgroup-by-treatment interaction as additional covariates.
Type 2 inflammatory asthma phenotype population is defined as the randomized patients with baseline blood eosinophils >= 0.15 Giga/L or baseline FeNO >= 20 ppb.
Only patients of age >=7 years old at randomization are included in the analysis.
PGM=DEVOPS/SAR231893/EFC14153/CSR_RWE/REPORT/PGM/eff_mmrm_ger_subg_i_t.sas OUT=REPORT/OUTPUT/eff_mmrm_aqlq_ger_wgt_i_t_x.rtf (21JUL2021 - 8:31)

Project Code / Study Number / Analysis: SAR231893 / EFC14153 / CSR_RWE

7 PAQLQ(S)-IA global score - ITT type 2 inflammatory asthma phenotype population

7.1 Summary of treatment effect on change from baseline at Week 52

7.1.8 By baseline weight (<=30 kg, >30 kg)

	Baseline weight (kg)			
	<=30		>30	
PAQLQ(S)-IA global score	**Placebo (N=29)**	**Dupilumab (N=56)**	**Placebo (N=78)**	**Dupilumab (N=155)**
p-value for heterogeneity[b]				0.360

[a]Derived from MMRM model with change from baseline in PAQLQ(S)-IA global score values up to Week 52 as the response variable, and treatment, region, age, baseline eosinophil level, baseline FeNO level, baseline ICS dose level, visit, treatment by-visit interaction, baseline PAQLQ(S)-IA global score value and baseline-by-visit interaction as covariates.
[b]Similar model as that mentioned in the footnote [a] with subgroup and subgroup-by-treatment interaction as additional covariates.
Type 2 inflammatory asthma phenotype population is defined as the randomized patients with baseline blood eosinophils >= 0.15 Giga/L or baseline FeNO >= 20 ppb.
Only patients of age >=7 years old at randomization are included in the analysis.
PGM=DEVOPS/SAR231893/EFC14153/CSR_RWE/REPORT/PGM/eff_mmrm_ger_subg_i_t.sas OUT=REPORT/OUTPUT/eff_mmrm_aqlq_ger_wgt_i_t_x.rtf (21JUL2021 - 8:31)

Project Code / Study Number / Analysis: SAR231893 / EFC14153 / CSR_RWE

7 PAQLQ(S)-IA global score - ITT type 2 inflammatory asthma phenotype population

7.1 Summary of treatment effect on change from baseline at Week 52

7.1.9 By atopic medical condition (Yes, No)

	Atopic medical condition			
	Yes		No	
PAQLQ(S)-IA global score	**Placebo (N=97)**	**Dupilumab (N=205)**	**Placebo (N=10)**	**Dupilumab (N=6)**
Baseline				
Value				
Number	94	197	10	6
Mean (SD)	4.89 (1.14)	4.95 (1.09)	5.19 (1.09)	5.13 (0.93)
Median	5.11	5.13	5.17	4.89
Q1 : Q3	4.17 : 5.87	4.26 : 5.70	4.57 : 6.17	4.43 : 6.13
Min : Max	1.8 : 6.9	1.3 : 6.8	3.0 : 6.4	4.0 : 6.4

[a]Derived from MMRM model with change from baseline in PAQLQ(S)-IA global score values up to Week 52 as the response variable, and treatment, baseline weight group, region, age, baseline eosinophil level, baseline FeNO level, baseline ICS dose level, visit, treatment by-visit interaction, baseline PAQLQ(S)-IA global score value and baseline-by-visit interaction as covariates.
[b]Similar model as that mentioned in the footnote [a] with subgroup and subgroup-by-treatment interaction as additional covariates.
Type 2 inflammatory asthma phenotype population is defined as the randomized patients with baseline blood eosinophils >= 0.15 Giga/L or baseline FeNO >= 20 ppb.
Only patients of age >=7 years old at randomization are included in the analysis.
PGM=DEVOPS/SAR231893/EFC14153/CSR_RWE/REPORT/PGM/eff_mmrm_ger_subg_i_t.sas OUT=REPORT/OUTPUT/eff_mmrm_aqlq_ger_amc_i_t_x.rtf (21JUL2021 - 8:31)

Project Code / Study Number / Analysis: SAR231893 / EFC14153 / CSR_RWE

7 PAQLQ(S)-IA global score - ITT type 2 inflammatory asthma phenotype population

7.1 Summary of treatment effect on change from baseline at Week 52

7.1.9 By atopic medical condition (Yes, No)

	Atopic medical condition			
	Yes		No	
PAQLQ(S)-IA global score	**Placebo (N=97)**	**Dupilumab (N=205)**	**Placebo (N=10)**	**Dupilumab (N=6)**
Week 52				
Value				
Number	93	185	10	6
Mean (SD)	6.16 (0.92)	6.52 (0.67)	6.43 (1.07)	6.92 (0.12)
Median	6.57	6.78	6.83	7.00
Q1 : Q3	5.83 : 6.83	6.35 : 6.96	6.35 : 6.96	6.78 : 7.00
Min : Max	3.1 : 7.0	3.3 : 7.0	3.5 : 7.0	6.7 : 7.0
Change from baseline				
Number	91	178	10	6
LS Mean (SE)[a]	1.19 (0.08)	1.54 (0.06)	1.30 (0.36)	1.82 (0.42)
LS Mean Diff (95% CI)[a]	-	0.35 (0.16 to 0.53)	-	0.53 (-0.59 to 1.65)
p-value[a]		<0.001		0.328
Hedges'g (95% CI)	-	0.487 (0.232 to 0.743)	-	0.554 (-0.627 to 1.735)

[a]Derived from MMRM model with change from baseline in PAQLQ(S)-IA global score values up to Week 52 as the response variable, and treatment, baseline weight group, region, age, baseline eosinophil level, baseline FeNO level, baseline ICS dose level, visit, treatment by-visit interaction, baseline PAQLQ(S)-IA global score value and baseline-by-visit interaction as covariates.
[b]Similar model as that mentioned in the footnote [a] with subgroup and subgroup-by-treatment interaction as additional covariates.
Type 2 inflammatory asthma phenotype population is defined as the randomized patients with baseline blood eosinophils >= 0.15 Giga/L or baseline FeNO >= 20 ppb.
Only patients of age >=7 years old at randomization are included in the analysis.
PGM=DEVOPS/SAR231893/EFC14153/CSR_RWE/REPORT/PGM/eff_mmrm_ger_subg_i_t.sas OUT=REPORT/OUTPUT/eff_mmrm_aqlq_ger_amc_i_t_x.rtf (21JUL2021 - 8:31)

Project Code / Study Number / Analysis: SAR231893 / EFC14153 / CSR_RWE

7 PAQLQ(S)-IA global score - ITT type 2 inflammatory asthma phenotype population

7.1 Summary of treatment effect on change from baseline at Week 52

7.1.9 By atopic medical condition (Yes, No)

	Atopic medical condition			
	Yes		No	
PAQLQ(S)-IA global score	**Placebo (N=97)**	**Dupilumab (N=205)**	**Placebo (N=10)**	**Dupilumab (N=6)**
p-value for heterogeneity[b]				0.759

[a]Derived from MMRM model with change from baseline in PAQLQ(S)-IA global score values up to Week 52 as the response variable, and treatment, baseline weight group, region, age, baseline eosinophil level, baseline FeNO level, baseline ICS dose level, visit, treatment by-visit interaction, baseline PAQLQ(S)-IA global score value and baseline-by-visit interaction as covariates.

[b]Similar model as that mentioned in the footnote [a] with subgroup and subgroup-by-treatment interaction as additional covariates.

Type 2 inflammatory asthma phenotype population is defined as the randomized patients with baseline blood eosinophils >= 0.15 Giga/L or baseline FeNO >= 20 ppb.

Only patients of age >=7 years old at randomization are included in the analysis.

PGM=DEVOPS/SAR231893/EFC14153/CSR_RWE/REPORT/PGM/eff_mmrm_ger_subg_i_t.sas OUT=REPORT/OUTPUT/eff_mmrm_aqlq_ger_amc_i_t_x.rtf (21JUL2021 - 8:31)

Project Code / Study Number / Analysis: SAR231893 / EFC14153 / CSR_RWE

7 PAQLQ(S)-IA global score - ITT type 2 inflammatory asthma phenotype population

7.1 Summary of treatment effect on change from baseline at Week 52

7.1.10 By baseline total IgE (<median, >= median)

	Baseline Total IgE (IU/mL)			
	<median		>=median	
PAQLQ(S)-IA global score	**Placebo (N=61)**	**Dupilumab (N=90)**	**Placebo (N=45)**	**Dupilumab (N=116)**
Baseline				
Value				
Number	60	86	43	112
Mean (SD)	4.89 (1.16)	5.05 (0.92)	5.02 (1.06)	4.88 (1.18)
Median	4.89	5.15	5.17	5.11
Q1 : Q3	4.20 : 5.89	4.39 : 5.91	4.26 : 5.91	4.13 : 5.65
Min : Max	1.8 : 6.9	2.2 : 6.6	2.3 : 6.6	1.3 : 6.8

[a]Derived from MMRM model with change from baseline in PAQLQ(S)-IA global score values up to Week 52 as the response variable, and treatment, baseline weight group, region, age, baseline eosinophil level, baseline FeNO level, baseline ICS dose level, visit, treatment by-visit interaction, baseline PAQLQ(S)-IA global score value and baseline-by-visit interaction as covariates.

[b]Similar model as that mentioned in the footnote [a] with subgroup and subgroup-by-treatment interaction as additional covariates.

Type 2 inflammatory asthma phenotype population is defined as the randomized patients with baseline blood eosinophils >= 0.15 Giga/L or baseline FeNO >= 20 ppb.

Only patients of age >=7 years old at randomization are included in the analysis.

PGM=DEVOPS/SAR231893/EFC14153/CSR_RWE/REPORT/PGM/eff_mmrm_ger_subg_i_t.sas OUT=REPORT/OUTPUT/eff_mmrm_aqlq_ger_igem_i_t_x.rtf (21JUL2021 - 8:31)

Project Code / Study Number / Analysis: SAR231893 / EFC14153 / CSR_RWE

7 PAQLQ(S)-IA global score - ITT type 2 inflammatory asthma phenotype population

7.1 Summary of treatment effect on change from baseline at Week 52

7.1.10 By baseline total IgE (<median, >= median)

	Baseline Total IgE (IU/mL)			
	<median		>=median	
PAQLQ(S)-IA global score	**Placebo (N=61)**	**Dupilumab (N=90)**	**Placebo (N=45)**	**Dupilumab (N=116)**
Week 52				
Value				
Number	60	83	42	105
Mean (SD)	6.21 (0.91)	6.58 (0.66)	6.18 (0.96)	6.51 (0.66)
Median	6.57	6.83	6.54	6.74
Q1 : Q3	5.93 : 6.91	6.52 : 6.96	5.87 : 6.78	6.30 : 6.96
Min : Max	3.3 : 7.0	3.3 : 7.0	3.1 : 7.0	3.7 : 7.0
Change from baseline				
Number	60	79	40	102
LS Mean (SE)[a]	1.22 (0.11)	1.52 (0.10)	1.12 (0.13)	1.53 (0.09)
LS Mean Diff (95% CI)[a]	-	0.31 (0.05 to 0.56)	-	0.41 (0.14 to 0.68)
p-value[a]		0.019		0.003
Hedges'g (95% CI)	-	0.415 (0.069 to 0.761)	-	0.554 (0.190 to 0.918)

[a]Derived from MMRM model with change from baseline in PAQLQ(S)-IA global score values up to Week 52 as the response variable, and treatment, baseline weight group, region, age, baseline eosinophil level, baseline FeNO level, baseline ICS dose level, visit, treatment by-visit interaction, baseline PAQLQ(S)-IA global score value and baseline-by-visit interaction as covariates.
[b]Similar model as that mentioned in the footnote [a] with subgroup and subgroup-by-treatment interaction as additional covariates.
Type 2 inflammatory asthma phenotype population is defined as the randomized patients with baseline blood eosinophils >= 0.15 Giga/L or baseline FeNO >= 20 ppb.
Only patients of age >=7 years old at randomization are included in the analysis.
PGM=DEVOPS/SAR231893/EFC14153/CSR_RWE/REPORT/PGM/eff_mmrm_ger_subg_i_t.sas OUT=REPORT/OUTPUT/eff_mmrm_aqlq_ger_igem_i_t_x.rtf (21JUL2021 - 8:31)

Project Code / Study Number / Analysis: SAR231893 / EFC14153 / CSR_RWE

7 PAQLQ(S)-IA global score - ITT type 2 inflammatory asthma phenotype population

7.1 Summary of treatment effect on change from baseline at Week 52

7.1.10 By baseline total IgE (<median, >= median)

	Baseline Total IgE (IU/mL)			
	<median		>=median	
PAQLQ(S)-IA global score	**Placebo (N=61)**	**Dupilumab (N=90)**	**Placebo (N=45)**	**Dupilumab (N=116)**
p-value for heterogeneity[b]				0.577

[a]Derived from MMRM model with change from baseline in PAQLQ(S)-IA global score values up to Week 52 as the response variable, and treatment, baseline weight group, region, age, baseline eosinophil level, baseline FeNO level, baseline ICS dose level, visit, treatment by-visit interaction, baseline PAQLQ(S)-IA global score value and baseline-by-visit interaction as covariates.

[b]Similar model as that mentioned in the footnote [a] with subgroup and subgroup-by-treatment interaction as additional covariates.

Type 2 inflammatory asthma phenotype population is defined as the randomized patients with baseline blood eosinophils >= 0.15 Giga/L or baseline FeNO >= 20 ppb.

Only patients of age >=7 years old at randomization are included in the analysis.

PGM=DEVOPS/SAR231893/EFC14153/CSR_RWE/REPORT/PGM/eff_mmrm_ger_subg_i_t.sas OUT=REPORT/OUTPUT/eff_mmrm_aqlq_ger_igem_i_t_x.rtf (21JUL2021 - 8:31)

Project Code / Study Number / Analysis: SAR231893 / EFC14153 / CSR_RWE

7 PAQLQ(S)-IA global score - ITT type 2 inflammatory asthma phenotype population

7.1 Summary of treatment effect on change from baseline at Week 52

7.1.11 By baseline total IgE (<100 IU/ml, >= 100 IU/ml)

	Baseline Total IgE (IU/mL)			
	< 100		>= 100	
PAQLQ(S)-IA global score	**Placebo (N=19)**	**Dupilumab (N=24)**	**Placebo (N=87)**	**Dupilumab (N=182)**
Baseline				
Value				
Number	19	24	84	174
Mean (SD)	4.75 (1.23)	5.03 (1.04)	4.98 (1.09)	4.95 (1.08)
Median	4.65	5.22	5.17	5.13
Q1 : Q3	4.39 : 5.61	4.20 : 5.87	4.20 : 5.91	4.26 : 5.70
Min : Max	1.8 : 6.8	2.7 : 6.4	2.3 : 6.9	1.3 : 6.8

[a]Derived from MMRM model with change from baseline in PAQLQ(S)-IA global score values up to Week 52 as the response variable, and treatment, baseline weight group, region, age, baseline eosinophil level, baseline FeNO level, baseline ICS dose level, visit, treatment by-visit interaction, baseline PAQLQ(S)-IA global score value and baseline-by-visit interaction as covariates.

[b]Similar model as that mentioned in the footnote [a] with subgroup and subgroup-by-treatment interaction as additional covariates.

Type 2 inflammatory asthma phenotype population is defined as the randomized patients with baseline blood eosinophils >= 0.15 Giga/L or baseline FeNO >= 20 ppb.

Only patients of age >=7 years old at randomization are included in the analysis.

PGM=DEVOPS/SAR231893/EFC14153/CSR_RWE/REPORT/PGM/eff_mmrm_ger_subg_i_t.sas OUT=REPORT/OUTPUT/eff_mmrm_aqlq_ger_ige_i_t_x.rtf (21JUL2021 - 8:31)

Project Code / Study Number / Analysis: SAR231893 / EFC14153 / CSR_RWE

7 PAQLQ(S)-IA global score - ITT type 2 inflammatory asthma phenotype population

7.1 Summary of treatment effect on change from baseline at Week 52

7.1.11 By baseline total IgE (<100 IU/ml, >= 100 IU/ml)

	Baseline Total IgE (IU/mL)			
	< 100		>= 100	
PAQLQ(S)-IA global score	**Placebo (N=19)**	**Dupilumab (N=24)**	**Placebo (N=87)**	**Dupilumab (N=182)**
Week 52				
Value				
Number	19	23	83	165
Mean (SD)	6.29 (1.00)	6.43 (0.98)	6.18 (0.92)	6.55 (0.60)
Median	6.70	6.87	6.57	6.74
Q1 : Q3	6.30 : 6.96	6.43 : 7.00	5.83 : 6.83	6.35 : 6.96
Min : Max	3.3 : 7.0	3.3 : 7.0	3.1 : 7.0	3.7 : 7.0
Change from baseline				
Number	19	23	81	158
LS Mean (SE)[a]	1.24 (0.27)	1.21 (0.27)	1.19 (0.09)	1.56 (0.07)
LS Mean Diff (95% CI)[a]	-	-0.03 (-0.65 to 0.59)	-	0.37 (0.18 to 0.56)
p-value[a]		0.923		<0.001
Hedges'g (95% CI)	-	-0.031 (-0.679 to 0.616)	-	0.533 (0.261 to 0.805)

[a]Derived from MMRM model with change from baseline in PAQLQ(S)-IA global score values up to Week 52 as the response variable, and treatment, baseline weight group, region, age, baseline eosinophil level, baseline FeNO level, baseline ICS dose level, visit, treatment by-visit interaction, baseline PAQLQ(S)-IA global score value and baseline-by-visit interaction as covariates.
[b]Similar model as that mentioned in the footnote [a] with subgroup and subgroup-by-treatment interaction as additional covariates.
Type 2 inflammatory asthma phenotype population is defined as the randomized patients with baseline blood eosinophils >= 0.15 Giga/L or baseline FeNO >= 20 ppb.
Only patients of age >=7 years old at randomization are included in the analysis.
PGM=DEVOPS/SAR231893/EFC14153/CSR_RWE/REPORT/PGM/eff_mmrm_ger_subg_i_t.sas OUT=REPORT/OUTPUT/eff_mmrm_aqlq_ger_ige_i_t_x.rtf (21JUL2021 - 8:31)

Project Code / Study Number / Analysis: SAR231893 / EFC14153 / CSR_RWE

7 PAQLQ(S)-IA global score - ITT type 2 inflammatory asthma phenotype population

7.1 Summary of treatment effect on change from baseline at Week 52

7.1.11 By baseline total IgE (<100 IU/ml, >= 100 IU/ml)

	Baseline Total IgE (IU/mL)			
	< 100		>= 100	
PAQLQ(S)-IA global score	**Placebo (N=19)**	**Dupilumab (N=24)**	**Placebo (N=87)**	**Dupilumab (N=182)**
p-value for heterogeneity[b]				0.188

[a]Derived from MMRM model with change from baseline in PAQLQ(S)-IA global score values up to Week 52 as the response variable, and treatment, baseline weight group, region, age, baseline eosinophil level, baseline FeNO level, baseline ICS dose level, visit, treatment by-visit interaction, baseline PAQLQ(S)-IA global score value and baseline-by-visit interaction as covariates.

[b]Similar model as that mentioned in the footnote [a] with subgroup and subgroup-by-treatment interaction as additional covariates.

Type 2 inflammatory asthma phenotype population is defined as the randomized patients with baseline blood eosinophils >= 0.15 Giga/L or baseline FeNO >= 20 ppb.

Only patients of age >=7 years old at randomization are included in the analysis.

PGM=DEVOPS/SAR231893/EFC14153/CSR_RWE/REPORT/PGM/eff_mmrm_ger_subg_i_t.sas OUT=REPORT/OUTPUT/eff_mmrm_aqlq_ger_ige_i_t_x.rtf (21JUL2021 - 8:31)

Project Code / Study Number / Analysis: SAR231893 / EFC14153 / CSR_RWE

7 PAQLQ(S)-IA global score - ITT type 2 inflammatory asthma phenotype population

7.1 Summary of treatment effect on change from baseline at Week 52

7.1.12 By age at onset of asthma (0-2, 3-5, >=6 years)

	Age of onset of asthma (years)					
	0-2		3-5		>= 6	
PAQLQ(S)-IA global score	**Placebo (N=36)**	**Dupilumab (N=89)**	**Placebo (N=36)**	**Dupilumab (N=77)**	**Placebo (N=35)**	**Dupilumab (N=45)**
Baseline						
Value						
Number	35	85	35	74	34	44
Mean (SD)	5.10 (1.06)	4.81 (1.15)	4.74 (1.08)	5.02 (1.13)	4.92 (1.24)	5.11 (0.80)
Median	5.39	4.91	4.61	5.24	5.15	5.26
Q1 : Q3	4.30 : 5.91	4.13 : 5.65	3.70 : 5.87	4.30 : 5.91	4.17 : 5.91	4.41 : 5.70
Min : Max	3.0 : 6.9	1.3 : 6.8	3.0 : 6.2	1.3 : 6.8	1.8 : 6.8	3.4 : 6.6

[a]Derived from MMRM model with change from baseline in PAQLQ(S)-IA global score values up to Week 52 as the response variable, and treatment, baseline weight group, region, age, baseline eosinophil level, baseline FeNO level, baseline ICS dose level, visit, treatment by-visit interaction, baseline PAQLQ(S)-IA global score value and baseline-by-visit interaction as covariates.
[b]Similar model as that mentioned in the footnote [a] with subgroup and subgroup-by-treatment interaction as additional covariates.
Type 2 inflammatory asthma phenotype population is defined as the randomized patients with baseline blood eosinophils >= 0.15 Giga/L or baseline FeNO >= 20 ppb.
Only patients of age >=7 years old at randomization are included in the analysis.
PGM=DEVOPS/SAR231893/EFC14153/CSR_RWE/REPORT/PGM/eff_mmrm_ger_subg_i_t.sas OUT=REPORT/OUTPUT/eff_mmrm_aqlq_ger_onsa_i_t_x.rtf (10AUG2021 - 9:54)

Project Code / Study Number / Analysis: SAR231893 / EFC14153 / CSR_RWE

7 PAQLQ(S)-IA global score - ITT type 2 inflammatory asthma phenotype population

7.1 Summary of treatment effect on change from baseline at Week 52

7.1.12 By age at onset of asthma (0-2, 3-5, >=6 years)

	Age of onset of asthma (years)					
	0-2		3-5		>= 6	
PAQLQ(S)-IA global score	**Placebo (N=36)**	**Dupilumab (N=89)**	**Placebo (N=36)**	**Dupilumab (N=77)**	**Placebo (N=35)**	**Dupilumab (N=45)**
Week 52						
Value						
Number	34	80	34	70	35	41
Mean (SD)	6.12 (0.99)	6.61 (0.50)	6.15 (0.99)	6.39 (0.88)	6.28 (0.84)	6.65 (0.42)
Median	6.46	6.78	6.57	6.74	6.65	6.83
Q1 : Q3	5.70 : 6.91	6.39 : 6.96	5.83 : 6.91	6.13 : 6.96	6.00 : 6.83	6.48 : 6.91
Min : Max	3.1 : 7.0	4.2 : 7.0	3.3 : 7.0	3.3 : 7.0	3.5 : 7.0	5.2 : 7.0
Change from baseline						
Number	33	76	34	68	34	40
LS Mean (SE)[a]	1.14 (0.13)	1.66 (0.10)	1.10 (0.15)	1.31 (0.11)	1.22 (0.14)	1.48 (0.14)
LS Mean Diff (95% CI)[a]	-	0.51 (0.24 to 0.79)	-	0.21 (-0.12 to 0.54)	-	0.26 (-0.08 to 0.60)
p-value[a]		<0.001		0.204		0.129

[a]Derived from MMRM model with change from baseline in PAQLQ(S)-IA global score values up to Week 52 as the response variable, and treatment, baseline weight group, region, age, baseline eosinophil level, baseline FeNO level, baseline ICS dose level, visit, treatment by-visit interaction, baseline PAQLQ(S)-IA global score value and baseline-by-visit interaction as covariates.
[b]Similar model as that mentioned in the footnote [a] with subgroup and subgroup-by-treatment interaction as additional covariates.
Type 2 inflammatory asthma phenotype population is defined as the randomized patients with baseline blood eosinophils >= 0.15 Giga/L or baseline FeNO >= 20 ppb.
Only patients of age >=7 years old at randomization are included in the analysis.
PGM=DEVOPS/SAR231893/EFC14153/CSR_RWE/REPORT/PGM/eff_mmrm_ger_subg_i_t.sas OUT=REPORT/OUTPUT/eff_mmrm_aqlq_ger_onsa_i_t_x.rtf (10AUG2021 - 9:54)

Project Code / Study Number / Analysis: SAR231893 / EFC14153 / CSR_RWE

7 PAQLQ(S)-IA global score - ITT type 2 inflammatory asthma phenotype population

7.1 Summary of treatment effect on change from baseline at Week 52

7.1.12 By age at onset of asthma (0-2, 3-5, >=6 years)

	Age of onset of asthma (years)					
	0-2		3-5		>= 6	
PAQLQ(S)-IA global score	**Placebo (N=36)**	**Dupilumab (N=89)**	**Placebo (N=36)**	**Dupilumab (N=77)**	**Placebo (N=35)**	**Dupilumab (N=45)**
Hedges'g (95% CI)	-	0.791 (0.368 to 1.214)	-	0.272 (-0.150 to 0.693)	-	0.365 (-0.110 to 0.840)
p-value for heterogeneity[b]:						
0-2, 3-5						0.119
0-2, >= 6						0.163
3-5, >= 6						0.939
overall						0.224

[a]Derived from MMRM model with change from baseline in PAQLQ(S)-IA global score values up to Week 52 as the response variable, and treatment, baseline weight group, region, age, baseline eosinophil level, baseline FeNO level, baseline ICS dose level, visit, treatment by-visit interaction, baseline PAQLQ(S)-IA global score value and baseline-by-visit interaction as covariates.

[b]Similar model as that mentioned in the footnote [a] with subgroup and subgroup-by-treatment interaction as additional covariates.

Type 2 inflammatory asthma phenotype population is defined as the randomized patients with baseline blood eosinophils >= 0.15 Giga/L or baseline FeNO >= 20 ppb.

Only patients of age >=7 years old at randomization are included in the analysis.

PGM=DEVOPS/SAR231893/EFC14153/CSR_RWE/REPORT/PGM/eff_mmrm_ger_subg_i_t.sas OUT=REPORT/OUTPUT/eff_mmrm_aqlq_ger_onsa_i_t_x.rtf (10AUG2021 - 9:54)

Project Code / Study Number / Analysis: SAR231893 / EFC14153 / CSR_RWE

7 PAQLQ(S)-IA global score - ITT type 2 inflammatory asthma phenotype population

7.1 Summary of treatment effect on change from baseline at Week 52

7.1.13 By number of severe asthma exacerbation prior to the study (<=1, 2, >2)

	Number of severe asthma exacerbation prior to the study					
	<=1		2		>2	
PAQLQ(S)-IA global score	**Placebo (N=43)**	**Dupilumab (N=78)**	**Placebo (N=30)**	**Dupilumab (N=66)**	**Placebo (N=34)**	**Dupilumab (N=67)**
Baseline						
Value						
Number	42	74	30	64	32	65
Mean (SD)	5.06 (1.11)	5.11 (1.07)	5.04 (1.22)	5.03 (1.04)	4.64 (1.05)	4.70 (1.10)
Median	5.17	5.33	5.28	5.35	4.59	4.74
Q1 : Q3	4.35 : 5.91	4.61 : 5.83	4.30 : 6.00	4.37 : 5.83	3.61 : 5.54	4.04 : 5.30
Min : Max	1.8 : 6.8	1.3 : 6.8	2.3 : 6.9	2.2 : 6.7	3.0 : 6.2	1.3 : 6.8

[a]Derived from MMRM model with change from baseline in PAQLQ(S)-IA global score values up to Week 52 as the response variable, and treatment, baseline weight group, region, age, baseline eosinophil level, baseline FeNO level, baseline ICS dose level, visit, treatment by-visit interaction, baseline PAQLQ(S)-IA global score value and baseline-by-visit interaction as covariates.

[b]Similar model as that mentioned in the footnote [a] with subgroup and subgroup-by-treatment interaction as additional covariates.

Type 2 inflammatory asthma phenotype population is defined as the randomized patients with baseline blood eosinophils >= 0.15 Giga/L or baseline FeNO >= 20 ppb.

Only patients of age >=7 years old at randomization are included in the analysis.

PGM=DEVOPS/SAR231893/EFC14153/CSR_RWE/REPORT/PGM/eff_mmrm_ger_subg_i_t.sas OUT=REPORT/OUTPUT/eff_mmrm_aqlq_ger_exa_i_t_x.rtf (21JUL2021 - 8:32)

Project Code / Study Number / Analysis: SAR231893 / EFC14153 / CSR_RWE

7 PAQLQ(S)-IA global score - ITT type 2 inflammatory asthma phenotype population

7.1 Summary of treatment effect on change from baseline at Week 52

7.1.13 By number of severe asthma exacerbation prior to the study (<=1, 2, >2)

	Number of severe asthma exacerbation prior to the study					
	<=1		2		>2	
PAQLQ(S)-IA global score	**Placebo (N=43)**	**Dupilumab (N=78)**	**Placebo (N=30)**	**Dupilumab (N=66)**	**Placebo (N=34)**	**Dupilumab (N=67)**
Week 52						
Value						
Number	41	73	30	58	32	60
Mean (SD)	6.43 (0.74)	6.51 (0.60)	6.12 (1.05)	6.59 (0.63)	5.93 (1.00)	6.52 (0.75)
Median	6.70	6.74	6.61	6.87	6.28	6.78
Q1 : Q3	6.22 : 6.91	6.26 : 6.91	5.22 : 6.87	6.52 : 6.96	5.87 : 6.57	6.35 : 6.96
Min : Max	3.3 : 7.0	3.7 : 7.0	3.5 : 7.0	4.2 : 7.0	3.1 : 7.0	3.3 : 7.0
Change from baseline						
Number	41	69	30	57	30	58
LS Mean (SE)[a]	1.27 (0.11)	1.49 (0.09)	0.97 (0.14)	1.34 (0.11)	1.21 (0.19)	1.76 (0.14)
LS Mean Diff (95% CI)[a]	-	0.22 (-0.03 to 0.47)	-	0.37 (0.04 to 0.70)	-	0.56 (0.17 to 0.94)
p-value[a]		0.090		0.030		0.005

[a]Derived from MMRM model with change from baseline in PAQLQ(S)-IA global score values up to Week 52 as the response variable, and treatment, baseline weight group, region, age, baseline eosinophil level, baseline FeNO level, baseline ICS dose level, visit, treatment by-visit interaction, baseline PAQLQ(S)-IA global score value and baseline-by-visit interaction as covariates.

[b]Similar model as that mentioned in the footnote [a] with subgroup and subgroup-by-treatment interaction as additional covariates.

Type 2 inflammatory asthma phenotype population is defined as the randomized patients with baseline blood eosinophils >= 0.15 Giga/L or baseline FeNO >= 20 ppb.

Only patients of age >=7 years old at randomization are included in the analysis.

PGM=DEVOPS/SAR231893/EFC14153/CSR_RWE/REPORT/PGM/eff_mmrm_ger_subg_i_t.sas OUT=REPORT/OUTPUT/eff_mmrm_aqlq_ger_exa_i_t_x.rtf (21JUL2021 - 8:32)

Project Code / Study Number / Analysis: SAR231893 / EFC14153 / CSR_RWE

7 PAQLQ(S)-IA global score - ITT type 2 inflammatory asthma phenotype population

7.1 Summary of treatment effect on change from baseline at Week 52

7.1.13 By number of severe asthma exacerbation prior to the study (<=1, 2, >2)

	Number of severe asthma exacerbation prior to the study					
	<=1		2		>2	
PAQLQ(S)-IA global score	**Placebo (N=43)**	**Dupilumab (N=78)**	**Placebo (N=30)**	**Dupilumab (N=66)**	**Placebo (N=34)**	**Dupilumab (N=67)**
Hedges'g (95% CI)	-	0.344 (-0.054 to 0.743)	-	0.507 (0.050 to 0.964)	-	0.670 (0.209 to 1.131)
p-value for heterogeneity[b]:						
<=1, 2						0.409
<=1, >2						0.244
2, >2						0.752
overall						0.475

[a]Derived from MMRM model with change from baseline in PAQLQ(S)-IA global score values up to Week 52 as the response variable, and treatment, baseline weight group, region, age, baseline eosinophil level, baseline FeNO level, baseline ICS dose level, visit, treatment by-visit interaction, baseline PAQLQ(S)-IA global score value and baseline-by-visit interaction as covariates.

[b]Similar model as that mentioned in the footnote [a] with subgroup and subgroup-by-treatment interaction as additional covariates.

Type 2 inflammatory asthma phenotype population is defined as the randomized patients with baseline blood eosinophils >= 0.15 Giga/L or baseline FeNO >= 20 ppb.

Only patients of age >=7 years old at randomization are included in the analysis.

PGM=DEVOPS/SAR231893/EFC14153/CSR_RWE/REPORT/PGM/eff_mmrm_ger_subg_i_t.sas OUT=REPORT/OUTPUT/eff_mmrm_aqlq_ger_exa_i_t_x.rtf (21JUL2021 - 8:32)

Project Code / Study Number / Analysis: SAR231893 / EFC14153 / CSR_RWE

8 EQ-VAS - ITT type 2 inflammatory asthma phenotype population

8.1 Change from baseline in EQ-VAS up to week 52

EQ-VAS	Placebo (N=87)	Dupilumab (N=181)
Baseline		
Value		
Number	84	180
Mean (SD)	72.92 (17.37)	73.56 (17.45)
Median	75.00	79.00
Q1 : Q3	65.00 : 85.00	62.50 : 85.50
Min : Max	5.0 : 100.0	9.0 : 100.0
Week 24		
Value		
Number	85	174
Mean (SD)	77.38 (15.32)	85.91 (13.13)
Median	80.00	90.00
Q1 : Q3	70.00 : 90.00	80.00 : 95.00
Min : Max	45.0 : 100.0	40.0 : 100.0

[a]Derived from MMRM model with change from baseline in EQ-VAS values up to Week 52 as the response variable, and treatment, baseline weight group, region, age, baseline eosinophil level, baseline FeNO level, baseline ICS dose level, visit, treatment by-visit interaction, baseline EQ-VAS value and baseline-by-visit interaction as covariates.

Type 2 inflammatory asthma phenotype population is defined as the randomized patients with baseline blood eosinophils >= 0.15 Giga/L or baseline FeNO >= 20 ppb. Only patients of age >=8 years old at randomization are included in the analysis.

PGM=DEVOPS/SAR231893/EFC14153/CSR_RWE/REPORT/PGM/eff_mmrm_i_t_intext.sas OUT=REPORT/OUTPUT/eff_eqvas_ger_chg_t2_t_x.rtf (11AUG2021 - 10:33)

Project Code / Study Number / Analysis: SAR231893 / EFC14153 / CSR_RWE

8 EQ-VAS - ITT type 2 inflammatory asthma phenotype population

8.1 Change from baseline in EQ-VAS up to week 52

EQ-VAS	Placebo (N=87)	Dupilumab (N=181)
Change from baseline		
Number	82	173
Mean (SD)	4.49 (20.49)	12.02 (19.08)
Median	5.00	10.00
Q1 : Q3	-9.00 : 15.00	0.00 : 20.00
Min : Max	-43.0 : 75.0	-40.0 : 86.0
Number of patients in the model	83	173
LS Mean (SE) [a]	4.05 (1.70)	11.84 (1.28)
LS Mean Diff vs. placebo (95% CI) [a]		7.79 (4.18, 11.40)
P-value vs. placebo [a]		<.001

[a]Derived from MMRM model with change from baseline in EQ-VAS values up to Week 52 as the response variable, and treatment, baseline weight group, region, age, baseline eosinophil level, baseline FeNO level, baseline ICS dose level, visit, treatment by-visit interaction, baseline EQ-VAS value and baseline-by-visit interaction as covariates.

Type 2 inflammatory asthma phenotype population is defined as the randomized patients with baseline blood eosinophils >= 0.15 Giga/L or baseline FeNO >= 20 ppb. Only patients of age >=8 years old at randomization are included in the analysis.

PGM=DEVOPS/SAR231893/EFC14153/CSR_RWE/REPORT/PGM/eff_mmrm_i_t_intext.sas OUT=REPORT/OUTPUT/eff_eqvas_ger_chg_t2_t_x.rtf (11AUG2021 - 10:33)

Project Code / Study Number / Analysis: SAR231893 / EFC14153 / CSR_RWE

8 EQ-VAS - ITT type 2 inflammatory asthma phenotype population

8.1 Change from baseline in EQ-VAS up to week 52

EQ-VAS	Placebo (N=87)	Dupilumab (N=181)
Week 52		
Value		
Number	83	170
Mean (SD)	83.28 (14.55)	87.84 (13.34)
Median	85.00	92.00
Q1 : Q3	75.00 : 95.00	85.00 : 96.00
Min : Max	45.0 : 100.0	30.0 : 100.0
Change from baseline		
Number	81	169
Mean (SD)	9.52 (20.85)	15.08 (19.75)
Median	7.00	15.00
Q1 : Q3	-1.00 : 20.00	5.00 : 25.00
Min : Max	-42.0 : 75.0	-40.0 : 90.0

[a]Derived from MMRM model with change from baseline in EQ-VAS values up to Week 52 as the response variable, and treatment, baseline weight group, region, age, baseline eosinophil level, baseline FeNO level, baseline ICS dose level, visit, treatment by-visit interaction, baseline EQ-VAS value and baseline-by-visit interaction as covariates.

Type 2 inflammatory asthma phenotype population is defined as the randomized patients with baseline blood eosinophils >= 0.15 Giga/L or baseline FeNO >= 20 ppb. Only patients of age >=8 years old at randomization are included in the analysis.

PGM=DEVOPS/SAR231893/EFC14153/CSR_RWE/REPORT/PGM/eff_mmrm_i_t_intext.sas OUT=REPORT/OUTPUT/eff_eqvas_ger_chg_t2_t_x.rtf (11AUG2021 - 10:33)

Project Code / Study Number / Analysis: SAR231893 / EFC14153 / CSR_RWE

8 EQ-VAS - ITT type 2 inflammatory asthma phenotype population

8.1 Change from baseline in EQ-VAS up to week 52

EQ-VAS	Placebo (N=87)	Dupilumab (N=181)
Number of patients in the model	83	173
LS Mean (SE) [a]	9.29 (1.68)	14.02 (1.26)
LS Mean Diff vs. placebo (95% CI) [a]		4.73 (1.18, 8.28)
P-value vs. placebo [a]		0.009

[a]Derived from MMRM model with change from baseline in EQ-VAS values up to Week 52 as the response variable, and treatment, baseline weight group, region, age, baseline eosinophil level, baseline FeNO level, baseline ICS dose level, visit, treatment by-visit interaction, baseline EQ-VAS value and baseline-by-visit interaction as covariates.

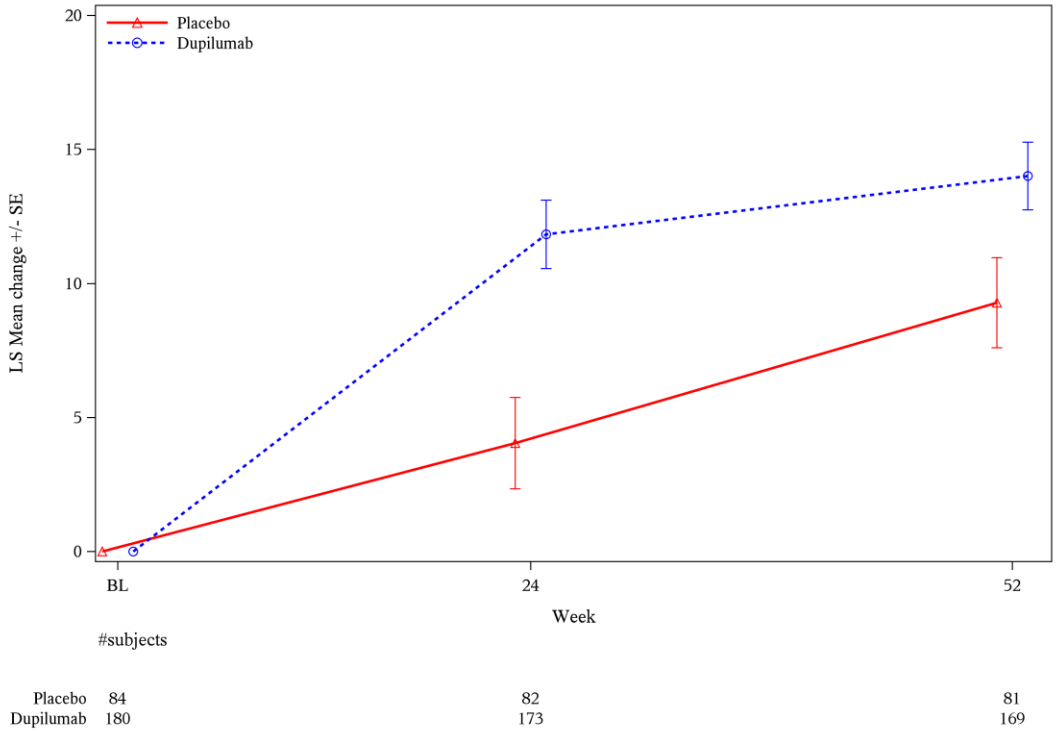
Type 2 inflammatory asthma phenotype population is defined as the randomized patients with baseline blood eosinophils >= 0.15 Giga/L or baseline FeNO >= 20 ppb. Only patients of age >=8 years old at randomization are included in the analysis.

PGM=DEVOPS/SAR231893/EFC14153/CSR_RWE/REPORT/PGM/eff_mmrm_i_t_intext.sas OUT=REPORT/OUTPUT/eff_eqvas_ger_chg_t2_t_x.rtf (11AUG2021 - 10:33)

Project Code / Study Number / Analysis: SAR231893 / EFC14153 / CSR_RWE

8 EQ-VAS - ITT type 2 inflammatory asthma phenotype population

8.2 Plot of LS mean change from baseline in EQ-VAS over time (MMRM including measurements up to Week 52)



BL=Baseline

Type 2 inflammatory asthma phenotype population is defined as the randomized patients with baseline blood eosinophils >= 0.15 Giga/L or baseline FeNO >= 20 ppb. Only patients of age >=8 years old at randomization are included in the analysis.

PGM=DEVOPS/SAR231893/EFC14153/CSR_RWE/REPORT/PGM/eff_mmrm_i_g_adqs.sas OUT=REPORT/OUTPUT/eff_eqvs_ger_chg_a52_t2_g_x.rtf (10AUG2021 - 9:32)

Project Code / Study Number / Analysis: SAR231893 / EFC14153 / CSR_RWE

8 EQ-VAS - ITT type 2 inflammatory asthma phenotype population

8.3 Summary of treatment effect on change from baseline at Week 52

EQ-VAS	Placebo (N=87)	Dupilumab (N=181)
Baseline		
Value		
Number	84	180
Mean (SD)	72.92 (17.37)	73.56 (17.45)
Median	75.00	79.00
Q1 : Q3	65.00 : 85.00	62.50 : 85.50
Min : Max	5.0 : 100.0	9.0 : 100.0
Week 52		
Value		
Number	83	170
Mean (SD)	83.28 (14.55)	87.84 (13.34)
Median	85.00	92.00
Q1 : Q3	75.00 : 95.00	85.00 : 96.00
Min : Max	45.0 : 100.0	30.0 : 100.0

[a]Derived from MMRM model with change from baseline in EQ-VAS values up to Week 52 as the response variable, and treatment, baseline weight group, region, age, baseline eosinophil level, baseline FeNO level, baseline ICS dose level, visit, treatment by-visit interaction, baseline EQ-VAS value and baseline-by-visit interaction as covariates.

Type 2 inflammatory asthma phenotype population is defined as the randomized patients with baseline blood eosinophils >= 0.15 Giga/L or baseline FeNO >= 20 ppb. Only patients of age >=8 years old at randomization are included in the analysis.

PGM=DEVOPS/SAR231893/EFC14153/CSR_RWE/REPORT/PGM/eff_mmrm_ger_i_t.sas OUT=REPORT/OUTPUT/eff_mmrm_eqvas_ger_i_t_x.rtf (10AUG2021 - 9:06)

Project Code / Study Number / Analysis: SAR231893 / EFC14153 / CSR_RWE

8 EQ-VAS - ITT type 2 inflammatory asthma phenotype population

8.3 Summary of treatment effect on change from baseline at Week 52

EQ-VAS	Placebo (N=87)	Dupilumab (N=181)
Change from baseline		
Number	81	169
LS Mean (SE)[a]	9.29 (1.68)	14.02 (1.26)
LS Mean Diff (95% CI)[a]	-	4.73 (1.18 to 8.28)
Hedges'g (95% CI)	-	0.293 (0.073 to 0.513)
p-value[a]		0.009

[a]Derived from MMRM model with change from baseline in EQ-VAS values up to Week 52 as the response variable, and treatment, baseline weight group, region, age, baseline eosinophil level, baseline FeNO level, baseline ICS dose level, visit, treatment by-visit interaction, baseline EQ-VAS value and baseline-by-visit interaction as covariates.

Type 2 inflammatory asthma phenotype population is defined as the randomized patients with baseline blood eosinophils >= 0.15 Giga/L or baseline FeNO >= 20 ppb. Only patients of age >=8 years old at randomization are included in the analysis.

PGM=DEVOPS/SAR231893/EFC14153/CSR_RWE/REPORT/PGM/eff_mmrm_ger_i_t.sas OUT=REPORT/OUTPUT/eff_mmrm_eqvas_ger_i_t_x.rtf (10AUG2021 - 9:06)

Project Code / Study Number / Analysis: SAR231893 / EFC14153 / CSR_RWE

8 EQ-VAS - ITT type 2 inflammatory asthma phenotype population

8.3 Summary of treatment effect on change from baseline at Week 52

8.3.1 By gender (Male, Female)

	Gender			
	Male		Female	
EQ-VAS	**Placebo (N=60)**	**Dupilumab (N=119)**	**Placebo (N=27)**	**Dupilumab (N=62)**
Baseline				
Value				
Number	58	118	26	62
Mean (SD)	71.74 (19.41)	73.83 (17.83)	75.54 (11.52)	73.05 (16.83)
Median	71.00	78.50	80.00	79.00
Q1 : Q3	60.00 : 90.00	60.00 : 89.00	67.00 : 85.00	65.00 : 85.00
Min : Max	5.0 : 100.0	9.0 : 100.0	50.0 : 95.0	10.0 : 95.0

[a]Derived from MMRM model with change from baseline in EQ-VAS values up to Week 52 as the response variable, and treatment, baseline weight group, region, age, baseline eosinophil level, baseline FeNO level, baseline ICS dose level, visit, treatment by-visit interaction, baseline EQ-VAS value and baseline-by-visit interaction as covariates.

[b]Similar model as that mentioned in the footnote [a] with subgroup and subgroup-by-treatment interaction as additional covariates.

Type 2 inflammatory asthma phenotype population is defined as the randomized patients with baseline blood eosinophils >= 0.15 Giga/L or baseline FeNO >= 20 ppb.

Only patients of age >=8 years old at randomization are included in the analysis.

PGM=DEVOPS/SAR231893/EFC14153/CSR_RWE/REPORT/PGM/eff_mmrm_ger_subg_i_t.sas OUT=REPORT/OUTPUT/eff_mmrm_eqvas_ger_sex_i_t_x.rtf (10AUG2021 - 10:56)

Project Code / Study Number / Analysis: SAR231893 / EFC14153 / CSR_RWE

8 EQ-VAS - ITT type 2 inflammatory asthma phenotype population

8.3 Summary of treatment effect on change from baseline at Week 52

8.3.1 By gender (Male, Female)

	Gender			
	Male		Female	
EQ-VAS	**Placebo (N=60)**	**Dupilumab (N=119)**	**Placebo (N=27)**	**Dupilumab (N=62)**
Week 52				
Value				
Number	59	111	24	59
Mean (SD)	82.58 (14.19)	88.22 (12.68)	85.00 (15.58)	87.14 (14.57)
Median	85.00	91.00	90.00	94.00
Q1 : Q3	75.00 : 95.00	85.00 : 95.00	77.00 : 96.50	82.00 : 97.00
Min : Max	45.0 : 100.0	40.0 : 100.0	50.0 : 100.0	30.0 : 100.0
Change from baseline				
Number	57	110	24	59
LS Mean (SE)[a]	8.95 (2.01)	14.44 (1.61)	10.35 (3.23)	13.45 (2.19)
LS Mean Diff (95% CI)[a]	-	5.49 (1.27 to 9.72)	-	3.10 (-3.94 to 10.14)
p-value[a]		0.011		0.383
Hedges'g (95% CI)	-	0.333 (0.077 to 0.589)	-	0.186 (-0.236 to 0.607)

[a]Derived from MMRM model with change from baseline in EQ-VAS values up to Week 52 as the response variable, and treatment, baseline weight group, region, age, baseline eosinophil level, baseline FeNO level, baseline ICS dose level, visit, treatment by-visit interaction, baseline EQ-VAS value and baseline-by-visit interaction as covariates.

[b]Similar model as that mentioned in the footnote [a] with subgroup and subgroup-by-treatment interaction as additional covariates.

Type 2 inflammatory asthma phenotype population is defined as the randomized patients with baseline blood eosinophils >= 0.15 Giga/L or baseline FeNO >= 20 ppb.

Only patients of age >=8 years old at randomization are included in the analysis.

PGM=DEVOPS/SAR231893/EFC14153/CSR_RWE/REPORT/PGM/eff_mmrm_ger_subg_i_t.sas OUT=REPORT/OUTPUT/eff_mmrm_eqvas_ger_sex_i_t_x.rtf (10AUG2021 - 10:56)

Project Code / Study Number / Analysis: SAR231893 / EFC14153 / CSR_RWE

8 EQ-VAS - ITT type 2 inflammatory asthma phenotype population

8.3 Summary of treatment effect on change from baseline at Week 52

8.3.1 By gender (Male, Female)

	Gender			
	Male		Female	
EQ-VAS	**Placebo (N=60)**	**Dupilumab (N=119)**	**Placebo (N=27)**	**Dupilumab (N=62)**
p-value for heterogeneity[b]				0.541

[a]Derived from MMRM model with change from baseline in EQ-VAS values up to Week 52 as the response variable, and treatment, baseline weight group, region, age, baseline eosinophil level, baseline FeNO level, baseline ICS dose level, visit, treatment by-visit interaction, baseline EQ-VAS value and baseline-by-visit interaction as covariates.

[b]Similar model as that mentioned in the footnote [a] with subgroup and subgroup-by-treatment interaction as additional covariates.

Type 2 inflammatory asthma phenotype population is defined as the randomized patients with baseline blood eosinophils >= 0.15 Giga/L or baseline FeNO >= 20 ppb.

Only patients of age >=8 years old at randomization are included in the analysis.

PGM=DEVOPS/SAR231893/EFC14153/CSR_RWE/REPORT/PGM/eff_mmrm_ger_subg_i_t.sas OUT=REPORT/OUTPUT/eff_mmrm_eqvas_ger_sex_i_t_x.rtf (10AUG2021 - 10:56)

Project Code / Study Number / Analysis: SAR231893 / EFC14153 / CSR_RWE

8 EQ-VAS - ITT type 2 inflammatory asthma phenotype population

8.3 Summary of treatment effect on change from baseline at Week 52

8.3.2 By region (Latin America, East Europe, Western Countries)

	Region					
	Latin America		East Europe		Western countries	
EQ-VAS	Placebo (N=41)	Dupilumab (N=82)	Placebo (N=31)	Dupilumab (N=56)	Placebo (N=15)	Dupilumab (N=43)
Baseline						
Value						
Number	39	81	31	56	14	43
Mean (SD)	73.87 (17.56)	70.35 (16.35)	70.10 (17.57)	75.66 (15.88)	76.50 (16.68)	76.88 (20.53)
Median	75.00	70.00	70.00	80.00	80.00	80.00
Q1 : Q3	65.00 : 85.00	60.00 : 80.00	60.00 : 85.00	70.00 : 88.00	65.00 : 91.00	65.00 : 90.00
Min : Max	5.0 : 100.0	9.0 : 100.0	32.0 : 100.0	30.0 : 97.0	50.0 : 98.0	10.0 : 100.0
Week 52						
Value						
Number	40	79	30	55	13	36
Mean (SD)	84.80 (15.34)	89.86 (11.40)	82.97 (13.14)	87.13 (12.66)	79.31 (15.48)	84.50 (17.33)
Median	90.00	94.00	85.00	90.00	75.00	91.50
Q1 : Q3	80.00 : 96.50	85.00 : 97.00	80.00 : 95.00	85.00 : 95.00	70.00 : 95.00	75.00 : 96.00
Min : Max	45.0 : 100.0	40.0 : 100.0	55.0 : 99.0	40.0 : 100.0	50.0 : 99.0	30.0 : 100.0

[a]Derived from MMRM model with change from baseline in EQ-VAS values up to Week 52 as the response variable, and treatment, baseline weight group, age, baseline eosinophil level, baseline FeNO level, baseline ICS dose level, visit, treatment by-visit interaction, baseline EQ-VAS value and baseline-by-visit interaction as covariates.
[b]Similar model as that mentioned in the footnote [a] with subgroup and subgroup-by-treatment interaction as additional covariates.
Type 2 inflammatory asthma phenotype population is defined as the randomized patients with baseline blood eosinophils >= 0.15 Giga/L or baseline FeNO >= 20 ppb.
Only patients of age >=8 years old at randomization are included in the analysis.
PGM=DEVOPS/SAR231893/EFC14153/CSR_RWE/REPORT/PGM/eff_mmrm_ger_subg_i_t.sas OUT=REPORT/OUTPUT/eff_mmrm_eqvas_ger_cty_i_t_x.rtf (10AUG2021 - 10:56)

Project Code / Study Number / Analysis: SAR231893 / EFC14153 / CSR_RWE

8 EQ-VAS - ITT type 2 inflammatory asthma phenotype population

8.3 Summary of treatment effect on change from baseline at Week 52

8.3.2 By region (Latin America, East Europe, Western Countries)

	Region					
	Latin America		East Europe		Western countries	
EQ-VAS	Placebo (N=41)	Dupilumab (N=82)	Placebo (N=31)	Dupilumab (N=56)	Placebo (N=15)	Dupilumab (N=43)
Change from baseline						
Number	38	78	30	55	13	36
LS Mean (SE)[a]	11.72 (2.28)	18.43 (1.73)	8.46 (2.77)	11.28 (2.22)	1.58 (5.66)	7.89 (3.76)
LS Mean Diff (95% CI)[a]	-	6.71 (1.97 to 11.45)	-	2.82 (-3.11 to 8.74)	-	6.31 (-5.29 to 17.92)
p-value[a]		0.006		0.347		0.279
Hedges'g (95% CI)	-	0.441 (0.130 to 0.753)	-	0.174 (-0.192 to 0.540)	-	0.282 (-0.236 to 0.800)
p-value for heterogeneity[b]:						
Latin America, East Europe						0.374
Latin America, Western countries						0.618
East Europe, Western countries						0.860
overall						0.668

[a]Derived from MMRM model with change from baseline in EQ-VAS values up to Week 52 as the response variable, and treatment, baseline weight group, age, baseline eosinophil level, baseline FeNO level, baseline ICS dose level, visit, treatment by-visit interaction, baseline EQ-VAS value and baseline-by-visit interaction as covariates.
[b]Similar model as that mentioned in the footnote [a] with subgroup and subgroup-by-treatment interaction as additional covariates.
Type 2 inflammatory asthma phenotype population is defined as the randomized patients with baseline blood eosinophils >= 0.15 Giga/L or baseline FeNO >= 20 ppb.
Only patients of age >=8 years old at randomization are included in the analysis.
PGM=DEVOPS/SAR231893/EFC14153/CSR_RWE/REPORT/PGM/eff_mmrm_ger_subg_i_t.sas OUT=REPORT/OUTPUT/eff_mmrm_eqvas_ger_cty_i_t_x.rtf (10AUG2021 - 10:56)

Project Code / Study Number / Analysis: SAR231893 / EFC14153 / CSR_RWE

8 EQ-VAS - ITT type 2 inflammatory asthma phenotype population

8.3 Summary of treatment effect on change from baseline at Week 52

8.3.3 By race (Caucasian/white, Black/of African descent, Other)

	Race					
	Caucasian/White		Black/of African descent		Other	
EQ-VAS	Placebo (N=78)	Dupilumab (N=155)	Placebo (N=4)	Dupilumab (N=7)	Placebo (N=5)	Dupilumab (N=19)
Baseline						
Value						
Number	76	154	3	7	5	19
Mean (SD)	72.87 (17.43)	73.33 (16.71)	79.00 (25.16)	78.86 (12.55)	70.00 (14.58)	73.47 (24.30)
Median	75.00	75.50	92.00	80.00	70.00	80.00
Q1 : Q3	65.00 : 85.00	65.00 : 85.00	50.00 : 95.00	65.00 : 88.00	65.00 : 75.00	60.00 : 90.00
Min : Max	5.0 : 100.0	9.0 : 100.0	50.0 : 95.0	60.0 : 95.0	50.0 : 90.0	10.0 : 100.0

[a]Derived from MMRM model with change from baseline in EQ-VAS values up to Week 52 as the response variable, and treatment, baseline weight group, region, age, baseline eosinophil level, baseline FeNO level, baseline ICS dose level, visit, treatment by-visit interaction, baseline EQ-VAS value and baseline-by-visit interaction as covariates.

[b]Similar model as that mentioned in the footnote [a] with subgroup and subgroup-by-treatment interaction as additional covariates.

Type 2 inflammatory asthma phenotype population is defined as the randomized patients with baseline blood eosinophils >= 0.15 Giga/L or baseline FeNO >= 20 ppb.

Only patients of age >=8 years old at randomization are included in the analysis.

PGM=DEVOPS/SAR231893/EFC14153/CSR_RWE/REPORT/PGM/eff_mmrm_ger_subg_i_t.sas OUT=REPORT/OUTPUT/eff_mmrm_eqvas_ger_race_i_t_x.rtf (10AUG2021 - 10:57)

Project Code / Study Number / Analysis: SAR231893 / EFC14153 / CSR_RWE

8 EQ-VAS - ITT type 2 inflammatory asthma phenotype population

8.3 Summary of treatment effect on change from baseline at Week 52

8.3.3 By race (Caucasian/white, Black/of African descent, Other)

	Race					
	Caucasian/White		Black/of African descent		Other	
EQ-VAS	Placebo (N=78)	Dupilumab (N=155)	Placebo (N=4)	Dupilumab (N=7)	Placebo (N=5)	Dupilumab (N=19)
Week 52						
Value						
Number	76	148	2	6	5	16
Mean (SD)	84.28 (13.64)	88.69 (12.98)	74.50 (34.65)	82.17 (12.64)	71.60 (17.94)	82.13 (15.65)
Median	86.50	94.00	74.50	79.00	71.00	87.50
Q1 : Q3	80.00 : 95.00	85.00 : 96.00	50.00 : 99.00	70.00 : 95.00	70.00 : 77.00	73.00 : 93.50
Min : Max	49.0 : 100.0	30.0 : 100.0	50.0 : 99.0	70.0 : 100.0	45.0 : 95.0	50.0 : 100.0
Change from baseline						
Number	74	147	2	6	5	16
LS Mean (SE)[a]	9.80 (1.71)	14.22 (1.35)	58.91 (40654.55)	98.20 (46208.63)	4.77 (9.97)	9.31 (6.34)
LS Mean Diff (95% CI)[a]	-	4.42 (0.88 to 7.96)	-	39.29 (-242534 to 242612.2)	-	4.54 (-18.75 to 27.83)
p-value[a]		0.015		0.999		0.685

[a]Derived from MMRM model with change from baseline in EQ-VAS values up to Week 52 as the response variable, and treatment, baseline weight group, region, age, baseline eosinophil level, baseline FeNO level, baseline ICS dose level, visit, treatment by-visit interaction, baseline EQ-VAS value and baseline-by-visit interaction as covariates.

[b]Similar model as that mentioned in the footnote [a] with subgroup and subgroup-by-treatment interaction as additional covariates.

Type 2 inflammatory asthma phenotype population is defined as the randomized patients with baseline blood eosinophils >= 0.15 Giga/L or baseline FeNO >= 20 ppb. Only patients of age >=8 years old at randomization are included in the analysis.

PGM=DEVOPS/SAR231893/EFC14153/CSR_RWE/REPORT/PGM/eff_mmrm_ger_subg_i_t.sas OUT=REPORT/OUTPUT/eff_mmrm_eqvas_ger_race_i_t_x.rtf (10AUG2021 - 10:57)

Project Code / Study Number / Analysis: SAR231893 / EFC14153 / CSR_RWE

8 EQ-VAS - ITT type 2 inflammatory asthma phenotype population

8.3 Summary of treatment effect on change from baseline at Week 52

8.3.3 By race (Caucasian/white, Black/of African descent, Other)

	Race					
	Caucasian/White		Black/of African descent		Other	
EQ-VAS	Placebo (N=78)	Dupilumab (N=155)	Placebo (N=4)	Dupilumab (N=7)	Placebo (N=5)	Dupilumab (N=19)
Hedges'g (95% CI)	-	0.276 (0.055 to 0.497)	-	0.000 (0.000 to 0.000)	-	0.175 (-0.722 to 1.072)
p-value for heterogeneity[b]:						
Caucasian/White, Black/of African descent						0.840
Caucasian/White, Other						0.619
Black/of African descent, Other						0.263
overall						0.528

[a]Derived from MMRM model with change from baseline in EQ-VAS values up to Week 52 as the response variable, and treatment, baseline weight group, region, age, baseline eosinophil level, baseline FeNO level, baseline ICS dose level, visit, treatment by-visit interaction, baseline EQ-VAS value and baseline-by-visit interaction as covariates.

[b]Similar model as that mentioned in the footnote [a] with subgroup and subgroup-by-treatment interaction as additional covariates.

Type 2 inflammatory asthma phenotype population is defined as the randomized patients with baseline blood eosinophils >= 0.15 Giga/L or baseline FeNO >= 20 ppb. Only patients of age >=8 years old at randomization are included in the analysis.

PGM=DEVOPS/SAR231893/EFC14153/CSR_RWE/REPORT/PGM/eff_mmrm_ger_subg_i_t.sas OUT=REPORT/OUTPUT/eff_mmrm_eqvas_ger_race_i_t_x.rtf (10AUG2021 - 10:57)

Project Code / Study Number / Analysis: SAR231893 / EFC14153 / CSR_RWE

8 EQ-VAS - ITT type 2 inflammatory asthma phenotype population

8.3 Summary of treatment effect on change from baseline at Week 52

8.3.4 By baseline ICS dose level (Medium, High)

	Baseline ICS dose level			
	High		Medium	
EQ-VAS	**Placebo (N=38)**	**Dupilumab (N=81)**	**Placebo (N=49)**	**Dupilumab (N=99)**
Baseline				
Value				
Number	38	81	46	98
Mean (SD)	73.37 (15.81)	72.31 (17.39)	72.54 (18.73)	74.33 (17.42)
Median	77.50	75.00	73.50	80.00
Q1 : Q3	65.00 : 85.00	60.00 : 86.00	65.00 : 85.00	65.00 : 85.00
Min : Max	32.0 : 98.0	35.0 : 100.0	5.0 : 100.0	9.0 : 100.0

[a]Derived from MMRM model with change from baseline in EQ-VAS values up to Week 52 as the response variable, and treatment, baseline weight group, region, age, baseline eosinophil level, baseline FeNO level, visit, treatment by-visit interaction, baseline EQ-VAS value and baseline-by-visit interaction as covariates.
[b]Similar model as that mentioned in the footnote [a] with subgroup and subgroup-by-treatment interaction as additional covariates.
Type 2 inflammatory asthma phenotype population is defined as the randomized patients with baseline blood eosinophils >= 0.15 Giga/L or baseline FeNO >= 20 ppb.
Only patients of age >=8 years old at randomization are included in the analysis.
PGM=DEVOPS/SAR231893/EFC14153/CSR_RWE/REPORT/PGM/eff_mmrm_ger_subg_i_t.sas OUT=REPORT/OUTPUT/eff_mmrm_eqvas_ger_ics_i_t_x.rtf (10AUG2021 - 10:57)

Project Code / Study Number / Analysis: SAR231893 / EFC14153 / CSR_RWE

8 EQ-VAS - ITT type 2 inflammatory asthma phenotype population

8.3 Summary of treatment effect on change from baseline at Week 52

8.3.4 By baseline ICS dose level (Medium, High)

	Baseline ICS dose level			
	High		Medium	
EQ-VAS	**Placebo (N=38)**	**Dupilumab (N=81)**	**Placebo (N=49)**	**Dupilumab (N=99)**
Week 52				
Value				
Number	36	79	47	91
Mean (SD)	81.83 (14.34)	84.92 (15.38)	84.38 (14.77)	90.37 (10.73)
Median	85.00	90.00	88.00	94.00
Q1 : Q3	72.50 : 94.50	80.00 : 96.00	79.00 : 96.00	90.00 : 96.00
Min : Max	49.0 : 100.0	40.0 : 100.0	45.0 : 100.0	30.0 : 100.0
Change from baseline				
Number	36	79	45	90
LS Mean (SE)[a]	8.30 (2.75)	12.21 (1.98)	9.06 (2.20)	14.78 (1.71)
LS Mean Diff (95% CI)[a]	-	3.91 (-2.03 to 9.86)	-	5.72 (1.29 to 10.16)
p-value[a]		0.195		0.012
Hedges'g (95% CI)	-	0.225 (-0.117 to 0.566)	-	0.357 (0.081 to 0.634)
p-value for heterogeneity[b]				0.664

[a]Derived from MMRM model with change from baseline in EQ-VAS values up to Week 52 as the response variable, and treatment, baseline weight group, region, age, baseline eosinophil level, baseline FeNO level, visit, treatment by-visit interaction, baseline EQ-VAS value and baseline-by-visit interaction as covariates.
[b]Similar model as that mentioned in the footnote [a] with subgroup and subgroup-by-treatment interaction as additional covariates.
Type 2 inflammatory asthma phenotype population is defined as the randomized patients with baseline blood eosinophils >= 0.15 Giga/L or baseline FeNO >= 20 ppb.
Only patients of age >=8 years old at randomization are included in the analysis.
PGM=DEVOPS/SAR231893/EFC14153/CSR_RWE/REPORT/PGM/eff_mmrm_ger_subg_i_t.sas OUT=REPORT/OUTPUT/eff_mmrm_eqvas_ger_ics_i_t_x.rtf (10AUG2021 - 10:57)

Project Code / Study Number / Analysis: SAR231893 / EFC14153 / CSR_RWE

8 EQ-VAS - ITT type 2 inflammatory asthma phenotype population

8.3 Summary of treatment effect on change from baseline at Week 52

8.3.5 By baseline ICS dose level 2 (Medium, High)

	Baseline ICS dose level 2			
	High		Medium	
EQ-VAS	**Placebo (N=72)**	**Dupilumab (N=156)**	**Placebo (N=15)**	**Dupilumab (N=25)**
Baseline				
Value				
Number	72	155	12	25
Mean (SD)	72.93 (16.50)	72.59 (17.26)	72.83 (22.81)	79.60 (17.75)
Median	70.00	75.00	80.00	80.00
Q1 : Q3	62.00 : 85.00	60.00 : 85.00	71.00 : 82.50	75.00 : 90.00
Min : Max	32.0 : 100.0	9.0 : 100.0	5.0 : 92.0	10.0 : 100.0

[a]Derived from MMRM model with change from baseline in EQ-VAS values up to Week 52 as the response variable, and treatment, baseline weight group, region, age, baseline eosinophil level, baseline FeNO level, visit, treatment by-visit interaction, baseline EQ-VAS value and baseline-by-visit interaction as covariates.
[b]Similar model as that mentioned in the footnote [a] with subgroup and subgroup-by-treatment interaction as additional covariates.
Type 2 inflammatory asthma phenotype population is defined as the randomized patients with baseline blood eosinophils >= 0.15 Giga/L or baseline FeNO >= 20 ppb.
Only patients of age >=8 years old at randomization are included in the analysis.
PGM=DEVOPS/SAR231893/EFC14153/CSR_RWE/REPORT/PGM/eff_mmrm_ger_subg_i_t.sas OUT=REPORT/OUTPUT/eff_mmrm_eqvas_ger_ics2_i_t_x.rtf (01SEP2021 - 17:20)

Project Code / Study Number / Analysis: SAR231893 / EFC14153 / CSR_RWE

8 EQ-VAS - ITT type 2 inflammatory asthma phenotype population

8.3 Summary of treatment effect on change from baseline at Week 52

8.3.5 By baseline ICS dose level 2 (Medium, High)

	Baseline ICS dose level 2			
	High		Medium	
EQ-VAS	**Placebo (N=72)**	**Dupilumab (N=156)**	**Placebo (N=15)**	**Dupilumab (N=25)**
Week 52				
Value				
Number	69	150	14	20
Mean (SD)	83.32 (14.13)	87.06 (13.97)	83.07 (17.05)	93.70 (3.36)
Median	85.00	90.50	88.50	95.00
Q1 : Q3	75.00 : 95.00	80.00 : 96.00	79.00 : 96.00	90.00 : 96.00
Min : Max	49.0 : 100.0	30.0 : 100.0	45.0 : 100.0	88.0 : 100.0
Change from baseline				
Number	69	149	12	20
LS Mean (SE)[a]	9.94 (1.86)	13.80 (1.37)	3.56 (4.78)	15.45 (3.81)
LS Mean Diff (95% CI)[a]	-	3.86 (-0.08 to 7.81)	-	11.89 (1.63 to 22.14)
p-value[a]		0.055		0.025
Hedges'g (95% CI)	-	0.235 (-0.005 to 0.474)	-	0.658 (0.090 to 1.225)
p-value for heterogeneity[b]				0.166

[a]Derived from MMRM model with change from baseline in EQ-VAS values up to Week 52 as the response variable, and treatment, baseline weight group, region, age, baseline eosinophil level, baseline FeNO level, visit, treatment by-visit interaction, baseline EQ-VAS value and baseline-by-visit interaction as covariates.
[b]Similar model as that mentioned in the footnote [a] with subgroup and subgroup-by-treatment interaction as additional covariates.
Type 2 inflammatory asthma phenotype population is defined as the randomized patients with baseline blood eosinophils >= 0.15 Giga/L or baseline FeNO >= 20 ppb.
Only patients of age >=8 years old at randomization are included in the analysis.
PGM=DEVOPS/SAR231893/EFC14153/CSR_RWE/REPORT/PGM/eff_mmrm_ger_subg_i_t.sas OUT=REPORT/OUTPUT/eff_mmrm_eqvas_ger_ics2_i_t_x.rtf (01SEP2021 - 17:20)

Project Code / Study Number / Analysis: SAR231893 / EFC14153 / CSR_RWE

8 EQ-VAS - ITT type 2 inflammatory asthma phenotype population

8.3 Summary of treatment effect on change from baseline at Week 52

8.3.6 By baseline predicted FEV1 (<80%, >=80%)

	Baseline Predicted FEV1			
	<80%		>=80%	
EQ-VAS	**Placebo (N=48)**	**Dupilumab (N=91)**	**Placebo (N=39)**	**Dupilumab (N=90)**
Baseline				
Value				
Number	47	91	37	89
Mean (SD)	72.74 (18.97)	71.26 (17.90)	73.14 (15.37)	75.91 (16.76)
Median	80.00	75.00	75.00	80.00
Q1 : Q3	65.00 : 85.00	60.00 : 80.00	65.00 : 85.00	70.00 : 90.00
Min : Max	5.0 : 100.0	9.0 : 100.0	35.0 : 95.0	10.0 : 100.0

[a]Derived from MMRM model with change from baseline in EQ-VAS values up to Week 52 as the response variable, and treatment, baseline weight group, region, age, baseline eosinophil level, baseline FeNO level, baseline ICS dose level, visit, treatment by-visit interaction, baseline EQ-VAS value and baseline-by-visit interaction as covariates.

[b]Similar model as that mentioned in the footnote [a] with subgroup and subgroup-by-treatment interaction as additional covariates.

Type 2 inflammatory asthma phenotype population is defined as the randomized patients with baseline blood eosinophils >= 0.15 Giga/L or baseline FeNO >= 20 ppb.

Only patients of age >=8 years old at randomization are included in the analysis.

PGM=DEVOPS/SAR231893/EFC14153/CSR_RWE/REPORT/PGM/eff_mmrm_ger_subg_i_t.sas OUT=REPORT/OUTPUT/eff_mmrm_eqvas_ger_pfev1_i_t_x.rtf (10AUG2021 - 10:57)

Project Code / Study Number / Analysis: SAR231893 / EFC14153 / CSR_RWE

8 EQ-VAS - ITT type 2 inflammatory asthma phenotype population

8.3 Summary of treatment effect on change from baseline at Week 52

8.3.6 By baseline predicted FEV1 (<80%, >=80%)

	Baseline Predicted FEV1			
	<80%		>=80%	
EQ-VAS	Placebo (N=48)	Dupilumab (N=91)	Placebo (N=39)	Dupilumab (N=90)
Week 52				
Value				
Number	45	88	38	82
Mean (SD)	82.47 (13.69)	87.35 (13.01)	84.24 (15.64)	88.37 (13.74)
Median	82.00	90.00	89.50	93.50
Q1 : Q3	75.00 : 95.00	80.00 : 95.00	80.00 : 96.00	85.00 : 97.00
Min : Max	49.0 : 100.0	40.0 : 100.0	45.0 : 100.0	30.0 : 100.0
Change from baseline				
Number	45	88	36	81
LS Mean (SE)[a]	10.81 (2.29)	15.96 (1.84)	7.68 (2.59)	12.20 (1.83)
LS Mean Diff (95% CI)[a]	-	5.15 (0.37 to 9.94)	-	4.53 (-1.00 to 10.06)
p-value[a]		0.035		0.108
Hedges'g (95% CI)	-	0.308 (0.022 to 0.593)	-	0.275 (-0.061 to 0.610)

[a]Derived from MMRM model with change from baseline in EQ-VAS values up to Week 52 as the response variable, and treatment, baseline weight group, region, age, baseline eosinophil level, baseline FeNO level, baseline ICS dose level, visit, treatment by-visit interaction, baseline EQ-VAS value and baseline-by-visit interaction as covariates.

[b]Similar model as that mentioned in the footnote [a] with subgroup and subgroup-by-treatment interaction as additional covariates.

Type 2 inflammatory asthma phenotype population is defined as the randomized patients with baseline blood eosinophils >= 0.15 Giga/L or baseline FeNO >= 20 ppb. Only patients of age >=8 years old at randomization are included in the analysis.

PGM=DEVOPS/SAR231893/EFC14153/CSR_RWE/REPORT/PGM/eff_mmrm_ger_subg_i_t.sas OUT=REPORT/OUTPUT/eff_mmrm_eqvas_ger_pfev1_i_t_x.rtf (10AUG2021 - 10:57)

Project Code / Study Number / Analysis: SAR231893 / EFC14153 / CSR_RWE

8 EQ-VAS - ITT type 2 inflammatory asthma phenotype population

8.3 Summary of treatment effect on change from baseline at Week 52

8.3.6 By baseline predicted FEV1 (<80%, >=80%)

	Baseline Predicted FEV1			
	<80%		>=80%	
EQ-VAS	Placebo (N=48)	Dupilumab (N=91)	Placebo (N=39)	Dupilumab (N=90)
p-value for heterogeneity[b]				0.969

[a]Derived from MMRM model with change from baseline in EQ-VAS values up to Week 52 as the response variable, and treatment, baseline weight group, region, age, baseline eosinophil level, baseline FeNO level, baseline ICS dose level, visit, treatment by-visit interaction, baseline EQ-VAS value and baseline-by-visit interaction as covariates.

[b]Similar model as that mentioned in the footnote [a] with subgroup and subgroup-by-treatment interaction as additional covariates.

Type 2 inflammatory asthma phenotype population is defined as the randomized patients with baseline blood eosinophils >= 0.15 Giga/L or baseline FeNO >= 20 ppb. Only patients of age >=8 years old at randomization are included in the analysis.

PGM=DEVOPS/SAR231893/EFC14153/CSR_RWE/REPORT/PGM/eff_mmrm_ger_subg_i_t.sas OUT=REPORT/OUTPUT/eff_mmrm_eqvas_ger_pfev1_i_t_x.rtf (10AUG2021 - 10:57)

Project Code / Study Number / Analysis: SAR231893 / EFC14153 / CSR_RWE

8 EQ-VAS - ITT type 2 inflammatory asthma phenotype population

8.3 Summary of treatment effect on change from baseline at Week 52

8.3.7 By baseline ACQ-7-IA (<=2, >2)

	Baseline ACQ-7-IA			
	<=2		>2	
EQ-VAS	**Placebo (N=45)**	**Dupilumab (N=100)**	**Placebo (N=42)**	**Dupilumab (N=81)**
Baseline				
Value				
Number	44	99	40	81
Mean (SD)	78.70 (15.53)	78.34 (15.02)	66.55 (17.23)	67.72 (18.49)
Median	80.00	80.00	70.00	70.00
Q1 : Q3	70.00 : 90.00	70.00 : 90.00	57.00 : 80.00	55.00 : 80.00
Min : Max	35.0 : 100.0	10.0 : 100.0	5.0 : 100.0	9.0 : 100.0

[a]Derived from MMRM model with change from baseline in EQ-VAS values up to Week 52 as the response variable, and treatment, baseline weight group, region, age, baseline eosinophil level, baseline FeNO level, baseline ICS dose level, visit, treatment by-visit interaction, baseline EQ-VAS value and baseline-by-visit interaction as covariates.

[b]Similar model as that mentioned in the footnote [a] with subgroup and subgroup-by-treatment interaction as additional covariates.

Type 2 inflammatory asthma phenotype population is defined as the randomized patients with baseline blood eosinophils >= 0.15 Giga/L or baseline FeNO >= 20 ppb.

Only patients of age >=8 years old at randomization are included in the analysis.

PGM=DEVOPS/SAR231893/EFC14153/CSR_RWE/REPORT/PGM/eff_mmrm_ger_subg_i_t.sas OUT=REPORT/OUTPUT/eff_mmrm_eqvas_ger_acq7_i_t_x.rtf (10AUG2021 - 10:58)

Project Code / Study Number / Analysis: SAR231893 / EFC14153 / CSR_RWE

8 EQ-VAS - ITT type 2 inflammatory asthma phenotype population

8.3 Summary of treatment effect on change from baseline at Week 52

8.3.7 By baseline ACQ-7-IA (<=2, >2)

	Baseline ACQ-7-IA			
	<=2		>2	
EQ-VAS	**Placebo (N=45)**	**Dupilumab (N=100)**	**Placebo (N=42)**	**Dupilumab (N=81)**
Week 52				
Value				
Number	44	92	39	78
Mean (SD)	85.98 (12.75)	88.21 (13.41)	80.23 (15.96)	87.41 (13.32)
Median	90.00	92.50	82.00	91.50
Q1 : Q3	80.00 : 95.00	85.00 : 96.00	70.00 : 95.00	80.00 : 95.00
Min : Max	50.0 : 100.0	30.0 : 100.0	45.0 : 100.0	40.0 : 100.0
Change from baseline				
Number	44	91	37	78
LS Mean (SE)[a]	6.41 (2.09)	9.23 (1.57)	12.94 (2.62)	20.51 (2.01)
LS Mean Diff (95% CI)[a]	-	2.82 (-1.69 to 7.34)	-	7.57 (2.15 to 13.00)
p-value[a]		0.218		0.007
Hedges'g (95% CI)	-	0.191 (-0.114 to 0.496)	-	0.435 (0.123 to 0.746)

[a]Derived from MMRM model with change from baseline in EQ-VAS values up to Week 52 as the response variable, and treatment, baseline weight group, region, age, baseline eosinophil level, baseline FeNO level, baseline ICS dose level, visit, treatment by-visit interaction, baseline EQ-VAS value and baseline-by-visit interaction as covariates.

[b]Similar model as that mentioned in the footnote [a] with subgroup and subgroup-by-treatment interaction as additional covariates.

Type 2 inflammatory asthma phenotype population is defined as the randomized patients with baseline blood eosinophils >= 0.15 Giga/L or baseline FeNO >= 20 ppb. Only patients of age >=8 years old at randomization are included in the analysis.

PGM=DEVOPS/SAR231893/EFC14153/CSR_RWE/REPORT/PGM/eff_mmrm_ger_subg_i_t.sas OUT=REPORT/OUTPUT/eff_mmrm_eqvas_ger_acq7_i_t_x.rtf (10AUG2021 - 10:58)

Project Code / Study Number / Analysis: SAR231893 / EFC14153 / CSR_RWE

8 EQ-VAS - ITT type 2 inflammatory asthma phenotype population

8.3 Summary of treatment effect on change from baseline at Week 52

8.3.7 By baseline ACQ-7-IA (<=2, >2)

	Baseline ACQ-7-IA			
	<=2		>2	
EQ-VAS	**Placebo (N=45)**	**Dupilumab (N=100)**	**Placebo (N=42)**	**Dupilumab (N=81)**
p-value for heterogeneity[b]				0.142

[a]Derived from MMRM model with change from baseline in EQ-VAS values up to Week 52 as the response variable, and treatment, baseline weight group, region, age, baseline eosinophil level, baseline FeNO level, baseline ICS dose level, visit, treatment by-visit interaction, baseline EQ-VAS value and baseline-by-visit interaction as covariates.

[b]Similar model as that mentioned in the footnote [a] with subgroup and subgroup-by-treatment interaction as additional covariates.

Type 2 inflammatory asthma phenotype population is defined as the randomized patients with baseline blood eosinophils >= 0.15 Giga/L or baseline FeNO >= 20 ppb. Only patients of age >=8 years old at randomization are included in the analysis.

PGM=DEVOPS/SAR231893/EFC14153/CSR_RWE/REPORT/PGM/eff_mmrm_ger_subg_i_t.sas OUT=REPORT/OUTPUT/eff_mmrm_eqvas_ger_acq7_i_t_x.rtf (10AUG2021 - 10:58)

Project Code / Study Number / Analysis: SAR231893 / EFC14153 / CSR_RWE

8 EQ-VAS - ITT type 2 inflammatory asthma phenotype population

8.3 Summary of treatment effect on change from baseline at Week 52

8.3.8 By baseline weight (<=30 kg, >30 kg)

	Baseline weight (kg)			
	<=30		>30	
EQ-VAS	**Placebo (N=16)**	**Dupilumab (N=38)**	**Placebo (N=71)**	**Dupilumab (N=143)**
Baseline				
Value				
Number	15	38	69	142
Mean (SD)	78.20 (15.35)	74.82 (18.86)	71.77 (17.68)	73.23 (17.11)
Median	80.00	80.00	70.00	75.00
Q1 : Q3	70.00 : 90.00	60.00 : 89.00	64.00 : 85.00	65.00 : 85.00
Min : Max	40.0 : 98.0	10.0 : 100.0	5.0 : 100.0	9.0 : 100.0

[a]Derived from MMRM model with change from baseline in EQ-VAS values up to Week 52 as the response variable, and treatment, region, age, baseline eosinophil level, baseline FeNO level, baseline ICS dose level, visit, treatment by-visit interaction, baseline EQ-VAS value and baseline-by-visit interaction as covariates.
[b]Similar model as that mentioned in the footnote [a] with subgroup and subgroup-by-treatment interaction as additional covariates.
Type 2 inflammatory asthma phenotype population is defined as the randomized patients with baseline blood eosinophils >= 0.15 Giga/L or baseline FeNO >= 20 ppb.
Only patients of age >=8 years old at randomization are included in the analysis.
PGM=DEVOPS/SAR231893/EFC14153/CSR_RWE/REPORT/PGM/eff_mmrm_ger_subg_i_t.sas OUT=REPORT/OUTPUT/eff_mmrm_eqvas_ger_wgt_i_t_x.rtf (10AUG2021 - 10:58)

Project Code / Study Number / Analysis: SAR231893 / EFC14153 / CSR_RWE

8 EQ-VAS - ITT type 2 inflammatory asthma phenotype population

8.3 Summary of treatment effect on change from baseline at Week 52

8.3.8 By baseline weight (<=30 kg, >30 kg)

	Baseline weight (kg)			
	<=30		>30	
EQ-VAS	**Placebo (N=16)**	**Dupilumab (N=38)**	**Placebo (N=71)**	**Dupilumab (N=143)**
Week 52				
Value				
Number	15	35	68	135
Mean (SD)	86.33 (12.14)	90.66 (12.63)	82.60 (15.03)	87.11 (13.46)
Median	90.00	95.00	85.00	90.00
Q1 : Q3	79.00 : 98.00	90.00 : 99.00	75.00 : 95.00	82.00 : 95.00
Min : Max	60.0 : 100.0	40.0 : 100.0	45.0 : 100.0	30.0 : 100.0
Change from baseline				
Number	15	35	66	134
LS Mean (SE)[a]	11.34 (3.63)	15.45 (2.45)	7.47 (1.80)	12.48 (1.32)
LS Mean Diff (95% CI)[a]	-	4.11 (-3.98 to 12.21)	-	5.01 (0.99 to 9.03)
p-value[a]		0.312		0.015
Hedges'g (95% CI)	-	0.281 (-0.273 to 0.835)	-	0.330 (0.065 to 0.594)
p-value for heterogeneity[b]				0.888

[a]Derived from MMRM model with change from baseline in EQ-VAS values up to Week 52 as the response variable, and treatment, region, age, baseline eosinophil level, baseline FeNO level, baseline ICS dose level, visit, treatment by-visit interaction, baseline EQ-VAS value and baseline-by-visit interaction as covariates.
[b]Similar model as that mentioned in the footnote [a] with subgroup and subgroup-by-treatment interaction as additional covariates.
Type 2 inflammatory asthma phenotype population is defined as the randomized patients with baseline blood eosinophils >= 0.15 Giga/L or baseline FeNO >= 20 ppb.
Only patients of age >=8 years old at randomization are included in the analysis.
PGM=DEVOPS/SAR231893/EFC14153/CSR_RWE/REPORT/PGM/eff_mmrm_ger_subg_i_t.sas OUT=REPORT/OUTPUT/eff_mmrm_eqvas_ger_wgt_i_t_x.rtf (10AUG2021 - 10:58)

Project Code / Study Number / Analysis: SAR231893 / EFC14153 / CSR_RWE

8 EQ-VAS - ITT type 2 inflammatory asthma phenotype population

8.3 Summary of treatment effect on change from baseline at Week 52

8.3.9 By atopic medical condition (Yes, No)

	Atopic medical condition			
	Yes		No	
EQ-VAS	**Placebo (N=79)**	**Dupilumab (N=175)**	**Placebo (N=8)**	**Dupilumab (N=6)**
Baseline				
Value				
Number	76	174	8	6
Mean (SD)	72.00 (17.47)	73.45 (17.64)	81.63 (14.58)	76.67 (11.25)
Median	73.50	78.50	86.50	82.50
Q1 : Q3	64.50 : 85.00	60.00 : 87.00	67.50 : 95.00	65.00 : 85.00
Min : Max	5.0 : 100.0	9.0 : 100.0	60.0 : 95.0	60.0 : 85.0

[a]Derived from MMRM model with change from baseline in EQ-VAS values up to Week 52 as the response variable, and treatment, baseline weight group, region, age, baseline eosinophil level, baseline FeNO level, baseline ICS dose level, visit, treatment by-visit interaction, baseline EQ-VAS value and baseline-by-visit interaction as covariates.

[b]Similar model as that mentioned in the footnote [a] with subgroup and subgroup-by-treatment interaction as additional covariates.

Type 2 inflammatory asthma phenotype population is defined as the randomized patients with baseline blood eosinophils >= 0.15 Giga/L or baseline FeNO >= 20 ppb.

Only patients of age >=8 years old at randomization are included in the analysis.

PGM=DEVOPS/SAR231893/EFC14153/CSR_RWE/REPORT/PGM/eff_mmrm_ger_subg_i_t.sas OUT=REPORT/OUTPUT/eff_mmrm_eqvas_ger_amc_i_t_x.rtf (10AUG2021 - 10:58)

Project Code / Study Number / Analysis: SAR231893 / EFC14153 / CSR_RWE

8 EQ-VAS - ITT type 2 inflammatory asthma phenotype population

8.3 Summary of treatment effect on change from baseline at Week 52

8.3.9 By atopic medical condition (Yes, No)

	Atopic medical condition			
	Yes		No	
EQ-VAS	Placebo (N=79)	Dupilumab (N=175)	Placebo (N=8)	Dupilumab (N=6)
Week 52				
Value				
Number	75	164	8	6
Mean (SD)	82.33 (14.85)	87.55 (13.48)	92.13 (7.04)	95.83 (3.31)
Median	85.00	90.50	95.50	96.50
Q1 : Q3	75.00 : 95.00	83.00 : 95.50	86.50 : 96.50	92.00 : 99.00
Min : Max	45.0 : 100.0	30.0 : 100.0	80.0 : 100.0	92.0 : 99.0
Change from baseline				
Number	73	163	8	6
LS Mean (SE)[a]	8.81 (1.78)	14.13 (1.34)	2.30 (4.46)	6.05 (5.05)
LS Mean Diff (95% CI)[a]	-	5.32 (1.55 to 9.10)	-	3.75 (-13.93 to 21.43)
p-value[a]		0.006		0.600
Hedges'g (95% CI)	-	0.319 (0.093 to 0.546)	-	0.247 (-0.917 to 1.411)

[a]Derived from MMRM model with change from baseline in EQ-VAS values up to Week 52 as the response variable, and treatment, baseline weight group, region, age, baseline eosinophil level, baseline FeNO level, baseline ICS dose level, visit, treatment by-visit interaction, baseline EQ-VAS value and baseline-by-visit interaction as covariates.

[b]Similar model as that mentioned in the footnote [a] with subgroup and subgroup-by-treatment interaction as additional covariates.

Type 2 inflammatory asthma phenotype population is defined as the randomized patients with baseline blood eosinophils >= 0.15 Giga/L or baseline FeNO >= 20 ppb.

Only patients of age >=8 years old at randomization are included in the analysis.

PGM=DEVOPS/SAR231893/EFC14153/CSR_RWE/REPORT/PGM/eff_mmrm_ger_subg_i_t.sas OUT=REPORT/OUTPUT/eff_mmrm_eqvas_ger_amc_i_t_x.rtf (10AUG2021 - 10:58)

Project Code / Study Number / Analysis: SAR231893 / EFC14153 / CSR_RWE

8 EQ-VAS - ITT type 2 inflammatory asthma phenotype population

8.3 Summary of treatment effect on change from baseline at Week 52

8.3.9 By atopic medical condition (Yes, No)

	Atopic medical condition			
	Yes		No	
EQ-VAS	**Placebo (N=79)**	**Dupilumab (N=175)**	**Placebo (N=8)**	**Dupilumab (N=6)**
p-value for heterogeneity[b]				0.622

[a]Derived from MMRM model with change from baseline in EQ-VAS values up to Week 52 as the response variable, and treatment, baseline weight group, region, age, baseline eosinophil level, baseline FeNO level, baseline ICS dose level, visit, treatment by-visit interaction, baseline EQ-VAS value and baseline-by-visit interaction as covariates.

[b]Similar model as that mentioned in the footnote [a] with subgroup and subgroup-by-treatment interaction as additional covariates.

Type 2 inflammatory asthma phenotype population is defined as the randomized patients with baseline blood eosinophils >= 0.15 Giga/L or baseline FeNO >= 20 ppb.

Only patients of age >=8 years old at randomization are included in the analysis.

PGM=DEVOPS/SAR231893/EFC14153/CSR_RWE/REPORT/PGM/eff_mmrm_ger_subg_i_t.sas OUT=REPORT/OUTPUT/eff_mmrm_eqvas_ger_amc_i_t_x.rtf (10AUG2021 - 10:58)

Project Code / Study Number / Analysis: SAR231893 / EFC14153 / CSR_RWE

8 EQ-VAS - ITT type 2 inflammatory asthma phenotype population

8.3 Summary of treatment effect on change from baseline at Week 52

8.3.10 By baseline total IgE (<median, >= median)

	Baseline Total IgE (IU/mL)			
	<median		>=median	
EQ-VAS	**Placebo (N=50)**	**Dupilumab (N=77)**	**Placebo (N=36)**	**Dupilumab (N=99)**
Baseline				
Value				
Number	49	77	34	98
Mean (SD)	74.47 (17.05)	75.81 (14.19)	70.76 (18.11)	71.57 (19.69)
Median	80.00	80.00	70.00	75.00
Q1 : Q3	65.00 : 85.00	70.00 : 85.00	64.00 : 85.00	58.00 : 88.00
Min : Max	32.0 : 100.0	35.0 : 100.0	5.0 : 97.0	9.0 : 100.0

[a]Derived from MMRM model with change from baseline in EQ-VAS values up to Week 52 as the response variable, and treatment, baseline weight group, region, age, baseline eosinophil level, baseline FeNO level, baseline ICS dose level, visit, treatment by-visit interaction, baseline EQ-VAS value and baseline-by-visit interaction as covariates.

[b]Similar model as that mentioned in the footnote [a] with subgroup and subgroup-by-treatment interaction as additional covariates.

Type 2 inflammatory asthma phenotype population is defined as the randomized patients with baseline blood eosinophils >= 0.15 Giga/L or baseline FeNO >= 20 ppb.

Only patients of age >=8 years old at randomization are included in the analysis.

PGM=DEVOPS/SAR231893/EFC14153/CSR_RWE/REPORT/PGM/eff_mmrm_ger_subg_i_t.sas OUT=REPORT/OUTPUT/eff_mmrm_eqvas_ger_igem_i_t_x.rtf (10AUG2021 - 10:58)

Project Code / Study Number / Analysis: SAR231893 / EFC14153 / CSR_RWE

8 EQ-VAS - ITT type 2 inflammatory asthma phenotype population

8.3 Summary of treatment effect on change from baseline at Week 52

8.3.10 By baseline total IgE (<median, >= median)

	Baseline Total IgE (IU/mL)			
	<median		>=median	
EQ-VAS	Placebo (N=50)	Dupilumab (N=77)	Placebo (N=36)	Dupilumab (N=99)
Week 52				
Value				
Number	49	76	33	91
Mean (SD)	82.82 (16.01)	87.59 (14.60)	84.36 (12.30)	87.71 (12.36)
Median	85.00	92.50	85.00	90.00
Q1 : Q3	77.00 : 96.00	85.00 : 96.00	80.00 : 95.00	80.00 : 95.00
Min : Max	45.0 : 100.0	30.0 : 100.0	49.0 : 99.0	40.0 : 100.0
Change from baseline				
Number	48	76	32	90
LS Mean (SE)[a]	6.77 (2.55)	12.06 (2.11)	14.23 (2.37)	18.17 (1.70)
LS Mean Diff (95% CI)[a]	-	5.29 (-0.33 to 10.91)	-	3.95 (-0.65 to 8.54)
p-value[a]		0.065		0.092
Hedges'g (95% CI)	-	0.289 (-0.018 to 0.597)	-	0.252 (-0.042 to 0.545)

[a]Derived from MMRM model with change from baseline in EQ-VAS values up to Week 52 as the response variable, and treatment, baseline weight group, region, age, baseline eosinophil level, baseline FeNO level, baseline ICS dose level, visit, treatment by-visit interaction, baseline EQ-VAS value and baseline-by-visit interaction as covariates.

[b]Similar model as that mentioned in the footnote [a] with subgroup and subgroup-by-treatment interaction as additional covariates.

Type 2 inflammatory asthma phenotype population is defined as the randomized patients with baseline blood eosinophils >= 0.15 Giga/L or baseline FeNO >= 20 ppb.

Only patients of age >=8 years old at randomization are included in the analysis.

PGM=DEVOPS/SAR231893/EFC14153/CSR_RWE/REPORT/PGM/eff_mmrm_ger_subg_i_t.sas OUT=REPORT/OUTPUT/eff_mmrm_eqvas_ger_igem_i_t_x.rtf (10AUG2021 - 10:58)

Project Code / Study Number / Analysis: SAR231893 / EFC14153 / CSR_RWE

8 EQ-VAS - ITT type 2 inflammatory asthma phenotype population

8.3 Summary of treatment effect on change from baseline at Week 52

8.3.10 By baseline total IgE (<median, >= median)

	Baseline Total IgE (IU/mL)			
	<median		>=median	
EQ-VAS	Placebo (N=50)	Dupilumab (N=77)	Placebo (N=36)	Dupilumab (N=99)
p-value for heterogeneity[b]				0.676

[a]Derived from MMRM model with change from baseline in EQ-VAS values up to Week 52 as the response variable, and treatment, baseline weight group, region, age, baseline eosinophil level, baseline FeNO level, baseline ICS dose level, visit, treatment by-visit interaction, baseline EQ-VAS value and baseline-by-visit interaction as covariates.

[b]Similar model as that mentioned in the footnote [a] with subgroup and subgroup-by-treatment interaction as additional covariates.

Type 2 inflammatory asthma phenotype population is defined as the randomized patients with baseline blood eosinophils >= 0.15 Giga/L or baseline FeNO >= 20 ppb. Only patients of age >=8 years old at randomization are included in the analysis.

PGM=DEVOPS/SAR231893/EFC14153/CSR_RWE/REPORT/PGM/eff_mmrm_ger_subg_i_t.sas OUT=REPORT/OUTPUT/eff_mmrm_eqvas_ger_igem_i_t_x.rtf (10AUG2021 - 10:58)

Project Code / Study Number / Analysis: SAR231893 / EFC14153 / CSR_RWE

8 EQ-VAS - ITT type 2 inflammatory asthma phenotype population

8.3 Summary of treatment effect on change from baseline at Week 52

8.3.11 By baseline total IgE (<100 IU/ml, >= 100 IU/ml)

	Baseline Total IgE (IU/mL)			
	< 100		>= 100	
EQ-VAS	**Placebo (N=16)**	**Dupilumab (N=21)**	**Placebo (N=70)**	**Dupilumab (N=155)**
Baseline				
Value				
Number	16	21	67	154
Mean (SD)	75.13 (13.95)	77.33 (13.69)	72.43 (18.27)	72.90 (18.00)
Median	75.00	80.00	75.00	77.50
Q1 : Q3	62.50 : 85.00	70.00 : 87.00	65.00 : 85.00	60.00 : 85.00
Min : Max	55.0 : 100.0	45.0 : 100.0	5.0 : 100.0	9.0 : 100.0

[a]Derived from MMRM model with change from baseline in EQ-VAS values up to Week 52 as the response variable, and treatment, baseline weight group, region, age, baseline eosinophil level, baseline FeNO level, baseline ICS dose level, visit, treatment by-visit interaction, baseline EQ-VAS value and baseline-by-visit interaction as covariates.

[b]Similar model as that mentioned in the footnote [a] with subgroup and subgroup-by-treatment interaction as additional covariates.

Type 2 inflammatory asthma phenotype population is defined as the randomized patients with baseline blood eosinophils >= 0.15 Giga/L or baseline FeNO >= 20 ppb.

Only patients of age >=8 years old at randomization are included in the analysis.

PGM=DEVOPS/SAR231893/EFC14153/CSR_RWE/REPORT/PGM/eff_mmrm_ger_subg_i_t.sas OUT=REPORT/OUTPUT/eff_mmrm_eqvas_ger_ige_i_t_x.rtf (10AUG2021 - 10:59)

Project Code / Study Number / Analysis: SAR231893 / EFC14153 / CSR_RWE

8 EQ-VAS - ITT type 2 inflammatory asthma phenotype population

8.3 Summary of treatment effect on change from baseline at Week 52

8.3.11 By baseline total IgE (<100 IU/ml, >= 100 IU/ml)

	Baseline Total IgE (IU/mL)			
	< 100		>= 100	
EQ-VAS	**Placebo (N=16)**	**Dupilumab (N=21)**	**Placebo (N=70)**	**Dupilumab (N=155)**
Week 52				
Value				
Number	16	21	66	146
Mean (SD)	81.19 (15.67)	83.33 (20.62)	83.98 (14.36)	88.28 (11.97)
Median	83.50	92.00	86.50	91.00
Q1 : Q3	70.00 : 95.00	85.00 : 95.00	77.00 : 95.00	83.00 : 96.00
Min : Max	50.0 : 100.0	30.0 : 100.0	45.0 : 100.0	40.0 : 100.0
Change from baseline				
Number	16	21	64	145
LS Mean (SE)[a]	6.18 (5.86)	8.62 (5.53)	10.49 (1.80)	15.13 (1.32)
LS Mean Diff (95% CI)[a]	-	2.44 (-10.60 to 15.48)	-	4.63 (0.95 to 8.32)
p-value[a]		0.704		0.014
Hedges'g (95% CI)	-	0.097 (-0.420 to 0.614)	-	0.297 (0.061 to 0.532)

[a]Derived from MMRM model with change from baseline in EQ-VAS values up to Week 52 as the response variable, and treatment, baseline weight group, region, age, baseline eosinophil level, baseline FeNO level, baseline ICS dose level, visit, treatment by-visit interaction, baseline EQ-VAS value and baseline-by-visit interaction as covariates.

[b]Similar model as that mentioned in the footnote [a] with subgroup and subgroup-by-treatment interaction as additional covariates.

Type 2 inflammatory asthma phenotype population is defined as the randomized patients with baseline blood eosinophils >= 0.15 Giga/L or baseline FeNO >= 20 ppb. Only patients of age >=8 years old at randomization are included in the analysis.

PGM=DEVOPS/SAR231893/EFC14153/CSR_RWE/REPORT/PGM/eff_mmrm_ger_subg_i_t.sas OUT=REPORT/OUTPUT/eff_mmrm_eqvas_ger_ige_i_t_x.rtf (10AUG2021 - 10:59)

Project Code / Study Number / Analysis: SAR231893 / EFC14153 / CSR_RWE

8 EQ-VAS - ITT type 2 inflammatory asthma phenotype population

8.3 Summary of treatment effect on change from baseline at Week 52

8.3.11 By baseline total IgE (<100 IU/ml, >= 100 IU/ml)

	Baseline Total IgE (IU/mL)			
	< 100		>= 100	
EQ-VAS	**Placebo (N=16)**	**Dupilumab (N=21)**	**Placebo (N=70)**	**Dupilumab (N=155)**
p-value for heterogeneity[b]				0.546

[a]Derived from MMRM model with change from baseline in EQ-VAS values up to Week 52 as the response variable, and treatment, baseline weight group, region, age, baseline eosinophil level, baseline FeNO level, baseline ICS dose level, visit, treatment by-visit interaction, baseline EQ-VAS value and baseline-by-visit interaction as covariates.

[b]Similar model as that mentioned in the footnote [a] with subgroup and subgroup-by-treatment interaction as additional covariates.

Type 2 inflammatory asthma phenotype population is defined as the randomized patients with baseline blood eosinophils >= 0.15 Giga/L or baseline FeNO >= 20 ppb. Only patients of age >=8 years old at randomization are included in the analysis.

PGM=DEVOPS/SAR231893/EFC14153/CSR_RWE/REPORT/PGM/eff_mmrm_ger_subg_i_t.sas OUT=REPORT/OUTPUT/eff_mmrm_eqvas_ger_ige_i_t_x.rtf (10AUG2021 - 10:59)

Project Code / Study Number / Analysis: SAR231893 / EFC14153 / CSR_RWE

8 EQ-VAS - ITT type 2 inflammatory asthma phenotype population

8.3 Summary of treatment effect on change from baseline at Week 52

8.3.12 By age at onset of asthma (0-2, 3-5, >=6 years)

	Age of onset of asthma (years)					
	0-2		3-5		>= 6	
EQ-VAS	Placebo (N=26)	Dupilumab (N=77)	Placebo (N=27)	Dupilumab (N=62)	Placebo (N=34)	Dupilumab (N=42)
Baseline						
Value						
Number	25	77	26	61	33	42
Mean (SD)	72.60 (15.82)	71.48 (18.47)	69.27 (14.80)	75.54 (15.77)	76.03 (20.08)	74.50 (17.85)
Median	70.00	75.00	70.00	76.00	80.00	80.00
Q1 : Q3	60.00 : 85.00	60.00 : 85.00	60.00 : 80.00	69.00 : 90.00	70.00 : 90.00	70.00 : 85.00
Min : Max	50.0 : 98.0	10.0 : 100.0	35.0 : 100.0	30.0 : 100.0	5.0 : 100.0	9.0 : 100.0

[a]Derived from MMRM model with change from baseline in EQ-VAS values up to Week 52 as the response variable, and treatment, baseline weight group, region, age, baseline eosinophil level, baseline FeNO level, baseline ICS dose level, visit, treatment by-visit interaction, baseline EQ-VAS value and baseline-by-visit interaction as covariates.

[b]Similar model as that mentioned in the footnote [a] with subgroup and subgroup-by-treatment interaction as additional covariates.

Type 2 inflammatory asthma phenotype population is defined as the randomized patients with baseline blood eosinophils >= 0.15 Giga/L or baseline FeNO >= 20 ppb.

Only patients of age >=8 years old at randomization are included in the analysis.

PGM=DEVOPS/SAR231893/EFC14153/CSR_RWE/REPORT/PGM/eff_mmrm_ger_subg_i_t.sas OUT=REPORT/OUTPUT/eff_mmrm_eqvas_ger_onsa_i_t_x.rtf (10AUG2021 - 10:59)

Project Code / Study Number / Analysis: SAR231893 / EFC14153 / CSR_RWE

8 EQ-VAS - ITT type 2 inflammatory asthma phenotype population

8.3 Summary of treatment effect on change from baseline at Week 52

8.3.12 By age at onset of asthma (0-2, 3-5, >=6 years)

	Age of onset of asthma (years)					
	0-2		3-5		>= 6	
EQ-VAS	**Placebo (N=26)**	**Dupilumab (N=77)**	**Placebo (N=27)**	**Dupilumab (N=62)**	**Placebo (N=34)**	**Dupilumab (N=42)**
Week 52						
Value						
Number	24	73	25	57	34	40
Mean (SD)	83.46 (12.54)	85.79 (15.05)	80.44 (17.67)	89.42 (12.47)	85.24 (13.40)	89.33 (10.75)
Median	85.00	91.00	85.00	95.00	90.00	90.00
Q1 : Q3	80.00 : 92.00	79.00 : 95.00	60.00 : 96.00	89.00 : 95.00	80.00 : 95.00	85.00 : 97.00
Min : Max	45.0 : 100.0	40.0 : 100.0	49.0 : 100.0	30.0 : 100.0	50.0 : 100.0	40.0 : 100.0
Change from baseline						
Number	23	73	25	56	33	40
LS Mean (SE)[a]	9.44 (3.25)	13.60 (2.22)	6.73 (3.51)	11.94 (2.46)	8.79 (2.53)	12.68 (2.45)
LS Mean Diff (95% CI)[a]	-	4.16 (-2.50 to 10.81)	-	5.21 (-1.85 to 12.26)	-	3.89 (-1.95 to 9.73)
p-value[a]		0.218		0.145		0.188

[a]Derived from MMRM model with change from baseline in EQ-VAS values up to Week 52 as the response variable, and treatment, baseline weight group, region, age, baseline eosinophil level, baseline FeNO level, baseline ICS dose level, visit, treatment by-visit interaction, baseline EQ-VAS value and baseline-by-visit interaction as covariates.

[b]Similar model as that mentioned in the footnote [a] with subgroup and subgroup-by-treatment interaction as additional covariates.

Type 2 inflammatory asthma phenotype population is defined as the randomized patients with baseline blood eosinophils >= 0.15 Giga/L or baseline FeNO >= 20 ppb. Only patients of age >=8 years old at randomization are included in the analysis.

PGM=DEVOPS/SAR231893/EFC14153/CSR_RWE/REPORT/PGM/eff_mmrm_ger_subg_i_t.sas OUT=REPORT/OUTPUT/eff_mmrm_eqvas_ger_onsa_i_t_x.rtf (10AUG2021 - 10:59)

Project Code / Study Number / Analysis: SAR231893 / EFC14153 / CSR_RWE

8 EQ-VAS - ITT type 2 inflammatory asthma phenotype population

8.3 Summary of treatment effect on change from baseline at Week 52

8.3.12 By age at onset of asthma (0-2, 3-5, >=6 years)

	Age of onset of asthma (years)					
	0-2		3-5		>= 6	
EQ-VAS	**Placebo (N=26)**	**Dupilumab (N=77)**	**Placebo (N=27)**	**Dupilumab (N=62)**	**Placebo (N=34)**	**Dupilumab (N=42)**
Hedges'g (95% CI)	-	0.226 (-0.136 to 0.587)	-	0.283 (-0.100 to 0.665)	-	0.254 (-0.127 to 0.635)
p-value for heterogeneity[b]:						
0-2, 3-5						0.558
0-2, >= 6						0.979
3-5, >= 6						0.570
overall						0.803

[a]Derived from MMRM model with change from baseline in EQ-VAS values up to Week 52 as the response variable, and treatment, baseline weight group, region, age, baseline eosinophil level, baseline FeNO level, baseline ICS dose level, visit, treatment by-visit interaction, baseline EQ-VAS value and baseline-by-visit interaction as covariates.

[b]Similar model as that mentioned in the footnote [a] with subgroup and subgroup-by-treatment interaction as additional covariates.

Type 2 inflammatory asthma phenotype population is defined as the randomized patients with baseline blood eosinophils >= 0.15 Giga/L or baseline FeNO >= 20 ppb. Only patients of age >=8 years old at randomization are included in the analysis.

PGM=DEVOPS/SAR231893/EFC14153/CSR_RWE/REPORT/PGM/eff_mmrm_ger_subg_i_t.sas OUT=REPORT/OUTPUT/eff_mmrm_eqvas_ger_onsa_i_t_x.rtf (10AUG2021 - 10:59)

Project Code / Study Number / Analysis: SAR231893 / EFC14153 / CSR_RWE

8 EQ-VAS - ITT type 2 inflammatory asthma phenotype population

8.3 Summary of treatment effect on change from baseline at Week 52

8.3.13 By number of severe asthma exacerbation prior to the study (<=1, 2, >2)

	Number of severe asthma exacerbation prior to the study					
	<=1		2		>2	
EQ-VAS	**Placebo (N=35)**	**Dupilumab (N=68)**	**Placebo (N=24)**	**Dupilumab (N=59)**	**Placebo (N=28)**	**Dupilumab (N=54)**
Baseline						
Value						
Number	34	68	24	58	26	54
Mean (SD)	77.06 (16.59)	73.57 (18.20)	71.58 (20.06)	75.38 (17.07)	68.73 (15.02)	71.59 (17.00)
Median	80.00	80.00	72.50	80.00	70.00	71.00
Q1 : Q3	70.00 : 90.00	65.00 : 87.00	62.50 : 85.00	70.00 : 87.00	59.00 : 80.00	60.00 : 83.00
Min : Max	35.0 : 100.0	10.0 : 100.0	5.0 : 98.0	9.0 : 100.0	32.0 : 95.0	30.0 : 100.0

[a]Derived from MMRM model with change from baseline in EQ-VAS values up to Week 52 as the response variable, and treatment, baseline weight group, region, age, baseline eosinophil level, baseline FeNO level, baseline ICS dose level, visit, treatment by-visit interaction, baseline EQ-VAS value and baseline-by-visit interaction as covariates.

[b]Similar model as that mentioned in the footnote [a] with subgroup and subgroup-by-treatment interaction as additional covariates.

Type 2 inflammatory asthma phenotype population is defined as the randomized patients with baseline blood eosinophils >= 0.15 Giga/L or baseline FeNO >= 20 ppb.

Only patients of age >=8 years old at randomization are included in the analysis.

PGM=DEVOPS/SAR231893/EFC14153/CSR_RWE/REPORT/PGM/eff_mmrm_ger_subg_i_t.sas OUT=REPORT/OUTPUT/eff_mmrm_eqvas_ger_exa_i_t_x.rtf (10AUG2021 - 10:59)

Project Code / Study Number / Analysis: SAR231893 / EFC14153 / CSR_RWE

8 EQ-VAS - ITT type 2 inflammatory asthma phenotype population

8.3 Summary of treatment effect on change from baseline at Week 52

8.3.13 By number of severe asthma exacerbation prior to the study (<=1, 2, >2)

	Number of severe asthma exacerbation prior to the study					
	<=1		2		>2	
EQ-VAS	**Placebo (N=35)**	**Dupilumab (N=68)**	**Placebo (N=24)**	**Dupilumab (N=59)**	**Placebo (N=28)**	**Dupilumab (N=54)**
Week 52						
Value						
Number	34	64	24	54	25	52
Mean (SD)	85.06 (13.75)	87.69 (13.49)	84.75 (13.74)	89.15 (10.48)	79.44 (16.14)	86.67 (15.73)
Median	89.50	92.50	89.50	90.00	80.00	92.50
Q1 : Q3	75.00 : 96.00	82.50 : 95.50	80.00 : 95.50	85.00 : 96.00	75.00 : 91.00	81.50 : 96.50
Min : Max	55.0 : 100.0	40.0 : 100.0	50.0 : 100.0	50.0 : 100.0	45.0 : 99.0	30.0 : 100.0
Change from baseline						
Number	33	64	24	53	24	52
LS Mean (SE)[a]	8.38 (2.25)	13.72 (1.72)	9.27 (2.75)	11.97 (2.30)	8.17 (4.18)	16.07 (3.06)
LS Mean Diff (95% CI)[a]	-	5.33 (0.23 to 10.43)	-	2.70 (-3.14 to 8.55)	-	7.90 (-0.28 to 16.09)
p-value[a]		0.041		0.360		0.058

[a]Derived from MMRM model with change from baseline in EQ-VAS values up to Week 52 as the response variable, and treatment, baseline weight group, region, age, baseline eosinophil level, baseline FeNO level, baseline ICS dose level, visit, treatment by-visit interaction, baseline EQ-VAS value and baseline-by-visit interaction as covariates.

[b]Similar model as that mentioned in the footnote [a] with subgroup and subgroup-by-treatment interaction as additional covariates.

Type 2 inflammatory asthma phenotype population is defined as the randomized patients with baseline blood eosinophils >= 0.15 Giga/L or baseline FeNO >= 20 ppb. Only patients of age >=8 years old at randomization are included in the analysis.

PGM=DEVOPS/SAR231893/EFC14153/CSR_RWE/REPORT/PGM/eff_mmrm_ger_subg_i_t.sas OUT=REPORT/OUTPUT/eff_mmrm_eqvas_ger_exa_i_t_x.rtf (10AUG2021 - 10:59)

Project Code / Study Number / Analysis: SAR231893 / EFC14153 / CSR_RWE

8 EQ-VAS - ITT type 2 inflammatory asthma phenotype population

8.3 Summary of treatment effect on change from baseline at Week 52

8.3.13 By number of severe asthma exacerbation prior to the study (<=1, 2, >2)

	Number of severe asthma exacerbation prior to the study					
	<=1		2		>2	
EQ-VAS	**Placebo (N=35)**	**Dupilumab (N=68)**	**Placebo (N=24)**	**Dupilumab (N=59)**	**Placebo (N=28)**	**Dupilumab (N=54)**
Hedges'g (95% CI)	-	0.391 (0.017 to 0.765)	-	0.167 (-0.195 to 0.529)	-	0.360 (-0.013 to 0.734)
p-value for heterogeneity[b]:						
<=1, 2						0.625
<=1, >2						0.591
2, >2						0.332
overall						0.625

[a]Derived from MMRM model with change from baseline in EQ-VAS values up to Week 52 as the response variable, and treatment, baseline weight group, region, age, baseline eosinophil level, baseline FeNO level, baseline ICS dose level, visit, treatment by-visit interaction, baseline EQ-VAS value and baseline-by-visit interaction as covariates.

[b]Similar model as that mentioned in the footnote [a] with subgroup and subgroup-by-treatment interaction as additional covariates.

Type 2 inflammatory asthma phenotype population is defined as the randomized patients with baseline blood eosinophils >= 0.15 Giga/L or baseline FeNO >= 20 ppb.

Only patients of age >=8 years old at randomization are included in the analysis.

PGM=DEVOPS/SAR231893/EFC14153/CSR_RWE/REPORT/PGM/eff_mmrm_ger_subg_i_t.sas OUT=REPORT/OUTPUT/eff_mmrm_eqvas_ger_exa_i_t_x.rtf (10AUG2021 - 10:59)

Subgruppenanalysen: unerwünschtes Ereignisse

Project Code / Study Number / Analysis: SAR231893 / EFC14153 / CSR_RWE

2 Adverse events - Safety type 2 inflammatory asthma phenotype population

2.1 Patients with any TEAE

Safety type 2 inflammatory asthma phenotype population	Placebo (N=113)	Dupilumab (N=234)
Patients with any TEAE [n(%)]	89 (78.8%)	194 (82.9%)
Odds Ratio (95% CI)	-	1.31 (0.74 to 2.30)
p-value for Odds Ratio		0.352
Risk Ratio (95% CI)	-	1.05 (0.94 to 1.18)
Reversed Risk Ratio (95% CI)	-	0.95 (0.85 to 1.06)
p-value for Risk Ratio		0.370
Risk Difference (95% CI)	-	4.14 (-4.84 to 13.13)
p-value for Risk Difference		0.365

Odds Ratio and related p-value are estimated by Wald's method using the SAS LOGISTIC procedure.
Peto OR calculation is based on Yusuf S et al. (Prog Cardiovasc Dis. 1985 Mar-Apr;27(5):335-71) and its p-value is derived using a normal approximation.
Risk Ratio and related p-value are estimated by using the SAS FREQ procedure.
Risk Difference and related p-value are estimated by using the SAS GLIMMIX procedure with the following model: criterion = treatment.
PGM=DEVOPS/SAR231893/EFC14153/CSR_RWE/REPORT/PGM/ae_evt_ger_s2_t.sas OUT=REPORT/OUTPUT/ae_teae_ger_s2_t_x.rtf (30JUL2021 - 15:49)

Project Code / Study Number / Analysis: SAR231893 / EFC14153 / CSR_RWE

2 Adverse events - Safety type 2 inflammatory asthma phenotype population

2.1 Patients with any TEAE

2.1.1 By gender (Male, Female)

	Gender			
	Male		Female	
Safety type 2 inflammatory asthma phenotype population	**Placebo (N=77)**	**Dupilumab (N=153)**	**Placebo (N=36)**	**Dupilumab (N=81)**
Patients with any TEAE [n(%)]	62 (80.5%)	122 (79.7%)	27 (75.0%)	72 (88.9%)
Odds Ratio (95% CI)	-	0.95 (0.48 to 1.89)	-	2.67 (0.96 to 7.43)
p-value for Odds Ratio		0.889		0.061
p-value for heterogeneity of Odds Ratio				0.103
Risk Ratio (95% CI)	-	0.99 (0.86 to 1.13)	-	1.19 (0.97 to 1.45)
Reversed Risk ratio (95% CI)			-	0.84 (0.69 to 1.03)
p-value for Risk Ratio		0.888		0.102
p-value for heterogeneity of Risk Ratio				0.151
Risk Difference (95% CI)	-	-0.78 (-11.74 to 10.18)	-	13.89 (-1.99 to 29.77)

Odds Ratio and related p-value are estimated by Wald's method using the SAS LOGISTIC procedure.
Peto OR calculation is based on Yusuf S et al. (Prog Cardiovasc Dis. 1985 Mar-Apr;27(5):335-71) and its p-value is derived using a normal approximation.
Risk Ratio and related p-value are estimated by using the SAS FREQ procedure.
Risk Difference and related p-value are estimated by using the SAS GLIMMIX procedure with the following model: criterion = treatment.
p-values for heterogeneity are estimated by using the SAS GLIMMIX procedure with the following model: criterion = treatment subgroup treatment*subgroup.
p-value for heterogeneity of Peto Odds Ratio is estimated by using normal approximation.
PGM=DEVOPS/SAR231893/EFC14153/CSR_RWE/REPORT/PGM/ae_evt_ger_subg_s2_t.sas OUT=REPORT/OUTPUT/ae_teae_ger_sex_s2_t_x.rtf (29JUL2021 - 14:40)

Project Code / Study Number / Analysis: SAR231893 / EFC14153 / CSR_RWE

2 Adverse events - Safety type 2 inflammatory asthma phenotype population

2.1 Patients with any TEAE

2.1.1 By gender (Male, Female)

	Gender			
	Male		Female	
Safety type 2 inflammatory asthma phenotype population	**Placebo (N=77)**	**Dupilumab (N=153)**	**Placebo (N=36)**	**Dupilumab (N=81)**
p-value for Risk Difference		0.888		0.086
p-value for heterogeneity of Risk Difference				0.134

Odds Ratio and related p-value are estimated by Wald's method using the SAS LOGISTIC procedure.
Peto OR calculation is based on Yusuf S et al. (Prog Cardiovasc Dis. 1985 Mar-Apr;27(5):335-71) and its p-value is derived using a normal approximation.
Risk Ratio and related p-value are estimated by using the SAS FREQ procedure.
Risk Difference and related p-value are estimated by using the SAS GLIMMIX procedure with the following model: criterion = treatment.
p-values for heterogeneity are estimated by using the SAS GLIMMIX procedure with the following model: criterion = treatment subgroup treatment*subgroup.
p-value for heterogeneity of Peto Odds Ratio is estimated by using normal approximation.
PGM=DEVOPS/SAR231893/EFC14153/CSR_RWE/REPORT/PGM/ae_evt_ger_subg_s2_t.sas OUT=REPORT/OUTPUT/ae_teae_ger_sex_s2_t_x.rtf (29JUL2021 - 14:40)

Project Code / Study Number / Analysis: SAR231893 / EFC14153 / CSR_RWE

2 Adverse events - Safety type 2 inflammatory asthma phenotype population

2.1 Patients with any TEAE

2.1.2 By region (Latin America, East Europe, Western Countries)

	Region					
	Latin America		East Europe		Western countries	
Safety type 2 inflammatory asthma phenotype population	**Placebo (N=51)**	**Dupilumab (N=105)**	**Placebo (N=43)**	**Dupilumab (N=78)**	**Placebo (N=19)**	**Dupilumab (N=51)**
Patients with any TEAE [n(%)]	40 (78.4%)	81 (77.1%)	31 (72.1%)	64 (82.1%)	18 (94.7%)	49 (96.1%)
Odds Ratio (95% CI)	-	0.93 (0.41 to 2.08)	-	1.77 (0.73 to 4.28)	-	1.36 (0.12 to 15.94)
p-value for Odds Ratio		0.856		0.205		0.806
p-value for heterogeneity of Odds Ratio:						
Latin America, East Europe						0.291
Latin America, Western countries						0.772
East Europe, Western countries						0.844
overall						0.571
Risk Ratio (95% CI)	-	0.98 (0.82 to 1.17)	-	1.14 (0.92 to 1.41)	-	1.01 (0.90 to 1.14)
Reversed Risk ratio (95% CI)			-	0.88 (0.71 to 1.09)	-	0.99 (0.87 to 1.11)

Odds Ratio and related p-value are estimated by Wald's method using the SAS LOGISTIC procedure.
Peto OR calculation is based on Yusuf S et al. (Prog Cardiovasc Dis. 1985 Mar-Apr;27(5):335-71) and its p-value is derived using a normal approximation.
Risk Ratio and related p-value are estimated by using the SAS FREQ procedure.
Risk Difference and related p-value are estimated by using the SAS GLIMMIX procedure with the following model: criterion = treatment.
p-values for heterogeneity are estimated by using the SAS GLIMMIX procedure with the following model: criterion = treatment subgroup treatment*subgroup.
p-value for heterogeneity of Peto Odds Ratio is estimated by using normal approximation.
PGM=DEVOPS/SAR231893/EFC14153/CSR_RWE/REPORT/PGM/ae_evt_ger_subg_s2_t.sas OUT=REPORT/OUTPUT/ae_teae_ger_cty_s2_t_x.rtf (29JUL2021 - 14:41)

Project Code / Study Number / Analysis: SAR231893 / EFC14153 / CSR_RWE

2 Adverse events - Safety type 2 inflammatory asthma phenotype population

2.1 Patients with any TEAE

2.1.2 By region (Latin America, East Europe, Western Countries)

	Region					
	Latin America		East Europe		Western countries	
Safety type 2 inflammatory asthma phenotype population	**Placebo (N=51)**	**Dupilumab (N=105)**	**Placebo (N=43)**	**Dupilumab (N=78)**	**Placebo (N=19)**	**Dupilumab (N=51)**
p-value for Risk Ratio		0.855		0.234		0.818
p-value for heterogeneity of Risk Ratio:						
Latin America, East Europe						0.303
Latin America, Western countries						0.779
East Europe, Western countries						0.355
overall						0.559
Risk Difference (95% CI)	-	-1.29 (-15.25 to 12.68)	-	9.96 (-6.09 to 26.00)	-	1.34 (-10.23 to 12.91)
p-value for Risk Difference		0.856		0.222		0.818
p-value for heterogeneity of Risk Difference:						
Latin America, East Europe						0.296
Latin America, Western countries						0.774

Odds Ratio and related p-value are estimated by Wald's method using the SAS LOGISTIC procedure.
Peto OR calculation is based on Yusuf S et al. (Prog Cardiovasc Dis. 1985 Mar-Apr;27(5):335-71) and its p-value is derived using a normal approximation.
Risk Ratio and related p-value are estimated by using the SAS FREQ procedure.
Risk Difference and related p-value are estimated by using the SAS GLIMMIX procedure with the following model: criterion = treatment.
p-values for heterogeneity are estimated by using the SAS GLIMMIX procedure with the following model: criterion = treatment subgroup treatment*subgroup.
p-value for heterogeneity of Peto Odds Ratio is estimated by using normal approximation.
PGM=DEVOPS/SAR231893/EFC14153/CSR_RWE/REPORT/PGM/ae_evt_ger_subg_s2_t.sas OUT=REPORT/OUTPUT/ae_teae_ger_cty_s2_t_x.rtf (29JUL2021 - 14:41)

Project Code / Study Number / Analysis: SAR231893 / EFC14153 / CSR_RWE

2 Adverse events - Safety type 2 inflammatory asthma phenotype population

2.1 Patients with any TEAE

2.1.2 By region (Latin America, East Europe, Western Countries)

	Region					
	Latin America		East Europe		Western countries	
Safety type 2 inflammatory asthma phenotype population	**Placebo (N=51)**	**Dupilumab (N=105)**	**Placebo (N=43)**	**Dupilumab (N=78)**	**Placebo (N=19)**	**Dupilumab (N=51)**
East Europe, Western countries						0.388
overall						0.557

Odds Ratio and related p-value are estimated by Wald's method using the SAS LOGISTIC procedure.
Peto OR calculation is based on Yusuf S et al. (Prog Cardiovasc Dis. 1985 Mar-Apr;27(5):335-71) and its p-value is derived using a normal approximation.
Risk Ratio and related p-value are estimated by using the SAS FREQ procedure.
Risk Difference and related p-value are estimated by using the SAS GLIMMIX procedure with the following model: criterion = treatment.
p-values for heterogeneity are estimated by using the SAS GLIMMIX procedure with the following model: criterion = treatment subgroup treatment*subgroup.
p-value for heterogeneity of Peto Odds Ratio is estimated by using normal approximation.
PGM=DEVOPS/SAR231893/EFC14153/CSR_RWE/REPORT/PGM/ae_evt_ger_subg_s2_t.sas OUT=REPORT/OUTPUT/ae_teae_ger_cty_s2_t_x.rtf (29JUL2021 - 14:41)

Project Code / Study Number / Analysis: SAR231893 / EFC14153 / CSR_RWE

2 Adverse events - Safety type 2 inflammatory asthma phenotype population

2.1 Patients with any TEAE

2.1.3 By race (Caucasian/white, Black/of African descent, Other)

	Race					
	Caucasian/White		Black/of African descent		Other	
Safety type 2 inflammatory asthma phenotype population	**Placebo (N=101)**	**Dupilumab (N=207)**	**Placebo (N=5)**	**Dupilumab (N=9)**	**Placebo (N=7)**	**Dupilumab (N=18)**
Patients with any TEAE [n(%)]	78 (77.2%)	169 (81.6%)	5 (100%)	8 (88.9%)	6 (85.7%)	17 (94.4%)
Odds Ratio (95% CI)	-	1.31 (0.73 to 2.35)	-	0.00 (NE to NE)	-	2.83 (0.15 to 52.74)
p-value for Odds Ratio		0.362		NE		0.485
p-value for heterogeneity of Odds Ratio:						
Caucasian/White, Black/of African descent						0.976
Caucasian/White, Other						0.613
Black/of African descent, Other						0.975
overall						0.879
Risk Ratio (95% CI)	-	1.06 (0.93 to 1.20)	-	0.89 (NE to NE)	-	1.10 (0.80 to 1.52)
Reversed Risk ratio (95% CI)	-	0.95 (0.84 to 1.07)			-	0.91 (0.66 to 1.25)

Odds Ratio and related p-value are estimated by Wald's method using the SAS LOGISTIC procedure.
Peto OR calculation is based on Yusuf S et al. (Prog Cardiovasc Dis. 1985 Mar-Apr;27(5):335-71) and its p-value is derived using a normal approximation.
Risk Ratio and related p-value are estimated by using the SAS FREQ procedure.
Risk Difference and related p-value are estimated by using the SAS GLIMMIX procedure with the following model: criterion = treatment.
p-values for heterogeneity are estimated by using the SAS GLIMMIX procedure with the following model: criterion = treatment subgroup treatment*subgroup.
p-value for heterogeneity of Peto Odds Ratio is estimated by using normal approximation.
PGM=DEVOPS/SAR231893/EFC14153/CSR_RWE/REPORT/PGM/ae_evt_ger_subg_s2_t.sas OUT=REPORT/OUTPUT/ae_teae_ger_race_s2_t_x.rtf (29JUL2021 - 14:41)

Project Code / Study Number / Analysis: SAR231893 / EFC14153 / CSR_RWE

2 Adverse events - Safety type 2 inflammatory asthma phenotype population

2.1 Patients with any TEAE

2.1.3 By race (Caucasian/white, Black/of African descent, Other)

	Race					
	Caucasian/White		Black/of African descent		Other	
Safety type 2 inflammatory asthma phenotype population	**Placebo (N=101)**	**Dupilumab (N=207)**	**Placebo (N=5)**	**Dupilumab (N=9)**	**Placebo (N=7)**	**Dupilumab (N=18)**
p-value for Risk Ratio		0.380		NE		0.556
p-value for heterogeneity of Risk Ratio:						
Caucasian/White, Black/of African descent						0.371
Caucasian/White, Other						0.904
Black/of African descent, Other						<0.001
overall						0.904
Risk Difference (95% CI)	-	4.41 (-5.36 to 14.18)	-	-11.11 (NE to NE)	-	8.73 (-20.82 to 38.28)
p-value for Risk Difference		0.375		<0.001		0.547
p-value for heterogeneity of Risk Difference:						
Caucasian/White, Black/of African descent						0.305
Caucasian/White, Other						0.776
Black/of African descent, Other						<0.001

Odds Ratio and related p-value are estimated by Wald's method using the SAS LOGISTIC procedure.
Peto OR calculation is based on Yusuf S et al. (Prog Cardiovasc Dis. 1985 Mar-Apr;27(5):335-71) and its p-value is derived using a normal approximation.
Risk Ratio and related p-value are estimated by using the SAS FREQ procedure.
Risk Difference and related p-value are estimated by using the SAS GLIMMIX procedure with the following model: criterion = treatment.
p-values for heterogeneity are estimated by using the SAS GLIMMIX procedure with the following model: criterion = treatment subgroup treatment*subgroup.
p-value for heterogeneity of Peto Odds Ratio is estimated by using normal approximation.
PGM=DEVOPS/SAR231893/EFC14153/CSR_RWE/REPORT/PGM/ae_evt_ger_subg_s2_t.sas OUT=REPORT/OUTPUT/ae_teae_ger_race_s2_t_x.rtf (29JUL2021 - 14:41)

Project Code / Study Number / Analysis: SAR231893 / EFC14153 / CSR_RWE

2 Adverse events - Safety type 2 inflammatory asthma phenotype population

2.1 Patients with any TEAE

2.1.3 By race (Caucasian/white, Black/of African descent, Other)

	Race					
	Caucasian/White		Black/of African descent		Other	
Safety type 2 inflammatory asthma phenotype population	**Placebo (N=101)**	**Dupilumab (N=207)**	**Placebo (N=5)**	**Dupilumab (N=9)**	**Placebo (N=7)**	**Dupilumab (N=18)**
overall						0.776

Odds Ratio and related p-value are estimated by Wald's method using the SAS LOGISTIC procedure.
Peto OR calculation is based on Yusuf S et al. (Prog Cardiovasc Dis. 1985 Mar-Apr;27(5):335-71) and its p-value is derived using a normal approximation.
Risk Ratio and related p-value are estimated by using the SAS FREQ procedure.
Risk Difference and related p-value are estimated by using the SAS GLIMMIX procedure with the following model: criterion = treatment.
p-values for heterogeneity are estimated by using the SAS GLIMMIX procedure with the following model: criterion = treatment subgroup treatment*subgroup.
p-value for heterogeneity of Peto Odds Ratio is estimated by using normal approximation.
PGM=DEVOPS/SAR231893/EFC14153/CSR_RWE/REPORT/PGM/ae_evt_ger_subg_s2_t.sas OUT=REPORT/OUTPUT/ae_teae_ger_race_s2_t_x.rtf (29JUL2021 - 14:41)

Project Code / Study Number / Analysis: SAR231893 / EFC14153 / CSR_RWE

2 Adverse events - Safety type 2 inflammatory asthma phenotype population

2.1 Patients with any TEAE

2.1.4 By baseline ICS dose level (Medium, High)

	Baseline ICS dose level			
	High		Medium	
Safety type 2 inflammatory asthma phenotype population	**Placebo (N=50)**	**Dupilumab (N=101)**	**Placebo (N=63)**	**Dupilumab (N=131)**
Patients with any TEAE [n(%)]	36 (72.0%)	86 (85.1%)	53 (84.1%)	107 (81.7%)
Odds Ratio (95% CI)	-	2.23 (0.98 to 5.09)	-	0.84 (0.38 to 1.89)
p-value for Odds Ratio		0.057		0.675
p-value for heterogeneity of Odds Ratio				0.099
Risk Ratio (95% CI)	-	1.18 (0.98 to 1.43)	-	0.97 (0.85 to 1.11)
Reversed Risk ratio (95% CI)	-	0.85 (0.70 to 1.02)		
p-value for Risk Ratio		0.085		0.667
p-value for heterogeneity of Risk Ratio				0.099
Risk Difference (95% CI)	-	13.15 (-1.22 to 27.51)	-	-2.45 (-13.71 to 8.82)

Odds Ratio and related p-value are estimated by Wald's method using the SAS LOGISTIC procedure.
Peto OR calculation is based on Yusuf S et al. (Prog Cardiovasc Dis. 1985 Mar-Apr;27(5):335-71) and its p-value is derived using a normal approximation.
Risk Ratio and related p-value are estimated by using the SAS FREQ procedure.
Risk Difference and related p-value are estimated by using the SAS GLIMMIX procedure with the following model: criterion = treatment.
p-values for heterogeneity are estimated by using the SAS GLIMMIX procedure with the following model: criterion = treatment subgroup treatment*subgroup.
p-value for heterogeneity of Peto Odds Ratio is estimated by using normal approximation.
PGM=DEVOPS/SAR231893/EFC14153/CSR_RWE/REPORT/PGM/ae_evt_ger_subg_s2_t.sas OUT=REPORT/OUTPUT/ae_teae_ger_ics_s2_t_x.rtf (29JUL2021 - 14:41)

Project Code / Study Number / Analysis: SAR231893 / EFC14153 / CSR_RWE

2 Adverse events - Safety type 2 inflammatory asthma phenotype population

2.1 Patients with any TEAE

2.1.4 By baseline ICS dose level (Medium, High)

	Baseline ICS dose level			
	High		Medium	
Safety type 2 inflammatory asthma phenotype population	**Placebo (N=50)**	**Dupilumab (N=101)**	**Placebo (N=63)**	**Dupilumab (N=131)**
p-value for Risk Difference		0.072		0.669
p-value for heterogeneity of Risk Difference				0.093

Odds Ratio and related p-value are estimated by Wald's method using the SAS LOGISTIC procedure.
Peto OR calculation is based on Yusuf S et al. (Prog Cardiovasc Dis. 1985 Mar-Apr;27(5):335-71) and its p-value is derived using a normal approximation.
Risk Ratio and related p-value are estimated by using the SAS FREQ procedure.
Risk Difference and related p-value are estimated by using the SAS GLIMMIX procedure with the following model: criterion = treatment.
p-values for heterogeneity are estimated by using the SAS GLIMMIX procedure with the following model: criterion = treatment subgroup treatment*subgroup.
p-value for heterogeneity of Peto Odds Ratio is estimated by using normal approximation.
PGM=DEVOPS/SAR231893/EFC14153/CSR_RWE/REPORT/PGM/ae_evt_ger_subg_s2_t.sas OUT=REPORT/OUTPUT/ae_teae_ger_ics_s2_t_x.rtf (29JUL2021 - 14:41)

Project Code / Study Number / Analysis: SAR231893 / EFC14153 / CSR_RWE

2 Adverse events - Safety type 2 inflammatory asthma phenotype population

2.1 Patients with any TEAE

2.1.5 By baseline ICS dose level 2 (Medium, High)

Safety type 2 inflammatory asthma phenotype population	Baseline ICS dose level 2			
	High		Medium	
	Placebo (N=94)	Dupilumab (N=199)	Placebo (N=19)	Dupilumab (N=35)
Patients with any TEAE [n(%)]	75 (79.8%)	163 (81.9%)	14 (73.7%)	31 (88.6%)
Odds Ratio (95% CI)	-	1.15 (0.62 to 2.13)	-	2.77 (0.64 to 11.90)
p-value for Odds Ratio		0.664		0.171
p-value for heterogeneity of Odds Ratio				0.277
Risk Ratio (95% CI)	-	1.03 (0.91 to 1.16)	-	1.20 (0.90 to 1.61)
Reversed Risk ratio (95% CI)	-	0.97 (0.86 to 1.10)	-	0.83 (0.62 to 1.12)
p-value for Risk Ratio		0.670		0.220
p-value for heterogeneity of Risk Ratio				0.331
Risk Difference (95% CI)	-	2.12 (-7.64 to 11.88)	-	14.89 (-8.08 to 37.85)

Odds Ratio and related p-value are estimated by Wald's method using the SAS LOGISTIC procedure.
Peto OR calculation is based on Yusuf S et al. (Prog Cardiovasc Dis. 1985 Mar-Apr;27(5):335-71) and its p-value is derived using a normal approximation.
Risk Ratio and related p-value are estimated by using the SAS FREQ procedure.
Risk Difference and related p-value are estimated by using the SAS GLIMMIX procedure with the following model: criterion = treatment.
p-values for heterogeneity are estimated by using the SAS GLIMMIX procedure with the following model: criterion = treatment subgroup treatment*subgroup.
p-value for heterogeneity of Peto Odds Ratio is estimated by using normal approximation.
PGM=DEVOPS/SAR231893/EFC14153/CSR_RWE/REPORT/PGM/ae_evt_ger_subg_s2_t.sas OUT=REPORT/OUTPUT/ae_teae_ger_ics2_s2_t_x.rtf (01SEP2021 - 16:08)

Project Code / Study Number / Analysis: SAR231893 / EFC14153 / CSR_RWE

2 Adverse events - Safety type 2 inflammatory asthma phenotype population

2.1 Patients with any TEAE

2.1.5 By baseline ICS dose level 2 (Medium, High)

	Baseline ICS dose level 2			
	High		Medium	
Safety type 2 inflammatory asthma phenotype population	**Placebo (N=94)**	**Dupilumab (N=199)**	**Placebo (N=19)**	**Dupilumab (N=35)**
p-value for Risk Difference		0.669		0.199
p-value for heterogeneity of Risk Difference				0.307

Odds Ratio and related p-value are estimated by Wald's method using the SAS LOGISTIC procedure.
Peto OR calculation is based on Yusuf S et al. (Prog Cardiovasc Dis. 1985 Mar-Apr;27(5):335-71) and its p-value is derived using a normal approximation.
Risk Ratio and related p-value are estimated by using the SAS FREQ procedure.
Risk Difference and related p-value are estimated by using the SAS GLIMMIX procedure with the following model: criterion = treatment.
p-values for heterogeneity are estimated by using the SAS GLIMMIX procedure with the following model: criterion = treatment subgroup treatment*subgroup.
p-value for heterogeneity of Peto Odds Ratio is estimated by using normal approximation.
PGM=DEVOPS/SAR231893/EFC14153/CSR_RWE/REPORT/PGM/ae_evt_ger_subg_s2_t.sas OUT=REPORT/OUTPUT/ae_teae_ger_ics2_s2_t_x.rtf (01SEP2021 - 16:08)

Project Code / Study Number / Analysis: SAR231893 / EFC14153 / CSR_RWE

2 Adverse events - Safety type 2 inflammatory asthma phenotype population

2.1 Patients with any TEAE

2.1.6 By baseline predicted FEV1 (<80%, >=80%)

	Baseline Predicted FEV1			
	<80%		>=80%	
Safety type 2 inflammatory asthma phenotype population	**Placebo (N=58)**	**Dupilumab (N=116)**	**Placebo (N=55)**	**Dupilumab (N=118)**
Patients with any TEAE [n(%)]	46 (79.3%)	101 (87.1%)	43 (78.2%)	93 (78.8%)
Odds Ratio (95% CI)	-	1.76 (0.76 to 4.05)	-	1.04 (0.48 to 2.26)
p-value for Odds Ratio		0.186		0.925
p-value for heterogeneity of Odds Ratio				0.367
Risk Ratio (95% CI)	-	1.10 (0.95 to 1.27)	-	1.01 (0.85 to 1.19)
Reversed Risk ratio (95% CI)	-	0.91 (0.78 to 1.06)	-	0.99 (0.84 to 1.17)
p-value for Risk Ratio		0.220		0.925
p-value for heterogeneity of Risk Ratio				0.457
Risk Difference (95% CI)	-	7.76 (-4.41 to 19.93)	-	0.63 (-12.63 to 13.90)

Odds Ratio and related p-value are estimated by Wald's method using the SAS LOGISTIC procedure.
Peto OR calculation is based on Yusuf S et al. (Prog Cardiovasc Dis. 1985 Mar-Apr;27(5):335-71) and its p-value is derived using a normal approximation.
Risk Ratio and related p-value are estimated by using the SAS FREQ procedure.
Risk Difference and related p-value are estimated by using the SAS GLIMMIX procedure with the following model: criterion = treatment.
p-values for heterogeneity are estimated by using the SAS GLIMMIX procedure with the following model: criterion = treatment subgroup treatment*subgroup.
p-value for heterogeneity of Peto Odds Ratio is estimated by using normal approximation.
PGM=DEVOPS/SAR231893/EFC14153/CSR_RWE/REPORT/PGM/ae_evt_ger_subg_s2_t.sas OUT=REPORT/OUTPUT/ae_teae_ger_pfev1_s2_t_x.rtf (29JUL2021 - 14:41)

Project Code / Study Number / Analysis: SAR231893 / EFC14153 / CSR_RWE

2 Adverse events - Safety type 2 inflammatory asthma phenotype population

2.1 Patients with any TEAE

2.1.6 By baseline predicted FEV1 (<80%, >=80%)

	Baseline Predicted FEV1			
	<80%		>=80%	
Safety type 2 inflammatory asthma phenotype population	**Placebo (N=58)**	**Dupilumab (N=116)**	**Placebo (N=55)**	**Dupilumab (N=118)**
p-value for Risk Difference		0.210		0.925
p-value for heterogeneity of Risk Difference				0.435

Odds Ratio and related p-value are estimated by Wald's method using the SAS LOGISTIC procedure.
Peto OR calculation is based on Yusuf S et al. (Prog Cardiovasc Dis. 1985 Mar-Apr;27(5):335-71) and its p-value is derived using a normal approximation.
Risk Ratio and related p-value are estimated by using the SAS FREQ procedure.
Risk Difference and related p-value are estimated by using the SAS GLIMMIX procedure with the following model: criterion = treatment.
p-values for heterogeneity are estimated by using the SAS GLIMMIX procedure with the following model: criterion = treatment subgroup treatment*subgroup.
p-value for heterogeneity of Peto Odds Ratio is estimated by using normal approximation.
PGM=DEVOPS/SAR231893/EFC14153/CSR_RWE/REPORT/PGM/ae_evt_ger_subg_s2_t.sas OUT=REPORT/OUTPUT/ae_teae_ger_pfev1_s2_t_x.rtf (29JUL2021 - 14:41)

Project Code / Study Number / Analysis: SAR231893 / EFC14153 / CSR_RWE

2 Adverse events - Safety type 2 inflammatory asthma phenotype population

2.1 Patients with any TEAE

2.1.7 By baseline ACQ-7-IA (<=2, >2)

	Baseline ACQ-7-IA			
	<=2		>2	
Safety type 2 inflammatory asthma phenotype population	**Placebo (N=61)**	**Dupilumab (N=125)**	**Placebo (N=52)**	**Dupilumab (N=109)**
Patients with any TEAE [n(%)]	48 (78.7%)	103 (82.4%)	41 (78.8%)	91 (83.5%)
Odds Ratio (95% CI)	-	1.27 (0.59 to 2.73)	-	1.36 (0.59 to 3.13)
p-value for Odds Ratio		0.544		0.475
p-value for heterogeneity of Odds Ratio				0.907
Risk Ratio (95% CI)	-	1.05 (0.90 to 1.22)	-	1.06 (0.90 to 1.25)
Reversed Risk ratio (95% CI)	-	0.95 (0.82 to 1.11)	-	0.94 (0.80 to 1.11)
p-value for Risk Ratio		0.557		0.494
p-value for heterogeneity of Risk Ratio				0.923
Risk Difference (95% CI)	-	3.71 (-8.62 to 16.05)	-	4.64 (-8.57 to 17.85)

Odds Ratio and related p-value are estimated by Wald's method using the SAS LOGISTIC procedure.
Peto OR calculation is based on Yusuf S et al. (Prog Cardiovasc Dis. 1985 Mar-Apr;27(5):335-71) and its p-value is derived using a normal approximation.
Risk Ratio and related p-value are estimated by using the SAS FREQ procedure.
Risk Difference and related p-value are estimated by using the SAS GLIMMIX procedure with the following model: criterion = treatment.
p-values for heterogeneity are estimated by using the SAS GLIMMIX procedure with the following model: criterion = treatment subgroup treatment*subgroup.
p-value for heterogeneity of Peto Odds Ratio is estimated by using normal approximation.
PGM=DEVOPS/SAR231893/EFC14153/CSR_RWE/REPORT/PGM/ae_evt_ger_subg_s2_t.sas OUT=REPORT/OUTPUT/ae_teae_ger_acq7_s2_t_x.rtf (29JUL2021 - 14:42)

Project Code / Study Number / Analysis: SAR231893 / EFC14153 / CSR_RWE

2 Adverse events - Safety type 2 inflammatory asthma phenotype population

2.1 Patients with any TEAE

2.1.7 By baseline ACQ-7-IA (<=2, >2)

	Baseline ACQ-7-IA			
	<=2		>2	
Safety type 2 inflammatory asthma phenotype population	**Placebo (N=61)**	**Dupilumab (N=125)**	**Placebo (N=52)**	**Dupilumab (N=109)**
p-value for Risk Difference		0.554		0.489
p-value for heterogeneity of Risk Difference				0.919

Odds Ratio and related p-value are estimated by Wald's method using the SAS LOGISTIC procedure.
Peto OR calculation is based on Yusuf S et al. (Prog Cardiovasc Dis. 1985 Mar-Apr;27(5):335-71) and its p-value is derived using a normal approximation.
Risk Ratio and related p-value are estimated by using the SAS FREQ procedure.
Risk Difference and related p-value are estimated by using the SAS GLIMMIX procedure with the following model: criterion = treatment.
p-values for heterogeneity are estimated by using the SAS GLIMMIX procedure with the following model: criterion = treatment subgroup treatment*subgroup.
p-value for heterogeneity of Peto Odds Ratio is estimated by using normal approximation.
PGM=DEVOPS/SAR231893/EFC14153/CSR_RWE/REPORT/PGM/ae_evt_ger_subg_s2_t.sas OUT=REPORT/OUTPUT/ae_teae_ger_acq7_s2_t_x.rtf (29JUL2021 - 14:42)

Project Code / Study Number / Analysis: SAR231893 / EFC14153 / CSR_RWE

2 Adverse events - Safety type 2 inflammatory asthma phenotype population

2.1 Patients with any TEAE

2.1.8 By baseline weight (<=30 kg, >30 kg)

	Baseline weight (kg)			
	<=30		>30	
Safety type 2 inflammatory asthma phenotype population	**Placebo (N=36)**	**Dupilumab (N=74)**	**Placebo (N=77)**	**Dupilumab (N=160)**
Patients with any TEAE [n(%)]	30 (83.3%)	58 (78.4%)	59 (76.6%)	136 (85.0%)
Odds Ratio (95% CI)	-	0.73 (0.26 to 2.04)	-	1.73 (0.87 to 3.42)
p-value for Odds Ratio		0.543		0.116
p-value for heterogeneity of Odds Ratio				0.171
Risk Ratio (95% CI)	-	0.94 (0.78 to 1.14)	-	1.11 (0.96 to 1.28)
Reversed Risk ratio (95% CI)			-	0.90 (0.78 to 1.04)
p-value for Risk Ratio		0.525		0.145
p-value for heterogeneity of Risk Ratio				0.169
Risk Difference (95% CI)	-	-4.95 (-20.50 to 10.59)	-	8.38 (-2.63 to 19.39)

Odds Ratio and related p-value are estimated by Wald's method using the SAS LOGISTIC procedure.
Peto OR calculation is based on Yusuf S et al. (Prog Cardiovasc Dis. 1985 Mar-Apr;27(5):335-71) and its p-value is derived using a normal approximation.
Risk Ratio and related p-value are estimated by using the SAS FREQ procedure.
Risk Difference and related p-value are estimated by using the SAS GLIMMIX procedure with the following model: criterion = treatment.
p-values for heterogeneity are estimated by using the SAS GLIMMIX procedure with the following model: criterion = treatment subgroup treatment*subgroup.
p-value for heterogeneity of Peto Odds Ratio is estimated by using normal approximation.
PGM=DEVOPS/SAR231893/EFC14153/CSR_RWE/REPORT/PGM/ae_evt_ger_subg_s2_t.sas OUT=REPORT/OUTPUT/ae_teae_ger_wgt_s2_t_x.rtf (29JUL2021 - 14:42)

Project Code / Study Number / Analysis: SAR231893 / EFC14153 / CSR_RWE

2 Adverse events - Safety type 2 inflammatory asthma phenotype population

2.1 Patients with any TEAE

2.1.8 By baseline weight (<=30 kg, >30 kg)

	Baseline weight (kg)			
	<=30		>30	
Safety type 2 inflammatory asthma phenotype population	**Placebo (N=36)**	**Dupilumab (N=74)**	**Placebo (N=77)**	**Dupilumab (N=160)**
p-value for Risk Difference		0.529		0.135
p-value for heterogeneity of Risk Difference				0.167

Odds Ratio and related p-value are estimated by Wald's method using the SAS LOGISTIC procedure.
Peto OR calculation is based on Yusuf S et al. (Prog Cardiovasc Dis. 1985 Mar-Apr;27(5):335-71) and its p-value is derived using a normal approximation.
Risk Ratio and related p-value are estimated by using the SAS FREQ procedure.
Risk Difference and related p-value are estimated by using the SAS GLIMMIX procedure with the following model: criterion = treatment.
p-values for heterogeneity are estimated by using the SAS GLIMMIX procedure with the following model: criterion = treatment subgroup treatment*subgroup.
p-value for heterogeneity of Peto Odds Ratio is estimated by using normal approximation.
PGM=DEVOPS/SAR231893/EFC14153/CSR_RWE/REPORT/PGM/ae_evt_ger_subg_s2_t.sas OUT=REPORT/OUTPUT/ae_teae_ger_wgt_s2_t_x.rtf (29JUL2021 - 14:42)

Project Code / Study Number / Analysis: SAR231893 / EFC14153 / CSR_RWE

2 Adverse events - Safety type 2 inflammatory asthma phenotype population

2.1 Patients with any TEAE

2.1.9 By atopic medical condition (Yes, No)

	Atopic medical condition			
	Yes		No	
Safety type 2 inflammatory asthma phenotype population	**Placebo (N=102)**	**Dupilumab (N=225)**	**Placebo (N=11)**	**Dupilumab (N=9)**
Patients with any TEAE [n(%)]	82 (80.4%)	187 (83.1%)	7 (63.6%)	7 (77.8%)
Odds Ratio (95% CI)	-	1.20 (0.66 to 2.19)	-	2.00 (0.27 to 14.70)
p-value for Odds Ratio		0.551		0.496
p-value for heterogeneity of Odds Ratio				0.631
Risk Ratio (95% CI)	-	1.03 (0.92 to 1.16)	-	1.22 (0.69 to 2.15)
Reversed Risk ratio (95% CI)	-	0.97 (0.86 to 1.08)	-	0.82 (0.46 to 1.44)
p-value for Risk Ratio		0.562		0.488
p-value for heterogeneity of Risk Ratio				0.571
Risk Difference (95% CI)	-	2.72 (-6.44 to 11.88)	-	14.14 (-28.00 to 56.29)

Odds Ratio and related p-value are estimated by Wald's method using the SAS LOGISTIC procedure.
Peto OR calculation is based on Yusuf S et al. (Prog Cardiovasc Dis. 1985 Mar-Apr;27(5):335-71) and its p-value is derived using a normal approximation.
Risk Ratio and related p-value are estimated by using the SAS FREQ procedure.
Risk Difference and related p-value are estimated by using the SAS GLIMMIX procedure with the following model: criterion = treatment.
p-values for heterogeneity are estimated by using the SAS GLIMMIX procedure with the following model: criterion = treatment subgroup treatment*subgroup.
p-value for heterogeneity of Peto Odds Ratio is estimated by using normal approximation.
PGM=DEVOPS/SAR231893/EFC14153/CSR_RWE/REPORT/PGM/ae_evt_ger_subg_s2_t.sas OUT=REPORT/OUTPUT/ae_teae_ger_amc_s2_t_x.rtf (29JUL2021 - 14:42)

Project Code / Study Number / Analysis: SAR231893 / EFC14153 / CSR_RWE

2 Adverse events - Safety type 2 inflammatory asthma phenotype population

2.1 Patients with any TEAE

2.1.9 By atopic medical condition (Yes, No)

	Atopic medical condition			
	Yes		No	
Safety type 2 inflammatory asthma phenotype population	**Placebo (N=102)**	**Dupilumab (N=225)**	**Placebo (N=11)**	**Dupilumab (N=9)**
p-value for Risk Difference		0.560		0.490
p-value for heterogeneity of Risk Difference				0.579

Odds Ratio and related p-value are estimated by Wald's method using the SAS LOGISTIC procedure.
Peto OR calculation is based on Yusuf S et al. (Prog Cardiovasc Dis. 1985 Mar-Apr;27(5):335-71) and its p-value is derived using a normal approximation.
Risk Ratio and related p-value are estimated by using the SAS FREQ procedure.
Risk Difference and related p-value are estimated by using the SAS GLIMMIX procedure with the following model: criterion = treatment.
p-values for heterogeneity are estimated by using the SAS GLIMMIX procedure with the following model: criterion = treatment subgroup treatment*subgroup.
p-value for heterogeneity of Peto Odds Ratio is estimated by using normal approximation.
PGM=DEVOPS/SAR231893/EFC14153/CSR_RWE/REPORT/PGM/ae_evt_ger_subg_s2_t.sas OUT=REPORT/OUTPUT/ae_teae_ger_amc_s2_t_x.rtf (29JUL2021 - 14:42)

Project Code / Study Number / Analysis: SAR231893 / EFC14153 / CSR_RWE

2 Adverse events - Safety type 2 inflammatory asthma phenotype population

2.1 Patients with any TEAE

2.1.10 By baseline total IgE (<median, >= median)

	Baseline Total IgE (IU/mL)			
	<median		>=median	
Safety type 2 inflammatory asthma phenotype population	**Placebo (N=65)**	**Dupilumab (N=106)**	**Placebo (N=47)**	**Dupilumab (N=124)**
Patients with any TEAE [n(%)]	49 (75.4%)	85 (80.2%)	39 (83.0%)	105 (84.7%)
Odds Ratio (95% CI)	-	1.32 (0.63 to 2.77)	-	1.13 (0.46 to 2.80)
p-value for Odds Ratio		0.460		0.786
p-value for heterogeneity of Odds Ratio				0.797
Risk Ratio (95% CI)	-	1.06 (0.90 to 1.26)	-	1.02 (0.88 to 1.19)
Reversed Risk ratio (95% CI)	-	0.94 (0.79 to 1.11)	-	0.98 (0.84 to 1.14)
p-value for Risk Ratio		0.471		0.791
p-value for heterogeneity of Risk Ratio				0.718
Risk Difference (95% CI)	-	4.80 (-8.22 to 17.83)	-	1.70 (-10.87 to 14.26)

Odds Ratio and related p-value are estimated by Wald's method using the SAS LOGISTIC procedure.
Peto OR calculation is based on Yusuf S et al. (Prog Cardiovasc Dis. 1985 Mar-Apr;27(5):335-71) and its p-value is derived using a normal approximation.
Risk Ratio and related p-value are estimated by using the SAS FREQ procedure.
Risk Difference and related p-value are estimated by using the SAS GLIMMIX procedure with the following model: criterion = treatment.
p-values for heterogeneity are estimated by using the SAS GLIMMIX procedure with the following model: criterion = treatment subgroup treatment*subgroup.
p-value for heterogeneity of Peto Odds Ratio is estimated by using normal approximation.
PGM=DEVOPS/SAR231893/EFC14153/CSR_RWE/REPORT/PGM/ae_evt_ger_subg_s2_t.sas OUT=REPORT/OUTPUT/ae_teae_ger_igem_s2_t_x.rtf (29JUL2021 - 14:42)

Project Code / Study Number / Analysis: SAR231893 / EFC14153 / CSR_RWE

2 Adverse events - Safety type 2 inflammatory asthma phenotype population

2.1 Patients with any TEAE

2.1.10 By baseline total IgE (<median, >= median)

	Baseline Total IgE (IU/mL)			
	<median		>=median	
Safety type 2 inflammatory asthma phenotype population	**Placebo (N=65)**	**Dupilumab (N=106)**	**Placebo (N=47)**	**Dupilumab (N=124)**
p-value for Risk Difference		0.468		0.790
p-value for heterogeneity of Risk Difference				0.735

Odds Ratio and related p-value are estimated by Wald's method using the SAS LOGISTIC procedure.
Peto OR calculation is based on Yusuf S et al. (Prog Cardiovasc Dis. 1985 Mar-Apr;27(5):335-71) and its p-value is derived using a normal approximation.
Risk Ratio and related p-value are estimated by using the SAS FREQ procedure.
Risk Difference and related p-value are estimated by using the SAS GLIMMIX procedure with the following model: criterion = treatment.
p-values for heterogeneity are estimated by using the SAS GLIMMIX procedure with the following model: criterion = treatment subgroup treatment*subgroup.
p-value for heterogeneity of Peto Odds Ratio is estimated by using normal approximation.
PGM=DEVOPS/SAR231893/EFC14153/CSR_RWE/REPORT/PGM/ae_evt_ger_subg_s2_t.sas OUT=REPORT/OUTPUT/ae_teae_ger_igem_s2_t_x.rtf (29JUL2021 - 14:42)

Project Code / Study Number / Analysis: SAR231893 / EFC14153 / CSR_RWE

2 Adverse events - Safety type 2 inflammatory asthma phenotype population

2.1 Patients with any TEAE

2.1.11 By baseline total IgE (<100 IU/ml, >= 100 IU/ml)

	Baseline Total IgE (IU/mL)			
	< 100		>= 100	
Safety type 2 inflammatory asthma phenotype population	**Placebo (N=22)**	**Dupilumab (N=29)**	**Placebo (N=90)**	**Dupilumab (N=201)**
Patients with any TEAE [n(%)]	15 (68.2%)	24 (82.8%)	73 (81.1%)	166 (82.6%)
Odds Ratio (95% CI)	-	2.24 (0.60 to 8.36)	-	1.10 (0.58 to 2.10)
p-value for Odds Ratio		0.230		0.761
p-value for heterogeneity of Odds Ratio				0.345
Risk Ratio (95% CI)	-	1.21 (0.87 to 1.69)	-	1.02 (0.90 to 1.15)
Reversed Risk ratio (95% CI)	-	0.82 (0.59 to 1.15)	-	0.98 (0.87 to 1.11)
p-value for Risk Ratio		0.250		0.765
p-value for heterogeneity of Risk Ratio				0.327
Risk Difference (95% CI)	-	14.58 (-9.86 to 39.01)	-	1.48 (-8.20 to 11.15)

Odds Ratio and related p-value are estimated by Wald's method using the SAS LOGISTIC procedure.
Peto OR calculation is based on Yusuf S et al. (Prog Cardiovasc Dis. 1985 Mar-Apr;27(5):335-71) and its p-value is derived using a normal approximation.
Risk Ratio and related p-value are estimated by using the SAS FREQ procedure.
Risk Difference and related p-value are estimated by using the SAS GLIMMIX procedure with the following model: criterion = treatment.
p-values for heterogeneity are estimated by using the SAS GLIMMIX procedure with the following model: criterion = treatment subgroup treatment*subgroup.
p-value for heterogeneity of Peto Odds Ratio is estimated by using normal approximation.
PGM=DEVOPS/SAR231893/EFC14153/CSR_RWE/REPORT/PGM/ae_evt_ger_subg_s2_t.sas OUT=REPORT/OUTPUT/ae_teae_ger_ige_s2_t_x.rtf (29JUL2021 - 14:43)

Project Code / Study Number / Analysis: SAR231893 / EFC14153 / CSR_RWE

2 Adverse events - Safety type 2 inflammatory asthma phenotype population

2.1 Patients with any TEAE

2.1.11 By baseline total IgE (<100 IU/ml, >= 100 IU/ml)

	Baseline Total IgE (IU/mL)			
	< 100		>= 100	
Safety type 2 inflammatory asthma phenotype population	**Placebo (N=22)**	**Dupilumab (N=29)**	**Placebo (N=90)**	**Dupilumab (N=201)**
p-value for Risk Difference		0.236		0.764
p-value for heterogeneity of Risk Difference				0.319

Odds Ratio and related p-value are estimated by Wald's method using the SAS LOGISTIC procedure.
Peto OR calculation is based on Yusuf S et al. (Prog Cardiovasc Dis. 1985 Mar-Apr;27(5):335-71) and its p-value is derived using a normal approximation.
Risk Ratio and related p-value are estimated by using the SAS FREQ procedure.
Risk Difference and related p-value are estimated by using the SAS GLIMMIX procedure with the following model: criterion = treatment.
p-values for heterogeneity are estimated by using the SAS GLIMMIX procedure with the following model: criterion = treatment subgroup treatment*subgroup.
p-value for heterogeneity of Peto Odds Ratio is estimated by using normal approximation.
PGM=DEVOPS/SAR231893/EFC14153/CSR_RWE/REPORT/PGM/ae_evt_ger_subg_s2_t.sas OUT=REPORT/OUTPUT/ae_teae_ger_ige_s2_t_x.rtf (29JUL2021 - 14:43)

Project Code / Study Number / Analysis: SAR231893 / EFC14153 / CSR_RWE

2 Adverse events - Safety type 2 inflammatory asthma phenotype population

2.1 Patients with any TEAE

2.1.12 By age at onset of asthma (0-2, 3-5, >=6 years)

	Age of onset of asthma (years)					
	0-2		3-5		>= 6	
Safety type 2 inflammatory asthma phenotype population	**Placebo (N=40)**	**Dupilumab (N=104)**	**Placebo (N=38)**	**Dupilumab (N=85)**	**Placebo (N=35)**	**Dupilumab (N=45)**
Patients with any TEAE [n(%)]	33 (82.5%)	90 (86.5%)	33 (86.8%)	70 (82.4%)	23 (65.7%)	34 (75.6%)
Odds Ratio (95% CI)	-	1.36 (0.51 to 3.67)	-	0.71 (0.24 to 2.11)	-	1.61 (0.61 to 4.27)
p-value for Odds Ratio		0.540		0.535		0.336
p-value for heterogeneity of Odds Ratio:						
0-2, 3-5						0.384
0-2, >= 6						0.813
3-5, >= 6						0.271
overall						0.518
Risk Ratio (95% CI)	-	1.05 (0.89 to 1.23)	-	0.95 (0.81 to 1.11)	-	1.15 (0.86 to 1.54)
Reversed Risk ratio (95% CI)	-	0.95 (0.81 to 1.12)			-	0.87 (0.65 to 1.16)

Odds Ratio and related p-value are estimated by Wald's method using the SAS LOGISTIC procedure.
Peto OR calculation is based on Yusuf S et al. (Prog Cardiovasc Dis. 1985 Mar-Apr;27(5):335-71) and its p-value is derived using a normal approximation.
Risk Ratio and related p-value are estimated by using the SAS FREQ procedure.
Risk Difference and related p-value are estimated by using the SAS GLIMMIX procedure with the following model: criterion = treatment.
p-values for heterogeneity are estimated by using the SAS GLIMMIX procedure with the following model: criterion = treatment subgroup treatment*subgroup.
p-value for heterogeneity of Peto Odds Ratio is estimated by using normal approximation.
PGM=DEVOPS/SAR231893/EFC14153/CSR_RWE/REPORT/PGM/ae_evt_ger_subg_s2_t.sas OUT=REPORT/OUTPUT/ae_teae_ger_onsa_s2_t_x.rtf (10AUG2021 - 8:06)

Project Code / Study Number / Analysis: SAR231893 / EFC14153 / CSR_RWE

2 Adverse events - Safety type 2 inflammatory asthma phenotype population

2.1 Patients with any TEAE

2.1.12 By age at onset of asthma (0-2, 3-5, >=6 years)

	Age of onset of asthma (years)					
	0-2		3-5		>= 6	
Safety type 2 inflammatory asthma phenotype population	**Placebo (N=40)**	**Dupilumab (N=104)**	**Placebo (N=38)**	**Dupilumab (N=85)**	**Placebo (N=35)**	**Dupilumab (N=45)**
p-value for Risk Ratio		0.562		0.511		0.348
p-value for heterogeneity of Risk Ratio:						
0-2, 3-5						0.383
0-2, >= 6						0.590
3-5, >= 6						0.256
overall						0.456
Risk Difference (95% CI)	-	4.04 (-9.56 to 17.63)	-	-4.49 (-18.09 to 9.11)	-	9.84 (-10.60 to 30.28)
p-value for Risk Difference		0.558		0.515		0.341
p-value for heterogeneity of Risk Difference:						
0-2, 3-5						0.381
0-2, >= 6						0.639

Odds Ratio and related p-value are estimated by Wald's method using the SAS LOGISTIC procedure.
Peto OR calculation is based on Yusuf S et al. (Prog Cardiovasc Dis. 1985 Mar-Apr;27(5):335-71) and its p-value is derived using a normal approximation.
Risk Ratio and related p-value are estimated by using the SAS FREQ procedure.
Risk Difference and related p-value are estimated by using the SAS GLIMMIX procedure with the following model: criterion = treatment.
p-values for heterogeneity are estimated by using the SAS GLIMMIX procedure with the following model: criterion = treatment subgroup treatment*subgroup.
p-value for heterogeneity of Peto Odds Ratio is estimated by using normal approximation.
PGM=DEVOPS/SAR231893/EFC14153/CSR_RWE/REPORT/PGM/ae_evt_ger_subg_s2_t.sas OUT=REPORT/OUTPUT/ae_teae_ger_onsa_s2_t_x.rtf (10AUG2021 - 8:06)

Project Code / Study Number / Analysis: SAR231893 / EFC14153 / CSR_RWE

2 Adverse events - Safety type 2 inflammatory asthma phenotype population

2.1 Patients with any TEAE

2.1.12 By age at onset of asthma (0-2, 3-5, >=6 years)

	Age of onset of asthma (years)					
	0-2		3-5		>= 6	
Safety type 2 inflammatory asthma phenotype population	**Placebo (N=40)**	**Dupilumab (N=104)**	**Placebo (N=38)**	**Dupilumab (N=85)**	**Placebo (N=35)**	**Dupilumab (N=45)**
3-5, >= 6						0.247
overall						0.460

Odds Ratio and related p-value are estimated by Wald's method using the SAS LOGISTIC procedure.
Peto OR calculation is based on Yusuf S et al. (Prog Cardiovasc Dis. 1985 Mar-Apr;27(5):335-71) and its p-value is derived using a normal approximation.
Risk Ratio and related p-value are estimated by using the SAS FREQ procedure.
Risk Difference and related p-value are estimated by using the SAS GLIMMIX procedure with the following model: criterion = treatment.
p-values for heterogeneity are estimated by using the SAS GLIMMIX procedure with the following model: criterion = treatment subgroup treatment*subgroup.
p-value for heterogeneity of Peto Odds Ratio is estimated by using normal approximation.
PGM=DEVOPS/SAR231893/EFC14153/CSR_RWE/REPORT/PGM/ae_evt_ger_subg_s2_t.sas OUT=REPORT/OUTPUT/ae_teae_ger_onsa_s2_t_x.rtf (10AUG2021 - 8:06)

Project Code / Study Number / Analysis: SAR231893 / EFC14153 / CSR_RWE

2 Adverse events - Safety type 2 inflammatory asthma phenotype population

2.1 Patients with any TEAE

2.1.13 By number of severe asthma exacerbation prior to the study (<=1, 2, >2)

	Number of severe asthma exacerbation prior to the study					
	<=1		2		>2	
Safety type 2 inflammatory asthma phenotype population	**Placebo (N=46)**	**Dupilumab (N=85)**	**Placebo (N=32)**	**Dupilumab (N=75)**	**Placebo (N=35)**	**Dupilumab (N=74)**
Patients with any TEAE [n(%)]	37 (80.4%)	72 (84.7%)	22 (68.8%)	57 (76.0%)	30 (85.7%)	65 (87.8%)
Odds Ratio (95% CI)	-	1.35 (0.53 to 3.44)	-	1.44 (0.58 to 3.60)	-	1.20 (0.37 to 3.90)
p-value for Odds Ratio		0.533		0.436		0.757
p-value for heterogeneity of Odds Ratio:						
<=1, 2						0.921
<=1, >2						0.883
2, >2						0.814
overall						0.973
Risk Ratio (95% CI)	-	1.05 (0.89 to 1.25)	-	1.11 (0.85 to 1.44)	-	1.02 (0.87 to 1.20)
Reversed Risk ratio (95% CI)	-	0.95 (0.80 to 1.12)	-	0.90 (0.69 to 1.18)	-	0.98 (0.83 to 1.14)

Odds Ratio and related p-value are estimated by Wald's method using the SAS LOGISTIC procedure.
Peto OR calculation is based on Yusuf S et al. (Prog Cardiovasc Dis. 1985 Mar-Apr;27(5):335-71) and its p-value is derived using a normal approximation.
Risk Ratio and related p-value are estimated by using the SAS FREQ procedure.
Risk Difference and related p-value are estimated by using the SAS GLIMMIX procedure with the following model: criterion = treatment.
p-values for heterogeneity are estimated by using the SAS GLIMMIX procedure with the following model: criterion = treatment subgroup treatment*subgroup.
p-value for heterogeneity of Peto Odds Ratio is estimated by using normal approximation.
PGM=DEVOPS/SAR231893/EFC14153/CSR_RWE/REPORT/PGM/ae_evt_ger_subg_s2_t.sas OUT=REPORT/OUTPUT/ae_teae_ger_exa_s2_t_x.rtf (29JUL2021 - 14:43)

Project Code / Study Number / Analysis: SAR231893 / EFC14153 / CSR_RWE

2 Adverse events - Safety type 2 inflammatory asthma phenotype population

2.1 Patients with any TEAE

2.1.13 By number of severe asthma exacerbation prior to the study (<=1, 2, >2)

	Number of severe asthma exacerbation prior to the study					
	<=1		2		>2	
Safety type 2 inflammatory asthma phenotype population	**Placebo (N=46)**	**Dupilumab (N=85)**	**Placebo (N=32)**	**Dupilumab (N=75)**	**Placebo (N=35)**	**Dupilumab (N=74)**
p-value for Risk Ratio		0.548		0.460		0.764
p-value for heterogeneity of Risk Ratio:						
<=1, 2						0.763
<=1, >2						0.818
2, >2						0.632
overall						0.890
Risk Difference (95% CI)	-	4.27 (-9.64 to 18.18)	-	7.25 (-11.71 to 26.21)	-	2.12 (-11.81 to 16.06)
p-value for Risk Difference		0.545		0.450		0.763
p-value for heterogeneity of Risk Difference:						
<=1, 2						0.802
<=1, >2						0.829

Odds Ratio and related p-value are estimated by Wald's method using the SAS LOGISTIC procedure.
Peto OR calculation is based on Yusuf S et al. (Prog Cardiovasc Dis. 1985 Mar-Apr;27(5):335-71) and its p-value is derived using a normal approximation.
Risk Ratio and related p-value are estimated by using the SAS FREQ procedure.
Risk Difference and related p-value are estimated by using the SAS GLIMMIX procedure with the following model: criterion = treatment.
p-values for heterogeneity are estimated by using the SAS GLIMMIX procedure with the following model: criterion = treatment subgroup treatment*subgroup.
p-value for heterogeneity of Peto Odds Ratio is estimated by using normal approximation.
PGM=DEVOPS/SAR231893/EFC14153/CSR_RWE/REPORT/PGM/ae_evt_ger_subg_s2_t.sas OUT=REPORT/OUTPUT/ae_teae_ger_exa_s2_t_x.rtf (29JUL2021 - 14:43)

Project Code / Study Number / Analysis: SAR231893 / EFC14153 / CSR_RWE

2 Adverse events - Safety type 2 inflammatory asthma phenotype population

2.1 Patients with any TEAE

2.1.13 By number of severe asthma exacerbation prior to the study (<=1, 2, >2)

	Number of severe asthma exacerbation prior to the study					
	<=1		2		>2	
Safety type 2 inflammatory asthma phenotype population	**Placebo (N=46)**	**Dupilumab (N=85)**	**Placebo (N=32)**	**Dupilumab (N=75)**	**Placebo (N=35)**	**Dupilumab (N=74)**
2, >2						0.666
overall						0.910

Odds Ratio and related p-value are estimated by Wald's method using the SAS LOGISTIC procedure.
Peto OR calculation is based on Yusuf S et al. (Prog Cardiovasc Dis. 1985 Mar-Apr;27(5):335-71) and its p-value is derived using a normal approximation.
Risk Ratio and related p-value are estimated by using the SAS FREQ procedure.
Risk Difference and related p-value are estimated by using the SAS GLIMMIX procedure with the following model: criterion = treatment.
p-values for heterogeneity are estimated by using the SAS GLIMMIX procedure with the following model: criterion = treatment subgroup treatment*subgroup.
p-value for heterogeneity of Peto Odds Ratio is estimated by using normal approximation.
PGM=DEVOPS/SAR231893/EFC14153/CSR_RWE/REPORT/PGM/ae_evt_ger_subg_s2_t.sas OUT=REPORT/OUTPUT/ae_teae_ger_exa_s2_t_x.rtf (29JUL2021 - 14:43)

Project Code / Study Number / Analysis: SAR231893 / EFC14153 / CSR_RWE

2 Adverse events - Safety type 2 inflammatory asthma phenotype population

2.2 Patients with any TEAE not severe

Safety type 2 inflammatory asthma phenotype population	Placebo (N=113)	Dupilumab (N=234)
Patients with any TEAE not severe [n(%)]	89 (78.8%)	192 (82.1%)
Odds Ratio (95% CI)	-	1.23 (0.70 to 2.16)
p-value for Odds Ratio		0.465
Risk Ratio (95% CI)	-	1.04 (0.93 to 1.17)
Reversed Risk Ratio (95% CI)	-	0.96 (0.86 to 1.07)
p-value for Risk Ratio		0.478
Risk Difference (95% CI)	-	3.29 (-5.74 to 12.32)
p-value for Risk Difference		0.474

Odds Ratio and related p-value are estimated by Wald's method using the SAS LOGISTIC procedure.
Peto OR calculation is based on Yusuf S et al. (Prog Cardiovasc Dis. 1985 Mar-Apr;27(5):335-71) and its p-value is derived using a normal approximation.
Risk Ratio and related p-value are estimated by using the SAS FREQ procedure.
Risk Difference and related p-value are estimated by using the SAS GLIMMIX procedure with the following model: criterion = treatment.
PGM=DEVOPS/SAR231893/EFC14153/CSR_RWE/REPORT/PGM/ae_evt_ger_s2_t.sas OUT=REPORT/OUTPUT/ae_teaensev_ger_s2_t_x.rtf (12AUG2021 - 9:08)

Project Code / Study Number / Analysis: SAR231893 / EFC14153 / CSR_RWE

2 Adverse events - Safety type 2 inflammatory asthma phenotype population

2.2 Patients with any TEAE not severe

2.2.1 By gender (Male, Female)

	Gender			
	Male		Female	
Safety type 2 inflammatory asthma phenotype population	**Placebo (N=77)**	**Dupilumab (N=153)**	**Placebo (N=36)**	**Dupilumab (N=81)**
Patients with any TEAE not severe [n(%)]	62 (80.5%)	121 (79.1%)	27 (75.0%)	71 (87.7%)
Odds Ratio (95% CI)	-	0.91 (0.46 to 1.82)	-	2.37 (0.87 to 6.46)
p-value for Odds Ratio		0.799		0.093
p-value for heterogeneity of Odds Ratio				0.126
Risk Ratio (95% CI)	-	0.98 (0.86 to 1.13)	-	1.17 (0.95 to 1.44)
Reversed Risk ratio (95% CI)			-	0.86 (0.70 to 1.05)
p-value for Risk Ratio		0.797		0.137
p-value for heterogeneity of Risk Ratio				0.168
Risk Difference (95% CI)	-	-1.43 (-12.44 to 9.57)	-	12.65 (-3.37 to 28.68)

Odds Ratio and related p-value are estimated by Wald's method using the SAS LOGISTIC procedure.
Peto OR calculation is based on Yusuf S et al. (Prog Cardiovasc Dis. 1985 Mar-Apr;27(5):335-71) and its p-value is derived using a normal approximation.
Risk Ratio and related p-value are estimated by using the SAS FREQ procedure.
Risk Difference and related p-value are estimated by using the SAS GLIMMIX procedure with the following model: criterion = treatment.
p-values for heterogeneity are estimated by using the SAS GLIMMIX procedure with the following model: criterion = treatment subgroup treatment*subgroup.
p-value for heterogeneity of Peto Odds Ratio is estimated by using normal approximation.
PGM=DEVOPS/SAR231893/EFC14153/CSR_RWE/REPORT/PGM/ae_evt_ger_subg_s2_t.sas OUT=REPORT/OUTPUT/ae_teaensev_ger_sex_s2_t_x.rtf (12AUG2021 - 9:08)

Project Code / Study Number / Analysis: SAR231893 / EFC14153 / CSR_RWE

2 Adverse events - Safety type 2 inflammatory asthma phenotype population

2.2 Patients with any TEAE not severe

2.2.1 By gender (Male, Female)

	Gender			
	Male		Female	
Safety type 2 inflammatory asthma phenotype population	**Placebo (N=77)**	**Dupilumab (N=153)**	**Placebo (N=36)**	**Dupilumab (N=81)**
p-value for Risk Difference		0.797		0.121
p-value for heterogeneity of Risk Difference				0.153

Odds Ratio and related p-value are estimated by Wald's method using the SAS LOGISTIC procedure.
Peto OR calculation is based on Yusuf S et al. (Prog Cardiovasc Dis. 1985 Mar-Apr;27(5):335-71) and its p-value is derived using a normal approximation.
Risk Ratio and related p-value are estimated by using the SAS FREQ procedure.
Risk Difference and related p-value are estimated by using the SAS GLIMMIX procedure with the following model: criterion = treatment.
p-values for heterogeneity are estimated by using the SAS GLIMMIX procedure with the following model: criterion = treatment subgroup treatment*subgroup.
p-value for heterogeneity of Peto Odds Ratio is estimated by using normal approximation.
PGM=DEVOPS/SAR231893/EFC14153/CSR_RWE/REPORT/PGM/ae_evt_ger_subg_s2_t.sas OUT=REPORT/OUTPUT/ae_teaensev_ger_sex_s2_t_x.rtf (12AUG2021 - 9:08)

Project Code / Study Number / Analysis: SAR231893 / EFC14153 / CSR_RWE

2 Adverse events - Safety type 2 inflammatory asthma phenotype population

2.2 Patients with any TEAE not severe

2.2.2 By region (Latin America, East Europe, Western Countries)

	Region					
	Latin America		East Europe		Western countries	
Safety type 2 inflammatory asthma phenotype population	**Placebo (N=51)**	**Dupilumab (N=105)**	**Placebo (N=43)**	**Dupilumab (N=78)**	**Placebo (N=19)**	**Dupilumab (N=51)**
Patients with any TEAE not severe [n(%)]	40 (78.4%)	79 (75.2%)	31 (72.1%)	64 (82.1%)	18 (94.7%)	49 (96.1%)
Odds Ratio (95% CI)	-	0.84 (0.38 to 1.86)	-	1.77 (0.73 to 4.28)	-	1.36 (0.12 to 15.94)
p-value for Odds Ratio		0.660		0.205		0.806
p-value for heterogeneity of Odds Ratio:						
Latin America, East Europe						0.218
Latin America, Western countries						0.712
East Europe, Western countries						0.844
overall						0.465
Risk Ratio (95% CI)	-	0.96 (0.80 to 1.15)	-	1.14 (0.92 to 1.41)	-	1.01 (0.90 to 1.14)
Reversed Risk ratio (95% CI)			-	0.88 (0.71 to 1.09)	-	0.99 (0.87 to 1.11)

Odds Ratio and related p-value are estimated by Wald's method using the SAS LOGISTIC procedure.
Peto OR calculation is based on Yusuf S et al. (Prog Cardiovasc Dis. 1985 Mar-Apr;27(5):335-71) and its p-value is derived using a normal approximation.
Risk Ratio and related p-value are estimated by using the SAS FREQ procedure.
Risk Difference and related p-value are estimated by using the SAS GLIMMIX procedure with the following model: criterion = treatment.
p-values for heterogeneity are estimated by using the SAS GLIMMIX procedure with the following model: criterion = treatment subgroup treatment*subgroup.
p-value for heterogeneity of Peto Odds Ratio is estimated by using normal approximation.
PGM=DEVOPS/SAR231893/EFC14153/CSR_RWE/REPORT/PGM/ae_evt_ger_subg_s2_t.sas OUT=REPORT/OUTPUT/ae_teaensev_ger_cty_s2_t_x.rtf (12AUG2021 - 9:08)

Project Code / Study Number / Analysis: SAR231893 / EFC14153 / CSR_RWE

2 Adverse events - Safety type 2 inflammatory asthma phenotype population

2.2 Patients with any TEAE not severe

2.2.2 By region (Latin America, East Europe, Western Countries)

	Region					
	Latin America		East Europe		Western countries	
Safety type 2 inflammatory asthma phenotype population	**Placebo (N=51)**	**Dupilumab (N=105)**	**Placebo (N=43)**	**Dupilumab (N=78)**	**Placebo (N=19)**	**Dupilumab (N=51)**
p-value for Risk Ratio		0.653		0.234		0.818
p-value for heterogeneity of Risk Ratio:						
Latin America, East Europe						0.231
Latin America, Western countries						0.616
East Europe, Western countries						0.355
overall						0.481
Risk Difference (95% CI)	-	-3.19 (-17.29 to 10.90)	-	9.96 (-6.09 to 26.00)	-	1.34 (-10.23 to 12.91)
p-value for Risk Difference		0.655		0.222		0.818
p-value for heterogeneity of Risk Difference:						
Latin America, East Europe						0.224
Latin America, Western countries						0.622

Odds Ratio and related p-value are estimated by Wald's method using the SAS LOGISTIC procedure.
Peto OR calculation is based on Yusuf S et al. (Prog Cardiovasc Dis. 1985 Mar-Apr;27(5):335-71) and its p-value is derived using a normal approximation.
Risk Ratio and related p-value are estimated by using the SAS FREQ procedure.
Risk Difference and related p-value are estimated by using the SAS GLIMMIX procedure with the following model: criterion = treatment.
p-values for heterogeneity are estimated by using the SAS GLIMMIX procedure with the following model: criterion = treatment subgroup treatment*subgroup.
p-value for heterogeneity of Peto Odds Ratio is estimated by using normal approximation.
PGM=DEVOPS/SAR231893/EFC14153/CSR_RWE/REPORT/PGM/ae_evt_ger_subg_s2_t.sas OUT=REPORT/OUTPUT/ae_teaensev_ger_cty_s2_t_x.rtf (12AUG2021 - 9:08)

Project Code / Study Number / Analysis: SAR231893 / EFC14153 / CSR_RWE

2 Adverse events - Safety type 2 inflammatory asthma phenotype population

2.2 Patients with any TEAE not severe

2.2.2 By region (Latin America, East Europe, Western Countries)

	Region					
	Latin America		East Europe		Western countries	
Safety type 2 inflammatory asthma phenotype population	**Placebo (N=51)**	**Dupilumab (N=105)**	**Placebo (N=43)**	**Dupilumab (N=78)**	**Placebo (N=19)**	**Dupilumab (N=51)**
East Europe, Western countries						0.388
overall						0.471

Odds Ratio and related p-value are estimated by Wald's method using the SAS LOGISTIC procedure.
Peto OR calculation is based on Yusuf S et al. (Prog Cardiovasc Dis. 1985 Mar-Apr;27(5):335-71) and its p-value is derived using a normal approximation.
Risk Ratio and related p-value are estimated by using the SAS FREQ procedure.
Risk Difference and related p-value are estimated by using the SAS GLIMMIX procedure with the following model: criterion = treatment.
p-values for heterogeneity are estimated by using the SAS GLIMMIX procedure with the following model: criterion = treatment subgroup treatment*subgroup.
p-value for heterogeneity of Peto Odds Ratio is estimated by using normal approximation.
PGM=DEVOPS/SAR231893/EFC14153/CSR_RWE/REPORT/PGM/ae_evt_ger_subg_s2_t.sas OUT=REPORT/OUTPUT/ae_teaensev_ger_cty_s2_t_x.rtf (12AUG2021 - 9:08)

Project Code / Study Number / Analysis: SAR231893 / EFC14153 / CSR_RWE

2 Adverse events - Safety type 2 inflammatory asthma phenotype population

2.2 Patients with any TEAE not severe

2.2.3 By race (Caucasian/white, Black/of African descent, Other)

	Race					
	Caucasian/White		Black/of African descent		Other	
Safety type 2 inflammatory asthma phenotype population	**Placebo (N=101)**	**Dupilumab (N=207)**	**Placebo (N=5)**	**Dupilumab (N=9)**	**Placebo (N=7)**	**Dupilumab (N=18)**
Patients with any TEAE not severe [n(%)]	78 (77.2%)	167 (80.7%)	5 (100%)	8 (88.9%)	6 (85.7%)	17 (94.4%)
Odds Ratio (95% CI)	-	1.23 (0.69 to 2.20)	-	0.00 (NE to NE)	-	2.83 (0.15 to 52.74)
p-value for Odds Ratio		0.482		NE		0.485
p-value for heterogeneity of Odds Ratio:						
Caucasian/White, Black/of African descent						0.976
Caucasian/White, Other						0.584
Black/of African descent, Other						0.975
overall						0.860
Risk Ratio (95% CI)	-	1.04 (0.92 to 1.18)	-	0.89 (NE to NE)	-	1.10 (0.80 to 1.52)
Reversed Risk ratio (95% CI)	-	0.96 (0.84 to 1.08)			-	0.91 (0.66 to 1.25)

Odds Ratio and related p-value are estimated by Wald's method using the SAS LOGISTIC procedure.
Peto OR calculation is based on Yusuf S et al. (Prog Cardiovasc Dis. 1985 Mar-Apr;27(5):335-71) and its p-value is derived using a normal approximation.
Risk Ratio and related p-value are estimated by using the SAS FREQ procedure.
Risk Difference and related p-value are estimated by using the SAS GLIMMIX procedure with the following model: criterion = treatment.
p-values for heterogeneity are estimated by using the SAS GLIMMIX procedure with the following model: criterion = treatment subgroup treatment*subgroup.
p-value for heterogeneity of Peto Odds Ratio is estimated by using normal approximation.
PGM=DEVOPS/SAR231893/EFC14153/CSR_RWE/REPORT/PGM/ae_evt_ger_subg_s2_t.sas OUT=REPORT/OUTPUT/ae_teaensev_ger_race_s2_t_x.rtf (12AUG2021 - 9:09)

Project Code / Study Number / Analysis: SAR231893 / EFC14153 / CSR_RWE

2 Adverse events - Safety type 2 inflammatory asthma phenotype population

2.2 Patients with any TEAE not severe

2.2.3 By race (Caucasian/white, Black/of African descent, Other)

	Race					
	Caucasian/White		Black/of African descent		Other	
Safety type 2 inflammatory asthma phenotype population	**Placebo (N=101)**	**Dupilumab (N=207)**	**Placebo (N=5)**	**Dupilumab (N=9)**	**Placebo (N=7)**	**Dupilumab (N=18)**
p-value for Risk Ratio		0.494		NE		0.556
p-value for heterogeneity of Risk Ratio:						
Caucasian/White, Black/of African descent						0.334
Caucasian/White, Other						0.815
Black/of African descent, Other						<0.001
overall						0.815
Risk Difference (95% CI)	-	3.45 (-6.38 to 13.28)	-	-11.11 (NE to NE)	-	8.73 (-20.82 to 38.28)
p-value for Risk Difference		0.490		<0.001		0.547
p-value for heterogeneity of Risk Difference:						
Caucasian/White, Black/of African descent						0.337
Caucasian/White, Other						0.727
Black/of African descent, Other						<0.001

Odds Ratio and related p-value are estimated by Wald's method using the SAS LOGISTIC procedure.
Peto OR calculation is based on Yusuf S et al. (Prog Cardiovasc Dis. 1985 Mar-Apr;27(5):335-71) and its p-value is derived using a normal approximation.
Risk Ratio and related p-value are estimated by using the SAS FREQ procedure.
Risk Difference and related p-value are estimated by using the SAS GLIMMIX procedure with the following model: criterion = treatment.
p-values for heterogeneity are estimated by using the SAS GLIMMIX procedure with the following model: criterion = treatment subgroup treatment*subgroup.
p-value for heterogeneity of Peto Odds Ratio is estimated by using normal approximation.
PGM=DEVOPS/SAR231893/EFC14153/CSR_RWE/REPORT/PGM/ae_evt_ger_subg_s2_t.sas OUT=REPORT/OUTPUT/ae_teaensev_ger_race_s2_t_x.rtf (12AUG2021 - 9:09)

Project Code / Study Number / Analysis: SAR231893 / EFC14153 / CSR_RWE

2 Adverse events - Safety type 2 inflammatory asthma phenotype population

2.2 Patients with any TEAE not severe

2.2.3 By race (Caucasian/white, Black/of African descent, Other)

	Race					
	Caucasian/White		Black/of African descent		Other	
Safety type 2 inflammatory asthma phenotype population	**Placebo (N=101)**	**Dupilumab (N=207)**	**Placebo (N=5)**	**Dupilumab (N=9)**	**Placebo (N=7)**	**Dupilumab (N=18)**
overall						0.727

Odds Ratio and related p-value are estimated by Wald's method using the SAS LOGISTIC procedure.
Peto OR calculation is based on Yusuf S et al. (Prog Cardiovasc Dis. 1985 Mar-Apr;27(5):335-71) and its p-value is derived using a normal approximation.
Risk Ratio and related p-value are estimated by using the SAS FREQ procedure.
Risk Difference and related p-value are estimated by using the SAS GLIMMIX procedure with the following model: criterion = treatment.
p-values for heterogeneity are estimated by using the SAS GLIMMIX procedure with the following model: criterion = treatment subgroup treatment*subgroup.
p-value for heterogeneity of Peto Odds Ratio is estimated by using normal approximation.
PGM=DEVOPS/SAR231893/EFC14153/CSR_RWE/REPORT/PGM/ae_evt_ger_subg_s2_t.sas OUT=REPORT/OUTPUT/ae_teaensev_ger_race_s2_t_x.rtf (12AUG2021 - 9:09)

Project Code / Study Number / Analysis: SAR231893 / EFC14153 / CSR_RWE

2 Adverse events - Safety type 2 inflammatory asthma phenotype population

2.2 Patients with any TEAE not severe

2.2.4 By baseline ICS dose level (Medium, High)

	Baseline ICS dose level			
	High		Medium	
Safety type 2 inflammatory asthma phenotype population	**Placebo (N=50)**	**Dupilumab (N=101)**	**Placebo (N=63)**	**Dupilumab (N=131)**
Patients with any TEAE not severe [n(%)]	36 (72.0%)	84 (83.2%)	53 (84.1%)	107 (81.7%)
Odds Ratio (95% CI)	-	1.92 (0.86 to 4.31)	-	0.84 (0.38 to 1.89)
p-value for Odds Ratio		0.113		0.675
p-value for heterogeneity of Odds Ratio				0.157
Risk Ratio (95% CI)	-	1.16 (0.95 to 1.40)	-	0.97 (0.85 to 1.11)
Reversed Risk ratio (95% CI)	-	0.87 (0.71 to 1.05)		
p-value for Risk Ratio		0.145		0.667
p-value for heterogeneity of Risk Ratio				0.150
Risk Difference (95% CI)	-	11.17 (-3.38 to 25.71)	-	-2.45 (-13.71 to 8.82)

Odds Ratio and related p-value are estimated by Wald's method using the SAS LOGISTIC procedure.
Peto OR calculation is based on Yusuf S et al. (Prog Cardiovasc Dis. 1985 Mar-Apr;27(5):335-71) and its p-value is derived using a normal approximation.
Risk Ratio and related p-value are estimated by using the SAS FREQ procedure.
Risk Difference and related p-value are estimated by using the SAS GLIMMIX procedure with the following model: criterion = treatment.
p-values for heterogeneity are estimated by using the SAS GLIMMIX procedure with the following model: criterion = treatment subgroup treatment*subgroup.
p-value for heterogeneity of Peto Odds Ratio is estimated by using normal approximation.
PGM=DEVOPS/SAR231893/EFC14153/CSR_RWE/REPORT/PGM/ae_evt_ger_subg_s2_t.sas OUT=REPORT/OUTPUT/ae_teaensev_ger_ics_s2_t_x.rtf (12AUG2021 - 9:09)

Project Code / Study Number / Analysis: SAR231893 / EFC14153 / CSR_RWE

2 Adverse events - Safety type 2 inflammatory asthma phenotype population

2.2 Patients with any TEAE not severe

2.2.4 By baseline ICS dose level (Medium, High)

	Baseline ICS dose level			
	High		Medium	
Safety type 2 inflammatory asthma phenotype population	**Placebo (N=50)**	**Dupilumab (N=101)**	**Placebo (N=63)**	**Dupilumab (N=131)**
p-value for Risk Difference		0.131		0.669
p-value for heterogeneity of Risk Difference				0.145

Odds Ratio and related p-value are estimated by Wald's method using the SAS LOGISTIC procedure.
Peto OR calculation is based on Yusuf S et al. (Prog Cardiovasc Dis. 1985 Mar-Apr;27(5):335-71) and its p-value is derived using a normal approximation.
Risk Ratio and related p-value are estimated by using the SAS FREQ procedure.
Risk Difference and related p-value are estimated by using the SAS GLIMMIX procedure with the following model: criterion = treatment.
p-values for heterogeneity are estimated by using the SAS GLIMMIX procedure with the following model: criterion = treatment subgroup treatment*subgroup.
p-value for heterogeneity of Peto Odds Ratio is estimated by using normal approximation.
PGM=DEVOPS/SAR231893/EFC14153/CSR_RWE/REPORT/PGM/ae_evt_ger_subg_s2_t.sas OUT=REPORT/OUTPUT/ae_teaensev_ger_ics_s2_t_x.rtf (12AUG2021 - 9:09)

Project Code / Study Number / Analysis: SAR231893 / EFC14153 / CSR_RWE

2 Adverse events - Safety type 2 inflammatory asthma phenotype population

2.2 Patients with any TEAE not severe

2.2.5 By baseline ICS dose level 2 (Medium, High)

Safety type 2 inflammatory asthma phenotype population	Baseline ICS dose level 2			
	High		Medium	
	Placebo (N=94)	Dupilumab (N=199)	Placebo (N=19)	Dupilumab (N=35)
Patients with any TEAE not severe [n(%)]	75 (79.8%)	161 (80.9%)	14 (73.7%)	31 (88.6%)
Odds Ratio (95% CI)	-	1.07 (0.58 to 1.99)	-	2.77 (0.64 to 11.90)
p-value for Odds Ratio		0.822		0.171
p-value for heterogeneity of Odds Ratio				0.242
Risk Ratio (95% CI)	-	1.01 (0.90 to 1.15)	-	1.20 (0.90 to 1.61)
Reversed Risk ratio (95% CI)	-	0.99 (0.87 to 1.11)	-	0.83 (0.62 to 1.12)
p-value for Risk Ratio		0.823		0.220
p-value for heterogeneity of Risk Ratio				0.296
Risk Difference (95% CI)	-	1.12 (-8.71 to 10.94)	-	14.89 (-8.08 to 37.85)

Odds Ratio and related p-value are estimated by Wald's method using the SAS LOGISTIC procedure.
Peto OR calculation is based on Yusuf S et al. (Prog Cardiovasc Dis. 1985 Mar-Apr;27(5):335-71) and its p-value is derived using a normal approximation.
Risk Ratio and related p-value are estimated by using the SAS FREQ procedure.
Risk Difference and related p-value are estimated by using the SAS GLIMMIX procedure with the following model: criterion = treatment.
p-values for heterogeneity are estimated by using the SAS GLIMMIX procedure with the following model: criterion = treatment subgroup treatment*subgroup.
p-value for heterogeneity of Peto Odds Ratio is estimated by using normal approximation.
PGM=DEVOPS/SAR231893/EFC14153/CSR_RWE/REPORT/PGM/ae_evt_ger_subg_s2_t.sas OUT=REPORT/OUTPUT/ae_teaensev_ger_ics2_s2_t_x.rtf (01SEP2021 - 16:09)

Project Code / Study Number / Analysis: SAR231893 / EFC14153 / CSR_RWE

2 Adverse events - Safety type 2 inflammatory asthma phenotype population

2.2 Patients with any TEAE not severe

2.2.5 By baseline ICS dose level 2 (Medium, High)

	Baseline ICS dose level 2			
	High		Medium	
Safety type 2 inflammatory asthma phenotype population	**Placebo (N=94)**	**Dupilumab (N=199)**	**Placebo (N=19)**	**Dupilumab (N=35)**
p-value for Risk Difference		0.823		0.199
p-value for heterogeneity of Risk Difference				0.271

Odds Ratio and related p-value are estimated by Wald's method using the SAS LOGISTIC procedure.
Peto OR calculation is based on Yusuf S et al. (Prog Cardiovasc Dis. 1985 Mar-Apr;27(5):335-71) and its p-value is derived using a normal approximation.
Risk Ratio and related p-value are estimated by using the SAS FREQ procedure.
Risk Difference and related p-value are estimated by using the SAS GLIMMIX procedure with the following model: criterion = treatment.
p-values for heterogeneity are estimated by using the SAS GLIMMIX procedure with the following model: criterion = treatment subgroup treatment*subgroup.
p-value for heterogeneity of Peto Odds Ratio is estimated by using normal approximation.
PGM=DEVOPS/SAR231893/EFC14153/CSR_RWE/REPORT/PGM/ae_evt_ger_subg_s2_t.sas OUT=REPORT/OUTPUT/ae_teaensev_ger_ics2_s2_t_x.rtf (01SEP2021 - 16:09)

Project Code / Study Number / Analysis: SAR231893 / EFC14153 / CSR_RWE

2 Adverse events - Safety type 2 inflammatory asthma phenotype population

2.2 Patients with any TEAE not severe

2.2.6 By baseline predicted FEV1 (<80%, >=80%)

	Baseline Predicted FEV1			
	<80%		>=80%	
Safety type 2 inflammatory asthma phenotype population	**Placebo (N=58)**	**Dupilumab (N=116)**	**Placebo (N=55)**	**Dupilumab (N=118)**
Patients with any TEAE not severe [n(%)]	46 (79.3%)	100 (86.2%)	43 (78.2%)	92 (78.0%)
Odds Ratio (95% CI)	-	1.63 (0.71 to 3.72)	-	0.99 (0.46 to 2.14)
p-value for Odds Ratio		0.246		0.975
p-value for heterogeneity of Odds Ratio				0.386
Risk Ratio (95% CI)	-	1.09 (0.94 to 1.26)	-	1.00 (0.84 to 1.18)
Reversed Risk ratio (95% CI)	-	0.92 (0.79 to 1.07)		
p-value for Risk Ratio		0.277		0.974
p-value for heterogeneity of Risk Ratio				0.456
Risk Difference (95% CI)	-	6.90 (-5.36 to 19.15)	-	-0.22 (-13.54 to 13.11)

Odds Ratio and related p-value are estimated by Wald's method using the SAS LOGISTIC procedure.
Peto OR calculation is based on Yusuf S et al. (Prog Cardiovasc Dis. 1985 Mar-Apr;27(5):335-71) and its p-value is derived using a normal approximation.
Risk Ratio and related p-value are estimated by using the SAS FREQ procedure.
Risk Difference and related p-value are estimated by using the SAS GLIMMIX procedure with the following model: criterion = treatment.
p-values for heterogeneity are estimated by using the SAS GLIMMIX procedure with the following model: criterion = treatment subgroup treatment*subgroup.
p-value for heterogeneity of Peto Odds Ratio is estimated by using normal approximation.
PGM=DEVOPS/SAR231893/EFC14153/CSR_RWE/REPORT/PGM/ae_evt_ger_subg_s2_t.sas OUT=REPORT/OUTPUT/ae_teaensev_ger_pfev1_s2_t_x.rtf (12AUG2021 - 9:09)

Project Code / Study Number / Analysis: SAR231893 / EFC14153 / CSR_RWE

2 Adverse events - Safety type 2 inflammatory asthma phenotype population

2.2 Patients with any TEAE not severe

2.2.6 By baseline predicted FEV1 (<80%, >=80%)

	Baseline Predicted FEV1			
	<80%		>=80%	
Safety type 2 inflammatory asthma phenotype population	**Placebo (N=58)**	**Dupilumab (N=116)**	**Placebo (N=55)**	**Dupilumab (N=118)**
p-value for Risk Difference		0.268		0.975
p-value for heterogeneity of Risk Difference				0.439

Odds Ratio and related p-value are estimated by Wald's method using the SAS LOGISTIC procedure.
Peto OR calculation is based on Yusuf S et al. (Prog Cardiovasc Dis. 1985 Mar-Apr;27(5):335-71) and its p-value is derived using a normal approximation.
Risk Ratio and related p-value are estimated by using the SAS FREQ procedure.
Risk Difference and related p-value are estimated by using the SAS GLIMMIX procedure with the following model: criterion = treatment.
p-values for heterogeneity are estimated by using the SAS GLIMMIX procedure with the following model: criterion = treatment subgroup treatment*subgroup.
p-value for heterogeneity of Peto Odds Ratio is estimated by using normal approximation.
PGM=DEVOPS/SAR231893/EFC14153/CSR_RWE/REPORT/PGM/ae_evt_ger_subg_s2_t.sas OUT=REPORT/OUTPUT/ae_teaensev_ger_pfev1_s2_t_x.rtf (12AUG2021 - 9:09)

Project Code / Study Number / Analysis: SAR231893 / EFC14153 / CSR_RWE

2 Adverse events - Safety type 2 inflammatory asthma phenotype population

2.2 Patients with any TEAE not severe

2.2.7 By baseline ACQ-7-IA (<=2, >2)

	Baseline ACQ-7-IA			
	<=2		>2	
Safety type 2 inflammatory asthma phenotype population	**Placebo (N=61)**	**Dupilumab (N=125)**	**Placebo (N=52)**	**Dupilumab (N=109)**
Patients with any TEAE not severe [n(%)]	48 (78.7%)	102 (81.6%)	41 (78.8%)	90 (82.6%)
Odds Ratio (95% CI)	-	1.20 (0.56 to 2.57)	-	1.27 (0.55 to 2.91)
p-value for Odds Ratio		0.637		0.571
p-value for heterogeneity of Odds Ratio				0.922
Risk Ratio (95% CI)	-	1.04 (0.89 to 1.21)	-	1.05 (0.89 to 1.24)
Reversed Risk ratio (95% CI)	-	0.96 (0.83 to 1.13)	-	0.95 (0.81 to 1.13)
p-value for Risk Ratio		0.646		0.584
p-value for heterogeneity of Risk Ratio				0.932
Risk Difference (95% CI)	-	2.91 (-9.49 to 15.31)	-	3.72 (-9.57 to 17.01)

Odds Ratio and related p-value are estimated by Wald's method using the SAS LOGISTIC procedure.
Peto OR calculation is based on Yusuf S et al. (Prog Cardiovasc Dis. 1985 Mar-Apr;27(5):335-71) and its p-value is derived using a normal approximation.
Risk Ratio and related p-value are estimated by using the SAS FREQ procedure.
Risk Difference and related p-value are estimated by using the SAS GLIMMIX procedure with the following model: criterion = treatment.
p-values for heterogeneity are estimated by using the SAS GLIMMIX procedure with the following model: criterion = treatment subgroup treatment*subgroup.
p-value for heterogeneity of Peto Odds Ratio is estimated by using normal approximation.
PGM=DEVOPS/SAR231893/EFC14153/CSR_RWE/REPORT/PGM/ae_evt_ger_subg_s2_t.sas OUT=REPORT/OUTPUT/ae_teaensev_ger_acq7_s2_t_x.rtf (12AUG2021 - 9:09)

Project Code / Study Number / Analysis: SAR231893 / EFC14153 / CSR_RWE

2 Adverse events - Safety type 2 inflammatory asthma phenotype population

2.2 Patients with any TEAE not severe

2.2.7 By baseline ACQ-7-IA (<=2, >2)

	Baseline ACQ-7-IA			
	<=2		>2	
Safety type 2 inflammatory asthma phenotype population	**Placebo (N=61)**	**Dupilumab (N=125)**	**Placebo (N=52)**	**Dupilumab (N=109)**
p-value for Risk Difference		0.644		0.581
p-value for heterogeneity of Risk Difference				0.930

Odds Ratio and related p-value are estimated by Wald's method using the SAS LOGISTIC procedure.
Peto OR calculation is based on Yusuf S et al. (Prog Cardiovasc Dis. 1985 Mar-Apr;27(5):335-71) and its p-value is derived using a normal approximation.
Risk Ratio and related p-value are estimated by using the SAS FREQ procedure.
Risk Difference and related p-value are estimated by using the SAS GLIMMIX procedure with the following model: criterion = treatment.
p-values for heterogeneity are estimated by using the SAS GLIMMIX procedure with the following model: criterion = treatment subgroup treatment*subgroup.
p-value for heterogeneity of Peto Odds Ratio is estimated by using normal approximation.
PGM=DEVOPS/SAR231893/EFC14153/CSR_RWE/REPORT/PGM/ae_evt_ger_subg_s2_t.sas OUT=REPORT/OUTPUT/ae_teaensev_ger_acq7_s2_t_x.rtf (12AUG2021 - 9:09)

Project Code / Study Number / Analysis: SAR231893 / EFC14153 / CSR_RWE

2 Adverse events - Safety type 2 inflammatory asthma phenotype population

2.2 Patients with any TEAE not severe

2.2.8 By baseline weight (<=30 kg, >30 kg)

	Baseline weight (kg)			
	<=30		>30	
Safety type 2 inflammatory asthma phenotype population	**Placebo (N=36)**	**Dupilumab (N=74)**	**Placebo (N=77)**	**Dupilumab (N=160)**
Patients with any TEAE not severe [n(%)]	30 (83.3%)	58 (78.4%)	59 (76.6%)	134 (83.8%)
Odds Ratio (95% CI)	-	0.73 (0.26 to 2.04)	-	1.57 (0.80 to 3.09)
p-value for Odds Ratio		0.543		0.188
p-value for heterogeneity of Odds Ratio				0.221
Risk Ratio (95% CI)	-	0.94 (0.78 to 1.14)	-	1.09 (0.95 to 1.26)
Reversed Risk ratio (95% CI)			-	0.91 (0.79 to 1.05)
p-value for Risk Ratio		0.525		0.216
p-value for heterogeneity of Risk Ratio				0.212
Risk Difference (95% CI)	-	-4.95 (-20.50 to 10.59)	-	7.13 (-3.98 to 18.23)

Odds Ratio and related p-value are estimated by Wald's method using the SAS LOGISTIC procedure.
Peto OR calculation is based on Yusuf S et al. (Prog Cardiovasc Dis. 1985 Mar-Apr;27(5):335-71) and its p-value is derived using a normal approximation.
Risk Ratio and related p-value are estimated by using the SAS FREQ procedure.
Risk Difference and related p-value are estimated by using the SAS GLIMMIX procedure with the following model: criterion = treatment.
p-values for heterogeneity are estimated by using the SAS GLIMMIX procedure with the following model: criterion = treatment subgroup treatment*subgroup.
p-value for heterogeneity of Peto Odds Ratio is estimated by using normal approximation.
PGM=DEVOPS/SAR231893/EFC14153/CSR_RWE/REPORT/PGM/ae_evt_ger_subg_s2_t.sas OUT=REPORT/OUTPUT/ae_teaensev_ger_wgt_s2_t_x.rtf (12AUG2021 - 9:09)

Project Code / Study Number / Analysis: SAR231893 / EFC14153 / CSR_RWE

2 Adverse events - Safety type 2 inflammatory asthma phenotype population

2.2 Patients with any TEAE not severe

2.2.8 By baseline weight (<=30 kg, >30 kg)

	Baseline weight (kg)			
	<=30		>30	
Safety type 2 inflammatory asthma phenotype population	**Placebo (N=36)**	**Dupilumab (N=74)**	**Placebo (N=77)**	**Dupilumab (N=160)**
p-value for Risk Difference		0.529		0.207
p-value for heterogeneity of Risk Difference				0.212

Odds Ratio and related p-value are estimated by Wald's method using the SAS LOGISTIC procedure.
Peto OR calculation is based on Yusuf S et al. (Prog Cardiovasc Dis. 1985 Mar-Apr;27(5):335-71) and its p-value is derived using a normal approximation.
Risk Ratio and related p-value are estimated by using the SAS FREQ procedure.
Risk Difference and related p-value are estimated by using the SAS GLIMMIX procedure with the following model: criterion = treatment.
p-values for heterogeneity are estimated by using the SAS GLIMMIX procedure with the following model: criterion = treatment subgroup treatment*subgroup.
p-value for heterogeneity of Peto Odds Ratio is estimated by using normal approximation.
PGM=DEVOPS/SAR231893/EFC14153/CSR_RWE/REPORT/PGM/ae_evt_ger_subg_s2_t.sas OUT=REPORT/OUTPUT/ae_teaensev_ger_wgt_s2_t_x.rtf (12AUG2021 - 9:09)

Project Code / Study Number / Analysis: SAR231893 / EFC14153 / CSR_RWE

2 Adverse events - Safety type 2 inflammatory asthma phenotype population

2.2 Patients with any TEAE not severe

2.2.9 By atopic medical condition (Yes, No)

	Atopic medical condition			
	Yes		No	
Safety type 2 inflammatory asthma phenotype population	**Placebo (N=102)**	**Dupilumab (N=225)**	**Placebo (N=11)**	**Dupilumab (N=9)**
Patients with any TEAE not severe [n(%)]	82 (80.4%)	185 (82.2%)	7 (63.6%)	7 (77.8%)
Odds Ratio (95% CI)	-	1.13 (0.62 to 2.05)	-	2.00 (0.27 to 14.70)
p-value for Odds Ratio		0.692		0.496
p-value for heterogeneity of Odds Ratio				0.590
Risk Ratio (95% CI)	-	1.02 (0.91 to 1.15)	-	1.22 (0.69 to 2.15)
Reversed Risk ratio (95% CI)	-	0.98 (0.87 to 1.10)	-	0.82 (0.46 to 1.44)
p-value for Risk Ratio		0.697		0.488
p-value for heterogeneity of Risk Ratio				0.546
Risk Difference (95% CI)	-	1.83 (-7.39 to 11.05)	-	14.14 (-28.00 to 56.29)

Odds Ratio and related p-value are estimated by Wald's method using the SAS LOGISTIC procedure.
Peto OR calculation is based on Yusuf S et al. (Prog Cardiovasc Dis. 1985 Mar-Apr;27(5):335-71) and its p-value is derived using a normal approximation.
Risk Ratio and related p-value are estimated by using the SAS FREQ procedure.
Risk Difference and related p-value are estimated by using the SAS GLIMMIX procedure with the following model: criterion = treatment.
p-values for heterogeneity are estimated by using the SAS GLIMMIX procedure with the following model: criterion = treatment subgroup treatment*subgroup.
p-value for heterogeneity of Peto Odds Ratio is estimated by using normal approximation.
PGM=DEVOPS/SAR231893/EFC14153/CSR_RWE/REPORT/PGM/ae_evt_ger_subg_s2_t.sas OUT=REPORT/OUTPUT/ae_teaensev_ger_amc_s2_t_x.rtf (12AUG2021 - 9:09)

Project Code / Study Number / Analysis: SAR231893 / EFC14153 / CSR_RWE

2 Adverse events - Safety type 2 inflammatory asthma phenotype population

2.2 Patients with any TEAE not severe

2.2.9 By atopic medical condition (Yes, No)

	Atopic medical condition			
	Yes		No	
Safety type 2 inflammatory asthma phenotype population	**Placebo (N=102)**	**Dupilumab (N=225)**	**Placebo (N=11)**	**Dupilumab (N=9)**
p-value for Risk Difference		0.696		0.490
p-value for heterogeneity of Risk Difference				0.550

Odds Ratio and related p-value are estimated by Wald's method using the SAS LOGISTIC procedure.
Peto OR calculation is based on Yusuf S et al. (Prog Cardiovasc Dis. 1985 Mar-Apr;27(5):335-71) and its p-value is derived using a normal approximation.
Risk Ratio and related p-value are estimated by using the SAS FREQ procedure.
Risk Difference and related p-value are estimated by using the SAS GLIMMIX procedure with the following model: criterion = treatment.
p-values for heterogeneity are estimated by using the SAS GLIMMIX procedure with the following model: criterion = treatment subgroup treatment*subgroup.
p-value for heterogeneity of Peto Odds Ratio is estimated by using normal approximation.
PGM=DEVOPS/SAR231893/EFC14153/CSR_RWE/REPORT/PGM/ae_evt_ger_subg_s2_t.sas OUT=REPORT/OUTPUT/ae_teaensev_ger_amc_s2_t_x.rtf (12AUG2021 - 9:09)

Project Code / Study Number / Analysis: SAR231893 / EFC14153 / CSR_RWE

2 Adverse events - Safety type 2 inflammatory asthma phenotype population

2.2 Patients with any TEAE not severe

2.2.10 By baseline total IgE (<median, >= median)

	Baseline Total IgE (IU/mL)			
	<median		>=median	
Safety type 2 inflammatory asthma phenotype population	**Placebo (N=65)**	**Dupilumab (N=106)**	**Placebo (N=47)**	**Dupilumab (N=124)**
Patients with any TEAE not severe [n(%)]	49 (75.4%)	84 (79.2%)	39 (83.0%)	104 (83.9%)
Odds Ratio (95% CI)	-	1.25 (0.60 to 2.60)	-	1.07 (0.43 to 2.62)
p-value for Odds Ratio		0.556		0.888
p-value for heterogeneity of Odds Ratio				0.792
Risk Ratio (95% CI)	-	1.05 (0.89 to 1.25)	-	1.01 (0.87 to 1.18)
Reversed Risk ratio (95% CI)	-	0.95 (0.80 to 1.13)	-	0.99 (0.85 to 1.15)
p-value for Risk Ratio		0.564		0.889
p-value for heterogeneity of Risk Ratio				0.735
Risk Difference (95% CI)	-	3.86 (-9.24 to 16.96)	-	0.89 (-11.74 to 13.53)

Odds Ratio and related p-value are estimated by Wald's method using the SAS LOGISTIC procedure.
Peto OR calculation is based on Yusuf S et al. (Prog Cardiovasc Dis. 1985 Mar-Apr;27(5):335-71) and its p-value is derived using a normal approximation.
Risk Ratio and related p-value are estimated by using the SAS FREQ procedure.
Risk Difference and related p-value are estimated by using the SAS GLIMMIX procedure with the following model: criterion = treatment.
p-values for heterogeneity are estimated by using the SAS GLIMMIX procedure with the following model: criterion = treatment subgroup treatment*subgroup.
p-value for heterogeneity of Peto Odds Ratio is estimated by using normal approximation.
PGM=DEVOPS/SAR231893/EFC14153/CSR_RWE/REPORT/PGM/ae_evt_ger_subg_s2_t.sas OUT=REPORT/OUTPUT/ae_teaensev_ger_igem_s2_t_x.rtf (12AUG2021 - 9:10)

Project Code / Study Number / Analysis: SAR231893 / EFC14153 / CSR_RWE

2 Adverse events - Safety type 2 inflammatory asthma phenotype population

2.2 Patients with any TEAE not severe

2.2.10 By baseline total IgE (<median, >= median)

	Baseline Total IgE (IU/mL)			
	<median		>=median	
Safety type 2 inflammatory asthma phenotype population	**Placebo (N=65)**	**Dupilumab (N=106)**	**Placebo (N=47)**	**Dupilumab (N=124)**
p-value for Risk Difference		0.562		0.889
p-value for heterogeneity of Risk Difference				0.748

Odds Ratio and related p-value are estimated by Wald's method using the SAS LOGISTIC procedure.
Peto OR calculation is based on Yusuf S et al. (Prog Cardiovasc Dis. 1985 Mar-Apr;27(5):335-71) and its p-value is derived using a normal approximation.
Risk Ratio and related p-value are estimated by using the SAS FREQ procedure.
Risk Difference and related p-value are estimated by using the SAS GLIMMIX procedure with the following model: criterion = treatment.
p-values for heterogeneity are estimated by using the SAS GLIMMIX procedure with the following model: criterion = treatment subgroup treatment*subgroup.
p-value for heterogeneity of Peto Odds Ratio is estimated by using normal approximation.
PGM=DEVOPS/SAR231893/EFC14153/CSR_RWE/REPORT/PGM/ae_evt_ger_subg_s2_t.sas OUT=REPORT/OUTPUT/ae_teaensev_ger_igem_s2_t_x.rtf (12AUG2021 - 9:10)

Project Code / Study Number / Analysis: SAR231893 / EFC14153 / CSR_RWE

2 Adverse events - Safety type 2 inflammatory asthma phenotype population

2.2 Patients with any TEAE not severe

2.2.11 By baseline total IgE (<100 IU/ml, >= 100 IU/ml)

	Baseline Total IgE (IU/mL)			
	< 100		>= 100	
Safety type 2 inflammatory asthma phenotype population	**Placebo (N=22)**	**Dupilumab (N=29)**	**Placebo (N=90)**	**Dupilumab (N=201)**
Patients with any TEAE not severe [n(%)]	15 (68.2%)	23 (79.3%)	73 (81.1%)	165 (82.1%)
Odds Ratio (95% CI)	-	1.79 (0.50 to 6.37)	-	1.07 (0.56 to 2.02)
p-value for Odds Ratio		0.369		0.842
p-value for heterogeneity of Odds Ratio				0.477
Risk Ratio (95% CI)	-	1.16 (0.83 to 1.64)	-	1.01 (0.90 to 1.14)
Reversed Risk ratio (95% CI)	-	0.86 (0.61 to 1.21)	-	0.99 (0.88 to 1.11)
p-value for Risk Ratio		0.384		0.843
p-value for heterogeneity of Risk Ratio				0.450
Risk Difference (95% CI)	-	11.13 (-13.91 to 36.16)	-	0.98 (-8.73 to 10.69)

Odds Ratio and related p-value are estimated by Wald's method using the SAS LOGISTIC procedure.
Peto OR calculation is based on Yusuf S et al. (Prog Cardiovasc Dis. 1985 Mar-Apr;27(5):335-71) and its p-value is derived using a normal approximation.
Risk Ratio and related p-value are estimated by using the SAS FREQ procedure.
Risk Difference and related p-value are estimated by using the SAS GLIMMIX procedure with the following model: criterion = treatment.
p-values for heterogeneity are estimated by using the SAS GLIMMIX procedure with the following model: criterion = treatment subgroup treatment*subgroup.
p-value for heterogeneity of Peto Odds Ratio is estimated by using normal approximation.
PGM=DEVOPS/SAR231893/EFC14153/CSR_RWE/REPORT/PGM/ae_evt_ger_subg_s2_t.sas OUT=REPORT/OUTPUT/ae_teaensev_ger_ige_s2_t_x.rtf (12AUG2021 - 9:10)

Project Code / Study Number / Analysis: SAR231893 / EFC14153 / CSR_RWE

2 Adverse events - Safety type 2 inflammatory asthma phenotype population

2.2 Patients with any TEAE not severe

2.2.11 By baseline total IgE (<100 IU/ml, >= 100 IU/ml)

	Baseline Total IgE (IU/mL)			
	< 100		>= 100	
Safety type 2 inflammatory asthma phenotype population	**Placebo (N=22)**	**Dupilumab (N=29)**	**Placebo (N=90)**	**Dupilumab (N=201)**
p-value for Risk Difference		0.376		0.843
p-value for heterogeneity of Risk Difference				0.449

Odds Ratio and related p-value are estimated by Wald's method using the SAS LOGISTIC procedure.
Peto OR calculation is based on Yusuf S et al. (Prog Cardiovasc Dis. 1985 Mar-Apr;27(5):335-71) and its p-value is derived using a normal approximation.
Risk Ratio and related p-value are estimated by using the SAS FREQ procedure.
Risk Difference and related p-value are estimated by using the SAS GLIMMIX procedure with the following model: criterion = treatment.
p-values for heterogeneity are estimated by using the SAS GLIMMIX procedure with the following model: criterion = treatment subgroup treatment*subgroup.
p-value for heterogeneity of Peto Odds Ratio is estimated by using normal approximation.
PGM=DEVOPS/SAR231893/EFC14153/CSR_RWE/REPORT/PGM/ae_evt_ger_subg_s2_t.sas OUT=REPORT/OUTPUT/ae_teaensev_ger_ige_s2_t_x.rtf (12AUG2021 - 9:10)

Project Code / Study Number / Analysis: SAR231893 / EFC14153 / CSR_RWE

2 Adverse events - Safety type 2 inflammatory asthma phenotype population

2.2 Patients with any TEAE not severe

2.2.12 By age at onset of asthma (0-2, 3-5, >=6 years)

	Age of onset of asthma (years)					
	0-2		3-5		>= 6	
Safety type 2 inflammatory asthma phenotype population	**Placebo (N=40)**	**Dupilumab (N=104)**	**Placebo (N=38)**	**Dupilumab (N=85)**	**Placebo (N=35)**	**Dupilumab (N=45)**
Patients with any TEAE not severe [n(%)]	33 (82.5%)	88 (84.6%)	33 (86.8%)	70 (82.4%)	23 (65.7%)	34 (75.6%)
Odds Ratio (95% CI)	-	1.17 (0.44 to 3.09)	-	0.71 (0.24 to 2.11)	-	1.61 (0.61 to 4.27)
p-value for Odds Ratio		0.756		0.535		0.336
p-value for heterogeneity of Odds Ratio:						
0-2, 3-5						0.503
0-2, >= 6						0.645
3-5, >= 6						0.271
overall						0.543
Risk Ratio (95% CI)	-	1.03 (0.87 to 1.21)	-	0.95 (0.81 to 1.11)	-	1.15 (0.86 to 1.54)
Reversed Risk ratio (95% CI)	-	0.98 (0.83 to 1.15)			-	0.87 (0.65 to 1.16)
p-value for Risk Ratio		0.763		0.511		0.348

Odds Ratio and related p-value are estimated by Wald's method using the SAS LOGISTIC procedure.
Peto OR calculation is based on Yusuf S et al. (Prog Cardiovasc Dis. 1985 Mar-Apr;27(5):335-71) and its p-value is derived using a normal approximation.
Risk Ratio and related p-value are estimated by using the SAS FREQ procedure.
Risk Difference and related p-value are estimated by using the SAS GLIMMIX procedure with the following model: criterion = treatment.
p-values for heterogeneity are estimated by using the SAS GLIMMIX procedure with the following model: criterion = treatment subgroup treatment*subgroup.
p-value for heterogeneity of Peto Odds Ratio is estimated by using normal approximation.
PGM=DEVOPS/SAR231893/EFC14153/CSR_RWE/REPORT/PGM/ae_evt_ger_subg_s2_t.sas OUT=REPORT/OUTPUT/ae_teaensev_ger_onsa_s2_t_x.rtf (12AUG2021 - 9:10)

Project Code / Study Number / Analysis: SAR231893 / EFC14153 / CSR_RWE

2 Adverse events - Safety type 2 inflammatory asthma phenotype population

2.2 Patients with any TEAE not severe

2.2.12 By age at onset of asthma (0-2, 3-5, >=6 years)

	Age of onset of asthma (years)					
	0-2		3-5		>= 6	
Safety type 2 inflammatory asthma phenotype population	**Placebo (N=40)**	**Dupilumab (N=104)**	**Placebo (N=38)**	**Dupilumab (N=85)**	**Placebo (N=35)**	**Dupilumab (N=45)**
p-value for heterogeneity of Risk Ratio:						
0-2, 3-5						0.501
0-2, >= 6						0.504
3-5, >= 6						0.256
overall						0.498
Risk Difference (95% CI)	-	2.12 (-11.67 to 15.90)	-	-4.49 (-18.09 to 9.11)	-	9.84 (-10.60 to 30.28)
p-value for Risk Difference		0.762		0.515		0.341
p-value for heterogeneity of Risk Difference:						
0-2, 3-5						0.500
0-2, >= 6						0.534
3-5, >= 6						0.247
overall						0.496

Odds Ratio and related p-value are estimated by Wald's method using the SAS LOGISTIC procedure.
Peto OR calculation is based on Yusuf S et al. (Prog Cardiovasc Dis. 1985 Mar-Apr;27(5):335-71) and its p-value is derived using a normal approximation.
Risk Ratio and related p-value are estimated by using the SAS FREQ procedure.
Risk Difference and related p-value are estimated by using the SAS GLIMMIX procedure with the following model: criterion = treatment.
p-values for heterogeneity are estimated by using the SAS GLIMMIX procedure with the following model: criterion = treatment subgroup treatment*subgroup.
p-value for heterogeneity of Peto Odds Ratio is estimated by using normal approximation.
PGM=DEVOPS/SAR231893/EFC14153/CSR_RWE/REPORT/PGM/ae_evt_ger_subg_s2_t.sas OUT=REPORT/OUTPUT/ae_teaensev_ger_onsa_s2_t_x.rtf (12AUG2021 - 9:10)

Project Code / Study Number / Analysis: SAR231893 / EFC14153 / CSR_RWE

2 Adverse events - Safety type 2 inflammatory asthma phenotype population

2.2 Patients with any TEAE not severe

2.2.13 By number of severe asthma exacerbation prior to the study (<=1, 2, >2)

	Number of severe asthma exacerbation prior to the study					
	<=1		2		>2	
Safety type 2 inflammatory asthma phenotype population	**Placebo (N=46)**	**Dupilumab (N=85)**	**Placebo (N=32)**	**Dupilumab (N=75)**	**Placebo (N=35)**	**Dupilumab (N=74)**
Patients with any TEAE not severe [n(%)]	37 (80.4%)	72 (84.7%)	22 (68.8%)	57 (76.0%)	30 (85.7%)	63 (85.1%)
Odds Ratio (95% CI)	-	1.35 (0.53 to 3.44)	-	1.44 (0.58 to 3.60)	-	0.95 (0.30 to 2.99)
p-value for Odds Ratio		0.533		0.436		0.936
p-value for heterogeneity of Odds Ratio:						
<=1, 2						0.921
<=1, >2						0.648
2, >2						0.583
overall						0.849
Risk Ratio (95% CI)	-	1.05 (0.89 to 1.25)	-	1.11 (0.85 to 1.44)	-	0.99 (0.84 to 1.17)
Reversed Risk ratio (95% CI)	-	0.95 (0.80 to 1.12)	-	0.90 (0.69 to 1.18)		

Odds Ratio and related p-value are estimated by Wald's method using the SAS LOGISTIC procedure.
Peto OR calculation is based on Yusuf S et al. (Prog Cardiovasc Dis. 1985 Mar-Apr;27(5):335-71) and its p-value is derived using a normal approximation.
Risk Ratio and related p-value are estimated by using the SAS FREQ procedure.
Risk Difference and related p-value are estimated by using the SAS GLIMMIX procedure with the following model: criterion = treatment.
p-values for heterogeneity are estimated by using the SAS GLIMMIX procedure with the following model: criterion = treatment subgroup treatment*subgroup.
p-value for heterogeneity of Peto Odds Ratio is estimated by using normal approximation.
PGM=DEVOPS/SAR231893/EFC14153/CSR_RWE/REPORT/PGM/ae_evt_ger_subg_s2_t.sas OUT=REPORT/OUTPUT/ae_teaensev_ger_exa_s2_t_x.rtf (12AUG2021 - 9:10)

Project Code / Study Number / Analysis: SAR231893 / EFC14153 / CSR_RWE

2 Adverse events - Safety type 2 inflammatory asthma phenotype population

2.2 Patients with any TEAE not severe

2.2.13 By number of severe asthma exacerbation prior to the study (<=1, 2, >2)

	Number of severe asthma exacerbation prior to the study					
	<=1		2		>2	
Safety type 2 inflammatory asthma phenotype population	**Placebo (N=46)**	**Dupilumab (N=85)**	**Placebo (N=32)**	**Dupilumab (N=75)**	**Placebo (N=35)**	**Dupilumab (N=74)**
p-value for Risk Ratio		0.548		0.460		0.936
p-value for heterogeneity of Risk Ratio:						
<=1, 2						0.763
<=1, >2						0.628
2, >2						0.503
overall						0.773
Risk Difference (95% CI)	-	4.27 (-9.64 to 18.18)	-	7.25 (-11.71 to 26.21)	-	-0.58 (-14.89 to 13.73)
p-value for Risk Difference		0.545		0.450		0.936
p-value for heterogeneity of Risk Difference:						
<=1, 2						0.802
<=1, >2						0.631

Odds Ratio and related p-value are estimated by Wald's method using the SAS LOGISTIC procedure.
Peto OR calculation is based on Yusuf S et al. (Prog Cardiovasc Dis. 1985 Mar-Apr;27(5):335-71) and its p-value is derived using a normal approximation.
Risk Ratio and related p-value are estimated by using the SAS FREQ procedure.
Risk Difference and related p-value are estimated by using the SAS GLIMMIX procedure with the following model: criterion = treatment.
p-values for heterogeneity are estimated by using the SAS GLIMMIX procedure with the following model: criterion = treatment subgroup treatment*subgroup.
p-value for heterogeneity of Peto Odds Ratio is estimated by using normal approximation.
PGM=DEVOPS/SAR231893/EFC14153/CSR_RWE/REPORT/PGM/ae_evt_ger_subg_s2_t.sas OUT=REPORT/OUTPUT/ae_teaensev_ger_exa_s2_t_x.rtf (12AUG2021 - 9:10)

Project Code / Study Number / Analysis: SAR231893 / EFC14153 / CSR_RWE

2 Adverse events - Safety type 2 inflammatory asthma phenotype population

2.2 Patients with any TEAE not severe

2.2.13 By number of severe asthma exacerbation prior to the study (<=1, 2, >2)

	Number of severe asthma exacerbation prior to the study					
	<=1		2		>2	
Safety type 2 inflammatory asthma phenotype population	**Placebo (N=46)**	**Dupilumab (N=85)**	**Placebo (N=32)**	**Dupilumab (N=75)**	**Placebo (N=35)**	**Dupilumab (N=74)**
2, >2						0.514
overall						0.788

Odds Ratio and related p-value are estimated by Wald's method using the SAS LOGISTIC procedure.
Peto OR calculation is based on Yusuf S et al. (Prog Cardiovasc Dis. 1985 Mar-Apr;27(5):335-71) and its p-value is derived using a normal approximation.
Risk Ratio and related p-value are estimated by using the SAS FREQ procedure.
Risk Difference and related p-value are estimated by using the SAS GLIMMIX procedure with the following model: criterion = treatment.
p-values for heterogeneity are estimated by using the SAS GLIMMIX procedure with the following model: criterion = treatment subgroup treatment*subgroup.
p-value for heterogeneity of Peto Odds Ratio is estimated by using normal approximation.
PGM=DEVOPS/SAR231893/EFC14153/CSR_RWE/REPORT/PGM/ae_evt_ger_subg_s2_t.sas OUT=REPORT/OUTPUT/ae_teaensev_ger_exa_s2_t_x.rtf (12AUG2021 - 9:10)

Project Code / Study Number / Analysis: SAR231893 / EFC14153 / CSR_RWE

2 Adverse events - Safety type 2 inflammatory asthma phenotype population

2.3 Patients with any TEAE severe

Safety type 2 inflammatory asthma phenotype population	Placebo (N=113)	Dupilumab (N=234)
Patients with any TEAE severe [n(%)]	6 (5.3%)	8 (3.4%)
Odds Ratio (95% CI)	-	0.63 (0.21 to 1.86)
p-value for Odds Ratio		0.405
Risk Ratio (95% CI)	-	0.64 (0.23 to 1.81)
p-value for Risk Ratio		0.404
Risk Difference (95% CI)	-	-1.89 (-6.65 to 2.87)
p-value for Risk Difference		0.435

Odds Ratio and related p-value are estimated by Wald's method using the SAS LOGISTIC procedure.
Peto OR calculation is based on Yusuf S et al. (Prog Cardiovasc Dis. 1985 Mar-Apr;27(5):335-71) and its p-value is derived using a normal approximation.
Risk Ratio and related p-value are estimated by using the SAS FREQ procedure.
Risk Difference and related p-value are estimated by using the SAS GLIMMIX procedure with the following model: criterion = treatment.
PGM=DEVOPS/SAR231893/EFC14153/CSR_RWE/REPORT/PGM/ae_evt_ger_s2_t.sas OUT=REPORT/OUTPUT/ae_teaesev_ger_s2_t_x.rtf (12AUG2021 - 9:08)

Project Code / Study Number / Analysis: SAR231893 / EFC14153 / CSR_RWE

2 Adverse events - Safety type 2 inflammatory asthma phenotype population

2.3 Patients with any TEAE severe

2.3.1 By gender (Male, Female)

	Gender			
	Male		Female	
Safety type 2 inflammatory asthma phenotype population	**Placebo (N=77)**	**Dupilumab (N=153)**	**Placebo (N=36)**	**Dupilumab (N=81)**
Patients with any TEAE severe [n(%)]	6 (7.8%)	4 (2.6%)	0	4 (4.9%)
Odds Ratio (95% CI)	-	0.32 (0.09 to 1.16)	-	NE (NE to NE)
p-value for Odds Ratio		0.083		NE
Peto Odds Ratio (95% CI)	-	0.29 (0.08 to 1.11)	-	4.41 (0.51 to 37.87)
Reversed Peto Odds Ratio (95% CI)			-	0.23 (0.03 to 1.96)
p-value for Peto Odds Ratio		0.070		0.177
p-value for heterogeneity of Peto Odds Ratio				0.035
Risk Ratio (95% CI)	-	0.34 (0.10 to 1.15)	-	NE (NE to NE)
p-value for Risk Ratio		0.083		NE
p-value for heterogeneity of Risk Ratio				0.969

Odds Ratio and related p-value are estimated by Wald's method using the SAS LOGISTIC procedure.
Peto OR calculation is based on Yusuf S et al. (Prog Cardiovasc Dis. 1985 Mar-Apr;27(5):335-71) and its p-value is derived using a normal approximation.
Risk Ratio and related p-value are estimated by using the SAS FREQ procedure.
Risk Difference and related p-value are estimated by using the SAS GLIMMIX procedure with the following model: criterion = treatment.
p-values for heterogeneity are estimated by using the SAS GLIMMIX procedure with the following model: criterion = treatment subgroup treatment*subgroup.
p-value for heterogeneity of Peto Odds Ratio is estimated by using normal approximation.
PGM=DEVOPS/SAR231893/EFC14153/CSR_RWE/REPORT/PGM/ae_evt_ger_subg_s2_t.sas OUT=REPORT/OUTPUT/ae_teaesev_ger_sex_s2_t_x.rtf (12AUG2021 - 9:10)

Project Code / Study Number / Analysis: SAR231893 / EFC14153 / CSR_RWE

2 Adverse events - Safety type 2 inflammatory asthma phenotype population

2.3 Patients with any TEAE severe

2.3.1 By gender (Male, Female)

	Gender			
	Male		Female	
Safety type 2 inflammatory asthma phenotype population	**Placebo (N=77)**	**Dupilumab (N=153)**	**Placebo (N=36)**	**Dupilumab (N=81)**
Risk Difference (95% CI)	-	-5.18 (-11.71 to 1.36)	-	4.94 (NE to NE)
p-value for Risk Difference		0.120		<0.001
p-value for heterogeneity of Risk Difference				<0.001

Odds Ratio and related p-value are estimated by Wald's method using the SAS LOGISTIC procedure.
Peto OR calculation is based on Yusuf S et al. (Prog Cardiovasc Dis. 1985 Mar-Apr;27(5):335-71) and its p-value is derived using a normal approximation.
Risk Ratio and related p-value are estimated by using the SAS FREQ procedure.
Risk Difference and related p-value are estimated by using the SAS GLIMMIX procedure with the following model: criterion = treatment.
p-values for heterogeneity are estimated by using the SAS GLIMMIX procedure with the following model: criterion = treatment subgroup treatment*subgroup.
p-value for heterogeneity of Peto Odds Ratio is estimated by using normal approximation.
PGM=DEVOPS/SAR231893/EFC14153/CSR_RWE/REPORT/PGM/ae_evt_ger_subg_s2_t.sas OUT=REPORT/OUTPUT/ae_teaesev_ger_sex_s2_t_x.rtf (12AUG2021 - 9:10)

Project Code / Study Number / Analysis: SAR231893 / EFC14153 / CSR_RWE

2 Adverse events - Safety type 2 inflammatory asthma phenotype population

2.3 Patients with any TEAE severe

2.3.2 By region (Latin America, East Europe, Western Countries)

	Region					
	Latin America		East Europe		Western countries	
Safety type 2 inflammatory asthma phenotype population	**Placebo (N=51)**	**Dupilumab (N=105)**	**Placebo (N=43)**	**Dupilumab (N=78)**	**Placebo (N=19)**	**Dupilumab (N=51)**
Patients with any TEAE severe [n(%)]	4 (7.8%)	4 (3.8%)	0	1 (1.3%)	2 (10.5%)	3 (5.9%)
Odds Ratio (95% CI)	-	0.47 (0.11 to 1.94)	-	NE (NE to NE)	-	0.53 (0.08 to 3.46)
p-value for Odds Ratio		0.294		NE		0.508
Peto Odds Ratio (95% CI)	-	0.44 (0.10 to 1.99)	-	4.72 (0.08 to 283.23)	-	0.50 (0.07 to 3.82)
Reversed Peto Odds Ratio (95% CI)			-	0.21 (0.00 to 12.50)		
p-value for Peto Odds Ratio		0.286		0.458		0.505
p-value for heterogeneity of Peto Odds Ratio:						
Latin America, East Europe						0.286
Latin America, Western countries						0.918
East Europe, Western countries						0.337

Odds Ratio and related p-value are estimated by Wald's method using the SAS LOGISTIC procedure.
Peto OR calculation is based on Yusuf S et al. (Prog Cardiovasc Dis. 1985 Mar-Apr;27(5):335-71) and its p-value is derived using a normal approximation.
Risk Ratio and related p-value are estimated by using the SAS FREQ procedure.
Risk Difference and related p-value are estimated by using the SAS GLIMMIX procedure with the following model: criterion = treatment.
p-values for heterogeneity are estimated by using the SAS GLIMMIX procedure with the following model: criterion = treatment subgroup treatment*subgroup.
p-value for heterogeneity of Peto Odds Ratio is estimated by using normal approximation.
PGM=DEVOPS/SAR231893/EFC14153/CSR_RWE/REPORT/PGM/ae_evt_ger_subg_s2_t.sas OUT=REPORT/OUTPUT/ae_teaesev_ger_cty_s2_t_x.rtf (12AUG2021 - 9:11)

Project Code / Study Number / Analysis: SAR231893 / EFC14153 / CSR_RWE

2 Adverse events - Safety type 2 inflammatory asthma phenotype population

2.3 Patients with any TEAE severe

2.3.2 By region (Latin America, East Europe, Western Countries)

	Region					
	Latin America		East Europe		Western countries	
Safety type 2 inflammatory asthma phenotype population	**Placebo (N=51)**	**Dupilumab (N=105)**	**Placebo (N=43)**	**Dupilumab (N=78)**	**Placebo (N=19)**	**Dupilumab (N=51)**
overall						0.562
Risk Ratio (95% CI)	-	0.49 (0.13 to 1.86)	-	NE (NE to NE)	-	0.56 (0.10 to 3.09)
p-value for Risk Ratio		0.293		NE		0.505
p-value for heterogeneity of Risk Ratio:						
Latin America, East Europe						0.980
Latin America, Western countries						0.900
East Europe, Western countries						0.981
overall						0.992
Risk Difference (95% CI)	-	-4.03 (-12.34 to 4.27)	-	1.28 (NE to NE)	-	-4.64 (-20.16 to 10.87)
p-value for Risk Difference		0.339		<0.001		0.552

Odds Ratio and related p-value are estimated by Wald's method using the SAS LOGISTIC procedure.
Peto OR calculation is based on Yusuf S et al. (Prog Cardiovasc Dis. 1985 Mar-Apr;27(5):335-71) and its p-value is derived using a normal approximation.
Risk Ratio and related p-value are estimated by using the SAS FREQ procedure.
Risk Difference and related p-value are estimated by using the SAS GLIMMIX procedure with the following model: criterion = treatment.
p-values for heterogeneity are estimated by using the SAS GLIMMIX procedure with the following model: criterion = treatment subgroup treatment*subgroup.
p-value for heterogeneity of Peto Odds Ratio is estimated by using normal approximation.
PGM=DEVOPS/SAR231893/EFC14153/CSR_RWE/REPORT/PGM/ae_evt_ger_subg_s2_t.sas OUT=REPORT/OUTPUT/ae_teaesev_ger_cty_s2_t_x.rtf (12AUG2021 - 9:11)

Project Code / Study Number / Analysis: SAR231893 / EFC14153 / CSR_RWE

2 Adverse events - Safety type 2 inflammatory asthma phenotype population

2.3 Patients with any TEAE severe

2.3.2 By region (Latin America, East Europe, Western Countries)

	Region					
	Latin America		East Europe		Western countries	
Safety type 2 inflammatory asthma phenotype population	**Placebo (N=51)**	**Dupilumab (N=105)**	**Placebo (N=43)**	**Dupilumab (N=78)**	**Placebo (N=19)**	**Dupilumab (N=51)**
p-value for heterogeneity of Risk Difference:						
Latin America, East Europe						0.548
Latin America, Western countries						0.945
East Europe, Western countries						<0.001
overall						0.945

Odds Ratio and related p-value are estimated by Wald's method using the SAS LOGISTIC procedure.
Peto OR calculation is based on Yusuf S et al. (Prog Cardiovasc Dis. 1985 Mar-Apr;27(5):335-71) and its p-value is derived using a normal approximation.
Risk Ratio and related p-value are estimated by using the SAS FREQ procedure.
Risk Difference and related p-value are estimated by using the SAS GLIMMIX procedure with the following model: criterion = treatment.
p-values for heterogeneity are estimated by using the SAS GLIMMIX procedure with the following model: criterion = treatment subgroup treatment*subgroup.
p-value for heterogeneity of Peto Odds Ratio is estimated by using normal approximation.
PGM=DEVOPS/SAR231893/EFC14153/CSR_RWE/REPORT/PGM/ae_evt_ger_subg_s2_t.sas OUT=REPORT/OUTPUT/ae_teaesev_ger_cty_s2_t_x.rtf (12AUG2021 - 9:11)

Project Code / Study Number / Analysis: SAR231893 / EFC14153 / CSR_RWE

2 Adverse events - Safety type 2 inflammatory asthma phenotype population

2.3 Patients with any TEAE severe

2.3.3 By race (Caucasian/white, Black/of African descent, Other)

	Race					
	Caucasian/White		Black/of African descent		Other	
Safety type 2 inflammatory asthma phenotype population	**Placebo (N=101)**	**Dupilumab (N=207)**	**Placebo (N=5)**	**Dupilumab (N=9)**	**Placebo (N=7)**	**Dupilumab (N=18)**
Patients with any TEAE severe [n(%)]	5 (5.0%)	7 (3.4%)	0	0	1 (14.3%)	1 (5.6%)
Odds Ratio (95% CI)	-	0.67 (0.21 to 2.17)	-	NE (NE to NE)	-	0.35 (0.02 to 6.57)
p-value for Odds Ratio		0.507		NE		0.485
Peto Odds Ratio (95% CI)	-	0.66 (0.19 to 2.25)	-	NE (NE to NE)	-	0.32 (0.01 to 7.50)
p-value for Peto Odds Ratio		0.505		NE		0.479
p-value for heterogeneity of Peto Odds Ratio:						
Caucasian/White, Black/of African descent						NE
Caucasian/White, Other						0.676
Black/of African descent, Other						NE
overall						NE
Risk Ratio (95% CI)	-	0.68 (0.22 to 2.10)	-	NE (NE to NE)	-	0.39 (0.03 to 5.40)

Odds Ratio and related p-value are estimated by Wald's method using the SAS LOGISTIC procedure.
Peto OR calculation is based on Yusuf S et al. (Prog Cardiovasc Dis. 1985 Mar-Apr;27(5):335-71) and its p-value is derived using a normal approximation.
Risk Ratio and related p-value are estimated by using the SAS FREQ procedure.
Risk Difference and related p-value are estimated by using the SAS GLIMMIX procedure with the following model: criterion = treatment.
p-values for heterogeneity are estimated by using the SAS GLIMMIX procedure with the following model: criterion = treatment subgroup treatment*subgroup.
p-value for heterogeneity of Peto Odds Ratio is estimated by using normal approximation.
PGM=DEVOPS/SAR231893/EFC14153/CSR_RWE/REPORT/PGM/ae_evt_ger_subg_s2_t.sas OUT=REPORT/OUTPUT/ae_teaesev_ger_race_s2_t_x.rtf (12AUG2021 - 9:11)

Project Code / Study Number / Analysis: SAR231893 / EFC14153 / CSR_RWE

2 Adverse events - Safety type 2 inflammatory asthma phenotype population

2.3 Patients with any TEAE severe

2.3.3 By race (Caucasian/white, Black/of African descent, Other)

	Race					
	Caucasian/White		Black/of African descent		Other	
Safety type 2 inflammatory asthma phenotype population	**Placebo (N=101)**	**Dupilumab (N=207)**	**Placebo (N=5)**	**Dupilumab (N=9)**	**Placebo (N=7)**	**Dupilumab (N=18)**
p-value for Risk Ratio		0.506		NE		0.482
p-value for heterogeneity of Risk Ratio:						
Caucasian/White, Black/of African descent						1.000
Caucasian/White, Other						0.700
Black/of African descent, Other						0.999
overall						0.928
Risk Difference (95% CI)	-	-1.57 (-6.48 to 3.35)	-	0.00 (NE to NE)	-	-8.73 (-38.28 to 20.82)
p-value for Risk Difference		0.530		NE		0.547
p-value for heterogeneity of Risk Difference:						
Caucasian/White, Black/of African descent						0.914
Caucasian/White, Other						0.622
Black/of African descent, Other						<0.001
overall						0.622

Odds Ratio and related p-value are estimated by Wald's method using the SAS LOGISTIC procedure.
Peto OR calculation is based on Yusuf S et al. (Prog Cardiovasc Dis. 1985 Mar-Apr;27(5):335-71) and its p-value is derived using a normal approximation.
Risk Ratio and related p-value are estimated by using the SAS FREQ procedure.
Risk Difference and related p-value are estimated by using the SAS GLIMMIX procedure with the following model: criterion = treatment.
p-values for heterogeneity are estimated by using the SAS GLIMMIX procedure with the following model: criterion = treatment subgroup treatment*subgroup.
p-value for heterogeneity of Peto Odds Ratio is estimated by using normal approximation.
PGM=DEVOPS/SAR231893/EFC14153/CSR_RWE/REPORT/PGM/ae_evt_ger_subg_s2_t.sas OUT=REPORT/OUTPUT/ae_teaesev_ger_race_s2_t_x.rtf (12AUG2021 - 9:11)

Project Code / Study Number / Analysis: SAR231893 / EFC14153 / CSR_RWE

2 Adverse events - Safety type 2 inflammatory asthma phenotype population

2.3 Patients with any TEAE severe

2.3.4 By baseline ICS dose level (Medium, High)

	Baseline ICS dose level			
	High		Medium	
Safety type 2 inflammatory asthma phenotype population	**Placebo (N=50)**	**Dupilumab (N=101)**	**Placebo (N=63)**	**Dupilumab (N=131)**
Patients with any TEAE severe [n(%)]	1 (2.0%)	3 (3.0%)	5 (7.9%)	5 (3.8%)
Odds Ratio (95% CI)	-	1.50 (0.15 to 14.80)	-	0.46 (0.13 to 1.65)
p-value for Odds Ratio		0.728		0.234
p-value for heterogeneity of Odds Ratio				0.378
Risk Ratio (95% CI)	-	1.49 (0.16 to 13.92)	-	0.48 (0.14 to 1.60)
Reversed Risk ratio (95% CI)	-	0.67 (0.07 to 6.31)		
p-value for Risk Ratio		0.729		0.233
p-value for heterogeneity of Risk Ratio				0.385
Risk Difference (95% CI)	-	0.97 (-4.17 to 6.11)	-	-4.12 (-11.60 to 3.37)

Odds Ratio and related p-value are estimated by Wald's method using the SAS LOGISTIC procedure.
Peto OR calculation is based on Yusuf S et al. (Prog Cardiovasc Dis. 1985 Mar-Apr;27(5):335-71) and its p-value is derived using a normal approximation.
Risk Ratio and related p-value are estimated by using the SAS FREQ procedure.
Risk Difference and related p-value are estimated by using the SAS GLIMMIX procedure with the following model: criterion = treatment.
p-values for heterogeneity are estimated by using the SAS GLIMMIX procedure with the following model: criterion = treatment subgroup treatment*subgroup.
p-value for heterogeneity of Peto Odds Ratio is estimated by using normal approximation.
PGM=DEVOPS/SAR231893/EFC14153/CSR_RWE/REPORT/PGM/ae_evt_ger_subg_s2_t.sas OUT=REPORT/OUTPUT/ae_teaesev_ger_ics_s2_t_x.rtf (12AUG2021 - 9:11)

Project Code / Study Number / Analysis: SAR231893 / EFC14153 / CSR_RWE

2 Adverse events - Safety type 2 inflammatory asthma phenotype population

2.3 Patients with any TEAE severe

2.3.4 By baseline ICS dose level (Medium, High)

	Baseline ICS dose level			
	High		Medium	
Safety type 2 inflammatory asthma phenotype population	**Placebo (N=50)**	**Dupilumab (N=101)**	**Placebo (N=63)**	**Dupilumab (N=131)**
p-value for Risk Difference		0.710		0.279
p-value for heterogeneity of Risk Difference				0.269

Odds Ratio and related p-value are estimated by Wald's method using the SAS LOGISTIC procedure.
Peto OR calculation is based on Yusuf S et al. (Prog Cardiovasc Dis. 1985 Mar-Apr;27(5):335-71) and its p-value is derived using a normal approximation.
Risk Ratio and related p-value are estimated by using the SAS FREQ procedure.
Risk Difference and related p-value are estimated by using the SAS GLIMMIX procedure with the following model: criterion = treatment.
p-values for heterogeneity are estimated by using the SAS GLIMMIX procedure with the following model: criterion = treatment subgroup treatment*subgroup.
p-value for heterogeneity of Peto Odds Ratio is estimated by using normal approximation.
PGM=DEVOPS/SAR231893/EFC14153/CSR_RWE/REPORT/PGM/ae_evt_ger_subg_s2_t.sas OUT=REPORT/OUTPUT/ae_teaesev_ger_ics_s2_t_x.rtf (12AUG2021 - 9:11)

Project Code / Study Number / Analysis: SAR231893 / EFC14153 / CSR_RWE

2 Adverse events - Safety type 2 inflammatory asthma phenotype population

2.3 Patients with any TEAE severe

2.3.5 By baseline ICS dose level 2 (Medium, High)

Safety type 2 inflammatory asthma phenotype population	Baseline ICS dose level 2			
	High		Medium	
	Placebo (N=94)	Dupilumab (N=199)	Placebo (N=19)	Dupilumab (N=35)
Patients with any TEAE severe [n(%)]	5 (5.3%)	5 (2.5%)	1 (5.3%)	3 (8.6%)
Odds Ratio (95% CI)	-	0.46 (0.13 to 1.62)	-	1.69 (0.16 to 17.44)
p-value for Odds Ratio		0.227		0.661
p-value for heterogeneity of Odds Ratio				0.337
Risk Ratio (95% CI)	-	0.47 (0.14 to 1.59)	-	1.63 (0.18 to 14.60)
Reversed Risk ratio (95% CI)			-	0.61 (0.07 to 5.50)
p-value for Risk Ratio		0.226		0.663
p-value for heterogeneity of Risk Ratio				0.334
Risk Difference (95% CI)	-	-2.81 (-7.86 to 2.25)	-	3.31 (-10.69 to 17.30)

Odds Ratio and related p-value are estimated by Wald's method using the SAS LOGISTIC procedure.
Peto OR calculation is based on Yusuf S et al. (Prog Cardiovasc Dis. 1985 Mar-Apr;27(5):335-71) and its p-value is derived using a normal approximation.
Risk Ratio and related p-value are estimated by using the SAS FREQ procedure.
Risk Difference and related p-value are estimated by using the SAS GLIMMIX procedure with the following model: criterion = treatment.
p-values for heterogeneity are estimated by using the SAS GLIMMIX procedure with the following model: criterion = treatment subgroup treatment*subgroup.
p-value for heterogeneity of Peto Odds Ratio is estimated by using normal approximation.
PGM=DEVOPS/SAR231893/EFC14153/CSR_RWE/REPORT/PGM/ae_evt_ger_subg_s2_t.sas OUT=REPORT/OUTPUT/ae_teaesev_ger_ics2_s2_t_x.rtf (01SEP2021 - 16:10)

Project Code / Study Number / Analysis: SAR231893 / EFC14153 / CSR_RWE

2 Adverse events - Safety type 2 inflammatory asthma phenotype population

2.3 Patients with any TEAE severe

2.3.5 By baseline ICS dose level 2 (Medium, High)

	Baseline ICS dose level 2			
	High		Medium	
Safety type 2 inflammatory asthma phenotype population	**Placebo (N=94)**	**Dupilumab (N=199)**	**Placebo (N=19)**	**Dupilumab (N=35)**
p-value for Risk Difference		0.275		0.637
p-value for heterogeneity of Risk Difference				0.411

Odds Ratio and related p-value are estimated by Wald's method using the SAS LOGISTIC procedure.
Peto OR calculation is based on Yusuf S et al. (Prog Cardiovasc Dis. 1985 Mar-Apr;27(5):335-71) and its p-value is derived using a normal approximation.
Risk Ratio and related p-value are estimated by using the SAS FREQ procedure.
Risk Difference and related p-value are estimated by using the SAS GLIMMIX procedure with the following model: criterion = treatment.
p-values for heterogeneity are estimated by using the SAS GLIMMIX procedure with the following model: criterion = treatment subgroup treatment*subgroup.
p-value for heterogeneity of Peto Odds Ratio is estimated by using normal approximation.
PGM=DEVOPS/SAR231893/EFC14153/CSR_RWE/REPORT/PGM/ae_evt_ger_subg_s2_t.sas OUT=REPORT/OUTPUT/ae_teaesev_ger_ics2_s2_t_x.rtf (01SEP2021 - 16:10)

Project Code / Study Number / Analysis: SAR231893 / EFC14153 / CSR_RWE

2 Adverse events - Safety type 2 inflammatory asthma phenotype population

2.3 Patients with any TEAE severe

2.3.6 By baseline predicted FEV1 (<80%, >=80%)

	Baseline Predicted FEV1			
	<80%		>=80%	
Safety type 2 inflammatory asthma phenotype population	**Placebo (N=58)**	**Dupilumab (N=116)**	**Placebo (N=55)**	**Dupilumab (N=118)**
Patients with any TEAE severe [n(%)]	3 (5.2%)	4 (3.4%)	3 (5.5%)	4 (3.4%)
Odds Ratio (95% CI)	-	0.65 (0.14 to 3.03)	-	0.61 (0.13 to 2.82)
p-value for Odds Ratio		0.588		0.525
p-value for heterogeneity of Odds Ratio				0.947
Risk Ratio (95% CI)	-	0.67 (0.15 to 2.88)	-	0.62 (0.14 to 2.68)
p-value for Risk Ratio		0.587		0.524
p-value for heterogeneity of Risk Ratio				0.947
Risk Difference (95% CI)	-	-1.72 (-8.37 to 4.92)	-	-2.06 (-8.95 to 4.82)
p-value for Risk Difference		0.609		0.554

Odds Ratio and related p-value are estimated by Wald's method using the SAS LOGISTIC procedure.
Peto OR calculation is based on Yusuf S et al. (Prog Cardiovasc Dis. 1985 Mar-Apr;27(5):335-71) and its p-value is derived using a normal approximation.
Risk Ratio and related p-value are estimated by using the SAS FREQ procedure.
Risk Difference and related p-value are estimated by using the SAS GLIMMIX procedure with the following model: criterion = treatment.
p-values for heterogeneity are estimated by using the SAS GLIMMIX procedure with the following model: criterion = treatment subgroup treatment*subgroup.
p-value for heterogeneity of Peto Odds Ratio is estimated by using normal approximation.
PGM=DEVOPS/SAR231893/EFC14153/CSR_RWE/REPORT/PGM/ae_evt_ger_subg_s2_t.sas OUT=REPORT/OUTPUT/ae_teaesev_ger_pfev1_s2_t_x.rtf (12AUG2021 - 9:11)

Project Code / Study Number / Analysis: SAR231893 / EFC14153 / CSR_RWE

2 Adverse events - Safety type 2 inflammatory asthma phenotype population

2.3 Patients with any TEAE severe

2.3.6 By baseline predicted FEV1 (<80%, >=80%)

	Baseline Predicted FEV1			
	<80%		>=80%	
Safety type 2 inflammatory asthma phenotype population	**Placebo (N=58)**	**Dupilumab (N=116)**	**Placebo (N=55)**	**Dupilumab (N=118)**
p-value for heterogeneity of Risk Difference				0.944

Odds Ratio and related p-value are estimated by Wald's method using the SAS LOGISTIC procedure.
Peto OR calculation is based on Yusuf S et al. (Prog Cardiovasc Dis. 1985 Mar-Apr;27(5):335-71) and its p-value is derived using a normal approximation.
Risk Ratio and related p-value are estimated by using the SAS FREQ procedure.
Risk Difference and related p-value are estimated by using the SAS GLIMMIX procedure with the following model: criterion = treatment.
p-values for heterogeneity are estimated by using the SAS GLIMMIX procedure with the following model: criterion = treatment subgroup treatment*subgroup.
p-value for heterogeneity of Peto Odds Ratio is estimated by using normal approximation.
PGM=DEVOPS/SAR231893/EFC14153/CSR_RWE/REPORT/PGM/ae_evt_ger_subg_s2_t.sas OUT=REPORT/OUTPUT/ae_teaesev_ger_pfev1_s2_t_x.rtf (12AUG2021 - 9:11)

Project Code / Study Number / Analysis: SAR231893 / EFC14153 / CSR_RWE

2 Adverse events - Safety type 2 inflammatory asthma phenotype population

2.3 Patients with any TEAE severe

2.3.7 By baseline ACQ-7-IA (<=2, >2)

	Baseline ACQ-7-IA			
	<=2		>2	
Safety type 2 inflammatory asthma phenotype population	**Placebo (N=61)**	**Dupilumab (N=125)**	**Placebo (N=52)**	**Dupilumab (N=109)**
Patients with any TEAE severe [n(%)]	4 (6.6%)	5 (4.0%)	2 (3.8%)	3 (2.8%)
Odds Ratio (95% CI)	-	0.59 (0.15 to 2.30)	-	0.71 (0.11 to 4.37)
p-value for Odds Ratio		0.450		0.709
p-value for heterogeneity of Odds Ratio				0.880
Risk Ratio (95% CI)	-	0.61 (0.17 to 2.19)	-	0.72 (0.12 to 4.15)
p-value for Risk Ratio		0.449		0.709
p-value for heterogeneity of Risk Ratio				0.886
Risk Difference (95% CI)	-	-2.56 (-9.70 to 4.59)	-	-1.09 (-7.20 to 5.02)
p-value for Risk Difference		0.481		0.724

Odds Ratio and related p-value are estimated by Wald's method using the SAS LOGISTIC procedure.
Peto OR calculation is based on Yusuf S et al. (Prog Cardiovasc Dis. 1985 Mar-Apr;27(5):335-71) and its p-value is derived using a normal approximation.
Risk Ratio and related p-value are estimated by using the SAS FREQ procedure.
Risk Difference and related p-value are estimated by using the SAS GLIMMIX procedure with the following model: criterion = treatment.
p-values for heterogeneity are estimated by using the SAS GLIMMIX procedure with the following model: criterion = treatment subgroup treatment*subgroup.
p-value for heterogeneity of Peto Odds Ratio is estimated by using normal approximation.
PGM=DEVOPS/SAR231893/EFC14153/CSR_RWE/REPORT/PGM/ae_evt_ger_subg_s2_t.sas OUT=REPORT/OUTPUT/ae_teaesev_ger_acq7_s2_t_x.rtf (12AUG2021 - 9:11)

Project Code / Study Number / Analysis: SAR231893 / EFC14153 / CSR_RWE

2 Adverse events - Safety type 2 inflammatory asthma phenotype population

2.3 Patients with any TEAE severe

2.3.7 By baseline ACQ-7-IA (<=2, >2)

	Baseline ACQ-7-IA			
	<=2		>2	
Safety type 2 inflammatory asthma phenotype population	**Placebo (N=61)**	**Dupilumab (N=125)**	**Placebo (N=52)**	**Dupilumab (N=109)**
p-value for heterogeneity of Risk Difference				0.759

Odds Ratio and related p-value are estimated by Wald's method using the SAS LOGISTIC procedure.
Peto OR calculation is based on Yusuf S et al. (Prog Cardiovasc Dis. 1985 Mar-Apr;27(5):335-71) and its p-value is derived using a normal approximation.
Risk Ratio and related p-value are estimated by using the SAS FREQ procedure.
Risk Difference and related p-value are estimated by using the SAS GLIMMIX procedure with the following model: criterion = treatment.
p-values for heterogeneity are estimated by using the SAS GLIMMIX procedure with the following model: criterion = treatment subgroup treatment*subgroup.
p-value for heterogeneity of Peto Odds Ratio is estimated by using normal approximation.
PGM=DEVOPS/SAR231893/EFC14153/CSR_RWE/REPORT/PGM/ae_evt_ger_subg_s2_t.sas OUT=REPORT/OUTPUT/ae_teaesev_ger_acq7_s2_t_x.rtf (12AUG2021 - 9:11)

Project Code / Study Number / Analysis: SAR231893 / EFC14153 / CSR_RWE

2 Adverse events - Safety type 2 inflammatory asthma phenotype population

2.3 Patients with any TEAE severe

2.3.8 By baseline weight (<=30 kg, >30 kg)

	Baseline weight (kg)			
	<=30		>30	
Safety type 2 inflammatory asthma phenotype population	**Placebo (N=36)**	**Dupilumab (N=74)**	**Placebo (N=77)**	**Dupilumab (N=160)**
Patients with any TEAE severe [n(%)]	1 (2.8%)	1 (1.4%)	5 (6.5%)	7 (4.4%)
Odds Ratio (95% CI)	-	0.48 (0.03 to 7.89)	-	0.66 (0.20 to 2.15)
p-value for Odds Ratio		0.607		0.489
p-value for heterogeneity of Odds Ratio				0.838
Risk Ratio (95% CI)	-	0.49 (0.03 to 7.56)	-	0.67 (0.22 to 2.05)
p-value for Risk Ratio		0.607		0.488
p-value for heterogeneity of Risk Ratio				0.829
Risk Difference (95% CI)	-	-1.43 (-7.47 to 4.62)	-	-2.12 (-8.50 to 4.27)
p-value for Risk Difference		0.641		0.514

Odds Ratio and related p-value are estimated by Wald's method using the SAS LOGISTIC procedure.
Peto OR calculation is based on Yusuf S et al. (Prog Cardiovasc Dis. 1985 Mar-Apr;27(5):335-71) and its p-value is derived using a normal approximation.
Risk Ratio and related p-value are estimated by using the SAS FREQ procedure.
Risk Difference and related p-value are estimated by using the SAS GLIMMIX procedure with the following model: criterion = treatment.
p-values for heterogeneity are estimated by using the SAS GLIMMIX procedure with the following model: criterion = treatment subgroup treatment*subgroup.
p-value for heterogeneity of Peto Odds Ratio is estimated by using normal approximation.
PGM=DEVOPS/SAR231893/EFC14153/CSR_RWE/REPORT/PGM/ae_evt_ger_subg_s2_t.sas OUT=REPORT/OUTPUT/ae_teaesev_ger_wgt_s2_t_x.rtf (12AUG2021 - 9:12)

Project Code / Study Number / Analysis: SAR231893 / EFC14153 / CSR_RWE

2 Adverse events - Safety type 2 inflammatory asthma phenotype population

2.3 Patients with any TEAE severe

2.3.8 By baseline weight (<=30 kg, >30 kg)

	Baseline weight (kg)			
	<=30		>30	
Safety type 2 inflammatory asthma phenotype population	**Placebo (N=36)**	**Dupilumab (N=74)**	**Placebo (N=77)**	**Dupilumab (N=160)**
p-value for heterogeneity of Risk Difference				0.877

Odds Ratio and related p-value are estimated by Wald's method using the SAS LOGISTIC procedure.
Peto OR calculation is based on Yusuf S et al. (Prog Cardiovasc Dis. 1985 Mar-Apr;27(5):335-71) and its p-value is derived using a normal approximation.
Risk Ratio and related p-value are estimated by using the SAS FREQ procedure.
Risk Difference and related p-value are estimated by using the SAS GLIMMIX procedure with the following model: criterion = treatment.
p-values for heterogeneity are estimated by using the SAS GLIMMIX procedure with the following model: criterion = treatment subgroup treatment*subgroup.
p-value for heterogeneity of Peto Odds Ratio is estimated by using normal approximation.
PGM=DEVOPS/SAR231893/EFC14153/CSR_RWE/REPORT/PGM/ae_evt_ger_subg_s2_t.sas OUT=REPORT/OUTPUT/ae_teaesev_ger_wgt_s2_t_x.rtf (12AUG2021 - 9:12)

Project Code / Study Number / Analysis: SAR231893 / EFC14153 / CSR_RWE

2 Adverse events - Safety type 2 inflammatory asthma phenotype population

2.3 Patients with any TEAE severe

2.3.9 By atopic medical condition (Yes, No)

	Atopic medical condition			
	Yes		No	
Safety type 2 inflammatory asthma phenotype population	**Placebo (N=102)**	**Dupilumab (N=225)**	**Placebo (N=11)**	**Dupilumab (N=9)**
Patients with any TEAE severe [n(%)]	6 (5.9%)	7 (3.1%)	0	1 (11.1%)
Odds Ratio (95% CI)	-	0.51 (0.17 to 1.57)	-	NE (NE to NE)
p-value for Odds Ratio		0.242		NE
Peto Odds Ratio (95% CI)	-	0.48 (0.15 to 1.60)	-	9.23 (0.18 to 474.33)
Reversed Peto Odds Ratio (95% CI)			-	0.11 (0.00 to 5.56)
p-value for Peto Odds Ratio		0.235		0.269
p-value for heterogeneity of Peto Odds Ratio				0.161
Risk Ratio (95% CI)	-	0.53 (0.18 to 1.53)	-	NE (NE to NE)
p-value for Risk Ratio		0.241		NE
p-value for heterogeneity of Risk Ratio				0.973

Odds Ratio and related p-value are estimated by Wald's method using the SAS LOGISTIC procedure.
Peto OR calculation is based on Yusuf S et al. (Prog Cardiovasc Dis. 1985 Mar-Apr;27(5):335-71) and its p-value is derived using a normal approximation.
Risk Ratio and related p-value are estimated by using the SAS FREQ procedure.
Risk Difference and related p-value are estimated by using the SAS GLIMMIX procedure with the following model: criterion = treatment.
p-values for heterogeneity are estimated by using the SAS GLIMMIX procedure with the following model: criterion = treatment subgroup treatment*subgroup.
p-value for heterogeneity of Peto Odds Ratio is estimated by using normal approximation.
PGM=DEVOPS/SAR231893/EFC14153/CSR_RWE/REPORT/PGM/ae_evt_ger_subg_s2_t.sas OUT=REPORT/OUTPUT/ae_teaesev_ger_amc_s2_t_x.rtf (12AUG2021 - 9:12)

Project Code / Study Number / Analysis: SAR231893 / EFC14153 / CSR_RWE

2 Adverse events - Safety type 2 inflammatory asthma phenotype population

2.3 Patients with any TEAE severe

2.3.9 By atopic medical condition (Yes, No)

	Atopic medical condition			
	Yes		No	
Safety type 2 inflammatory asthma phenotype population	**Placebo (N=102)**	**Dupilumab (N=225)**	**Placebo (N=11)**	**Dupilumab (N=9)**
Risk Difference (95% CI)	-	-2.77 (-7.89 to 2.35)	-	11.11 (NE to NE)
p-value for Risk Difference		0.288		<0.001
p-value for heterogeneity of Risk Difference				<0.001

Odds Ratio and related p-value are estimated by Wald's method using the SAS LOGISTIC procedure.
Peto OR calculation is based on Yusuf S et al. (Prog Cardiovasc Dis. 1985 Mar-Apr;27(5):335-71) and its p-value is derived using a normal approximation.
Risk Ratio and related p-value are estimated by using the SAS FREQ procedure.
Risk Difference and related p-value are estimated by using the SAS GLIMMIX procedure with the following model: criterion = treatment.
p-values for heterogeneity are estimated by using the SAS GLIMMIX procedure with the following model: criterion = treatment subgroup treatment*subgroup.
p-value for heterogeneity of Peto Odds Ratio is estimated by using normal approximation.
PGM=DEVOPS/SAR231893/EFC14153/CSR_RWE/REPORT/PGM/ae_evt_ger_subg_s2_t.sas OUT=REPORT/OUTPUT/ae_teaesev_ger_amc_s2_t_x.rtf (12AUG2021 - 9:12)

Project Code / Study Number / Analysis: SAR231893 / EFC14153 / CSR_RWE

2 Adverse events - Safety type 2 inflammatory asthma phenotype population

2.3 Patients with any TEAE severe

2.3.10 By baseline total IgE (<median, >= median)

	Baseline Total IgE (IU/mL)			
	<median		>=median	
Safety type 2 inflammatory asthma phenotype population	**Placebo (N=65)**	**Dupilumab (N=106)**	**Placebo (N=47)**	**Dupilumab (N=124)**
Patients with any TEAE severe [n(%)]	1 (1.5%)	5 (4.7%)	5 (10.6%)	2 (1.6%)
Odds Ratio (95% CI)	-	3.17 (0.36 to 27.72)	-	0.14 (0.03 to 0.74)
p-value for Odds Ratio		0.298		0.020
p-value for heterogeneity of Odds Ratio				0.026
Risk Ratio (95% CI)	-	3.07 (0.37 to 25.66)	-	0.15 (0.03 to 0.75)
Reversed Risk ratio (95% CI)	-	0.33 (0.04 to 2.73)		
p-value for Risk Ratio		0.301		0.021
p-value for heterogeneity of Risk Ratio				0.028
Risk Difference (95% CI)	-	3.18 (-1.88 to 8.24)	-	-9.03 (-18.18 to 0.13)

Odds Ratio and related p-value are estimated by Wald's method using the SAS LOGISTIC procedure.
Peto OR calculation is based on Yusuf S et al. (Prog Cardiovasc Dis. 1985 Mar-Apr;27(5):335-71) and its p-value is derived using a normal approximation.
Risk Ratio and related p-value are estimated by using the SAS FREQ procedure.
Risk Difference and related p-value are estimated by using the SAS GLIMMIX procedure with the following model: criterion = treatment.
p-values for heterogeneity are estimated by using the SAS GLIMMIX procedure with the following model: criterion = treatment subgroup treatment*subgroup.
p-value for heterogeneity of Peto Odds Ratio is estimated by using normal approximation.
PGM=DEVOPS/SAR231893/EFC14153/CSR_RWE/REPORT/PGM/ae_evt_ger_subg_s2_t.sas OUT=REPORT/OUTPUT/ae_teaesev_ger_igem_s2_t_x.rtf (12AUG2021 - 9:12)

Project Code / Study Number / Analysis: SAR231893 / EFC14153 / CSR_RWE

2 Adverse events - Safety type 2 inflammatory asthma phenotype population

2.3 Patients with any TEAE severe

2.3.10 By baseline total IgE (<median, >= median)

	Baseline Total IgE (IU/mL)			
	<median		>=median	
Safety type 2 inflammatory asthma phenotype population	**Placebo (N=65)**	**Dupilumab (N=106)**	**Placebo (N=47)**	**Dupilumab (N=124)**
p-value for Risk Difference		0.217		0.053
p-value for heterogeneity of Risk Difference				0.022

Odds Ratio and related p-value are estimated by Wald's method using the SAS LOGISTIC procedure.
Peto OR calculation is based on Yusuf S et al. (Prog Cardiovasc Dis. 1985 Mar-Apr;27(5):335-71) and its p-value is derived using a normal approximation.
Risk Ratio and related p-value are estimated by using the SAS FREQ procedure.
Risk Difference and related p-value are estimated by using the SAS GLIMMIX procedure with the following model: criterion = treatment.
p-values for heterogeneity are estimated by using the SAS GLIMMIX procedure with the following model: criterion = treatment subgroup treatment*subgroup.
p-value for heterogeneity of Peto Odds Ratio is estimated by using normal approximation.
PGM=DEVOPS/SAR231893/EFC14153/CSR_RWE/REPORT/PGM/ae_evt_ger_subg_s2_t.sas OUT=REPORT/OUTPUT/ae_teaesev_ger_igem_s2_t_x.rtf (12AUG2021 - 9:12)

Project Code / Study Number / Analysis: SAR231893 / EFC14153 / CSR_RWE

2 Adverse events - Safety type 2 inflammatory asthma phenotype population

2.3 Patients with any TEAE severe

2.3.11 By baseline total IgE (<100 IU/ml, >= 100 IU/ml)

	Baseline Total IgE (IU/mL)			
	< 100		>= 100	
Safety type 2 inflammatory asthma phenotype population	**Placebo (N=22)**	**Dupilumab (N=29)**	**Placebo (N=90)**	**Dupilumab (N=201)**
Patients with any TEAE severe [n(%)]	0	2 (6.9%)	6 (6.7%)	5 (2.5%)
Odds Ratio (95% CI)	-	NE (NE to NE)	-	0.36 (0.11 to 1.20)
p-value for Odds Ratio		NE		0.096
Peto Odds Ratio (95% CI)	-	6.02 (0.36 to 101.62)	-	0.32 (0.09 to 1.17)
Reversed Peto Odds Ratio (95% CI)	-	0.17 (0.01 to 2.78)		
p-value for Peto Odds Ratio		0.213		0.085
p-value for heterogeneity of Peto Odds Ratio				0.064
Risk Ratio (95% CI)	-	NE (NE to NE)	-	0.37 (0.12 to 1.19)
p-value for Risk Ratio		NE		0.096
p-value for heterogeneity of Risk Ratio				0.975

Odds Ratio and related p-value are estimated by Wald's method using the SAS LOGISTIC procedure.
Peto OR calculation is based on Yusuf S et al. (Prog Cardiovasc Dis. 1985 Mar-Apr;27(5):335-71) and its p-value is derived using a normal approximation.
Risk Ratio and related p-value are estimated by using the SAS FREQ procedure.
Risk Difference and related p-value are estimated by using the SAS GLIMMIX procedure with the following model: criterion = treatment.
p-values for heterogeneity are estimated by using the SAS GLIMMIX procedure with the following model: criterion = treatment subgroup treatment*subgroup.
p-value for heterogeneity of Peto Odds Ratio is estimated by using normal approximation.
PGM=DEVOPS/SAR231893/EFC14153/CSR_RWE/REPORT/PGM/ae_evt_ger_subg_s2_t.sas OUT=REPORT/OUTPUT/ae_teaesev_ger_ige_s2_t_x.rtf (12AUG2021 - 9:12)

Project Code / Study Number / Analysis: SAR231893 / EFC14153 / CSR_RWE

2 Adverse events - Safety type 2 inflammatory asthma phenotype population

2.3 Patients with any TEAE severe

2.3.11 By baseline total IgE (<100 IU/ml, >= 100 IU/ml)

	Baseline Total IgE (IU/mL)			
	< 100		>= 100	
Safety type 2 inflammatory asthma phenotype population	**Placebo (N=22)**	**Dupilumab (N=29)**	**Placebo (N=90)**	**Dupilumab (N=201)**
Risk Difference (95% CI)	-	6.90 (NE to NE)	-	-4.18 (-9.79 to 1.43)
p-value for Risk Difference		<0.001		0.144
p-value for heterogeneity of Risk Difference				<0.001

Odds Ratio and related p-value are estimated by Wald's method using the SAS LOGISTIC procedure.
Peto OR calculation is based on Yusuf S et al. (Prog Cardiovasc Dis. 1985 Mar-Apr;27(5):335-71) and its p-value is derived using a normal approximation.
Risk Ratio and related p-value are estimated by using the SAS FREQ procedure.
Risk Difference and related p-value are estimated by using the SAS GLIMMIX procedure with the following model: criterion = treatment.
p-values for heterogeneity are estimated by using the SAS GLIMMIX procedure with the following model: criterion = treatment subgroup treatment*subgroup.
p-value for heterogeneity of Peto Odds Ratio is estimated by using normal approximation.
PGM=DEVOPS/SAR231893/EFC14153/CSR_RWE/REPORT/PGM/ae_evt_ger_subg_s2_t.sas OUT=REPORT/OUTPUT/ae_teaesev_ger_ige_s2_t_x.rtf (12AUG2021 - 9:12)

Project Code / Study Number / Analysis: SAR231893 / EFC14153 / CSR_RWE

2 Adverse events - Safety type 2 inflammatory asthma phenotype population

2.3 Patients with any TEAE severe

2.3.12 By age at onset of asthma (0-2, 3-5, >=6 years)

	Age of onset of asthma (years)					
	0-2		3-5		>= 6	
Safety type 2 inflammatory asthma phenotype population	**Placebo (N=40)**	**Dupilumab (N=104)**	**Placebo (N=38)**	**Dupilumab (N=85)**	**Placebo (N=35)**	**Dupilumab (N=45)**
Patients with any TEAE severe [n(%)]	2 (5.0%)	8 (7.7%)	3 (7.9%)	0	1 (2.9%)	0
Odds Ratio (95% CI)	-	1.58 (0.32 to 7.80)	-	0.00 (NE to NE)	-	0.00 (NE to NE)
p-value for Odds Ratio		0.572		NE		NE
Peto Odds Ratio (95% CI)	-	1.51 (0.36 to 6.32)	-	0.04 (0.00 to 0.44)	-	0.10 (0.00 to 5.29)
Reversed Peto Odds Ratio (95% CI)	-	0.66 (0.16 to 2.78)				
p-value for Peto Odds Ratio		0.571		0.009		0.257
p-value for heterogeneity of Peto Odds Ratio:						
0-2, 3-5						0.011
0-2, >= 6						0.208
3-5, >= 6						0.672
overall						0.028

Odds Ratio and related p-value are estimated by Wald's method using the SAS LOGISTIC procedure.
Peto OR calculation is based on Yusuf S et al. (Prog Cardiovasc Dis. 1985 Mar-Apr;27(5):335-71) and its p-value is derived using a normal approximation.
Risk Ratio and related p-value are estimated by using the SAS FREQ procedure.
Risk Difference and related p-value are estimated by using the SAS GLIMMIX procedure with the following model: criterion = treatment.
p-values for heterogeneity are estimated by using the SAS GLIMMIX procedure with the following model: criterion = treatment subgroup treatment*subgroup.
p-value for heterogeneity of Peto Odds Ratio is estimated by using normal approximation.
PGM=DEVOPS/SAR231893/EFC14153/CSR_RWE/REPORT/PGM/ae_evt_ger_subg_s2_t.sas OUT=REPORT/OUTPUT/ae_teaesev_ger_onsa_s2_t_x.rtf (12AUG2021 - 9:12)

Project Code / Study Number / Analysis: SAR231893 / EFC14153 / CSR_RWE

2 Adverse events - Safety type 2 inflammatory asthma phenotype population

2.3 Patients with any TEAE severe

2.3.12 By age at onset of asthma (0-2, 3-5, >=6 years)

	Age of onset of asthma (years)					
	0-2		3-5		>= 6	
Safety type 2 inflammatory asthma phenotype population	**Placebo (N=40)**	**Dupilumab (N=104)**	**Placebo (N=38)**	**Dupilumab (N=85)**	**Placebo (N=35)**	**Dupilumab (N=45)**
Risk Ratio (95% CI)	-	1.54 (0.34 to 6.94)	-	0.00 (NE to NE)	-	0.00 (NE to NE)
Reversed Risk ratio (95% CI)	-	0.65 (0.14 to 2.93)				
p-value for Risk Ratio		0.575		NE		NE
p-value for heterogeneity of Risk Ratio:						
0-2, 3-5						0.980
0-2, >= 6						0.986
3-5, >= 6						0.999
overall						1.000
Risk Difference (95% CI)	-	2.69 (-5.86 to 11.24)	-	-7.89 (NE to NE)	-	-2.86 (NE to NE)
p-value for Risk Difference		0.535		<0.001		<0.001
p-value for heterogeneity of Risk Difference:						

Odds Ratio and related p-value are estimated by Wald's method using the SAS LOGISTIC procedure.
Peto OR calculation is based on Yusuf S et al. (Prog Cardiovasc Dis. 1985 Mar-Apr;27(5):335-71) and its p-value is derived using a normal approximation.
Risk Ratio and related p-value are estimated by using the SAS FREQ procedure.
Risk Difference and related p-value are estimated by using the SAS GLIMMIX procedure with the following model: criterion = treatment.
p-values for heterogeneity are estimated by using the SAS GLIMMIX procedure with the following model: criterion = treatment subgroup treatment*subgroup.
p-value for heterogeneity of Peto Odds Ratio is estimated by using normal approximation.
PGM=DEVOPS/SAR231893/EFC14153/CSR_RWE/REPORT/PGM/ae_evt_ger_subg_s2_t.sas OUT=REPORT/OUTPUT/ae_teaesev_ger_onsa_s2_t_x.rtf (12AUG2021 - 9:12)

Project Code / Study Number / Analysis: SAR231893 / EFC14153 / CSR_RWE

2 Adverse events - Safety type 2 inflammatory asthma phenotype population

2.3 Patients with any TEAE severe

2.3.12 By age at onset of asthma (0-2, 3-5, >=6 years)

	Age of onset of asthma (years)					
	0-2		3-5		>= 6	
Safety type 2 inflammatory asthma phenotype population	**Placebo (N=40)**	**Dupilumab (N=104)**	**Placebo (N=38)**	**Dupilumab (N=85)**	**Placebo (N=35)**	**Dupilumab (N=45)**
0-2, 3-5						<0.001
0-2, >= 6						<0.001
3-5, >= 6						<0.001
overall						<0.001

Odds Ratio and related p-value are estimated by Wald's method using the SAS LOGISTIC procedure.
Peto OR calculation is based on Yusuf S et al. (Prog Cardiovasc Dis. 1985 Mar-Apr;27(5):335-71) and its p-value is derived using a normal approximation.
Risk Ratio and related p-value are estimated by using the SAS FREQ procedure.
Risk Difference and related p-value are estimated by using the SAS GLIMMIX procedure with the following model: criterion = treatment.
p-values for heterogeneity are estimated by using the SAS GLIMMIX procedure with the following model: criterion = treatment subgroup treatment*subgroup.
p-value for heterogeneity of Peto Odds Ratio is estimated by using normal approximation.
PGM=DEVOPS/SAR231893/EFC14153/CSR_RWE/REPORT/PGM/ae_evt_ger_subg_s2_t.sas OUT=REPORT/OUTPUT/ae_teaesev_ger_onsa_s2_t_x.rtf (12AUG2021 - 9:12)

Project Code / Study Number / Analysis: SAR231893 / EFC14153 / CSR_RWE

2 Adverse events - Safety type 2 inflammatory asthma phenotype population

2.3 Patients with any TEAE severe

2.3.13 By number of severe asthma exacerbation prior to the study (<=1, 2, >2)

	Number of severe asthma exacerbation prior to the study					
	<=1		2		>2	
Safety type 2 inflammatory asthma phenotype population	**Placebo (N=46)**	**Dupilumab (N=85)**	**Placebo (N=32)**	**Dupilumab (N=75)**	**Placebo (N=35)**	**Dupilumab (N=74)**
Patients with any TEAE severe [n(%)]	4 (8.7%)	2 (2.4%)	2 (6.3%)	1 (1.3%)	0	5 (6.8%)
Odds Ratio (95% CI)	-	0.25 (0.04 to 1.44)	-	0.20 (0.02 to 2.32)	-	NE (NE to NE)
p-value for Odds Ratio		0.121		0.199		NE
Peto Odds Ratio (95% CI)	-	0.24 (0.04 to 1.31)	-	0.17 (0.01 to 2.03)	-	4.62 (0.68 to 31.27)
Reversed Peto Odds Ratio (95% CI)					-	0.22 (0.03 to 1.47)
p-value for Peto Odds Ratio		0.099		0.160		0.117
p-value for heterogeneity of Peto Odds Ratio:						
<=1, 2						0.822
<=1, >2						0.023
2, >2						0.039

Odds Ratio and related p-value are estimated by Wald's method using the SAS LOGISTIC procedure.
Peto OR calculation is based on Yusuf S et al. (Prog Cardiovasc Dis. 1985 Mar-Apr;27(5):335-71) and its p-value is derived using a normal approximation.
Risk Ratio and related p-value are estimated by using the SAS FREQ procedure.
Risk Difference and related p-value are estimated by using the SAS GLIMMIX procedure with the following model: criterion = treatment.
p-values for heterogeneity are estimated by using the SAS GLIMMIX procedure with the following model: criterion = treatment subgroup treatment*subgroup.
p-value for heterogeneity of Peto Odds Ratio is estimated by using normal approximation.
PGM=DEVOPS/SAR231893/EFC14153/CSR_RWE/REPORT/PGM/ae_evt_ger_subg_s2_t.sas OUT=REPORT/OUTPUT/ae_teaesev_ger_exa_s2_t_x.rtf (12AUG2021 - 9:13)

Project Code / Study Number / Analysis: SAR231893 / EFC14153 / CSR_RWE

2 Adverse events - Safety type 2 inflammatory asthma phenotype population

2.3 Patients with any TEAE severe

2.3.13 By number of severe asthma exacerbation prior to the study (<=1, 2, >2)

	Number of severe asthma exacerbation prior to the study					
	<=1		2		>2	
Safety type 2 inflammatory asthma phenotype population	**Placebo (N=46)**	**Dupilumab (N=85)**	**Placebo (N=32)**	**Dupilumab (N=75)**	**Placebo (N=35)**	**Dupilumab (N=74)**
overall						0.039
Risk Ratio (95% CI)	-	0.27 (0.05 to 1.42)	-	0.21 (0.02 to 2.27)	-	NE (NE to NE)
p-value for Risk Ratio		0.123		0.200		NE
p-value for heterogeneity of Risk Ratio:						
<=1, 2						0.872
<=1, >2						0.968
2, >2						0.967
overall						0.986
Risk Difference (95% CI)	-	-6.34 (-15.18 to 2.50)	-	-4.92 (-13.80 to 3.97)	-	6.76 (NE to NE)
p-value for Risk Difference		0.158		0.275		<0.001

Odds Ratio and related p-value are estimated by Wald's method using the SAS LOGISTIC procedure.
Peto OR calculation is based on Yusuf S et al. (Prog Cardiovasc Dis. 1985 Mar-Apr;27(5):335-71) and its p-value is derived using a normal approximation.
Risk Ratio and related p-value are estimated by using the SAS FREQ procedure.
Risk Difference and related p-value are estimated by using the SAS GLIMMIX procedure with the following model: criterion = treatment.
p-values for heterogeneity are estimated by using the SAS GLIMMIX procedure with the following model: criterion = treatment subgroup treatment*subgroup.
p-value for heterogeneity of Peto Odds Ratio is estimated by using normal approximation.
PGM=DEVOPS/SAR231893/EFC14153/CSR_RWE/REPORT/PGM/ae_evt_ger_subg_s2_t.sas OUT=REPORT/OUTPUT/ae_teaesev_ger_exa_s2_t_x.rtf (12AUG2021 - 9:13)

Project Code / Study Number / Analysis: SAR231893 / EFC14153 / CSR_RWE

2 Adverse events - Safety type 2 inflammatory asthma phenotype population

2.3 Patients with any TEAE severe

2.3.13 By number of severe asthma exacerbation prior to the study (<=1, 2, >2)

	Number of severe asthma exacerbation prior to the study					
	<=1		2		>2	
Safety type 2 inflammatory asthma phenotype population	**Placebo (N=46)**	**Dupilumab (N=85)**	**Placebo (N=32)**	**Dupilumab (N=75)**	**Placebo (N=35)**	**Dupilumab (N=74)**
p-value for heterogeneity of Risk Difference:						
<=1, 2						0.822
<=1, >2						0.039
2, >2						<0.001
overall						0.039

Odds Ratio and related p-value are estimated by Wald's method using the SAS LOGISTIC procedure.
Peto OR calculation is based on Yusuf S et al. (Prog Cardiovasc Dis. 1985 Mar-Apr;27(5):335-71) and its p-value is derived using a normal approximation.
Risk Ratio and related p-value are estimated by using the SAS FREQ procedure.
Risk Difference and related p-value are estimated by using the SAS GLIMMIX procedure with the following model: criterion = treatment.
p-values for heterogeneity are estimated by using the SAS GLIMMIX procedure with the following model: criterion = treatment subgroup treatment*subgroup.
p-value for heterogeneity of Peto Odds Ratio is estimated by using normal approximation.
PGM=DEVOPS/SAR231893/EFC14153/CSR_RWE/REPORT/PGM/ae_evt_ger_subg_s2_t.sas OUT=REPORT/OUTPUT/ae_teaesev_ger_exa_s2_t_x.rtf (12AUG2021 - 9:13)

Project Code / Study Number / Analysis: SAR231893 / EFC14153 / CSR_RWE

2 Adverse events - Safety type 2 inflammatory asthma phenotype population

2.4 Patients with any treatment emergent SAE

Safety type 2 inflammatory asthma phenotype population	Placebo (N=113)	Dupilumab (N=234)
Patients with any treatment emergent SAE [n(%)]	6 (5.3%)	13 (5.6%)
Odds Ratio (95% CI)	-	1.05 (0.39 to 2.84)
p-value for Odds Ratio		0.925
Risk Ratio (95% CI)	-	1.05 (0.41 to 2.68)
Reversed Risk Ratio (95% CI)	-	0.96 (0.37 to 2.45)
p-value for Risk Ratio		0.925
Risk Difference (95% CI)	-	0.25 (-4.84 to 5.33)
p-value for Risk Difference		0.924

Odds Ratio and related p-value are estimated by Wald's method using the SAS LOGISTIC procedure.
Peto OR calculation is based on Yusuf S et al. (Prog Cardiovasc Dis. 1985 Mar-Apr;27(5):335-71) and its p-value is derived using a normal approximation.
Risk Ratio and related p-value are estimated by using the SAS FREQ procedure.
Risk Difference and related p-value are estimated by using the SAS GLIMMIX procedure with the following model: criterion = treatment.
PGM=DEVOPS/SAR231893/EFC14153/CSR_RWE/REPORT/PGM/ae_evt_ger_s2_t.sas OUT=REPORT/OUTPUT/ae_sae_ger_s2_t_x.rtf (30JUL2021 - 15:49)

Project Code / Study Number / Analysis: SAR231893 / EFC14153 / CSR_RWE

2 Adverse events - Safety type 2 inflammatory asthma phenotype population

2.4 Patients with any treatment emergent SAE

2.4.1 By gender (Male, Female)

	Gender			
	Male		Female	
Safety type 2 inflammatory asthma phenotype population	**Placebo (N=77)**	**Dupilumab (N=153)**	**Placebo (N=36)**	**Dupilumab (N=81)**
Patients with any treatment emergent SAE [n(%)]	6 (7.8%)	9 (5.9%)	0	4 (4.9%)
Odds Ratio (95% CI)	-	0.74 (0.25 to 2.16)	-	NE (NE to NE)
p-value for Odds Ratio		0.581		NE
Peto Odds Ratio (95% CI)	-	0.73 (0.24 to 2.21)	-	4.41 (0.51 to 37.87)
Reversed Peto Odds Ratio (95% CI)			-	0.23 (0.03 to 1.96)
p-value for Peto Odds Ratio		0.581		0.177
p-value for heterogeneity of Peto Odds Ratio				0.146
Risk Ratio (95% CI)	-	0.75 (0.28 to 2.04)	-	NE (NE to NE)
p-value for Risk Ratio		0.580		NE
p-value for heterogeneity of Risk Ratio				0.971

Odds Ratio and related p-value are estimated by Wald's method using the SAS LOGISTIC procedure.
Peto OR calculation is based on Yusuf S et al. (Prog Cardiovasc Dis. 1985 Mar-Apr;27(5):335-71) and its p-value is derived using a normal approximation.
Risk Ratio and related p-value are estimated by using the SAS FREQ procedure.
Risk Difference and related p-value are estimated by using the SAS GLIMMIX procedure with the following model: criterion = treatment.
p-values for heterogeneity are estimated by using the SAS GLIMMIX procedure with the following model: criterion = treatment subgroup treatment*subgroup.
p-value for heterogeneity of Peto Odds Ratio is estimated by using normal approximation.
PGM=DEVOPS/SAR231893/EFC14153/CSR_RWE/REPORT/PGM/ae_evt_ger_subg_s2_t.sas OUT=REPORT/OUTPUT/ae_sae_ger_sex_s2_t_x.rtf (29JUL2021 - 14:44)

Project Code / Study Number / Analysis: SAR231893 / EFC14153 / CSR_RWE

2 Adverse events - Safety type 2 inflammatory asthma phenotype population

2.4 Patients with any treatment emergent SAE

2.4.1 By gender (Male, Female)

	Gender			
	Male		Female	
Safety type 2 inflammatory asthma phenotype population	**Placebo (N=77)**	**Dupilumab (N=153)**	**Placebo (N=36)**	**Dupilumab (N=81)**
Risk Difference (95% CI)	-	-1.91 (-9.00 to 5.18)	-	4.94 (NE to NE)
p-value for Risk Difference		0.596		<0.001
p-value for heterogeneity of Risk Difference				<0.001

Odds Ratio and related p-value are estimated by Wald's method using the SAS LOGISTIC procedure.
Peto OR calculation is based on Yusuf S et al. (Prog Cardiovasc Dis. 1985 Mar-Apr;27(5):335-71) and its p-value is derived using a normal approximation.
Risk Ratio and related p-value are estimated by using the SAS FREQ procedure.
Risk Difference and related p-value are estimated by using the SAS GLIMMIX procedure with the following model: criterion = treatment.
p-values for heterogeneity are estimated by using the SAS GLIMMIX procedure with the following model: criterion = treatment subgroup treatment*subgroup.
p-value for heterogeneity of Peto Odds Ratio is estimated by using normal approximation.
PGM=DEVOPS/SAR231893/EFC14153/CSR_RWE/REPORT/PGM/ae_evt_ger_subg_s2_t.sas OUT=REPORT/OUTPUT/ae_sae_ger_sex_s2_t_x.rtf (29JUL2021 - 14:44)

Project Code / Study Number / Analysis: SAR231893 / EFC14153 / CSR_RWE

2 Adverse events - Safety type 2 inflammatory asthma phenotype population

2.4 Patients with any treatment emergent SAE

2.4.2 By region (Latin America, East Europe, Western Countries)

	Region					
	Latin America		East Europe		Western countries	
Safety type 2 inflammatory asthma phenotype population	**Placebo (N=51)**	**Dupilumab (N=105)**	**Placebo (N=43)**	**Dupilumab (N=78)**	**Placebo (N=19)**	**Dupilumab (N=51)**
Patients with any treatment emergent SAE [n(%)]	4 (7.8%)	2 (1.9%)	1 (2.3%)	5 (6.4%)	1 (5.3%)	6 (11.8%)
Odds Ratio (95% CI)	-	0.23 (0.04 to 1.29)	-	2.88 (0.33 to 25.45)	-	2.40 (0.27 to 21.37)
p-value for Odds Ratio		0.094		0.342		0.433
p-value for heterogeneity of Odds Ratio:						
Latin America, East Europe						0.075
Latin America, Western countries						0.099
East Europe, Western countries						0.909
overall						0.120
Risk Ratio (95% CI)	-	0.24 (0.05 to 1.28)	-	2.76 (0.33 to 22.84)	-	2.24 (0.29 to 17.37)

Odds Ratio and related p-value are estimated by Wald's method using the SAS LOGISTIC procedure.
Peto OR calculation is based on Yusuf S et al. (Prog Cardiovasc Dis. 1985 Mar-Apr;27(5):335-71) and its p-value is derived using a normal approximation.
Risk Ratio and related p-value are estimated by using the SAS FREQ procedure.
Risk Difference and related p-value are estimated by using the SAS GLIMMIX procedure with the following model: criterion = treatment.
p-values for heterogeneity are estimated by using the SAS GLIMMIX procedure with the following model: criterion = treatment subgroup treatment*subgroup.
p-value for heterogeneity of Peto Odds Ratio is estimated by using normal approximation.
PGM=DEVOPS/SAR231893/EFC14153/CSR_RWE/REPORT/PGM/ae_evt_ger_subg_s2_t.sas OUT=REPORT/OUTPUT/ae_sae_ger_cty_s2_t_x.rtf (29JUL2021 - 14:44)

Project Code / Study Number / Analysis: SAR231893 / EFC14153 / CSR_RWE

2 Adverse events - Safety type 2 inflammatory asthma phenotype population

2.4 Patients with any treatment emergent SAE

2.4.2 By region (Latin America, East Europe, Western Countries)

	Region					
	Latin America		East Europe		Western countries	
Safety type 2 inflammatory asthma phenotype population	**Placebo (N=51)**	**Dupilumab (N=105)**	**Placebo (N=43)**	**Dupilumab (N=78)**	**Placebo (N=19)**	**Dupilumab (N=51)**
Reversed Risk ratio (95% CI)			-	0.36 (0.04 to 3.01)	-	0.45 (0.06 to 3.48)
p-value for Risk Ratio		0.096		0.347		0.442
p-value for heterogeneity of Risk Ratio:						
Latin America, East Europe						0.078
Latin America, Western countries						0.100
East Europe, Western countries						0.889
overall						0.123
Risk Difference (95% CI)	-	-5.94 (-13.83 to 1.95)	-	4.08 (-3.05 to 11.22)	-	6.50 (-7.12 to 20.12)
p-value for Risk Difference		0.139		0.259		0.344
p-value for heterogeneity of Risk Difference:						
Latin America, East Europe						0.063
Latin America, Western countries						0.117

Odds Ratio and related p-value are estimated by Wald's method using the SAS LOGISTIC procedure.
Peto OR calculation is based on Yusuf S et al. (Prog Cardiovasc Dis. 1985 Mar-Apr;27(5):335-71) and its p-value is derived using a normal approximation.
Risk Ratio and related p-value are estimated by using the SAS FREQ procedure.
Risk Difference and related p-value are estimated by using the SAS GLIMMIX procedure with the following model: criterion = treatment.
p-values for heterogeneity are estimated by using the SAS GLIMMIX procedure with the following model: criterion = treatment subgroup treatment*subgroup.
p-value for heterogeneity of Peto Odds Ratio is estimated by using normal approximation.
PGM=DEVOPS/SAR231893/EFC14153/CSR_RWE/REPORT/PGM/ae_evt_ger_subg_s2_t.sas OUT=REPORT/OUTPUT/ae_sae_ger_cty_s2_t_x.rtf (29JUL2021 - 14:44)

Project Code / Study Number / Analysis: SAR231893 / EFC14153 / CSR_RWE

2 Adverse events - Safety type 2 inflammatory asthma phenotype population

2.4 Patients with any treatment emergent SAE

2.4.2 By region (Latin America, East Europe, Western Countries)

	Region					
	Latin America		East Europe		Western countries	
Safety type 2 inflammatory asthma phenotype population	**Placebo (N=51)**	**Dupilumab (N=105)**	**Placebo (N=43)**	**Dupilumab (N=78)**	**Placebo (N=19)**	**Dupilumab (N=51)**
East Europe, Western countries						0.754
overall						0.115

Odds Ratio and related p-value are estimated by Wald's method using the SAS LOGISTIC procedure.
Peto OR calculation is based on Yusuf S et al. (Prog Cardiovasc Dis. 1985 Mar-Apr;27(5):335-71) and its p-value is derived using a normal approximation.
Risk Ratio and related p-value are estimated by using the SAS FREQ procedure.
Risk Difference and related p-value are estimated by using the SAS GLIMMIX procedure with the following model: criterion = treatment.
p-values for heterogeneity are estimated by using the SAS GLIMMIX procedure with the following model: criterion = treatment subgroup treatment*subgroup.
p-value for heterogeneity of Peto Odds Ratio is estimated by using normal approximation.
PGM=DEVOPS/SAR231893/EFC14153/CSR_RWE/REPORT/PGM/ae_evt_ger_subg_s2_t.sas OUT=REPORT/OUTPUT/ae_sae_ger_cty_s2_t_x.rtf (29JUL2021 - 14:44)

Project Code / Study Number / Analysis: SAR231893 / EFC14153 / CSR_RWE

2 Adverse events - Safety type 2 inflammatory asthma phenotype population

2.4 Patients with any treatment emergent SAE

2.4.3 By race (Caucasian/white, Black/of African descent, Other)

	Race					
	Caucasian/White		Black/of African descent		Other	
Safety type 2 inflammatory asthma phenotype population	**Placebo (N=101)**	**Dupilumab (N=207)**	**Placebo (N=5)**	**Dupilumab (N=9)**	**Placebo (N=7)**	**Dupilumab (N=18)**
Patients with any treatment emergent SAE [n(%)]	5 (5.0%)	11 (5.3%)	0	1 (11.1%)	1 (14.3%)	1 (5.6%)
Odds Ratio (95% CI)	-	1.08 (0.36 to 3.19)	-	NE (NE to NE)	-	0.35 (0.02 to 6.57)
p-value for Odds Ratio		0.893		NE		0.485
Peto Odds Ratio (95% CI)	-	1.08 (0.37 to 3.14)	-	4.74 (0.08 to 283.15)	-	0.32 (0.01 to 7.50)
Reversed Peto Odds Ratio (95% CI)	-	0.93 (0.32 to 2.70)	-	0.21 (0.00 to 12.50)		
p-value for Peto Odds Ratio		0.893		0.456		0.479
p-value for heterogeneity of Peto Odds Ratio:						
Caucasian/White, Black/of African descent						0.492
Caucasian/White, Other						0.476

Odds Ratio and related p-value are estimated by Wald's method using the SAS LOGISTIC procedure.
Peto OR calculation is based on Yusuf S et al. (Prog Cardiovasc Dis. 1985 Mar-Apr;27(5):335-71) and its p-value is derived using a normal approximation.
Risk Ratio and related p-value are estimated by using the SAS FREQ procedure.
Risk Difference and related p-value are estimated by using the SAS GLIMMIX procedure with the following model: criterion = treatment.
p-values for heterogeneity are estimated by using the SAS GLIMMIX procedure with the following model: criterion = treatment subgroup treatment*subgroup.
p-value for heterogeneity of Peto Odds Ratio is estimated by using normal approximation.
PGM=DEVOPS/SAR231893/EFC14153/CSR_RWE/REPORT/PGM/ae_evt_ger_subg_s2_t.sas OUT=REPORT/OUTPUT/ae_sae_ger_race_s2_t_x.rtf (29JUL2021 - 14:44)

Project Code / Study Number / Analysis: SAR231893 / EFC14153 / CSR_RWE

2 Adverse events - Safety type 2 inflammatory asthma phenotype population

2.4 Patients with any treatment emergent SAE

2.4.3 By race (Caucasian/white, Black/of African descent, Other)

	Race					
	Caucasian/White		Black/of African descent		Other	
Safety type 2 inflammatory asthma phenotype population	**Placebo (N=101)**	**Dupilumab (N=207)**	**Placebo (N=5)**	**Dupilumab (N=9)**	**Placebo (N=7)**	**Dupilumab (N=18)**
Black/of African descent, Other						0.307
overall						0.586
Risk Ratio (95% CI)	-	1.07 (0.38 to 3.01)	-	NE (NE to NE)	-	0.39 (0.03 to 5.40)
Reversed Risk ratio (95% CI)	-	0.93 (0.33 to 2.61)				
p-value for Risk Ratio		0.893		NE		0.482
p-value for heterogeneity of Risk Ratio:						
Caucasian/White, Black/of African descent						0.974
Caucasian/White, Other						0.482
Black/of African descent, Other						0.971
overall						0.780

Odds Ratio and related p-value are estimated by Wald's method using the SAS LOGISTIC procedure.
Peto OR calculation is based on Yusuf S et al. (Prog Cardiovasc Dis. 1985 Mar-Apr;27(5):335-71) and its p-value is derived using a normal approximation.
Risk Ratio and related p-value are estimated by using the SAS FREQ procedure.
Risk Difference and related p-value are estimated by using the SAS GLIMMIX procedure with the following model: criterion = treatment.
p-values for heterogeneity are estimated by using the SAS GLIMMIX procedure with the following model: criterion = treatment subgroup treatment*subgroup.
p-value for heterogeneity of Peto Odds Ratio is estimated by using normal approximation.
PGM=DEVOPS/SAR231893/EFC14153/CSR_RWE/REPORT/PGM/ae_evt_ger_subg_s2_t.sas OUT=REPORT/OUTPUT/ae_sae_ger_race_s2_t_x.rtf (29JUL2021 - 14:44)

Project Code / Study Number / Analysis: SAR231893 / EFC14153 / CSR_RWE

2 Adverse events - Safety type 2 inflammatory asthma phenotype population

2.4 Patients with any treatment emergent SAE

2.4.3 By race (Caucasian/white, Black/of African descent, Other)

	Race					
	Caucasian/White		Black/of African descent		Other	
Safety type 2 inflammatory asthma phenotype population	**Placebo (N=101)**	**Dupilumab (N=207)**	**Placebo (N=5)**	**Dupilumab (N=9)**	**Placebo (N=7)**	**Dupilumab (N=18)**
Risk Difference (95% CI)	-	0.36 (-4.88 to 5.60)	-	11.11 (NE to NE)	-	-8.73 (-38.28 to 20.82)
p-value for Risk Difference		0.891		<0.001		0.547
p-value for heterogeneity of Risk Difference:						
Caucasian/White, Black/of African descent						0.460
Caucasian/White, Other						0.532
Black/of African descent, Other						<0.001
overall						0.532

Odds Ratio and related p-value are estimated by Wald's method using the SAS LOGISTIC procedure.
Peto OR calculation is based on Yusuf S et al. (Prog Cardiovasc Dis. 1985 Mar-Apr;27(5):335-71) and its p-value is derived using a normal approximation.
Risk Ratio and related p-value are estimated by using the SAS FREQ procedure.
Risk Difference and related p-value are estimated by using the SAS GLIMMIX procedure with the following model: criterion = treatment.
p-values for heterogeneity are estimated by using the SAS GLIMMIX procedure with the following model: criterion = treatment subgroup treatment*subgroup.
p-value for heterogeneity of Peto Odds Ratio is estimated by using normal approximation.
PGM=DEVOPS/SAR231893/EFC14153/CSR_RWE/REPORT/PGM/ae_evt_ger_subg_s2_t.sas OUT=REPORT/OUTPUT/ae_sae_ger_race_s2_t_x.rtf (29JUL2021 - 14:44)

Project Code / Study Number / Analysis: SAR231893 / EFC14153 / CSR_RWE

2 Adverse events - Safety type 2 inflammatory asthma phenotype population

2.4 Patients with any treatment emergent SAE

2.4.4 By baseline ICS dose level (Medium, High)

	Baseline ICS dose level			
	High		Medium	
Safety type 2 inflammatory asthma phenotype population	**Placebo (N=50)**	**Dupilumab (N=101)**	**Placebo (N=63)**	**Dupilumab (N=131)**
Patients with any treatment emergent SAE [n(%)]	0	6 (5.9%)	6 (9.5%)	7 (5.3%)
Odds Ratio (95% CI)	-	NE (NE to NE)	-	0.54 (0.17 to 1.67)
p-value for Odds Ratio		NE		0.282
Peto Odds Ratio (95% CI)	-	4.70 (0.83 to 26.47)	-	0.51 (0.16 to 1.70)
Reversed Peto Odds Ratio (95% CI)	-	0.21 (0.04 to 1.20)		
p-value for Peto Odds Ratio		0.080		0.277
p-value for heterogeneity of Peto Odds Ratio				0.039
Risk Ratio (95% CI)	-	NE (NE to NE)	-	0.56 (0.20 to 1.60)
p-value for Risk Ratio		NE		0.280
p-value for heterogeneity of Risk Ratio				0.976

Odds Ratio and related p-value are estimated by Wald's method using the SAS LOGISTIC procedure.
Peto OR calculation is based on Yusuf S et al. (Prog Cardiovasc Dis. 1985 Mar-Apr;27(5):335-71) and its p-value is derived using a normal approximation.
Risk Ratio and related p-value are estimated by using the SAS FREQ procedure.
Risk Difference and related p-value are estimated by using the SAS GLIMMIX procedure with the following model: criterion = treatment.
p-values for heterogeneity are estimated by using the SAS GLIMMIX procedure with the following model: criterion = treatment subgroup treatment*subgroup.
p-value for heterogeneity of Peto Odds Ratio is estimated by using normal approximation.
PGM=DEVOPS/SAR231893/EFC14153/CSR_RWE/REPORT/PGM/ae_evt_ger_subg_s2_t.sas OUT=REPORT/OUTPUT/ae_sae_ger_ics_s2_t_x.rtf (29JUL2021 - 14:44)

Project Code / Study Number / Analysis: SAR231893 / EFC14153 / CSR_RWE

2 Adverse events - Safety type 2 inflammatory asthma phenotype population

2.4 Patients with any treatment emergent SAE

2.4.4 By baseline ICS dose level (Medium, High)

Safety type 2 inflammatory asthma phenotype population	Baseline ICS dose level			
	High		Medium	
	Placebo (N=50)	Dupilumab (N=101)	Placebo (N=63)	Dupilumab (N=131)
Risk Difference (95% CI)	-	5.94 (NE to NE)	-	-4.18 (-12.44 to 4.08)
p-value for Risk Difference		<0.001		0.319
p-value for heterogeneity of Risk Difference				<0.001

Odds Ratio and related p-value are estimated by Wald's method using the SAS LOGISTIC procedure.
Peto OR calculation is based on Yusuf S et al. (Prog Cardiovasc Dis. 1985 Mar-Apr;27(5):335-71) and its p-value is derived using a normal approximation.
Risk Ratio and related p-value are estimated by using the SAS FREQ procedure.
Risk Difference and related p-value are estimated by using the SAS GLIMMIX procedure with the following model: criterion = treatment.
p-values for heterogeneity are estimated by using the SAS GLIMMIX procedure with the following model: criterion = treatment subgroup treatment*subgroup.
p-value for heterogeneity of Peto Odds Ratio is estimated by using normal approximation.
PGM=DEVOPS/SAR231893/EFC14153/CSR_RWE/REPORT/PGM/ae_evt_ger_subg_s2_t.sas OUT=REPORT/OUTPUT/ae_sae_ger_ics_s2_t_x.rtf (29JUL2021 - 14:44)

Project Code / Study Number / Analysis: SAR231893 / EFC14153 / CSR_RWE

2 Adverse events - Safety type 2 inflammatory asthma phenotype population

2.4 Patients with any treatment emergent SAE

2.4.5 By baseline ICS dose level 2 (Medium, High)

	Baseline ICS dose level 2			
	High		Medium	
Safety type 2 inflammatory asthma phenotype population	**Placebo (N=94)**	**Dupilumab (N=199)**	**Placebo (N=19)**	**Dupilumab (N=35)**
Patients with any treatment emergent SAE [n(%)]	4 (4.3%)	10 (5.0%)	2 (10.5%)	3 (8.6%)
Odds Ratio (95% CI)	-	1.19 (0.36 to 3.90)	-	0.80 (0.12 to 5.24)
p-value for Odds Ratio		0.773		0.813
p-value for heterogeneity of Odds Ratio				0.724
Risk Ratio (95% CI)	-	1.18 (0.38 to 3.67)	-	0.81 (0.15 to 4.46)
Reversed Risk ratio (95% CI)	-	0.85 (0.27 to 2.63)		
p-value for Risk Ratio		0.774		0.813
p-value for heterogeneity of Risk Ratio				0.722
Risk Difference (95% CI)	-	0.77 (-4.34 to 5.88)	-	-1.95 (-18.98 to 15.07)

Odds Ratio and related p-value are estimated by Wald's method using the SAS LOGISTIC procedure.
Peto OR calculation is based on Yusuf S et al. (Prog Cardiovasc Dis. 1985 Mar-Apr;27(5):335-71) and its p-value is derived using a normal approximation.
Risk Ratio and related p-value are estimated by using the SAS FREQ procedure.
Risk Difference and related p-value are estimated by using the SAS GLIMMIX procedure with the following model: criterion = treatment.
p-values for heterogeneity are estimated by using the SAS GLIMMIX procedure with the following model: criterion = treatment subgroup treatment*subgroup.
p-value for heterogeneity of Peto Odds Ratio is estimated by using normal approximation.
PGM=DEVOPS/SAR231893/EFC14153/CSR_RWE/REPORT/PGM/ae_evt_ger_subg_s2_t.sas OUT=REPORT/OUTPUT/ae_sae_ger_ics2_s2_t_x.rtf (01SEP2021 - 16:08)

Project Code / Study Number / Analysis: SAR231893 / EFC14153 / CSR_RWE

2 Adverse events - Safety type 2 inflammatory asthma phenotype population

2.4 Patients with any treatment emergent SAE

2.4.5 By baseline ICS dose level 2 (Medium, High)

	Baseline ICS dose level 2			
	High		Medium	
Safety type 2 inflammatory asthma phenotype population	**Placebo (N=94)**	**Dupilumab (N=199)**	**Placebo (N=19)**	**Dupilumab (N=35)**
p-value for Risk Difference		0.767		0.819
p-value for heterogeneity of Risk Difference				0.759

Odds Ratio and related p-value are estimated by Wald's method using the SAS LOGISTIC procedure.
Peto OR calculation is based on Yusuf S et al. (Prog Cardiovasc Dis. 1985 Mar-Apr;27(5):335-71) and its p-value is derived using a normal approximation.
Risk Ratio and related p-value are estimated by using the SAS FREQ procedure.
Risk Difference and related p-value are estimated by using the SAS GLIMMIX procedure with the following model: criterion = treatment.
p-values for heterogeneity are estimated by using the SAS GLIMMIX procedure with the following model: criterion = treatment subgroup treatment*subgroup.
p-value for heterogeneity of Peto Odds Ratio is estimated by using normal approximation.
PGM=DEVOPS/SAR231893/EFC14153/CSR_RWE/REPORT/PGM/ae_evt_ger_subg_s2_t.sas OUT=REPORT/OUTPUT/ae_sae_ger_ics2_s2_t_x.rtf (01SEP2021 - 16:08)

Project Code / Study Number / Analysis: SAR231893 / EFC14153 / CSR_RWE

2 Adverse events - Safety type 2 inflammatory asthma phenotype population

2.4 Patients with any treatment emergent SAE

2.4.6 By baseline predicted FEV1 (<80%, >=80%)

	Baseline Predicted FEV1			
	<80%		>=80%	
Safety type 2 inflammatory asthma phenotype population	**Placebo (N=58)**	**Dupilumab (N=116)**	**Placebo (N=55)**	**Dupilumab (N=118)**
Patients with any treatment emergent SAE [n(%)]	3 (5.2%)	6 (5.2%)	3 (5.5%)	7 (5.9%)
Odds Ratio (95% CI)	-	1.00 (0.24 to 4.15)	-	1.09 (0.27 to 4.40)
p-value for Odds Ratio		1.000		0.900
p-value for heterogeneity of Odds Ratio				0.930
Risk Ratio (95% CI)	-	1.00 (0.26 to 3.86)	-	1.09 (0.29 to 4.05)
Reversed Risk ratio (95% CI)			-	0.92 (0.25 to 3.42)
p-value for Risk Ratio		1.000		0.900
p-value for heterogeneity of Risk Ratio				0.930
Risk Difference (95% CI)	-	-0.00 (-7.03 to 7.03)	-	0.48 (-6.94 to 7.89)

Odds Ratio and related p-value are estimated by Wald's method using the SAS LOGISTIC procedure.
Peto OR calculation is based on Yusuf S et al. (Prog Cardiovasc Dis. 1985 Mar-Apr;27(5):335-71) and its p-value is derived using a normal approximation.
Risk Ratio and related p-value are estimated by using the SAS FREQ procedure.
Risk Difference and related p-value are estimated by using the SAS GLIMMIX procedure with the following model: criterion = treatment.
p-values for heterogeneity are estimated by using the SAS GLIMMIX procedure with the following model: criterion = treatment subgroup treatment*subgroup.
p-value for heterogeneity of Peto Odds Ratio is estimated by using normal approximation.
PGM=DEVOPS/SAR231893/EFC14153/CSR_RWE/REPORT/PGM/ae_evt_ger_subg_s2_t.sas OUT=REPORT/OUTPUT/ae_sae_ger_pfev1_s2_t_x.rtf (29JUL2021 - 14:45)

Project Code / Study Number / Analysis: SAR231893 / EFC14153 / CSR_RWE

2 Adverse events - Safety type 2 inflammatory asthma phenotype population

2.4 Patients with any treatment emergent SAE

2.4.6 By baseline predicted FEV1 (<80%, >=80%)

	Baseline Predicted FEV1			
	<80%		>=80%	
Safety type 2 inflammatory asthma phenotype population	**Placebo (N=58)**	**Dupilumab (N=116)**	**Placebo (N=55)**	**Dupilumab (N=118)**
p-value for Risk Difference		1.000		0.899
p-value for heterogeneity of Risk Difference				0.927

Odds Ratio and related p-value are estimated by Wald's method using the SAS LOGISTIC procedure.
Peto OR calculation is based on Yusuf S et al. (Prog Cardiovasc Dis. 1985 Mar-Apr;27(5):335-71) and its p-value is derived using a normal approximation.
Risk Ratio and related p-value are estimated by using the SAS FREQ procedure.
Risk Difference and related p-value are estimated by using the SAS GLIMMIX procedure with the following model: criterion = treatment.
p-values for heterogeneity are estimated by using the SAS GLIMMIX procedure with the following model: criterion = treatment subgroup treatment*subgroup.
p-value for heterogeneity of Peto Odds Ratio is estimated by using normal approximation.
PGM=DEVOPS/SAR231893/EFC14153/CSR_RWE/REPORT/PGM/ae_evt_ger_subg_s2_t.sas OUT=REPORT/OUTPUT/ae_sae_ger_pfev1_s2_t_x.rtf (29JUL2021 - 14:45)

Project Code / Study Number / Analysis: SAR231893 / EFC14153 / CSR_RWE

2 Adverse events - Safety type 2 inflammatory asthma phenotype population

2.4 Patients with any treatment emergent SAE

2.4.7 By baseline ACQ-7-IA (<=2, >2)

	Baseline ACQ-7-IA			
	<=2		>2	
Safety type 2 inflammatory asthma phenotype population	**Placebo (N=61)**	**Dupilumab (N=125)**	**Placebo (N=52)**	**Dupilumab (N=109)**
Patients with any treatment emergent SAE [n(%)]	4 (6.6%)	7 (5.6%)	2 (3.8%)	6 (5.5%)
Odds Ratio (95% CI)	-	0.85 (0.24 to 3.01)	-	1.46 (0.28 to 7.47)
p-value for Odds Ratio		0.795		0.652
p-value for heterogeneity of Odds Ratio				0.607
Risk Ratio (95% CI)	-	0.85 (0.26 to 2.81)	-	1.43 (0.30 to 6.85)
Reversed Risk ratio (95% CI)			-	0.70 (0.15 to 3.34)
p-value for Risk Ratio		0.795		0.654
p-value for heterogeneity of Risk Ratio				0.607
Risk Difference (95% CI)	-	-0.96 (-8.41 to 6.50)	-	1.66 (-5.15 to 8.47)

Odds Ratio and related p-value are estimated by Wald's method using the SAS LOGISTIC procedure.
Peto OR calculation is based on Yusuf S et al. (Prog Cardiovasc Dis. 1985 Mar-Apr;27(5):335-71) and its p-value is derived using a normal approximation.
Risk Ratio and related p-value are estimated by using the SAS FREQ procedure.
Risk Difference and related p-value are estimated by using the SAS GLIMMIX procedure with the following model: criterion = treatment.
p-values for heterogeneity are estimated by using the SAS GLIMMIX procedure with the following model: criterion = treatment subgroup treatment*subgroup.
p-value for heterogeneity of Peto Odds Ratio is estimated by using normal approximation.
PGM=DEVOPS/SAR231893/EFC14153/CSR_RWE/REPORT/PGM/ae_evt_ger_subg_s2_t.sas OUT=REPORT/OUTPUT/ae_sae_ger_acq7_s2_t_x.rtf (29JUL2021 - 14:45)

Project Code / Study Number / Analysis: SAR231893 / EFC14153 / CSR_RWE

2 Adverse events - Safety type 2 inflammatory asthma phenotype population

2.4 Patients with any treatment emergent SAE

2.4.7 By baseline ACQ-7-IA (<=2, >2)

	Baseline ACQ-7-IA			
	<=2		>2	
Safety type 2 inflammatory asthma phenotype population	**Placebo (N=61)**	**Dupilumab (N=125)**	**Placebo (N=52)**	**Dupilumab (N=109)**
p-value for Risk Difference		0.800		0.631
p-value for heterogeneity of Risk Difference				0.609

Odds Ratio and related p-value are estimated by Wald's method using the SAS LOGISTIC procedure.
Peto OR calculation is based on Yusuf S et al. (Prog Cardiovasc Dis. 1985 Mar-Apr;27(5):335-71) and its p-value is derived using a normal approximation.
Risk Ratio and related p-value are estimated by using the SAS FREQ procedure.
Risk Difference and related p-value are estimated by using the SAS GLIMMIX procedure with the following model: criterion = treatment.
p-values for heterogeneity are estimated by using the SAS GLIMMIX procedure with the following model: criterion = treatment subgroup treatment*subgroup.
p-value for heterogeneity of Peto Odds Ratio is estimated by using normal approximation.
PGM=DEVOPS/SAR231893/EFC14153/CSR_RWE/REPORT/PGM/ae_evt_ger_subg_s2_t.sas OUT=REPORT/OUTPUT/ae_sae_ger_acq7_s2_t_x.rtf (29JUL2021 - 14:45)

Project Code / Study Number / Analysis: SAR231893 / EFC14153 / CSR_RWE

2 Adverse events - Safety type 2 inflammatory asthma phenotype population

2.4 Patients with any treatment emergent SAE

2.4.8 By baseline weight (<=30 kg, >30 kg)

	Baseline weight (kg)			
	<=30		>30	
Safety type 2 inflammatory asthma phenotype population	**Placebo (N=36)**	**Dupilumab (N=74)**	**Placebo (N=77)**	**Dupilumab (N=160)**
Patients with any treatment emergent SAE [n(%)]	2 (5.6%)	3 (4.1%)	4 (5.2%)	10 (6.3%)
Odds Ratio (95% CI)	-	0.72 (0.11 to 4.50)	-	1.22 (0.37 to 4.01)
p-value for Odds Ratio		0.724		0.747
p-value for heterogeneity of Odds Ratio				0.637
Risk Ratio (95% CI)	-	0.73 (0.13 to 4.18)	-	1.20 (0.39 to 3.71)
Reversed Risk ratio (95% CI)			-	0.83 (0.27 to 2.57)
p-value for Risk Ratio		0.723		0.748
p-value for heterogeneity of Risk Ratio				0.637
Risk Difference (95% CI)	-	-1.50 (-10.33 to 7.33)	-	1.06 (-5.19 to 7.30)

Odds Ratio and related p-value are estimated by Wald's method using the SAS LOGISTIC procedure.
Peto OR calculation is based on Yusuf S et al. (Prog Cardiovasc Dis. 1985 Mar-Apr;27(5):335-71) and its p-value is derived using a normal approximation.
Risk Ratio and related p-value are estimated by using the SAS FREQ procedure.
Risk Difference and related p-value are estimated by using the SAS GLIMMIX procedure with the following model: criterion = treatment.
p-values for heterogeneity are estimated by using the SAS GLIMMIX procedure with the following model: criterion = treatment subgroup treatment*subgroup.
p-value for heterogeneity of Peto Odds Ratio is estimated by using normal approximation.
PGM=DEVOPS/SAR231893/EFC14153/CSR_RWE/REPORT/PGM/ae_evt_ger_subg_s2_t.sas OUT=REPORT/OUTPUT/ae_sae_ger_wgt_s2_t_x.rtf (29JUL2021 - 14:45)

Project Code / Study Number / Analysis: SAR231893 / EFC14153 / CSR_RWE

2 Adverse events - Safety type 2 inflammatory asthma phenotype population

2.4 Patients with any treatment emergent SAE

2.4.8 By baseline weight (<=30 kg, >30 kg)

	Baseline weight (kg)			
	<=30		>30	
Safety type 2 inflammatory asthma phenotype population	**Placebo (N=36)**	**Dupilumab (N=74)**	**Placebo (N=77)**	**Dupilumab (N=160)**
p-value for Risk Difference		0.737		0.740
p-value for heterogeneity of Risk Difference				0.640

Odds Ratio and related p-value are estimated by Wald's method using the SAS LOGISTIC procedure.
Peto OR calculation is based on Yusuf S et al. (Prog Cardiovasc Dis. 1985 Mar-Apr;27(5):335-71) and its p-value is derived using a normal approximation.
Risk Ratio and related p-value are estimated by using the SAS FREQ procedure.
Risk Difference and related p-value are estimated by using the SAS GLIMMIX procedure with the following model: criterion = treatment.
p-values for heterogeneity are estimated by using the SAS GLIMMIX procedure with the following model: criterion = treatment subgroup treatment*subgroup.
p-value for heterogeneity of Peto Odds Ratio is estimated by using normal approximation.
PGM=DEVOPS/SAR231893/EFC14153/CSR_RWE/REPORT/PGM/ae_evt_ger_subg_s2_t.sas OUT=REPORT/OUTPUT/ae_sae_ger_wgt_s2_t_x.rtf (29JUL2021 - 14:45)

Project Code / Study Number / Analysis: SAR231893 / EFC14153 / CSR_RWE

2 Adverse events - Safety type 2 inflammatory asthma phenotype population

2.4 Patients with any treatment emergent SAE

2.4.9 By atopic medical condition (Yes, No)

	Atopic medical condition			
	Yes		No	
Safety type 2 inflammatory asthma phenotype population	**Placebo (N=102)**	**Dupilumab (N=225)**	**Placebo (N=11)**	**Dupilumab (N=9)**
Patients with any treatment emergent SAE [n(%)]	6 (5.9%)	12 (5.3%)	0	1 (11.1%)
Odds Ratio (95% CI)	-	0.90 (0.33 to 2.47)	-	NE (NE to NE)
p-value for Odds Ratio		0.840		NE
Peto Odds Ratio (95% CI)	-	0.90 (0.32 to 2.51)	-	9.23 (0.18 to 474.33)
Reversed Peto Odds Ratio (95% CI)			-	0.11 (0.00 to 5.56)
p-value for Peto Odds Ratio		0.840		0.269
p-value for heterogeneity of Peto Odds Ratio				0.262
Risk Ratio (95% CI)	-	0.91 (0.35 to 2.35)	-	NE (NE to NE)
p-value for Risk Ratio		0.840		NE
p-value for heterogeneity of Risk Ratio				0.974

Odds Ratio and related p-value are estimated by Wald's method using the SAS LOGISTIC procedure.
Peto OR calculation is based on Yusuf S et al. (Prog Cardiovasc Dis. 1985 Mar-Apr;27(5):335-71) and its p-value is derived using a normal approximation.
Risk Ratio and related p-value are estimated by using the SAS FREQ procedure.
Risk Difference and related p-value are estimated by using the SAS GLIMMIX procedure with the following model: criterion = treatment.
p-values for heterogeneity are estimated by using the SAS GLIMMIX procedure with the following model: criterion = treatment subgroup treatment*subgroup.
p-value for heterogeneity of Peto Odds Ratio is estimated by using normal approximation.
PGM=DEVOPS/SAR231893/EFC14153/CSR_RWE/REPORT/PGM/ae_evt_ger_subg_s2_t.sas OUT=REPORT/OUTPUT/ae_sae_ger_amc_s2_t_x.rtf (29JUL2021 - 14:45)

Project Code / Study Number / Analysis: SAR231893 / EFC14153 / CSR_RWE

2 Adverse events - Safety type 2 inflammatory asthma phenotype population

2.4 Patients with any treatment emergent SAE

2.4.9 By atopic medical condition (Yes, No)

	Atopic medical condition			
	Yes		No	
Safety type 2 inflammatory asthma phenotype population	**Placebo (N=102)**	**Dupilumab (N=225)**	**Placebo (N=11)**	**Dupilumab (N=9)**
Risk Difference (95% CI)	-	-0.55 (-6.00 to 4.90)	-	11.11 (NE to NE)
p-value for Risk Difference		0.843		<0.001
p-value for heterogeneity of Risk Difference				<0.001

Odds Ratio and related p-value are estimated by Wald's method using the SAS LOGISTIC procedure.
Peto OR calculation is based on Yusuf S et al. (Prog Cardiovasc Dis. 1985 Mar-Apr;27(5):335-71) and its p-value is derived using a normal approximation.
Risk Ratio and related p-value are estimated by using the SAS FREQ procedure.
Risk Difference and related p-value are estimated by using the SAS GLIMMIX procedure with the following model: criterion = treatment.
p-values for heterogeneity are estimated by using the SAS GLIMMIX procedure with the following model: criterion = treatment subgroup treatment*subgroup.
p-value for heterogeneity of Peto Odds Ratio is estimated by using normal approximation.
PGM=DEVOPS/SAR231893/EFC14153/CSR_RWE/REPORT/PGM/ae_evt_ger_subg_s2_t.sas OUT=REPORT/OUTPUT/ae_sae_ger_amc_s2_t_x.rtf (29JUL2021 - 14:45)

Project Code / Study Number / Analysis: SAR231893 / EFC14153 / CSR_RWE

2 Adverse events - Safety type 2 inflammatory asthma phenotype population

2.4 Patients with any treatment emergent SAE

2.4.10 By baseline total IgE (<median, >= median)

	Baseline Total IgE (IU/mL)			
	<median		>=median	
Safety type 2 inflammatory asthma phenotype population	**Placebo (N=65)**	**Dupilumab (N=106)**	**Placebo (N=47)**	**Dupilumab (N=124)**
Patients with any treatment emergent SAE [n(%)]	1 (1.5%)	5 (4.7%)	5 (10.6%)	7 (5.6%)
Odds Ratio (95% CI)	-	3.17 (0.36 to 27.72)	-	0.50 (0.15 to 1.67)
p-value for Odds Ratio		0.298		0.261
p-value for heterogeneity of Odds Ratio				0.147
Risk Ratio (95% CI)	-	3.07 (0.37 to 25.66)	-	0.53 (0.18 to 1.59)
Reversed Risk ratio (95% CI)	-	0.33 (0.04 to 2.73)		
p-value for Risk Ratio		0.301		0.258
p-value for heterogeneity of Risk Ratio				0.151
Risk Difference (95% CI)	-	3.18 (-1.88 to 8.24)	-	-4.99 (-14.77 to 4.78)

Odds Ratio and related p-value are estimated by Wald's method using the SAS LOGISTIC procedure.
Peto OR calculation is based on Yusuf S et al. (Prog Cardiovasc Dis. 1985 Mar-Apr;27(5):335-71) and its p-value is derived using a normal approximation.
Risk Ratio and related p-value are estimated by using the SAS FREQ procedure.
Risk Difference and related p-value are estimated by using the SAS GLIMMIX procedure with the following model: criterion = treatment.
p-values for heterogeneity are estimated by using the SAS GLIMMIX procedure with the following model: criterion = treatment subgroup treatment*subgroup.
p-value for heterogeneity of Peto Odds Ratio is estimated by using normal approximation.
PGM=DEVOPS/SAR231893/EFC14153/CSR_RWE/REPORT/PGM/ae_evt_ger_subg_s2_t.sas OUT=REPORT/OUTPUT/ae_sae_ger_igem_s2_t_x.rtf (29JUL2021 - 14:46)

Project Code / Study Number / Analysis: SAR231893 / EFC14153 / CSR_RWE

2 Adverse events - Safety type 2 inflammatory asthma phenotype population

2.4 Patients with any treatment emergent SAE

2.4.10 By baseline total IgE (<median, >= median)

	Baseline Total IgE (IU/mL)			
	<median		>=median	
Safety type 2 inflammatory asthma phenotype population	**Placebo (N=65)**	**Dupilumab (N=106)**	**Placebo (N=47)**	**Dupilumab (N=124)**
p-value for Risk Difference		0.217		0.315
p-value for heterogeneity of Risk Difference				0.144

Odds Ratio and related p-value are estimated by Wald's method using the SAS LOGISTIC procedure.
Peto OR calculation is based on Yusuf S et al. (Prog Cardiovasc Dis. 1985 Mar-Apr;27(5):335-71) and its p-value is derived using a normal approximation.
Risk Ratio and related p-value are estimated by using the SAS FREQ procedure.
Risk Difference and related p-value are estimated by using the SAS GLIMMIX procedure with the following model: criterion = treatment.
p-values for heterogeneity are estimated by using the SAS GLIMMIX procedure with the following model: criterion = treatment subgroup treatment*subgroup.
p-value for heterogeneity of Peto Odds Ratio is estimated by using normal approximation.
PGM=DEVOPS/SAR231893/EFC14153/CSR_RWE/REPORT/PGM/ae_evt_ger_subg_s2_t.sas OUT=REPORT/OUTPUT/ae_sae_ger_igem_s2_t_x.rtf (29JUL2021 - 14:46)

Project Code / Study Number / Analysis: SAR231893 / EFC14153 / CSR_RWE

2 Adverse events - Safety type 2 inflammatory asthma phenotype population

2.4 Patients with any treatment emergent SAE

2.4.11 By baseline total IgE (<100 IU/ml, >= 100 IU/ml)

	Baseline Total IgE (IU/mL)			
	< 100		>= 100	
Safety type 2 inflammatory asthma phenotype population	**Placebo (N=22)**	**Dupilumab (N=29)**	**Placebo (N=90)**	**Dupilumab (N=201)**
Patients with any treatment emergent SAE [n(%)]	0	1 (3.4%)	6 (6.7%)	11 (5.5%)
Odds Ratio (95% CI)	-	NE (NE to NE)	-	0.81 (0.29 to 2.26)
p-value for Odds Ratio		NE		0.689
Peto Odds Ratio (95% CI)	-	5.80 (0.11 to 303.69)	-	0.81 (0.28 to 2.32)
Reversed Peto Odds Ratio (95% CI)	-	0.17 (0.00 to 9.09)		
p-value for Peto Odds Ratio		0.384		0.689
p-value for heterogeneity of Peto Odds Ratio				0.345
Risk Ratio (95% CI)	-	NE (NE to NE)	-	0.82 (0.31 to 2.15)
p-value for Risk Ratio		NE		0.688
p-value for heterogeneity of Risk Ratio				0.978

Odds Ratio and related p-value are estimated by Wald's method using the SAS LOGISTIC procedure.
Peto OR calculation is based on Yusuf S et al. (Prog Cardiovasc Dis. 1985 Mar-Apr;27(5):335-71) and its p-value is derived using a normal approximation.
Risk Ratio and related p-value are estimated by using the SAS FREQ procedure.
Risk Difference and related p-value are estimated by using the SAS GLIMMIX procedure with the following model: criterion = treatment.
p-values for heterogeneity are estimated by using the SAS GLIMMIX procedure with the following model: criterion = treatment subgroup treatment*subgroup.
p-value for heterogeneity of Peto Odds Ratio is estimated by using normal approximation.
PGM=DEVOPS/SAR231893/EFC14153/CSR_RWE/REPORT/PGM/ae_evt_ger_subg_s2_t.sas OUT=REPORT/OUTPUT/ae_sae_ger_ige_s2_t_x.rtf (29JUL2021 - 14:46)

Project Code / Study Number / Analysis: SAR231893 / EFC14153 / CSR_RWE

2 Adverse events - Safety type 2 inflammatory asthma phenotype population

2.4 Patients with any treatment emergent SAE

2.4.11 By baseline total IgE (<100 IU/ml, >= 100 IU/ml)

	Baseline Total IgE (IU/mL)			
	< 100		>= 100	
Safety type 2 inflammatory asthma phenotype population	**Placebo (N=22)**	**Dupilumab (N=29)**	**Placebo (N=90)**	**Dupilumab (N=201)**
Risk Difference (95% CI)	-	3.45 (NE to NE)	-	-1.19 (-7.26 to 4.87)
p-value for Risk Difference		<0.001		0.699
p-value for heterogeneity of Risk Difference				<0.001

Odds Ratio and related p-value are estimated by Wald's method using the SAS LOGISTIC procedure.
Peto OR calculation is based on Yusuf S et al. (Prog Cardiovasc Dis. 1985 Mar-Apr;27(5):335-71) and its p-value is derived using a normal approximation.
Risk Ratio and related p-value are estimated by using the SAS FREQ procedure.
Risk Difference and related p-value are estimated by using the SAS GLIMMIX procedure with the following model: criterion = treatment.
p-values for heterogeneity are estimated by using the SAS GLIMMIX procedure with the following model: criterion = treatment subgroup treatment*subgroup.
p-value for heterogeneity of Peto Odds Ratio is estimated by using normal approximation.
PGM=DEVOPS/SAR231893/EFC14153/CSR_RWE/REPORT/PGM/ae_evt_ger_subg_s2_t.sas OUT=REPORT/OUTPUT/ae_sae_ger_ige_s2_t_x.rtf (29JUL2021 - 14:46)

Project Code / Study Number / Analysis: SAR231893 / EFC14153 / CSR_RWE

2 Adverse events - Safety type 2 inflammatory asthma phenotype population

2.4 Patients with any treatment emergent SAE

2.4.12 By age at onset of asthma (0-2, 3-5, >=6 years)

	Age of onset of asthma (years)					
	0-2		3-5		>= 6	
Safety type 2 inflammatory asthma phenotype population	**Placebo (N=40)**	**Dupilumab (N=104)**	**Placebo (N=38)**	**Dupilumab (N=85)**	**Placebo (N=35)**	**Dupilumab (N=45)**
Patients with any treatment emergent SAE [n(%)]	2 (5.0%)	10 (9.6%)	2 (5.3%)	3 (3.5%)	2 (5.7%)	0
Odds Ratio (95% CI)	-	2.02 (0.42 to 9.66)	-	0.66 (0.11 to 4.11)	-	0.00 (NE to NE)
p-value for Odds Ratio		0.378		0.655		NE
Peto Odds Ratio (95% CI)	-	1.82 (0.49 to 6.79)	-	0.64 (0.09 to 4.43)	-	0.10 (0.01 to 1.64)
Reversed Peto Odds Ratio (95% CI)	-	0.55 (0.15 to 2.04)				
p-value for Peto Odds Ratio		0.371		0.654		0.107
p-value for heterogeneity of Peto Odds Ratio:						
0-2, 3-5						0.382
0-2, >= 6						0.066
3-5, >= 6						0.281

Odds Ratio and related p-value are estimated by Wald's method using the SAS LOGISTIC procedure.
Peto OR calculation is based on Yusuf S et al. (Prog Cardiovasc Dis. 1985 Mar-Apr;27(5):335-71) and its p-value is derived using a normal approximation.
Risk Ratio and related p-value are estimated by using the SAS FREQ procedure.
Risk Difference and related p-value are estimated by using the SAS GLIMMIX procedure with the following model: criterion = treatment.
p-values for heterogeneity are estimated by using the SAS GLIMMIX procedure with the following model: criterion = treatment subgroup treatment*subgroup.
p-value for heterogeneity of Peto Odds Ratio is estimated by using normal approximation.
PGM=DEVOPS/SAR231893/EFC14153/CSR_RWE/REPORT/PGM/ae_evt_ger_subg_s2_t.sas OUT=REPORT/OUTPUT/ae_sae_ger_onsa_s2_t_x.rtf (10AUG2021 - 8:07)

Project Code / Study Number / Analysis: SAR231893 / EFC14153 / CSR_RWE

2 Adverse events - Safety type 2 inflammatory asthma phenotype population

2.4 Patients with any treatment emergent SAE

2.4.12 By age at onset of asthma (0-2, 3-5, >=6 years)

	Age of onset of asthma (years)					
	0-2		3-5		>= 6	
Safety type 2 inflammatory asthma phenotype population	**Placebo (N=40)**	**Dupilumab (N=104)**	**Placebo (N=38)**	**Dupilumab (N=85)**	**Placebo (N=35)**	**Dupilumab (N=45)**
overall						0.166
Risk Ratio (95% CI)	-	1.92 (0.44 to 8.40)	-	0.67 (0.12 to 3.85)	-	0.00 (NE to NE)
Reversed Risk ratio (95% CI)	-	0.52 (0.12 to 2.27)				
p-value for Risk Ratio		0.384		0.654		NE
p-value for heterogeneity of Risk Ratio:						
0-2, 3-5						0.367
0-2, >= 6						0.978
3-5, >= 6						0.979
overall						0.665
Risk Difference (95% CI)	-	4.62 (-4.28 to 13.51)	-	-1.73 (-9.93 to 6.46)	-	-5.71 (NE to NE)
p-value for Risk Difference		0.307		0.676		<0.001

Odds Ratio and related p-value are estimated by Wald's method using the SAS LOGISTIC procedure.
Peto OR calculation is based on Yusuf S et al. (Prog Cardiovasc Dis. 1985 Mar-Apr;27(5):335-71) and its p-value is derived using a normal approximation.
Risk Ratio and related p-value are estimated by using the SAS FREQ procedure.
Risk Difference and related p-value are estimated by using the SAS GLIMMIX procedure with the following model: criterion = treatment.
p-values for heterogeneity are estimated by using the SAS GLIMMIX procedure with the following model: criterion = treatment subgroup treatment*subgroup.
p-value for heterogeneity of Peto Odds Ratio is estimated by using normal approximation.
PGM=DEVOPS/SAR231893/EFC14153/CSR_RWE/REPORT/PGM/ae_evt_ger_subg_s2_t.sas OUT=REPORT/OUTPUT/ae_sae_ger_onsa_s2_t_x.rtf (10AUG2021 - 8:07)

Project Code / Study Number / Analysis: SAR231893 / EFC14153 / CSR_RWE

2 Adverse events - Safety type 2 inflammatory asthma phenotype population

2.4 Patients with any treatment emergent SAE

2.4.12 By age at onset of asthma (0-2, 3-5, >=6 years)

	Age of onset of asthma (years)					
	0-2		3-5		>= 6	
Safety type 2 inflammatory asthma phenotype population	**Placebo (N=40)**	**Dupilumab (N=104)**	**Placebo (N=38)**	**Dupilumab (N=85)**	**Placebo (N=35)**	**Dupilumab (N=45)**
p-value for heterogeneity of Risk Difference:						
0-2, 3-5						0.300
0-2, >= 6						0.092
3-5, >= 6						<0.001
overall						0.092

Odds Ratio and related p-value are estimated by Wald's method using the SAS LOGISTIC procedure.
Peto OR calculation is based on Yusuf S et al. (Prog Cardiovasc Dis. 1985 Mar-Apr;27(5):335-71) and its p-value is derived using a normal approximation.
Risk Ratio and related p-value are estimated by using the SAS FREQ procedure.
Risk Difference and related p-value are estimated by using the SAS GLIMMIX procedure with the following model: criterion = treatment.
p-values for heterogeneity are estimated by using the SAS GLIMMIX procedure with the following model: criterion = treatment subgroup treatment*subgroup.
p-value for heterogeneity of Peto Odds Ratio is estimated by using normal approximation.
PGM=DEVOPS/SAR231893/EFC14153/CSR_RWE/REPORT/PGM/ae_evt_ger_subg_s2_t.sas OUT=REPORT/OUTPUT/ae_sae_ger_onsa_s2_t_x.rtf (10AUG2021 - 8:07)

Project Code / Study Number / Analysis: SAR231893 / EFC14153 / CSR_RWE

2 Adverse events - Safety type 2 inflammatory asthma phenotype population

2.4 Patients with any treatment emergent SAE

2.4.13 By number of severe asthma exacerbation prior to the study (<=1, 2, >2)

	Number of severe asthma exacerbation prior to the study					
	<=1		**2**		**>2**	
Safety type 2 inflammatory asthma phenotype population	**Placebo (N=46)**	**Dupilumab (N=85)**	**Placebo (N=32)**	**Dupilumab (N=75)**	**Placebo (N=35)**	**Dupilumab (N=74)**
Patients with any treatment emergent SAE [n(%)]	4 (8.7%)	4 (4.7%)	1 (3.1%)	3 (4.0%)	1 (2.9%)	6 (8.1%)
Odds Ratio (95% CI)	-	0.52 (0.12 to 2.18)	-	1.29 (0.13 to 12.91)	-	3.00 (0.35 to 25.91)
p-value for Odds Ratio		0.370		0.828		0.318
p-value for heterogeneity of Odds Ratio:						
<=1, 2						0.510
<=1, >2						0.185
2, >2						0.601
overall						0.399
Risk Ratio (95% CI)	-	0.54 (0.14 to 2.06)	-	1.28 (0.14 to 11.84)	-	2.84 (0.36 to 22.68)

Odds Ratio and related p-value are estimated by Wald's method using the SAS LOGISTIC procedure.
Peto OR calculation is based on Yusuf S et al. (Prog Cardiovasc Dis. 1985 Mar-Apr;27(5):335-71) and its p-value is derived using a normal approximation.
Risk Ratio and related p-value are estimated by using the SAS FREQ procedure.
Risk Difference and related p-value are estimated by using the SAS GLIMMIX procedure with the following model: criterion = treatment.
p-values for heterogeneity are estimated by using the SAS GLIMMIX procedure with the following model: criterion = treatment subgroup treatment*subgroup.
p-value for heterogeneity of Peto Odds Ratio is estimated by using normal approximation.
PGM=DEVOPS/SAR231893/EFC14153/CSR_RWE/REPORT/PGM/ae_evt_ger_subg_s2_t.sas OUT=REPORT/OUTPUT/ae_sae_ger_exa_s2_t_x.rtf (29JUL2021 - 14:47)

Project Code / Study Number / Analysis: SAR231893 / EFC14153 / CSR_RWE

2 Adverse events - Safety type 2 inflammatory asthma phenotype population

2.4 Patients with any treatment emergent SAE

2.4.13 By number of severe asthma exacerbation prior to the study (<=1, 2, >2)

	Number of severe asthma exacerbation prior to the study					
	<=1		2		>2	
Safety type 2 inflammatory asthma phenotype population	**Placebo (N=46)**	**Dupilumab (N=85)**	**Placebo (N=32)**	**Dupilumab (N=75)**	**Placebo (N=35)**	**Dupilumab (N=74)**
Reversed Risk ratio (95% CI)			-	0.78 (0.08 to 7.23)	-	0.35 (0.04 to 2.82)
p-value for Risk Ratio		0.369		0.828		0.325
p-value for heterogeneity of Risk Ratio:						
<=1, 2						0.516
<=1, >2						0.190
2, >2						0.609
overall						0.405
Risk Difference (95% CI)	-	-3.99 (-13.38 to 5.40)	-	0.88 (-6.70 to 8.45)	-	5.25 (-3.16 to 13.66)
p-value for Risk Difference		0.402		0.819		0.219
p-value for heterogeneity of Risk Difference:						
<=1, 2						0.425
<=1, >2						0.148

Odds Ratio and related p-value are estimated by Wald's method using the SAS LOGISTIC procedure.
Peto OR calculation is based on Yusuf S et al. (Prog Cardiovasc Dis. 1985 Mar-Apr;27(5):335-71) and its p-value is derived using a normal approximation.
Risk Ratio and related p-value are estimated by using the SAS FREQ procedure.
Risk Difference and related p-value are estimated by using the SAS GLIMMIX procedure with the following model: criterion = treatment.
p-values for heterogeneity are estimated by using the SAS GLIMMIX procedure with the following model: criterion = treatment subgroup treatment*subgroup.
p-value for heterogeneity of Peto Odds Ratio is estimated by using normal approximation.
PGM=DEVOPS/SAR231893/EFC14153/CSR_RWE/REPORT/PGM/ae_evt_ger_subg_s2_t.sas OUT=REPORT/OUTPUT/ae_sae_ger_exa_s2_t_x.rtf (29JUL2021 - 14:47)

Project Code / Study Number / Analysis: SAR231893 / EFC14153 / CSR_RWE

2 Adverse events - Safety type 2 inflammatory asthma phenotype population

2.4 Patients with any treatment emergent SAE

2.4.13 By number of severe asthma exacerbation prior to the study (<=1, 2, >2)

	Number of severe asthma exacerbation prior to the study					
	<=1		2		>2	
Safety type 2 inflammatory asthma phenotype population	**Placebo (N=46)**	**Dupilumab (N=85)**	**Placebo (N=32)**	**Dupilumab (N=75)**	**Placebo (N=35)**	**Dupilumab (N=74)**
2, >2						0.444
overall						0.349

Odds Ratio and related p-value are estimated by Wald's method using the SAS LOGISTIC procedure.
Peto OR calculation is based on Yusuf S et al. (Prog Cardiovasc Dis. 1985 Mar-Apr;27(5):335-71) and its p-value is derived using a normal approximation.
Risk Ratio and related p-value are estimated by using the SAS FREQ procedure.
Risk Difference and related p-value are estimated by using the SAS GLIMMIX procedure with the following model: criterion = treatment.
p-values for heterogeneity are estimated by using the SAS GLIMMIX procedure with the following model: criterion = treatment subgroup treatment*subgroup.
p-value for heterogeneity of Peto Odds Ratio is estimated by using normal approximation.
PGM=DEVOPS/SAR231893/EFC14153/CSR_RWE/REPORT/PGM/ae_evt_ger_subg_s2_t.sas OUT=REPORT/OUTPUT/ae_sae_ger_exa_s2_t_x.rtf (29JUL2021 - 14:47)

Project Code / Study Number / Analysis: SAR231893 / EFC14153 / CSR_RWE

2 Adverse events - Safety type 2 inflammatory asthma phenotype population

2.12 Patients with at least one TEAE in SOC: Blood and lymphatic system disorders

Safety type 2 inflammatory asthma phenotype population	Placebo (N=113)	Dupilumab (N=234)
Patients with at least one TEAE in SOC: Blood and lymphatic system disorders [n(%)]	4 (3.5%)	20 (8.5%)
Odds Ratio (95% CI)	-	2.55 (0.85 to 7.63)
p-value for Odds Ratio		0.095
Risk Ratio (95% CI)	-	2.41 (0.85 to 6.90)
Reversed Risk Ratio (95% CI)	-	0.41 (0.14 to 1.18)
p-value for Risk Ratio		0.100
Risk Difference (95% CI)	-	5.01 (0.05 to 9.97)
p-value for Risk Difference		0.048

Odds Ratio and related p-value are estimated by Wald's method using the SAS LOGISTIC procedure.
Peto OR calculation is based on Yusuf S et al. (Prog Cardiovasc Dis. 1985 Mar-Apr;27(5):335-71) and its p-value is derived using a normal approximation.
Risk Ratio and related p-value are estimated by using the SAS FREQ procedure.
Risk Difference and related p-value are estimated by using the SAS GLIMMIX procedure with the following model: criterion = treatment.
p-value for heterogeneity of Peto Odds Ratio is estimated by using normal approximation.
PGM=DEVOPS/SAR231893/EFC14153/CSR_RWE/REPORT/PGM/ae_evt_ger_s2_t.sas OUT=REPORT/OUTPUT/ae_socblood_ger_s2_t_x.rtf (30JUL2021 - 15:50)

Project Code / Study Number / Analysis: SAR231893 / EFC14153 / CSR_RWE

2 Adverse events - Safety type 2 inflammatory asthma phenotype population

2.12 Patients with at least one TEAE in SOC: Blood and lymphatic system disorders

2.12.1 By gender (Male, Female)

	Gender			
	Male		Female	
Safety type 2 inflammatory asthma phenotype population	**Placebo (N=77)**	**Dupilumab (N=153)**	**Placebo (N=36)**	**Dupilumab (N=81)**
Patients with at least one TEAE in SOC: Blood and lymphatic system disorders [n(%)]	2 (2.6%)	15 (9.8%)	2 (5.6%)	5 (6.2%)
Odds Ratio (95% CI)	-	4.08 (0.91 to 18.30)	-	1.12 (0.21 to 6.05)
p-value for Odds Ratio		0.067		0.897
p-value for heterogeneity of Odds Ratio				0.263
Risk Ratio (95% CI)	-	3.77 (0.89 to 16.09)	-	1.11 (0.23 to 5.46)
Reversed Risk ratio (95% CI)	-	0.26 (0.06 to 1.13)	-	0.90 (0.18 to 4.42)
p-value for Risk Ratio		0.073		0.897
p-value for heterogeneity of Risk Ratio				0.266

Odds Ratio and related p-value are estimated by Wald's method using the SAS LOGISTIC procedure.
Peto OR calculation is based on Yusuf S et al. (Prog Cardiovasc Dis. 1985 Mar-Apr;27(5):335-71) and its p-value is derived using a normal approximation.
Risk Ratio and related p-value are estimated by using the SAS FREQ procedure.
Risk Difference and related p-value are estimated by using the SAS GLIMMIX procedure with the following model: criterion = treatment.
p-values for heterogeneity are estimated by using the SAS GLIMMIX procedure with the following model: criterion = treatment subgroup treatment*subgroup.
p-value for heterogeneity of Peto Odds Ratio is estimated by using normal approximation.
PGM=DEVOPS/SAR231893/EFC14153/CSR_RWE/REPORT/PGM/ae_evt_ger_subg_s2_t.sas OUT=REPORT/OUTPUT/ae_socblood_ger_sex_s2_t_x.rtf (10AUG2021 - 8:09)

Project Code / Study Number / Analysis: SAR231893 / EFC14153 / CSR_RWE

2 Adverse events - Safety type 2 inflammatory asthma phenotype population

2.12 Patients with at least one TEAE in SOC: Blood and lymphatic system disorders

2.12.1 By gender (Male, Female)

	Gender			
	Male		Female	
Safety type 2 inflammatory asthma phenotype population	**Placebo (N=77)**	**Dupilumab (N=153)**	**Placebo (N=36)**	**Dupilumab (N=81)**
Risk Difference (95% CI)	-	7.21 (1.27 to 13.14)	-	0.62 (-8.62 to 9.85)
p-value for Risk Difference		0.017		0.895
p-value for heterogeneity of Risk Difference				0.236

Odds Ratio and related p-value are estimated by Wald's method using the SAS LOGISTIC procedure.
Peto OR calculation is based on Yusuf S et al. (Prog Cardiovasc Dis. 1985 Mar-Apr;27(5):335-71) and its p-value is derived using a normal approximation.
Risk Ratio and related p-value are estimated by using the SAS FREQ procedure.
Risk Difference and related p-value are estimated by using the SAS GLIMMIX procedure with the following model: criterion = treatment.
p-values for heterogeneity are estimated by using the SAS GLIMMIX procedure with the following model: criterion = treatment subgroup treatment*subgroup.
p-value for heterogeneity of Peto Odds Ratio is estimated by using normal approximation.
PGM=DEVOPS/SAR231893/EFC14153/CSR_RWE/REPORT/PGM/ae_evt_ger_subg_s2_t.sas OUT=REPORT/OUTPUT/ae_socblood_ger_sex_s2_t_x.rtf (10AUG2021 - 8:09)

Project Code / Study Number / Analysis: SAR231893 / EFC14153 / CSR_RWE

2 Adverse events - Safety type 2 inflammatory asthma phenotype population

2.12 Patients with at least one TEAE in SOC: Blood and lymphatic system disorders

2.12.2 By region (Latin America, East Europe, Western Countries)

	Region					
	Latin America		East Europe		Western countries	
Safety type 2 inflammatory asthma phenotype population	**Placebo (N=51)**	**Dupilumab (N=105)**	**Placebo (N=43)**	**Dupilumab (N=78)**	**Placebo (N=19)**	**Dupilumab (N=51)**
Patients with at least one TEAE in SOC: Blood and lymphatic system disorders [n(%)]	1 (2.0%)	7 (6.7%)	2 (4.7%)	8 (10.3%)	1 (5.3%)	5 (9.8%)
Odds Ratio (95% CI)	-	3.57 (0.43 to 29.84)	-	2.34 (0.47 to 11.57)	-	1.96 (0.21 to 17.93)
p-value for Odds Ratio		0.240		0.296		0.553
p-value for heterogeneity of Odds Ratio:						
Latin America, East Europe						0.756
Latin America, Western countries						0.701
East Europe, Western countries						0.897
overall						0.922

Odds Ratio and related p-value are estimated by Wald's method using the SAS LOGISTIC procedure.
Peto OR calculation is based on Yusuf S et al. (Prog Cardiovasc Dis. 1985 Mar-Apr;27(5):335-71) and its p-value is derived using a normal approximation.
Risk Ratio and related p-value are estimated by using the SAS FREQ procedure.
Risk Difference and related p-value are estimated by using the SAS GLIMMIX procedure with the following model: criterion = treatment.
p-values for heterogeneity are estimated by using the SAS GLIMMIX procedure with the following model: criterion = treatment subgroup treatment*subgroup.
p-value for heterogeneity of Peto Odds Ratio is estimated by using normal approximation.
PGM=DEVOPS/SAR231893/EFC14153/CSR_RWE/REPORT/PGM/ae_evt_ger_subg_s2_t.sas OUT=REPORT/OUTPUT/ae_socblood_ger_cty_s2_t_x.rtf (10AUG2021 - 8:09)

Project Code / Study Number / Analysis: SAR231893 / EFC14153 / CSR_RWE

2 Adverse events - Safety type 2 inflammatory asthma phenotype population

2.12 Patients with at least one TEAE in SOC: Blood and lymphatic system disorders

2.12.2 By region (Latin America, East Europe, Western Countries)

	Region					
	Latin America		East Europe		Western countries	
Safety type 2 inflammatory asthma phenotype population	**Placebo (N=51)**	**Dupilumab (N=105)**	**Placebo (N=43)**	**Dupilumab (N=78)**	**Placebo (N=19)**	**Dupilumab (N=51)**
Risk Ratio (95% CI)	-	3.40 (0.43 to 26.90)	-	2.21 (0.49 to 9.92)	-	1.86 (0.23 to 14.93)
Reversed Risk ratio (95% CI)	-	0.29 (0.04 to 2.33)	-	0.45 (0.10 to 2.04)	-	0.54 (0.07 to 4.30)
p-value for Risk Ratio		0.246		0.303		0.558
p-value for heterogeneity of Risk Ratio:						
Latin America, East Europe						0.740
Latin America, Western countries						0.688
East Europe, Western countries						0.898
overall						0.915
Risk Difference (95% CI)	-	4.71 (-1.45 to 10.86)	-	5.61 (-3.71 to 14.92)	-	4.54 (-8.63 to 17.71)
p-value for Risk Difference		0.133		0.236		0.494
p-value for heterogeneity of Risk Difference:						
Latin America, East Europe						0.873

Odds Ratio and related p-value are estimated by Wald's method using the SAS LOGISTIC procedure.
Peto OR calculation is based on Yusuf S et al. (Prog Cardiovasc Dis. 1985 Mar-Apr;27(5):335-71) and its p-value is derived using a normal approximation.
Risk Ratio and related p-value are estimated by using the SAS FREQ procedure.
Risk Difference and related p-value are estimated by using the SAS GLIMMIX procedure with the following model: criterion = treatment.
p-values for heterogeneity are estimated by using the SAS GLIMMIX procedure with the following model: criterion = treatment subgroup treatment*subgroup.
p-value for heterogeneity of Peto Odds Ratio is estimated by using normal approximation.
PGM=DEVOPS/SAR231893/EFC14153/CSR_RWE/REPORT/PGM/ae_evt_ger_subg_s2_t.sas OUT=REPORT/OUTPUT/ae_socblood_ger_cty_s2_t_x.rtf (10AUG2021 - 8:09)

Project Code / Study Number / Analysis: SAR231893 / EFC14153 / CSR_RWE

2 Adverse events - Safety type 2 inflammatory asthma phenotype population

2.12 Patients with at least one TEAE in SOC: Blood and lymphatic system disorders

2.12.2 By region (Latin America, East Europe, Western Countries)

	Region					
	Latin America		East Europe		Western countries	
Safety type 2 inflammatory asthma phenotype population	**Placebo (N=51)**	**Dupilumab (N=105)**	**Placebo (N=43)**	**Dupilumab (N=78)**	**Placebo (N=19)**	**Dupilumab (N=51)**
Latin America, Western countries						0.982
East Europe, Western countries						0.896
overall						0.985

Odds Ratio and related p-value are estimated by Wald's method using the SAS LOGISTIC procedure.
Peto OR calculation is based on Yusuf S et al. (Prog Cardiovasc Dis. 1985 Mar-Apr;27(5):335-71) and its p-value is derived using a normal approximation.
Risk Ratio and related p-value are estimated by using the SAS FREQ procedure.
Risk Difference and related p-value are estimated by using the SAS GLIMMIX procedure with the following model: criterion = treatment.
p-values for heterogeneity are estimated by using the SAS GLIMMIX procedure with the following model: criterion = treatment subgroup treatment*subgroup.
p-value for heterogeneity of Peto Odds Ratio is estimated by using normal approximation.
PGM=DEVOPS/SAR231893/EFC14153/CSR_RWE/REPORT/PGM/ae_evt_ger_subg_s2_t.sas OUT=REPORT/OUTPUT/ae_socblood_ger_cty_s2_t_x.rtf (10AUG2021 - 8:09)

Project Code / Study Number / Analysis: SAR231893 / EFC14153 / CSR_RWE

2 Adverse events - Safety type 2 inflammatory asthma phenotype population

2.12 Patients with at least one TEAE in SOC: Blood and lymphatic system disorders

2.12.3 By race (Caucasian/white, Black/of African descent, Other)

	Race					
	Caucasian/White		Black/of African descent		Other	
Safety type 2 inflammatory asthma phenotype population	**Placebo (N=101)**	**Dupilumab (N=207)**	**Placebo (N=5)**	**Dupilumab (N=9)**	**Placebo (N=7)**	**Dupilumab (N=18)**
Patients with at least one TEAE in SOC: Blood and lymphatic system disorders [n(%)]	3 (3.0%)	19 (9.2%)	1 (20.0%)	1 (11.1%)	0	0
Odds Ratio (95% CI)	-	3.30 (0.95 to 11.43)	-	0.50 (0.02 to 10.25)	-	NE (NE to NE)
p-value for Odds Ratio		0.059		0.653		NE
Peto Odds Ratio (95% CI)	-	2.54 (1.01 to 6.39)	-	0.51 (0.03 to 10.34)	-	NE (NE to NE)
Reversed Peto Odds Ratio (95% CI)	-	0.39 (0.16 to 0.99)				
p-value for Peto Odds Ratio		0.047		0.661		NE
p-value for heterogeneity of Peto Odds Ratio:						
Caucasian/White, Black/of African descent						0.317
Caucasian/White, Other						NE
Black/of African descent, Other						NE
overall						NE

Odds Ratio and related p-value are estimated by Wald's method using the SAS LOGISTIC procedure.
Peto OR calculation is based on Yusuf S et al. (Prog Cardiovasc Dis. 1985 Mar-Apr;27(5):335-71) and its p-value is derived using a normal approximation.
Risk Ratio and related p-value are estimated by using the SAS FREQ procedure.
Risk Difference and related p-value are estimated by using the SAS GLIMMIX procedure with the following model: criterion = treatment.
p-values for heterogeneity are estimated by using the SAS GLIMMIX procedure with the following model: criterion = treatment subgroup treatment*subgroup.
p-value for heterogeneity of Peto Odds Ratio is estimated by using normal approximation.
PGM=DEVOPS/SAR231893/EFC14153/CSR_RWE/REPORT/PGM/ae_evt_ger_subg_s2_t.sas OUT=REPORT/OUTPUT/ae_socblood_ger_race_s2_t_x.rtf (10AUG2021 - 8:09)

Project Code / Study Number / Analysis: SAR231893 / EFC14153 / CSR_RWE

2 Adverse events - Safety type 2 inflammatory asthma phenotype population

2.12 Patients with at least one TEAE in SOC: Blood and lymphatic system disorders

2.12.3 By race (Caucasian/white, Black/of African descent, Other)

	Race					
	Caucasian/White		Black/of African descent		Other	
Safety type 2 inflammatory asthma phenotype population	**Placebo (N=101)**	**Dupilumab (N=207)**	**Placebo (N=5)**	**Dupilumab (N=9)**	**Placebo (N=7)**	**Dupilumab (N=18)**
Risk Ratio (95% CI)	-	3.09 (0.94 to 10.20)	-	0.56 (0.04 to 7.09)	-	NE (NE to NE)
Reversed Risk ratio (95% CI)	-	0.32 (0.10 to 1.07)				
p-value for Risk Ratio		0.064		0.651		NE
p-value for heterogeneity of Risk Ratio:						
Caucasian/White, Black/of African descent						0.233
Caucasian/White, Other						0.999
Black/of African descent, Other						0.999
overall						0.490
Risk Difference (95% CI)	-	6.21 (1.05 to 11.37)	-	-8.89 (-54.06 to 36.28)	-	0.00 (NE to NE)
p-value for Risk Difference		0.019		0.676		NE
p-value for heterogeneity of Risk Difference:						
Caucasian/White, Black/of African descent						0.470

Odds Ratio and related p-value are estimated by Wald's method using the SAS LOGISTIC procedure.
Peto OR calculation is based on Yusuf S et al. (Prog Cardiovasc Dis. 1985 Mar-Apr;27(5):335-71) and its p-value is derived using a normal approximation.
Risk Ratio and related p-value are estimated by using the SAS FREQ procedure.
Risk Difference and related p-value are estimated by using the SAS GLIMMIX procedure with the following model: criterion = treatment.
p-values for heterogeneity are estimated by using the SAS GLIMMIX procedure with the following model: criterion = treatment subgroup treatment*subgroup.
p-value for heterogeneity of Peto Odds Ratio is estimated by using normal approximation.
PGM=DEVOPS/SAR231893/EFC14153/CSR_RWE/REPORT/PGM/ae_evt_ger_subg_s2_t.sas OUT=REPORT/OUTPUT/ae_socblood_ger_race_s2_t_x.rtf (10AUG2021 - 8:09)

Project Code / Study Number / Analysis: SAR231893 / EFC14153 / CSR_RWE

2 Adverse events - Safety type 2 inflammatory asthma phenotype population

2.12 Patients with at least one TEAE in SOC: Blood and lymphatic system disorders

2.12.3 By race (Caucasian/white, Black/of African descent, Other)

	Race					
	Caucasian/White		Black/of African descent		Other	
Safety type 2 inflammatory asthma phenotype population	**Placebo (N=101)**	**Dupilumab (N=207)**	**Placebo (N=5)**	**Dupilumab (N=9)**	**Placebo (N=7)**	**Dupilumab (N=18)**
Caucasian/White, Other						0.767
Black/of African descent, Other						<0.001
overall						0.767

Odds Ratio and related p-value are estimated by Wald's method using the SAS LOGISTIC procedure.
Peto OR calculation is based on Yusuf S et al. (Prog Cardiovasc Dis. 1985 Mar-Apr;27(5):335-71) and its p-value is derived using a normal approximation.
Risk Ratio and related p-value are estimated by using the SAS FREQ procedure.
Risk Difference and related p-value are estimated by using the SAS GLIMMIX procedure with the following model: criterion = treatment.
p-values for heterogeneity are estimated by using the SAS GLIMMIX procedure with the following model: criterion = treatment subgroup treatment*subgroup.
p-value for heterogeneity of Peto Odds Ratio is estimated by using normal approximation.
PGM=DEVOPS/SAR231893/EFC14153/CSR_RWE/REPORT/PGM/ae_evt_ger_subg_s2_t.sas OUT=REPORT/OUTPUT/ae_socblood_ger_race_s2_t_x.rtf (10AUG2021 - 8:09)

Project Code / Study Number / Analysis: SAR231893 / EFC14153 / CSR_RWE

2 Adverse events - Safety type 2 inflammatory asthma phenotype population

2.12 Patients with at least one TEAE in SOC: Blood and lymphatic system disorders

2.12.4 By baseline ICS dose level (Medium, High)

	Baseline ICS dose level			
	High		Medium	
Safety type 2 inflammatory asthma phenotype population	**Placebo (N=50)**	**Dupilumab (N=101)**	**Placebo (N=63)**	**Dupilumab (N=131)**
Patients with at least one TEAE in SOC: Blood and lymphatic system disorders [n(%)]	0	5 (5.0%)	4 (6.3%)	15 (11.5%)
Odds Ratio (95% CI)	-	NE (NE to NE)	-	1.91 (0.61 to 6.00)
p-value for Odds Ratio		NE		0.270
Peto Odds Ratio (95% CI)	-	4.65 (0.70 to 30.69)	-	1.78 (0.65 to 4.87)
Reversed Peto Odds Ratio (95% CI)	-	0.22 (0.03 to 1.43)	-	0.56 (0.21 to 1.54)
p-value for Peto Odds Ratio		0.111		0.264
p-value for heterogeneity of Peto Odds Ratio				0.379
Risk Ratio (95% CI)	-	NE (NE to NE)	-	1.80 (0.62 to 5.21)
Reversed Risk ratio (95% CI)			-	0.55 (0.19 to 1.60)

Odds Ratio and related p-value are estimated by Wald's method using the SAS LOGISTIC procedure.
Peto OR calculation is based on Yusuf S et al. (Prog Cardiovasc Dis. 1985 Mar-Apr;27(5):335-71) and its p-value is derived using a normal approximation.
Risk Ratio and related p-value are estimated by using the SAS FREQ procedure.
Risk Difference and related p-value are estimated by using the SAS GLIMMIX procedure with the following model: criterion = treatment.
p-values for heterogeneity are estimated by using the SAS GLIMMIX procedure with the following model: criterion = treatment subgroup treatment*subgroup.
p-value for heterogeneity of Peto Odds Ratio is estimated by using normal approximation.
PGM=DEVOPS/SAR231893/EFC14153/CSR_RWE/REPORT/PGM/ae_evt_ger_subg_s2_t.sas OUT=REPORT/OUTPUT/ae_socblood_ger_ics_s2_t_x.rtf (10AUG2021 - 8:09)

Project Code / Study Number / Analysis: SAR231893 / EFC14153 / CSR_RWE

2 Adverse events - Safety type 2 inflammatory asthma phenotype population

2.12 Patients with at least one TEAE in SOC: Blood and lymphatic system disorders

2.12.4 By baseline ICS dose level (Medium, High)

	Baseline ICS dose level			
	High		Medium	
Safety type 2 inflammatory asthma phenotype population	**Placebo (N=50)**	**Dupilumab (N=101)**	**Placebo (N=63)**	**Dupilumab (N=131)**
p-value for Risk Ratio		NE		0.276
p-value for heterogeneity of Risk Ratio				0.979
Risk Difference (95% CI)	-	4.95 (NE to NE)	-	5.10 (-3.07 to 13.28)
p-value for Risk Difference		<0.001		0.220
p-value for heterogeneity of Risk Difference				<0.001

Odds Ratio and related p-value are estimated by Wald's method using the SAS LOGISTIC procedure.
Peto OR calculation is based on Yusuf S et al. (Prog Cardiovasc Dis. 1985 Mar-Apr;27(5):335-71) and its p-value is derived using a normal approximation.
Risk Ratio and related p-value are estimated by using the SAS FREQ procedure.
Risk Difference and related p-value are estimated by using the SAS GLIMMIX procedure with the following model: criterion = treatment.
p-values for heterogeneity are estimated by using the SAS GLIMMIX procedure with the following model: criterion = treatment subgroup treatment*subgroup.
p-value for heterogeneity of Peto Odds Ratio is estimated by using normal approximation.
PGM=DEVOPS/SAR231893/EFC14153/CSR_RWE/REPORT/PGM/ae_evt_ger_subg_s2_t.sas OUT=REPORT/OUTPUT/ae_socblood_ger_ics_s2_t_x.rtf (10AUG2021 - 8:09)

Project Code / Study Number / Analysis: SAR231893 / EFC14153 / CSR_RWE

2 Adverse events - Safety type 2 inflammatory asthma phenotype population

2.12 Patients with at least one TEAE in SOC: Blood and lymphatic system disorders

2.12.5 By baseline ICS dose level 2 (Medium, High)

	Baseline ICS dose level 2			
	High		Medium	
Safety type 2 inflammatory asthma phenotype population	**Placebo (N=94)**	**Dupilumab (N=199)**	**Placebo (N=19)**	**Dupilumab (N=35)**
Patients with at least one TEAE in SOC: Blood and lymphatic system disorders [n(%)]	4 (4.3%)	16 (8.0%)	0	4 (11.4%)
Odds Ratio (95% CI)	-	1.97 (0.64 to 6.06)	-	NE (NE to NE)
p-value for Odds Ratio		0.238		NE
Peto Odds Ratio (95% CI)	-	1.81 (0.69 to 4.78)	-	5.13 (0.62 to 42.44)
Reversed Peto Odds Ratio (95% CI)	-	0.55 (0.21 to 1.45)	-	0.19 (0.02 to 1.61)
p-value for Peto Odds Ratio		0.231		0.129
p-value for heterogeneity of Peto Odds Ratio				0.380
Risk Ratio (95% CI)	-	1.89 (0.65 to 5.50)	-	NE (NE to NE)
Reversed Risk ratio (95% CI)	-	0.53 (0.18 to 1.54)		

Odds Ratio and related p-value are estimated by Wald's method using the SAS LOGISTIC procedure.
Peto OR calculation is based on Yusuf S et al. (Prog Cardiovasc Dis. 1985 Mar-Apr;27(5):335-71) and its p-value is derived using a normal approximation.
Risk Ratio and related p-value are estimated by using the SAS FREQ procedure.
Risk Difference and related p-value are estimated by using the SAS GLIMMIX procedure with the following model: criterion = treatment.
p-values for heterogeneity are estimated by using the SAS GLIMMIX procedure with the following model: criterion = treatment subgroup treatment*subgroup.
p-value for heterogeneity of Peto Odds Ratio is estimated by using normal approximation.
PGM=DEVOPS/SAR231893/EFC14153/CSR_RWE/REPORT/PGM/ae_evt_ger_subg_s2_t.sas OUT=REPORT/OUTPUT/ae_socblood_ger_ics2_s2_t_x.rtf (01SEP2021 - 16:08)

Project Code / Study Number / Analysis: SAR231893 / EFC14153 / CSR_RWE

2 Adverse events - Safety type 2 inflammatory asthma phenotype population

2.12 Patients with at least one TEAE in SOC: Blood and lymphatic system disorders

2.12.5 By baseline ICS dose level 2 (Medium, High)

	Baseline ICS dose level 2			
	High		Medium	
Safety type 2 inflammatory asthma phenotype population	**Placebo (N=94)**	**Dupilumab (N=199)**	**Placebo (N=19)**	**Dupilumab (N=35)**
p-value for Risk Ratio		0.243		NE
p-value for heterogeneity of Risk Ratio				0.979
Risk Difference (95% CI)	-	3.78 (-1.80 to 9.37)	-	11.43 (NE to NE)
p-value for Risk Difference		0.183		<0.001
p-value for heterogeneity of Risk Difference				<0.001

Odds Ratio and related p-value are estimated by Wald's method using the SAS LOGISTIC procedure.
Peto OR calculation is based on Yusuf S et al. (Prog Cardiovasc Dis. 1985 Mar-Apr;27(5):335-71) and its p-value is derived using a normal approximation.
Risk Ratio and related p-value are estimated by using the SAS FREQ procedure.
Risk Difference and related p-value are estimated by using the SAS GLIMMIX procedure with the following model: criterion = treatment.
p-values for heterogeneity are estimated by using the SAS GLIMMIX procedure with the following model: criterion = treatment subgroup treatment*subgroup.
p-value for heterogeneity of Peto Odds Ratio is estimated by using normal approximation.
PGM=DEVOPS/SAR231893/EFC14153/CSR_RWE/REPORT/PGM/ae_evt_ger_subg_s2_t.sas OUT=REPORT/OUTPUT/ae_socblood_ger_ics2_s2_t_x.rtf (01SEP2021 - 16:08)

Project Code / Study Number / Analysis: SAR231893 / EFC14153 / CSR_RWE

2 Adverse events - Safety type 2 inflammatory asthma phenotype population

2.12 Patients with at least one TEAE in SOC: Blood and lymphatic system disorders

2.12.6 By baseline predicted FEV1 (<80%, >=80%)

	Baseline Predicted FEV1			
	<80%		>=80%	
Safety type 2 inflammatory asthma phenotype population	**Placebo (N=58)**	**Dupilumab (N=116)**	**Placebo (N=55)**	**Dupilumab (N=118)**
Patients with at least one TEAE in SOC: Blood and lymphatic system disorders [n(%)]	3 (5.2%)	9 (7.8%)	1 (1.8%)	11 (9.3%)
Odds Ratio (95% CI)	-	1.54 (0.40 to 5.93)	-	5.55 (0.70 to 44.13)
p-value for Odds Ratio		0.528		0.105
p-value for heterogeneity of Odds Ratio				0.311
Risk Ratio (95% CI)	-	1.50 (0.42 to 5.33)	-	5.13 (0.68 to 38.73)
Reversed Risk ratio (95% CI)	-	0.67 (0.19 to 2.37)	-	0.20 (0.03 to 1.47)
p-value for Risk Ratio		0.531		0.113
p-value for heterogeneity of Risk Ratio				0.314

Odds Ratio and related p-value are estimated by Wald's method using the SAS LOGISTIC procedure.
Peto OR calculation is based on Yusuf S et al. (Prog Cardiovasc Dis. 1985 Mar-Apr;27(5):335-71) and its p-value is derived using a normal approximation.
Risk Ratio and related p-value are estimated by using the SAS FREQ procedure.
Risk Difference and related p-value are estimated by using the SAS GLIMMIX procedure with the following model: criterion = treatment.
p-values for heterogeneity are estimated by using the SAS GLIMMIX procedure with the following model: criterion = treatment subgroup treatment*subgroup.
p-value for heterogeneity of Peto Odds Ratio is estimated by using normal approximation.
PGM=DEVOPS/SAR231893/EFC14153/CSR_RWE/REPORT/PGM/ae_evt_ger_subg_s2_t.sas OUT=REPORT/OUTPUT/ae_socblood_ger_pfev1_s2_t_x.rtf (10AUG2021 - 8:10)

Project Code / Study Number / Analysis: SAR231893 / EFC14153 / CSR_RWE

2 Adverse events - Safety type 2 inflammatory asthma phenotype population

2.12 Patients with at least one TEAE in SOC: Blood and lymphatic system disorders

2.12.6 By baseline predicted FEV1 (<80%, >=80%)

	Baseline Predicted FEV1			
	<80%		>=80%	
Safety type 2 inflammatory asthma phenotype population	**Placebo (N=58)**	**Dupilumab (N=116)**	**Placebo (N=55)**	**Dupilumab (N=118)**
Risk Difference (95% CI)	-	2.59 (-4.96 to 10.14)	-	7.50 (1.14 to 13.87)
p-value for Risk Difference		0.500		0.021
p-value for heterogeneity of Risk Difference				0.326

Odds Ratio and related p-value are estimated by Wald's method using the SAS LOGISTIC procedure.
Peto OR calculation is based on Yusuf S et al. (Prog Cardiovasc Dis. 1985 Mar-Apr;27(5):335-71) and its p-value is derived using a normal approximation.
Risk Ratio and related p-value are estimated by using the SAS FREQ procedure.
Risk Difference and related p-value are estimated by using the SAS GLIMMIX procedure with the following model: criterion = treatment.
p-values for heterogeneity are estimated by using the SAS GLIMMIX procedure with the following model: criterion = treatment subgroup treatment*subgroup.
p-value for heterogeneity of Peto Odds Ratio is estimated by using normal approximation.
PGM=DEVOPS/SAR231893/EFC14153/CSR_RWE/REPORT/PGM/ae_evt_ger_subg_s2_t.sas OUT=REPORT/OUTPUT/ae_socblood_ger_pfev1_s2_t_x.rtf (10AUG2021 - 8:10)

Project Code / Study Number / Analysis: SAR231893 / EFC14153 / CSR_RWE

2 Adverse events - Safety type 2 inflammatory asthma phenotype population

2.12 Patients with at least one TEAE in SOC: Blood and lymphatic system disorders

2.12.7 By baseline ACQ-7-IA (<=2, >2)

	Baseline ACQ-7-IA			
	<=2		>2	
Safety type 2 inflammatory asthma phenotype population	**Placebo (N=61)**	**Dupilumab (N=125)**	**Placebo (N=52)**	**Dupilumab (N=109)**
Patients with at least one TEAE in SOC: Blood and lymphatic system disorders [n(%)]	3 (4.9%)	8 (6.4%)	1 (1.9%)	12 (11.0%)
Odds Ratio (95% CI)	-	1.32 (0.34 to 5.17)	-	6.31 (0.80 to 49.89)
p-value for Odds Ratio		0.688		0.081
p-value for heterogeneity of Odds Ratio				0.217
Risk Ratio (95% CI)	-	1.30 (0.36 to 4.73)	-	5.72 (0.76 to 42.86)
Reversed Risk ratio (95% CI)	-	0.77 (0.21 to 2.79)	-	0.17 (0.02 to 1.31)
p-value for Risk Ratio		0.689		0.089
p-value for heterogeneity of Risk Ratio				0.226

Odds Ratio and related p-value are estimated by Wald's method using the SAS LOGISTIC procedure.
Peto OR calculation is based on Yusuf S et al. (Prog Cardiovasc Dis. 1985 Mar-Apr;27(5):335-71) and its p-value is derived using a normal approximation.
Risk Ratio and related p-value are estimated by using the SAS FREQ procedure.
Risk Difference and related p-value are estimated by using the SAS GLIMMIX procedure with the following model: criterion = treatment.
p-values for heterogeneity are estimated by using the SAS GLIMMIX procedure with the following model: criterion = treatment subgroup treatment*subgroup.
p-value for heterogeneity of Peto Odds Ratio is estimated by using normal approximation.
PGM=DEVOPS/SAR231893/EFC14153/CSR_RWE/REPORT/PGM/ae_evt_ger_subg_s2_t.sas OUT=REPORT/OUTPUT/ae_socblood_ger_acq7_s2_t_x.rtf (10AUG2021 - 8:10)

Project Code / Study Number / Analysis: SAR231893 / EFC14153 / CSR_RWE

2 Adverse events - Safety type 2 inflammatory asthma phenotype population

2.12 Patients with at least one TEAE in SOC: Blood and lymphatic system disorders

2.12.7 By baseline ACQ-7-IA (<=2, >2)

	Baseline ACQ-7-IA			
	<=2		>2	
Safety type 2 inflammatory asthma phenotype population	**Placebo (N=61)**	**Dupilumab (N=125)**	**Placebo (N=52)**	**Dupilumab (N=109)**
Risk Difference (95% CI)	-	1.48 (-5.48 to 8.45)	-	9.09 (2.07 to 16.10)
p-value for Risk Difference		0.675		0.011
p-value for heterogeneity of Risk Difference				0.130

Odds Ratio and related p-value are estimated by Wald's method using the SAS LOGISTIC procedure.
Peto OR calculation is based on Yusuf S et al. (Prog Cardiovasc Dis. 1985 Mar-Apr;27(5):335-71) and its p-value is derived using a normal approximation.
Risk Ratio and related p-value are estimated by using the SAS FREQ procedure.
Risk Difference and related p-value are estimated by using the SAS GLIMMIX procedure with the following model: criterion = treatment.
p-values for heterogeneity are estimated by using the SAS GLIMMIX procedure with the following model: criterion = treatment subgroup treatment*subgroup.
p-value for heterogeneity of Peto Odds Ratio is estimated by using normal approximation.
PGM=DEVOPS/SAR231893/EFC14153/CSR_RWE/REPORT/PGM/ae_evt_ger_subg_s2_t.sas OUT=REPORT/OUTPUT/ae_socblood_ger_acq7_s2_t_x.rtf (10AUG2021 - 8:10)

Project Code / Study Number / Analysis: SAR231893 / EFC14153 / CSR_RWE

2 Adverse events - Safety type 2 inflammatory asthma phenotype population

2.12 Patients with at least one TEAE in SOC: Blood and lymphatic system disorders

2.12.8 By baseline weight (<=30 kg, >30 kg)

	Baseline weight (kg)			
	<=30		>30	
Safety type 2 inflammatory asthma phenotype population	**Placebo (N=36)**	**Dupilumab (N=74)**	**Placebo (N=77)**	**Dupilumab (N=160)**
Patients with at least one TEAE in SOC: Blood and lymphatic system disorders [n(%)]	1 (2.8%)	9 (12.2%)	3 (3.9%)	11 (6.9%)
Odds Ratio (95% CI)	-	4.85 (0.59 to 39.83)	-	1.82 (0.49 to 6.73)
p-value for Odds Ratio		0.142		0.369
p-value for heterogeneity of Odds Ratio				0.440
Risk Ratio (95% CI)	-	4.38 (0.58 to 33.25)	-	1.76 (0.51 to 6.14)
Reversed Risk ratio (95% CI)	-	0.23 (0.03 to 1.73)	-	0.57 (0.16 to 1.97)
p-value for Risk Ratio		0.153		0.372
p-value for heterogeneity of Risk Ratio				0.455

Odds Ratio and related p-value are estimated by Wald's method using the SAS LOGISTIC procedure.
Peto OR calculation is based on Yusuf S et al. (Prog Cardiovasc Dis. 1985 Mar-Apr;27(5):335-71) and its p-value is derived using a normal approximation.
Risk Ratio and related p-value are estimated by using the SAS FREQ procedure.
Risk Difference and related p-value are estimated by using the SAS GLIMMIX procedure with the following model: criterion = treatment.
p-values for heterogeneity are estimated by using the SAS GLIMMIX procedure with the following model: criterion = treatment subgroup treatment*subgroup.
p-value for heterogeneity of Peto Odds Ratio is estimated by using normal approximation.
PGM=DEVOPS/SAR231893/EFC14153/CSR_RWE/REPORT/PGM/ae_evt_ger_subg_s2_t.sas OUT=REPORT/OUTPUT/ae_socblood_ger_wgt_s2_t_x.rtf (10AUG2021 - 8:10)

Project Code / Study Number / Analysis: SAR231893 / EFC14153 / CSR_RWE

2 Adverse events - Safety type 2 inflammatory asthma phenotype population

2.12 Patients with at least one TEAE in SOC: Blood and lymphatic system disorders

2.12.8 By baseline weight (<=30 kg, >30 kg)

	Baseline weight (kg)			
	<=30		>30	
Safety type 2 inflammatory asthma phenotype population	**Placebo (N=36)**	**Dupilumab (N=74)**	**Placebo (N=77)**	**Dupilumab (N=160)**
Risk Difference (95% CI)	-	9.38 (0.10 to 18.67)	-	2.98 (-2.89 to 8.84)
p-value for Risk Difference		0.048		0.318
p-value for heterogeneity of Risk Difference				0.249

Odds Ratio and related p-value are estimated by Wald's method using the SAS LOGISTIC procedure.
Peto OR calculation is based on Yusuf S et al. (Prog Cardiovasc Dis. 1985 Mar-Apr;27(5):335-71) and its p-value is derived using a normal approximation.
Risk Ratio and related p-value are estimated by using the SAS FREQ procedure.
Risk Difference and related p-value are estimated by using the SAS GLIMMIX procedure with the following model: criterion = treatment.
p-values for heterogeneity are estimated by using the SAS GLIMMIX procedure with the following model: criterion = treatment subgroup treatment*subgroup.
p-value for heterogeneity of Peto Odds Ratio is estimated by using normal approximation.
PGM=DEVOPS/SAR231893/EFC14153/CSR_RWE/REPORT/PGM/ae_evt_ger_subg_s2_t.sas OUT=REPORT/OUTPUT/ae_socblood_ger_wgt_s2_t_x.rtf (10AUG2021 - 8:10)

Project Code / Study Number / Analysis: SAR231893 / EFC14153 / CSR_RWE

2 Adverse events - Safety type 2 inflammatory asthma phenotype population

2.12 Patients with at least one TEAE in SOC: Blood and lymphatic system disorders

2.12.9 By atopic medical condition (Yes, No)

	Atopic medical condition			
	Yes		No	
Safety type 2 inflammatory asthma phenotype population	**Placebo (N=102)**	**Dupilumab (N=225)**	**Placebo (N=11)**	**Dupilumab (N=9)**
Patients with at least one TEAE in SOC: Blood and lymphatic system disorders [n(%)]	4 (3.9%)	19 (8.4%)	0	1 (11.1%)
Odds Ratio (95% CI)	-	2.26 (0.75 to 6.82)	-	NE (NE to NE)
p-value for Odds Ratio		0.148		NE
Peto Odds Ratio (95% CI)	-	1.99 (0.80 to 4.97)	-	9.23 (0.18 to 474.33)
Reversed Peto Odds Ratio (95% CI)	-	0.50 (0.20 to 1.25)	-	0.11 (0.00 to 5.56)
p-value for Peto Odds Ratio		0.139		0.269
p-value for heterogeneity of Peto Odds Ratio				0.458
Risk Ratio (95% CI)	-	2.15 (0.75 to 6.17)	-	NE (NE to NE)
Reversed Risk ratio (95% CI)	-	0.46 (0.16 to 1.33)		

Odds Ratio and related p-value are estimated by Wald's method using the SAS LOGISTIC procedure.
Peto OR calculation is based on Yusuf S et al. (Prog Cardiovasc Dis. 1985 Mar-Apr;27(5):335-71) and its p-value is derived using a normal approximation.
Risk Ratio and related p-value are estimated by using the SAS FREQ procedure.
Risk Difference and related p-value are estimated by using the SAS GLIMMIX procedure with the following model: criterion = treatment.
p-values for heterogeneity are estimated by using the SAS GLIMMIX procedure with the following model: criterion = treatment subgroup treatment*subgroup.
p-value for heterogeneity of Peto Odds Ratio is estimated by using normal approximation.
PGM=DEVOPS/SAR231893/EFC14153/CSR_RWE/REPORT/PGM/ae_evt_ger_subg_s2_t.sas OUT=REPORT/OUTPUT/ae_socblood_ger_amc_s2_t_x.rtf (10AUG2021 - 8:10)

Project Code / Study Number / Analysis: SAR231893 / EFC14153 / CSR_RWE

2 Adverse events - Safety type 2 inflammatory asthma phenotype population

2.12 Patients with at least one TEAE in SOC: Blood and lymphatic system disorders

2.12.9 By atopic medical condition (Yes, No)

	Atopic medical condition			
	Yes		No	
Safety type 2 inflammatory asthma phenotype population	**Placebo (N=102)**	**Dupilumab (N=225)**	**Placebo (N=11)**	**Dupilumab (N=9)**
p-value for Risk Ratio		0.153		NE
p-value for heterogeneity of Risk Ratio				0.976
Risk Difference (95% CI)	-	4.52 (-0.73 to 9.78)	-	11.11 (NE to NE)
p-value for Risk Difference		0.091		<0.001
p-value for heterogeneity of Risk Difference				<0.001

Odds Ratio and related p-value are estimated by Wald's method using the SAS LOGISTIC procedure.
Peto OR calculation is based on Yusuf S et al. (Prog Cardiovasc Dis. 1985 Mar-Apr;27(5):335-71) and its p-value is derived using a normal approximation.
Risk Ratio and related p-value are estimated by using the SAS FREQ procedure.
Risk Difference and related p-value are estimated by using the SAS GLIMMIX procedure with the following model: criterion = treatment.
p-values for heterogeneity are estimated by using the SAS GLIMMIX procedure with the following model: criterion = treatment subgroup treatment*subgroup.
p-value for heterogeneity of Peto Odds Ratio is estimated by using normal approximation.
PGM=DEVOPS/SAR231893/EFC14153/CSR_RWE/REPORT/PGM/ae_evt_ger_subg_s2_t.sas OUT=REPORT/OUTPUT/ae_socblood_ger_amc_s2_t_x.rtf (10AUG2021 - 8:10)

Project Code / Study Number / Analysis: SAR231893 / EFC14153 / CSR_RWE

2 Adverse events - Safety type 2 inflammatory asthma phenotype population

2.12 Patients with at least one TEAE in SOC: Blood and lymphatic system disorders

2.12.10 By baseline total IgE (<median, >= median)

	Baseline Total IgE (IU/mL)			
	<median		>=median	
Safety type 2 inflammatory asthma phenotype population	**Placebo (N=65)**	**Dupilumab (N=106)**	**Placebo (N=47)**	**Dupilumab (N=124)**
Patients with at least one TEAE in SOC: Blood and lymphatic system disorders [n(%)]	1 (1.5%)	4 (3.8%)	3 (6.4%)	14 (11.3%)
Odds Ratio (95% CI)	-	2.51 (0.27 to 22.96)	-	1.87 (0.51 to 6.82)
p-value for Odds Ratio		0.415		0.345
p-value for heterogeneity of Odds Ratio				0.821
Risk Ratio (95% CI)	-	2.45 (0.28 to 21.47)	-	1.77 (0.53 to 5.88)
Reversed Risk ratio (95% CI)	-	0.41 (0.05 to 3.57)	-	0.57 (0.17 to 1.88)
p-value for Risk Ratio		0.418		0.352
p-value for heterogeneity of Risk Ratio				0.796

Odds Ratio and related p-value are estimated by Wald's method using the SAS LOGISTIC procedure.
Peto OR calculation is based on Yusuf S et al. (Prog Cardiovasc Dis. 1985 Mar-Apr;27(5):335-71) and its p-value is derived using a normal approximation.
Risk Ratio and related p-value are estimated by using the SAS FREQ procedure.
Risk Difference and related p-value are estimated by using the SAS GLIMMIX procedure with the following model: criterion = treatment.
p-values for heterogeneity are estimated by using the SAS GLIMMIX procedure with the following model: criterion = treatment subgroup treatment*subgroup.
p-value for heterogeneity of Peto Odds Ratio is estimated by using normal approximation.
PGM=DEVOPS/SAR231893/EFC14153/CSR_RWE/REPORT/PGM/ae_evt_ger_subg_s2_t.sas OUT=REPORT/OUTPUT/ae_socblood_ger_igem_s2_t_x.rtf (10AUG2021 - 8:10)

Project Code / Study Number / Analysis: SAR231893 / EFC14153 / CSR_RWE

2 Adverse events - Safety type 2 inflammatory asthma phenotype population

2.12 Patients with at least one TEAE in SOC: Blood and lymphatic system disorders

2.12.10 By baseline total IgE (<median, >= median)

	Baseline Total IgE (IU/mL)			
	<median		>=median	
Safety type 2 inflammatory asthma phenotype population	**Placebo (N=65)**	**Dupilumab (N=106)**	**Placebo (N=47)**	**Dupilumab (N=124)**
Risk Difference (95% CI)	-	2.24 (-2.50 to 6.97)	-	4.91 (-4.09 to 13.91)
p-value for Risk Difference		0.353		0.283
p-value for heterogeneity of Risk Difference				0.604

Odds Ratio and related p-value are estimated by Wald's method using the SAS LOGISTIC procedure.
Peto OR calculation is based on Yusuf S et al. (Prog Cardiovasc Dis. 1985 Mar-Apr;27(5):335-71) and its p-value is derived using a normal approximation.
Risk Ratio and related p-value are estimated by using the SAS FREQ procedure.
Risk Difference and related p-value are estimated by using the SAS GLIMMIX procedure with the following model: criterion = treatment.
p-values for heterogeneity are estimated by using the SAS GLIMMIX procedure with the following model: criterion = treatment subgroup treatment*subgroup.
p-value for heterogeneity of Peto Odds Ratio is estimated by using normal approximation.
PGM=DEVOPS/SAR231893/EFC14153/CSR_RWE/REPORT/PGM/ae_evt_ger_subg_s2_t.sas OUT=REPORT/OUTPUT/ae_socblood_ger_igem_s2_t_x.rtf (10AUG2021 - 8:10)

Project Code / Study Number / Analysis: SAR231893 / EFC14153 / CSR_RWE

2 Adverse events - Safety type 2 inflammatory asthma phenotype population

2.12 Patients with at least one TEAE in SOC: Blood and lymphatic system disorders

2.12.11 By baseline total IgE (<100 IU/ml, >= 100 IU/ml)

	Baseline Total IgE (IU/mL)			
	< 100		>= 100	
Safety type 2 inflammatory asthma phenotype population	**Placebo (N=22)**	**Dupilumab (N=29)**	**Placebo (N=90)**	**Dupilumab (N=201)**
Patients with at least one TEAE in SOC: Blood and lymphatic system disorders [n(%)]	0	0	4 (4.4%)	18 (9.0%)
Odds Ratio (95% CI)	-	NE (NE to NE)	-	2.11 (0.69 to 6.44)
p-value for Odds Ratio		NE		0.187
Peto Odds Ratio (95% CI)	-	NE (NE to NE)	-	1.90 (0.74 to 4.86)
Reversed Peto Odds Ratio (95% CI)			-	0.53 (0.21 to 1.35)
p-value for Peto Odds Ratio		NE		0.179
p-value for heterogeneity of Peto Odds Ratio				NE
Risk Ratio (95% CI)	-	NE (NE to NE)	-	2.01 (0.70 to 5.78)
Reversed Risk ratio (95% CI)			-	0.50 (0.17 to 1.42)

Odds Ratio and related p-value are estimated by Wald's method using the SAS LOGISTIC procedure.
Peto OR calculation is based on Yusuf S et al. (Prog Cardiovasc Dis. 1985 Mar-Apr;27(5):335-71) and its p-value is derived using a normal approximation.
Risk Ratio and related p-value are estimated by using the SAS FREQ procedure.
Risk Difference and related p-value are estimated by using the SAS GLIMMIX procedure with the following model: criterion = treatment.
p-values for heterogeneity are estimated by using the SAS GLIMMIX procedure with the following model: criterion = treatment subgroup treatment*subgroup.
p-value for heterogeneity of Peto Odds Ratio is estimated by using normal approximation.
PGM=DEVOPS/SAR231893/EFC14153/CSR_RWE/REPORT/PGM/ae_evt_ger_subg_s2_t.sas OUT=REPORT/OUTPUT/ae_socblood_ger_ige_s2_t_x.rtf (10AUG2021 - 8:11)

Project Code / Study Number / Analysis: SAR231893 / EFC14153 / CSR_RWE

2 Adverse events - Safety type 2 inflammatory asthma phenotype population

2.12 Patients with at least one TEAE in SOC: Blood and lymphatic system disorders

2.12.11 By baseline total IgE (<100 IU/ml, >= 100 IU/ml)

	Baseline Total IgE (IU/mL)			
	< 100		>= 100	
Safety type 2 inflammatory asthma phenotype population	**Placebo (N=22)**	**Dupilumab (N=29)**	**Placebo (N=90)**	**Dupilumab (N=201)**
p-value for Risk Ratio		NE		0.193
p-value for heterogeneity of Risk Ratio				0.999
Risk Difference (95% CI)	-	0.00 (NE to NE)	-	4.51 (-1.32 to 10.34)
p-value for Risk Difference		NE		0.129
p-value for heterogeneity of Risk Difference				<0.001

Odds Ratio and related p-value are estimated by Wald's method using the SAS LOGISTIC procedure.
Peto OR calculation is based on Yusuf S et al. (Prog Cardiovasc Dis. 1985 Mar-Apr;27(5):335-71) and its p-value is derived using a normal approximation.
Risk Ratio and related p-value are estimated by using the SAS FREQ procedure.
Risk Difference and related p-value are estimated by using the SAS GLIMMIX procedure with the following model: criterion = treatment.
p-values for heterogeneity are estimated by using the SAS GLIMMIX procedure with the following model: criterion = treatment subgroup treatment*subgroup.
p-value for heterogeneity of Peto Odds Ratio is estimated by using normal approximation.
PGM=DEVOPS/SAR231893/EFC14153/CSR_RWE/REPORT/PGM/ae_evt_ger_subg_s2_t.sas OUT=REPORT/OUTPUT/ae_socblood_ger_ige_s2_t_x.rtf (10AUG2021 - 8:11)

Project Code / Study Number / Analysis: SAR231893 / EFC14153 / CSR_RWE

2 Adverse events - Safety type 2 inflammatory asthma phenotype population

2.12 Patients with at least one TEAE in SOC: Blood and lymphatic system disorders

2.12.12 By age at onset of asthma (0-2, 3-5, >=6 years)

	Age of onset of asthma (years)					
	0-2		3-5		>= 6	
Safety type 2 inflammatory asthma phenotype population	**Placebo (N=40)**	**Dupilumab (N=104)**	**Placebo (N=38)**	**Dupilumab (N=85)**	**Placebo (N=35)**	**Dupilumab (N=45)**
Patients with at least one TEAE in SOC: Blood and lymphatic system disorders [n(%)]	3 (7.5%)	7 (6.7%)	1 (2.6%)	6 (7.1%)	0	7 (15.6%)
Odds Ratio (95% CI)	-	0.89 (0.22 to 3.63)	-	2.81 (0.33 to 24.18)	-	NE (NE to NE)
p-value for Odds Ratio		0.871		0.347		NE
Peto Odds Ratio (95% CI)	-	0.89 (0.21 to 3.71)	-	2.27 (0.44 to 11.73)	-	6.85 (1.45 to 32.37)
Reversed Peto Odds Ratio (95% CI)			-	0.44 (0.09 to 2.27)	-	0.15 (0.03 to 0.69)
p-value for Peto Odds Ratio		0.871		0.329		0.015
p-value for heterogeneity of Peto Odds Ratio:						
0-2, 3-5						0.400
0-2, >= 6						0.058

Odds Ratio and related p-value are estimated by Wald's method using the SAS LOGISTIC procedure.
Peto OR calculation is based on Yusuf S et al. (Prog Cardiovasc Dis. 1985 Mar-Apr;27(5):335-71) and its p-value is derived using a normal approximation.
Risk Ratio and related p-value are estimated by using the SAS FREQ procedure.
Risk Difference and related p-value are estimated by using the SAS GLIMMIX procedure with the following model: criterion = treatment.
p-values for heterogeneity are estimated by using the SAS GLIMMIX procedure with the following model: criterion = treatment subgroup treatment*subgroup.
p-value for heterogeneity of Peto Odds Ratio is estimated by using normal approximation.
PGM=DEVOPS/SAR231893/EFC14153/CSR_RWE/REPORT/PGM/ae_evt_ger_subg_s2_t.sas OUT=REPORT/OUTPUT/ae_socblood_ger_onsa_s2_t_x.rtf (10AUG2021 - 8:11)

Project Code / Study Number / Analysis: SAR231893 / EFC14153 / CSR_RWE

2 Adverse events - Safety type 2 inflammatory asthma phenotype population

2.12 Patients with at least one TEAE in SOC: Blood and lymphatic system disorders

2.12.12 By age at onset of asthma (0-2, 3-5, >=6 years)

	Age of onset of asthma (years)					
	0-2		3-5		>= 6	
Safety type 2 inflammatory asthma phenotype population	**Placebo (N=40)**	**Dupilumab (N=104)**	**Placebo (N=38)**	**Dupilumab (N=85)**	**Placebo (N=35)**	**Dupilumab (N=45)**
3-5, >= 6						0.338
overall						0.166
Risk Ratio (95% CI)	-	0.90 (0.24 to 3.30)	-	2.68 (0.33 to 21.52)	-	NE (NE to NE)
Reversed Risk ratio (95% CI)			-	0.37 (0.05 to 2.99)		
p-value for Risk Ratio		0.871		0.353		NE
p-value for heterogeneity of Risk Ratio:						
0-2, 3-5						0.383
0-2, >= 6						0.969
3-5, >= 6						0.971
overall						0.682
Risk Difference (95% CI)	-	-0.77 (-10.33 to 8.79)	-	4.43 (-3.10 to 11.96)	-	15.56 (NE to NE)

Odds Ratio and related p-value are estimated by Wald's method using the SAS LOGISTIC procedure.
Peto OR calculation is based on Yusuf S et al. (Prog Cardiovasc Dis. 1985 Mar-Apr;27(5):335-71) and its p-value is derived using a normal approximation.
Risk Ratio and related p-value are estimated by using the SAS FREQ procedure.
Risk Difference and related p-value are estimated by using the SAS GLIMMIX procedure with the following model: criterion = treatment.
p-values for heterogeneity are estimated by using the SAS GLIMMIX procedure with the following model: criterion = treatment subgroup treatment*subgroup.
p-value for heterogeneity of Peto Odds Ratio is estimated by using normal approximation.
PGM=DEVOPS/SAR231893/EFC14153/CSR_RWE/REPORT/PGM/ae_evt_ger_subg_s2_t.sas OUT=REPORT/OUTPUT/ae_socblood_ger_onsa_s2_t_x.rtf (10AUG2021 - 8:11)

Project Code / Study Number / Analysis: SAR231893 / EFC14153 / CSR_RWE

2 Adverse events - Safety type 2 inflammatory asthma phenotype population

2.12 Patients with at least one TEAE in SOC: Blood and lymphatic system disorders

2.12.12 By age at onset of asthma (0-2, 3-5, >=6 years)

	Age of onset of asthma (years)					
	0-2		3-5		>= 6	
Safety type 2 inflammatory asthma phenotype population	**Placebo (N=40)**	**Dupilumab (N=104)**	**Placebo (N=38)**	**Dupilumab (N=85)**	**Placebo (N=35)**	**Dupilumab (N=45)**
p-value for Risk Difference		0.874		0.247		<0.001
p-value for heterogeneity of Risk Difference:						
0-2, 3-5						0.399
0-2, >= 6						0.008
3-5, >= 6						<0.001
overall						0.008

Odds Ratio and related p-value are estimated by Wald's method using the SAS LOGISTIC procedure.
Peto OR calculation is based on Yusuf S et al. (Prog Cardiovasc Dis. 1985 Mar-Apr;27(5):335-71) and its p-value is derived using a normal approximation.
Risk Ratio and related p-value are estimated by using the SAS FREQ procedure.
Risk Difference and related p-value are estimated by using the SAS GLIMMIX procedure with the following model: criterion = treatment.
p-values for heterogeneity are estimated by using the SAS GLIMMIX procedure with the following model: criterion = treatment subgroup treatment*subgroup.
p-value for heterogeneity of Peto Odds Ratio is estimated by using normal approximation.
PGM=DEVOPS/SAR231893/EFC14153/CSR_RWE/REPORT/PGM/ae_evt_ger_subg_s2_t.sas OUT=REPORT/OUTPUT/ae_socblood_ger_onsa_s2_t_x.rtf (10AUG2021 - 8:11)

Project Code / Study Number / Analysis: SAR231893 / EFC14153 / CSR_RWE

2 Adverse events - Safety type 2 inflammatory asthma phenotype population

2.12 Patients with at least one TEAE in SOC: Blood and lymphatic system disorders

2.12.13 By number of severe asthma exacerbation prior to the study (<=1, 2, >2)

	Number of severe asthma exacerbation prior to the study					
	<=1		2		>2	
Safety type 2 inflammatory asthma phenotype population	**Placebo (N=46)**	**Dupilumab (N=85)**	**Placebo (N=32)**	**Dupilumab (N=75)**	**Placebo (N=35)**	**Dupilumab (N=74)**
Patients with at least one TEAE in SOC: Blood and lymphatic system disorders [n(%)]	3 (6.5%)	6 (7.1%)	0	9 (12.0%)	1 (2.9%)	5 (6.8%)
Odds Ratio (95% CI)	-	1.09 (0.26 to 4.57)	-	NE (NE to NE)	-	2.46 (0.28 to 21.92)
p-value for Odds Ratio		0.908		NE		0.419
Peto Odds Ratio (95% CI)	-	1.09 (0.26 to 4.46)	-	4.68 (1.06 to 20.64)	-	2.10 (0.36 to 12.15)
Reversed Peto Odds Ratio (95% CI)	-	0.92 (0.22 to 3.85)	-	0.21 (0.05 to 0.94)	-	0.48 (0.08 to 2.78)
p-value for Peto Odds Ratio		0.908		0.042		0.407
p-value for heterogeneity of Peto Odds Ratio:						
<=1, 2						0.163
<=1, >2						0.566
2, >2						0.495

Odds Ratio and related p-value are estimated by Wald's method using the SAS LOGISTIC procedure.
Peto OR calculation is based on Yusuf S et al. (Prog Cardiovasc Dis. 1985 Mar-Apr;27(5):335-71) and its p-value is derived using a normal approximation.
Risk Ratio and related p-value are estimated by using the SAS FREQ procedure.
Risk Difference and related p-value are estimated by using the SAS GLIMMIX procedure with the following model: criterion = treatment.
p-values for heterogeneity are estimated by using the SAS GLIMMIX procedure with the following model: criterion = treatment subgroup treatment*subgroup.
p-value for heterogeneity of Peto Odds Ratio is estimated by using normal approximation.
PGM=DEVOPS/SAR231893/EFC14153/CSR_RWE/REPORT/PGM/ae_evt_ger_subg_s2_t.sas OUT=REPORT/OUTPUT/ae_socblood_ger_exa_s2_t_x.rtf (10AUG2021 - 8:11)

Project Code / Study Number / Analysis: SAR231893 / EFC14153 / CSR_RWE

2 Adverse events - Safety type 2 inflammatory asthma phenotype population

2.12 Patients with at least one TEAE in SOC: Blood and lymphatic system disorders

2.12.13 By number of severe asthma exacerbation prior to the study (<=1, 2, >2)

	Number of severe asthma exacerbation prior to the study					
	<=1		2		>2	
Safety type 2 inflammatory asthma phenotype population	**Placebo (N=46)**	**Dupilumab (N=85)**	**Placebo (N=32)**	**Dupilumab (N=75)**	**Placebo (N=35)**	**Dupilumab (N=74)**
overall						0.377
Risk Ratio (95% CI)	-	1.08 (0.28 to 4.13)	-	NE (NE to NE)	-	2.36 (0.29 to 19.49)
Reversed Risk ratio (95% CI)	-	0.92 (0.24 to 3.52)			-	0.42 (0.05 to 3.48)
p-value for Risk Ratio		0.908		NE		0.424
p-value for heterogeneity of Risk Ratio:						
<=1, 2						0.971
<=1, >2						0.540
2, >2						0.973
overall						0.828
Risk Difference (95% CI)	-	0.54 (-8.52 to 9.60)	-	12.00 (NE to NE)	-	3.90 (-4.14 to 11.94)
p-value for Risk Difference		0.907		<0.001		0.338

Odds Ratio and related p-value are estimated by Wald's method using the SAS LOGISTIC procedure.
Peto OR calculation is based on Yusuf S et al. (Prog Cardiovasc Dis. 1985 Mar-Apr;27(5):335-71) and its p-value is derived using a normal approximation.
Risk Ratio and related p-value are estimated by using the SAS FREQ procedure.
Risk Difference and related p-value are estimated by using the SAS GLIMMIX procedure with the following model: criterion = treatment.
p-values for heterogeneity are estimated by using the SAS GLIMMIX procedure with the following model: criterion = treatment subgroup treatment*subgroup.
p-value for heterogeneity of Peto Odds Ratio is estimated by using normal approximation.
PGM=DEVOPS/SAR231893/EFC14153/CSR_RWE/REPORT/PGM/ae_evt_ger_subg_s2_t.sas OUT=REPORT/OUTPUT/ae_socblood_ger_exa_s2_t_x.rtf (10AUG2021 - 8:11)

Project Code / Study Number / Analysis: SAR231893 / EFC14153 / CSR_RWE

2 Adverse events - Safety type 2 inflammatory asthma phenotype population

2.12 Patients with at least one TEAE in SOC: Blood and lymphatic system disorders

2.12.13 By number of severe asthma exacerbation prior to the study (<=1, 2, >2)

	Number of severe asthma exacerbation prior to the study					
	<=1		2		>2	
Safety type 2 inflammatory asthma phenotype population	**Placebo (N=46)**	**Dupilumab (N=85)**	**Placebo (N=32)**	**Dupilumab (N=75)**	**Placebo (N=35)**	**Dupilumab (N=74)**
p-value for heterogeneity of Risk Difference:						
<=1, 2						0.062
<=1, >2						0.583
2, >2						<0.001
overall						0.583

Odds Ratio and related p-value are estimated by Wald's method using the SAS LOGISTIC procedure.
Peto OR calculation is based on Yusuf S et al. (Prog Cardiovasc Dis. 1985 Mar-Apr;27(5):335-71) and its p-value is derived using a normal approximation.
Risk Ratio and related p-value are estimated by using the SAS FREQ procedure.
Risk Difference and related p-value are estimated by using the SAS GLIMMIX procedure with the following model: criterion = treatment.
p-values for heterogeneity are estimated by using the SAS GLIMMIX procedure with the following model: criterion = treatment subgroup treatment*subgroup.
p-value for heterogeneity of Peto Odds Ratio is estimated by using normal approximation.
PGM=DEVOPS/SAR231893/EFC14153/CSR_RWE/REPORT/PGM/ae_evt_ger_subg_s2_t.sas OUT=REPORT/OUTPUT/ae_socblood_ger_exa_s2_t_x.rtf (10AUG2021 - 8:11)

overall	0.028

Odds Ratio and related p-value are estimated by Wald's method using the SAS LOGISTIC procedure.
Peto OR calculation is based on Yusuf S et al. (Prog Cardiovasc Dis. 1985 Mar-Apr;27(5):335-71) and its p-value is derived using a normal approximation.
Risk Ratio and related p-value are estimated by using the SAS FREQ procedure.
Risk Difference and related p-value are estimated by using the SAS GLIMMIX procedure with the following model: criterion = treatment.
p-values for heterogeneity are estimated by using the SAS GLIMMIX procedure with the following model: criterion = treatment subgroup treatment*subgroup.
p-value for heterogeneity of Peto Odds Ratio is estimated by using normal approximation.
PGM=DEVOPS/SAR231893/EFC14153/CSR_RWE/REPORT/PGM/ae_evt_ger_subg_s2_t.sas OUT=REPORT/OUTPUT/ae_socnerv_ger_exa_s2_t_x.rtf (10AUG2021 - 8:13)

Project Code / Study Number / Analysis: SAR231893 / EFC14153 / CSR_RWE

2 Adverse events - Safety type 2 inflammatory asthma phenotype population

2.14 Patients with at least one TEAE in SOC: Respiratory, thoracic and mediastinal disorders

Safety type 2 inflammatory asthma phenotype population	Placebo (N=113)	Dupilumab (N=234)
Patients with at least one TEAE in SOC: Respiratory, thoracic and mediastinal disorders [n(%)]	31 (27.4%)	42 (17.9%)
Odds Ratio (95% CI)	-	0.58 (0.34 to 0.98)
p-value for Odds Ratio		0.043
Risk Ratio (95% CI)	-	0.65 (0.44 to 0.98)
p-value for Risk Ratio		0.041
Risk Difference (95% CI)	-	-9.48 (-19.10 to 0.13)
p-value for Risk Difference		0.053

Odds Ratio and related p-value are estimated by Wald's method using the SAS LOGISTIC procedure.
Peto OR calculation is based on Yusuf S et al. (Prog Cardiovasc Dis. 1985 Mar-Apr;27(5):335-71) and its p-value is derived using a normal approximation.
Risk Ratio and related p-value are estimated by using the SAS FREQ procedure.
Risk Difference and related p-value are estimated by using the SAS GLIMMIX procedure with the following model: criterion = treatment.
p-value for heterogeneity of Peto Odds Ratio is estimated by using normal approximation.
PGM=DEVOPS/SAR231893/EFC14153/CSR_RWE/REPORT/PGM/ae_evt_ger_s2_t.sas OUT=REPORT/OUTPUT/ae_socrtmd_ger_s2_t_x.rtf (30JUL2021 - 15:50)

Project Code / Study Number / Analysis: SAR231893 / EFC14153 / CSR_RWE

2 Adverse events - Safety type 2 inflammatory asthma phenotype population

2.14 Patients with at least one TEAE in SOC: Respiratory, thoracic and mediastinal disorders

2.14.1 By gender (Male, Female)

	Gender			
	Male		Female	
Safety type 2 inflammatory asthma phenotype population	**Placebo (N=77)**	**Dupilumab (N=153)**	**Placebo (N=36)**	**Dupilumab (N=81)**
Patients with at least one TEAE in SOC: Respiratory, thoracic and mediastinal disorders [n(%)]	24 (31.2%)	26 (17.0%)	7 (19.4%)	16 (19.8%)
Odds Ratio (95% CI)	-	0.45 (0.24 to 0.86)	-	1.02 (0.38 to 2.74)
p-value for Odds Ratio		0.015		0.969
p-value for heterogeneity of Odds Ratio				0.177
Risk Ratio (95% CI)	-	0.55 (0.34 to 0.88)	-	1.02 (0.46 to 2.25)
Reversed Risk ratio (95% CI)			-	0.98 (0.44 to 2.18)
p-value for Risk Ratio		0.014		0.969
p-value for heterogeneity of Risk Ratio				0.191

Odds Ratio and related p-value are estimated by Wald's method using the SAS LOGISTIC procedure.
Peto OR calculation is based on Yusuf S et al. (Prog Cardiovasc Dis. 1985 Mar-Apr;27(5):335-71) and its p-value is derived using a normal approximation.
Risk Ratio and related p-value are estimated by using the SAS FREQ procedure.
Risk Difference and related p-value are estimated by using the SAS GLIMMIX procedure with the following model: criterion = treatment.
p-values for heterogeneity are estimated by using the SAS GLIMMIX procedure with the following model: criterion = treatment subgroup treatment*subgroup.
p-value for heterogeneity of Peto Odds Ratio is estimated by using normal approximation.
PGM=DEVOPS/SAR231893/EFC14153/CSR_RWE/REPORT/PGM/ae_evt_ger_subg_s2_t.sas OUT=REPORT/OUTPUT/ae_socrtmd_ger_sex_s2_t_x.rtf (10AUG2021 - 8:14)

Project Code / Study Number / Analysis: SAR231893 / EFC14153 / CSR_RWE

2 Adverse events - Safety type 2 inflammatory asthma phenotype population

2.14 Patients with at least one TEAE in SOC: Respiratory, thoracic and mediastinal disorders

2.14.1 By gender (Male, Female)

	Gender			
	Male		Female	
Safety type 2 inflammatory asthma phenotype population	**Placebo (N=77)**	**Dupilumab (N=153)**	**Placebo (N=36)**	**Dupilumab (N=81)**
Risk Difference (95% CI)	-	-14.18 (-26.17 to -2.18)	-	0.31 (-15.42 to 16.04)
p-value for Risk Difference		0.021		0.969
p-value for heterogeneity of Risk Difference				0.149

Odds Ratio and related p-value are estimated by Wald's method using the SAS LOGISTIC procedure.
Peto OR calculation is based on Yusuf S et al. (Prog Cardiovasc Dis. 1985 Mar-Apr;27(5):335-71) and its p-value is derived using a normal approximation.
Risk Ratio and related p-value are estimated by using the SAS FREQ procedure.
Risk Difference and related p-value are estimated by using the SAS GLIMMIX procedure with the following model: criterion = treatment.
p-values for heterogeneity are estimated by using the SAS GLIMMIX procedure with the following model: criterion = treatment subgroup treatment*subgroup.
p-value for heterogeneity of Peto Odds Ratio is estimated by using normal approximation.
PGM=DEVOPS/SAR231893/EFC14153/CSR_RWE/REPORT/PGM/ae_evt_ger_subg_s2_t.sas OUT=REPORT/OUTPUT/ae_socrtmd_ger_sex_s2_t_x.rtf (10AUG2021 - 8:14)

Project Code / Study Number / Analysis: SAR231893 / EFC14153 / CSR_RWE

2 Adverse events - Safety type 2 inflammatory asthma phenotype population

2.14 Patients with at least one TEAE in SOC: Respiratory, thoracic and mediastinal disorders

2.14.2 By region (Latin America, East Europe, Western Countries)

	Region					
	Latin America		East Europe		Western countries	
Safety type 2 inflammatory asthma phenotype population	**Placebo (N=51)**	**Dupilumab (N=105)**	**Placebo (N=43)**	**Dupilumab (N=78)**	**Placebo (N=19)**	**Dupilumab (N=51)**
Patients with at least one TEAE in SOC: Respiratory, thoracic and mediastinal disorders [n(%)]	12 (23.5%)	15 (14.3%)	10 (23.3%)	10 (12.8%)	9 (47.4%)	17 (33.3%)
Odds Ratio (95% CI)	-	0.54 (0.23 to 1.26)	-	0.49 (0.18 to 1.28)	-	0.56 (0.19 to 1.62)
p-value for Odds Ratio		0.156		0.144		0.283
p-value for heterogeneity of Odds Ratio:						
Latin America, East Europe						0.867
Latin America, Western countries						0.971
East Europe, Western countries						0.855
overall						0.980

Odds Ratio and related p-value are estimated by Wald's method using the SAS LOGISTIC procedure.
Peto OR calculation is based on Yusuf S et al. (Prog Cardiovasc Dis. 1985 Mar-Apr;27(5):335-71) and its p-value is derived using a normal approximation.
Risk Ratio and related p-value are estimated by using the SAS FREQ procedure.
Risk Difference and related p-value are estimated by using the SAS GLIMMIX procedure with the following model: criterion = treatment.
p-values for heterogeneity are estimated by using the SAS GLIMMIX procedure with the following model: criterion = treatment subgroup treatment*subgroup.
p-value for heterogeneity of Peto Odds Ratio is estimated by using normal approximation.
PGM=DEVOPS/SAR231893/EFC14153/CSR_RWE/REPORT/PGM/ae_evt_ger_subg_s2_t.sas OUT=REPORT/OUTPUT/ae_socrtmd_ger_cty_s2_t_x.rtf (10AUG2021 - 8:14)

Project Code / Study Number / Analysis: SAR231893 / EFC14153 / CSR_RWE

2 Adverse events - Safety type 2 inflammatory asthma phenotype population

2.14 Patients with at least one TEAE in SOC: Respiratory, thoracic and mediastinal disorders

2.14.2 By region (Latin America, East Europe, Western Countries)

	Region					
	Latin America		East Europe		Western countries	
Safety type 2 inflammatory asthma phenotype population	**Placebo (N=51)**	**Dupilumab (N=105)**	**Placebo (N=43)**	**Dupilumab (N=78)**	**Placebo (N=19)**	**Dupilumab (N=51)**
Risk Ratio (95% CI)	-	0.61 (0.31 to 1.20)	-	0.55 (0.25 to 1.22)	-	0.70 (0.38 to 1.30)
p-value for Risk Ratio		0.151		0.141		0.261
p-value for heterogeneity of Risk Ratio:						
Latin America, East Europe						0.857
Latin America, Western countries						0.752
East Europe, Western countries						0.633
overall						0.885
Risk Difference (95% CI)	-	-9.24 (-22.78 to 4.29)	-	-10.44 (-25.23 to 4.36)	-	-14.04 (-40.42 to 12.35)
p-value for Risk Difference		0.179		0.165		0.292
p-value for heterogeneity of Risk Difference:						

Odds Ratio and related p-value are estimated by Wald's method using the SAS LOGISTIC procedure.
Peto OR calculation is based on Yusuf S et al. (Prog Cardiovasc Dis. 1985 Mar-Apr;27(5):335-71) and its p-value is derived using a normal approximation.
Risk Ratio and related p-value are estimated by using the SAS FREQ procedure.
Risk Difference and related p-value are estimated by using the SAS GLIMMIX procedure with the following model: criterion = treatment.
p-values for heterogeneity are estimated by using the SAS GLIMMIX procedure with the following model: criterion = treatment subgroup treatment*subgroup.
p-value for heterogeneity of Peto Odds Ratio is estimated by using normal approximation.
PGM=DEVOPS/SAR231893/EFC14153/CSR_RWE/REPORT/PGM/ae_evt_ger_subg_s2_t.sas OUT=REPORT/OUTPUT/ae_socrtmd_ger_cty_s2_t_x.rtf (10AUG2021 - 8:14)

Project Code / Study Number / Analysis: SAR231893 / EFC14153 / CSR_RWE

2 Adverse events - Safety type 2 inflammatory asthma phenotype population

2.14 Patients with at least one TEAE in SOC: Respiratory, thoracic and mediastinal disorders

2.14.2 By region (Latin America, East Europe, Western Countries)

	Region					
	Latin America		East Europe		Western countries	
Safety type 2 inflammatory asthma phenotype population	**Placebo (N=51)**	**Dupilumab (N=105)**	**Placebo (N=43)**	**Dupilumab (N=78)**	**Placebo (N=19)**	**Dupilumab (N=51)**
Latin America, East Europe						0.907
Latin America, Western countries						0.748
East Europe, Western countries						0.813
overall						0.949

Odds Ratio and related p-value are estimated by Wald's method using the SAS LOGISTIC procedure.
Peto OR calculation is based on Yusuf S et al. (Prog Cardiovasc Dis. 1985 Mar-Apr;27(5):335-71) and its p-value is derived using a normal approximation.
Risk Ratio and related p-value are estimated by using the SAS FREQ procedure.
Risk Difference and related p-value are estimated by using the SAS GLIMMIX procedure with the following model: criterion = treatment.
p-values for heterogeneity are estimated by using the SAS GLIMMIX procedure with the following model: criterion = treatment subgroup treatment*subgroup.
p-value for heterogeneity of Peto Odds Ratio is estimated by using normal approximation.
PGM=DEVOPS/SAR231893/EFC14153/CSR_RWE/REPORT/PGM/ae_evt_ger_subg_s2_t.sas OUT=REPORT/OUTPUT/ae_socrtmd_ger_cty_s2_t_x.rtf (10AUG2021 - 8:14)

Project Code / Study Number / Analysis: SAR231893 / EFC14153 / CSR_RWE

2 Adverse events - Safety type 2 inflammatory asthma phenotype population

2.14 Patients with at least one TEAE in SOC: Respiratory, thoracic and mediastinal disorders

2.14.3 By race (Caucasian/white, Black/of African descent, Other)

	Race					
	Caucasian/White		Black/of African descent		Other	
Safety type 2 inflammatory asthma phenotype population	**Placebo (N=101)**	**Dupilumab (N=207)**	**Placebo (N=5)**	**Dupilumab (N=9)**	**Placebo (N=7)**	**Dupilumab (N=18)**
Patients with at least one TEAE in SOC: Respiratory, thoracic and mediastinal disorders [n(%)]	26 (25.7%)	32 (15.5%)	2 (40.0%)	4 (44.4%)	3 (42.9%)	6 (33.3%)
Odds Ratio (95% CI)	-	0.53 (0.29 to 0.95)	-	1.20 (0.13 to 11.05)	-	0.67 (0.11 to 3.99)
p-value for Odds Ratio		0.032		0.872		0.657
p-value for heterogeneity of Odds Ratio:						
Caucasian/White, Black/of African descent						0.483
Caucasian/White, Other						0.807
Black/of African descent, Other						0.686
overall						0.768

Odds Ratio and related p-value are estimated by Wald's method using the SAS LOGISTIC procedure.
Peto OR calculation is based on Yusuf S et al. (Prog Cardiovasc Dis. 1985 Mar-Apr;27(5):335-71) and its p-value is derived using a normal approximation.
Risk Ratio and related p-value are estimated by using the SAS FREQ procedure.
Risk Difference and related p-value are estimated by using the SAS GLIMMIX procedure with the following model: criterion = treatment.
p-values for heterogeneity are estimated by using the SAS GLIMMIX procedure with the following model: criterion = treatment subgroup treatment*subgroup.
p-value for heterogeneity of Peto Odds Ratio is estimated by using normal approximation.
PGM=DEVOPS/SAR231893/EFC14153/CSR_RWE/REPORT/PGM/ae_evt_ger_subg_s2_t.sas OUT=REPORT/OUTPUT/ae_socrtmd_ger_race_s2_t_x.rtf (10AUG2021 - 8:14)

Project Code / Study Number / Analysis: SAR231893 / EFC14153 / CSR_RWE

2 Adverse events - Safety type 2 inflammatory asthma phenotype population

2.14 Patients with at least one TEAE in SOC: Respiratory, thoracic and mediastinal disorders

2.14.3 By race (Caucasian/white, Black/of African descent, Other)

	Race					
	Caucasian/White		Black/of African descent		Other	
Safety type 2 inflammatory asthma phenotype population	**Placebo (N=101)**	**Dupilumab (N=207)**	**Placebo (N=5)**	**Dupilumab (N=9)**	**Placebo (N=7)**	**Dupilumab (N=18)**
Risk Ratio (95% CI)	-	0.60 (0.38 to 0.95)	-	1.11 (0.30 to 4.07)	-	0.78 (0.27 to 2.28)
Reversed Risk ratio (95% CI)			-	0.90 (0.25 to 3.30)		
p-value for Risk Ratio		0.030		0.874		0.647
p-value for heterogeneity of Risk Ratio:						
Caucasian/White, Black/of African descent						0.382
Caucasian/White, Other						0.665
Black/of African descent, Other						0.679
overall						0.648
Risk Difference (95% CI)	-	-10.28 (-20.17 to -0.40)	-	4.44 (-55.40 to 64.29)	-	-9.52 (-54.53 to 35.48)

Odds Ratio and related p-value are estimated by Wald's method using the SAS LOGISTIC procedure.
Peto OR calculation is based on Yusuf S et al. (Prog Cardiovasc Dis. 1985 Mar-Apr;27(5):335-71) and its p-value is derived using a normal approximation.
Risk Ratio and related p-value are estimated by using the SAS FREQ procedure.
Risk Difference and related p-value are estimated by using the SAS GLIMMIX procedure with the following model: criterion = treatment.
p-values for heterogeneity are estimated by using the SAS GLIMMIX procedure with the following model: criterion = treatment subgroup treatment*subgroup.
p-value for heterogeneity of Peto Odds Ratio is estimated by using normal approximation.
PGM=DEVOPS/SAR231893/EFC14153/CSR_RWE/REPORT/PGM/ae_evt_ger_subg_s2_t.sas OUT=REPORT/OUTPUT/ae_socrtmd_ger_race_s2_t_x.rtf (10AUG2021 - 8:14)

Project Code / Study Number / Analysis: SAR231893 / EFC14153 / CSR_RWE

2 Adverse events - Safety type 2 inflammatory asthma phenotype population

2.14 Patients with at least one TEAE in SOC: Respiratory, thoracic and mediastinal disorders

2.14.3 By race (Caucasian/white, Black/of African descent, Other)

	Race					
	Caucasian/White		Black/of African descent		Other	
Safety type 2 inflammatory asthma phenotype population	**Placebo (N=101)**	**Dupilumab (N=207)**	**Placebo (N=5)**	**Dupilumab (N=9)**	**Placebo (N=7)**	**Dupilumab (N=18)**
p-value for Risk Difference		0.042		0.874		0.666
p-value for heterogeneity of Risk Difference:						
Caucasian/White, Black/of African descent						0.598
Caucasian/White, Other						0.973
Black/of African descent, Other						0.690
overall						0.870

Odds Ratio and related p-value are estimated by Wald's method using the SAS LOGISTIC procedure.
Peto OR calculation is based on Yusuf S et al. (Prog Cardiovasc Dis. 1985 Mar-Apr;27(5):335-71) and its p-value is derived using a normal approximation.
Risk Ratio and related p-value are estimated by using the SAS FREQ procedure.
Risk Difference and related p-value are estimated by using the SAS GLIMMIX procedure with the following model: criterion = treatment.
p-values for heterogeneity are estimated by using the SAS GLIMMIX procedure with the following model: criterion = treatment subgroup treatment*subgroup.
p-value for heterogeneity of Peto Odds Ratio is estimated by using normal approximation.
PGM=DEVOPS/SAR231893/EFC14153/CSR_RWE/REPORT/PGM/ae_evt_ger_subg_s2_t.sas OUT=REPORT/OUTPUT/ae_socrtmd_ger_race_s2_t_x.rtf (10AUG2021 - 8:14)

Project Code / Study Number / Analysis: SAR231893 / EFC14153 / CSR_RWE

2 Adverse events - Safety type 2 inflammatory asthma phenotype population

2.14 Patients with at least one TEAE in SOC: Respiratory, thoracic and mediastinal disorders

2.14.4 By baseline ICS dose level (Medium, High)

	Baseline ICS dose level			
	High		Medium	
Safety type 2 inflammatory asthma phenotype population	**Placebo (N=50)**	**Dupilumab (N=101)**	**Placebo (N=63)**	**Dupilumab (N=131)**
Patients with at least one TEAE in SOC: Respiratory, thoracic and mediastinal disorders [n(%)]	12 (24.0%)	22 (21.8%)	19 (30.2%)	19 (14.5%)
Odds Ratio (95% CI)	-	0.88 (0.40 to 1.97)	-	0.39 (0.19 to 0.81)
p-value for Odds Ratio		0.759		0.012
p-value for heterogeneity of Odds Ratio				0.144
Risk Ratio (95% CI)	-	0.91 (0.49 to 1.68)	-	0.48 (0.27 to 0.84)
p-value for Risk Ratio		0.758		0.010
p-value for heterogeneity of Risk Ratio				0.136
Risk Difference (95% CI)	-	-2.22 (-16.65 to 12.22)	-	-15.65 (-28.57 to -2.74)

Odds Ratio and related p-value are estimated by Wald's method using the SAS LOGISTIC procedure.
Peto OR calculation is based on Yusuf S et al. (Prog Cardiovasc Dis. 1985 Mar-Apr;27(5):335-71) and its p-value is derived using a normal approximation.
Risk Ratio and related p-value are estimated by using the SAS FREQ procedure.
Risk Difference and related p-value are estimated by using the SAS GLIMMIX procedure with the following model: criterion = treatment.
p-values for heterogeneity are estimated by using the SAS GLIMMIX procedure with the following model: criterion = treatment subgroup treatment*subgroup.
p-value for heterogeneity of Peto Odds Ratio is estimated by using normal approximation.
PGM=DEVOPS/SAR231893/EFC14153/CSR_RWE/REPORT/PGM/ae_evt_ger_subg_s2_t.sas OUT=REPORT/OUTPUT/ae_socrtmd_ger_ics_s2_t_x.rtf (10AUG2021 - 8:14)

Project Code / Study Number / Analysis: SAR231893 / EFC14153 / CSR_RWE

2 Adverse events - Safety type 2 inflammatory asthma phenotype population

2.14 Patients with at least one TEAE in SOC: Respiratory, thoracic and mediastinal disorders

2.14.4 By baseline ICS dose level (Medium, High)

	Baseline ICS dose level			
	High		Medium	
Safety type 2 inflammatory asthma phenotype population	**Placebo (N=50)**	**Dupilumab (N=101)**	**Placebo (N=63)**	**Dupilumab (N=131)**
p-value for Risk Difference		0.762		0.018
p-value for heterogeneity of Risk Difference				0.172

Odds Ratio and related p-value are estimated by Wald's method using the SAS LOGISTIC procedure.
Peto OR calculation is based on Yusuf S et al. (Prog Cardiovasc Dis. 1985 Mar-Apr;27(5):335-71) and its p-value is derived using a normal approximation.
Risk Ratio and related p-value are estimated by using the SAS FREQ procedure.
Risk Difference and related p-value are estimated by using the SAS GLIMMIX procedure with the following model: criterion = treatment.
p-values for heterogeneity are estimated by using the SAS GLIMMIX procedure with the following model: criterion = treatment subgroup treatment*subgroup.
p-value for heterogeneity of Peto Odds Ratio is estimated by using normal approximation.
PGM=DEVOPS/SAR231893/EFC14153/CSR_RWE/REPORT/PGM/ae_evt_ger_subg_s2_t.sas OUT=REPORT/OUTPUT/ae_socrtmd_ger_ics_s2_t_x.rtf (10AUG2021 - 8:14)

Project Code / Study Number / Analysis: SAR231893 / EFC14153 / CSR_RWE

2 Adverse events - Safety type 2 inflammatory asthma phenotype population

2.14 Patients with at least one TEAE in SOC: Respiratory, thoracic and mediastinal disorders

2.14.5 By baseline ICS dose level 2 (Medium, High)

	Baseline ICS dose level 2			
	High		Medium	
Safety type 2 inflammatory asthma phenotype population	**Placebo (N=94)**	**Dupilumab (N=199)**	**Placebo (N=19)**	**Dupilumab (N=35)**
Patients with at least one TEAE in SOC: Respiratory, thoracic and mediastinal disorders [n(%)]	26 (27.7%)	34 (17.1%)	5 (26.3%)	8 (22.9%)
Odds Ratio (95% CI)	-	0.54 (0.30 to 0.97)	-	0.83 (0.23 to 3.02)
p-value for Odds Ratio		0.038		0.777
p-value for heterogeneity of Odds Ratio				0.551
Risk Ratio (95% CI)	-	0.62 (0.39 to 0.97)	-	0.87 (0.33 to 2.29)
p-value for Risk Ratio		0.035		0.775
p-value for heterogeneity of Risk Ratio				0.531
Risk Difference (95% CI)	-	-10.57 (-21.06 to -0.08)	-	-3.46 (-28.23 to 21.32)

Odds Ratio and related p-value are estimated by Wald's method using the SAS LOGISTIC procedure.
Peto OR calculation is based on Yusuf S et al. (Prog Cardiovasc Dis. 1985 Mar-Apr;27(5):335-71) and its p-value is derived using a normal approximation.
Risk Ratio and related p-value are estimated by using the SAS FREQ procedure.
Risk Difference and related p-value are estimated by using the SAS GLIMMIX procedure with the following model: criterion = treatment.
p-values for heterogeneity are estimated by using the SAS GLIMMIX procedure with the following model: criterion = treatment subgroup treatment*subgroup.
p-value for heterogeneity of Peto Odds Ratio is estimated by using normal approximation.
PGM=DEVOPS/SAR231893/EFC14153/CSR_RWE/REPORT/PGM/ae_evt_ger_subg_s2_t.sas OUT=REPORT/OUTPUT/ae_socrtmd_ger_ics2_s2_t_x.rtf (01SEP2021 - 16:09)

Project Code / Study Number / Analysis: SAR231893 / EFC14153 / CSR_RWE

2 Adverse events - Safety type 2 inflammatory asthma phenotype population

2.14 Patients with at least one TEAE in SOC: Respiratory, thoracic and mediastinal disorders

2.14.5 By baseline ICS dose level 2 (Medium, High)

	Baseline ICS dose level 2			
	High		Medium	
Safety type 2 inflammatory asthma phenotype population	**Placebo (N=94)**	**Dupilumab (N=199)**	**Placebo (N=19)**	**Dupilumab (N=35)**
p-value for Risk Difference		0.048		0.780
p-value for heterogeneity of Risk Difference				0.597

Odds Ratio and related p-value are estimated by Wald's method using the SAS LOGISTIC procedure.
Peto OR calculation is based on Yusuf S et al. (Prog Cardiovasc Dis. 1985 Mar-Apr;27(5):335-71) and its p-value is derived using a normal approximation.
Risk Ratio and related p-value are estimated by using the SAS FREQ procedure.
Risk Difference and related p-value are estimated by using the SAS GLIMMIX procedure with the following model: criterion = treatment.
p-values for heterogeneity are estimated by using the SAS GLIMMIX procedure with the following model: criterion = treatment subgroup treatment*subgroup.
p-value for heterogeneity of Peto Odds Ratio is estimated by using normal approximation.
PGM=DEVOPS/SAR231893/EFC14153/CSR_RWE/REPORT/PGM/ae_evt_ger_subg_s2_t.sas OUT=REPORT/OUTPUT/ae_socrtmd_ger_ics2_s2_t_x.rtf (01SEP2021 - 16:09)

Project Code / Study Number / Analysis: SAR231893 / EFC14153 / CSR_RWE

2 Adverse events - Safety type 2 inflammatory asthma phenotype population

2.14 Patients with at least one TEAE in SOC: Respiratory, thoracic and mediastinal disorders

2.14.6 By baseline predicted FEV1 (<80%, >=80%)

	Baseline Predicted FEV1			
	<80%		>=80%	
Safety type 2 inflammatory asthma phenotype population	**Placebo (N=58)**	**Dupilumab (N=116)**	**Placebo (N=55)**	**Dupilumab (N=118)**
Patients with at least one TEAE in SOC: Respiratory, thoracic and mediastinal disorders [n(%)]	15 (25.9%)	23 (19.8%)	16 (29.1%)	19 (16.1%)
Odds Ratio (95% CI)	-	0.71 (0.34 to 1.49)	-	0.47 (0.22 to 1.00)
p-value for Odds Ratio		0.365		0.050
p-value for heterogeneity of Odds Ratio				0.445
Risk Ratio (95% CI)	-	0.77 (0.43 to 1.35)	-	0.55 (0.31 to 0.99)
p-value for Risk Ratio		0.360		0.047
p-value for heterogeneity of Risk Ratio				0.434
Risk Difference (95% CI)	-	-6.03 (-19.53 to 7.46)	-	-12.99 (-26.80 to 0.82)

Odds Ratio and related p-value are estimated by Wald's method using the SAS LOGISTIC procedure.
Peto OR calculation is based on Yusuf S et al. (Prog Cardiovasc Dis. 1985 Mar-Apr;27(5):335-71) and its p-value is derived using a normal approximation.
Risk Ratio and related p-value are estimated by using the SAS FREQ procedure.
Risk Difference and related p-value are estimated by using the SAS GLIMMIX procedure with the following model: criterion = treatment.
p-values for heterogeneity are estimated by using the SAS GLIMMIX procedure with the following model: criterion = treatment subgroup treatment*subgroup.
p-value for heterogeneity of Peto Odds Ratio is estimated by using normal approximation.
PGM=DEVOPS/SAR231893/EFC14153/CSR_RWE/REPORT/PGM/ae_evt_ger_subg_s2_t.sas OUT=REPORT/OUTPUT/ae_socrtmd_ger_pfev1_s2_t_x.rtf (10AUG2021 - 8:14)

Project Code / Study Number / Analysis: SAR231893 / EFC14153 / CSR_RWE

2 Adverse events - Safety type 2 inflammatory asthma phenotype population

2.14 Patients with at least one TEAE in SOC: Respiratory, thoracic and mediastinal disorders

2.14.6 By baseline predicted FEV1 (<80%, >=80%)

	Baseline Predicted FEV1			
	<80%		>=80%	
Safety type 2 inflammatory asthma phenotype population	**Placebo (N=58)**	**Dupilumab (N=116)**	**Placebo (N=55)**	**Dupilumab (N=118)**
p-value for Risk Difference		0.379		0.065
p-value for heterogeneity of Risk Difference				0.478

Odds Ratio and related p-value are estimated by Wald's method using the SAS LOGISTIC procedure.
Peto OR calculation is based on Yusuf S et al. (Prog Cardiovasc Dis. 1985 Mar-Apr;27(5):335-71) and its p-value is derived using a normal approximation.
Risk Ratio and related p-value are estimated by using the SAS FREQ procedure.
Risk Difference and related p-value are estimated by using the SAS GLIMMIX procedure with the following model: criterion = treatment.
p-values for heterogeneity are estimated by using the SAS GLIMMIX procedure with the following model: criterion = treatment subgroup treatment*subgroup.
p-value for heterogeneity of Peto Odds Ratio is estimated by using normal approximation.
PGM=DEVOPS/SAR231893/EFC14153/CSR_RWE/REPORT/PGM/ae_evt_ger_subg_s2_t.sas OUT=REPORT/OUTPUT/ae_socrtmd_ger_pfev1_s2_t_x.rtf (10AUG2021 - 8:14)

Project Code / Study Number / Analysis: SAR231893 / EFC14153 / CSR_RWE

2 Adverse events - Safety type 2 inflammatory asthma phenotype population

2.14 Patients with at least one TEAE in SOC: Respiratory, thoracic and mediastinal disorders

2.14.7 By baseline ACQ-7-IA (<=2, >2)

	Baseline ACQ-7-IA			
	<=2		>2	
Safety type 2 inflammatory asthma phenotype population	**Placebo (N=61)**	**Dupilumab (N=125)**	**Placebo (N=52)**	**Dupilumab (N=109)**
Patients with at least one TEAE in SOC: Respiratory, thoracic and mediastinal disorders [n(%)]	16 (26.2%)	21 (16.8%)	15 (28.8%)	21 (19.3%)
Odds Ratio (95% CI)	-	0.57 (0.27 to 1.19)	-	0.59 (0.27 to 1.27)
p-value for Odds Ratio		0.133		0.175
p-value for heterogeneity of Odds Ratio				0.947
Risk Ratio (95% CI)	-	0.64 (0.36 to 1.14)	-	0.67 (0.38 to 1.19)
p-value for Risk Ratio		0.128		0.168
p-value for heterogeneity of Risk Ratio				0.920
Risk Difference (95% CI)	-	-9.43 (-22.35 to 3.49)	-	-9.58 (-24.06 to 4.90)

Odds Ratio and related p-value are estimated by Wald's method using the SAS LOGISTIC procedure.
Peto OR calculation is based on Yusuf S et al. (Prog Cardiovasc Dis. 1985 Mar-Apr;27(5):335-71) and its p-value is derived using a normal approximation.
Risk Ratio and related p-value are estimated by using the SAS FREQ procedure.
Risk Difference and related p-value are estimated by using the SAS GLIMMIX procedure with the following model: criterion = treatment.
p-values for heterogeneity are estimated by using the SAS GLIMMIX procedure with the following model: criterion = treatment subgroup treatment*subgroup.
p-value for heterogeneity of Peto Odds Ratio is estimated by using normal approximation.
PGM=DEVOPS/SAR231893/EFC14153/CSR_RWE/REPORT/PGM/ae_evt_ger_subg_s2_t.sas OUT=REPORT/OUTPUT/ae_socrtmd_ger_acq7_s2_t_x.rtf (10AUG2021 - 8:15)

Project Code / Study Number / Analysis: SAR231893 / EFC14153 / CSR_RWE

2 Adverse events - Safety type 2 inflammatory asthma phenotype population

2.14 Patients with at least one TEAE in SOC: Respiratory, thoracic and mediastinal disorders

2.14.7 By baseline ACQ-7-IA (<=2, >2)

	Baseline ACQ-7-IA			
	<=2		>2	
Safety type 2 inflammatory asthma phenotype population	**Placebo (N=61)**	**Dupilumab (N=125)**	**Placebo (N=52)**	**Dupilumab (N=109)**
p-value for Risk Difference		0.152		0.193
p-value for heterogeneity of Risk Difference				0.988

Odds Ratio and related p-value are estimated by Wald's method using the SAS LOGISTIC procedure.
Peto OR calculation is based on Yusuf S et al. (Prog Cardiovasc Dis. 1985 Mar-Apr;27(5):335-71) and its p-value is derived using a normal approximation.
Risk Ratio and related p-value are estimated by using the SAS FREQ procedure.
Risk Difference and related p-value are estimated by using the SAS GLIMMIX procedure with the following model: criterion = treatment.
p-values for heterogeneity are estimated by using the SAS GLIMMIX procedure with the following model: criterion = treatment subgroup treatment*subgroup.
p-value for heterogeneity of Peto Odds Ratio is estimated by using normal approximation.
PGM=DEVOPS/SAR231893/EFC14153/CSR_RWE/REPORT/PGM/ae_evt_ger_subg_s2_t.sas OUT=REPORT/OUTPUT/ae_socrtmd_ger_acq7_s2_t_x.rtf (10AUG2021 - 8:15)

Project Code / Study Number / Analysis: SAR231893 / EFC14153 / CSR_RWE

2 Adverse events - Safety type 2 inflammatory asthma phenotype population

2.14 Patients with at least one TEAE in SOC: Respiratory, thoracic and mediastinal disorders

2.14.8 By baseline weight (<=30 kg, >30 kg)

	Baseline weight (kg)			
	<=30		>30	
Safety type 2 inflammatory asthma phenotype population	**Placebo (N=36)**	**Dupilumab (N=74)**	**Placebo (N=77)**	**Dupilumab (N=160)**
Patients with at least one TEAE in SOC: Respiratory, thoracic and mediastinal disorders [n(%)]	9 (25.0%)	12 (16.2%)	22 (28.6%)	30 (18.8%)
Odds Ratio (95% CI)	-	0.58 (0.22 to 1.54)	-	0.58 (0.31 to 1.09)
p-value for Odds Ratio		0.275		0.089
p-value for heterogeneity of Odds Ratio				0.991
Risk Ratio (95% CI)	-	0.65 (0.30 to 1.40)	-	0.66 (0.41 to 1.06)
p-value for Risk Ratio		0.269		0.084
p-value for heterogeneity of Risk Ratio				0.980
Risk Difference (95% CI)	-	-8.78 (-25.42 to 7.85)	-	-9.82 (-21.65 to 2.00)

Odds Ratio and related p-value are estimated by Wald's method using the SAS LOGISTIC procedure.
Peto OR calculation is based on Yusuf S et al. (Prog Cardiovasc Dis. 1985 Mar-Apr;27(5):335-71) and its p-value is derived using a normal approximation.
Risk Ratio and related p-value are estimated by using the SAS FREQ procedure.
Risk Difference and related p-value are estimated by using the SAS GLIMMIX procedure with the following model: criterion = treatment.
p-values for heterogeneity are estimated by using the SAS GLIMMIX procedure with the following model: criterion = treatment subgroup treatment*subgroup.
p-value for heterogeneity of Peto Odds Ratio is estimated by using normal approximation.
PGM=DEVOPS/SAR231893/EFC14153/CSR_RWE/REPORT/PGM/ae_evt_ger_subg_s2_t.sas OUT=REPORT/OUTPUT/ae_socrtmd_ger_wgt_s2_t_x.rtf (10AUG2021 - 8:15)

Project Code / Study Number / Analysis: SAR231893 / EFC14153 / CSR_RWE

2 Adverse events - Safety type 2 inflammatory asthma phenotype population

2.14 Patients with at least one TEAE in SOC: Respiratory, thoracic and mediastinal disorders

2.14.8 By baseline weight (<=30 kg, >30 kg)

	Baseline weight (kg)			
	<=30		>30	
Safety type 2 inflammatory asthma phenotype population	**Placebo (N=36)**	**Dupilumab (N=74)**	**Placebo (N=77)**	**Dupilumab (N=160)**
p-value for Risk Difference		0.298		0.103
p-value for heterogeneity of Risk Difference				0.920

Odds Ratio and related p-value are estimated by Wald's method using the SAS LOGISTIC procedure.
Peto OR calculation is based on Yusuf S et al. (Prog Cardiovasc Dis. 1985 Mar-Apr;27(5):335-71) and its p-value is derived using a normal approximation.
Risk Ratio and related p-value are estimated by using the SAS FREQ procedure.
Risk Difference and related p-value are estimated by using the SAS GLIMMIX procedure with the following model: criterion = treatment.
p-values for heterogeneity are estimated by using the SAS GLIMMIX procedure with the following model: criterion = treatment subgroup treatment*subgroup.
p-value for heterogeneity of Peto Odds Ratio is estimated by using normal approximation.
PGM=DEVOPS/SAR231893/EFC14153/CSR_RWE/REPORT/PGM/ae_evt_ger_subg_s2_t.sas OUT=REPORT/OUTPUT/ae_socrtmd_ger_wgt_s2_t_x.rtf (10AUG2021 - 8:15)

Project Code / Study Number / Analysis: SAR231893 / EFC14153 / CSR_RWE

2 Adverse events - Safety type 2 inflammatory asthma phenotype population

2.14 Patients with at least one TEAE in SOC: Respiratory, thoracic and mediastinal disorders

2.14.9 By atopic medical condition (Yes, No)

Safety type 2 inflammatory asthma phenotype population	Atopic medical condition: Yes – Placebo (N=102)	Atopic medical condition: Yes – Dupilumab (N=225)	Atopic medical condition: No – Placebo (N=11)	Atopic medical condition: No – Dupilumab (N=9)
Patients with at least one TEAE in SOC: Respiratory, thoracic and mediastinal disorders [n(%)]	30 (29.4%)	42 (18.7%)	1 (9.1%)	0
Odds Ratio (95% CI)	-	0.55 (0.32 to 0.95)	-	0.00 (NE to NE)
p-value for Odds Ratio		0.031		NE
Peto Odds Ratio (95% CI)	-	0.54 (0.30 to 0.94)	-	0.16 (0.00 to 8.34)
p-value for Peto Odds Ratio		0.030		0.366
p-value for heterogeneity of Peto Odds Ratio				0.556
Risk Ratio (95% CI)	-	0.63 (0.42 to 0.95)	-	0.00 (NE to NE)
p-value for Risk Ratio		0.028		NE
p-value for heterogeneity of Risk Ratio				0.978

Odds Ratio and related p-value are estimated by Wald's method using the SAS LOGISTIC procedure.
Peto OR calculation is based on Yusuf S et al. (Prog Cardiovasc Dis. 1985 Mar-Apr;27(5):335-71) and its p-value is derived using a normal approximation.
Risk Ratio and related p-value are estimated by using the SAS FREQ procedure.
Risk Difference and related p-value are estimated by using the SAS GLIMMIX procedure with the following model: criterion = treatment.
p-values for heterogeneity are estimated by using the SAS GLIMMIX procedure with the following model: criterion = treatment subgroup treatment*subgroup.
p-value for heterogeneity of Peto Odds Ratio is estimated by using normal approximation.
PGM=DEVOPS/SAR231893/EFC14153/CSR_RWE/REPORT/PGM/ae_evt_ger_subg_s2_t.sas OUT=REPORT/OUTPUT/ae_socrtmd_ger_amc_s2_t_x.rtf (10AUG2021 - 8:15)

Project Code / Study Number / Analysis: SAR231893 / EFC14153 / CSR_RWE

2 Adverse events - Safety type 2 inflammatory asthma phenotype population

2.14 Patients with at least one TEAE in SOC: Respiratory, thoracic and mediastinal disorders

2.14.9 By atopic medical condition (Yes, No)

	Atopic medical condition			
	Yes		No	
Safety type 2 inflammatory asthma phenotype population	**Placebo (N=102)**	**Dupilumab (N=225)**	**Placebo (N=11)**	**Dupilumab (N=9)**
Risk Difference (95% CI)	-	-10.75 (-20.99 to -0.50)	-	-9.09 (NE to NE)
p-value for Risk Difference		0.040		<0.001
p-value for heterogeneity of Risk Difference				<0.001

Odds Ratio and related p-value are estimated by Wald's method using the SAS LOGISTIC procedure.
Peto OR calculation is based on Yusuf S et al. (Prog Cardiovasc Dis. 1985 Mar-Apr;27(5):335-71) and its p-value is derived using a normal approximation.
Risk Ratio and related p-value are estimated by using the SAS FREQ procedure.
Risk Difference and related p-value are estimated by using the SAS GLIMMIX procedure with the following model: criterion = treatment.
p-values for heterogeneity are estimated by using the SAS GLIMMIX procedure with the following model: criterion = treatment subgroup treatment*subgroup.
p-value for heterogeneity of Peto Odds Ratio is estimated by using normal approximation.
PGM=DEVOPS/SAR231893/EFC14153/CSR_RWE/REPORT/PGM/ae_evt_ger_subg_s2_t.sas OUT=REPORT/OUTPUT/ae_socrtmd_ger_amc_s2_t_x.rtf (10AUG2021 - 8:15)

Project Code / Study Number / Analysis: SAR231893 / EFC14153 / CSR_RWE

2 Adverse events - Safety type 2 inflammatory asthma phenotype population

2.14 Patients with at least one TEAE in SOC: Respiratory, thoracic and mediastinal disorders

2.14.10 By baseline total IgE (<median, >= median)

	Baseline Total IgE (IU/mL)			
	<median		>=median	
Safety type 2 inflammatory asthma phenotype population	**Placebo (N=65)**	**Dupilumab (N=106)**	**Placebo (N=47)**	**Dupilumab (N=124)**
Patients with at least one TEAE in SOC: Respiratory, thoracic and mediastinal disorders [n(%)]	19 (29.2%)	17 (16.0%)	11 (23.4%)	24 (19.4%)
Odds Ratio (95% CI)	-	0.46 (0.22 to 0.97)	-	0.79 (0.35 to 1.76)
p-value for Odds Ratio		0.042		0.558
p-value for heterogeneity of Odds Ratio				0.346
Risk Ratio (95% CI)	-	0.55 (0.31 to 0.98)	-	0.83 (0.44 to 1.55)
p-value for Risk Ratio		0.041		0.554
p-value for heterogeneity of Risk Ratio				0.347
Risk Difference (95% CI)	-	-13.19 (-26.37 to -0.02)	-	-4.05 (-18.11 to 10.01)

Odds Ratio and related p-value are estimated by Wald's method using the SAS LOGISTIC procedure.
Peto OR calculation is based on Yusuf S et al. (Prog Cardiovasc Dis. 1985 Mar-Apr;27(5):335-71) and its p-value is derived using a normal approximation.
Risk Ratio and related p-value are estimated by using the SAS FREQ procedure.
Risk Difference and related p-value are estimated by using the SAS GLIMMIX procedure with the following model: criterion = treatment.
p-values for heterogeneity are estimated by using the SAS GLIMMIX procedure with the following model: criterion = treatment subgroup treatment*subgroup.
p-value for heterogeneity of Peto Odds Ratio is estimated by using normal approximation.
PGM=DEVOPS/SAR231893/EFC14153/CSR_RWE/REPORT/PGM/ae_evt_ger_subg_s2_t.sas OUT=REPORT/OUTPUT/ae_socrtmd_ger_igem_s2_t_x.rtf (10AUG2021 - 8:15)

Project Code / Study Number / Analysis: SAR231893 / EFC14153 / CSR_RWE

2 Adverse events - Safety type 2 inflammatory asthma phenotype population

2.14 Patients with at least one TEAE in SOC: Respiratory, thoracic and mediastinal disorders

2.14.10 By baseline total IgE (<median, >= median)

	Baseline Total IgE (IU/mL)			
	<median		>=median	
Safety type 2 inflammatory asthma phenotype population	**Placebo (N=65)**	**Dupilumab (N=106)**	**Placebo (N=47)**	**Dupilumab (N=124)**
p-value for Risk Difference		0.050		0.570
p-value for heterogeneity of Risk Difference				0.350

Odds Ratio and related p-value are estimated by Wald's method using the SAS LOGISTIC procedure.
Peto OR calculation is based on Yusuf S et al. (Prog Cardiovasc Dis. 1985 Mar-Apr;27(5):335-71) and its p-value is derived using a normal approximation.
Risk Ratio and related p-value are estimated by using the SAS FREQ procedure.
Risk Difference and related p-value are estimated by using the SAS GLIMMIX procedure with the following model: criterion = treatment.
p-values for heterogeneity are estimated by using the SAS GLIMMIX procedure with the following model: criterion = treatment subgroup treatment*subgroup.
p-value for heterogeneity of Peto Odds Ratio is estimated by using normal approximation.
PGM=DEVOPS/SAR231893/EFC14153/CSR_RWE/REPORT/PGM/ae_evt_ger_subg_s2_t.sas OUT=REPORT/OUTPUT/ae_socrtmd_ger_igem_s2_t_x.rtf (10AUG2021 - 8:15)

Project Code / Study Number / Analysis: SAR231893 / EFC14153 / CSR_RWE

2 Adverse events - Safety type 2 inflammatory asthma phenotype population

2.14 Patients with at least one TEAE in SOC: Respiratory, thoracic and mediastinal disorders

2.14.11 By baseline total IgE (<100 IU/ml, >= 100 IU/ml)

	Baseline Total IgE (IU/mL)			
	< 100		>= 100	
Safety type 2 inflammatory asthma phenotype population	**Placebo (N=22)**	**Dupilumab (N=29)**	**Placebo (N=90)**	**Dupilumab (N=201)**
Patients with at least one TEAE in SOC: Respiratory, thoracic and mediastinal disorders [n(%)]	4 (18.2%)	6 (20.7%)	26 (28.9%)	35 (17.4%)
Odds Ratio (95% CI)	-	1.17 (0.29 to 4.80)	-	0.52 (0.29 to 0.93)
p-value for Odds Ratio		0.823		0.028
p-value for heterogeneity of Odds Ratio				0.295
Risk Ratio (95% CI)	-	1.14 (0.36 to 3.55)	-	0.60 (0.39 to 0.94)
Reversed Risk ratio (95% CI)	-	0.88 (0.28 to 2.74)		
p-value for Risk Ratio		0.824		0.025
p-value for heterogeneity of Risk Ratio				0.308

Odds Ratio and related p-value are estimated by Wald's method using the SAS LOGISTIC procedure.
Peto OR calculation is based on Yusuf S et al. (Prog Cardiovasc Dis. 1985 Mar-Apr;27(5):335-71) and its p-value is derived using a normal approximation.
Risk Ratio and related p-value are estimated by using the SAS FREQ procedure.
Risk Difference and related p-value are estimated by using the SAS GLIMMIX procedure with the following model: criterion = treatment.
p-values for heterogeneity are estimated by using the SAS GLIMMIX procedure with the following model: criterion = treatment subgroup treatment*subgroup.
p-value for heterogeneity of Peto Odds Ratio is estimated by using normal approximation.
PGM=DEVOPS/SAR231893/EFC14153/CSR_RWE/REPORT/PGM/ae_evt_ger_subg_s2_t.sas OUT=REPORT/OUTPUT/ae_socrtmd_ger_ige_s2_t_x.rtf (10AUG2021 - 8:15)

Project Code / Study Number / Analysis: SAR231893 / EFC14153 / CSR_RWE

2 Adverse events - Safety type 2 inflammatory asthma phenotype population

2.14 Patients with at least one TEAE in SOC: Respiratory, thoracic and mediastinal disorders

2.14.11 By baseline total IgE (<100 IU/ml, >= 100 IU/ml)

	Baseline Total IgE (IU/mL)			
	< 100		>= 100	
Safety type 2 inflammatory asthma phenotype population	**Placebo (N=22)**	**Dupilumab (N=29)**	**Placebo (N=90)**	**Dupilumab (N=201)**
Risk Difference (95% CI)	-	2.51 (-19.89 to 24.90)	-	-11.48 (-22.25 to -0.70)
p-value for Risk Difference		0.823		0.037
p-value for heterogeneity of Risk Difference				0.261

Odds Ratio and related p-value are estimated by Wald's method using the SAS LOGISTIC procedure.
Peto OR calculation is based on Yusuf S et al. (Prog Cardiovasc Dis. 1985 Mar-Apr;27(5):335-71) and its p-value is derived using a normal approximation.
Risk Ratio and related p-value are estimated by using the SAS FREQ procedure.
Risk Difference and related p-value are estimated by using the SAS GLIMMIX procedure with the following model: criterion = treatment.
p-values for heterogeneity are estimated by using the SAS GLIMMIX procedure with the following model: criterion = treatment subgroup treatment*subgroup.
p-value for heterogeneity of Peto Odds Ratio is estimated by using normal approximation.
PGM=DEVOPS/SAR231893/EFC14153/CSR_RWE/REPORT/PGM/ae_evt_ger_subg_s2_t.sas OUT=REPORT/OUTPUT/ae_socrtmd_ger_ige_s2_t_x.rtf (10AUG2021 - 8:15)

Project Code / Study Number / Analysis: SAR231893 / EFC14153 / CSR_RWE

2 Adverse events - Safety type 2 inflammatory asthma phenotype population

2.14 Patients with at least one TEAE in SOC: Respiratory, thoracic and mediastinal disorders

2.14.12 By age at onset of asthma (0-2, 3-5, >=6 years)

	Age of onset of asthma (years)					
	0-2		3-5		>= 6	
Safety type 2 inflammatory asthma phenotype population	**Placebo (N=40)**	**Dupilumab (N=104)**	**Placebo (N=38)**	**Dupilumab (N=85)**	**Placebo (N=35)**	**Dupilumab (N=45)**
Patients with at least one TEAE in SOC: Respiratory, thoracic and mediastinal disorders [n(%)]	13 (32.5%)	23 (22.1%)	10 (26.3%)	17 (20.0%)	8 (22.9%)	2 (4.4%)
Odds Ratio (95% CI)	-	0.59 (0.26 to 1.32)	-	0.70 (0.29 to 1.72)	-	0.16 (0.03 to 0.80)
p-value for Odds Ratio		0.200		0.435		0.025
p-value for heterogeneity of Odds Ratio:						
0-2, 3-5						0.781
0-2, >= 6						0.153
3-5, >= 6						0.115
overall						0.275

Odds Ratio and related p-value are estimated by Wald's method using the SAS LOGISTIC procedure.
Peto OR calculation is based on Yusuf S et al. (Prog Cardiovasc Dis. 1985 Mar-Apr;27(5):335-71) and its p-value is derived using a normal approximation.
Risk Ratio and related p-value are estimated by using the SAS FREQ procedure.
Risk Difference and related p-value are estimated by using the SAS GLIMMIX procedure with the following model: criterion = treatment.
p-values for heterogeneity are estimated by using the SAS GLIMMIX procedure with the following model: criterion = treatment subgroup treatment*subgroup.
p-value for heterogeneity of Peto Odds Ratio is estimated by using normal approximation.
PGM=DEVOPS/SAR231893/EFC14153/CSR_RWE/REPORT/PGM/ae_evt_ger_subg_s2_t.sas OUT=REPORT/OUTPUT/ae_socrtmd_ger_onsa_s2_t_x.rtf (10AUG2021 - 8:16)

Project Code / Study Number / Analysis: SAR231893 / EFC14153 / CSR_RWE

2 Adverse events - Safety type 2 inflammatory asthma phenotype population

2.14 Patients with at least one TEAE in SOC: Respiratory, thoracic and mediastinal disorders

2.14.12 By age at onset of asthma (0-2, 3-5, >=6 years)

	Age of onset of asthma (years)					
	0-2		3-5		>= 6	
Safety type 2 inflammatory asthma phenotype population	**Placebo (N=40)**	**Dupilumab (N=104)**	**Placebo (N=38)**	**Dupilumab (N=85)**	**Placebo (N=35)**	**Dupilumab (N=45)**
Risk Ratio (95% CI)	-	0.68 (0.38 to 1.21)	-	0.76 (0.38 to 1.50)	-	0.19 (0.04 to 0.86)
p-value for Risk Ratio		0.189		0.430		0.031
p-value for heterogeneity of Risk Ratio:						
0-2, 3-5						0.808
0-2, >= 6						0.124
3-5, >= 6						0.103
overall						0.253
Risk Difference (95% CI)	-	-10.38 (-27.09 to 6.32)	-	-6.32 (-22.86 to 10.23)	-	-18.41 (-33.81 to -3.02)
p-value for Risk Difference		0.221		0.451		0.020
p-value for heterogeneity of Risk Difference:						

Odds Ratio and related p-value are estimated by Wald's method using the SAS LOGISTIC procedure.
Peto OR calculation is based on Yusuf S et al. (Prog Cardiovasc Dis. 1985 Mar-Apr;27(5):335-71) and its p-value is derived using a normal approximation.
Risk Ratio and related p-value are estimated by using the SAS FREQ procedure.
Risk Difference and related p-value are estimated by using the SAS GLIMMIX procedure with the following model: criterion = treatment.
p-values for heterogeneity are estimated by using the SAS GLIMMIX procedure with the following model: criterion = treatment subgroup treatment*subgroup.
p-value for heterogeneity of Peto Odds Ratio is estimated by using normal approximation.
PGM=DEVOPS/SAR231893/EFC14153/CSR_RWE/REPORT/PGM/ae_evt_ger_subg_s2_t.sas OUT=REPORT/OUTPUT/ae_socrtmd_ger_onsa_s2_t_x.rtf (10AUG2021 - 8:16)

Project Code / Study Number / Analysis: SAR231893 / EFC14153 / CSR_RWE

2 Adverse events - Safety type 2 inflammatory asthma phenotype population

2.14 Patients with at least one TEAE in SOC: Respiratory, thoracic and mediastinal disorders

2.14.12 By age at onset of asthma (0-2, 3-5, >=6 years)

	Age of onset of asthma (years)					
	0-2		3-5		>= 6	
Safety type 2 inflammatory asthma phenotype population	**Placebo (N=40)**	**Dupilumab (N=104)**	**Placebo (N=38)**	**Dupilumab (N=85)**	**Placebo (N=35)**	**Dupilumab (N=45)**
0-2, 3-5						0.732
0-2, >= 6						0.484
3-5, >= 6						0.289
overall						0.553

Odds Ratio and related p-value are estimated by Wald's method using the SAS LOGISTIC procedure.
Peto OR calculation is based on Yusuf S et al. (Prog Cardiovasc Dis. 1985 Mar-Apr;27(5):335-71) and its p-value is derived using a normal approximation.
Risk Ratio and related p-value are estimated by using the SAS FREQ procedure.
Risk Difference and related p-value are estimated by using the SAS GLIMMIX procedure with the following model: criterion = treatment.
p-values for heterogeneity are estimated by using the SAS GLIMMIX procedure with the following model: criterion = treatment subgroup treatment*subgroup.
p-value for heterogeneity of Peto Odds Ratio is estimated by using normal approximation.
PGM=DEVOPS/SAR231893/EFC14153/CSR_RWE/REPORT/PGM/ae_evt_ger_subg_s2_t.sas OUT=REPORT/OUTPUT/ae_socrtmd_ger_onsa_s2_t_x.rtf (10AUG2021 - 8:16)

Project Code / Study Number / Analysis: SAR231893 / EFC14153 / CSR_RWE

2 Adverse events - Safety type 2 inflammatory asthma phenotype population

2.14 Patients with at least one TEAE in SOC: Respiratory, thoracic and mediastinal disorders

2.14.13 By number of severe asthma exacerbation prior to the study (<=1, 2, >2)

	Number of severe asthma exacerbation prior to the study					
	<=1		2		>2	
Safety type 2 inflammatory asthma phenotype population	**Placebo (N=46)**	**Dupilumab (N=85)**	**Placebo (N=32)**	**Dupilumab (N=75)**	**Placebo (N=35)**	**Dupilumab (N=74)**
Patients with at least one TEAE in SOC: Respiratory, thoracic and mediastinal disorders [n(%)]	12 (26.1%)	15 (17.6%)	8 (25.0%)	5 (6.7%)	11 (31.4%)	22 (29.7%)
Odds Ratio (95% CI)	-	0.61 (0.26 to 1.44)	-	0.21 (0.06 to 0.72)	-	0.92 (0.39 to 2.20)
p-value for Odds Ratio		0.257		0.013		0.857
p-value for heterogeneity of Odds Ratio:						
<=1, 2						0.170
<=1, >2						0.503
2, >2						0.056
overall						0.158

Odds Ratio and related p-value are estimated by Wald's method using the SAS LOGISTIC procedure.
Peto OR calculation is based on Yusuf S et al. (Prog Cardiovasc Dis. 1985 Mar-Apr;27(5):335-71) and its p-value is derived using a normal approximation.
Risk Ratio and related p-value are estimated by using the SAS FREQ procedure.
Risk Difference and related p-value are estimated by using the SAS GLIMMIX procedure with the following model: criterion = treatment.
p-values for heterogeneity are estimated by using the SAS GLIMMIX procedure with the following model: criterion = treatment subgroup treatment*subgroup.
p-value for heterogeneity of Peto Odds Ratio is estimated by using normal approximation.
PGM=DEVOPS/SAR231893/EFC14153/CSR_RWE/REPORT/PGM/ae_evt_ger_subg_s2_t.sas OUT=REPORT/OUTPUT/ae_socrtmd_ger_exa_s2_t_x.rtf (10AUG2021 - 8:16)

Project Code / Study Number / Analysis: SAR231893 / EFC14153 / CSR_RWE

2 Adverse events - Safety type 2 inflammatory asthma phenotype population

2.14 Patients with at least one TEAE in SOC: Respiratory, thoracic and mediastinal disorders

2.14.13 By number of severe asthma exacerbation prior to the study (<=1, 2, >2)

	Number of severe asthma exacerbation prior to the study					
	<=1		2		>2	
Safety type 2 inflammatory asthma phenotype population	**Placebo (N=46)**	**Dupilumab (N=85)**	**Placebo (N=32)**	**Dupilumab (N=75)**	**Placebo (N=35)**	**Dupilumab (N=74)**
Risk Ratio (95% CI)	-	0.68 (0.35 to 1.32)	-	0.27 (0.09 to 0.75)	-	0.95 (0.52 to 1.73)
p-value for Risk Ratio		0.252		0.013		0.856
p-value for heterogeneity of Risk Ratio:						
<=1, 2						0.140
<=1, >2						0.466
2, >2						0.039
overall						0.119
Risk Difference (95% CI)	-	-8.44 (-23.64 to 6.76)	-	-18.33 (-34.55 to -2.12)	-	-1.70 (-20.49 to 17.09)
p-value for Risk Difference		0.274		0.027		0.858
p-value for heterogeneity of Risk Difference:						
<=1, 2						0.379
<=1, >2						0.581

Odds Ratio and related p-value are estimated by Wald's method using the SAS LOGISTIC procedure.
Peto OR calculation is based on Yusuf S et al. (Prog Cardiovasc Dis. 1985 Mar-Apr;27(5):335-71) and its p-value is derived using a normal approximation.
Risk Ratio and related p-value are estimated by using the SAS FREQ procedure.
Risk Difference and related p-value are estimated by using the SAS GLIMMIX procedure with the following model: criterion = treatment.
p-values for heterogeneity are estimated by using the SAS GLIMMIX procedure with the following model: criterion = treatment subgroup treatment*subgroup.
p-value for heterogeneity of Peto Odds Ratio is estimated by using normal approximation.
PGM=DEVOPS/SAR231893/EFC14153/CSR_RWE/REPORT/PGM/ae_evt_ger_subg_s2_t.sas OUT=REPORT/OUTPUT/ae_socrtmd_ger_exa_s2_t_x.rtf (10AUG2021 - 8:16)

Project Code / Study Number / Analysis: SAR231893 / EFC14153 / CSR_RWE

2 Adverse events - Safety type 2 inflammatory asthma phenotype population

2.14 Patients with at least one TEAE in SOC: Respiratory, thoracic and mediastinal disorders

2.14.13 By number of severe asthma exacerbation prior to the study (<=1, 2, >2)

	Number of severe asthma exacerbation prior to the study					
	<=1		2		>2	
Safety type 2 inflammatory asthma phenotype population	**Placebo (N=46)**	**Dupilumab (N=85)**	**Placebo (N=32)**	**Dupilumab (N=75)**	**Placebo (N=35)**	**Dupilumab (N=74)**
2, >2						0.185
overall						0.398

Odds Ratio and related p-value are estimated by Wald's method using the SAS LOGISTIC procedure.
Peto OR calculation is based on Yusuf S et al. (Prog Cardiovasc Dis. 1985 Mar-Apr;27(5):335-71) and its p-value is derived using a normal approximation.
Risk Ratio and related p-value are estimated by using the SAS FREQ procedure.
Risk Difference and related p-value are estimated by using the SAS GLIMMIX procedure with the following model: criterion = treatment.
p-values for heterogeneity are estimated by using the SAS GLIMMIX procedure with the following model: criterion = treatment subgroup treatment*subgroup.
p-value for heterogeneity of Peto Odds Ratio is estimated by using normal approximation.
PGM=DEVOPS/SAR231893/EFC14153/CSR_RWE/REPORT/PGM/ae_evt_ger_subg_s2_t.sas OUT=REPORT/OUTPUT/ae_socrtmd_ger_exa_s2_t_x.rtf (10AUG2021 - 8:16)

Project Code / Study Number / Analysis: SAR231893 / EFC14153 / CSR_RWE

2 Adverse events - Safety type 2 inflammatory asthma phenotype population

2.32 Patients with any TEAE: Eosinophilia

Safety type 2 inflammatory asthma phenotype population	Placebo (N=113)	Dupilumab (N=234)
Patients with any TEAE: Eosinophilia [n(%)]	1 (0.9%)	16 (6.8%)
Odds Ratio (95% CI)	-	8.21 (1.08 to 62.70)
p-value for Odds Ratio		0.042
Peto Odds Ratio (95% CI)	-	3.57 (1.27 to 10.10)
Reversed Peto Odds Ratio (95% CI)	-	0.28 (0.10 to 0.79)
p-value for Peto Odds Ratio		0.016
Risk Ratio (95% CI)	-	7.73 (1.04 to 57.54)
Reversed Risk Ratio (95% CI)	-	0.13 (0.02 to 0.96)
p-value for Risk Ratio		0.046
Risk Difference (95% CI)	-	5.95 (2.27 to 9.63)
p-value for Risk Difference		0.002

Odds Ratio and related p-value are estimated by Wald's method using the SAS LOGISTIC procedure.
Peto OR calculation is based on Yusuf S et al. (Prog Cardiovasc Dis. 1985 Mar-Apr;27(5):335-71) and its p-value is derived using a normal approximation.
Risk Ratio and related p-value are estimated by using the SAS FREQ procedure.
Risk Difference and related p-value are estimated by using the SAS GLIMMIX procedure with the following model: criterion = treatment.
p-value for heterogeneity of Peto Odds Ratio is estimated by using normal approximation.
PGM=DEVOPS/SAR231893/EFC14153/CSR_RWE/REPORT/PGM/ae_evt_ger_s2_t.sas OUT=REPORT/OUTPUT/ae_pteos_ger_s2_t_x.rtf (12AUG2021 - 11:36)

Project Code / Study Number / Analysis: SAR231893 / EFC14153 / CSR_RWE

2 Adverse events - Safety type 2 inflammatory asthma phenotype population

2.32 Patients with any TEAE: Eosinophilia

2.32.1 By gender (Male, Female)

	Gender			
	Male		Female	
Safety type 2 inflammatory asthma phenotype population	**Placebo (N=77)**	**Dupilumab (N=153)**	**Placebo (N=36)**	**Dupilumab (N=81)**
Patients with any TEAE: Eosinophilia [n(%)]	0	11 (7.2%)	1 (2.8%)	5 (6.2%)
Odds Ratio (95% CI)	-	NE (NE to NE)	-	2.30 (0.26 to 20.45)
p-value for Odds Ratio		NE		0.454
Peto Odds Ratio (95% CI)	-	4.82 (1.34 to 17.33)	-	2.00 (0.34 to 11.75)
Reversed Peto Odds Ratio (95% CI)	-	0.21 (0.06 to 0.75)	-	0.50 (0.09 to 2.94)
p-value for Peto Odds Ratio		0.016		0.444
p-value for heterogeneity of Peto Odds Ratio				0.430
Risk Ratio (95% CI)	-	NE (NE to NE)	-	2.22 (0.27 to 18.34)
Reversed Risk ratio (95% CI)			-	0.45 (0.05 to 3.71)
p-value for Risk Ratio		NE		0.458

Odds Ratio and related p-value are estimated by Wald's method using the SAS LOGISTIC procedure.
Peto OR calculation is based on Yusuf S et al. (Prog Cardiovasc Dis. 1985 Mar-Apr;27(5):335-71) and its p-value is derived using a normal approximation.
Risk Ratio and related p-value are estimated by using the SAS FREQ procedure.
Risk Difference and related p-value are estimated by using the SAS GLIMMIX procedure with the following model: criterion = treatment.
p-values for heterogeneity are estimated by using the SAS GLIMMIX procedure with the following model: criterion = treatment subgroup treatment*subgroup.
p-value for heterogeneity of Peto Odds Ratio is estimated by using normal approximation.
PGM=DEVOPS/SAR231893/EFC14153/CSR_RWE/REPORT/PGM/ae_evt_ger_subg_s2_t.sas OUT=REPORT/OUTPUT/ae_pteos_ger_sex_s2_t_x.rtf (12AUG2021 - 12:03)

Project Code / Study Number / Analysis: SAR231893 / EFC14153 / CSR_RWE

2 Adverse events - Safety type 2 inflammatory asthma phenotype population

2.32 Patients with any TEAE: Eosinophilia

2.32.1 By gender (Male, Female)

	Gender			
	Male		Female	
Safety type 2 inflammatory asthma phenotype population	**Placebo (N=77)**	**Dupilumab (N=153)**	**Placebo (N=36)**	**Dupilumab (N=81)**
p-value for heterogeneity of Risk Ratio				0.973
Risk Difference (95% CI)	-	7.19 (NE to NE)	-	3.40 (-4.19 to 10.98)
p-value for Risk Difference		<0.001		0.377
p-value for heterogeneity of Risk Difference				<0.001

Odds Ratio and related p-value are estimated by Wald's method using the SAS LOGISTIC procedure.
Peto OR calculation is based on Yusuf S et al. (Prog Cardiovasc Dis. 1985 Mar-Apr;27(5):335-71) and its p-value is derived using a normal approximation.
Risk Ratio and related p-value are estimated by using the SAS FREQ procedure.
Risk Difference and related p-value are estimated by using the SAS GLIMMIX procedure with the following model: criterion = treatment.
p-values for heterogeneity are estimated by using the SAS GLIMMIX procedure with the following model: criterion = treatment subgroup treatment*subgroup.
p-value for heterogeneity of Peto Odds Ratio is estimated by using normal approximation.
PGM=DEVOPS/SAR231893/EFC14153/CSR_RWE/REPORT/PGM/ae_evt_ger_subg_s2_t.sas OUT=REPORT/OUTPUT/ae_pteos_ger_sex_s2_t_x.rtf (12AUG2021 - 12:03)

Project Code / Study Number / Analysis: SAR231893 / EFC14153 / CSR_RWE

2 Adverse events - Safety type 2 inflammatory asthma phenotype population

2.32 Patients with any TEAE: Eosinophilia

2.32.2 By region (Latin America, East Europe, Western Countries)

	Region					
	Latin America		East Europe		Western countries	
Safety type 2 inflammatory asthma phenotype population	**Placebo (N=51)**	**Dupilumab (N=105)**	**Placebo (N=43)**	**Dupilumab (N=78)**	**Placebo (N=19)**	**Dupilumab (N=51)**
Patients with any TEAE: Eosinophilia [n(%)]	0	6 (5.7%)	1 (2.3%)	7 (9.0%)	0	3 (5.9%)
Odds Ratio (95% CI)	-	NE (NE to NE)	-	4.14 (0.49 to 34.84)	-	NE (NE to NE)
p-value for Odds Ratio		NE		0.191		NE
Peto Odds Ratio (95% CI)	-	4.64 (0.82 to 26.29)	-	2.91 (0.65 to 12.93)	-	4.11 (0.31 to 54.37)
Reversed Peto Odds Ratio (95% CI)	-	0.22 (0.04 to 1.22)	-	0.34 (0.08 to 1.54)	-	0.24 (0.02 to 3.23)
p-value for Peto Odds Ratio		0.083		0.161		0.283
p-value for heterogeneity of Peto Odds Ratio:						
Latin America, East Europe						0.689
Latin America, Western countries						0.939
East Europe, Western countries						0.820
overall						0.918

Odds Ratio and related p-value are estimated by Wald's method using the SAS LOGISTIC procedure.
Peto OR calculation is based on Yusuf S et al. (Prog Cardiovasc Dis. 1985 Mar-Apr;27(5):335-71) and its p-value is derived using a normal approximation.
Risk Ratio and related p-value are estimated by using the SAS FREQ procedure.
Risk Difference and related p-value are estimated by using the SAS GLIMMIX procedure with the following model: criterion = treatment.
p-values for heterogeneity are estimated by using the SAS GLIMMIX procedure with the following model: criterion = treatment subgroup treatment*subgroup.
p-value for heterogeneity of Peto Odds Ratio is estimated by using normal approximation.
PGM=DEVOPS/SAR231893/EFC14153/CSR_RWE/REPORT/PGM/ae_evt_ger_subg_s2_t.sas OUT=REPORT/OUTPUT/ae_pteos_ger_cty_s2_t_x.rtf (12AUG2021 - 12:04)

Project Code / Study Number / Analysis: SAR231893 / EFC14153 / CSR_RWE

2 Adverse events - Safety type 2 inflammatory asthma phenotype population

2.32 Patients with any TEAE: Eosinophilia

2.32.2 By region (Latin America, East Europe, Western Countries)

	Region					
	Latin America		East Europe		Western countries	
Safety type 2 inflammatory asthma phenotype population	**Placebo (N=51)**	**Dupilumab (N=105)**	**Placebo (N=43)**	**Dupilumab (N=78)**	**Placebo (N=19)**	**Dupilumab (N=51)**
Risk Ratio (95% CI)	-	NE (NE to NE)	-	3.86 (0.49 to 30.34)	-	NE (NE to NE)
Reversed Risk ratio (95% CI)			-	0.26 (0.03 to 2.04)		
p-value for Risk Ratio		NE		0.199		NE
p-value for heterogeneity of Risk Ratio:						
Latin America, East Europe						0.980
Latin America, Western countries						1.000
East Europe, Western countries						0.988
overall						1.000
Risk Difference (95% CI)	-	5.71 (NE to NE)	-	6.65 (-1.21 to 14.51)	-	5.88 (NE to NE)
p-value for Risk Difference		<0.001		0.097		<0.001
p-value for heterogeneity of Risk Difference:						

Odds Ratio and related p-value are estimated by Wald's method using the SAS LOGISTIC procedure.
Peto OR calculation is based on Yusuf S et al. (Prog Cardiovasc Dis. 1985 Mar-Apr;27(5):335-71) and its p-value is derived using a normal approximation.
Risk Ratio and related p-value are estimated by using the SAS FREQ procedure.
Risk Difference and related p-value are estimated by using the SAS GLIMMIX procedure with the following model: criterion = treatment.
p-values for heterogeneity are estimated by using the SAS GLIMMIX procedure with the following model: criterion = treatment subgroup treatment*subgroup.
p-value for heterogeneity of Peto Odds Ratio is estimated by using normal approximation.
PGM=DEVOPS/SAR231893/EFC14153/CSR_RWE/REPORT/PGM/ae_evt_ger_subg_s2_t.sas OUT=REPORT/OUTPUT/ae_pteos_ger_cty_s2_t_x.rtf (12AUG2021 - 12:04)

Project Code / Study Number / Analysis: SAR231893 / EFC14153 / CSR_RWE

2 Adverse events - Safety type 2 inflammatory asthma phenotype population

2.32 Patients with any TEAE: Eosinophilia

2.32.2 By region (Latin America, East Europe, Western Countries)

	Region					
	Latin America		East Europe		Western countries	
Safety type 2 inflammatory asthma phenotype population	**Placebo (N=51)**	**Dupilumab (N=105)**	**Placebo (N=43)**	**Dupilumab (N=78)**	**Placebo (N=19)**	**Dupilumab (N=51)**
Latin America, East Europe						<0.001
Latin America, Western countries						<0.001
East Europe, Western countries						<0.001
overall						<0.001

Odds Ratio and related p-value are estimated by Wald's method using the SAS LOGISTIC procedure.
Peto OR calculation is based on Yusuf S et al. (Prog Cardiovasc Dis. 1985 Mar-Apr;27(5):335-71) and its p-value is derived using a normal approximation.
Risk Ratio and related p-value are estimated by using the SAS FREQ procedure.
Risk Difference and related p-value are estimated by using the SAS GLIMMIX procedure with the following model: criterion = treatment.
p-values for heterogeneity are estimated by using the SAS GLIMMIX procedure with the following model: criterion = treatment subgroup treatment*subgroup.
p-value for heterogeneity of Peto Odds Ratio is estimated by using normal approximation.
PGM=DEVOPS/SAR231893/EFC14153/CSR_RWE/REPORT/PGM/ae_evt_ger_subg_s2_t.sas OUT=REPORT/OUTPUT/ae_pteos_ger_cty_s2_t_x.rtf (12AUG2021 - 12:04)

Project Code / Study Number / Analysis: SAR231893 / EFC14153 / CSR_RWE

2 Adverse events - Safety type 2 inflammatory asthma phenotype population

2.32 Patients with any TEAE: Eosinophilia

2.32.3 By race (Caucasian/white, Black/of African descent, Other)

	Race					
	Caucasian/White		Black/of African descent		Other	
Safety type 2 inflammatory asthma phenotype population	**Placebo (N=101)**	**Dupilumab (N=207)**	**Placebo (N=5)**	**Dupilumab (N=9)**	**Placebo (N=7)**	**Dupilumab (N=18)**
Patients with any TEAE: Eosinophilia [n(%)]	1 (1.0%)	16 (7.7%)	0	0	0	0
Odds Ratio (95% CI)	-	8.37 (1.09 to 63.99)	-	NE (NE to NE)	-	NE (NE to NE)
p-value for Odds Ratio		0.041		NE		NE
Peto Odds Ratio (95% CI)	-	3.63 (1.28 to 10.26)	-	NE (NE to NE)	-	NE (NE to NE)
Reversed Peto Odds Ratio (95% CI)	-	0.28 (0.10 to 0.78)				
p-value for Peto Odds Ratio		0.015		NE		NE
p-value for heterogeneity of Peto Odds Ratio:						
Caucasian/White, Black/of African descent						NE
Caucasian/White, Other						NE
Black/of African descent, Other						NE
overall						NE

Odds Ratio and related p-value are estimated by Wald's method using the SAS LOGISTIC procedure.
Peto OR calculation is based on Yusuf S et al. (Prog Cardiovasc Dis. 1985 Mar-Apr;27(5):335-71) and its p-value is derived using a normal approximation.
Risk Ratio and related p-value are estimated by using the SAS FREQ procedure.
Risk Difference and related p-value are estimated by using the SAS GLIMMIX procedure with the following model: criterion = treatment.
p-values for heterogeneity are estimated by using the SAS GLIMMIX procedure with the following model: criterion = treatment subgroup treatment*subgroup.
p-value for heterogeneity of Peto Odds Ratio is estimated by using normal approximation.
PGM=DEVOPS/SAR231893/EFC14153/CSR_RWE/REPORT/PGM/ae_evt_ger_subg_s2_t.sas OUT=REPORT/OUTPUT/ae_pteos_ger_race_s2_t_x.rtf (12AUG2021 - 12:04)

Project Code / Study Number / Analysis: SAR231893 / EFC14153 / CSR_RWE

2 Adverse events - Safety type 2 inflammatory asthma phenotype population

2.32 Patients with any TEAE: Eosinophilia

2.32.3 By race (Caucasian/white, Black/of African descent, Other)

	Race					
	Caucasian/White		Black/of African descent		Other	
Safety type 2 inflammatory asthma phenotype population	**Placebo (N=101)**	**Dupilumab (N=207)**	**Placebo (N=5)**	**Dupilumab (N=9)**	**Placebo (N=7)**	**Dupilumab (N=18)**
Risk Ratio (95% CI)	-	7.81 (1.05 to 58.05)	-	NE (NE to NE)	-	NE (NE to NE)
Reversed Risk ratio (95% CI)	-	0.13 (0.02 to 0.95)				
p-value for Risk Ratio		0.045		NE		NE
p-value for heterogeneity of Risk Ratio:						
Caucasian/White, Black/of African descent						0.999
Caucasian/White, Other						0.998
Black/of African descent, Other						1.000
overall						1.000
Risk Difference (95% CI)	-	6.74 (2.60 to 10.87)	-	0.00 (NE to NE)	-	0.00 (NE to NE)
p-value for Risk Difference		0.001		NE		NE
p-value for heterogeneity of Risk Difference:						

Odds Ratio and related p-value are estimated by Wald's method using the SAS LOGISTIC procedure.
Peto OR calculation is based on Yusuf S et al. (Prog Cardiovasc Dis. 1985 Mar-Apr;27(5):335-71) and its p-value is derived using a normal approximation.
Risk Ratio and related p-value are estimated by using the SAS FREQ procedure.
Risk Difference and related p-value are estimated by using the SAS GLIMMIX procedure with the following model: criterion = treatment.
p-values for heterogeneity are estimated by using the SAS GLIMMIX procedure with the following model: criterion = treatment subgroup treatment*subgroup.
p-value for heterogeneity of Peto Odds Ratio is estimated by using normal approximation.
PGM=DEVOPS/SAR231893/EFC14153/CSR_RWE/REPORT/PGM/ae_evt_ger_subg_s2_t.sas OUT=REPORT/OUTPUT/ae_pteos_ger_race_s2_t_x.rtf (12AUG2021 - 12:04)

Project Code / Study Number / Analysis: SAR231893 / EFC14153 / CSR_RWE

2 Adverse events - Safety type 2 inflammatory asthma phenotype population

2.32 Patients with any TEAE: Eosinophilia

2.32.3 By race (Caucasian/white, Black/of African descent, Other)

	Race					
	Caucasian/White		Black/of African descent		Other	
Safety type 2 inflammatory asthma phenotype population	**Placebo (N=101)**	**Dupilumab (N=207)**	**Placebo (N=5)**	**Dupilumab (N=9)**	**Placebo (N=7)**	**Dupilumab (N=18)**
Caucasian/White, Black/of African descent						<0.001
Caucasian/White, Other						<0.001
Black/of African descent, Other						NE
overall						NE

Odds Ratio and related p-value are estimated by Wald's method using the SAS LOGISTIC procedure.
Peto OR calculation is based on Yusuf S et al. (Prog Cardiovasc Dis. 1985 Mar-Apr;27(5):335-71) and its p-value is derived using a normal approximation.
Risk Ratio and related p-value are estimated by using the SAS FREQ procedure.
Risk Difference and related p-value are estimated by using the SAS GLIMMIX procedure with the following model: criterion = treatment.
p-values for heterogeneity are estimated by using the SAS GLIMMIX procedure with the following model: criterion = treatment subgroup treatment*subgroup.
p-value for heterogeneity of Peto Odds Ratio is estimated by using normal approximation.
PGM=DEVOPS/SAR231893/EFC14153/CSR_RWE/REPORT/PGM/ae_evt_ger_subg_s2_t.sas OUT=REPORT/OUTPUT/ae_pteos_ger_race_s2_t_x.rtf (12AUG2021 - 12:04)

Project Code / Study Number / Analysis: SAR231893 / EFC14153 / CSR_RWE

2 Adverse events - Safety type 2 inflammatory asthma phenotype population

2.32 Patients with any TEAE: Eosinophilia

2.32.4 By baseline ICS dose level (Medium, High)

	Baseline ICS dose level			
	High		Medium	
Safety type 2 inflammatory asthma phenotype population	**Placebo (N=50)**	**Dupilumab (N=101)**	**Placebo (N=63)**	**Dupilumab (N=131)**
Patients with any TEAE: Eosinophilia [n(%)]	0	4 (4.0%)	1 (1.6%)	12 (9.2%)
Odds Ratio (95% CI)	-	NE (NE to NE)	-	6.25 (0.79 to 49.19)
p-value for Odds Ratio		NE		0.082
Peto Odds Ratio (95% CI)	-	4.60 (0.56 to 37.68)	-	3.34 (1.01 to 11.06)
Reversed Peto Odds Ratio (95% CI)	-	0.22 (0.03 to 1.79)	-	0.30 (0.09 to 0.99)
p-value for Peto Odds Ratio		0.155		0.049
p-value for heterogeneity of Peto Odds Ratio				0.795
Risk Ratio (95% CI)	-	NE (NE to NE)	-	5.77 (0.77 to 43.41)
Reversed Risk ratio (95% CI)			-	0.17 (0.02 to 1.30)
p-value for Risk Ratio		NE		0.089

Odds Ratio and related p-value are estimated by Wald's method using the SAS LOGISTIC procedure.
Peto OR calculation is based on Yusuf S et al. (Prog Cardiovasc Dis. 1985 Mar-Apr;27(5):335-71) and its p-value is derived using a normal approximation.
Risk Ratio and related p-value are estimated by using the SAS FREQ procedure.
Risk Difference and related p-value are estimated by using the SAS GLIMMIX procedure with the following model: criterion = treatment.
p-values for heterogeneity are estimated by using the SAS GLIMMIX procedure with the following model: criterion = treatment subgroup treatment*subgroup.
p-value for heterogeneity of Peto Odds Ratio is estimated by using normal approximation.
PGM=DEVOPS/SAR231893/EFC14153/CSR_RWE/REPORT/PGM/ae_evt_ger_subg_s2_t.sas OUT=REPORT/OUTPUT/ae_pteos_ger_ics_s2_t_x.rtf (12AUG2021 - 12:04)

Project Code / Study Number / Analysis: SAR231893 / EFC14153 / CSR_RWE

2 Adverse events - Safety type 2 inflammatory asthma phenotype population

2.32 Patients with any TEAE: Eosinophilia

2.32.4 By baseline ICS dose level (Medium, High)

	Baseline ICS dose level			
	High		Medium	
Safety type 2 inflammatory asthma phenotype population	**Placebo (N=50)**	**Dupilumab (N=101)**	**Placebo (N=63)**	**Dupilumab (N=131)**
p-value for heterogeneity of Risk Ratio				0.981
Risk Difference (95% CI)	-	3.96 (NE to NE)	-	7.57 (1.71 to 13.43)
p-value for Risk Difference		<0.001		0.012
p-value for heterogeneity of Risk Difference				<0.001

Odds Ratio and related p-value are estimated by Wald's method using the SAS LOGISTIC procedure.
Peto OR calculation is based on Yusuf S et al. (Prog Cardiovasc Dis. 1985 Mar-Apr;27(5):335-71) and its p-value is derived using a normal approximation.
Risk Ratio and related p-value are estimated by using the SAS FREQ procedure.
Risk Difference and related p-value are estimated by using the SAS GLIMMIX procedure with the following model: criterion = treatment.
p-values for heterogeneity are estimated by using the SAS GLIMMIX procedure with the following model: criterion = treatment subgroup treatment*subgroup.
p-value for heterogeneity of Peto Odds Ratio is estimated by using normal approximation.
PGM=DEVOPS/SAR231893/EFC14153/CSR_RWE/REPORT/PGM/ae_evt_ger_subg_s2_t.sas OUT=REPORT/OUTPUT/ae_pteos_ger_ics_s2_t_x.rtf (12AUG2021 - 12:04)

Project Code / Study Number / Analysis: SAR231893 / EFC14153 / CSR_RWE

2 Adverse events - Safety type 2 inflammatory asthma phenotype population

2.32 Patients with any TEAE: Eosinophilia

2.32.5 By baseline ICS dose level 2 (Medium, High)

Safety type 2 inflammatory asthma phenotype population	Baseline ICS dose level 2			
	High		Medium	
	Placebo (N=94)	Dupilumab (N=199)	Placebo (N=19)	Dupilumab (N=35)
Patients with any TEAE: Eosinophilia [n(%)]	1 (1.1%)	14 (7.0%)	0	2 (5.7%)
Odds Ratio (95% CI)	-	7.04 (0.91 to 54.31)	-	NE (NE to NE)
p-value for Odds Ratio		0.061		NE
Peto Odds Ratio (95% CI)	-	3.40 (1.12 to 10.34)	-	4.82 (0.26 to 90.24)
Reversed Peto Odds Ratio (95% CI)	-	0.29 (0.10 to 0.89)	-	0.21 (0.01 to 3.85)
p-value for Peto Odds Ratio		0.031		0.293
p-value for heterogeneity of Peto Odds Ratio				0.828
Risk Ratio (95% CI)	-	6.61 (0.88 to 49.55)	-	NE (NE to NE)
Reversed Risk ratio (95% CI)	-	0.15 (0.02 to 1.13)		
p-value for Risk Ratio		0.066		NE

Odds Ratio and related p-value are estimated by Wald's method using the SAS LOGISTIC procedure.
Peto OR calculation is based on Yusuf S et al. (Prog Cardiovasc Dis. 1985 Mar-Apr;27(5):335-71) and its p-value is derived using a normal approximation.
Risk Ratio and related p-value are estimated by using the SAS FREQ procedure.
Risk Difference and related p-value are estimated by using the SAS GLIMMIX procedure with the following model: criterion = treatment.
p-values for heterogeneity are estimated by using the SAS GLIMMIX procedure with the following model: criterion = treatment subgroup treatment*subgroup.
p-value for heterogeneity of Peto Odds Ratio is estimated by using normal approximation.
PGM=DEVOPS/SAR231893/EFC14153/CSR_RWE/REPORT/PGM/ae_evt_ger_subg_s2_t.sas OUT=REPORT/OUTPUT/ae_pteos_ger_ics2_s2_t_x.rtf (01SEP2021 - 16:12)

Project Code / Study Number / Analysis: SAR231893 / EFC14153 / CSR_RWE

2 Adverse events - Safety type 2 inflammatory asthma phenotype population

2.32 Patients with any TEAE: Eosinophilia

2.32.5 By baseline ICS dose level 2 (Medium, High)

	Baseline ICS dose level 2			
	High		Medium	
Safety type 2 inflammatory asthma phenotype population	**Placebo (N=94)**	**Dupilumab (N=199)**	**Placebo (N=19)**	**Dupilumab (N=35)**
p-value for heterogeneity of Risk Ratio				0.982
Risk Difference (95% CI)	-	5.97 (1.84 to 10.10)	-	5.71 (NE to NE)
p-value for Risk Difference		0.005		<0.001
p-value for heterogeneity of Risk Difference				<0.001

Odds Ratio and related p-value are estimated by Wald's method using the SAS LOGISTIC procedure.
Peto OR calculation is based on Yusuf S et al. (Prog Cardiovasc Dis. 1985 Mar-Apr;27(5):335-71) and its p-value is derived using a normal approximation.
Risk Ratio and related p-value are estimated by using the SAS FREQ procedure.
Risk Difference and related p-value are estimated by using the SAS GLIMMIX procedure with the following model: criterion = treatment.
p-values for heterogeneity are estimated by using the SAS GLIMMIX procedure with the following model: criterion = treatment subgroup treatment*subgroup.
p-value for heterogeneity of Peto Odds Ratio is estimated by using normal approximation.
PGM=DEVOPS/SAR231893/EFC14153/CSR_RWE/REPORT/PGM/ae_evt_ger_subg_s2_t.sas OUT=REPORT/OUTPUT/ae_pteos_ger_ics2_s2_t_x.rtf (01SEP2021 - 16:12)

Project Code / Study Number / Analysis: SAR231893 / EFC14153 / CSR_RWE

2 Adverse events - Safety type 2 inflammatory asthma phenotype population

2.32 Patients with any TEAE: Eosinophilia

2.32.6 By baseline predicted FEV1 (<80%, >=80%)

	Baseline Predicted FEV1			
	<80%		>=80%	
Safety type 2 inflammatory asthma phenotype population	**Placebo (N=58)**	**Dupilumab (N=116)**	**Placebo (N=55)**	**Dupilumab (N=118)**
Patients with any TEAE: Eosinophilia [n(%)]	0	7 (6.0%)	1 (1.8%)	9 (7.6%)
Odds Ratio (95% CI)	-	NE (NE to NE)	-	4.46 (0.55 to 36.10)
p-value for Odds Ratio		NE		0.161
Peto Odds Ratio (95% CI)	-	4.73 (0.96 to 23.41)	-	2.89 (0.74 to 11.33)
Reversed Peto Odds Ratio (95% CI)	-	0.21 (0.04 to 1.04)	-	0.35 (0.09 to 1.35)
p-value for Peto Odds Ratio		0.057		0.128
p-value for heterogeneity of Peto Odds Ratio				0.646
Risk Ratio (95% CI)	-	NE (NE to NE)	-	4.19 (0.54 to 32.30)
Reversed Risk ratio (95% CI)			-	0.24 (0.03 to 1.84)
p-value for Risk Ratio		NE		0.169

Odds Ratio and related p-value are estimated by Wald's method using the SAS LOGISTIC procedure.
Peto OR calculation is based on Yusuf S et al. (Prog Cardiovasc Dis. 1985 Mar-Apr;27(5):335-71) and its p-value is derived using a normal approximation.
Risk Ratio and related p-value are estimated by using the SAS FREQ procedure.
Risk Difference and related p-value are estimated by using the SAS GLIMMIX procedure with the following model: criterion = treatment.
p-values for heterogeneity are estimated by using the SAS GLIMMIX procedure with the following model: criterion = treatment subgroup treatment*subgroup.
p-value for heterogeneity of Peto Odds Ratio is estimated by using normal approximation.
PGM=DEVOPS/SAR231893/EFC14153/CSR_RWE/REPORT/PGM/ae_evt_ger_subg_s2_t.sas OUT=REPORT/OUTPUT/ae_pteos_ger_pfev1_s2_t_x.rtf (12AUG2021 - 12:04)

Project Code / Study Number / Analysis: SAR231893 / EFC14153 / CSR_RWE

2 Adverse events - Safety type 2 inflammatory asthma phenotype population

2.32 Patients with any TEAE: Eosinophilia

2.32.6 By baseline predicted FEV1 (<80%, >=80%)

	Baseline Predicted FEV1			
	<80%		>=80%	
Safety type 2 inflammatory asthma phenotype population	**Placebo (N=58)**	**Dupilumab (N=116)**	**Placebo (N=55)**	**Dupilumab (N=118)**
p-value for heterogeneity of Risk Ratio				0.978
Risk Difference (95% CI)	-	6.03 (NE to NE)	-	5.81 (-0.18 to 11.80)
p-value for Risk Difference		<0.001		0.057
p-value for heterogeneity of Risk Difference				<0.001

Odds Ratio and related p-value are estimated by Wald's method using the SAS LOGISTIC procedure.
Peto OR calculation is based on Yusuf S et al. (Prog Cardiovasc Dis. 1985 Mar-Apr;27(5):335-71) and its p-value is derived using a normal approximation.
Risk Ratio and related p-value are estimated by using the SAS FREQ procedure.
Risk Difference and related p-value are estimated by using the SAS GLIMMIX procedure with the following model: criterion = treatment.
p-values for heterogeneity are estimated by using the SAS GLIMMIX procedure with the following model: criterion = treatment subgroup treatment*subgroup.
p-value for heterogeneity of Peto Odds Ratio is estimated by using normal approximation.
PGM=DEVOPS/SAR231893/EFC14153/CSR_RWE/REPORT/PGM/ae_evt_ger_subg_s2_t.sas OUT=REPORT/OUTPUT/ae_pteos_ger_pfev1_s2_t_x.rtf (12AUG2021 - 12:04)

Project Code / Study Number / Analysis: SAR231893 / EFC14153 / CSR_RWE

2 Adverse events - Safety type 2 inflammatory asthma phenotype population

2.32 Patients with any TEAE: Eosinophilia

2.32.7 By baseline ACQ-7-IA (<=2, >2)

	Baseline ACQ-7-IA			
	<=2		>2	
Safety type 2 inflammatory asthma phenotype population	**Placebo (N=61)**	**Dupilumab (N=125)**	**Placebo (N=52)**	**Dupilumab (N=109)**
Patients with any TEAE: Eosinophilia [n(%)]	1 (1.6%)	6 (4.8%)	0	10 (9.2%)
Odds Ratio (95% CI)	-	3.02 (0.36 to 25.68)	-	NE (NE to NE)
p-value for Odds Ratio		0.311		NE
Peto Odds Ratio (95% CI)	-	2.38 (0.48 to 11.85)	-	4.78 (1.22 to 18.72)
Reversed Peto Odds Ratio (95% CI)	-	0.42 (0.08 to 2.08)	-	0.21 (0.05 to 0.82)
p-value for Peto Odds Ratio		0.289		0.025
p-value for heterogeneity of Peto Odds Ratio				0.517
Risk Ratio (95% CI)	-	2.93 (0.36 to 23.79)	-	NE (NE to NE)
Reversed Risk ratio (95% CI)	-	0.34 (0.04 to 2.77)		
p-value for Risk Ratio		0.315		NE

Odds Ratio and related p-value are estimated by Wald's method using the SAS LOGISTIC procedure.
Peto OR calculation is based on Yusuf S et al. (Prog Cardiovasc Dis. 1985 Mar-Apr;27(5):335-71) and its p-value is derived using a normal approximation.
Risk Ratio and related p-value are estimated by using the SAS FREQ procedure.
Risk Difference and related p-value are estimated by using the SAS GLIMMIX procedure with the following model: criterion = treatment.
p-values for heterogeneity are estimated by using the SAS GLIMMIX procedure with the following model: criterion = treatment subgroup treatment*subgroup.
p-value for heterogeneity of Peto Odds Ratio is estimated by using normal approximation.
PGM=DEVOPS/SAR231893/EFC14153/CSR_RWE/REPORT/PGM/ae_evt_ger_subg_s2_t.sas OUT=REPORT/OUTPUT/ae_pteos_ger_acq7_s2_t_x.rtf (12AUG2021 - 12:04)

Project Code / Study Number / Analysis: SAR231893 / EFC14153 / CSR_RWE

2 Adverse events - Safety type 2 inflammatory asthma phenotype population

2.32 Patients with any TEAE: Eosinophilia

2.32.7 By baseline ACQ-7-IA (<=2, >2)

	Baseline ACQ-7-IA			
	<=2		>2	
Safety type 2 inflammatory asthma phenotype population	**Placebo (N=61)**	**Dupilumab (N=125)**	**Placebo (N=52)**	**Dupilumab (N=109)**
p-value for heterogeneity of Risk Ratio				0.978
Risk Difference (95% CI)	-	3.16 (-1.79 to 8.11)	-	9.17 (NE to NE)
p-value for Risk Difference		0.210		<0.001
p-value for heterogeneity of Risk Difference				<0.001

Odds Ratio and related p-value are estimated by Wald's method using the SAS LOGISTIC procedure.
Peto OR calculation is based on Yusuf S et al. (Prog Cardiovasc Dis. 1985 Mar-Apr;27(5):335-71) and its p-value is derived using a normal approximation.
Risk Ratio and related p-value are estimated by using the SAS FREQ procedure.
Risk Difference and related p-value are estimated by using the SAS GLIMMIX procedure with the following model: criterion = treatment.
p-values for heterogeneity are estimated by using the SAS GLIMMIX procedure with the following model: criterion = treatment subgroup treatment*subgroup.
p-value for heterogeneity of Peto Odds Ratio is estimated by using normal approximation.
PGM=DEVOPS/SAR231893/EFC14153/CSR_RWE/REPORT/PGM/ae_evt_ger_subg_s2_t.sas OUT=REPORT/OUTPUT/ae_pteos_ger_acq7_s2_t_x.rtf (12AUG2021 - 12:04)

Project Code / Study Number / Analysis: SAR231893 / EFC14153 / CSR_RWE

2 Adverse events - Safety type 2 inflammatory asthma phenotype population

2.32 Patients with any TEAE: Eosinophilia

2.32.8 By baseline weight (<=30 kg, >30 kg)

	Baseline weight (kg)			
	<=30		>30	
Safety type 2 inflammatory asthma phenotype population	**Placebo (N=36)**	**Dupilumab (N=74)**	**Placebo (N=77)**	**Dupilumab (N=160)**
Patients with any TEAE: Eosinophilia [n(%)]	0	8 (10.8%)	1 (1.3%)	8 (5.0%)
Odds Ratio (95% CI)	-	NE (NE to NE)	-	4.00 (0.49 to 32.57)
p-value for Odds Ratio		NE		0.195
Peto Odds Ratio (95% CI)	-	4.90 (1.06 to 22.54)	-	2.74 (0.66 to 11.34)
Reversed Peto Odds Ratio (95% CI)	-	0.20 (0.04 to 0.94)	-	0.36 (0.09 to 1.52)
p-value for Peto Odds Ratio		0.041		0.164
p-value for heterogeneity of Peto Odds Ratio				0.586
Risk Ratio (95% CI)	-	NE (NE to NE)	-	3.85 (0.49 to 30.24)
Reversed Risk ratio (95% CI)			-	0.26 (0.03 to 2.04)
p-value for Risk Ratio		NE		0.200

Odds Ratio and related p-value are estimated by Wald's method using the SAS LOGISTIC procedure.
Peto OR calculation is based on Yusuf S et al. (Prog Cardiovasc Dis. 1985 Mar-Apr;27(5):335-71) and its p-value is derived using a normal approximation.
Risk Ratio and related p-value are estimated by using the SAS FREQ procedure.
Risk Difference and related p-value are estimated by using the SAS GLIMMIX procedure with the following model: criterion = treatment.
p-values for heterogeneity are estimated by using the SAS GLIMMIX procedure with the following model: criterion = treatment subgroup treatment*subgroup.
p-value for heterogeneity of Peto Odds Ratio is estimated by using normal approximation.
PGM=DEVOPS/SAR231893/EFC14153/CSR_RWE/REPORT/PGM/ae_evt_ger_subg_s2_t.sas OUT=REPORT/OUTPUT/ae_pteos_ger_wgt_s2_t_x.rtf (12AUG2021 - 12:05)

Project Code / Study Number / Analysis: SAR231893 / EFC14153 / CSR_RWE

2 Adverse events - Safety type 2 inflammatory asthma phenotype population

2.32 Patients with any TEAE: Eosinophilia

2.32.8 By baseline weight (<=30 kg, >30 kg)

	Baseline weight (kg)			
	<=30		>30	
Safety type 2 inflammatory asthma phenotype population	**Placebo (N=36)**	**Dupilumab (N=74)**	**Placebo (N=77)**	**Dupilumab (N=160)**
p-value for heterogeneity of Risk Ratio				0.973
Risk Difference (95% CI)	-	10.81 (NE to NE)	-	3.70 (-0.54 to 7.94)
p-value for Risk Difference		<0.001		0.087
p-value for heterogeneity of Risk Difference				<0.001

Odds Ratio and related p-value are estimated by Wald's method using the SAS LOGISTIC procedure.
Peto OR calculation is based on Yusuf S et al. (Prog Cardiovasc Dis. 1985 Mar-Apr;27(5):335-71) and its p-value is derived using a normal approximation.
Risk Ratio and related p-value are estimated by using the SAS FREQ procedure.
Risk Difference and related p-value are estimated by using the SAS GLIMMIX procedure with the following model: criterion = treatment.
p-values for heterogeneity are estimated by using the SAS GLIMMIX procedure with the following model: criterion = treatment subgroup treatment*subgroup.
p-value for heterogeneity of Peto Odds Ratio is estimated by using normal approximation.
PGM=DEVOPS/SAR231893/EFC14153/CSR_RWE/REPORT/PGM/ae_evt_ger_subg_s2_t.sas OUT=REPORT/OUTPUT/ae_pteos_ger_wgt_s2_t_x.rtf (12AUG2021 - 12:05)

Project Code / Study Number / Analysis: SAR231893 / EFC14153 / CSR_RWE

2 Adverse events - Safety type 2 inflammatory asthma phenotype population

2.32 Patients with any TEAE: Eosinophilia

2.32.9 By atopic medical condition (Yes, No)

	Atopic medical condition			
	Yes		No	
Safety type 2 inflammatory asthma phenotype population	**Placebo (N=102)**	**Dupilumab (N=225)**	**Placebo (N=11)**	**Dupilumab (N=9)**
Patients with any TEAE: Eosinophilia [n(%)]	1 (1.0%)	15 (6.7%)	0	1 (11.1%)
Odds Ratio (95% CI)	-	7.21 (0.94 to 55.34)	-	NE (NE to NE)
p-value for Odds Ratio		0.057		NE
Peto Odds Ratio (95% CI)	-	3.38 (1.14 to 9.98)	-	9.23 (0.18 to 474.33)
Reversed Peto Odds Ratio (95% CI)	-	0.30 (0.10 to 0.88)	-	0.11 (0.00 to 5.56)
p-value for Peto Odds Ratio		0.027		0.269
p-value for heterogeneity of Peto Odds Ratio				0.630
Risk Ratio (95% CI)	-	6.80 (0.91 to 50.78)	-	NE (NE to NE)
Reversed Risk ratio (95% CI)	-	0.15 (0.02 to 1.10)		
p-value for Risk Ratio		0.062		NE

Odds Ratio and related p-value are estimated by Wald's method using the SAS LOGISTIC procedure.
Peto OR calculation is based on Yusuf S et al. (Prog Cardiovasc Dis. 1985 Mar-Apr;27(5):335-71) and its p-value is derived using a normal approximation.
Risk Ratio and related p-value are estimated by using the SAS FREQ procedure.
Risk Difference and related p-value are estimated by using the SAS GLIMMIX procedure with the following model: criterion = treatment.
p-values for heterogeneity are estimated by using the SAS GLIMMIX procedure with the following model: criterion = treatment subgroup treatment*subgroup.
p-value for heterogeneity of Peto Odds Ratio is estimated by using normal approximation.
PGM=DEVOPS/SAR231893/EFC14153/CSR_RWE/REPORT/PGM/ae_evt_ger_subg_s2_t.sas OUT=REPORT/OUTPUT/ae_pteos_ger_amc_s2_t_x.rtf (12AUG2021 - 12:05)

Project Code / Study Number / Analysis: SAR231893 / EFC14153 / CSR_RWE

2 Adverse events - Safety type 2 inflammatory asthma phenotype population

2.32 Patients with any TEAE: Eosinophilia

2.32.9 By atopic medical condition (Yes, No)

	Atopic medical condition			
	Yes		No	
Safety type 2 inflammatory asthma phenotype population	**Placebo (N=102)**	**Dupilumab (N=225)**	**Placebo (N=11)**	**Dupilumab (N=9)**
p-value for heterogeneity of Risk Ratio				0.978
Risk Difference (95% CI)	-	5.69 (1.89 to 9.48)	-	11.11 (NE to NE)
p-value for Risk Difference		0.003		<0.001
p-value for heterogeneity of Risk Difference				<0.001

Odds Ratio and related p-value are estimated by Wald's method using the SAS LOGISTIC procedure.
Peto OR calculation is based on Yusuf S et al. (Prog Cardiovasc Dis. 1985 Mar-Apr;27(5):335-71) and its p-value is derived using a normal approximation.
Risk Ratio and related p-value are estimated by using the SAS FREQ procedure.
Risk Difference and related p-value are estimated by using the SAS GLIMMIX procedure with the following model: criterion = treatment.
p-values for heterogeneity are estimated by using the SAS GLIMMIX procedure with the following model: criterion = treatment subgroup treatment*subgroup.
p-value for heterogeneity of Peto Odds Ratio is estimated by using normal approximation.
PGM=DEVOPS/SAR231893/EFC14153/CSR_RWE/REPORT/PGM/ae_evt_ger_subg_s2_t.sas OUT=REPORT/OUTPUT/ae_pteos_ger_amc_s2_t_x.rtf (12AUG2021 - 12:05)

Project Code / Study Number / Analysis: SAR231893 / EFC14153 / CSR_RWE

2 Adverse events - Safety type 2 inflammatory asthma phenotype population

2.32 Patients with any TEAE: Eosinophilia

2.32.10 By baseline total IgE (<median, >= median)

	Baseline Total IgE (IU/mL)			
	<median		>=median	
Safety type 2 inflammatory asthma phenotype population	**Placebo (N=65)**	**Dupilumab (N=106)**	**Placebo (N=47)**	**Dupilumab (N=124)**
Patients with any TEAE: Eosinophilia [n(%)]	0	4 (3.8%)	1 (2.1%)	10 (8.1%)
Odds Ratio (95% CI)	-	NE (NE to NE)	-	4.04 (0.50 to 32.43)
p-value for Odds Ratio		NE		0.190
Peto Odds Ratio (95% CI)	-	5.17 (0.67 to 39.61)	-	2.67 (0.68 to 10.43)
Reversed Peto Odds Ratio (95% CI)	-	0.19 (0.03 to 1.49)	-	0.37 (0.10 to 1.47)
p-value for Peto Odds Ratio		0.114		0.159
p-value for heterogeneity of Peto Odds Ratio				0.597
Risk Ratio (95% CI)	-	NE (NE to NE)	-	3.79 (0.50 to 28.80)
Reversed Risk ratio (95% CI)			-	0.26 (0.03 to 2.00)
p-value for Risk Ratio		NE		0.198

Odds Ratio and related p-value are estimated by Wald's method using the SAS LOGISTIC procedure.
Peto OR calculation is based on Yusuf S et al. (Prog Cardiovasc Dis. 1985 Mar-Apr;27(5):335-71) and its p-value is derived using a normal approximation.
Risk Ratio and related p-value are estimated by using the SAS FREQ procedure.
Risk Difference and related p-value are estimated by using the SAS GLIMMIX procedure with the following model: criterion = treatment.
p-values for heterogeneity are estimated by using the SAS GLIMMIX procedure with the following model: criterion = treatment subgroup treatment*subgroup.
p-value for heterogeneity of Peto Odds Ratio is estimated by using normal approximation.
PGM=DEVOPS/SAR231893/EFC14153/CSR_RWE/REPORT/PGM/ae_evt_ger_subg_s2_t.sas OUT=REPORT/OUTPUT/ae_pteos_ger_igem_s2_t_x.rtf (12AUG2021 - 12:05)

Project Code / Study Number / Analysis: SAR231893 / EFC14153 / CSR_RWE

2 Adverse events - Safety type 2 inflammatory asthma phenotype population

2.32 Patients with any TEAE: Eosinophilia

2.32.10 By baseline total IgE (<median, >= median)

	Baseline Total IgE (IU/mL)			
	<median		>=median	
Safety type 2 inflammatory asthma phenotype population	**Placebo (N=65)**	**Dupilumab (N=106)**	**Placebo (N=47)**	**Dupilumab (N=124)**
p-value for heterogeneity of Risk Ratio				0.978
Risk Difference (95% CI)	-	3.77 (NE to NE)	-	5.94 (-0.43 to 12.31)
p-value for Risk Difference		<0.001		0.068
p-value for heterogeneity of Risk Difference				<0.001

Odds Ratio and related p-value are estimated by Wald's method using the SAS LOGISTIC procedure.
Peto OR calculation is based on Yusuf S et al. (Prog Cardiovasc Dis. 1985 Mar-Apr;27(5):335-71) and its p-value is derived using a normal approximation.
Risk Ratio and related p-value are estimated by using the SAS FREQ procedure.
Risk Difference and related p-value are estimated by using the SAS GLIMMIX procedure with the following model: criterion = treatment.
p-values for heterogeneity are estimated by using the SAS GLIMMIX procedure with the following model: criterion = treatment subgroup treatment*subgroup.
p-value for heterogeneity of Peto Odds Ratio is estimated by using normal approximation.
PGM=DEVOPS/SAR231893/EFC14153/CSR_RWE/REPORT/PGM/ae_evt_ger_subg_s2_t.sas OUT=REPORT/OUTPUT/ae_pteos_ger_igem_s2_t_x.rtf (12AUG2021 - 12:05)

Project Code / Study Number / Analysis: SAR231893 / EFC14153 / CSR_RWE

2 Adverse events - Safety type 2 inflammatory asthma phenotype population

2.32 Patients with any TEAE: Eosinophilia

2.32.11 By baseline total IgE (<100 IU/ml, >= 100 IU/ml)

	Baseline Total IgE (IU/mL)			
	< 100		>= 100	
Safety type 2 inflammatory asthma phenotype population	**Placebo (N=22)**	**Dupilumab (N=29)**	**Placebo (N=90)**	**Dupilumab (N=201)**
Patients with any TEAE: Eosinophilia [n(%)]	0	0	1 (1.1%)	14 (7.0%)
Odds Ratio (95% CI)	-	NE (NE to NE)	-	6.66 (0.86 to 51.45)
p-value for Odds Ratio		NE		0.069
Peto Odds Ratio (95% CI)	-	NE (NE to NE)	-	3.30 (1.07 to 10.13)
Reversed Peto Odds Ratio (95% CI)			-	0.30 (0.10 to 0.93)
p-value for Peto Odds Ratio		NE		0.037
p-value for heterogeneity of Peto Odds Ratio				NE
Risk Ratio (95% CI)	-	NE (NE to NE)	-	6.27 (0.84 to 46.95)
Reversed Risk ratio (95% CI)			-	0.16 (0.02 to 1.19)
p-value for Risk Ratio		NE		0.074

Odds Ratio and related p-value are estimated by Wald's method using the SAS LOGISTIC procedure.
Peto OR calculation is based on Yusuf S et al. (Prog Cardiovasc Dis. 1985 Mar-Apr;27(5):335-71) and its p-value is derived using a normal approximation.
Risk Ratio and related p-value are estimated by using the SAS FREQ procedure.
Risk Difference and related p-value are estimated by using the SAS GLIMMIX procedure with the following model: criterion = treatment.
p-values for heterogeneity are estimated by using the SAS GLIMMIX procedure with the following model: criterion = treatment subgroup treatment*subgroup.
p-value for heterogeneity of Peto Odds Ratio is estimated by using normal approximation.
PGM=DEVOPS/SAR231893/EFC14153/CSR_RWE/REPORT/PGM/ae_evt_ger_subg_s2_t.sas OUT=REPORT/OUTPUT/ae_pteos_ger_ige_s2_t_x.rtf (12AUG2021 - 12:05)

Project Code / Study Number / Analysis: SAR231893 / EFC14153 / CSR_RWE

2 Adverse events - Safety type 2 inflammatory asthma phenotype population

2.32 Patients with any TEAE: Eosinophilia

2.32.11 By baseline total IgE (<100 IU/ml, >= 100 IU/ml)

	Baseline Total IgE (IU/mL)			
	< 100		>= 100	
Safety type 2 inflammatory asthma phenotype population	**Placebo (N=22)**	**Dupilumab (N=29)**	**Placebo (N=90)**	**Dupilumab (N=201)**
p-value for heterogeneity of Risk Ratio				0.998
Risk Difference (95% CI)	-	0.00 (NE to NE)	-	5.85 (1.70 to 10.00)
p-value for Risk Difference		NE		0.006
p-value for heterogeneity of Risk Difference				<0.001

Odds Ratio and related p-value are estimated by Wald's method using the SAS LOGISTIC procedure.
Peto OR calculation is based on Yusuf S et al. (Prog Cardiovasc Dis. 1985 Mar-Apr;27(5):335-71) and its p-value is derived using a normal approximation.
Risk Ratio and related p-value are estimated by using the SAS FREQ procedure.
Risk Difference and related p-value are estimated by using the SAS GLIMMIX procedure with the following model: criterion = treatment.
p-values for heterogeneity are estimated by using the SAS GLIMMIX procedure with the following model: criterion = treatment subgroup treatment*subgroup.
p-value for heterogeneity of Peto Odds Ratio is estimated by using normal approximation.
PGM=DEVOPS/SAR231893/EFC14153/CSR_RWE/REPORT/PGM/ae_evt_ger_subg_s2_t.sas OUT=REPORT/OUTPUT/ae_pteos_ger_ige_s2_t_x.rtf (12AUG2021 - 12:05)

Project Code / Study Number / Analysis: SAR231893 / EFC14153 / CSR_RWE

2 Adverse events - Safety type 2 inflammatory asthma phenotype population

2.32 Patients with any TEAE: Eosinophilia

2.32.12 By age at onset of asthma (0-2, 3-5, >=6 years)

	Age of onset of asthma (years)					
	0-2		3-5		>= 6	
Safety type 2 inflammatory asthma phenotype population	**Placebo (N=40)**	**Dupilumab (N=104)**	**Placebo (N=38)**	**Dupilumab (N=85)**	**Placebo (N=35)**	**Dupilumab (N=45)**
Patients with any TEAE: Eosinophilia [n(%)]	1 (2.5%)	6 (5.8%)	0	5 (5.9%)	0	5 (11.1%)
Odds Ratio (95% CI)	-	2.39 (0.28 to 20.48)	-	NE (NE to NE)	-	NE (NE to NE)
p-value for Odds Ratio		0.427		NE		NE
Peto Odds Ratio (95% CI)	-	2.02 (0.37 to 10.93)	-	4.46 (0.65 to 30.72)	-	6.51 (1.06 to 39.89)
Reversed Peto Odds Ratio (95% CI)	-	0.50 (0.09 to 2.70)	-	0.22 (0.03 to 1.54)	-	0.15 (0.03 to 0.94)
p-value for Peto Odds Ratio		0.416		0.128		0.043
p-value for heterogeneity of Peto Odds Ratio:						
0-2, 3-5						0.544
0-2, >= 6						0.355
3-5, >= 6						0.781
overall						0.637

Odds Ratio and related p-value are estimated by Wald's method using the SAS LOGISTIC procedure.
Peto OR calculation is based on Yusuf S et al. (Prog Cardiovasc Dis. 1985 Mar-Apr;27(5):335-71) and its p-value is derived using a normal approximation.
Risk Ratio and related p-value are estimated by using the SAS FREQ procedure.
Risk Difference and related p-value are estimated by using the SAS GLIMMIX procedure with the following model: criterion = treatment.
p-values for heterogeneity are estimated by using the SAS GLIMMIX procedure with the following model: criterion = treatment subgroup treatment*subgroup.
p-value for heterogeneity of Peto Odds Ratio is estimated by using normal approximation.
PGM=DEVOPS/SAR231893/EFC14153/CSR_RWE/REPORT/PGM/ae_evt_ger_subg_s2_t.sas OUT=REPORT/OUTPUT/ae_pteos_ger_onsa_s2_t_x.rtf (12AUG2021 - 12:06)

Project Code / Study Number / Analysis: SAR231893 / EFC14153 / CSR_RWE

2 Adverse events - Safety type 2 inflammatory asthma phenotype population

2.32 Patients with any TEAE: Eosinophilia

2.32.12 By age at onset of asthma (0-2, 3-5, >=6 years)

	Age of onset of asthma (years)					
	0-2		3-5		>= 6	
Safety type 2 inflammatory asthma phenotype population	**Placebo (N=40)**	**Dupilumab (N=104)**	**Placebo (N=38)**	**Dupilumab (N=85)**	**Placebo (N=35)**	**Dupilumab (N=45)**
Risk Ratio (95% CI)	-	2.31 (0.29 to 18.57)	-	NE (NE to NE)	-	NE (NE to NE)
Reversed Risk ratio (95% CI)	-	0.43 (0.05 to 3.49)				
p-value for Risk Ratio		0.432		NE		NE
p-value for heterogeneity of Risk Ratio:						
0-2, 3-5						0.982
0-2, >= 6						0.981
3-5, >= 6						0.999
overall						0.999
Risk Difference (95% CI)	-	3.27 (-3.38 to 9.92)	-	5.88 (NE to NE)	-	11.11 (NE to NE)
p-value for Risk Difference		0.333		<0.001		<0.001
p-value for heterogeneity of Risk Difference:						

Odds Ratio and related p-value are estimated by Wald's method using the SAS LOGISTIC procedure.
Peto OR calculation is based on Yusuf S et al. (Prog Cardiovasc Dis. 1985 Mar-Apr;27(5):335-71) and its p-value is derived using a normal approximation.
Risk Ratio and related p-value are estimated by using the SAS FREQ procedure.
Risk Difference and related p-value are estimated by using the SAS GLIMMIX procedure with the following model: criterion = treatment.
p-values for heterogeneity are estimated by using the SAS GLIMMIX procedure with the following model: criterion = treatment subgroup treatment*subgroup.
p-value for heterogeneity of Peto Odds Ratio is estimated by using normal approximation.
PGM=DEVOPS/SAR231893/EFC14153/CSR_RWE/REPORT/PGM/ae_evt_ger_subg_s2_t.sas OUT=REPORT/OUTPUT/ae_pteos_ger_onsa_s2_t_x.rtf (12AUG2021 - 12:06)

Project Code / Study Number / Analysis: SAR231893 / EFC14153 / CSR_RWE

2 Adverse events - Safety type 2 inflammatory asthma phenotype population

2.32 Patients with any TEAE: Eosinophilia

2.32.12 By age at onset of asthma (0-2, 3-5, >=6 years)

	Age of onset of asthma (years)					
	0-2		3-5		>= 6	
Safety type 2 inflammatory asthma phenotype population	**Placebo (N=40)**	**Dupilumab (N=104)**	**Placebo (N=38)**	**Dupilumab (N=85)**	**Placebo (N=35)**	**Dupilumab (N=45)**
0-2, 3-5						<0.001
0-2, >= 6						<0.001
3-5, >= 6						<0.001
overall						<0.001

Odds Ratio and related p-value are estimated by Wald's method using the SAS LOGISTIC procedure.
Peto OR calculation is based on Yusuf S et al. (Prog Cardiovasc Dis. 1985 Mar-Apr;27(5):335-71) and its p-value is derived using a normal approximation.
Risk Ratio and related p-value are estimated by using the SAS FREQ procedure.
Risk Difference and related p-value are estimated by using the SAS GLIMMIX procedure with the following model: criterion = treatment.
p-values for heterogeneity are estimated by using the SAS GLIMMIX procedure with the following model: criterion = treatment subgroup treatment*subgroup.
p-value for heterogeneity of Peto Odds Ratio is estimated by using normal approximation.
PGM=DEVOPS/SAR231893/EFC14153/CSR_RWE/REPORT/PGM/ae_evt_ger_subg_s2_t.sas OUT=REPORT/OUTPUT/ae_pteos_ger_onsa_s2_t_x.rtf (12AUG2021 - 12:06)

Project Code / Study Number / Analysis: SAR231893 / EFC14153 / CSR_RWE

2 Adverse events - Safety type 2 inflammatory asthma phenotype population

2.32 Patients with any TEAE: Eosinophilia

2.32.13 By number of severe asthma exacerbation prior to the study (<=1, 2, >2)

	Number of severe asthma exacerbation prior to the study					
	<=1		2		>2	
Safety type 2 inflammatory asthma phenotype population	**Placebo (N=46)**	**Dupilumab (N=85)**	**Placebo (N=32)**	**Dupilumab (N=75)**	**Placebo (N=35)**	**Dupilumab (N=74)**
Patients with any TEAE: Eosinophilia [n(%)]	0	4 (4.7%)	0	7 (9.3%)	1 (2.9%)	5 (6.8%)
Odds Ratio (95% CI)	-	NE (NE to NE)	-	NE (NE to NE)	-	2.46 (0.28 to 21.92)
p-value for Odds Ratio		NE		NE		0.419
Peto Odds Ratio (95% CI)	-	4.84 (0.61 to 38.66)	-	4.54 (0.86 to 24.00)	-	2.10 (0.36 to 12.15)
Reversed Peto Odds Ratio (95% CI)	-	0.21 (0.03 to 1.64)	-	0.22 (0.04 to 1.16)	-	0.48 (0.08 to 2.78)
p-value for Peto Odds Ratio		0.137		0.075		0.407
p-value for heterogeneity of Peto Odds Ratio:						
<=1, 2						0.962
<=1, >2						0.547
2, >2						0.533
overall						0.774

Odds Ratio and related p-value are estimated by Wald's method using the SAS LOGISTIC procedure.
Peto OR calculation is based on Yusuf S et al. (Prog Cardiovasc Dis. 1985 Mar-Apr;27(5):335-71) and its p-value is derived using a normal approximation.
Risk Ratio and related p-value are estimated by using the SAS FREQ procedure.
Risk Difference and related p-value are estimated by using the SAS GLIMMIX procedure with the following model: criterion = treatment.
p-values for heterogeneity are estimated by using the SAS GLIMMIX procedure with the following model: criterion = treatment subgroup treatment*subgroup.
p-value for heterogeneity of Peto Odds Ratio is estimated by using normal approximation.
PGM=DEVOPS/SAR231893/EFC14153/CSR_RWE/REPORT/PGM/ae_evt_ger_subg_s2_t.sas OUT=REPORT/OUTPUT/ae_pteos_ger_exa_s2_t_x.rtf (12AUG2021 - 12:06)

Project Code / Study Number / Analysis: SAR231893 / EFC14153 / CSR_RWE

2 Adverse events - Safety type 2 inflammatory asthma phenotype population

2.32 Patients with any TEAE: Eosinophilia

2.32.13 By number of severe asthma exacerbation prior to the study (<=1, 2, >2)

	Number of severe asthma exacerbation prior to the study					
	<=1		2		>2	
Safety type 2 inflammatory asthma phenotype population	**Placebo (N=46)**	**Dupilumab (N=85)**	**Placebo (N=32)**	**Dupilumab (N=75)**	**Placebo (N=35)**	**Dupilumab (N=74)**
Risk Ratio (95% CI)	-	NE (NE to NE)	-	NE (NE to NE)	-	2.36 (0.29 to 19.49)
Reversed Risk ratio (95% CI)					-	0.42 (0.05 to 3.48)
p-value for Risk Ratio		NE		NE		0.424
p-value for heterogeneity of Risk Ratio:						
<=1, 2						0.999
<=1, >2						0.980
2, >2						0.983
overall						0.999
Risk Difference (95% CI)	-	4.71 (NE to NE)	-	9.33 (NE to NE)	-	3.90 (-4.14 to 11.94)
p-value for Risk Difference		<0.001		<0.001		0.338
p-value for heterogeneity of Risk Difference:						
<=1, 2						<0.001
<=1, >2						<0.001

Odds Ratio and related p-value are estimated by Wald's method using the SAS LOGISTIC procedure.
Peto OR calculation is based on Yusuf S et al. (Prog Cardiovasc Dis. 1985 Mar-Apr;27(5):335-71) and its p-value is derived using a normal approximation.
Risk Ratio and related p-value are estimated by using the SAS FREQ procedure.
Risk Difference and related p-value are estimated by using the SAS GLIMMIX procedure with the following model: criterion = treatment.
p-values for heterogeneity are estimated by using the SAS GLIMMIX procedure with the following model: criterion = treatment subgroup treatment*subgroup.
p-value for heterogeneity of Peto Odds Ratio is estimated by using normal approximation.
PGM=DEVOPS/SAR231893/EFC14153/CSR_RWE/REPORT/PGM/ae_evt_ger_subg_s2_t.sas OUT=REPORT/OUTPUT/ae_pteos_ger_exa_s2_t_x.rtf (12AUG2021 - 12:06)

Project Code / Study Number / Analysis: SAR231893 / EFC14153 / CSR_RWE

2 Adverse events - Safety type 2 inflammatory asthma phenotype population

2.32 Patients with any TEAE: Eosinophilia

2.32.13 By number of severe asthma exacerbation prior to the study (<=1, 2, >2)

	Number of severe asthma exacerbation prior to the study					
	<=1		2		>2	
Safety type 2 inflammatory asthma phenotype population	**Placebo (N=46)**	**Dupilumab (N=85)**	**Placebo (N=32)**	**Dupilumab (N=75)**	**Placebo (N=35)**	**Dupilumab (N=74)**
2, >2						<0.001
overall						<0.001

Odds Ratio and related p-value are estimated by Wald's method using the SAS LOGISTIC procedure.
Peto OR calculation is based on Yusuf S et al. (Prog Cardiovasc Dis. 1985 Mar-Apr;27(5):335-71) and its p-value is derived using a normal approximation.
Risk Ratio and related p-value are estimated by using the SAS FREQ procedure.
Risk Difference and related p-value are estimated by using the SAS GLIMMIX procedure with the following model: criterion = treatment.
p-values for heterogeneity are estimated by using the SAS GLIMMIX procedure with the following model: criterion = treatment subgroup treatment*subgroup.
p-value for heterogeneity of Peto Odds Ratio is estimated by using normal approximation.
PGM=DEVOPS/SAR231893/EFC14153/CSR_RWE/REPORT/PGM/ae_evt_ger_subg_s2_t.sas OUT=REPORT/OUTPUT/ae_pteos_ger_exa_s2_t_x.rtf (12AUG2021 - 12:06)

Project Code / Study Number / Analysis: SAR231893 / EFC14153 / CSR_RWE

2 Adverse events - Safety type 2 inflammatory asthma phenotype population

2.36 Patients with any TEAE: Injection site nodule

Safety type 2 inflammatory asthma phenotype population	Placebo (N=113)	Dupilumab (N=234)
Patients with any TEAE: Injection site nodule [n(%)]	1 (0.9%)	15 (6.4%)
Odds Ratio (95% CI)	-	7.67 (1.00 to 58.76)
p-value for Odds Ratio		0.050
Peto Odds Ratio (95% CI)	-	3.50 (1.20 to 10.19)
Reversed Peto Odds Ratio (95% CI)	-	0.29 (0.10 to 0.83)
p-value for Peto Odds Ratio		0.022
Risk Ratio (95% CI)	-	7.24 (0.97 to 54.16)
Reversed Risk Ratio (95% CI)	-	0.14 (0.02 to 1.03)
p-value for Risk Ratio		0.054
Risk Difference (95% CI)	-	5.53 (1.93 to 9.12)
p-value for Risk Difference		0.003

Odds Ratio and related p-value are estimated by Wald's method using the SAS LOGISTIC procedure.
Peto OR calculation is based on Yusuf S et al. (Prog Cardiovasc Dis. 1985 Mar-Apr;27(5):335-71) and its p-value is derived using a normal approximation.
Risk Ratio and related p-value are estimated by using the SAS FREQ procedure.
Risk Difference and related p-value are estimated by using the SAS GLIMMIX procedure with the following model: criterion = treatment.
p-value for heterogeneity of Peto Odds Ratio is estimated by using normal approximation.
PGM=DEVOPS/SAR231893/EFC14153/CSR_RWE/REPORT/PGM/ae_evt_ger_s2_t.sas OUT=REPORT/OUTPUT/ae_ptinjn_ger_s2_t_x.rtf (12AUG2021 - 11:36)

Project Code / Study Number / Analysis: SAR231893 / EFC14153 / CSR_RWE

2 Adverse events - Safety type 2 inflammatory asthma phenotype population

2.36 Patients with any TEAE: Injection site nodule

2.36.1 By gender (Male, Female)

	Gender			
	Male		Female	
Safety type 2 inflammatory asthma phenotype population	**Placebo (N=77)**	**Dupilumab (N=153)**	**Placebo (N=36)**	**Dupilumab (N=81)**
Patients with any TEAE: Injection site nodule [n(%)]	1 (1.3%)	10 (6.5%)	0	5 (6.2%)
Odds Ratio (95% CI)	-	5.31 (0.67 to 42.30)	-	NE (NE to NE)
p-value for Odds Ratio		0.114		NE
Peto Odds Ratio (95% CI)	-	3.14 (0.87 to 11.31)	-	4.46 (0.65 to 30.84)
Reversed Peto Odds Ratio (95% CI)	-	0.32 (0.09 to 1.15)	-	0.22 (0.03 to 1.54)
p-value for Peto Odds Ratio		0.080		0.129
p-value for heterogeneity of Peto Odds Ratio				0.767
Risk Ratio (95% CI)	-	5.03 (0.66 to 38.60)	-	NE (NE to NE)
Reversed Risk ratio (95% CI)	-	0.20 (0.03 to 1.52)		
p-value for Risk Ratio		0.120		NE

Odds Ratio and related p-value are estimated by Wald's method using the SAS LOGISTIC procedure.
Peto OR calculation is based on Yusuf S et al. (Prog Cardiovasc Dis. 1985 Mar-Apr;27(5):335-71) and its p-value is derived using a normal approximation.
Risk Ratio and related p-value are estimated by using the SAS FREQ procedure.
Risk Difference and related p-value are estimated by using the SAS GLIMMIX procedure with the following model: criterion = treatment.
p-values for heterogeneity are estimated by using the SAS GLIMMIX procedure with the following model: criterion = treatment subgroup treatment*subgroup.
p-value for heterogeneity of Peto Odds Ratio is estimated by using normal approximation.
PGM=DEVOPS/SAR231893/EFC14153/CSR_RWE/REPORT/PGM/ae_evt_ger_subg_s2_t.sas OUT=REPORT/OUTPUT/ae_ptinjn_ger_sex_s2_t_x.rtf (12AUG2021 - 12:06)

Project Code / Study Number / Analysis: SAR231893 / EFC14153 / CSR_RWE

2 Adverse events - Safety type 2 inflammatory asthma phenotype population

2.36 Patients with any TEAE: Injection site nodule

2.36.1 By gender (Male, Female)

	Gender			
	Male		Female	
Safety type 2 inflammatory asthma phenotype population	**Placebo (N=77)**	**Dupilumab (N=153)**	**Placebo (N=36)**	**Dupilumab (N=81)**
p-value for heterogeneity of Risk Ratio				0.975
Risk Difference (95% CI)	-	5.24 (0.55 to 9.92)	-	6.17 (NE to NE)
p-value for Risk Difference		0.029		<0.001
p-value for heterogeneity of Risk Difference				<0.001

Odds Ratio and related p-value are estimated by Wald's method using the SAS LOGISTIC procedure.
Peto OR calculation is based on Yusuf S et al. (Prog Cardiovasc Dis. 1985 Mar-Apr;27(5):335-71) and its p-value is derived using a normal approximation.
Risk Ratio and related p-value are estimated by using the SAS FREQ procedure.
Risk Difference and related p-value are estimated by using the SAS GLIMMIX procedure with the following model: criterion = treatment.
p-values for heterogeneity are estimated by using the SAS GLIMMIX procedure with the following model: criterion = treatment subgroup treatment*subgroup.
p-value for heterogeneity of Peto Odds Ratio is estimated by using normal approximation.
PGM=DEVOPS/SAR231893/EFC14153/CSR_RWE/REPORT/PGM/ae_evt_ger_subg_s2_t.sas OUT=REPORT/OUTPUT/ae_ptinjn_ger_sex_s2_t_x.rtf (12AUG2021 - 12:06)

Project Code / Study Number / Analysis: SAR231893 / EFC14153 / CSR_RWE

2 Adverse events - Safety type 2 inflammatory asthma phenotype population

2.36 Patients with any TEAE: Injection site nodule

2.36.2 By region (Latin America, East Europe, Western Countries)

	Region					
	Latin America		East Europe		Western countries	
Safety type 2 inflammatory asthma phenotype population	**Placebo (N=51)**	**Dupilumab (N=105)**	**Placebo (N=43)**	**Dupilumab (N=78)**	**Placebo (N=19)**	**Dupilumab (N=51)**
Patients with any TEAE: Injection site nodule [n(%)]	0	0	1 (2.3%)	8 (10.3%)	0	7 (13.7%)
Odds Ratio (95% CI)	-	NE (NE to NE)	-	4.80 (0.58 to 39.74)	-	NE (NE to NE)
p-value for Odds Ratio		NE		0.146		NE
Peto Odds Ratio (95% CI)	-	NE (NE to NE)	-	3.13 (0.76 to 12.88)	-	4.50 (0.79 to 25.70)
Reversed Peto Odds Ratio (95% CI)			-	0.32 (0.08 to 1.32)	-	0.22 (0.04 to 1.27)
p-value for Peto Odds Ratio		NE		0.113		0.091
p-value for heterogeneity of Peto Odds Ratio:						
Latin America, East Europe						NE
Latin America, Western countries						NE
East Europe, Western countries						0.753

Odds Ratio and related p-value are estimated by Wald's method using the SAS LOGISTIC procedure.
Peto OR calculation is based on Yusuf S et al. (Prog Cardiovasc Dis. 1985 Mar-Apr;27(5):335-71) and its p-value is derived using a normal approximation.
Risk Ratio and related p-value are estimated by using the SAS FREQ procedure.
Risk Difference and related p-value are estimated by using the SAS GLIMMIX procedure with the following model: criterion = treatment.
p-values for heterogeneity are estimated by using the SAS GLIMMIX procedure with the following model: criterion = treatment subgroup treatment*subgroup.
p-value for heterogeneity of Peto Odds Ratio is estimated by using normal approximation.
PGM=DEVOPS/SAR231893/EFC14153/CSR_RWE/REPORT/PGM/ae_evt_ger_subg_s2_t.sas OUT=REPORT/OUTPUT/ae_ptinjn_ger_cty_s2_t_x.rtf (12AUG2021 - 12:06)

Project Code / Study Number / Analysis: SAR231893 / EFC14153 / CSR_RWE

2 Adverse events - Safety type 2 inflammatory asthma phenotype population

2.36 Patients with any TEAE: Injection site nodule

2.36.2 By region (Latin America, East Europe, Western Countries)

	Region					
	Latin America		East Europe		Western countries	
Safety type 2 inflammatory asthma phenotype population	**Placebo (N=51)**	**Dupilumab (N=105)**	**Placebo (N=43)**	**Dupilumab (N=78)**	**Placebo (N=19)**	**Dupilumab (N=51)**
overall						NE
Risk Ratio (95% CI)	-	NE (NE to NE)	-	4.41 (0.57 to 34.10)	-	NE (NE to NE)
Reversed Risk ratio (95% CI)			-	0.23 (0.03 to 1.75)		
p-value for Risk Ratio		NE		0.155		NE
p-value for heterogeneity of Risk Ratio:						
Latin America, East Europe						0.999
Latin America, Western countries						0.992
East Europe, Western countries						0.991
overall						1.000
Risk Difference (95% CI)	-	0.00 (NE to NE)	-	7.93 (-0.25 to 16.11)	-	13.73 (NE to NE)
p-value for Risk Difference		NE		0.057		<0.001

Odds Ratio and related p-value are estimated by Wald's method using the SAS LOGISTIC procedure.
Peto OR calculation is based on Yusuf S et al. (Prog Cardiovasc Dis. 1985 Mar-Apr;27(5):335-71) and its p-value is derived using a normal approximation.
Risk Ratio and related p-value are estimated by using the SAS FREQ procedure.
Risk Difference and related p-value are estimated by using the SAS GLIMMIX procedure with the following model: criterion = treatment.
p-values for heterogeneity are estimated by using the SAS GLIMMIX procedure with the following model: criterion = treatment subgroup treatment*subgroup.
p-value for heterogeneity of Peto Odds Ratio is estimated by using normal approximation.
PGM=DEVOPS/SAR231893/EFC14153/CSR_RWE/REPORT/PGM/ae_evt_ger_subg_s2_t.sas OUT=REPORT/OUTPUT/ae_ptinjn_ger_cty_s2_t_x.rtf (12AUG2021 - 12:06)

Project Code / Study Number / Analysis: SAR231893 / EFC14153 / CSR_RWE

2 Adverse events - Safety type 2 inflammatory asthma phenotype population

2.36 Patients with any TEAE: Injection site nodule

2.36.2 By region (Latin America, East Europe, Western Countries)

	Region					
	Latin America		East Europe		Western countries	
Safety type 2 inflammatory asthma phenotype population	**Placebo (N=51)**	**Dupilumab (N=105)**	**Placebo (N=43)**	**Dupilumab (N=78)**	**Placebo (N=19)**	**Dupilumab (N=51)**
p-value for heterogeneity of Risk Difference:						
Latin America, East Europe						<0.001
Latin America, Western countries						<0.001
East Europe, Western countries						<0.001
overall						<0.001

Odds Ratio and related p-value are estimated by Wald's method using the SAS LOGISTIC procedure.
Peto OR calculation is based on Yusuf S et al. (Prog Cardiovasc Dis. 1985 Mar-Apr;27(5):335-71) and its p-value is derived using a normal approximation.
Risk Ratio and related p-value are estimated by using the SAS FREQ procedure.
Risk Difference and related p-value are estimated by using the SAS GLIMMIX procedure with the following model: criterion = treatment.
p-values for heterogeneity are estimated by using the SAS GLIMMIX procedure with the following model: criterion = treatment subgroup treatment*subgroup.
p-value for heterogeneity of Peto Odds Ratio is estimated by using normal approximation.
PGM=DEVOPS/SAR231893/EFC14153/CSR_RWE/REPORT/PGM/ae_evt_ger_subg_s2_t.sas OUT=REPORT/OUTPUT/ae_ptinjn_ger_cty_s2_t_x.rtf (12AUG2021 - 12:06)

Project Code / Study Number / Analysis: SAR231893 / EFC14153 / CSR_RWE

2 Adverse events - Safety type 2 inflammatory asthma phenotype population

2.36 Patients with any TEAE: Injection site nodule

2.36.3 By race (Caucasian/white, Black/of African descent, Other)

	Race					
	Caucasian/White		Black/of African descent		Other	
Safety type 2 inflammatory asthma phenotype population	**Placebo (N=101)**	**Dupilumab (N=207)**	**Placebo (N=5)**	**Dupilumab (N=9)**	**Placebo (N=7)**	**Dupilumab (N=18)**
Patients with any TEAE: Injection site nodule [n(%)]	1 (1.0%)	15 (7.2%)	0	0	0	0
Odds Ratio (95% CI)	-	7.81 (1.02 to 59.94)	-	NE (NE to NE)	-	NE (NE to NE)
p-value for Odds Ratio		0.048		NE		NE
Peto Odds Ratio (95% CI)	-	3.55 (1.22 to 10.34)	-	NE (NE to NE)	-	NE (NE to NE)
Reversed Peto Odds Ratio (95% CI)	-	0.28 (0.10 to 0.82)				
p-value for Peto Odds Ratio		0.020		NE		NE
p-value for heterogeneity of Peto Odds Ratio:						
Caucasian/White, Black/of African descent						NE
Caucasian/White, Other						NE
Black/of African descent, Other						NE

Odds Ratio and related p-value are estimated by Wald's method using the SAS LOGISTIC procedure.
Peto OR calculation is based on Yusuf S et al. (Prog Cardiovasc Dis. 1985 Mar-Apr;27(5):335-71) and its p-value is derived using a normal approximation.
Risk Ratio and related p-value are estimated by using the SAS FREQ procedure.
Risk Difference and related p-value are estimated by using the SAS GLIMMIX procedure with the following model: criterion = treatment.
p-values for heterogeneity are estimated by using the SAS GLIMMIX procedure with the following model: criterion = treatment subgroup treatment*subgroup.
p-value for heterogeneity of Peto Odds Ratio is estimated by using normal approximation.
PGM=DEVOPS/SAR231893/EFC14153/CSR_RWE/REPORT/PGM/ae_evt_ger_subg_s2_t.sas OUT=REPORT/OUTPUT/ae_ptinjn_ger_race_s2_t_x.rtf (12AUG2021 - 12:07)

Project Code / Study Number / Analysis: SAR231893 / EFC14153 / CSR_RWE

2 Adverse events - Safety type 2 inflammatory asthma phenotype population

2.36 Patients with any TEAE: Injection site nodule

2.36.3 By race (Caucasian/white, Black/of African descent, Other)

	Race					
	Caucasian/White		Black/of African descent		Other	
Safety type 2 inflammatory asthma phenotype population	**Placebo (N=101)**	**Dupilumab (N=207)**	**Placebo (N=5)**	**Dupilumab (N=9)**	**Placebo (N=7)**	**Dupilumab (N=18)**
overall						NE
Risk Ratio (95% CI)	-	7.32 (0.98 to 54.63)	-	NE (NE to NE)	-	NE (NE to NE)
Reversed Risk ratio (95% CI)	-	0.14 (0.02 to 1.02)				
p-value for Risk Ratio		0.052		NE		NE
p-value for heterogeneity of Risk Ratio:						
Caucasian/White, Black/of African descent						0.999
Caucasian/White, Other						0.998
Black/of African descent, Other						1.000
overall						1.000
Risk Difference (95% CI)	-	6.26 (2.22 to 10.30)	-	0.00 (NE to NE)	-	0.00 (NE to NE)
p-value for Risk Difference		0.003		NE		NE

Odds Ratio and related p-value are estimated by Wald's method using the SAS LOGISTIC procedure.
Peto OR calculation is based on Yusuf S et al. (Prog Cardiovasc Dis. 1985 Mar-Apr;27(5):335-71) and its p-value is derived using a normal approximation.
Risk Ratio and related p-value are estimated by using the SAS FREQ procedure.
Risk Difference and related p-value are estimated by using the SAS GLIMMIX procedure with the following model: criterion = treatment.
p-values for heterogeneity are estimated by using the SAS GLIMMIX procedure with the following model: criterion = treatment subgroup treatment*subgroup.
p-value for heterogeneity of Peto Odds Ratio is estimated by using normal approximation.
PGM=DEVOPS/SAR231893/EFC14153/CSR_RWE/REPORT/PGM/ae_evt_ger_subg_s2_t.sas OUT=REPORT/OUTPUT/ae_ptinjn_ger_race_s2_t_x.rtf (12AUG2021 - 12:07)

Project Code / Study Number / Analysis: SAR231893 / EFC14153 / CSR_RWE

2 Adverse events - Safety type 2 inflammatory asthma phenotype population

2.36 Patients with any TEAE: Injection site nodule

2.36.3 By race (Caucasian/white, Black/of African descent, Other)

	Race					
	Caucasian/White		Black/of African descent		Other	
Safety type 2 inflammatory asthma phenotype population	**Placebo (N=101)**	**Dupilumab (N=207)**	**Placebo (N=5)**	**Dupilumab (N=9)**	**Placebo (N=7)**	**Dupilumab (N=18)**
p-value for heterogeneity of Risk Difference:						
Caucasian/White, Black/of African descent						<0.001
Caucasian/White, Other						<0.001
Black/of African descent, Other						NE
overall						NE

Odds Ratio and related p-value are estimated by Wald's method using the SAS LOGISTIC procedure.
Peto OR calculation is based on Yusuf S et al. (Prog Cardiovasc Dis. 1985 Mar-Apr;27(5):335-71) and its p-value is derived using a normal approximation.
Risk Ratio and related p-value are estimated by using the SAS FREQ procedure.
Risk Difference and related p-value are estimated by using the SAS GLIMMIX procedure with the following model: criterion = treatment.
p-values for heterogeneity are estimated by using the SAS GLIMMIX procedure with the following model: criterion = treatment subgroup treatment*subgroup.
p-value for heterogeneity of Peto Odds Ratio is estimated by using normal approximation.
PGM=DEVOPS/SAR231893/EFC14153/CSR_RWE/REPORT/PGM/ae_evt_ger_subg_s2_t.sas OUT=REPORT/OUTPUT/ae_ptinjn_ger_race_s2_t_x.rtf (12AUG2021 - 12:07)

Project Code / Study Number / Analysis: SAR231893 / EFC14153 / CSR_RWE

2 Adverse events - Safety type 2 inflammatory asthma phenotype population

2.36 Patients with any TEAE: Injection site nodule

2.36.4 By baseline ICS dose level (Medium, High)

	Baseline ICS dose level			
	High		Medium	
Safety type 2 inflammatory asthma phenotype population	**Placebo (N=50)**	**Dupilumab (N=101)**	**Placebo (N=63)**	**Dupilumab (N=131)**
Patients with any TEAE: Injection site nodule [n(%)]	1 (2.0%)	4 (4.0%)	0	11 (8.4%)
Odds Ratio (95% CI)	-	2.02 (0.22 to 18.57)	-	NE (NE to NE)
p-value for Odds Ratio		0.534		NE
Peto Odds Ratio (95% CI)	-	1.84 (0.28 to 12.13)	-	4.77 (1.30 to 17.42)
Reversed Peto Odds Ratio (95% CI)	-	0.54 (0.08 to 3.57)	-	0.21 (0.06 to 0.77)
p-value for Peto Odds Ratio		0.528		0.018
p-value for heterogeneity of Peto Odds Ratio				0.414
Risk Ratio (95% CI)	-	1.98 (0.23 to 17.26)	-	NE (NE to NE)
Reversed Risk ratio (95% CI)	-	0.51 (0.06 to 4.40)		
p-value for Risk Ratio		0.536		NE

Odds Ratio and related p-value are estimated by Wald's method using the SAS LOGISTIC procedure.
Peto OR calculation is based on Yusuf S et al. (Prog Cardiovasc Dis. 1985 Mar-Apr;27(5):335-71) and its p-value is derived using a normal approximation.
Risk Ratio and related p-value are estimated by using the SAS FREQ procedure.
Risk Difference and related p-value are estimated by using the SAS GLIMMIX procedure with the following model: criterion = treatment.
p-values for heterogeneity are estimated by using the SAS GLIMMIX procedure with the following model: criterion = treatment subgroup treatment*subgroup.
p-value for heterogeneity of Peto Odds Ratio is estimated by using normal approximation.
PGM=DEVOPS/SAR231893/EFC14153/CSR_RWE/REPORT/PGM/ae_evt_ger_subg_s2_t.sas OUT=REPORT/OUTPUT/ae_ptinjn_ger_ics_s2_t_x.rtf (12AUG2021 - 12:07)

Project Code / Study Number / Analysis: SAR231893 / EFC14153 / CSR_RWE

2 Adverse events - Safety type 2 inflammatory asthma phenotype population

2.36 Patients with any TEAE: Injection site nodule

2.36.4 By baseline ICS dose level (Medium, High)

	Baseline ICS dose level			
	High		Medium	
Safety type 2 inflammatory asthma phenotype population	**Placebo (N=50)**	**Dupilumab (N=101)**	**Placebo (N=63)**	**Dupilumab (N=131)**
p-value for heterogeneity of Risk Ratio				0.975
Risk Difference (95% CI)	-	1.96 (-3.52 to 7.44)	-	8.40 (NE to NE)
p-value for Risk Difference		0.481		<0.001
p-value for heterogeneity of Risk Difference				<0.001

Odds Ratio and related p-value are estimated by Wald's method using the SAS LOGISTIC procedure.
Peto OR calculation is based on Yusuf S et al. (Prog Cardiovasc Dis. 1985 Mar-Apr;27(5):335-71) and its p-value is derived using a normal approximation.
Risk Ratio and related p-value are estimated by using the SAS FREQ procedure.
Risk Difference and related p-value are estimated by using the SAS GLIMMIX procedure with the following model: criterion = treatment.
p-values for heterogeneity are estimated by using the SAS GLIMMIX procedure with the following model: criterion = treatment subgroup treatment*subgroup.
p-value for heterogeneity of Peto Odds Ratio is estimated by using normal approximation.
PGM=DEVOPS/SAR231893/EFC14153/CSR_RWE/REPORT/PGM/ae_evt_ger_subg_s2_t.sas OUT=REPORT/OUTPUT/ae_ptinjn_ger_ics_s2_t_x.rtf (12AUG2021 - 12:07)

Project Code / Study Number / Analysis: SAR231893 / EFC14153 / CSR_RWE

2 Adverse events - Safety type 2 inflammatory asthma phenotype population

2.36 Patients with any TEAE: Injection site nodule

2.36.5 By baseline ICS dose level 2 (Medium, High)

	Baseline ICS dose level 2			
	High		Medium	
Safety type 2 inflammatory asthma phenotype population	**Placebo (N=94)**	**Dupilumab (N=199)**	**Placebo (N=19)**	**Dupilumab (N=35)**
Patients with any TEAE: Injection site nodule [n(%)]	1 (1.1%)	10 (5.0%)	0	5 (14.3%)
Odds Ratio (95% CI)	-	4.92 (0.62 to 39.02)	-	NE (NE to NE)
p-value for Odds Ratio		0.131		NE
Peto Odds Ratio (95% CI)	-	2.98 (0.82 to 10.81)	-	5.31 (0.79 to 35.79)
Reversed Peto Odds Ratio (95% CI)	-	0.34 (0.09 to 1.22)	-	0.19 (0.03 to 1.27)
p-value for Peto Odds Ratio		0.096		0.087
p-value for heterogeneity of Peto Odds Ratio				0.624
Risk Ratio (95% CI)	-	4.72 (0.61 to 36.36)	-	NE (NE to NE)
Reversed Risk ratio (95% CI)	-	0.21 (0.03 to 1.63)		
p-value for Risk Ratio		0.136		NE

Odds Ratio and related p-value are estimated by Wald's method using the SAS LOGISTIC procedure.
Peto OR calculation is based on Yusuf S et al. (Prog Cardiovasc Dis. 1985 Mar-Apr;27(5):335-71) and its p-value is derived using a normal approximation.
Risk Ratio and related p-value are estimated by using the SAS FREQ procedure.
Risk Difference and related p-value are estimated by using the SAS GLIMMIX procedure with the following model: criterion = treatment.
p-values for heterogeneity are estimated by using the SAS GLIMMIX procedure with the following model: criterion = treatment subgroup treatment*subgroup.
p-value for heterogeneity of Peto Odds Ratio is estimated by using normal approximation.
PGM=DEVOPS/SAR231893/EFC14153/CSR_RWE/REPORT/PGM/ae_evt_ger_subg_s2_t.sas OUT=REPORT/OUTPUT/ae_ptinjn_ger_ics2_s2_t_x.rtf (01SEP2021 - 16:13)

Project Code / Study Number / Analysis: SAR231893 / EFC14153 / CSR_RWE

2 Adverse events - Safety type 2 inflammatory asthma phenotype population

2.36 Patients with any TEAE: Injection site nodule

2.36.5 By baseline ICS dose level 2 (Medium, High)

	Baseline ICS dose level 2			
	High		Medium	
Safety type 2 inflammatory asthma phenotype population	**Placebo (N=94)**	**Dupilumab (N=199)**	**Placebo (N=19)**	**Dupilumab (N=35)**
p-value for heterogeneity of Risk Ratio				0.980
Risk Difference (95% CI)	-	3.96 (0.27 to 7.65)	-	14.29 (NE to NE)
p-value for Risk Difference		0.036		<0.001
p-value for heterogeneity of Risk Difference				<0.001

Odds Ratio and related p-value are estimated by Wald's method using the SAS LOGISTIC procedure.
Peto OR calculation is based on Yusuf S et al. (Prog Cardiovasc Dis. 1985 Mar-Apr;27(5):335-71) and its p-value is derived using a normal approximation.
Risk Ratio and related p-value are estimated by using the SAS FREQ procedure.
Risk Difference and related p-value are estimated by using the SAS GLIMMIX procedure with the following model: criterion = treatment.
p-values for heterogeneity are estimated by using the SAS GLIMMIX procedure with the following model: criterion = treatment subgroup treatment*subgroup.
p-value for heterogeneity of Peto Odds Ratio is estimated by using normal approximation.
PGM=DEVOPS/SAR231893/EFC14153/CSR_RWE/REPORT/PGM/ae_evt_ger_subg_s2_t.sas OUT=REPORT/OUTPUT/ae_ptinjn_ger_ics2_s2_t_x.rtf (01SEP2021 - 16:13)

Project Code / Study Number / Analysis: SAR231893 / EFC14153 / CSR_RWE

2 Adverse events - Safety type 2 inflammatory asthma phenotype population

2.36 Patients with any TEAE: Injection site nodule

2.36.6 By baseline predicted FEV1 (<80%, >=80%)

	Baseline Predicted FEV1			
	<80%		>=80%	
Safety type 2 inflammatory asthma phenotype population	**Placebo (N=58)**	**Dupilumab (N=116)**	**Placebo (N=55)**	**Dupilumab (N=118)**
Patients with any TEAE: Injection site nodule [n(%)]	1 (1.7%)	9 (7.8%)	0	6 (5.1%)
Odds Ratio (95% CI)	-	4.79 (0.59 to 38.79)	-	NE (NE to NE)
p-value for Odds Ratio		0.142		NE
Peto Odds Ratio (95% CI)	-	3.03 (0.78 to 11.68)	-	4.53 (0.79 to 25.89)
Reversed Peto Odds Ratio (95% CI)	-	0.33 (0.09 to 1.28)	-	0.22 (0.04 to 1.27)
p-value for Peto Odds Ratio		0.108		0.090
p-value for heterogeneity of Peto Odds Ratio				0.721
Risk Ratio (95% CI)	-	4.50 (0.58 to 34.67)	-	NE (NE to NE)
Reversed Risk ratio (95% CI)	-	0.22 (0.03 to 1.71)		
p-value for Risk Ratio		0.149		NE

Odds Ratio and related p-value are estimated by Wald's method using the SAS LOGISTIC procedure.
Peto OR calculation is based on Yusuf S et al. (Prog Cardiovasc Dis. 1985 Mar-Apr;27(5):335-71) and its p-value is derived using a normal approximation.
Risk Ratio and related p-value are estimated by using the SAS FREQ procedure.
Risk Difference and related p-value are estimated by using the SAS GLIMMIX procedure with the following model: criterion = treatment.
p-values for heterogeneity are estimated by using the SAS GLIMMIX procedure with the following model: criterion = treatment subgroup treatment*subgroup.
p-value for heterogeneity of Peto Odds Ratio is estimated by using normal approximation.
PGM=DEVOPS/SAR231893/EFC14153/CSR_RWE/REPORT/PGM/ae_evt_ger_subg_s2_t.sas OUT=REPORT/OUTPUT/ae_ptinjn_ger_pfev1_s2_t_x.rtf (12AUG2021 - 12:07)

Project Code / Study Number / Analysis: SAR231893 / EFC14153 / CSR_RWE

2 Adverse events - Safety type 2 inflammatory asthma phenotype population

2.36 Patients with any TEAE: Injection site nodule

2.36.6 By baseline predicted FEV1 (<80%, >=80%)

	Baseline Predicted FEV1			
	<80%		>=80%	
Safety type 2 inflammatory asthma phenotype population	**Placebo (N=58)**	**Dupilumab (N=116)**	**Placebo (N=55)**	**Dupilumab (N=118)**
p-value for heterogeneity of Risk Ratio				0.979
Risk Difference (95% CI)	-	6.03 (0.08 to 11.99)	-	5.08 (NE to NE)
p-value for Risk Difference		0.047		<0.001
p-value for heterogeneity of Risk Difference				<0.001

Odds Ratio and related p-value are estimated by Wald's method using the SAS LOGISTIC procedure.
Peto OR calculation is based on Yusuf S et al. (Prog Cardiovasc Dis. 1985 Mar-Apr;27(5):335-71) and its p-value is derived using a normal approximation.
Risk Ratio and related p-value are estimated by using the SAS FREQ procedure.
Risk Difference and related p-value are estimated by using the SAS GLIMMIX procedure with the following model: criterion = treatment.
p-values for heterogeneity are estimated by using the SAS GLIMMIX procedure with the following model: criterion = treatment subgroup treatment*subgroup.
p-value for heterogeneity of Peto Odds Ratio is estimated by using normal approximation.
PGM=DEVOPS/SAR231893/EFC14153/CSR_RWE/REPORT/PGM/ae_evt_ger_subg_s2_t.sas OUT=REPORT/OUTPUT/ae_ptinjn_ger_pfev1_s2_t_x.rtf (12AUG2021 - 12:07)

Project Code / Study Number / Analysis: SAR231893 / EFC14153 / CSR_RWE

2 Adverse events - Safety type 2 inflammatory asthma phenotype population

2.36 Patients with any TEAE: Injection site nodule

2.36.7 By baseline ACQ-7-IA (<=2, >2)

	Baseline ACQ-7-IA			
	<=2		>2	
Safety type 2 inflammatory asthma phenotype population	**Placebo (N=61)**	**Dupilumab (N=125)**	**Placebo (N=52)**	**Dupilumab (N=109)**
Patients with any TEAE: Injection site nodule [n(%)]	1 (1.6%)	8 (6.4%)	0	7 (6.4%)
Odds Ratio (95% CI)	-	4.10 (0.50 to 33.57)	-	NE (NE to NE)
p-value for Odds Ratio		0.188		NE
Peto Odds Ratio (95% CI)	-	2.80 (0.67 to 11.60)	-	4.64 (0.92 to 23.32)
Reversed Peto Odds Ratio (95% CI)	-	0.36 (0.09 to 1.49)	-	0.22 (0.04 to 1.09)
p-value for Peto Odds Ratio		0.157		0.063
p-value for heterogeneity of Peto Odds Ratio				0.645
Risk Ratio (95% CI)	-	3.90 (0.50 to 30.51)	-	NE (NE to NE)
Reversed Risk ratio (95% CI)	-	0.26 (0.03 to 2.00)		
p-value for Risk Ratio		0.194		NE

Odds Ratio and related p-value are estimated by Wald's method using the SAS LOGISTIC procedure.
Peto OR calculation is based on Yusuf S et al. (Prog Cardiovasc Dis. 1985 Mar-Apr;27(5):335-71) and its p-value is derived using a normal approximation.
Risk Ratio and related p-value are estimated by using the SAS FREQ procedure.
Risk Difference and related p-value are estimated by using the SAS GLIMMIX procedure with the following model: criterion = treatment.
p-values for heterogeneity are estimated by using the SAS GLIMMIX procedure with the following model: criterion = treatment subgroup treatment*subgroup.
p-value for heterogeneity of Peto Odds Ratio is estimated by using normal approximation.
PGM=DEVOPS/SAR231893/EFC14153/CSR_RWE/REPORT/PGM/ae_evt_ger_subg_s2_t.sas OUT=REPORT/OUTPUT/ae_ptinjn_ger_acq7_s2_t_x.rtf (12AUG2021 - 12:07)

Project Code / Study Number / Analysis: SAR231893 / EFC14153 / CSR_RWE

2 Adverse events - Safety type 2 inflammatory asthma phenotype population

2.36 Patients with any TEAE: Injection site nodule

2.36.7 By baseline ACQ-7-IA (<=2, >2)

	Baseline ACQ-7-IA			
	<=2		>2	
Safety type 2 inflammatory asthma phenotype population	**Placebo (N=61)**	**Dupilumab (N=125)**	**Placebo (N=52)**	**Dupilumab (N=109)**
p-value for heterogeneity of Risk Ratio				0.979
Risk Difference (95% CI)	-	4.76 (-0.62 to 10.14)	-	6.42 (NE to NE)
p-value for Risk Difference		0.083		<0.001
p-value for heterogeneity of Risk Difference				<0.001

Odds Ratio and related p-value are estimated by Wald's method using the SAS LOGISTIC procedure.
Peto OR calculation is based on Yusuf S et al. (Prog Cardiovasc Dis. 1985 Mar-Apr;27(5):335-71) and its p-value is derived using a normal approximation.
Risk Ratio and related p-value are estimated by using the SAS FREQ procedure.
Risk Difference and related p-value are estimated by using the SAS GLIMMIX procedure with the following model: criterion = treatment.
p-values for heterogeneity are estimated by using the SAS GLIMMIX procedure with the following model: criterion = treatment subgroup treatment*subgroup.
p-value for heterogeneity of Peto Odds Ratio is estimated by using normal approximation.
PGM=DEVOPS/SAR231893/EFC14153/CSR_RWE/REPORT/PGM/ae_evt_ger_subg_s2_t.sas OUT=REPORT/OUTPUT/ae_ptinjn_ger_acq7_s2_t_x.rtf (12AUG2021 - 12:07)

Project Code / Study Number / Analysis: SAR231893 / EFC14153 / CSR_RWE

2 Adverse events - Safety type 2 inflammatory asthma phenotype population

2.36 Patients with any TEAE: Injection site nodule

2.36.8 By baseline weight (<=30 kg, >30 kg)

	Baseline weight (kg)			
	<=30		>30	
Safety type 2 inflammatory asthma phenotype population	**Placebo (N=36)**	**Dupilumab (N=74)**	**Placebo (N=77)**	**Dupilumab (N=160)**
Patients with any TEAE: Injection site nodule [n(%)]	0	7 (9.5%)	1 (1.3%)	8 (5.0%)
Odds Ratio (95% CI)	-	NE (NE to NE)	-	4.00 (0.49 to 32.57)
p-value for Odds Ratio		NE		0.195
Peto Odds Ratio (95% CI)	-	4.82 (0.95 to 24.46)	-	2.74 (0.66 to 11.34)
Reversed Peto Odds Ratio (95% CI)	-	0.21 (0.04 to 1.05)	-	0.36 (0.09 to 1.52)
p-value for Peto Odds Ratio		0.058		0.164
p-value for heterogeneity of Peto Odds Ratio				0.608
Risk Ratio (95% CI)	-	NE (NE to NE)	-	3.85 (0.49 to 30.24)
Reversed Risk ratio (95% CI)			-	0.26 (0.03 to 2.04)
p-value for Risk Ratio		NE		0.200

Odds Ratio and related p-value are estimated by Wald's method using the SAS LOGISTIC procedure.
Peto OR calculation is based on Yusuf S et al. (Prog Cardiovasc Dis. 1985 Mar-Apr;27(5):335-71) and its p-value is derived using a normal approximation.
Risk Ratio and related p-value are estimated by using the SAS FREQ procedure.
Risk Difference and related p-value are estimated by using the SAS GLIMMIX procedure with the following model: criterion = treatment.
p-values for heterogeneity are estimated by using the SAS GLIMMIX procedure with the following model: criterion = treatment subgroup treatment*subgroup.
p-value for heterogeneity of Peto Odds Ratio is estimated by using normal approximation.
PGM=DEVOPS/SAR231893/EFC14153/CSR_RWE/REPORT/PGM/ae_evt_ger_subg_s2_t.sas OUT=REPORT/OUTPUT/ae_ptinjn_ger_wgt_s2_t_x.rtf (12AUG2021 - 12:07)

Project Code / Study Number / Analysis: SAR231893 / EFC14153 / CSR_RWE

2 Adverse events - Safety type 2 inflammatory asthma phenotype population

2.36 Patients with any TEAE: Injection site nodule

2.36.8 By baseline weight (<=30 kg, >30 kg)

	Baseline weight (kg)			
	<=30		>30	
Safety type 2 inflammatory asthma phenotype population	**Placebo (N=36)**	**Dupilumab (N=74)**	**Placebo (N=77)**	**Dupilumab (N=160)**
p-value for heterogeneity of Risk Ratio				0.973
Risk Difference (95% CI)	-	9.46 (NE to NE)	-	3.70 (-0.54 to 7.94)
p-value for Risk Difference		<0.001		0.087
p-value for heterogeneity of Risk Difference				<0.001

Odds Ratio and related p-value are estimated by Wald's method using the SAS LOGISTIC procedure.
Peto OR calculation is based on Yusuf S et al. (Prog Cardiovasc Dis. 1985 Mar-Apr;27(5):335-71) and its p-value is derived using a normal approximation.
Risk Ratio and related p-value are estimated by using the SAS FREQ procedure.
Risk Difference and related p-value are estimated by using the SAS GLIMMIX procedure with the following model: criterion = treatment.
p-values for heterogeneity are estimated by using the SAS GLIMMIX procedure with the following model: criterion = treatment subgroup treatment*subgroup.
p-value for heterogeneity of Peto Odds Ratio is estimated by using normal approximation.
PGM=DEVOPS/SAR231893/EFC14153/CSR_RWE/REPORT/PGM/ae_evt_ger_subg_s2_t.sas OUT=REPORT/OUTPUT/ae_ptinjn_ger_wgt_s2_t_x.rtf (12AUG2021 - 12:07)

Project Code / Study Number / Analysis: SAR231893 / EFC14153 / CSR_RWE

2 Adverse events - Safety type 2 inflammatory asthma phenotype population

2.36 Patients with any TEAE: Injection site nodule

2.36.9 By atopic medical condition (Yes, No)

	Atopic medical condition			
	Yes		No	
Safety type 2 inflammatory asthma phenotype population	**Placebo (N=102)**	**Dupilumab (N=225)**	**Placebo (N=11)**	**Dupilumab (N=9)**
Patients with any TEAE: Injection site nodule [n(%)]	1 (1.0%)	15 (6.7%)	0	0
Odds Ratio (95% CI)	-	7.21 (0.94 to 55.34)	-	NE (NE to NE)
p-value for Odds Ratio		0.057		NE
Peto Odds Ratio (95% CI)	-	3.38 (1.14 to 9.98)	-	NE (NE to NE)
Reversed Peto Odds Ratio (95% CI)	-	0.30 (0.10 to 0.88)		
p-value for Peto Odds Ratio		0.027		NE
p-value for heterogeneity of Peto Odds Ratio				NE
Risk Ratio (95% CI)	-	6.80 (0.91 to 50.78)	-	NE (NE to NE)
Reversed Risk ratio (95% CI)	-	0.15 (0.02 to 1.10)		
p-value for Risk Ratio		0.062		NE

Odds Ratio and related p-value are estimated by Wald's method using the SAS LOGISTIC procedure.
Peto OR calculation is based on Yusuf S et al. (Prog Cardiovasc Dis. 1985 Mar-Apr;27(5):335-71) and its p-value is derived using a normal approximation.
Risk Ratio and related p-value are estimated by using the SAS FREQ procedure.
Risk Difference and related p-value are estimated by using the SAS GLIMMIX procedure with the following model: criterion = treatment.
p-values for heterogeneity are estimated by using the SAS GLIMMIX procedure with the following model: criterion = treatment subgroup treatment*subgroup.
p-value for heterogeneity of Peto Odds Ratio is estimated by using normal approximation.
PGM=DEVOPS/SAR231893/EFC14153/CSR_RWE/REPORT/PGM/ae_evt_ger_subg_s2_t.sas OUT=REPORT/OUTPUT/ae_ptinjn_ger_amc_s2_t_x.rtf (12AUG2021 - 12:07)

Project Code / Study Number / Analysis: SAR231893 / EFC14153 / CSR_RWE

2 Adverse events - Safety type 2 inflammatory asthma phenotype population

2.36 Patients with any TEAE: Injection site nodule

2.36.9 By atopic medical condition (Yes, No)

	Atopic medical condition			
	Yes		No	
Safety type 2 inflammatory asthma phenotype population	**Placebo (N=102)**	**Dupilumab (N=225)**	**Placebo (N=11)**	**Dupilumab (N=9)**
p-value for heterogeneity of Risk Ratio				0.998
Risk Difference (95% CI)	-	5.69 (1.89 to 9.48)	-	0.00 (NE to NE)
p-value for Risk Difference		0.003		NE
p-value for heterogeneity of Risk Difference				<0.001

Odds Ratio and related p-value are estimated by Wald's method using the SAS LOGISTIC procedure.
Peto OR calculation is based on Yusuf S et al. (Prog Cardiovasc Dis. 1985 Mar-Apr;27(5):335-71) and its p-value is derived using a normal approximation.
Risk Ratio and related p-value are estimated by using the SAS FREQ procedure.
Risk Difference and related p-value are estimated by using the SAS GLIMMIX procedure with the following model: criterion = treatment.
p-values for heterogeneity are estimated by using the SAS GLIMMIX procedure with the following model: criterion = treatment subgroup treatment*subgroup.
p-value for heterogeneity of Peto Odds Ratio is estimated by using normal approximation.
PGM=DEVOPS/SAR231893/EFC14153/CSR_RWE/REPORT/PGM/ae_evt_ger_subg_s2_t.sas OUT=REPORT/OUTPUT/ae_ptinjn_ger_amc_s2_t_x.rtf (12AUG2021 - 12:07)

Project Code / Study Number / Analysis: SAR231893 / EFC14153 / CSR_RWE

2 Adverse events - Safety type 2 inflammatory asthma phenotype population

2.36 Patients with any TEAE: Injection site nodule

2.36.10 By baseline total IgE (<median, >= median)

	Baseline Total IgE (IU/mL)			
	<median		>=median	
Safety type 2 inflammatory asthma phenotype population	**Placebo (N=65)**	**Dupilumab (N=106)**	**Placebo (N=47)**	**Dupilumab (N=124)**
Patients with any TEAE: Injection site nodule [n(%)]	0	9 (8.5%)	1 (2.1%)	6 (4.8%)
Odds Ratio (95% CI)	-	NE (NE to NE)	-	2.34 (0.27 to 19.96)
p-value for Odds Ratio		NE		0.437
Peto Odds Ratio (95% CI)	-	5.44 (1.37 to 21.58)	-	1.99 (0.37 to 10.76)
Reversed Peto Odds Ratio (95% CI)	-	0.18 (0.05 to 0.73)	-	0.50 (0.09 to 2.70)
p-value for Peto Odds Ratio		0.016		0.426
p-value for heterogeneity of Peto Odds Ratio				0.366
Risk Ratio (95% CI)	-	NE (NE to NE)	-	2.27 (0.28 to 18.39)
Reversed Risk ratio (95% CI)			-	0.44 (0.05 to 3.56)
p-value for Risk Ratio		NE		0.441

Odds Ratio and related p-value are estimated by Wald's method using the SAS LOGISTIC procedure.
Peto OR calculation is based on Yusuf S et al. (Prog Cardiovasc Dis. 1985 Mar-Apr;27(5):335-71) and its p-value is derived using a normal approximation.
Risk Ratio and related p-value are estimated by using the SAS FREQ procedure.
Risk Difference and related p-value are estimated by using the SAS GLIMMIX procedure with the following model: criterion = treatment.
p-values for heterogeneity are estimated by using the SAS GLIMMIX procedure with the following model: criterion = treatment subgroup treatment*subgroup.
p-value for heterogeneity of Peto Odds Ratio is estimated by using normal approximation.
PGM=DEVOPS/SAR231893/EFC14153/CSR_RWE/REPORT/PGM/ae_evt_ger_subg_s2_t.sas OUT=REPORT/OUTPUT/ae_ptinjn_ger_igem_s2_t_x.rtf (12AUG2021 - 12:08)

Project Code / Study Number / Analysis: SAR231893 / EFC14153 / CSR_RWE

2 Adverse events - Safety type 2 inflammatory asthma phenotype population

2.36 Patients with any TEAE: Injection site nodule

2.36.10 By baseline total IgE (<median, >= median)

	Baseline Total IgE (IU/mL)			
	<median		>=median	
Safety type 2 inflammatory asthma phenotype population	**Placebo (N=65)**	**Dupilumab (N=106)**	**Placebo (N=47)**	**Dupilumab (N=124)**
p-value for heterogeneity of Risk Ratio				0.975
Risk Difference (95% CI)	-	8.49 (NE to NE)	-	2.71 (-2.92 to 8.34)
p-value for Risk Difference		<0.001		0.343
p-value for heterogeneity of Risk Difference				<0.001

Odds Ratio and related p-value are estimated by Wald's method using the SAS LOGISTIC procedure.
Peto OR calculation is based on Yusuf S et al. (Prog Cardiovasc Dis. 1985 Mar-Apr;27(5):335-71) and its p-value is derived using a normal approximation.
Risk Ratio and related p-value are estimated by using the SAS FREQ procedure.
Risk Difference and related p-value are estimated by using the SAS GLIMMIX procedure with the following model: criterion = treatment.
p-values for heterogeneity are estimated by using the SAS GLIMMIX procedure with the following model: criterion = treatment subgroup treatment*subgroup.
p-value for heterogeneity of Peto Odds Ratio is estimated by using normal approximation.
PGM=DEVOPS/SAR231893/EFC14153/CSR_RWE/REPORT/PGM/ae_evt_ger_subg_s2_t.sas OUT=REPORT/OUTPUT/ae_ptinjn_ger_igem_s2_t_x.rtf (12AUG2021 - 12:08)

Project Code / Study Number / Analysis: SAR231893 / EFC14153 / CSR_RWE

2 Adverse events - Safety type 2 inflammatory asthma phenotype population

2.36 Patients with any TEAE: Injection site nodule

2.36.11 By baseline total IgE (<100 IU/ml, >= 100 IU/ml)

	Baseline Total IgE (IU/mL)			
	< 100		>= 100	
Safety type 2 inflammatory asthma phenotype population	**Placebo (N=22)**	**Dupilumab (N=29)**	**Placebo (N=90)**	**Dupilumab (N=201)**
Patients with any TEAE: Injection site nodule [n(%)]	0	1 (3.4%)	1 (1.1%)	14 (7.0%)
Odds Ratio (95% CI)	-	NE (NE to NE)	-	6.66 (0.86 to 51.45)
p-value for Odds Ratio		NE		0.069
Peto Odds Ratio (95% CI)	-	5.80 (0.11 to 303.69)	-	3.30 (1.07 to 10.13)
Reversed Peto Odds Ratio (95% CI)	-	0.17 (0.00 to 9.09)	-	0.30 (0.10 to 0.93)
p-value for Peto Odds Ratio		0.384		0.037
p-value for heterogeneity of Peto Odds Ratio				0.788
Risk Ratio (95% CI)	-	NE (NE to NE)	-	6.27 (0.84 to 46.95)
Reversed Risk ratio (95% CI)			-	0.16 (0.02 to 1.19)
p-value for Risk Ratio		NE		0.074

Odds Ratio and related p-value are estimated by Wald's method using the SAS LOGISTIC procedure.
Peto OR calculation is based on Yusuf S et al. (Prog Cardiovasc Dis. 1985 Mar-Apr;27(5):335-71) and its p-value is derived using a normal approximation.
Risk Ratio and related p-value are estimated by using the SAS FREQ procedure.
Risk Difference and related p-value are estimated by using the SAS GLIMMIX procedure with the following model: criterion = treatment.
p-values for heterogeneity are estimated by using the SAS GLIMMIX procedure with the following model: criterion = treatment subgroup treatment*subgroup.
p-value for heterogeneity of Peto Odds Ratio is estimated by using normal approximation.
PGM=DEVOPS/SAR231893/EFC14153/CSR_RWE/REPORT/PGM/ae_evt_ger_subg_s2_t.sas OUT=REPORT/OUTPUT/ae_ptinjn_ger_ige_s2_t_x.rtf (12AUG2021 - 12:08)

Project Code / Study Number / Analysis: SAR231893 / EFC14153 / CSR_RWE

2 Adverse events - Safety type 2 inflammatory asthma phenotype population

2.36 Patients with any TEAE: Injection site nodule

2.36.11 By baseline total IgE (<100 IU/ml, >= 100 IU/ml)

	Baseline Total IgE (IU/mL)			
	< 100		>= 100	
Safety type 2 inflammatory asthma phenotype population	**Placebo (N=22)**	**Dupilumab (N=29)**	**Placebo (N=90)**	**Dupilumab (N=201)**
p-value for heterogeneity of Risk Ratio				0.982
Risk Difference (95% CI)	-	3.45 (NE to NE)	-	5.85 (1.70 to 10.00)
p-value for Risk Difference		<0.001		0.006
p-value for heterogeneity of Risk Difference				<0.001

Odds Ratio and related p-value are estimated by Wald's method using the SAS LOGISTIC procedure.
Peto OR calculation is based on Yusuf S et al. (Prog Cardiovasc Dis. 1985 Mar-Apr;27(5):335-71) and its p-value is derived using a normal approximation.
Risk Ratio and related p-value are estimated by using the SAS FREQ procedure.
Risk Difference and related p-value are estimated by using the SAS GLIMMIX procedure with the following model: criterion = treatment.
p-values for heterogeneity are estimated by using the SAS GLIMMIX procedure with the following model: criterion = treatment subgroup treatment*subgroup.
p-value for heterogeneity of Peto Odds Ratio is estimated by using normal approximation.
PGM=DEVOPS/SAR231893/EFC14153/CSR_RWE/REPORT/PGM/ae_evt_ger_subg_s2_t.sas OUT=REPORT/OUTPUT/ae_ptinjn_ger_ige_s2_t_x.rtf (12AUG2021 - 12:08)

Project Code / Study Number / Analysis: SAR231893 / EFC14153 / CSR_RWE

2 Adverse events - Safety type 2 inflammatory asthma phenotype population

2.36 Patients with any TEAE: Injection site nodule

2.36.12 By age at onset of asthma (0-2, 3-5, >=6 years)

	Age of onset of asthma (years)					
	0-2		3-5		>= 6	
Safety type 2 inflammatory asthma phenotype population	**Placebo (N=40)**	**Dupilumab (N=104)**	**Placebo (N=38)**	**Dupilumab (N=85)**	**Placebo (N=35)**	**Dupilumab (N=45)**
Patients with any TEAE: Injection site nodule [n(%)]	0	5 (4.8%)	1 (2.6%)	6 (7.1%)	0	4 (8.9%)
Odds Ratio (95% CI)	-	NE (NE to NE)	-	2.81 (0.33 to 24.18)	-	NE (NE to NE)
p-value for Odds Ratio		NE		0.347		NE
Peto Odds Ratio (95% CI)	-	4.16 (0.57 to 30.25)	-	2.27 (0.44 to 11.73)	-	6.35 (0.85 to 47.56)
Reversed Peto Odds Ratio (95% CI)	-	0.24 (0.03 to 1.75)	-	0.44 (0.09 to 2.27)	-	0.16 (0.02 to 1.18)
p-value for Peto Odds Ratio		0.160		0.329		0.072
p-value for heterogeneity of Peto Odds Ratio:						
0-2, 3-5						0.645
0-2, >= 6						0.769
3-5, >= 6						0.438

Odds Ratio and related p-value are estimated by Wald's method using the SAS LOGISTIC procedure.
Peto OR calculation is based on Yusuf S et al. (Prog Cardiovasc Dis. 1985 Mar-Apr;27(5):335-71) and its p-value is derived using a normal approximation.
Risk Ratio and related p-value are estimated by using the SAS FREQ procedure.
Risk Difference and related p-value are estimated by using the SAS GLIMMIX procedure with the following model: criterion = treatment.
p-values for heterogeneity are estimated by using the SAS GLIMMIX procedure with the following model: criterion = treatment subgroup treatment*subgroup.
p-value for heterogeneity of Peto Odds Ratio is estimated by using normal approximation.
PGM=DEVOPS/SAR231893/EFC14153/CSR_RWE/REPORT/PGM/ae_evt_ger_subg_s2_t.sas OUT=REPORT/OUTPUT/ae_ptinjn_ger_onsa_s2_t_x.rtf (12AUG2021 - 12:08)

Project Code / Study Number / Analysis: SAR231893 / EFC14153 / CSR_RWE

2 Adverse events - Safety type 2 inflammatory asthma phenotype population

2.36 Patients with any TEAE: Injection site nodule

2.36.12 By age at onset of asthma (0-2, 3-5, >=6 years)

	Age of onset of asthma (years)					
	0-2		3-5		>= 6	
Safety type 2 inflammatory asthma phenotype population	**Placebo (N=40)**	**Dupilumab (N=104)**	**Placebo (N=38)**	**Dupilumab (N=85)**	**Placebo (N=35)**	**Dupilumab (N=45)**
overall						0.730
Risk Ratio (95% CI)	-	NE (NE to NE)	-	2.68 (0.33 to 21.52)	-	NE (NE to NE)
Reversed Risk ratio (95% CI)			-	0.37 (0.05 to 2.99)		
p-value for Risk Ratio		NE		0.353		NE
p-value for heterogeneity of Risk Ratio:						
0-2, 3-5						0.982
0-2, >= 6						0.999
3-5, >= 6						0.982
overall						0.999
Risk Difference (95% CI)	-	4.81 (NE to NE)	-	4.43 (-3.10 to 11.96)	-	8.89 (NE to NE)
p-value for Risk Difference		<0.001		0.247		<0.001

Odds Ratio and related p-value are estimated by Wald's method using the SAS LOGISTIC procedure.
Peto OR calculation is based on Yusuf S et al. (Prog Cardiovasc Dis. 1985 Mar-Apr;27(5):335-71) and its p-value is derived using a normal approximation.
Risk Ratio and related p-value are estimated by using the SAS FREQ procedure.
Risk Difference and related p-value are estimated by using the SAS GLIMMIX procedure with the following model: criterion = treatment.
p-values for heterogeneity are estimated by using the SAS GLIMMIX procedure with the following model: criterion = treatment subgroup treatment*subgroup.
p-value for heterogeneity of Peto Odds Ratio is estimated by using normal approximation.
PGM=DEVOPS/SAR231893/EFC14153/CSR_RWE/REPORT/PGM/ae_evt_ger_subg_s2_t.sas OUT=REPORT/OUTPUT/ae_ptinjn_ger_onsa_s2_t_x.rtf (12AUG2021 - 12:08)

Project Code / Study Number / Analysis: SAR231893 / EFC14153 / CSR_RWE

2 Adverse events - Safety type 2 inflammatory asthma phenotype population

2.36 Patients with any TEAE: Injection site nodule

2.36.12 By age at onset of asthma (0-2, 3-5, >=6 years)

	Age of onset of asthma (years)					
	0-2		3-5		>= 6	
Safety type 2 inflammatory asthma phenotype population	**Placebo (N=40)**	**Dupilumab (N=104)**	**Placebo (N=38)**	**Dupilumab (N=85)**	**Placebo (N=35)**	**Dupilumab (N=45)**
p-value for heterogeneity of Risk Difference:						
0-2, 3-5						<0.001
0-2, >= 6						<0.001
3-5, >= 6						<0.001
overall						<0.001

Odds Ratio and related p-value are estimated by Wald's method using the SAS LOGISTIC procedure.
Peto OR calculation is based on Yusuf S et al. (Prog Cardiovasc Dis. 1985 Mar-Apr;27(5):335-71) and its p-value is derived using a normal approximation.
Risk Ratio and related p-value are estimated by using the SAS FREQ procedure.
Risk Difference and related p-value are estimated by using the SAS GLIMMIX procedure with the following model: criterion = treatment.
p-values for heterogeneity are estimated by using the SAS GLIMMIX procedure with the following model: criterion = treatment subgroup treatment*subgroup.
p-value for heterogeneity of Peto Odds Ratio is estimated by using normal approximation.
PGM=DEVOPS/SAR231893/EFC14153/CSR_RWE/REPORT/PGM/ae_evt_ger_subg_s2_t.sas OUT=REPORT/OUTPUT/ae_ptinjn_ger_onsa_s2_t_x.rtf (12AUG2021 - 12:08)

Project Code / Study Number / Analysis: SAR231893 / EFC14153 / CSR_RWE

2 Adverse events - Safety type 2 inflammatory asthma phenotype population

2.36 Patients with any TEAE: Injection site nodule

2.36.13 By number of severe asthma exacerbation prior to the study (<=1, 2, >2)

	Number of severe asthma exacerbation prior to the study					
	<=1		2		>2	
Safety type 2 inflammatory asthma phenotype population	**Placebo (N=46)**	**Dupilumab (N=85)**	**Placebo (N=32)**	**Dupilumab (N=75)**	**Placebo (N=35)**	**Dupilumab (N=74)**
Patients with any TEAE: Injection site nodule [n(%)]	0	6 (7.1%)	0	4 (5.3%)	1 (2.9%)	5 (6.8%)
Odds Ratio (95% CI)	-	NE (NE to NE)	-	NE (NE to NE)	-	2.46 (0.28 to 21.92)
p-value for Odds Ratio		NE		NE		0.419
Peto Odds Ratio (95% CI)	-	4.97 (0.90 to 27.45)	-	4.34 (0.50 to 38.08)	-	2.10 (0.36 to 12.15)
Reversed Peto Odds Ratio (95% CI)	-	0.20 (0.04 to 1.11)	-	0.23 (0.03 to 2.00)	-	0.48 (0.08 to 2.78)
p-value for Peto Odds Ratio		0.066		0.185		0.407
p-value for heterogeneity of Peto Odds Ratio:						
<=1, 2						0.924
<=1, >2						0.491
2, >2						0.611

Odds Ratio and related p-value are estimated by Wald's method using the SAS LOGISTIC procedure.
Peto OR calculation is based on Yusuf S et al. (Prog Cardiovasc Dis. 1985 Mar-Apr;27(5):335-71) and its p-value is derived using a normal approximation.
Risk Ratio and related p-value are estimated by using the SAS FREQ procedure.
Risk Difference and related p-value are estimated by using the SAS GLIMMIX procedure with the following model: criterion = treatment.
p-values for heterogeneity are estimated by using the SAS GLIMMIX procedure with the following model: criterion = treatment subgroup treatment*subgroup.
p-value for heterogeneity of Peto Odds Ratio is estimated by using normal approximation.
PGM=DEVOPS/SAR231893/EFC14153/CSR_RWE/REPORT/PGM/ae_evt_ger_subg_s2_t.sas OUT=REPORT/OUTPUT/ae_ptinjn_ger_exa_s2_t_x.rtf (12AUG2021 - 12:08)

Project Code / Study Number / Analysis: SAR231893 / EFC14153 / CSR_RWE

2 Adverse events - Safety type 2 inflammatory asthma phenotype population

2.36 Patients with any TEAE: Injection site nodule

2.36.13 By number of severe asthma exacerbation prior to the study (<=1, 2, >2)

	Number of severe asthma exacerbation prior to the study					
	<=1		2		>2	
Safety type 2 inflammatory asthma phenotype population	**Placebo (N=46)**	**Dupilumab (N=85)**	**Placebo (N=32)**	**Dupilumab (N=75)**	**Placebo (N=35)**	**Dupilumab (N=74)**
overall						0.770
Risk Ratio (95% CI)	-	NE (NE to NE)	-	NE (NE to NE)	-	2.36 (0.29 to 19.49)
Reversed Risk ratio (95% CI)					-	0.42 (0.05 to 3.48)
p-value for Risk Ratio		NE		NE		0.424
p-value for heterogeneity of Risk Ratio:						
<=1, 2						1.000
<=1, >2						0.979
2, >2						0.983
overall						0.999
Risk Difference (95% CI)	-	7.06 (NE to NE)	-	5.33 (NE to NE)	-	3.90 (-4.14 to 11.94)
p-value for Risk Difference		<0.001		<0.001		0.338

Odds Ratio and related p-value are estimated by Wald's method using the SAS LOGISTIC procedure.
Peto OR calculation is based on Yusuf S et al. (Prog Cardiovasc Dis. 1985 Mar-Apr;27(5):335-71) and its p-value is derived using a normal approximation.
Risk Ratio and related p-value are estimated by using the SAS FREQ procedure.
Risk Difference and related p-value are estimated by using the SAS GLIMMIX procedure with the following model: criterion = treatment.
p-values for heterogeneity are estimated by using the SAS GLIMMIX procedure with the following model: criterion = treatment subgroup treatment*subgroup.
p-value for heterogeneity of Peto Odds Ratio is estimated by using normal approximation.
PGM=DEVOPS/SAR231893/EFC14153/CSR_RWE/REPORT/PGM/ae_evt_ger_subg_s2_t.sas OUT=REPORT/OUTPUT/ae_ptinjn_ger_exa_s2_t_x.rtf (12AUG2021 - 12:08)

Project Code / Study Number / Analysis: SAR231893 / EFC14153 / CSR_RWE

2 Adverse events - Safety type 2 inflammatory asthma phenotype population

2.36 Patients with any TEAE: Injection site nodule

2.36.13 By number of severe asthma exacerbation prior to the study (<=1, 2, >2)

	Number of severe asthma exacerbation prior to the study					
	<=1		2		>2	
Safety type 2 inflammatory asthma phenotype population	**Placebo (N=46)**	**Dupilumab (N=85)**	**Placebo (N=32)**	**Dupilumab (N=75)**	**Placebo (N=35)**	**Dupilumab (N=74)**
p-value for heterogeneity of Risk Difference:						
<=1, 2						<0.001
<=1, >2						<0.001
2, >2						<0.001
overall						<0.001

Odds Ratio and related p-value are estimated by Wald's method using the SAS LOGISTIC procedure.
Peto OR calculation is based on Yusuf S et al. (Prog Cardiovasc Dis. 1985 Mar-Apr;27(5):335-71) and its p-value is derived using a normal approximation.
Risk Ratio and related p-value are estimated by using the SAS FREQ procedure.
Risk Difference and related p-value are estimated by using the SAS GLIMMIX procedure with the following model: criterion = treatment.
p-values for heterogeneity are estimated by using the SAS GLIMMIX procedure with the following model: criterion = treatment subgroup treatment*subgroup.
p-value for heterogeneity of Peto Odds Ratio is estimated by using normal approximation.
PGM=DEVOPS/SAR231893/EFC14153/CSR_RWE/REPORT/PGM/ae_evt_ger_subg_s2_t.sas OUT=REPORT/OUTPUT/ae_ptinjn_ger_exa_s2_t_x.rtf (12AUG2021 - 12:08)

Project Code / Study Number / Analysis: SAR231893 / EFC14153 / CSR_RWE

2 Adverse events - Safety type 2 inflammatory asthma phenotype population

2.37 Patients with any TEAE: Injection site oedema

Safety type 2 inflammatory asthma phenotype population	Placebo (N=113)	Dupilumab (N=234)
Patients with any TEAE: Injection site oedema [n(%)]	4 (3.5%)	23 (9.8%)
Odds Ratio (95% CI)	-	2.97 (1.00 to 8.80)
p-value for Odds Ratio		0.050
Risk Ratio (95% CI)	-	2.78 (0.98 to 7.84)
Reversed Risk Ratio (95% CI)	-	0.36 (0.13 to 1.02)
p-value for Risk Ratio		0.054
Risk Difference (95% CI)	-	6.29 (1.16 to 11.42)
p-value for Risk Difference		0.016

Odds Ratio and related p-value are estimated by Wald's method using the SAS LOGISTIC procedure.
Peto OR calculation is based on Yusuf S et al. (Prog Cardiovasc Dis. 1985 Mar-Apr;27(5):335-71) and its p-value is derived using a normal approximation.
Risk Ratio and related p-value are estimated by using the SAS FREQ procedure.
Risk Difference and related p-value are estimated by using the SAS GLIMMIX procedure with the following model: criterion = treatment.
p-value for heterogeneity of Peto Odds Ratio is estimated by using normal approximation.
PGM=DEVOPS/SAR231893/EFC14153/CSR_RWE/REPORT/PGM/ae_evt_ger_s2_t.sas OUT=REPORT/OUTPUT/ae_ptinjo_ger_s2_t_x.rtf (12AUG2021 - 11:35)

Project Code / Study Number / Analysis: SAR231893 / EFC14153 / CSR_RWE

2 Adverse events - Safety type 2 inflammatory asthma phenotype population

2.37 Patients with any TEAE: Injection site oedema

2.37.1 By gender (Male, Female)

	Gender			
	Male		Female	
Safety type 2 inflammatory asthma phenotype population	**Placebo (N=77)**	**Dupilumab (N=153)**	**Placebo (N=36)**	**Dupilumab (N=81)**
Patients with any TEAE: Injection site oedema [n(%)]	2 (2.6%)	15 (9.8%)	2 (5.6%)	8 (9.9%)
Odds Ratio (95% CI)	-	4.08 (0.91 to 18.30)	-	1.86 (0.38 to 9.25)
p-value for Odds Ratio		0.067		0.447
p-value for heterogeneity of Odds Ratio				0.485
Risk Ratio (95% CI)	-	3.77 (0.89 to 16.09)	-	1.78 (0.40 to 7.96)
Reversed Risk ratio (95% CI)	-	0.26 (0.06 to 1.13)	-	0.56 (0.13 to 2.52)
p-value for Risk Ratio		0.073		0.452
p-value for heterogeneity of Risk Ratio				0.480

Odds Ratio and related p-value are estimated by Wald's method using the SAS LOGISTIC procedure.
Peto OR calculation is based on Yusuf S et al. (Prog Cardiovasc Dis. 1985 Mar-Apr;27(5):335-71) and its p-value is derived using a normal approximation.
Risk Ratio and related p-value are estimated by using the SAS FREQ procedure.
Risk Difference and related p-value are estimated by using the SAS GLIMMIX procedure with the following model: criterion = treatment.
p-values for heterogeneity are estimated by using the SAS GLIMMIX procedure with the following model: criterion = treatment subgroup treatment*subgroup.
p-value for heterogeneity of Peto Odds Ratio is estimated by using normal approximation.
PGM=DEVOPS/SAR231893/EFC14153/CSR_RWE/REPORT/PGM/ae_evt_ger_subg_s2_t.sas OUT=REPORT/OUTPUT/ae_ptinjo_ger_sex_s2_t_x.rtf (12AUG2021 - 11:42)

Project Code / Study Number / Analysis: SAR231893 / EFC14153 / CSR_RWE

2 Adverse events - Safety type 2 inflammatory asthma phenotype population

2.37 Patients with any TEAE: Injection site oedema

2.37.1 By gender (Male, Female)

	Gender			
	Male		Female	
Safety type 2 inflammatory asthma phenotype population	**Placebo (N=77)**	**Dupilumab (N=153)**	**Placebo (N=36)**	**Dupilumab (N=81)**
Risk Difference (95% CI)	-	7.21 (1.27 to 13.14)	-	4.32 (-5.69 to 14.34)
p-value for Risk Difference		0.017		0.395
p-value for heterogeneity of Risk Difference				0.624

Odds Ratio and related p-value are estimated by Wald's method using the SAS LOGISTIC procedure.
Peto OR calculation is based on Yusuf S et al. (Prog Cardiovasc Dis. 1985 Mar-Apr;27(5):335-71) and its p-value is derived using a normal approximation.
Risk Ratio and related p-value are estimated by using the SAS FREQ procedure.
Risk Difference and related p-value are estimated by using the SAS GLIMMIX procedure with the following model: criterion = treatment.
p-values for heterogeneity are estimated by using the SAS GLIMMIX procedure with the following model: criterion = treatment subgroup treatment*subgroup.
p-value for heterogeneity of Peto Odds Ratio is estimated by using normal approximation.
PGM=DEVOPS/SAR231893/EFC14153/CSR_RWE/REPORT/PGM/ae_evt_ger_subg_s2_t.sas OUT=REPORT/OUTPUT/ae_ptinjo_ger_sex_s2_t_x.rtf (12AUG2021 - 11:42)

Project Code / Study Number / Analysis: SAR231893 / EFC14153 / CSR_RWE

2 Adverse events - Safety type 2 inflammatory asthma phenotype population

2.37 Patients with any TEAE: Injection site oedema

2.37.2 By region (Latin America, East Europe, Western Countries)

	Region					
	Latin America		East Europe		Western countries	
Safety type 2 inflammatory asthma phenotype population	**Placebo (N=51)**	**Dupilumab (N=105)**	**Placebo (N=43)**	**Dupilumab (N=78)**	**Placebo (N=19)**	**Dupilumab (N=51)**
Patients with any TEAE: Injection site oedema [n(%)]	2 (3.9%)	9 (8.6%)	1 (2.3%)	9 (11.5%)	1 (5.3%)	5 (9.8%)
Odds Ratio (95% CI)	-	2.30 (0.48 to 11.04)	-	5.48 (0.67 to 44.79)	-	1.96 (0.21 to 17.93)
p-value for Odds Ratio		0.299		0.113		0.553
p-value for heterogeneity of Odds Ratio:						
Latin America, East Europe						0.516
Latin America, Western countries						0.908
East Europe, Western countries						0.509
overall						0.758
Risk Ratio (95% CI)	-	2.19 (0.49 to 9.75)	-	4.96 (0.65 to 37.86)	-	1.86 (0.23 to 14.93)

Odds Ratio and related p-value are estimated by Wald's method using the SAS LOGISTIC procedure.
Peto OR calculation is based on Yusuf S et al. (Prog Cardiovasc Dis. 1985 Mar-Apr;27(5):335-71) and its p-value is derived using a normal approximation.
Risk Ratio and related p-value are estimated by using the SAS FREQ procedure.
Risk Difference and related p-value are estimated by using the SAS GLIMMIX procedure with the following model: criterion = treatment.
p-values for heterogeneity are estimated by using the SAS GLIMMIX procedure with the following model: criterion = treatment subgroup treatment*subgroup.
p-value for heterogeneity of Peto Odds Ratio is estimated by using normal approximation.
PGM=DEVOPS/SAR231893/EFC14153/CSR_RWE/REPORT/PGM/ae_evt_ger_subg_s2_t.sas OUT=REPORT/OUTPUT/ae_ptinjo_ger_cty_s2_t_x.rtf (12AUG2021 - 11:43)

Project Code / Study Number / Analysis: SAR231893 / EFC14153 / CSR_RWE

2 Adverse events - Safety type 2 inflammatory asthma phenotype population

2.37 Patients with any TEAE: Injection site oedema

2.37.2 By region (Latin America, East Europe, Western Countries)

	Region					
	Latin America		East Europe		Western countries	
Safety type 2 inflammatory asthma phenotype population	**Placebo (N=51)**	**Dupilumab (N=105)**	**Placebo (N=43)**	**Dupilumab (N=78)**	**Placebo (N=19)**	**Dupilumab (N=51)**
Reversed Risk ratio (95% CI)	-	0.46 (0.10 to 2.04)	-	0.20 (0.03 to 1.54)	-	0.54 (0.07 to 4.30)
p-value for Risk Ratio		0.305		0.122		0.558
p-value for heterogeneity of Risk Ratio:						
Latin America, East Europe						0.525
Latin America, Western countries						0.903
East Europe, Western countries						0.510
overall						0.764
Risk Difference (95% CI)	-	4.65 (-2.96 to 12.26)	-	9.21 (0.73 to 17.70)	-	4.54 (-8.63 to 17.71)
p-value for Risk Difference		0.229		0.034		0.494
p-value for heterogeneity of Risk Difference:						
Latin America, East Europe						0.429
Latin America, Western countries						0.989

Odds Ratio and related p-value are estimated by Wald's method using the SAS LOGISTIC procedure.
Peto OR calculation is based on Yusuf S et al. (Prog Cardiovasc Dis. 1985 Mar-Apr;27(5):335-71) and its p-value is derived using a normal approximation.
Risk Ratio and related p-value are estimated by using the SAS FREQ procedure.
Risk Difference and related p-value are estimated by using the SAS GLIMMIX procedure with the following model: criterion = treatment.
p-values for heterogeneity are estimated by using the SAS GLIMMIX procedure with the following model: criterion = treatment subgroup treatment*subgroup.
p-value for heterogeneity of Peto Odds Ratio is estimated by using normal approximation.
PGM=DEVOPS/SAR231893/EFC14153/CSR_RWE/REPORT/PGM/ae_evt_ger_subg_s2_t.sas OUT=REPORT/OUTPUT/ae_ptinjo_ger_cty_s2_t_x.rtf (12AUG2021 - 11:43)

Project Code / Study Number / Analysis: SAR231893 / EFC14153 / CSR_RWE

2 Adverse events - Safety type 2 inflammatory asthma phenotype population

2.37 Patients with any TEAE: Injection site oedema

2.37.2 By region (Latin America, East Europe, Western Countries)

	Region					
	Latin America		East Europe		Western countries	
Safety type 2 inflammatory asthma phenotype population	**Placebo (N=51)**	**Dupilumab (N=105)**	**Placebo (N=43)**	**Dupilumab (N=78)**	**Placebo (N=19)**	**Dupilumab (N=51)**
East Europe, Western countries						0.553
overall						0.699

Odds Ratio and related p-value are estimated by Wald's method using the SAS LOGISTIC procedure.
Peto OR calculation is based on Yusuf S et al. (Prog Cardiovasc Dis. 1985 Mar-Apr;27(5):335-71) and its p-value is derived using a normal approximation.
Risk Ratio and related p-value are estimated by using the SAS FREQ procedure.
Risk Difference and related p-value are estimated by using the SAS GLIMMIX procedure with the following model: criterion = treatment.
p-values for heterogeneity are estimated by using the SAS GLIMMIX procedure with the following model: criterion = treatment subgroup treatment*subgroup.
p-value for heterogeneity of Peto Odds Ratio is estimated by using normal approximation.
PGM=DEVOPS/SAR231893/EFC14153/CSR_RWE/REPORT/PGM/ae_evt_ger_subg_s2_t.sas OUT=REPORT/OUTPUT/ae_ptinjo_ger_cty_s2_t_x.rtf (12AUG2021 - 11:43)

Project Code / Study Number / Analysis: SAR231893 / EFC14153 / CSR_RWE

2 Adverse events - Safety type 2 inflammatory asthma phenotype population

2.37 Patients with any TEAE: Injection site oedema

2.37.3 By race (Caucasian/white, Black/of African descent, Other)

	Race					
	Caucasian/White		Black/of African descent		Other	
Safety type 2 inflammatory asthma phenotype population	**Placebo (N=101)**	**Dupilumab (N=207)**	**Placebo (N=5)**	**Dupilumab (N=9)**	**Placebo (N=7)**	**Dupilumab (N=18)**
Patients with any TEAE: Injection site oedema [n(%)]	4 (4.0%)	21 (10.1%)	0	0	0	2 (11.1%)
Odds Ratio (95% CI)	-	2.74 (0.91 to 8.20)	-	NE (NE to NE)	-	NE (NE to NE)
p-value for Odds Ratio		0.072		NE		NE
Peto Odds Ratio (95% CI)	-	2.29 (0.96 to 5.45)	-	NE (NE to NE)	-	4.26 (0.18 to 99.71)
Reversed Peto Odds Ratio (95% CI)	-	0.44 (0.18 to 1.04)			-	0.23 (0.01 to 5.56)
p-value for Peto Odds Ratio		0.062		NE		0.368
p-value for heterogeneity of Peto Odds Ratio:						
Caucasian/White, Black/of African descent						NE
Caucasian/White, Other						0.709
Black/of African descent, Other						NE

Odds Ratio and related p-value are estimated by Wald's method using the SAS LOGISTIC procedure.
Peto OR calculation is based on Yusuf S et al. (Prog Cardiovasc Dis. 1985 Mar-Apr;27(5):335-71) and its p-value is derived using a normal approximation.
Risk Ratio and related p-value are estimated by using the SAS FREQ procedure.
Risk Difference and related p-value are estimated by using the SAS GLIMMIX procedure with the following model: criterion = treatment.
p-values for heterogeneity are estimated by using the SAS GLIMMIX procedure with the following model: criterion = treatment subgroup treatment*subgroup.
p-value for heterogeneity of Peto Odds Ratio is estimated by using normal approximation.
PGM=DEVOPS/SAR231893/EFC14153/CSR_RWE/REPORT/PGM/ae_evt_ger_subg_s2_t.sas OUT=REPORT/OUTPUT/ae_ptinjo_ger_race_s2_t_x.rtf (12AUG2021 - 11:43)

Project Code / Study Number / Analysis: SAR231893 / EFC14153 / CSR_RWE

2 Adverse events - Safety type 2 inflammatory asthma phenotype population

2.37 Patients with any TEAE: Injection site oedema

2.37.3 By race (Caucasian/white, Black/of African descent, Other)

	Race					
	Caucasian/White		Black/of African descent		Other	
Safety type 2 inflammatory asthma phenotype population	**Placebo (N=101)**	**Dupilumab (N=207)**	**Placebo (N=5)**	**Dupilumab (N=9)**	**Placebo (N=7)**	**Dupilumab (N=18)**
overall						NE
Risk Ratio (95% CI)	-	2.56 (0.90 to 7.27)	-	NE (NE to NE)	-	NE (NE to NE)
Reversed Risk ratio (95% CI)	-	0.39 (0.14 to 1.11)				
p-value for Risk Ratio		0.077		NE		NE
p-value for heterogeneity of Risk Ratio:						
Caucasian/White, Black/of African descent						0.999
Caucasian/White, Other						0.987
Black/of African descent, Other						0.992
overall						1.000
Risk Difference (95% CI)	-	6.18 (0.56 to 11.81)	-	0.00 (NE to NE)	-	11.11 (NE to NE)
p-value for Risk Difference		0.031		NE		<0.001

Odds Ratio and related p-value are estimated by Wald's method using the SAS LOGISTIC procedure.
Peto OR calculation is based on Yusuf S et al. (Prog Cardiovasc Dis. 1985 Mar-Apr;27(5):335-71) and its p-value is derived using a normal approximation.
Risk Ratio and related p-value are estimated by using the SAS FREQ procedure.
Risk Difference and related p-value are estimated by using the SAS GLIMMIX procedure with the following model: criterion = treatment.
p-values for heterogeneity are estimated by using the SAS GLIMMIX procedure with the following model: criterion = treatment subgroup treatment*subgroup.
p-value for heterogeneity of Peto Odds Ratio is estimated by using normal approximation.
PGM=DEVOPS/SAR231893/EFC14153/CSR_RWE/REPORT/PGM/ae_evt_ger_subg_s2_t.sas OUT=REPORT/OUTPUT/ae_ptinjo_ger_race_s2_t_x.rtf (12AUG2021 - 11:43)

Project Code / Study Number / Analysis: SAR231893 / EFC14153 / CSR_RWE

2 Adverse events - Safety type 2 inflammatory asthma phenotype population

2.37 Patients with any TEAE: Injection site oedema

2.37.3 By race (Caucasian/white, Black/of African descent, Other)

	Race					
	Caucasian/White		Black/of African descent		Other	
Safety type 2 inflammatory asthma phenotype population	**Placebo (N=101)**	**Dupilumab (N=207)**	**Placebo (N=5)**	**Dupilumab (N=9)**	**Placebo (N=7)**	**Dupilumab (N=18)**
p-value for heterogeneity of Risk Difference:						
Caucasian/White, Black/of African descent						<0.001
Caucasian/White, Other						<0.001
Black/of African descent, Other						<0.001
overall						<0.001

Odds Ratio and related p-value are estimated by Wald's method using the SAS LOGISTIC procedure.
Peto OR calculation is based on Yusuf S et al. (Prog Cardiovasc Dis. 1985 Mar-Apr;27(5):335-71) and its p-value is derived using a normal approximation.
Risk Ratio and related p-value are estimated by using the SAS FREQ procedure.
Risk Difference and related p-value are estimated by using the SAS GLIMMIX procedure with the following model: criterion = treatment.
p-values for heterogeneity are estimated by using the SAS GLIMMIX procedure with the following model: criterion = treatment subgroup treatment*subgroup.
p-value for heterogeneity of Peto Odds Ratio is estimated by using normal approximation.
PGM=DEVOPS/SAR231893/EFC14153/CSR_RWE/REPORT/PGM/ae_evt_ger_subg_s2_t.sas OUT=REPORT/OUTPUT/ae_ptinjo_ger_race_s2_t_x.rtf (12AUG2021 - 11:43)

Project Code / Study Number / Analysis: SAR231893 / EFC14153 / CSR_RWE

2 Adverse events - Safety type 2 inflammatory asthma phenotype population

2.37 Patients with any TEAE: Injection site oedema

2.37.4 By baseline ICS dose level (Medium, High)

Safety type 2 inflammatory asthma phenotype population	Baseline ICS dose level: High – Placebo (N=50)	High – Dupilumab (N=101)	Medium – Placebo (N=63)	Medium – Dupilumab (N=131)
Patients with any TEAE: Injection site oedema [n(%)]	3 (6.0%)	7 (6.9%)	1 (1.6%)	15 (11.5%)
Odds Ratio (95% CI)	-	1.17 (0.29 to 4.72)	-	8.01 (1.03 to 62.08)
p-value for Odds Ratio		0.829		0.046
p-value for heterogeneity of Odds Ratio				0.128
Risk Ratio (95% CI)	-	1.16 (0.31 to 4.28)	-	7.21 (0.97 to 53.40)
Reversed Risk ratio (95% CI)	-	0.87 (0.23 to 3.21)	-	0.14 (0.02 to 1.03)
p-value for Risk Ratio		0.829		0.053
p-value for heterogeneity of Risk Ratio				0.134

Odds Ratio and related p-value are estimated by Wald's method using the SAS LOGISTIC procedure.
Peto OR calculation is based on Yusuf S et al. (Prog Cardiovasc Dis. 1985 Mar-Apr;27(5):335-71) and its p-value is derived using a normal approximation.
Risk Ratio and related p-value are estimated by using the SAS FREQ procedure.
Risk Difference and related p-value are estimated by using the SAS GLIMMIX procedure with the following model: criterion = treatment.
p-values for heterogeneity are estimated by using the SAS GLIMMIX procedure with the following model: criterion = treatment subgroup treatment*subgroup.
p-value for heterogeneity of Peto Odds Ratio is estimated by using normal approximation.
PGM=DEVOPS/SAR231893/EFC14153/CSR_RWE/REPORT/PGM/ae_evt_ger_subg_s2_t.sas OUT=REPORT/OUTPUT/ae_ptinjo_ger_ics_s2_t_x.rtf (12AUG2021 - 11:43)

Project Code / Study Number / Analysis: SAR231893 / EFC14153 / CSR_RWE

2 Adverse events - Safety type 2 inflammatory asthma phenotype population

2.37 Patients with any TEAE: Injection site oedema

2.37.4 By baseline ICS dose level (Medium, High)

	Baseline ICS dose level			
	High		Medium	
Safety type 2 inflammatory asthma phenotype population	**Placebo (N=50)**	**Dupilumab (N=101)**	**Placebo (N=63)**	**Dupilumab (N=131)**
Risk Difference (95% CI)	-	0.93 (-7.37 to 9.24)	-	9.86 (3.56 to 16.17)
p-value for Risk Difference		0.825		0.002
p-value for heterogeneity of Risk Difference				0.092

Odds Ratio and related p-value are estimated by Wald's method using the SAS LOGISTIC procedure.
Peto OR calculation is based on Yusuf S et al. (Prog Cardiovasc Dis. 1985 Mar-Apr;27(5):335-71) and its p-value is derived using a normal approximation.
Risk Ratio and related p-value are estimated by using the SAS FREQ procedure.
Risk Difference and related p-value are estimated by using the SAS GLIMMIX procedure with the following model: criterion = treatment.
p-values for heterogeneity are estimated by using the SAS GLIMMIX procedure with the following model: criterion = treatment subgroup treatment*subgroup.
p-value for heterogeneity of Peto Odds Ratio is estimated by using normal approximation.
PGM=DEVOPS/SAR231893/EFC14153/CSR_RWE/REPORT/PGM/ae_evt_ger_subg_s2_t.sas OUT=REPORT/OUTPUT/ae_ptinjo_ger_ics_s2_t_x.rtf (12AUG2021 - 11:43)

Project Code / Study Number / Analysis: SAR231893 / EFC14153 / CSR_RWE

2 Adverse events - Safety type 2 inflammatory asthma phenotype population

2.37 Patients with any TEAE: Injection site oedema

2.37.5 By baseline ICS dose level 2 (Medium, High)

Safety type 2 inflammatory asthma phenotype population	Baseline ICS dose level 2			
	High		Medium	
	Placebo (N=94)	Dupilumab (N=199)	Placebo (N=19)	Dupilumab (N=35)
Patients with any TEAE: Injection site oedema [n(%)]	4 (4.3%)	20 (10.1%)	0	3 (8.6%)
Odds Ratio (95% CI)	-	2.51 (0.83 to 7.57)	-	NE (NE to NE)
p-value for Odds Ratio		0.101		NE
Peto Odds Ratio (95% CI)	-	2.16 (0.88 to 5.26)	-	4.97 (0.44 to 55.64)
Reversed Peto Odds Ratio (95% CI)	-	0.46 (0.19 to 1.14)	-	0.20 (0.02 to 2.27)
p-value for Peto Odds Ratio		0.092		0.193
p-value for heterogeneity of Peto Odds Ratio				0.525
Risk Ratio (95% CI)	-	2.36 (0.83 to 6.72)	-	NE (NE to NE)
Reversed Risk ratio (95% CI)	-	0.42 (0.15 to 1.20)		

Odds Ratio and related p-value are estimated by Wald's method using the SAS LOGISTIC procedure.
Peto OR calculation is based on Yusuf S et al. (Prog Cardiovasc Dis. 1985 Mar-Apr;27(5):335-71) and its p-value is derived using a normal approximation.
Risk Ratio and related p-value are estimated by using the SAS FREQ procedure.
Risk Difference and related p-value are estimated by using the SAS GLIMMIX procedure with the following model: criterion = treatment.
p-values for heterogeneity are estimated by using the SAS GLIMMIX procedure with the following model: criterion = treatment subgroup treatment*subgroup.
p-value for heterogeneity of Peto Odds Ratio is estimated by using normal approximation.
PGM=DEVOPS/SAR231893/EFC14153/CSR_RWE/REPORT/PGM/ae_evt_ger_subg_s2_t.sas OUT=REPORT/OUTPUT/ae_ptinjo_ger_ics2_s2_t_x.rtf (01SEP2021 - 16:11)

Project Code / Study Number / Analysis: SAR231893 / EFC14153 / CSR_RWE

2 Adverse events - Safety type 2 inflammatory asthma phenotype population

2.37 Patients with any TEAE: Injection site oedema

2.37.5 By baseline ICS dose level 2 (Medium, High)

	Baseline ICS dose level 2			
	High		Medium	
Safety type 2 inflammatory asthma phenotype population	**Placebo (N=94)**	**Dupilumab (N=199)**	**Placebo (N=19)**	**Dupilumab (N=35)**
p-value for Risk Ratio		0.107		NE
p-value for heterogeneity of Risk Ratio				0.980
Risk Difference (95% CI)	-	5.79 (-0.07 to 11.66)	-	8.57 (NE to NE)
p-value for Risk Difference		0.053		<0.001
p-value for heterogeneity of Risk Difference				<0.001

Odds Ratio and related p-value are estimated by Wald's method using the SAS LOGISTIC procedure.
Peto OR calculation is based on Yusuf S et al. (Prog Cardiovasc Dis. 1985 Mar-Apr;27(5):335-71) and its p-value is derived using a normal approximation.
Risk Ratio and related p-value are estimated by using the SAS FREQ procedure.
Risk Difference and related p-value are estimated by using the SAS GLIMMIX procedure with the following model: criterion = treatment.
p-values for heterogeneity are estimated by using the SAS GLIMMIX procedure with the following model: criterion = treatment subgroup treatment*subgroup.
p-value for heterogeneity of Peto Odds Ratio is estimated by using normal approximation.
PGM=DEVOPS/SAR231893/EFC14153/CSR_RWE/REPORT/PGM/ae_evt_ger_subg_s2_t.sas OUT=REPORT/OUTPUT/ae_ptinjo_ger_ics2_s2_t_x.rtf (01SEP2021 - 16:11)

Project Code / Study Number / Analysis: SAR231893 / EFC14153 / CSR_RWE

2 Adverse events - Safety type 2 inflammatory asthma phenotype population

2.37 Patients with any TEAE: Injection site oedema

2.37.6 By baseline predicted FEV1 (<80%, >=80%)

	Baseline Predicted FEV1			
	<80%		>=80%	
Safety type 2 inflammatory asthma phenotype population	**Placebo (N=58)**	**Dupilumab (N=116)**	**Placebo (N=55)**	**Dupilumab (N=118)**
Patients with any TEAE: Injection site oedema [n(%)]	2 (3.4%)	13 (11.2%)	2 (3.6%)	10 (8.5%)
Odds Ratio (95% CI)	-	3.53 (0.77 to 16.22)	-	2.45 (0.52 to 11.60)
p-value for Odds Ratio		0.104		0.257
p-value for heterogeneity of Odds Ratio				0.743
Risk Ratio (95% CI)	-	3.25 (0.76 to 13.92)	-	2.33 (0.53 to 10.28)
Reversed Risk ratio (95% CI)	-	0.31 (0.07 to 1.32)	-	0.43 (0.10 to 1.89)
p-value for Risk Ratio		0.112		0.264
p-value for heterogeneity of Risk Ratio				0.754

Odds Ratio and related p-value are estimated by Wald's method using the SAS LOGISTIC procedure.
Peto OR calculation is based on Yusuf S et al. (Prog Cardiovasc Dis. 1985 Mar-Apr;27(5):335-71) and its p-value is derived using a normal approximation.
Risk Ratio and related p-value are estimated by using the SAS FREQ procedure.
Risk Difference and related p-value are estimated by using the SAS GLIMMIX procedure with the following model: criterion = treatment.
p-values for heterogeneity are estimated by using the SAS GLIMMIX procedure with the following model: criterion = treatment subgroup treatment*subgroup.
p-value for heterogeneity of Peto Odds Ratio is estimated by using normal approximation.
PGM=DEVOPS/SAR231893/EFC14153/CSR_RWE/REPORT/PGM/ae_evt_ger_subg_s2_t.sas OUT=REPORT/OUTPUT/ae_ptinjo_ger_pfev1_s2_t_x.rtf (12AUG2021 - 11:43)

Project Code / Study Number / Analysis: SAR231893 / EFC14153 / CSR_RWE

2 Adverse events - Safety type 2 inflammatory asthma phenotype population

2.37 Patients with any TEAE: Injection site oedema

2.37.6 By baseline predicted FEV1 (<80%, >=80%)

	Baseline Predicted FEV1			
	<80%		>=80%	
Safety type 2 inflammatory asthma phenotype population	**Placebo (N=58)**	**Dupilumab (N=116)**	**Placebo (N=55)**	**Dupilumab (N=118)**
Risk Difference (95% CI)	-	7.76 (0.29 to 15.23)	-	4.84 (-2.26 to 11.94)
p-value for Risk Difference		0.042		0.180
p-value for heterogeneity of Risk Difference				0.576

Odds Ratio and related p-value are estimated by Wald's method using the SAS LOGISTIC procedure.
Peto OR calculation is based on Yusuf S et al. (Prog Cardiovasc Dis. 1985 Mar-Apr;27(5):335-71) and its p-value is derived using a normal approximation.
Risk Ratio and related p-value are estimated by using the SAS FREQ procedure.
Risk Difference and related p-value are estimated by using the SAS GLIMMIX procedure with the following model: criterion = treatment.
p-values for heterogeneity are estimated by using the SAS GLIMMIX procedure with the following model: criterion = treatment subgroup treatment*subgroup.
p-value for heterogeneity of Peto Odds Ratio is estimated by using normal approximation.
PGM=DEVOPS/SAR231893/EFC14153/CSR_RWE/REPORT/PGM/ae_evt_ger_subg_s2_t.sas OUT=REPORT/OUTPUT/ae_ptinjo_ger_pfev1_s2_t_x.rtf (12AUG2021 - 11:43)

Project Code / Study Number / Analysis: SAR231893 / EFC14153 / CSR_RWE

2 Adverse events - Safety type 2 inflammatory asthma phenotype population

2.37 Patients with any TEAE: Injection site oedema

2.37.7 By baseline ACQ-7-IA (<=2, >2)

	Baseline ACQ-7-IA			
	<=2		>2	
Safety type 2 inflammatory asthma phenotype population	**Placebo (N=61)**	**Dupilumab (N=125)**	**Placebo (N=52)**	**Dupilumab (N=109)**
Patients with any TEAE: Injection site oedema [n(%)]	0	16 (12.8%)	4 (7.7%)	7 (6.4%)
Odds Ratio (95% CI)	-	NE (NE to NE)	-	0.82 (0.23 to 2.95)
p-value for Odds Ratio		NE		0.765
Peto Odds Ratio (95% CI)	-	5.05 (1.70 to 15.00)	-	0.82 (0.22 to 3.02)
Reversed Peto Odds Ratio (95% CI)	-	0.20 (0.07 to 0.59)		
p-value for Peto Odds Ratio		0.004		0.766
p-value for heterogeneity of Peto Odds Ratio				0.036
Risk Ratio (95% CI)	-	NE (NE to NE)	-	0.83 (0.26 to 2.73)
p-value for Risk Ratio		NE		0.765

Odds Ratio and related p-value are estimated by Wald's method using the SAS LOGISTIC procedure.
Peto OR calculation is based on Yusuf S et al. (Prog Cardiovasc Dis. 1985 Mar-Apr;27(5):335-71) and its p-value is derived using a normal approximation.
Risk Ratio and related p-value are estimated by using the SAS FREQ procedure.
Risk Difference and related p-value are estimated by using the SAS GLIMMIX procedure with the following model: criterion = treatment.
p-values for heterogeneity are estimated by using the SAS GLIMMIX procedure with the following model: criterion = treatment subgroup treatment*subgroup.
p-value for heterogeneity of Peto Odds Ratio is estimated by using normal approximation.
PGM=DEVOPS/SAR231893/EFC14153/CSR_RWE/REPORT/PGM/ae_evt_ger_subg_s2_t.sas OUT=REPORT/OUTPUT/ae_ptinjo_ger_acq7_s2_t_x.rtf (12AUG2021 - 11:43)

Project Code / Study Number / Analysis: SAR231893 / EFC14153 / CSR_RWE

2 Adverse events - Safety type 2 inflammatory asthma phenotype population

2.37 Patients with any TEAE: Injection site oedema

2.37.7 By baseline ACQ-7-IA (<=2, >2)

	Baseline ACQ-7-IA			
	<=2		>2	
Safety type 2 inflammatory asthma phenotype population	**Placebo (N=61)**	**Dupilumab (N=125)**	**Placebo (N=52)**	**Dupilumab (N=109)**
p-value for heterogeneity of Risk Ratio				0.973
Risk Difference (95% CI)	-	12.80 (NE to NE)	-	-1.27 (-9.92 to 7.38)
p-value for Risk Difference		<0.001		0.772
p-value for heterogeneity of Risk Difference				<0.001

Odds Ratio and related p-value are estimated by Wald's method using the SAS LOGISTIC procedure.
Peto OR calculation is based on Yusuf S et al. (Prog Cardiovasc Dis. 1985 Mar-Apr;27(5):335-71) and its p-value is derived using a normal approximation.
Risk Ratio and related p-value are estimated by using the SAS FREQ procedure.
Risk Difference and related p-value are estimated by using the SAS GLIMMIX procedure with the following model: criterion = treatment.
p-values for heterogeneity are estimated by using the SAS GLIMMIX procedure with the following model: criterion = treatment subgroup treatment*subgroup.
p-value for heterogeneity of Peto Odds Ratio is estimated by using normal approximation.
PGM=DEVOPS/SAR231893/EFC14153/CSR_RWE/REPORT/PGM/ae_evt_ger_subg_s2_t.sas OUT=REPORT/OUTPUT/ae_ptinjo_ger_acq7_s2_t_x.rtf (12AUG2021 - 11:43)

Project Code / Study Number / Analysis: SAR231893 / EFC14153 / CSR_RWE

2 Adverse events - Safety type 2 inflammatory asthma phenotype population

2.37 Patients with any TEAE: Injection site oedema

2.37.8 By baseline weight (<=30 kg, >30 kg)

	Baseline weight (kg)			
	<=30		>30	
Safety type 2 inflammatory asthma phenotype population	**Placebo (N=36)**	**Dupilumab (N=74)**	**Placebo (N=77)**	**Dupilumab (N=160)**
Patients with any TEAE: Injection site oedema [n(%)]	0	6 (8.1%)	4 (5.2%)	17 (10.6%)
Odds Ratio (95% CI)	-	NE (NE to NE)	-	2.17 (0.70 to 6.68)
p-value for Odds Ratio		NE		0.177
Peto Odds Ratio (95% CI)	-	4.75 (0.83 to 27.21)	-	1.95 (0.75 to 5.07)
Reversed Peto Odds Ratio (95% CI)	-	0.21 (0.04 to 1.20)	-	0.51 (0.20 to 1.33)
p-value for Peto Odds Ratio		0.080		0.169
p-value for heterogeneity of Peto Odds Ratio				0.382
Risk Ratio (95% CI)	-	NE (NE to NE)	-	2.05 (0.71 to 5.87)
Reversed Risk ratio (95% CI)			-	0.49 (0.17 to 1.40)

Odds Ratio and related p-value are estimated by Wald's method using the SAS LOGISTIC procedure.
Peto OR calculation is based on Yusuf S et al. (Prog Cardiovasc Dis. 1985 Mar-Apr;27(5):335-71) and its p-value is derived using a normal approximation.
Risk Ratio and related p-value are estimated by using the SAS FREQ procedure.
Risk Difference and related p-value are estimated by using the SAS GLIMMIX procedure with the following model: criterion = treatment.
p-values for heterogeneity are estimated by using the SAS GLIMMIX procedure with the following model: criterion = treatment subgroup treatment*subgroup.
p-value for heterogeneity of Peto Odds Ratio is estimated by using normal approximation.
PGM=DEVOPS/SAR231893/EFC14153/CSR_RWE/REPORT/PGM/ae_evt_ger_subg_s2_t.sas OUT=REPORT/OUTPUT/ae_ptinjo_ger_wgt_s2_t_x.rtf (12AUG2021 - 11:44)

Project Code / Study Number / Analysis: SAR231893 / EFC14153 / CSR_RWE

2 Adverse events - Safety type 2 inflammatory asthma phenotype population

2.37 Patients with any TEAE: Injection site oedema

2.37.8 By baseline weight (<=30 kg, >30 kg)

	Baseline weight (kg)			
	<=30		>30	
Safety type 2 inflammatory asthma phenotype population	**Placebo (N=36)**	**Dupilumab (N=74)**	**Placebo (N=77)**	**Dupilumab (N=160)**
p-value for Risk Ratio		NE		0.184
p-value for heterogeneity of Risk Ratio				0.972
Risk Difference (95% CI)	-	8.11 (NE to NE)	-	5.43 (-1.49 to 12.35)
p-value for Risk Difference		<0.001		0.123
p-value for heterogeneity of Risk Difference				<0.001

Odds Ratio and related p-value are estimated by Wald's method using the SAS LOGISTIC procedure.
Peto OR calculation is based on Yusuf S et al. (Prog Cardiovasc Dis. 1985 Mar-Apr;27(5):335-71) and its p-value is derived using a normal approximation.
Risk Ratio and related p-value are estimated by using the SAS FREQ procedure.
Risk Difference and related p-value are estimated by using the SAS GLIMMIX procedure with the following model: criterion = treatment.
p-values for heterogeneity are estimated by using the SAS GLIMMIX procedure with the following model: criterion = treatment subgroup treatment*subgroup.
p-value for heterogeneity of Peto Odds Ratio is estimated by using normal approximation.
PGM=DEVOPS/SAR231893/EFC14153/CSR_RWE/REPORT/PGM/ae_evt_ger_subg_s2_t.sas OUT=REPORT/OUTPUT/ae_ptinjo_ger_wgt_s2_t_x.rtf (12AUG2021 - 11:44)

Project Code / Study Number / Analysis: SAR231893 / EFC14153 / CSR_RWE

2 Adverse events - Safety type 2 inflammatory asthma phenotype population

2.37 Patients with any TEAE: Injection site oedema

2.37.9 By atopic medical condition (Yes, No)

	Atopic medical condition			
	Yes		No	
Safety type 2 inflammatory asthma phenotype population	**Placebo (N=102)**	**Dupilumab (N=225)**	**Placebo (N=11)**	**Dupilumab (N=9)**
Patients with any TEAE: Injection site oedema [n(%)]	4 (3.9%)	23 (10.2%)	0	0
Odds Ratio (95% CI)	-	2.79 (0.94 to 8.29)	-	NE (NE to NE)
p-value for Odds Ratio		0.065		NE
Peto Odds Ratio (95% CI)	-	2.29 (0.98 to 5.35)	-	NE (NE to NE)
Reversed Peto Odds Ratio (95% CI)	-	0.44 (0.19 to 1.02)		
p-value for Peto Odds Ratio		0.056		NE
p-value for heterogeneity of Peto Odds Ratio				NE
Risk Ratio (95% CI)	-	2.61 (0.93 to 7.34)	-	NE (NE to NE)
Reversed Risk ratio (95% CI)	-	0.38 (0.14 to 1.08)		

Odds Ratio and related p-value are estimated by Wald's method using the SAS LOGISTIC procedure.
Peto OR calculation is based on Yusuf S et al. (Prog Cardiovasc Dis. 1985 Mar-Apr;27(5):335-71) and its p-value is derived using a normal approximation.
Risk Ratio and related p-value are estimated by using the SAS FREQ procedure.
Risk Difference and related p-value are estimated by using the SAS GLIMMIX procedure with the following model: criterion = treatment.
p-values for heterogeneity are estimated by using the SAS GLIMMIX procedure with the following model: criterion = treatment subgroup treatment*subgroup.
p-value for heterogeneity of Peto Odds Ratio is estimated by using normal approximation.
PGM=DEVOPS/SAR231893/EFC14153/CSR_RWE/REPORT/PGM/ae_evt_ger_subg_s2_t.sas OUT=REPORT/OUTPUT/ae_ptinjo_ger_amc_s2_t_x.rtf (12AUG2021 - 11:44)

Project Code / Study Number / Analysis: SAR231893 / EFC14153 / CSR_RWE

2 Adverse events - Safety type 2 inflammatory asthma phenotype population

2.37 Patients with any TEAE: Injection site oedema

2.37.9 By atopic medical condition (Yes, No)

	Atopic medical condition			
	Yes		No	
Safety type 2 inflammatory asthma phenotype population	**Placebo (N=102)**	**Dupilumab (N=225)**	**Placebo (N=11)**	**Dupilumab (N=9)**
p-value for Risk Ratio		0.070		NE
p-value for heterogeneity of Risk Ratio				0.999
Risk Difference (95% CI)	-	6.30 (0.82 to 11.79)	-	0.00 (NE to NE)
p-value for Risk Difference		0.024		NE
p-value for heterogeneity of Risk Difference				<0.001

Odds Ratio and related p-value are estimated by Wald's method using the SAS LOGISTIC procedure.
Peto OR calculation is based on Yusuf S et al. (Prog Cardiovasc Dis. 1985 Mar-Apr;27(5):335-71) and its p-value is derived using a normal approximation.
Risk Ratio and related p-value are estimated by using the SAS FREQ procedure.
Risk Difference and related p-value are estimated by using the SAS GLIMMIX procedure with the following model: criterion = treatment.
p-values for heterogeneity are estimated by using the SAS GLIMMIX procedure with the following model: criterion = treatment subgroup treatment*subgroup.
p-value for heterogeneity of Peto Odds Ratio is estimated by using normal approximation.
PGM=DEVOPS/SAR231893/EFC14153/CSR_RWE/REPORT/PGM/ae_evt_ger_subg_s2_t.sas OUT=REPORT/OUTPUT/ae_ptinjo_ger_amc_s2_t_x.rtf (12AUG2021 - 11:44)

Project Code / Study Number / Analysis: SAR231893 / EFC14153 / CSR_RWE

2 Adverse events - Safety type 2 inflammatory asthma phenotype population

2.37 Patients with any TEAE: Injection site oedema

2.37.10 By baseline total IgE (<median, >= median)

	Baseline Total IgE (IU/mL)			
	<median		>=median	
Safety type 2 inflammatory asthma phenotype population	**Placebo (N=65)**	**Dupilumab (N=106)**	**Placebo (N=47)**	**Dupilumab (N=124)**
Patients with any TEAE: Injection site oedema [n(%)]	3 (4.6%)	11 (10.4%)	1 (2.1%)	12 (9.7%)
Odds Ratio (95% CI)	-	2.39 (0.64 to 8.92)	-	4.93 (0.62 to 39.00)
p-value for Odds Ratio		0.194		0.131
p-value for heterogeneity of Odds Ratio				0.564
Risk Ratio (95% CI)	-	2.25 (0.65 to 7.76)	-	4.55 (0.61 to 34.02)
Reversed Risk ratio (95% CI)	-	0.44 (0.13 to 1.53)	-	0.22 (0.03 to 1.64)
p-value for Risk Ratio		0.200		0.140
p-value for heterogeneity of Risk Ratio				0.559

Odds Ratio and related p-value are estimated by Wald's method using the SAS LOGISTIC procedure.
Peto OR calculation is based on Yusuf S et al. (Prog Cardiovasc Dis. 1985 Mar-Apr;27(5):335-71) and its p-value is derived using a normal approximation.
Risk Ratio and related p-value are estimated by using the SAS FREQ procedure.
Risk Difference and related p-value are estimated by using the SAS GLIMMIX procedure with the following model: criterion = treatment.
p-values for heterogeneity are estimated by using the SAS GLIMMIX procedure with the following model: criterion = treatment subgroup treatment*subgroup.
p-value for heterogeneity of Peto Odds Ratio is estimated by using normal approximation.
PGM=DEVOPS/SAR231893/EFC14153/CSR_RWE/REPORT/PGM/ae_evt_ger_subg_s2_t.sas OUT=REPORT/OUTPUT/ae_ptinjo_ger_igem_s2_t_x.rtf (12AUG2021 - 11:44)

Project Code / Study Number / Analysis: SAR231893 / EFC14153 / CSR_RWE

2 Adverse events - Safety type 2 inflammatory asthma phenotype population

2.37 Patients with any TEAE: Injection site oedema

2.37.10 By baseline total IgE (<median, >= median)

	Baseline Total IgE (IU/mL)			
	<median		>=median	
Safety type 2 inflammatory asthma phenotype population	**Placebo (N=65)**	**Dupilumab (N=106)**	**Placebo (N=47)**	**Dupilumab (N=124)**
Risk Difference (95% CI)	-	5.76 (-2.02 to 13.55)	-	7.55 (0.86 to 14.24)
p-value for Risk Difference		0.146		0.027
p-value for heterogeneity of Risk Difference				0.731

Odds Ratio and related p-value are estimated by Wald's method using the SAS LOGISTIC procedure.
Peto OR calculation is based on Yusuf S et al. (Prog Cardiovasc Dis. 1985 Mar-Apr;27(5):335-71) and its p-value is derived using a normal approximation.
Risk Ratio and related p-value are estimated by using the SAS FREQ procedure.
Risk Difference and related p-value are estimated by using the SAS GLIMMIX procedure with the following model: criterion = treatment.
p-values for heterogeneity are estimated by using the SAS GLIMMIX procedure with the following model: criterion = treatment subgroup treatment*subgroup.
p-value for heterogeneity of Peto Odds Ratio is estimated by using normal approximation.
PGM=DEVOPS/SAR231893/EFC14153/CSR_RWE/REPORT/PGM/ae_evt_ger_subg_s2_t.sas OUT=REPORT/OUTPUT/ae_ptinjo_ger_igem_s2_t_x.rtf (12AUG2021 - 11:44)

Project Code / Study Number / Analysis: SAR231893 / EFC14153 / CSR_RWE

2 Adverse events - Safety type 2 inflammatory asthma phenotype population

2.37 Patients with any TEAE: Injection site oedema

2.37.11 By baseline total IgE (<100 IU/ml, >= 100 IU/ml)

	Baseline Total IgE (IU/mL)			
	< 100		>= 100	
Safety type 2 inflammatory asthma phenotype population	**Placebo (N=22)**	**Dupilumab (N=29)**	**Placebo (N=90)**	**Dupilumab (N=201)**
Patients with any TEAE: Injection site oedema [n(%)]	1 (4.5%)	5 (17.2%)	3 (3.3%)	18 (9.0%)
Odds Ratio (95% CI)	-	4.37 (0.47 to 40.50)	-	2.85 (0.82 to 9.94)
p-value for Odds Ratio		0.194		0.100
p-value for heterogeneity of Odds Ratio				0.743
Risk Ratio (95% CI)	-	3.79 (0.48 to 30.19)	-	2.69 (0.81 to 8.89)
Reversed Risk ratio (95% CI)	-	0.26 (0.03 to 2.10)	-	0.37 (0.11 to 1.23)
p-value for Risk Ratio		0.208		0.106
p-value for heterogeneity of Risk Ratio				0.778

Odds Ratio and related p-value are estimated by Wald's method using the SAS LOGISTIC procedure.
Peto OR calculation is based on Yusuf S et al. (Prog Cardiovasc Dis. 1985 Mar-Apr;27(5):335-71) and its p-value is derived using a normal approximation.
Risk Ratio and related p-value are estimated by using the SAS FREQ procedure.
Risk Difference and related p-value are estimated by using the SAS GLIMMIX procedure with the following model: criterion = treatment.
p-values for heterogeneity are estimated by using the SAS GLIMMIX procedure with the following model: criterion = treatment subgroup treatment*subgroup.
p-value for heterogeneity of Peto Odds Ratio is estimated by using normal approximation.
PGM=DEVOPS/SAR231893/EFC14153/CSR_RWE/REPORT/PGM/ae_evt_ger_subg_s2_t.sas OUT=REPORT/OUTPUT/ae_ptinjo_ger_ige_s2_t_x.rtf (12AUG2021 - 11:44)

Project Code / Study Number / Analysis: SAR231893 / EFC14153 / CSR_RWE

2 Adverse events - Safety type 2 inflammatory asthma phenotype population

2.37 Patients with any TEAE: Injection site oedema

2.37.11 By baseline total IgE (<100 IU/ml, >= 100 IU/ml)

	Baseline Total IgE (IU/mL)			
	< 100		>= 100	
Safety type 2 inflammatory asthma phenotype population	**Placebo (N=22)**	**Dupilumab (N=29)**	**Placebo (N=90)**	**Dupilumab (N=201)**
Risk Difference (95% CI)	-	12.70 (-3.99 to 29.38)	-	5.62 (0.18 to 11.06)
p-value for Risk Difference		0.133		0.043
p-value for heterogeneity of Risk Difference				0.419

Odds Ratio and related p-value are estimated by Wald's method using the SAS LOGISTIC procedure.
Peto OR calculation is based on Yusuf S et al. (Prog Cardiovasc Dis. 1985 Mar-Apr;27(5):335-71) and its p-value is derived using a normal approximation.
Risk Ratio and related p-value are estimated by using the SAS FREQ procedure.
Risk Difference and related p-value are estimated by using the SAS GLIMMIX procedure with the following model: criterion = treatment.
p-values for heterogeneity are estimated by using the SAS GLIMMIX procedure with the following model: criterion = treatment subgroup treatment*subgroup.
p-value for heterogeneity of Peto Odds Ratio is estimated by using normal approximation.
PGM=DEVOPS/SAR231893/EFC14153/CSR_RWE/REPORT/PGM/ae_evt_ger_subg_s2_t.sas OUT=REPORT/OUTPUT/ae_ptinjo_ger_ige_s2_t_x.rtf (12AUG2021 - 11:44)

Project Code / Study Number / Analysis: SAR231893 / EFC14153 / CSR_RWE

2 Adverse events - Safety type 2 inflammatory asthma phenotype population

2.37 Patients with any TEAE: Injection site oedema

2.37.12 By age at onset of asthma (0-2, 3-5, >=6 years)

	Age of onset of asthma (years)					
	0-2		3-5		>= 6	
Safety type 2 inflammatory asthma phenotype population	**Placebo (N=40)**	**Dupilumab (N=104)**	**Placebo (N=38)**	**Dupilumab (N=85)**	**Placebo (N=35)**	**Dupilumab (N=45)**
Patients with any TEAE: Injection site oedema [n(%)]	0	8 (7.7%)	2 (5.3%)	11 (12.9%)	2 (5.7%)	4 (8.9%)
Odds Ratio (95% CI)	-	NE (NE to NE)	-	2.68 (0.56 to 12.71)	-	1.61 (0.28 to 9.34)
p-value for Odds Ratio		NE		0.216		0.596
Peto Odds Ratio (95% CI)	-	4.29 (0.88 to 20.95)	-	2.24 (0.65 to 7.73)	-	1.57 (0.30 to 8.32)
Reversed Peto Odds Ratio (95% CI)	-	0.23 (0.05 to 1.14)	-	0.45 (0.13 to 1.54)	-	0.64 (0.12 to 3.33)
p-value for Peto Odds Ratio		0.072		0.202		0.595
p-value for heterogeneity of Peto Odds Ratio:						
0-2, 3-5						0.527
0-2, >= 6						0.392
3-5, >= 6						0.738

Odds Ratio and related p-value are estimated by Wald's method using the SAS LOGISTIC procedure.
Peto OR calculation is based on Yusuf S et al. (Prog Cardiovasc Dis. 1985 Mar-Apr;27(5):335-71) and its p-value is derived using a normal approximation.
Risk Ratio and related p-value are estimated by using the SAS FREQ procedure.
Risk Difference and related p-value are estimated by using the SAS GLIMMIX procedure with the following model: criterion = treatment.
p-values for heterogeneity are estimated by using the SAS GLIMMIX procedure with the following model: criterion = treatment subgroup treatment*subgroup.
p-value for heterogeneity of Peto Odds Ratio is estimated by using normal approximation.
PGM=DEVOPS/SAR231893/EFC14153/CSR_RWE/REPORT/PGM/ae_evt_ger_subg_s2_t.sas OUT=REPORT/OUTPUT/ae_ptinjo_ger_onsa_s2_t_x.rtf (12AUG2021 - 11:45)

Project Code / Study Number / Analysis: SAR231893 / EFC14153 / CSR_RWE

2 Adverse events - Safety type 2 inflammatory asthma phenotype population

2.37 Patients with any TEAE: Injection site oedema

2.37.12 By age at onset of asthma (0-2, 3-5, >=6 years)

	Age of onset of asthma (years)					
	0-2		3-5		>= 6	
Safety type 2 inflammatory asthma phenotype population	**Placebo (N=40)**	**Dupilumab (N=104)**	**Placebo (N=38)**	**Dupilumab (N=85)**	**Placebo (N=35)**	**Dupilumab (N=45)**
overall						0.680
Risk Ratio (95% CI)	-	NE (NE to NE)	-	2.46 (0.57 to 10.56)	-	1.56 (0.30 to 8.01)
Reversed Risk ratio (95% CI)			-	0.41 (0.09 to 1.75)	-	0.64 (0.12 to 3.31)
p-value for Risk Ratio		NE		0.226		0.597
p-value for heterogeneity of Risk Ratio:						
0-2, 3-5						0.971
0-2, >= 6						0.970
3-5, >= 6						0.683
overall						0.919
Risk Difference (95% CI)	-	7.69 (NE to NE)	-	7.68 (-2.49 to 17.85)	-	3.17 (-8.33 to 14.68)
p-value for Risk Difference		<0.001		0.138		0.584

Odds Ratio and related p-value are estimated by Wald's method using the SAS LOGISTIC procedure.
Peto OR calculation is based on Yusuf S et al. (Prog Cardiovasc Dis. 1985 Mar-Apr;27(5):335-71) and its p-value is derived using a normal approximation.
Risk Ratio and related p-value are estimated by using the SAS FREQ procedure.
Risk Difference and related p-value are estimated by using the SAS GLIMMIX procedure with the following model: criterion = treatment.
p-values for heterogeneity are estimated by using the SAS GLIMMIX procedure with the following model: criterion = treatment subgroup treatment*subgroup.
p-value for heterogeneity of Peto Odds Ratio is estimated by using normal approximation.
PGM=DEVOPS/SAR231893/EFC14153/CSR_RWE/REPORT/PGM/ae_evt_ger_subg_s2_t.sas OUT=REPORT/OUTPUT/ae_ptinjo_ger_onsa_s2_t_x.rtf (12AUG2021 - 11:45)

Project Code / Study Number / Analysis: SAR231893 / EFC14153 / CSR_RWE

2 Adverse events - Safety type 2 inflammatory asthma phenotype population

2.37 Patients with any TEAE: Injection site oedema

2.37.12 By age at onset of asthma (0-2, 3-5, >=6 years)

	Age of onset of asthma (years)					
	0-2		3-5		>= 6	
Safety type 2 inflammatory asthma phenotype population	**Placebo (N=40)**	**Dupilumab (N=104)**	**Placebo (N=38)**	**Dupilumab (N=85)**	**Placebo (N=35)**	**Dupilumab (N=45)**
p-value for heterogeneity of Risk Difference:						
0-2, 3-5						0.999
0-2, >= 6						<0.001
3-5, >= 6						0.561
overall						0.561

Odds Ratio and related p-value are estimated by Wald's method using the SAS LOGISTIC procedure.
Peto OR calculation is based on Yusuf S et al. (Prog Cardiovasc Dis. 1985 Mar-Apr;27(5):335-71) and its p-value is derived using a normal approximation.
Risk Ratio and related p-value are estimated by using the SAS FREQ procedure.
Risk Difference and related p-value are estimated by using the SAS GLIMMIX procedure with the following model: criterion = treatment.
p-values for heterogeneity are estimated by using the SAS GLIMMIX procedure with the following model: criterion = treatment subgroup treatment*subgroup.
p-value for heterogeneity of Peto Odds Ratio is estimated by using normal approximation.
PGM=DEVOPS/SAR231893/EFC14153/CSR_RWE/REPORT/PGM/ae_evt_ger_subg_s2_t.sas OUT=REPORT/OUTPUT/ae_ptinjo_ger_onsa_s2_t_x.rtf (12AUG2021 - 11:45)

Project Code / Study Number / Analysis: SAR231893 / EFC14153 / CSR_RWE

2 Adverse events - Safety type 2 inflammatory asthma phenotype population

2.37 Patients with any TEAE: Injection site oedema

2.37.13 By number of severe asthma exacerbation prior to the study (<=1, 2, >2)

	Number of severe asthma exacerbation prior to the study					
	<=1		2		>2	
Safety type 2 inflammatory asthma phenotype population	**Placebo (N=46)**	**Dupilumab (N=85)**	**Placebo (N=32)**	**Dupilumab (N=75)**	**Placebo (N=35)**	**Dupilumab (N=74)**
Patients with any TEAE: Injection site oedema [n(%)]	2 (4.3%)	9 (10.6%)	0	7 (9.3%)	2 (5.7%)	7 (9.5%)
Odds Ratio (95% CI)	-	2.61 (0.54 to 12.60)	-	NE (NE to NE)	-	1.72 (0.34 to 8.76)
p-value for Odds Ratio		0.234		NE		0.511
Peto Odds Ratio (95% CI)	-	2.24 (0.62 to 8.11)	-	4.54 (0.86 to 24.00)	-	1.63 (0.38 to 6.99)
Reversed Peto Odds Ratio (95% CI)	-	0.45 (0.12 to 1.61)	-	0.22 (0.04 to 1.16)	-	0.61 (0.14 to 2.63)
p-value for Peto Odds Ratio		0.221		0.075		0.509
p-value for heterogeneity of Peto Odds Ratio:						
<=1, 2						0.511
<=1, >2						0.751
2, >2						0.365

Odds Ratio and related p-value are estimated by Wald's method using the SAS LOGISTIC procedure.
Peto OR calculation is based on Yusuf S et al. (Prog Cardiovasc Dis. 1985 Mar-Apr;27(5):335-71) and its p-value is derived using a normal approximation.
Risk Ratio and related p-value are estimated by using the SAS FREQ procedure.
Risk Difference and related p-value are estimated by using the SAS GLIMMIX procedure with the following model: criterion = treatment.
p-values for heterogeneity are estimated by using the SAS GLIMMIX procedure with the following model: criterion = treatment subgroup treatment*subgroup.
p-value for heterogeneity of Peto Odds Ratio is estimated by using normal approximation.
PGM=DEVOPS/SAR231893/EFC14153/CSR_RWE/REPORT/PGM/ae_evt_ger_subg_s2_t.sas OUT=REPORT/OUTPUT/ae_ptinjo_ger_exa_s2_t_x.rtf (12AUG2021 - 11:45)

Project Code / Study Number / Analysis: SAR231893 / EFC14153 / CSR_RWE

2 Adverse events - Safety type 2 inflammatory asthma phenotype population

2.37 Patients with any TEAE: Injection site oedema

2.37.13 By number of severe asthma exacerbation prior to the study (<=1, 2, >2)

	Number of severe asthma exacerbation prior to the study					
	<=1		2		>2	
Safety type 2 inflammatory asthma phenotype population	**Placebo (N=46)**	**Dupilumab (N=85)**	**Placebo (N=32)**	**Dupilumab (N=75)**	**Placebo (N=35)**	**Dupilumab (N=74)**
overall						0.656
Risk Ratio (95% CI)	-	2.44 (0.55 to 10.80)	-	NE (NE to NE)	-	1.66 (0.36 to 7.56)
Reversed Risk ratio (95% CI)	-	0.41 (0.09 to 1.82)			-	0.60 (0.13 to 2.76)
p-value for Risk Ratio		0.242		NE		0.515
p-value for heterogeneity of Risk Ratio:						
<=1, 2						0.973
<=1, >2						0.722
2, >2						0.973
overall						0.938
Risk Difference (95% CI)	-	6.24 (-2.65 to 15.13)	-	9.33 (NE to NE)	-	3.75 (-6.55 to 14.04)
p-value for Risk Difference		0.167		<0.001		0.472

Odds Ratio and related p-value are estimated by Wald's method using the SAS LOGISTIC procedure.
Peto OR calculation is based on Yusuf S et al. (Prog Cardiovasc Dis. 1985 Mar-Apr;27(5):335-71) and its p-value is derived using a normal approximation.
Risk Ratio and related p-value are estimated by using the SAS FREQ procedure.
Risk Difference and related p-value are estimated by using the SAS GLIMMIX procedure with the following model: criterion = treatment.
p-values for heterogeneity are estimated by using the SAS GLIMMIX procedure with the following model: criterion = treatment subgroup treatment*subgroup.
p-value for heterogeneity of Peto Odds Ratio is estimated by using normal approximation.
PGM=DEVOPS/SAR231893/EFC14153/CSR_RWE/REPORT/PGM/ae_evt_ger_subg_s2_t.sas OUT=REPORT/OUTPUT/ae_ptinjo_ger_exa_s2_t_x.rtf (12AUG2021 - 11:45)

Project Code / Study Number / Analysis: SAR231893 / EFC14153 / CSR_RWE

2 Adverse events - Safety type 2 inflammatory asthma phenotype population

2.37 Patients with any TEAE: Injection site oedema

2.37.13 By number of severe asthma exacerbation prior to the study (<=1, 2, >2)

	Number of severe asthma exacerbation prior to the study					
	<=1		2		>2	
Safety type 2 inflammatory asthma phenotype population	**Placebo (N=46)**	**Dupilumab (N=85)**	**Placebo (N=32)**	**Dupilumab (N=75)**	**Placebo (N=35)**	**Dupilumab (N=74)**
p-value for heterogeneity of Risk Difference:						
<=1, 2						0.653
<=1, >2						0.717
2, >2						<0.001
overall						0.717

Odds Ratio and related p-value are estimated by Wald's method using the SAS LOGISTIC procedure.
Peto OR calculation is based on Yusuf S et al. (Prog Cardiovasc Dis. 1985 Mar-Apr;27(5):335-71) and its p-value is derived using a normal approximation.
Risk Ratio and related p-value are estimated by using the SAS FREQ procedure.
Risk Difference and related p-value are estimated by using the SAS GLIMMIX procedure with the following model: criterion = treatment.
p-values for heterogeneity are estimated by using the SAS GLIMMIX procedure with the following model: criterion = treatment subgroup treatment*subgroup.
p-value for heterogeneity of Peto Odds Ratio is estimated by using normal approximation.
PGM=DEVOPS/SAR231893/EFC14153/CSR_RWE/REPORT/PGM/ae_evt_ger_subg_s2_t.sas OUT=REPORT/OUTPUT/ae_ptinjo_ger_exa_s2_t_x.rtf (12AUG2021 - 11:45)

MMRM-Analysen und Zeitverläufe für PRO

16.2.6 Efficacy response data

16.2.6.6 ACQ-5-IA

16.2.6.6.1 Summary of ACQ-5-IA over time - Type 2 inflammatory asthma phenotype population and baseline blood eosinophils >=0.3 Giga/L population

	Type 2 inflammatory asthma phenotype population	
ACQ-5-IA	**Placebo (N=114)**	**Dupilumab (N=236)**
Baseline		
Value		
Number	114	236
Mean (SD)	2.15 (0.84)	2.18 (0.79)
Median	2.20	2.00
Q1 : Q3	1.60 : 2.60	1.80 : 2.60
Min : Max	0.0 : 5.0	0.0 : 5.6
Week 2		
Value		
Number	110	232
Mean (SD)	1.38 (0.91)	1.36 (0.99)
Median	1.40	1.20
Q1 : Q3	0.80 : 2.00	0.60 : 2.00
Min : Max	0.0 : 3.8	0.0 : 5.2

Type 2 inflammatory asthma phenotype population is defined as the randomized patients with baseline blood eosinophils >= 0.15 Giga/L or baseline FeNO >= 20 ppb.
PGM=PRODOPS/SAR231893/EFC14153/CSR/REPORT/PGM/eff_sum_vis_i_t.sas OUT=REPORT/OUTPUT/eff_sum_acq5_t2e3_t_x.rtf (27NOV2020 - 6:42)

16.2.6 Efficacy response data

16.2.6.6 ACQ-5-IA

16.2.6.6.1 Summary of ACQ-5-IA over time - Type 2 inflammatory asthma phenotype population and baseline blood eosinophils >=0.3 Giga/L population

	Type 2 inflammatory asthma phenotype population	
ACQ-5-IA	**Placebo (N=114)**	**Dupilumab (N=236)**
Change from baseline		
Number	110	232
Mean (SD)	-0.77 (1.05)	-0.82 (0.98)
Median	-0.60	-0.80
Q1 : Q3	-1.20 : -0.20	-1.40 : -0.20
Min : Max	-5.0 : 2.0	-4.0 : 2.6
Percent change from baseline		
Number	109	231
Mean (SD)	-25.55 (68.63)	-36.67 (43.47)
Median	-36.36	-40.00
Q1 : Q3	-58.33 : -7.69	-66.67 : -10.00
Min : Max	-100.0 : 400.0	-100.0 : 162.5

Type 2 inflammatory asthma phenotype population is defined as the randomized patients with baseline blood eosinophils >= 0.15 Giga/L or baseline FeNO >= 20 ppb.
PGM=PRODOPS/SAR231893/EFC14153/CSR/REPORT/PGM/eff_sum_vis_i_t.sas OUT=REPORT/OUTPUT/eff_sum_acq5_t2e3_t_x.rtf (27NOV2020 - 6:42)

16.2.6 Efficacy response data

16.2.6.6 ACQ-5-IA

16.2.6.6.1 Summary of ACQ-5-IA over time - Type 2 inflammatory asthma phenotype population and baseline blood eosinophils >=0.3 Giga/L population

	Type 2 inflammatory asthma phenotype population	
ACQ-5-IA	**Placebo (N=114)**	**Dupilumab (N=236)**
Week 4		
Value		
Number	110	226
Mean (SD)	1.25 (0.96)	1.02 (0.81)
Median	1.00	1.00
Q1 : Q3	0.40 : 2.00	0.40 : 1.60
Min : Max	0.0 : 3.8	0.0 : 3.6
Change from baseline		
Number	110	226
Mean (SD)	-0.90 (1.19)	-1.15 (0.97)
Median	-1.00	-1.00
Q1 : Q3	-1.60 : -0.20	-1.60 : -0.60
Min : Max	-5.0 : 3.2	-5.6 : 1.4

Type 2 inflammatory asthma phenotype population is defined as the randomized patients with baseline blood eosinophils >= 0.15 Giga/L or baseline FeNO >= 20 ppb.
PGM=PRODOPS/SAR231893/EFC14153/CSR/REPORT/PGM/eff_sum_vis_i_t.sas OUT=REPORT/OUTPUT/eff_sum_acq5_t2e3_t_x.rtf (27NOV2020 - 6:42)

16.2.6 Efficacy response data

16.2.6.6 ACQ-5-IA

16.2.6.6.1 Summary of ACQ-5-IA over time - Type 2 inflammatory asthma phenotype population and baseline blood eosinophils >=0.3 Giga/L population

	Type 2 inflammatory asthma phenotype population	
ACQ-5-IA	**Placebo (N=114)**	**Dupilumab (N=236)**
Percent change from baseline		
Number	109	225
Mean (SD)	-24.31 (112.69)	-50.37 (41.80)
Median	-50.00	-55.56
Q1 : Q3	-80.00 : -9.09	-81.82 : -27.27
Min : Max	-100.0 : 800.0	-100.0 : 100.0
Week 6		
Value		
Number	113	229
Mean (SD)	1.19 (1.03)	0.91 (0.92)
Median	0.80	0.60
Q1 : Q3	0.40 : 1.80	0.20 : 1.40
Min : Max	0.0 : 5.6	0.0 : 5.4

Type 2 inflammatory asthma phenotype population is defined as the randomized patients with baseline blood eosinophils >= 0.15 Giga/L or baseline FeNO >= 20 ppb.
PGM=PRODOPS/SAR231893/EFC14153/CSR/REPORT/PGM/eff_sum_vis_i_t.sas OUT=REPORT/OUTPUT/eff_sum_acq5_t2e3_t_x.rtf (27NOV2020 - 6:42)

16.2.6 Efficacy response data

16.2.6.6 ACQ-5-IA

16.2.6.6.1 Summary of ACQ-5-IA over time - Type 2 inflammatory asthma phenotype population and baseline blood eosinophils >=0.3 Giga/L population

	Type 2 inflammatory asthma phenotype population	
ACQ-5-IA	**Placebo (N=114)**	**Dupilumab (N=236)**
Change from baseline		
Number	113	229
Mean (SD)	-0.95 (1.20)	-1.25 (1.12)
Median	-1.00	-1.20
Q1 : Q3	-1.60 : -0.20	-2.00 : -0.60
Min : Max	-5.0 : 5.2	-5.6 : 3.6
Percent change from baseline		
Number	112	228
Mean (SD)	-33.30 (134.56)	-55.55 (46.53)
Median	-54.55	-66.67
Q1 : Q3	-78.89 : -20.00	-90.45 : -33.33
Min : Max	-100.0 : 1300.0	-100.0 : 200.0

Type 2 inflammatory asthma phenotype population is defined as the randomized patients with baseline blood eosinophils >= 0.15 Giga/L or baseline FeNO >= 20 ppb.
PGM=PRODOPS/SAR231893/EFC14153/CSR/REPORT/PGM/eff_sum_vis_i_t.sas OUT=REPORT/OUTPUT/eff_sum_acq5_t2e3_t_x.rtf (27NOV2020 - 6:42)

16.2.6 Efficacy response data

16.2.6.6 ACQ-5-IA

16.2.6.6.1 Summary of ACQ-5-IA over time - Type 2 inflammatory asthma phenotype population and baseline blood eosinophils >=0.3 Giga/L population

	Type 2 inflammatory asthma phenotype population	
ACQ-5-IA	**Placebo (N=114)**	**Dupilumab (N=236)**
Week 8		
Value		
Number	113	227
Mean (SD)	1.05 (0.99)	0.84 (0.90)
Median	0.80	0.60
Q1 : Q3	0.20 : 1.60	0.20 : 1.40
Min : Max	0.0 : 5.2	0.0 : 4.6
Change from baseline		
Number	113	227
Mean (SD)	-1.10 (1.24)	-1.34 (1.06)
Median	-1.20	-1.40
Q1 : Q3	-1.80 : -0.40	-2.00 : -0.80
Min : Max	-4.2 : 4.8	-5.2 : 2.6

Type 2 inflammatory asthma phenotype population is defined as the randomized patients with baseline blood eosinophils >= 0.15 Giga/L or baseline FeNO >= 20 ppb.
PGM=PRODOPS/SAR231893/EFC14153/CSR/REPORT/PGM/eff_sum_vis_i_t.sas OUT=REPORT/OUTPUT/eff_sum_acq5_t2e3_t_x.rtf (27NOV2020 - 6:42)

16.2.6 Efficacy response data

16.2.6.6 ACQ-5-IA

16.2.6.6.1 Summary of ACQ-5-IA over time - Type 2 inflammatory asthma phenotype population and baseline blood eosinophils >=0.3 Giga/L population

	Type 2 inflammatory asthma phenotype population	
ACQ-5-IA	**Placebo (N=114)**	**Dupilumab (N=236)**
Percent change from baseline		
Number	112	226
Mean (SD)	-32.54 (137.67)	-59.79 (45.34)
Median	-59.17	-71.43
Q1 : Q3	-88.19 : -17.91	-94.12 : -40.00
Min : Max	-100.0 : 1200.0	-100.0 : 175.0
Week 10		
Value		
Number	113	226
Mean (SD)	1.02 (0.96)	0.76 (0.81)
Median	0.80	0.60
Q1 : Q3	0.20 : 1.80	0.00 : 1.20
Min : Max	0.0 : 4.4	0.0 : 4.0

Type 2 inflammatory asthma phenotype population is defined as the randomized patients with baseline blood eosinophils >= 0.15 Giga/L or baseline FeNO >= 20 ppb.
PGM=PRODOPS/SAR231893/EFC14153/CSR/REPORT/PGM/eff_sum_vis_i_t.sas OUT=REPORT/OUTPUT/eff_sum_acq5_t2e3_t_x.rtf (27NOV2020 - 6:42)

16.2.6 Efficacy response data

16.2.6.6 ACQ-5-IA

16.2.6.6.1 Summary of ACQ-5-IA over time - Type 2 inflammatory asthma phenotype population and baseline blood eosinophils >=0.3 Giga/L population

	Type 2 inflammatory asthma phenotype population	
ACQ-5-IA	**Placebo (N=114)**	**Dupilumab (N=236)**
Change from baseline		
Number	113	226
Mean (SD)	-1.13 (1.04)	-1.40 (1.03)
Median	-1.20	-1.40
Q1 : Q3	-1.80 : -0.40	-2.00 : -0.80
Min : Max	-3.6 : 2.4	-5.6 : 2.8
Percent change from baseline		
Number	112	225
Mean (SD)	-44.18 (66.60)	-61.53 (52.90)
Median	-59.17	-75.00
Q1 : Q3	-91.29 : -19.09	-100.00 : -50.00
Min : Max	-100.0 : 400.0	-100.0 : 466.7

Type 2 inflammatory asthma phenotype population is defined as the randomized patients with baseline blood eosinophils >= 0.15 Giga/L or baseline FeNO >= 20 ppb.
PGM=PRODOPS/SAR231893/EFC14153/CSR/REPORT/PGM/eff_sum_vis_i_t.sas OUT=REPORT/OUTPUT/eff_sum_acq5_t2e3_t_x.rtf (27NOV2020 - 6:42)

16.2.6 Efficacy response data

16.2.6.6 ACQ-5-IA

16.2.6.6.1 Summary of ACQ-5-IA over time - Type 2 inflammatory asthma phenotype population and baseline blood eosinophils >=0.3 Giga/L population

	Type 2 inflammatory asthma phenotype population	
ACQ-5-IA	**Placebo (N=114)**	**Dupilumab (N=236)**
Week 12		
Value		
Number	113	229
Mean (SD)	1.04 (0.98)	0.74 (0.79)
Median	0.80	0.60
Q1 : Q3	0.20 : 1.80	0.00 : 1.20
Min : Max	0.0 : 3.8	0.0 : 3.6
Change from baseline		
Number	113	229
Mean (SD)	-1.12 (1.22)	-1.44 (1.01)
Median	-1.00	-1.40
Q1 : Q3	-2.00 : -0.40	-2.00 : -0.60
Min : Max	-5.0 : 3.4	-5.0 : 1.2

Type 2 inflammatory asthma phenotype population is defined as the randomized patients with baseline blood eosinophils >= 0.15 Giga/L or baseline FeNO >= 20 ppb.
PGM=PRODOPS/SAR231893/EFC14153/CSR/REPORT/PGM/eff_sum_vis_i_t.sas OUT=REPORT/OUTPUT/eff_sum_acq5_t2e3_t_x.rtf (27NOV2020 - 6:42)

16.2.6 Efficacy response data

16.2.6.6 ACQ-5-IA

16.2.6.6.1 Summary of ACQ-5-IA over time - Type 2 inflammatory asthma phenotype population and baseline blood eosinophils >=0.3 Giga/L population

	Type 2 inflammatory asthma phenotype population	
ACQ-5-IA	**Placebo (N=114)**	**Dupilumab (N=236)**
Percent change from baseline		
Number	112	228
Mean (SD)	-27.12 (181.99)	-65.14 (36.48)
Median	-59.94	-75.96
Q1 : Q3	-91.29 : -20.00	-100.00 : -39.23
Min : Max	-100.0 : 1700.0	-100.0 : 54.5
Week 16		
Value		
Number	110	227
Mean (SD)	0.88 (0.83)	0.74 (0.81)
Median	0.60	0.60
Q1 : Q3	0.20 : 1.40	0.00 : 1.20
Min : Max	0.0 : 3.4	0.0 : 3.8

Type 2 inflammatory asthma phenotype population is defined as the randomized patients with baseline blood eosinophils >= 0.15 Giga/L or baseline FeNO >= 20 ppb.
PGM=PRODOPS/SAR231893/EFC14153/CSR/REPORT/PGM/eff_sum_vis_i_t.sas OUT=REPORT/OUTPUT/eff_sum_acq5_t2e3_t_x.rtf (27NOV2020 - 6:42)

16.2.6 Efficacy response data

16.2.6.6 ACQ-5-IA

16.2.6.6.1 Summary of ACQ-5-IA over time - Type 2 inflammatory asthma phenotype population and baseline blood eosinophils >=0.3 Giga/L population

	Type 2 inflammatory asthma phenotype population	
ACQ-5-IA	**Placebo (N=114)**	**Dupilumab (N=236)**
Change from baseline		
Number	110	227
Mean (SD)	-1.26 (1.05)	-1.45 (1.03)
Median	-1.30	-1.60
Q1 : Q3	-2.00 : -0.40	-2.04 : -0.80
Min : Max	-4.6 : 1.0	-4.4 : 1.4
Percent change from baseline		
Number	109	226
Mean (SD)	-51.21 (58.58)	-63.82 (40.10)
Median	-66.67	-76.70
Q1 : Q3	-92.31 : -30.00	-100.00 : -45.45
Min : Max	-100.0 : 300.0	-100.0 : 100.0

Type 2 inflammatory asthma phenotype population is defined as the randomized patients with baseline blood eosinophils >= 0.15 Giga/L or baseline FeNO >= 20 ppb.
PGM=PRODOPS/SAR231893/EFC14153/CSR/REPORT/PGM/eff_sum_vis_i_t.sas OUT=REPORT/OUTPUT/eff_sum_acq5_t2e3_t_x.rtf (27NOV2020 - 6:42)

16.2.6 Efficacy response data

16.2.6.6 ACQ-5-IA

16.2.6.6.1 Summary of ACQ-5-IA over time - Type 2 inflammatory asthma phenotype population and baseline blood eosinophils >=0.3 Giga/L population

	Type 2 inflammatory asthma phenotype population	
ACQ-5-IA	**Placebo (N=114)**	**Dupilumab (N=236)**
Week 20		
Value		
Number	112	223
Mean (SD)	0.93 (0.93)	0.72 (0.86)
Median	0.60	0.40
Q1 : Q3	0.20 : 1.60	0.00 : 1.20
Min : Max	0.0 : 4.2	0.0 : 3.8
Change from baseline		
Number	112	223
Mean (SD)	-1.20 (1.12)	-1.45 (1.15)
Median	-1.20	-1.60
Q1 : Q3	-1.90 : -0.50	-2.20 : -0.80
Min : Max	-5.0 : 3.8	-5.6 : 3.0

Type 2 inflammatory asthma phenotype population is defined as the randomized patients with baseline blood eosinophils >= 0.15 Giga/L or baseline FeNO >= 20 ppb.
PGM=PRODOPS/SAR231893/EFC14153/CSR/REPORT/PGM/eff_sum_vis_i_t.sas OUT=REPORT/OUTPUT/eff_sum_acq5_t2e3_t_x.rtf (27NOV2020 - 6:42)

16.2.6 Efficacy response data

16.2.6.6 ACQ-5-IA

16.2.6.6.1 Summary of ACQ-5-IA over time - Type 2 inflammatory asthma phenotype population and baseline blood eosinophils >=0.3 Giga/L population

	Type 2 inflammatory asthma phenotype population	
ACQ-5-IA	**Placebo (N=114)**	**Dupilumab (N=236)**
Percent change from baseline		
Number	111	223
Mean (SD)	-43.60 (111.92)	-60.40 (64.33)
Median	-63.64	-80.00
Q1 : Q3	-94.12 : -25.00	-100.00 : -42.86
Min : Max	-100.0 : 950.0	-100.0 : 500.0
Week 24		
Value		
Number	112	228
Mean (SD)	0.92 (0.93)	0.65 (0.77)
Median	0.60	0.40
Q1 : Q3	0.20 : 1.40	0.00 : 1.00
Min : Max	0.0 : 3.8	0.0 : 3.4

Type 2 inflammatory asthma phenotype population is defined as the randomized patients with baseline blood eosinophils >= 0.15 Giga/L or baseline FeNO >= 20 ppb.
PGM=PRODOPS/SAR231893/EFC14153/CSR/REPORT/PGM/eff_sum_vis_i_t.sas OUT=REPORT/OUTPUT/eff_sum_acq5_t2e3_t_x.rtf (27NOV2020 - 6:42)

16.2.6 Efficacy response data

16.2.6.6 ACQ-5-IA

16.2.6.6.1 Summary of ACQ-5-IA over time - Type 2 inflammatory asthma phenotype population and baseline blood eosinophils >=0.3 Giga/L population

	Type 2 inflammatory asthma phenotype population	
ACQ-5-IA	**Placebo (N=114)**	**Dupilumab (N=236)**
Change from baseline		
Number	112	228
Mean (SD)	-1.22 (1.13)	-1.53 (1.09)
Median	-1.20	-1.60
Q1 : Q3	-2.00 : -0.50	-2.20 : -0.80
Min : Max	-4.8 : 2.4	-5.6 : 2.2
Percent change from baseline		
Number	111	227
Mean (SD)	-47.23 (77.74)	-65.31 (47.04)
Median	-63.64	-83.33
Q1 : Q3	-92.86 : -25.00	-100.00 : -41.67
Min : Max	-100.0 : 600.0	-100.0 : 233.3

Type 2 inflammatory asthma phenotype population is defined as the randomized patients with baseline blood eosinophils >= 0.15 Giga/L or baseline FeNO >= 20 ppb.
PGM=PRODOPS/SAR231893/EFC14153/CSR/REPORT/PGM/eff_sum_vis_i_t.sas OUT=REPORT/OUTPUT/eff_sum_acq5_t2e3_t_x.rtf (27NOV2020 - 6:42)

16.2.6 Efficacy response data

16.2.6.6 ACQ-5-IA

16.2.6.6.1 Summary of ACQ-5-IA over time - Type 2 inflammatory asthma phenotype population and baseline blood eosinophils >=0.3 Giga/L population

	Type 2 inflammatory asthma phenotype population	
ACQ-5-IA	**Placebo (N=114)**	**Dupilumab (N=236)**
Week 28		
Value		
Number	112	225
Mean (SD)	0.85 (0.98)	0.61 (0.78)
Median	0.60	0.20
Q1 : Q3	0.00 : 1.40	0.00 : 1.00
Min : Max	0.0 : 5.2	0.0 : 4.2
Change from baseline		
Number	112	225
Mean (SD)	-1.30 (1.25)	-1.58 (1.07)
Median	-1.40	-1.60
Q1 : Q3	-2.10 : -0.60	-2.20 : -1.00
Min : Max	-5.0 : 3.8	-5.6 : 3.6

Type 2 inflammatory asthma phenotype population is defined as the randomized patients with baseline blood eosinophils >= 0.15 Giga/L or baseline FeNO >= 20 ppb.
PGM=PRODOPS/SAR231893/EFC14153/CSR/REPORT/PGM/eff_sum_vis_i_t.sas OUT=REPORT/OUTPUT/eff_sum_acq5_t2e3_t_x.rtf (27NOV2020 - 6:42)

16.2.6 Efficacy response data

16.2.6.6 ACQ-5-IA

16.2.6.6.1 Summary of ACQ-5-IA over time - Type 2 inflammatory asthma phenotype population and baseline blood eosinophils >=0.3 Giga/L population

	Type 2 inflammatory asthma phenotype population	
ACQ-5-IA	**Placebo (N=114)**	**Dupilumab (N=236)**
Percent change from baseline		
Number	111	224
Mean (SD)	-46.72 (97.44)	-68.63 (57.05)
Median	-71.43	-83.33
Q1 : Q3	-100.00 : -33.33	-100.00 : -55.05
Min : Max	-100.0 : 566.7	-100.0 : 600.0
Week 32		
Value		
Number	110	223
Mean (SD)	0.80 (0.84)	0.64 (0.83)
Median	0.60	0.40
Q1 : Q3	0.20 : 1.20	0.00 : 1.00
Min : Max	0.0 : 3.2	0.0 : 5.6

Type 2 inflammatory asthma phenotype population is defined as the randomized patients with baseline blood eosinophils >= 0.15 Giga/L or baseline FeNO >= 20 ppb.
PGM=PRODOPS/SAR231893/EFC14153/CSR/REPORT/PGM/eff_sum_vis_i_t.sas OUT=REPORT/OUTPUT/eff_sum_acq5_t2e3_t_x.rtf (27NOV2020 - 6:42)

16.2.6 Efficacy response data

16.2.6.6 ACQ-5-IA

16.2.6.6.1 Summary of ACQ-5-IA over time - Type 2 inflammatory asthma phenotype population and baseline blood eosinophils >=0.3 Giga/L population

	Type 2 inflammatory asthma phenotype population	
ACQ-5-IA	**Placebo (N=114)**	**Dupilumab (N=236)**
Change from baseline		
Number	110	223
Mean (SD)	-1.34 (1.17)	-1.54 (1.05)
Median	-1.60	-1.60
Q1 : Q3	-2.00 : -0.80	-2.20 : -1.00
Min : Max	-5.0 : 2.2	-4.6 : 3.8
Percent change from baseline		
Number	109	222
Mean (SD)	-45.25 (105.20)	-68.26 (42.94)
Median	-72.22	-81.82
Q1 : Q3	-94.12 : -44.44	-100.00 : -50.00
Min : Max	-100.0 : 700.0	-100.0 : 211.1

Type 2 inflammatory asthma phenotype population is defined as the randomized patients with baseline blood eosinophils >= 0.15 Giga/L or baseline FeNO >= 20 ppb.
PGM=PRODOPS/SAR231893/EFC14153/CSR/REPORT/PGM/eff_sum_vis_i_t.sas OUT=REPORT/OUTPUT/eff_sum_acq5_t2e3_t_x.rtf (27NOV2020 - 6:42)

16.2.6 Efficacy response data

16.2.6.6 ACQ-5-IA

16.2.6.6.1 Summary of ACQ-5-IA over time - Type 2 inflammatory asthma phenotype population and baseline blood eosinophils >=0.3 Giga/L population

	Type 2 inflammatory asthma phenotype population	
ACQ-5-IA	**Placebo (N=114)**	**Dupilumab (N=236)**
Week 36		
Value		
Number	111	218
Mean (SD)	0.82 (0.91)	0.54 (0.72)
Median	0.60	0.20
Q1 : Q3	0.00 : 1.20	0.00 : 0.80
Min : Max	0.0 : 3.8	0.0 : 4.2
Change from baseline		
Number	111	218
Mean (SD)	-1.32 (1.18)	-1.65 (0.97)
Median	-1.60	-1.80
Q1 : Q3	-2.00 : -0.60	-2.20 : -1.00
Min : Max	-4.8 : 3.0	-5.0 : 2.0

Type 2 inflammatory asthma phenotype population is defined as the randomized patients with baseline blood eosinophils >= 0.15 Giga/L or baseline FeNO >= 20 ppb.
PGM=PRODOPS/SAR231893/EFC14153/CSR/REPORT/PGM/eff_sum_vis_i_t.sas OUT=REPORT/OUTPUT/eff_sum_acq5_t2e3_t_x.rtf (27NOV2020 - 6:42)

16.2.6 Efficacy response data

16.2.6.6 ACQ-5-IA

16.2.6.6.1 Summary of ACQ-5-IA over time - Type 2 inflammatory asthma phenotype population and baseline blood eosinophils >=0.3 Giga/L population

	Type 2 inflammatory asthma phenotype population	
ACQ-5-IA	**Placebo (N=114)**	**Dupilumab (N=236)**
Percent change from baseline		
Number	110	217
Mean (SD)	-51.96 (78.58)	-74.29 (34.24)
Median	-71.83	-88.89
Q1 : Q3	-100.00 : -38.46	-100.00 : -61.54
Min : Max	-100.0 : 500.0	-100.0 : 90.9
Week 40		
Value		
Number	106	220
Mean (SD)	0.80 (0.85)	0.56 (0.76)
Median	0.60	0.20
Q1 : Q3	0.00 : 1.40	0.00 : 1.00
Min : Max	0.0 : 3.2	0.0 : 3.8

Type 2 inflammatory asthma phenotype population is defined as the randomized patients with baseline blood eosinophils >= 0.15 Giga/L or baseline FeNO >= 20 ppb.
PGM=PRODOPS/SAR231893/EFC14153/CSR/REPORT/PGM/eff_sum_vis_i_t.sas OUT=REPORT/OUTPUT/eff_sum_acq5_t2e3_t_x.rtf (27NOV2020 - 6:42)

16.2.6 Efficacy response data

16.2.6.6 ACQ-5-IA

16.2.6.6.1 Summary of ACQ-5-IA over time - Type 2 inflammatory asthma phenotype population and baseline blood eosinophils >=0.3 Giga/L population

	Type 2 inflammatory asthma phenotype population	
ACQ-5-IA	**Placebo (N=114)**	**Dupilumab (N=236)**
Change from baseline		
Number	106	220
Mean (SD)	-1.35 (1.16)	-1.64 (1.02)
Median	-1.60	-1.80
Q1 : Q3	-2.00 : -0.60	-2.20 : -1.00
Min : Max	-5.0 : 1.6	-5.4 : 1.8
Percent change from baseline		
Number	105	219
Mean (SD)	-52.26 (71.80)	-73.44 (37.87)
Median	-75.00	-90.00
Q1 : Q3	-100.00 : -41.67	-100.00 : -58.33
Min : Max	-100.0 : 350.0	-100.0 : 128.6

Type 2 inflammatory asthma phenotype population is defined as the randomized patients with baseline blood eosinophils >= 0.15 Giga/L or baseline FeNO >= 20 ppb.
PGM=PRODOPS/SAR231893/EFC14153/CSR/REPORT/PGM/eff_sum_vis_i_t.sas OUT=REPORT/OUTPUT/eff_sum_acq5_t2e3_t_x.rtf (27NOV2020 - 6:42)

16.2.6 Efficacy response data

16.2.6.6 ACQ-5-IA

16.2.6.6.1 Summary of ACQ-5-IA over time - Type 2 inflammatory asthma phenotype population and baseline blood eosinophils >=0.3 Giga/L population

	Type 2 inflammatory asthma phenotype population	
ACQ-5-IA	**Placebo (N=114)**	**Dupilumab (N=236)**
Week 44		
Value		
Number	109	215
Mean (SD)	0.72 (0.76)	0.51 (0.71)
Median	0.60	0.20
Q1 : Q3	0.00 : 1.20	0.00 : 0.80
Min : Max	0.0 : 3.4	0.0 : 4.4
Change from baseline		
Number	109	215
Mean (SD)	-1.43 (1.05)	-1.69 (0.93)
Median	-1.60	-1.80
Q1 : Q3	-2.00 : -0.80	-2.20 : -1.00
Min : Max	-5.0 : 1.2	-5.2 : 1.2

Type 2 inflammatory asthma phenotype population is defined as the randomized patients with baseline blood eosinophils >= 0.15 Giga/L or baseline FeNO >= 20 ppb.
PGM=PRODOPS/SAR231893/EFC14153/CSR/REPORT/PGM/eff_sum_vis_i_t.sas OUT=REPORT/OUTPUT/eff_sum_acq5_t2e3_t_x.rtf (27NOV2020 - 6:42)

16.2.6 Efficacy response data

16.2.6.6 ACQ-5-IA

16.2.6.6.1 Summary of ACQ-5-IA over time - Type 2 inflammatory asthma phenotype population and baseline blood eosinophils >=0.3 Giga/L population

	Type 2 inflammatory asthma phenotype population	
ACQ-5-IA	**Placebo (N=114)**	**Dupilumab (N=236)**
Percent change from baseline		
Number	108	214
Mean (SD)	-59.29 (52.49)	-76.34 (31.56)
Median	-77.75	-90.00
Q1 : Q3	-100.00 : -44.95	-100.00 : -63.64
Min : Max	-100.0 : 200.0	-100.0 : 54.5
Week 48		
Value		
Number	110	219
Mean (SD)	0.73 (0.85)	0.48 (0.72)
Median	0.40	0.20
Q1 : Q3	0.00 : 1.20	0.00 : 0.80
Min : Max	0.0 : 3.4	0.0 : 4.0

Type 2 inflammatory asthma phenotype population is defined as the randomized patients with baseline blood eosinophils >= 0.15 Giga/L or baseline FeNO >= 20 ppb.
PGM=PRODOPS/SAR231893/EFC14153/CSR/REPORT/PGM/eff_sum_vis_i_t.sas OUT=REPORT/OUTPUT/eff_sum_acq5_t2e3_t_x.rtf (27NOV2020 - 6:42)

16.2.6 Efficacy response data

16.2.6.6 ACQ-5-IA

16.2.6.6.1 Summary of ACQ-5-IA over time - Type 2 inflammatory asthma phenotype population and baseline blood eosinophils >=0.3 Giga/L population

	Type 2 inflammatory asthma phenotype population	
ACQ-5-IA	**Placebo (N=114)**	**Dupilumab (N=236)**
Change from baseline		
Number	110	219
Mean (SD)	-1.42 (1.04)	-1.72 (0.94)
Median	-1.60	-1.80
Q1 : Q3	-2.20 : -0.80	-2.20 : -1.20
Min : Max	-5.0 : 0.8	-5.2 : 1.8
Percent change from baseline		
Number	109	218
Mean (SD)	-59.80 (57.76)	-77.77 (32.42)
Median	-75.00	-92.31
Q1 : Q3	-100.00 : -50.00	-100.00 : -66.67
Min : Max	-100.0 : 300.0	-100.0 : 81.8

Type 2 inflammatory asthma phenotype population is defined as the randomized patients with baseline blood eosinophils >= 0.15 Giga/L or baseline FeNO >= 20 ppb.
PGM=PRODOPS/SAR231893/EFC14153/CSR/REPORT/PGM/eff_sum_vis_i_t.sas OUT=REPORT/OUTPUT/eff_sum_acq5_t2e3_t_x.rtf (27NOV2020 - 6:42)

16.2.6 Efficacy response data

16.2.6.6 ACQ-5-IA

16.2.6.6.1 Summary of ACQ-5-IA over time - Type 2 inflammatory asthma phenotype population and baseline blood eosinophils >=0.3 Giga/L population

	Type 2 inflammatory asthma phenotype population	
ACQ-5-IA	**Placebo (N=114)**	**Dupilumab (N=236)**
Week 52		
Value		
Number	110	222
Mean (SD)	0.83 (0.94)	0.40 (0.64)
Median	0.60	0.00
Q1 : Q3	0.00 : 1.20	0.00 : 0.60
Min : Max	0.0 : 4.8	0.0 : 4.0
Change from baseline		
Number	110	222
Mean (SD)	-1.33 (1.15)	-1.80 (0.92)
Median	-1.50	-1.80
Q1 : Q3	-2.00 : -0.80	-2.40 : -1.20
Min : Max	-5.0 : 3.0	-4.8 : 1.8

Type 2 inflammatory asthma phenotype population is defined as the randomized patients with baseline blood eosinophils >= 0.15 Giga/L or baseline FeNO >= 20 ppb.
PGM=PRODOPS/SAR231893/EFC14153/CSR/REPORT/PGM/eff_sum_vis_i_t.sas OUT=REPORT/OUTPUT/eff_sum_acq5_t2e3_t_x.rtf (27NOV2020 - 6:42)

16.2.6 Efficacy response data

16.2.6.6 ACQ-5-IA

16.2.6.6.1 Summary of ACQ-5-IA over time - Type 2 inflammatory asthma phenotype population and baseline blood eosinophils >=0.3 Giga/L population

	Type 2 inflammatory asthma phenotype population	
ACQ-5-IA	**Placebo (N=114)**	**Dupilumab (N=236)**
Percent change from baseline		
Number	109	221
Mean (SD)	-55.86 (56.23)	-81.44 (29.86)
Median	-71.43	-100.00
Q1 : Q3	-100.00 : -44.44	-100.00 : -76.92
Min : Max	-100.0 : 200.0	-100.0 : 81.8
Week 64		
Value		
Number	2	15
Mean (SD)	2.40 (1.98)	0.40 (0.51)
Median	2.40	0.40
Q1 : Q3	1.00 : 3.80	0.00 : 0.80
Min : Max	1.0 : 3.8	0.0 : 1.8

Type 2 inflammatory asthma phenotype population is defined as the randomized patients with baseline blood eosinophils >= 0.15 Giga/L or baseline FeNO >= 20 ppb.
PGM=PRODOPS/SAR231893/EFC14153/CSR/REPORT/PGM/eff_sum_vis_i_t.sas OUT=REPORT/OUTPUT/eff_sum_acq5_t2e3_t_x.rtf (27NOV2020 - 6:42)

16.2.6 Efficacy response data

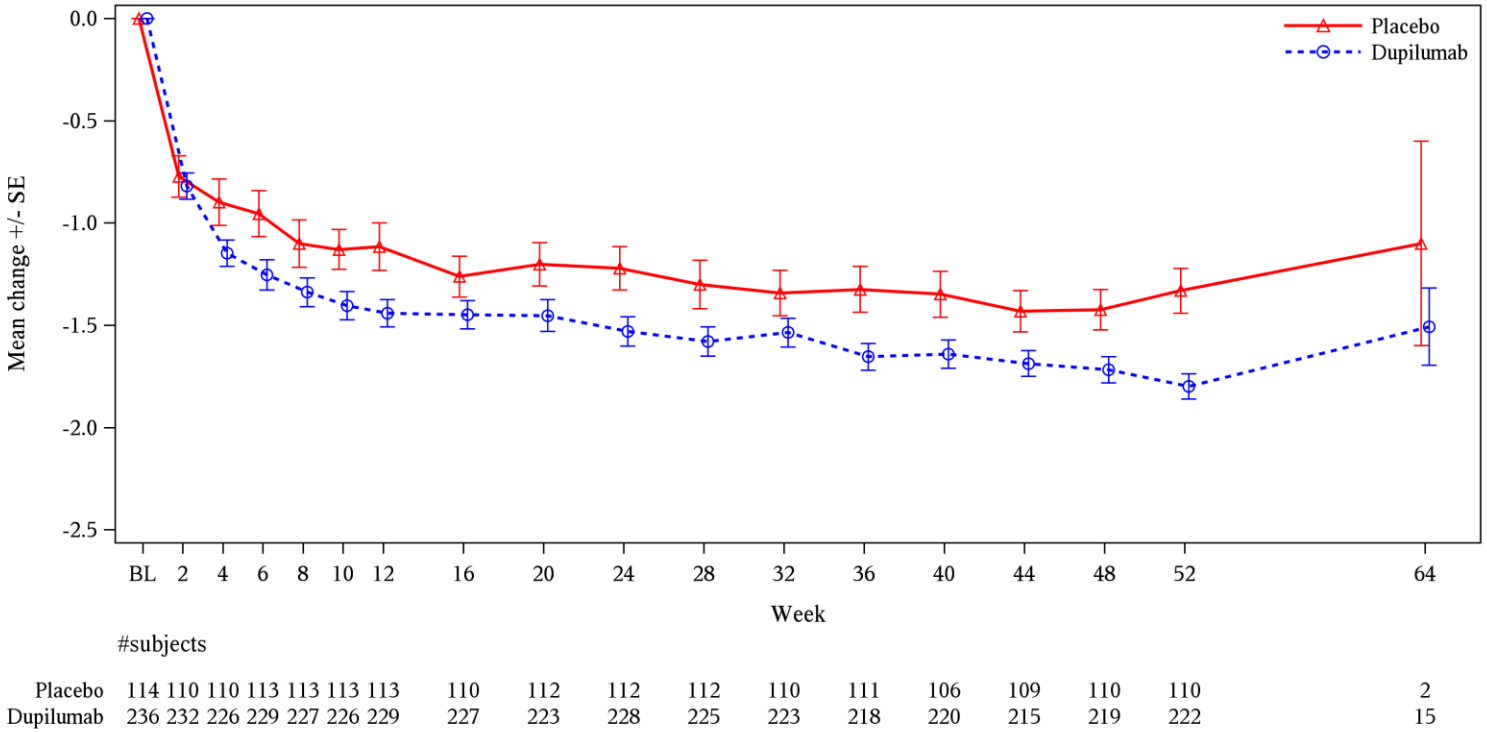
16.2.6.6 ACQ-5-IA

16.2.6.6.1 Summary of ACQ-5-IA over time - Type 2 inflammatory asthma phenotype population and baseline blood eosinophils >=0.3 Giga/L population

	Type 2 inflammatory asthma phenotype population	
ACQ-5-IA	**Placebo (N=114)**	**Dupilumab (N=236)**
Change from baseline		
Number	2	15
Mean (SD)	-1.10 (0.71)	-1.51 (0.73)
Median	-1.10	-1.60
Q1 : Q3	-1.60 : -0.60	-2.20 : -1.00
Min : Max	-1.6 : -0.6	-2.4 : -0.2
Percent change from baseline		
Number	2	15
Mean (SD)	-37.59 (33.87)	-75.93 (27.49)
Median	-37.59	-77.78
Q1 : Q3	-61.54 : -13.64	-100.00 : -55.56
Min : Max	-61.5 : -13.6	-100.0 : -18.2

Type 2 inflammatory asthma phenotype population is defined as the randomized patients with baseline blood eosinophils >= 0.15 Giga/L or baseline FeNO >= 20 ppb.
PGM=PRODOPS/SAR231893/EFC14153/CSR/REPORT/PGM/eff_sum_vis_i_t.sas OUT=REPORT/OUTPUT/eff_sum_acq5_t2e3_t_x.rtf (27NOV2020 - 6:42)

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen
Project Code / Study Number / Analysis: SAR231893 / EFC14153 / CSR
16.2.6 Efficacy response data
16.2.6.6 ACQ-5-IA
16.2.6.6.2 Plot of mean change from baseline in ACQ-5-IA over time - Type 2 inflammatory asthma phenotype population



BL=Baseline
Type 2 inflammatory asthma phenotype population is defined as the randomized patients with baseline blood eosinophils >= 0.15 Giga/L or baseline FeNO >= 20 ppb.
PGM=PRODOPS/SAR231893/EFC14153/CSR/REPORT/PGM/eff_sum_vis_i_g.sas OUT=REPORT/OUTPUT/eff_sum_acq5_t2_g_x.rtf (27NOV2020 - 6:36)

16.2.6.6.4 Change from baseline in ACQ-5-IA over time (MMRM including measurements up to Week 52) - Type 2 inflammatory asthma phenotype population and baseline blood eosinophils >=0.3 Giga/L population

	Type 2 inflammatory asthma phenotype population	
ACQ-5-IA	**Placebo (N=114)**	**Dupilumab (N=236)**
Baseline		
Value		
Number	114	236
Mean (SD)	2.15 (0.84)	2.18 (0.79)
Median	2.20	2.00
Q1 : Q3	1.60 : 2.60	1.80 : 2.60
Min : Max	0.0 : 5.0	0.0 : 5.6
Week 2		
Change from baseline		
Number of patients in the model	110	227
LS Mean (SE) [a]	-0.72 (0.09)	-0.77 (0.06)
LS Mean Diff vs. placebo (95% CI) [a]		-0.05 (-0.25, 0.15)
P-value vs. placebo [a]		0.6192

[a] Derived from MMRM model with change from baseline in ACQ-5-IA values up to Week 52 as the response variable, and treatment, age, baseline weight group, region, baseline eosinophil level, baseline FeNO level, baseline ICS dose level, visit, treatment by-visit interaction, baseline ACQ-5-IA value and baseline-by-visit interaction as covariates.
Type 2 inflammatory asthma phenotype population is defined as the randomized patients with baseline blood eosinophils >= 0.15 Giga/L or baseline FeNO >= 20 ppb.
PGM=PRODOPS/SAR231893/EFC14153/CSR/REPORT/PGM/eff_mmrm_i_t.sas OUT=REPORT/OUTPUT/eff_acq5_chg_a52_t2e3_t_x.rtf (27NOV2020 - 5:26)

16.2.6.6.4 Change from baseline in ACQ-5-IA over time (MMRM including measurements up to Week 52) - Type 2 inflammatory asthma phenotype population and baseline blood eosinophils >=0.3 Giga/L population

	Type 2 inflammatory asthma phenotype population	
ACQ-5-IA	**Placebo (N=114)**	**Dupilumab (N=236)**
Week 4		
Change from baseline		
Number of patients in the model	110	227
LS Mean (SE) [a]	-0.86 (0.08)	-1.09 (0.06)
LS Mean Diff vs. placebo (95% CI) [a]		-0.24 (-0.43, -0.04)
P-value vs. placebo [a]		0.0166
Week 6		
Change from baseline		
Number of patients in the model	110	227
LS Mean (SE) [a]	-0.90 (0.09)	-1.18 (0.07)
LS Mean Diff vs. placebo (95% CI) [a]		-0.29 (-0.50, -0.07)
P-value vs. placebo [a]		0.0094

[a] Derived from MMRM model with change from baseline in ACQ-5-IA values up to Week 52 as the response variable, and treatment, age, baseline weight group, region, baseline eosinophil level, baseline FeNO level, baseline ICS dose level, visit, treatment by-visit interaction, baseline ACQ-5-IA value and baseline-by-visit interaction as covariates.
Type 2 inflammatory asthma phenotype population is defined as the randomized patients with baseline blood eosinophils >= 0.15 Giga/L or baseline FeNO >= 20 ppb.
PGM=PRODOPS/SAR231893/EFC14153/CSR/REPORT/PGM/eff_mmrm_i_t.sas OUT=REPORT/OUTPUT/eff_acq5_chg_a52_t2e3_t_x.rtf (27NOV2020 - 5:26)

16.2.6.6.4 Change from baseline in ACQ-5-IA over time (MMRM including measurements up to Week 52) - Type 2 inflammatory asthma phenotype population and baseline blood eosinophils >=0.3 Giga/L population

	Type 2 inflammatory asthma phenotype population	
ACQ-5-IA	**Placebo (N=114)**	**Dupilumab (N=236)**
Week 8		
Change from baseline		
Number of patients in the model	110	227
LS Mean (SE) [a]	-1.04 (0.09)	-1.24 (0.07)
LS Mean Diff vs. placebo (95% CI) [a]		-0.20 (-0.41, 0.01)
P-value vs. placebo [a]		0.0634
Week 10		
Change from baseline		
Number of patients in the model	110	227
LS Mean (SE) [a]	-1.08 (0.08)	-1.34 (0.06)
LS Mean Diff vs. placebo (95% CI) [a]		-0.27 (-0.46, -0.08)
P-value vs. placebo [a]		0.0059

[a] Derived from MMRM model with change from baseline in ACQ-5-IA values up to Week 52 as the response variable, and treatment, age, baseline weight group, region, baseline eosinophil level, baseline FeNO level, baseline ICS dose level, visit, treatment by-visit interaction, baseline ACQ-5-IA value and baseline-by-visit interaction as covariates.
Type 2 inflammatory asthma phenotype population is defined as the randomized patients with baseline blood eosinophils >= 0.15 Giga/L or baseline FeNO >= 20 ppb.
PGM=PRODOPS/SAR231893/EFC14153/CSR/REPORT/PGM/eff_mmrm_i_t.sas OUT=REPORT/OUTPUT/eff_acq5_chg_a52_t2e3_t_x.rtf (27NOV2020 - 5:26)

16.2.6.6.4 Change from baseline in ACQ-5-IA over time (MMRM including measurements up to Week 52) - Type 2 inflammatory asthma phenotype population and baseline blood eosinophils >=0.3 Giga/L population

	Type 2 inflammatory asthma phenotype population	
ACQ-5-IA	**Placebo (N=114)**	**Dupilumab (N=236)**
Week 12		
Change from baseline		
Number of patients in the model	110	227
LS Mean (SE) [a]	-1.04 (0.08)	-1.35 (0.06)
LS Mean Diff vs. placebo (95% CI) [a]		-0.31 (-0.51, -0.12)
P-value vs. placebo [a]		0.0013
Week 16		
Change from baseline		
Number of patients in the model	110	227
LS Mean (SE) [a]	-1.23 (0.08)	-1.36 (0.06)
LS Mean Diff vs. placebo (95% CI) [a]		-0.14 (-0.32, 0.05)
P-value vs. placebo [a]		0.1402

[a] Derived from MMRM model with change from baseline in ACQ-5-IA values up to Week 52 as the response variable, and treatment, age, baseline weight group, region, baseline eosinophil level, baseline FeNO level, baseline ICS dose level, visit, treatment by-visit interaction, baseline ACQ-5-IA value and baseline-by-visit interaction as covariates.
Type 2 inflammatory asthma phenotype population is defined as the randomized patients with baseline blood eosinophils >= 0.15 Giga/L or baseline FeNO >= 20 ppb.
PGM=PRODOPS/SAR231893/EFC14153/CSR/REPORT/PGM/eff_mmrm_i_t.sas OUT=REPORT/OUTPUT/eff_acq5_chg_a52_t2e3_t_x.rtf (27NOV2020 - 5:26)

16.2.6.6.4 Change from baseline in ACQ-5-IA over time (MMRM including measurements up to Week 52) - Type 2 inflammatory asthma phenotype population and baseline blood eosinophils >=0.3 Giga/L population

	Type 2 inflammatory asthma phenotype population	
ACQ-5-IA	**Placebo (N=114)**	**Dupilumab (N=236)**
Week 20		
Change from baseline		
Number of patients in the model	110	227
LS Mean (SE) [a]	-1.17 (0.09)	-1.35 (0.06)
LS Mean Diff vs. placebo (95% CI) [a]		-0.18 (-0.38, 0.02)
P-value vs. placebo [a]		0.0738
Week 24		
Change from baseline		
Number of patients in the model	110	227
LS Mean (SE) [a]	-1.18 (0.08)	-1.46 (0.06)
LS Mean Diff vs. placebo (95% CI) [a]		-0.28 (-0.46, -0.09)
P-value vs. placebo [a]		0.0032

[a] Derived from MMRM model with change from baseline in ACQ-5-IA values up to Week 52 as the response variable, and treatment, age, baseline weight group, region, baseline eosinophil level, baseline FeNO level, baseline ICS dose level, visit, treatment by-visit interaction, baseline ACQ-5-IA value and baseline-by-visit interaction as covariates.

Type 2 inflammatory asthma phenotype population is defined as the randomized patients with baseline blood eosinophils >= 0.15 Giga/L or baseline FeNO >= 20 ppb.

PGM=PRODOPS/SAR231893/EFC14153/CSR/REPORT/PGM/eff_mmrm_i_t.sas OUT=REPORT/OUTPUT/eff_acq5_chg_a52_t2e3_t_x.rtf (27NOV2020 - 5:26)

16.2.6.6.4 Change from baseline in ACQ-5-IA over time (MMRM including measurements up to Week 52) - Type 2 inflammatory asthma phenotype population and baseline blood eosinophils >=0.3 Giga/L population

	Type 2 inflammatory asthma phenotype population	
ACQ-5-IA	**Placebo (N=114)**	**Dupilumab (N=236)**
Week 28		
Change from baseline		
Number of patients in the model	110	227
LS Mean (SE) [a]	-1.26 (0.08)	-1.49 (0.06)
LS Mean Diff vs. placebo (95% CI) [a]		-0.23 (-0.42, -0.04)
P-value vs. placebo [a]		0.0171
Week 32		
Change from baseline		
Number of patients in the model	110	227
LS Mean (SE) [a]	-1.30 (0.08)	-1.45 (0.06)
LS Mean Diff vs. placebo (95% CI) [a]		-0.16 (-0.35, 0.03)
P-value vs. placebo [a]		0.1010

[a] Derived from MMRM model with change from baseline in ACQ-5-IA values up to Week 52 as the response variable, and treatment, age, baseline weight group, region, baseline eosinophil level, baseline FeNO level, baseline ICS dose level, visit, treatment by-visit interaction, baseline ACQ-5-IA value and baseline-by-visit interaction as covariates.
Type 2 inflammatory asthma phenotype population is defined as the randomized patients with baseline blood eosinophils >= 0.15 Giga/L or baseline FeNO >= 20 ppb.
PGM=PRODOPS/SAR231893/EFC14153/CSR/REPORT/PGM/eff_mmrm_i_t.sas OUT=REPORT/OUTPUT/eff_acq5_chg_a52_t2e3_t_x.rtf (27NOV2020 - 5:26)

16.2.6.6.4 Change from baseline in ACQ-5-IA over time (MMRM including measurements up to Week 52) - Type 2 inflammatory asthma phenotype population and baseline blood eosinophils >=0.3 Giga/L population

	Type 2 inflammatory asthma phenotype population	
ACQ-5-IA	**Placebo (N=114)**	**Dupilumab (N=236)**
Week 36		
Change from baseline		
Number of patients in the model	110	227
LS Mean (SE) [a]	-1.25 (0.08)	-1.57 (0.06)
LS Mean Diff vs. placebo (95% CI) [a]		-0.31 (-0.49, -0.14)
P-value vs. placebo [a]		0.0005
Week 40		
Change from baseline		
Number of patients in the model	110	227
LS Mean (SE) [a]	-1.29 (0.08)	-1.54 (0.06)
LS Mean Diff vs. placebo (95% CI) [a]		-0.26 (-0.43, -0.08)
P-value vs. placebo [a]		0.0042

[a] Derived from MMRM model with change from baseline in ACQ-5-IA values up to Week 52 as the response variable, and treatment, age, baseline weight group, region, baseline eosinophil level, baseline FeNO level, baseline ICS dose level, visit, treatment by-visit interaction, baseline ACQ-5-IA value and baseline-by-visit interaction as covariates.
Type 2 inflammatory asthma phenotype population is defined as the randomized patients with baseline blood eosinophils >= 0.15 Giga/L or baseline FeNO >= 20 ppb.
PGM=PRODOPS/SAR231893/EFC14153/CSR/REPORT/PGM/eff_mmrm_i_t.sas OUT=REPORT/OUTPUT/eff_acq5_chg_a52_t2e3_t_x.rtf (27NOV2020 - 5:26)

16.2.6.6.4 Change from baseline in ACQ-5-IA over time (MMRM including measurements up to Week 52) - Type 2 inflammatory asthma phenotype population and baseline blood eosinophils >=0.3 Giga/L population

	Type 2 inflammatory asthma phenotype population	
ACQ-5-IA	**Placebo (N=114)**	**Dupilumab (N=236)**
Week 44		
Change from baseline		
Number of patients in the model	110	227
LS Mean (SE) [a]	-1.35 (0.07)	-1.58 (0.05)
LS Mean Diff vs. placebo (95% CI) [a]		-0.23 (-0.39, -0.07)
P-value vs. placebo [a]		0.0050
Week 48		
Change from baseline		
Number of patients in the model	110	227
LS Mean (SE) [a]	-1.36 (0.07)	-1.63 (0.06)
LS Mean Diff vs. placebo (95% CI) [a]		-0.27 (-0.44, -0.10)
P-value vs. placebo [a]		0.0022

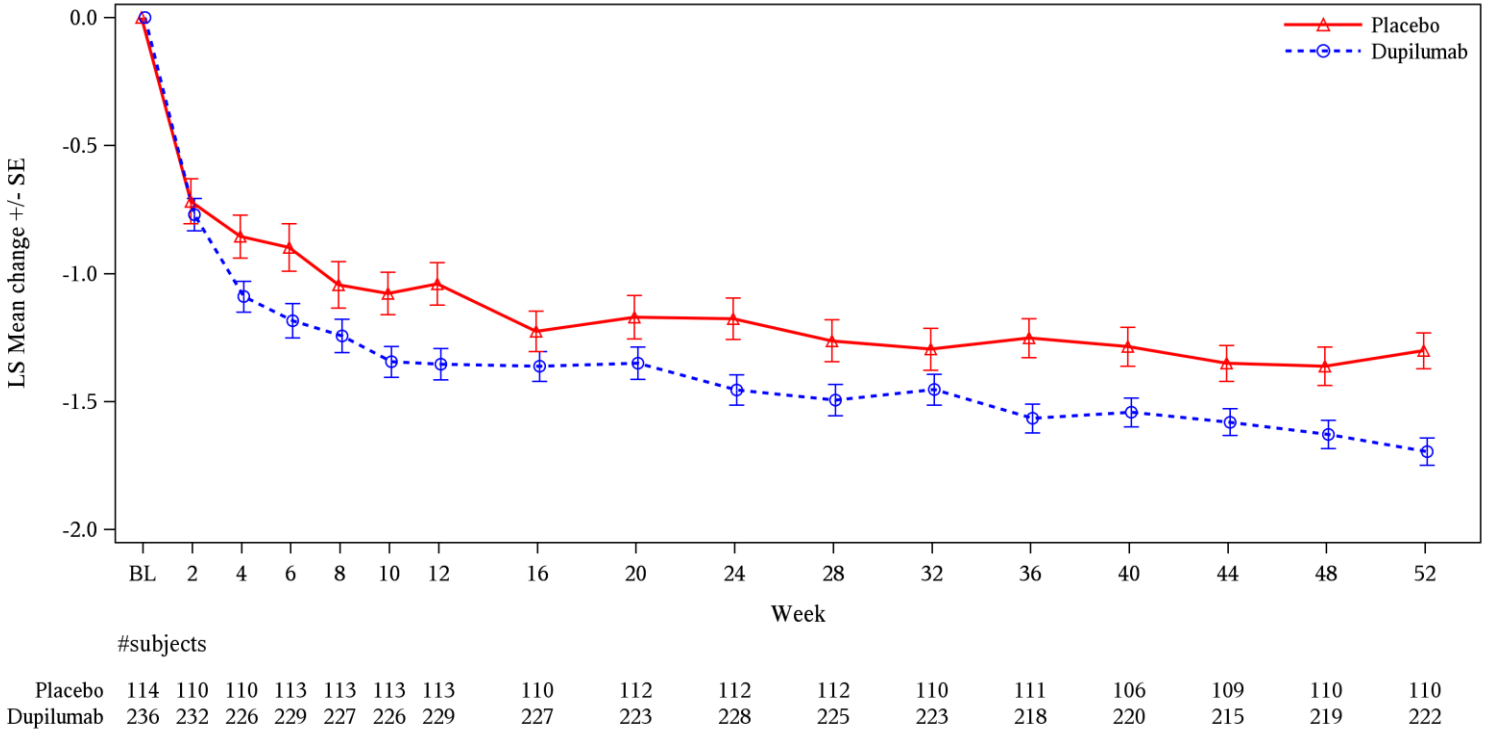
[a] Derived from MMRM model with change from baseline in ACQ-5-IA values up to Week 52 as the response variable, and treatment, age, baseline weight group, region, baseline eosinophil level, baseline FeNO level, baseline ICS dose level, visit, treatment by-visit interaction, baseline ACQ-5-IA value and baseline-by-visit interaction as covariates.
Type 2 inflammatory asthma phenotype population is defined as the randomized patients with baseline blood eosinophils >= 0.15 Giga/L or baseline FeNO >= 20 ppb.
PGM=PRODOPS/SAR231893/EFC14153/CSR/REPORT/PGM/eff_mmrm_i_t.sas OUT=REPORT/OUTPUT/eff_acq5_chg_a52_t2e3_t_x.rtf (27NOV2020 - 5:26)

16.2.6.6.4 Change from baseline in ACQ-5-IA over time (MMRM including measurements up to Week 52) - Type 2 inflammatory asthma phenotype population and baseline blood eosinophils >=0.3 Giga/L population

	Type 2 inflammatory asthma phenotype population	
ACQ-5-IA	**Placebo (N=114)**	**Dupilumab (N=236)**
Week 52		
Change from baseline		
Number of patients in the model	110	227
LS Mean (SE) [a]	-1.30 (0.07)	-1.70 (0.05)
LS Mean Diff vs. placebo (95% CI) [a]		-0.39 (-0.55, -0.23)
P-value vs. placebo [a]		<.0001

[a] Derived from MMRM model with change from baseline in ACQ-5-IA values up to Week 52 as the response variable, and treatment, age, baseline weight group, region, baseline eosinophil level, baseline FeNO level, baseline ICS dose level, visit, treatment by-visit interaction, baseline ACQ-5-IA value and baseline-by-visit interaction as covariates.
Type 2 inflammatory asthma phenotype population is defined as the randomized patients with baseline blood eosinophils >= 0.15 Giga/L or baseline FeNO >= 20 ppb.
PGM=PRODOPS/SAR231893/EFC14153/CSR/REPORT/PGM/eff_mmrm_i_t.sas OUT=REPORT/OUTPUT/eff_acq5_chg_a52_t2e3_t_x.rtf (27NOV2020 - 5:26)

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen
Project Code / Study Number / Analysis: SAR231893 / EFC14153 / CSR
16.2.6 Efficacy response data
16.2.6.6 ACQ-5-IA
16.2.6.6.5 Plot of LS mean change from baseline in ACQ-5-IA over time (MMRM including measurements up to Week 52) - Type 2 inflammatory asthma phenotype population



BL=Baseline
Type 2 inflammatory asthma phenotype population is defined as the randomized patients with baseline blood eosinophils >= 0.15 Giga/L or baseline FeNO >= 20 ppb.
PGM=PRODOPS/SAR231893/EFC14153/CSR/REPORT/PGM/eff_mmrm_i_g_intext_adqs.sas OUT=REPORT/OUTPUT/eff_acq5_chg_a52_t2_g_x.rtf (27NOV2020 - 3:23)

16.2.6 Efficacy response data

16.2.6.15 AM asthma symptom score

16.2.6.15.1 Summary of AM asthma symptom score over time - Type 2 inflammatory asthma phenotype population and baseline blood eosinophils >=0.3 Giga/L population

	Type 2 inflammatory asthma phenotype population	
AM asthma symptom score	**Placebo (N=114)**	**Dupilumab (N=236)**
Baseline		
Value		
Number	114	236
Mean (SD)	0.90 (0.72)	0.90 (0.78)
Median	0.86	0.86
Q1 : Q3	0.29 : 1.43	0.17 : 1.33
Min : Max	0.0 : 2.7	0.0 : 3.0
Week 2		
Value		
Number	114	234
Mean (SD)	0.69 (0.67)	0.72 (0.71)
Median	0.50	0.57
Q1 : Q3	0.14 : 1.15	0.10 : 1.07
Min : Max	0.0 : 3.0	0.0 : 3.0

Type 2 inflammatory asthma phenotype population is defined as the randomized patients with baseline blood eosinophils >= 0.15 Giga/L or baseline FeNO >= 20 ppb.

16.2.6 Efficacy response data

16.2.6.15 AM asthma symptom score

16.2.6.15.1 Summary of AM asthma symptom score over time - Type 2 inflammatory asthma phenotype population and baseline blood eosinophils >=0.3 Giga/L population

	Type 2 inflammatory asthma phenotype population	
AM asthma symptom score	**Placebo (N=114)**	**Dupilumab (N=236)**
Change from baseline		
Number	114	234
Mean (SD)	-0.21 (0.52)	-0.18 (0.45)
Median	-0.04	-0.03
Q1 : Q3	-0.43 : 0.01	-0.36 : 0.03
Min : Max	-2.7 : 0.7	-2.0 : 0.8
Percent change from baseline		
Number	94	187
Mean (SD)	-21.20 (57.77)	-12.21 (78.82)
Median	-19.62	-14.29
Q1 : Q3	-59.62 : 0.00	-53.85 : 1.54
Min : Max	-100.0 : 250.0	-100.0 : 500.0

Type 2 inflammatory asthma phenotype population is defined as the randomized patients with baseline blood eosinophils >= 0.15 Giga/L or baseline FeNO >= 20 ppb.

16.2.6 Efficacy response data

16.2.6.15 AM asthma symptom score

16.2.6.15.1 Summary of AM asthma symptom score over time - Type 2 inflammatory asthma phenotype population and baseline blood eosinophils >=0.3 Giga/L population

	Type 2 inflammatory asthma phenotype population	
AM asthma symptom score	**Placebo (N=114)**	**Dupilumab (N=236)**
Week 4		
Value		
Number	114	232
Mean (SD)	0.62 (0.67)	0.58 (0.65)
Median	0.36	0.35
Q1 : Q3	0.07 : 1.00	0.07 : 1.00
Min : Max	0.0 : 3.0	0.0 : 3.0
Change from baseline		
Number	114	232
Mean (SD)	-0.28 (0.63)	-0.33 (0.63)
Median	-0.12	-0.14
Q1 : Q3	-0.57 : 0.07	-0.64 : 0.00
Min : Max	-2.7 : 1.5	-2.8 : 1.1

Type 2 inflammatory asthma phenotype population is defined as the randomized patients with baseline blood eosinophils >= 0.15 Giga/L or baseline FeNO >= 20 ppb.

16.2.6 Efficacy response data

16.2.6.15 AM asthma symptom score

16.2.6.15.1 Summary of AM asthma symptom score over time - Type 2 inflammatory asthma phenotype population and baseline blood eosinophils >=0.3 Giga/L population

	Type 2 inflammatory asthma phenotype population	
AM asthma symptom score	**Placebo (N=114)**	**Dupilumab (N=236)**
Percent change from baseline		
Number	94	186
Mean (SD)	-26.76 (94.58)	-30.05 (75.15)
Median	-29.67	-41.67
Q1 : Q3	-85.71 : 0.00	-83.33 : 0.00
Min : Max	-100.0 : 707.7	-100.0 : 450.0
Week 6		
Value		
Number	114	232
Mean (SD)	0.59 (0.66)	0.52 (0.63)
Median	0.33	0.28
Q1 : Q3	0.00 : 1.00	0.00 : 1.00
Min : Max	0.0 : 2.5	0.0 : 3.0

Type 2 inflammatory asthma phenotype population is defined as the randomized patients with baseline blood eosinophils >= 0.15 Giga/L or baseline FeNO >= 20 ppb.

16.2.6 Efficacy response data

16.2.6.15 AM asthma symptom score

16.2.6.15.1 Summary of AM asthma symptom score over time - Type 2 inflammatory asthma phenotype population and baseline blood eosinophils >=0.3 Giga/L population

	Type 2 inflammatory asthma phenotype population	
AM asthma symptom score	**Placebo (N=114)**	**Dupilumab (N=236)**
Change from baseline		
Number	114	232
Mean (SD)	-0.31 (0.66)	-0.39 (0.65)
Median	-0.16	-0.14
Q1 : Q3	-0.65 : 0.00	-0.75 : 0.00
Min : Max	-2.3 : 1.6	-3.0 : 1.3
Percent change from baseline		
Number	94	186
Mean (SD)	-33.87 (85.28)	-35.99 (72.53)
Median	-48.08	-46.43
Q1 : Q3	-100.00 : 0.00	-91.43 : 0.00
Min : Max	-100.0 : 553.8	-100.0 : 400.0

Type 2 inflammatory asthma phenotype population is defined as the randomized patients with baseline blood eosinophils >= 0.15 Giga/L or baseline FeNO >= 20 ppb.

16.2.6 Efficacy response data

16.2.6.15 AM asthma symptom score

16.2.6.15.1 Summary of AM asthma symptom score over time - Type 2 inflammatory asthma phenotype population and baseline blood eosinophils >=0.3 Giga/L population

	Type 2 inflammatory asthma phenotype population	
AM asthma symptom score	**Placebo (N=114)**	**Dupilumab (N=236)**
Week 8		
Value		
Number	114	232
Mean (SD)	0.54 (0.64)	0.52 (0.65)
Median	0.22	0.29
Q1 : Q3	0.00 : 1.00	0.00 : 0.96
Min : Max	0.0 : 2.6	0.0 : 3.3
Change from baseline		
Number	114	232
Mean (SD)	-0.36 (0.67)	-0.38 (0.67)
Median	-0.20	-0.17
Q1 : Q3	-0.71 : 0.00	-0.76 : 0.00
Min : Max	-2.5 : 1.6	-2.9 : 1.5

Type 2 inflammatory asthma phenotype population is defined as the randomized patients with baseline blood eosinophils >= 0.15 Giga/L or baseline FeNO >= 20 ppb.

16.2.6 Efficacy response data

16.2.6.15 AM asthma symptom score

16.2.6.15.1 Summary of AM asthma symptom score over time - Type 2 inflammatory asthma phenotype population and baseline blood eosinophils >=0.3 Giga/L population

	Type 2 inflammatory asthma phenotype population	
AM asthma symptom score	**Placebo (N=114)**	**Dupilumab (N=236)**
Percent change from baseline		
Number	94	186
Mean (SD)	-40.63 (69.58)	-38.57 (72.58)
Median	-50.00	-50.00
Q1 : Q3	-100.00 : 0.00	-100.00 : 0.00
Min : Max	-100.0 : 328.6	-100.0 : 500.0
Week 10		
Value		
Number	114	230
Mean (SD)	0.60 (0.72)	0.45 (0.62)
Median	0.25	0.15
Q1 : Q3	0.00 : 1.00	0.00 : 0.82
Min : Max	0.0 : 3.0	0.0 : 3.0

Type 2 inflammatory asthma phenotype population is defined as the randomized patients with baseline blood eosinophils >= 0.15 Giga/L or baseline FeNO >= 20 ppb.

16.2.6 Efficacy response data

16.2.6.15 AM asthma symptom score

16.2.6.15.1 Summary of AM asthma symptom score over time - Type 2 inflammatory asthma phenotype population and baseline blood eosinophils >=0.3 Giga/L population

	Type 2 inflammatory asthma phenotype population	
AM asthma symptom score	**Placebo (N=114)**	**Dupilumab (N=236)**
Change from baseline		
Number	114	230
Mean (SD)	-0.30 (0.68)	-0.45 (0.69)
Median	-0.19	-0.25
Q1 : Q3	-0.69 : 0.00	-0.86 : 0.00
Min : Max	-2.3 : 1.9	-3.0 : 2.1
Percent change from baseline		
Number	94	185
Mean (SD)	-30.12 (87.06)	-40.80 (122.29)
Median	-47.73	-66.67
Q1 : Q3	-100.00 : 0.00	-100.00 : -8.16
Min : Max	-100.0 : 323.1	-100.0 : 1440.0

Type 2 inflammatory asthma phenotype population is defined as the randomized patients with baseline blood eosinophils >= 0.15 Giga/L or baseline FeNO >= 20 ppb.

16.2.6 Efficacy response data

16.2.6.15 AM asthma symptom score

16.2.6.15.1 Summary of AM asthma symptom score over time - Type 2 inflammatory asthma phenotype population and baseline blood eosinophils >=0.3 Giga/L population

	Type 2 inflammatory asthma phenotype population	
AM asthma symptom score	**Placebo (N=114)**	**Dupilumab (N=236)**
Week 12		
Value		
Number	113	229
Mean (SD)	0.56 (0.66)	0.43 (0.61)
Median	0.22	0.15
Q1 : Q3	0.00 : 1.00	0.00 : 0.63
Min : Max	0.0 : 2.9	0.0 : 3.0
Change from baseline		
Number	113	229
Mean (SD)	-0.35 (0.62)	-0.47 (0.70)
Median	-0.25	-0.24
Q1 : Q3	-0.57 : 0.00	-0.93 : 0.00
Min : Max	-2.3 : 1.0	-3.0 : 1.4

Type 2 inflammatory asthma phenotype population is defined as the randomized patients with baseline blood eosinophils >= 0.15 Giga/L or baseline FeNO >= 20 ppb.

16.2.6 Efficacy response data

16.2.6.15 AM asthma symptom score

16.2.6.15.1 Summary of AM asthma symptom score over time - Type 2 inflammatory asthma phenotype population and baseline blood eosinophils >=0.3 Giga/L population

	Type 2 inflammatory asthma phenotype population	
AM asthma symptom score	**Placebo (N=114)**	**Dupilumab (N=236)**
Percent change from baseline		
Number	93	183
Mean (SD)	-41.13 (65.86)	-45.89 (84.22)
Median	-51.79	-64.10
Q1 : Q3	-100.00 : -8.33	-100.00 : -14.29
Min : Max	-100.0 : 191.7	-100.0 : 653.8
Week 16		
Value		
Number	113	230
Mean (SD)	0.47 (0.60)	0.43 (0.60)
Median	0.18	0.13
Q1 : Q3	0.00 : 0.85	0.00 : 0.83
Min : Max	0.0 : 3.1	0.0 : 3.0

Type 2 inflammatory asthma phenotype population is defined as the randomized patients with baseline blood eosinophils >= 0.15 Giga/L or baseline FeNO >= 20 ppb.

16.2.6 Efficacy response data

16.2.6.15 AM asthma symptom score

16.2.6.15.1 Summary of AM asthma symptom score over time - Type 2 inflammatory asthma phenotype population and baseline blood eosinophils >=0.3 Giga/L population

	Type 2 inflammatory asthma phenotype population	
AM asthma symptom score	**Placebo (N=114)**	**Dupilumab (N=236)**
Change from baseline		
Number	113	230
Mean (SD)	-0.44 (0.62)	-0.47 (0.68)
Median	-0.33	-0.18
Q1 : Q3	-0.72 : 0.00	-0.86 : 0.00
Min : Max	-2.3 : 0.8	-3.0 : 1.2
Percent change from baseline		
Number	93	184
Mean (SD)	-52.14 (52.57)	-49.52 (66.47)
Median	-60.29	-73.07
Q1 : Q3	-100.00 : -17.39	-100.00 : -12.25
Min : Max	-100.0 : 169.2	-100.0 : 444.4

Type 2 inflammatory asthma phenotype population is defined as the randomized patients with baseline blood eosinophils >= 0.15 Giga/L or baseline FeNO >= 20 ppb.

16.2.6 Efficacy response data

16.2.6.15 AM asthma symptom score

16.2.6.15.1 Summary of AM asthma symptom score over time - Type 2 inflammatory asthma phenotype population and baseline blood eosinophils >=0.3 Giga/L population

	Type 2 inflammatory asthma phenotype population	
AM asthma symptom score	**Placebo (N=114)**	**Dupilumab (N=236)**
Week 20		
Value		
Number	113	229
Mean (SD)	0.48 (0.59)	0.39 (0.56)
Median	0.21	0.08
Q1 : Q3	0.00 : 1.00	0.00 : 0.67
Min : Max	0.0 : 3.0	0.0 : 2.8
Change from baseline		
Number	113	229
Mean (SD)	-0.42 (0.65)	-0.52 (0.70)
Median	-0.33	-0.31
Q1 : Q3	-0.80 : 0.00	-0.89 : 0.00
Min : Max	-2.5 : 0.9	-3.0 : 0.7

Type 2 inflammatory asthma phenotype population is defined as the randomized patients with baseline blood eosinophils >= 0.15 Giga/L or baseline FeNO >= 20 ppb.

16.2.6 Efficacy response data

16.2.6.15 AM asthma symptom score

16.2.6.15.1 Summary of AM asthma symptom score over time - Type 2 inflammatory asthma phenotype population and baseline blood eosinophils >=0.3 Giga/L population

	Type 2 inflammatory asthma phenotype population	
AM asthma symptom score	**Placebo (N=114)**	**Dupilumab (N=236)**
Percent change from baseline		
Number	93	185
Mean (SD)	-48.69 (61.96)	-52.57 (65.36)
Median	-69.57	-76.00
Q1 : Q3	-100.00 : -16.67	-100.00 : -14.29
Min : Max	-100.0 : 225.0	-100.0 : 384.6
Week 24		
Value		
Number	113	229
Mean (SD)	0.45 (0.61)	0.36 (0.58)
Median	0.14	0.06
Q1 : Q3	0.00 : 0.88	0.00 : 0.52
Min : Max	0.0 : 3.0	0.0 : 3.1

Type 2 inflammatory asthma phenotype population is defined as the randomized patients with baseline blood eosinophils >= 0.15 Giga/L or baseline FeNO >= 20 ppb.

16.2.6 Efficacy response data

16.2.6.15 AM asthma symptom score

16.2.6.15.1 Summary of AM asthma symptom score over time - Type 2 inflammatory asthma phenotype population and baseline blood eosinophils >=0.3 Giga/L population

	Type 2 inflammatory asthma phenotype population	
AM asthma symptom score	**Placebo (N=114)**	**Dupilumab (N=236)**
Change from baseline		
Number	113	229
Mean (SD)	-0.46 (0.66)	-0.55 (0.73)
Median	-0.33	-0.29
Q1 : Q3	-0.83 : 0.00	-1.00 : 0.00
Min : Max	-2.5 : 1.7	-3.0 : 1.0
Percent change from baseline		
Number	93	185
Mean (SD)	-51.13 (61.16)	-53.74 (73.16)
Median	-73.91	-87.50
Q1 : Q3	-100.00 : -22.22	-100.00 : -19.44
Min : Max	-100.0 : 191.7	-100.0 : 524.0

Type 2 inflammatory asthma phenotype population is defined as the randomized patients with baseline blood eosinophils >= 0.15 Giga/L or baseline FeNO >= 20 ppb.

16.2.6 Efficacy response data

16.2.6.15 AM asthma symptom score

16.2.6.15.1 Summary of AM asthma symptom score over time - Type 2 inflammatory asthma phenotype population and baseline blood eosinophils >=0.3 Giga/L population

	Type 2 inflammatory asthma phenotype population	
AM asthma symptom score	**Placebo (N=114)**	**Dupilumab (N=236)**
Week 28		
Value		
Number	111	227
Mean (SD)	0.41 (0.58)	0.37 (0.60)
Median	0.07	0.04
Q1 : Q3	0.00 : 0.89	0.00 : 0.63
Min : Max	0.0 : 3.0	0.0 : 3.5
Change from baseline		
Number	111	227
Mean (SD)	-0.49 (0.69)	-0.54 (0.72)
Median	-0.35	-0.29
Q1 : Q3	-0.95 : 0.00	-0.96 : 0.00
Min : Max	-2.7 : 1.1	-3.0 : 1.4

Type 2 inflammatory asthma phenotype population is defined as the randomized patients with baseline blood eosinophils >= 0.15 Giga/L or baseline FeNO >= 20 ppb.

16.2.6 Efficacy response data

16.2.6.15 AM asthma symptom score

16.2.6.15.1 Summary of AM asthma symptom score over time - Type 2 inflammatory asthma phenotype population and baseline blood eosinophils >=0.3 Giga/L population

	Type 2 inflammatory asthma phenotype population	
AM asthma symptom score	**Placebo (N=114)**	**Dupilumab (N=236)**
Percent change from baseline		
Number	91	183
Mean (SD)	-57.36 (57.39)	-53.40 (69.89)
Median	-80.00	-85.71
Q1 : Q3	-100.00 : -30.86	-100.00 : -15.00
Min : Max	-100.0 : 250.0	-100.0 : 303.8
Week 32		
Value		
Number	111	225
Mean (SD)	0.39 (0.57)	0.37 (0.60)
Median	0.07	0.07
Q1 : Q3	0.00 : 0.75	0.00 : 0.59
Min : Max	0.0 : 3.0	0.0 : 4.0

Type 2 inflammatory asthma phenotype population is defined as the randomized patients with baseline blood eosinophils >= 0.15 Giga/L or baseline FeNO >= 20 ppb.

16.2.6 Efficacy response data

16.2.6.15 AM asthma symptom score

16.2.6.15.1 Summary of AM asthma symptom score over time - Type 2 inflammatory asthma phenotype population and baseline blood eosinophils >=0.3 Giga/L population

	Type 2 inflammatory asthma phenotype population	
AM asthma symptom score	**Placebo (N=114)**	**Dupilumab (N=236)**
Change from baseline		
Number	111	225
Mean (SD)	-0.51 (0.71)	-0.54 (0.73)
Median	-0.33	-0.29
Q1 : Q3	-1.00 : 0.00	-1.00 : 0.00
Min : Max	-2.7 : 0.9	-3.0 : 1.0
Percent change from baseline		
Number	91	181
Mean (SD)	-55.26 (62.94)	-54.04 (60.84)
Median	-86.67	-83.33
Q1 : Q3	-100.00 : -22.22	-100.00 : -14.29
Min : Max	-100.0 : 225.0	-100.0 : 250.0

Type 2 inflammatory asthma phenotype population is defined as the randomized patients with baseline blood eosinophils >= 0.15 Giga/L or baseline FeNO >= 20 ppb.

16.2.6 Efficacy response data

16.2.6.15 AM asthma symptom score

16.2.6.15.1 Summary of AM asthma symptom score over time - Type 2 inflammatory asthma phenotype population and baseline blood eosinophils >=0.3 Giga/L population

	Type 2 inflammatory asthma phenotype population	
AM asthma symptom score	**Placebo (N=114)**	**Dupilumab (N=236)**
Week 36		
Value		
Number	110	225
Mean (SD)	0.41 (0.58)	0.36 (0.59)
Median	0.09	0.00
Q1 : Q3	0.00 : 0.86	0.00 : 0.60
Min : Max	0.0 : 3.0	0.0 : 3.7
Change from baseline		
Number	110	225
Mean (SD)	-0.49 (0.70)	-0.55 (0.74)
Median	-0.31	-0.33
Q1 : Q3	-0.91 : 0.00	-0.96 : 0.00
Min : Max	-2.7 : 1.0	-3.0 : 2.0

Type 2 inflammatory asthma phenotype population is defined as the randomized patients with baseline blood eosinophils >= 0.15 Giga/L or baseline FeNO >= 20 ppb.

16.2.6 Efficacy response data

16.2.6.15 AM asthma symptom score

16.2.6.15.1 Summary of AM asthma symptom score over time - Type 2 inflammatory asthma phenotype population and baseline blood eosinophils >=0.3 Giga/L population

	Type 2 inflammatory asthma phenotype population	
AM asthma symptom score	**Placebo (N=114)**	**Dupilumab (N=236)**
Percent change from baseline		
Number	90	181
Mean (SD)	-53.10 (62.00)	-53.61 (74.82)
Median	-86.81	-88.89
Q1 : Q3	-100.00 : -6.52	-100.00 : -22.22
Min : Max	-100.0 : 211.1	-100.0 : 430.8
Week 40		
Value		
Number	111	224
Mean (SD)	0.42 (0.58)	0.32 (0.55)
Median	0.09	0.00
Q1 : Q3	0.00 : 0.95	0.00 : 0.48
Min : Max	0.0 : 3.0	0.0 : 3.0

Type 2 inflammatory asthma phenotype population is defined as the randomized patients with baseline blood eosinophils >= 0.15 Giga/L or baseline FeNO >= 20 ppb.

16.2.6 Efficacy response data

16.2.6.15 AM asthma symptom score

16.2.6.15.1 Summary of AM asthma symptom score over time - Type 2 inflammatory asthma phenotype population and baseline blood eosinophils >=0.3 Giga/L population

	Type 2 inflammatory asthma phenotype population	
AM asthma symptom score	**Placebo (N=114)**	**Dupilumab (N=236)**
Change from baseline		
Number	111	224
Mean (SD)	-0.47 (0.71)	-0.59 (0.76)
Median	-0.29	-0.30
Q1 : Q3	-0.89 : 0.00	-1.00 : 0.00
Min : Max	-2.7 : 0.9	-3.0 : 1.9
Percent change from baseline		
Number	91	180
Mean (SD)	-47.71 (75.00)	-58.56 (65.90)
Median	-79.81	-93.89
Q1 : Q3	-100.00 : -13.04	-100.00 : -22.22
Min : Max	-100.0 : 320.0	-100.0 : 316.7

Type 2 inflammatory asthma phenotype population is defined as the randomized patients with baseline blood eosinophils >= 0.15 Giga/L or baseline FeNO >= 20 ppb.

16.2.6 Efficacy response data

16.2.6.15 AM asthma symptom score

16.2.6.15.1 Summary of AM asthma symptom score over time - Type 2 inflammatory asthma phenotype population and baseline blood eosinophils >=0.3 Giga/L population

	Type 2 inflammatory asthma phenotype population	
AM asthma symptom score	**Placebo (N=114)**	**Dupilumab (N=236)**
Week 44		
Value		
Number	111	224
Mean (SD)	0.42 (0.60)	0.31 (0.55)
Median	0.04	0.00
Q1 : Q3	0.00 : 0.93	0.00 : 0.33
Min : Max	0.0 : 3.0	0.0 : 3.0
Change from baseline		
Number	111	224
Mean (SD)	-0.48 (0.72)	-0.60 (0.76)
Median	-0.33	-0.39
Q1 : Q3	-0.88 : 0.00	-1.00 : 0.00
Min : Max	-2.7 : 1.0	-2.9 : 2.1

Type 2 inflammatory asthma phenotype population is defined as the randomized patients with baseline blood eosinophils >= 0.15 Giga/L or baseline FeNO >= 20 ppb.

16.2.6 Efficacy response data

16.2.6.15 AM asthma symptom score

16.2.6.15.1 Summary of AM asthma symptom score over time - Type 2 inflammatory asthma phenotype population and baseline blood eosinophils >=0.3 Giga/L population

	Type 2 inflammatory asthma phenotype population	
AM asthma symptom score	**Placebo (N=114)**	**Dupilumab (N=236)**
Percent change from baseline		
Number	91	180
Mean (SD)	-56.24 (65.06)	-60.80 (66.85)
Median	-93.00	-93.63
Q1 : Q3	-100.00 : -22.22	-100.00 : -30.00
Min : Max	-100.0 : 279.2	-100.0 : 344.4
Week 48		
Value		
Number	111	221
Mean (SD)	0.43 (0.57)	0.29 (0.51)
Median	0.10	0.00
Q1 : Q3	0.00 : 0.92	0.00 : 0.31
Min : Max	0.0 : 3.0	0.0 : 2.9

Type 2 inflammatory asthma phenotype population is defined as the randomized patients with baseline blood eosinophils >= 0.15 Giga/L or baseline FeNO >= 20 ppb.

16.2.6 Efficacy response data

16.2.6.15 AM asthma symptom score

16.2.6.15.1 Summary of AM asthma symptom score over time - Type 2 inflammatory asthma phenotype population and baseline blood eosinophils >=0.3 Giga/L population

	Type 2 inflammatory asthma phenotype population	
AM asthma symptom score	**Placebo (N=114)**	**Dupilumab (N=236)**
Change from baseline		
Number	111	221
Mean (SD)	-0.47 (0.68)	-0.62 (0.75)
Median	-0.33	-0.43
Q1 : Q3	-0.76 : 0.00	-1.00 : 0.00
Min : Max	-2.7 : 1.1	-3.0 : 0.7
Percent change from baseline		
Number	91	177
Mean (SD)	-50.25 (64.73)	-66.21 (53.86)
Median	-72.22	-100.00
Q1 : Q3	-100.00 : -13.07	-100.00 : -40.00
Min : Max	-100.0 : 236.0	-100.0 : 250.0

Type 2 inflammatory asthma phenotype population is defined as the randomized patients with baseline blood eosinophils >= 0.15 Giga/L or baseline FeNO >= 20 ppb.

16.2.6 Efficacy response data

16.2.6.15 AM asthma symptom score

16.2.6.15.1 Summary of AM asthma symptom score over time - Type 2 inflammatory asthma phenotype population and baseline blood eosinophils >=0.3 Giga/L population

	Type 2 inflammatory asthma phenotype population	
AM asthma symptom score	**Placebo (N=114)**	**Dupilumab (N=236)**
Week 52		
Value		
Number	111	222
Mean (SD)	0.40 (0.58)	0.30 (0.55)
Median	0.05	0.00
Q1 : Q3	0.00 : 0.87	0.00 : 0.41
Min : Max	0.0 : 3.0	0.0 : 3.0
Change from baseline		
Number	111	222
Mean (SD)	-0.50 (0.71)	-0.60 (0.78)
Median	-0.33	-0.43
Q1 : Q3	-0.86 : 0.00	-1.00 : 0.00
Min : Max	-2.7 : 1.4	-3.0 : 2.4

Type 2 inflammatory asthma phenotype population is defined as the randomized patients with baseline blood eosinophils >= 0.15 Giga/L or baseline FeNO >= 20 ppb.

16.2.6 Efficacy response data

16.2.6.15 AM asthma symptom score

16.2.6.15.1 Summary of AM asthma symptom score over time - Type 2 inflammatory asthma phenotype population and baseline blood eosinophils >=0.3 Giga/L population

	Type 2 inflammatory asthma phenotype population	
AM asthma symptom score	**Placebo (N=114)**	**Dupilumab (N=236)**
Percent change from baseline		
Number	91	178
Mean (SD)	-53.16 (73.22)	-59.30 (75.63)
Median	-90.00	-98.50
Q1 : Q3	-100.00 : -22.22	-100.00 : -30.86
Min : Max	-100.0 : 350.0	-100.0 : 453.8
Week 56		
Value		
Number	35	84
Mean (SD)	0.48 (0.66)	0.23 (0.45)
Median	0.00	0.00
Q1 : Q3	0.00 : 1.00	0.00 : 0.00
Min : Max	0.0 : 2.3	0.0 : 2.0

Type 2 inflammatory asthma phenotype population is defined as the randomized patients with baseline blood eosinophils >= 0.15 Giga/L or baseline FeNO >= 20 ppb.

16.2.6 Efficacy response data

16.2.6.15 AM asthma symptom score

16.2.6.15.1 Summary of AM asthma symptom score over time - Type 2 inflammatory asthma phenotype population and baseline blood eosinophils >=0.3 Giga/L population

	Type 2 inflammatory asthma phenotype population	
AM asthma symptom score	**Placebo (N=114)**	**Dupilumab (N=236)**
Change from baseline		
Number	35	84
Mean (SD)	-0.46 (0.71)	-0.59 (0.66)
Median	-0.25	-0.46
Q1 : Q3	-0.86 : 0.00	-1.00 : 0.00
Min : Max	-2.3 : 0.9	-2.2 : 1.0
Percent change from baseline		
Number	30	68
Mean (SD)	-50.15 (60.46)	-70.11 (62.55)
Median	-59.81	-100.00
Q1 : Q3	-100.00 : -5.56	-100.00 : -50.00
Min : Max	-100.0 : 100.0	-100.0 : 250.0

Type 2 inflammatory asthma phenotype population is defined as the randomized patients with baseline blood eosinophils >= 0.15 Giga/L or baseline FeNO >= 20 ppb.

16.2.6 Efficacy response data

16.2.6.15 AM asthma symptom score

16.2.6.15.1 Summary of AM asthma symptom score over time - Type 2 inflammatory asthma phenotype population and baseline blood eosinophils >=0.3 Giga/L population

	Type 2 inflammatory asthma phenotype population	
AM asthma symptom score	**Placebo (N=114)**	**Dupilumab (N=236)**
Week 60		
Value		
Number	3	14
Mean (SD)	0.07 (0.12)	0.23 (0.42)
Median	0.00	0.00
Q1 : Q3	0.00 : 0.21	0.00 : 0.10
Min : Max	0.0 : 0.2	0.0 : 1.0
Change from baseline		
Number	3	14
Mean (SD)	-1.04 (1.12)	-0.75 (0.68)
Median	-0.43	-0.83
Q1 : Q3	-2.33 : -0.36	-1.29 : 0.00
Min : Max	-2.3 : -0.4	-2.1 : 0.0

Type 2 inflammatory asthma phenotype population is defined as the randomized patients with baseline blood eosinophils >= 0.15 Giga/L or baseline FeNO >= 20 ppb.

16.2.6 Efficacy response data

16.2.6.15 AM asthma symptom score

16.2.6.15.1 Summary of AM asthma symptom score over time - Type 2 inflammatory asthma phenotype population and baseline blood eosinophils >=0.3 Giga/L population

	Type 2 inflammatory asthma phenotype population	
AM asthma symptom score	**Placebo (N=114)**	**Dupilumab (N=236)**
Percent change from baseline		
Number	3	11
Mean (SD)	-87.72 (21.27)	-75.20 (40.32)
Median	-100.00	-96.88
Q1 : Q3	-100.00 : -63.16	-100.00 : -25.00
Min : Max	-100.0 : -63.2	-100.0 : 0.0
Week 64		
Value		
Number	2	14
Mean (SD)	0.65 (0.21)	0.37 (0.56)
Median	0.65	0.00
Q1 : Q3	0.50 : 0.79	0.00 : 1.00
Min : Max	0.5 : 0.8	0.0 : 1.7

Type 2 inflammatory asthma phenotype population is defined as the randomized patients with baseline blood eosinophils >= 0.15 Giga/L or baseline FeNO >= 20 ppb.

16.2.6 Efficacy response data

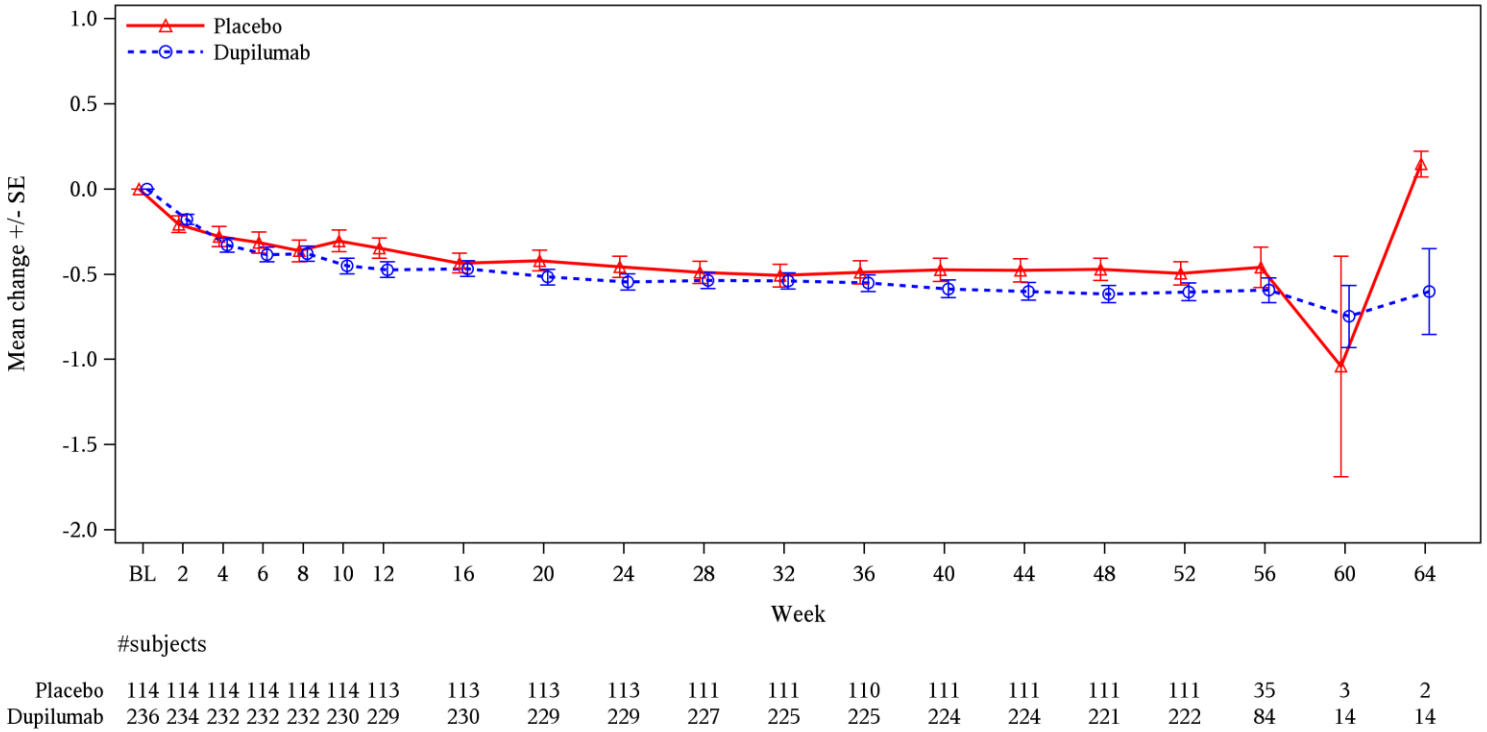
16.2.6.15 AM asthma symptom score

16.2.6.15.1 Summary of AM asthma symptom score over time - Type 2 inflammatory asthma phenotype population and baseline blood eosinophils >=0.3 Giga/L population

	Type 2 inflammatory asthma phenotype population	
AM asthma symptom score	**Placebo (N=114)**	**Dupilumab (N=236)**
Change from baseline		
Number	2	14
Mean (SD)	0.15 (0.11)	-0.60 (0.94)
Median	0.15	-0.58
Q1 : Q3	0.07 : 0.22	-1.29 : 0.00
Min : Max	0.1 : 0.2	-2.2 : 1.7
Percent change from baseline		
Number	2	11
Mean (SD)	27.60 (15.47)	-70.55 (41.75)
Median	27.60	-100.00
Q1 : Q3	16.67 : 38.54	-100.00 : -25.00
Min : Max	16.7 : 38.5	-100.0 : 0.0

Type 2 inflammatory asthma phenotype population is defined as the randomized patients with baseline blood eosinophils >= 0.15 Giga/L or baseline FeNO >= 20 ppb.

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen
Project Code / Study Number / Analysis: SAR231893 / EFC14153 / CSR
16.2.6 Efficacy response data
16.2.6.15 AM asthma symptom score
16.2.6.15.2 Plot of mean change from baseline in AM asthma symptom score over time - Type 2 inflammatory asthma phenotype population



#subjects

	BL	2	4	6	8	10	12	16	20	24	28	32	36	40	44	48	52	56	60	64
Placebo	114	114	114	114	114	114	113	113	113	113	111	111	110	111	111	111	111	35	3	2
Dupilumab	236	234	232	232	232	230	229	230	229	229	227	225	225	224	224	221	222	84	14	14

BL=Baseline
Type 2 inflammatory asthma phenotype population is defined as the randomized patients with baseline blood eosinophils >= 0.15 Giga/L or baseline FeNO >= 20 ppb.
PGM=PRODOPS/SAR231893/EFC14153/CSR/REPORT/PGM/eff_sum_vis_i_g.sas OUT=REPORT/OUTPUT/eff_sum_asam_t2_g_x.rtf (27NOV2020 - 6:37)

Project Code / Study Number / Analysis: SAR231893 / EFC14153 / CSR

16.2.6 Efficacy response data

16.2.6.15 AM asthma symptom score

16.2.6.15.4 Change from baseline in AM asthma symptom score over time (MMRM including measurements up to Week 52) - Type 2 inflammatory asthma phenotype population and baseline blood eosinophils >=0.3 Giga/L population

	Type 2 inflammatory asthma phenotype population	
AM asthma symptom score	**Placebo (N=114)**	**Dupilumab (N=236)**
Baseline		
Value		
Number	114	236
Mean (SD)	0.90 (0.72)	0.90 (0.78)
Median	0.86	0.86
Q1 : Q3	0.29 : 1.43	0.17 : 1.33
Min : Max	0.0 : 2.7	0.0 : 3.0
Week 2		
Change from baseline		
Number of patients in the model	110	228
LS Mean (SE) [a]	-0.22 (0.04)	-0.18 (0.03)
LS Mean Diff vs. placebo (95% CI) [a]		0.03 (-0.06, 0.13)
P-value vs. placebo [a]		0.4961

[a] Derived from MMRM model with change from baseline in AM asthma symptom score values up to Week 52 as the response variable, and treatment, age, baseline weight group, region, baseline eosinophil level, baseline FeNO level, baseline ICS dose level, visit, treatment by-visit interaction, baseline AM asthma symptom score value and baseline-by-visit interaction as covariates.

Type 2 inflammatory asthma phenotype population is defined as the randomized patients with baseline blood eosinophils >= 0.15 Giga/L or baseline FeNO >= 20 ppb.

PGM=PRODOPS/SAR231893/EFC14153/CSR/REPORT/PGM/eff_mmrm_i_t_aded.sas OUT=REPORT/OUTPUT/eff_asam_chg_a52_t2e3_t_x.rtf (27NOV2020 - 2:53)

Project Code / Study Number / Analysis: SAR231893 / EFC14153 / CSR

16.2.6 Efficacy response data

16.2.6.15 AM asthma symptom score

16.2.6.15.4 Change from baseline in AM asthma symptom score over time (MMRM including measurements up to Week 52) - Type 2 inflammatory asthma phenotype population and baseline blood eosinophils >=0.3 Giga/L population

	Type 2 inflammatory asthma phenotype population	
AM asthma symptom score	**Placebo (N=114)**	**Dupilumab (N=236)**
Week 4		
Change from baseline		
Number of patients in the model	110	228
LS Mean (SE) [a]	-0.29 (0.05)	-0.34 (0.04)
LS Mean Diff vs. placebo (95% CI) [a]		-0.05 (-0.17, 0.07)
P-value vs. placebo [a]		0.3899
Week 6		
Change from baseline		
Number of patients in the model	110	228
LS Mean (SE) [a]	-0.32 (0.05)	-0.39 (0.04)
LS Mean Diff vs. placebo (95% CI) [a]		-0.07 (-0.19, 0.05)
P-value vs. placebo [a]		0.2364

[a] Derived from MMRM model with change from baseline in AM asthma symptom score values up to Week 52 as the response variable, and treatment, age, baseline weight group, region, baseline eosinophil level, baseline FeNO level, baseline ICS dose level, visit, treatment by-visit interaction, baseline AM asthma symptom score value and baseline-by-visit interaction as covariates.

Type 2 inflammatory asthma phenotype population is defined as the randomized patients with baseline blood eosinophils >= 0.15 Giga/L or baseline FeNO >= 20 ppb.

PGM=PRODOPS/SAR231893/EFC14153/CSR/REPORT/PGM/eff_mmrm_i_t_aded.sas OUT=REPORT/OUTPUT/eff_asam_chg_a52_t2e3_t_x.rtf (27NOV2020 - 2:53)

Project Code / Study Number / Analysis: SAR231893 / EFC14153 / CSR

16.2.6 Efficacy response data

16.2.6.15 AM asthma symptom score

16.2.6.15.4 Change from baseline in AM asthma symptom score over time (MMRM including measurements up to Week 52) - Type 2 inflammatory asthma phenotype population and baseline blood eosinophils >=0.3 Giga/L population

	Type 2 inflammatory asthma phenotype population	
AM asthma symptom score	**Placebo (N=114)**	**Dupilumab (N=236)**
Week 8		
Change from baseline		
Number of patients in the model	110	228
LS Mean (SE) [a]	-0.37 (0.05)	-0.39 (0.04)
LS Mean Diff vs. placebo (95% CI) [a]		-0.02 (-0.15, 0.10)
P-value vs. placebo [a]		0.7514
Week 10		
Change from baseline		
Number of patients in the model	110	228
LS Mean (SE) [a]	-0.31 (0.06)	-0.46 (0.04)
LS Mean Diff vs. placebo (95% CI) [a]		-0.15 (-0.28, -0.03)
P-value vs. placebo [a]		0.0186

[a] Derived from MMRM model with change from baseline in AM asthma symptom score values up to Week 52 as the response variable, and treatment, age, baseline weight group, region, baseline eosinophil level, baseline FeNO level, baseline ICS dose level, visit, treatment by-visit interaction, baseline AM asthma symptom score value and baseline-by-visit interaction as covariates.

Type 2 inflammatory asthma phenotype population is defined as the randomized patients with baseline blood eosinophils >= 0.15 Giga/L or baseline FeNO >= 20 ppb.

PGM=PRODOPS/SAR231893/EFC14153/CSR/REPORT/PGM/eff_mmrm_i_t_aded.sas OUT=REPORT/OUTPUT/eff_asam_chg_a52_t2e3_t_x.rtf (27NOV2020 - 2:53)

Project Code / Study Number / Analysis: SAR231893 / EFC14153 / CSR

16.2.6 Efficacy response data

16.2.6.15 AM asthma symptom score

16.2.6.15.4 Change from baseline in AM asthma symptom score over time (MMRM including measurements up to Week 52) - Type 2 inflammatory asthma phenotype population and baseline blood eosinophils >=0.3 Giga/L population

	Type 2 inflammatory asthma phenotype population	
AM asthma symptom score	**Placebo (N=114)**	**Dupilumab (N=236)**
Week 12		
Change from baseline		
Number of patients in the model	110	228
LS Mean (SE) [a]	-0.34 (0.05)	-0.48 (0.04)
LS Mean Diff vs. placebo (95% CI) [a]		-0.15 (-0.27, -0.02)
P-value vs. placebo [a]		0.0187
Week 16		
Change from baseline		
Number of patients in the model	110	228
LS Mean (SE) [a]	-0.43 (0.05)	-0.48 (0.04)
LS Mean Diff vs. placebo (95% CI) [a]		-0.05 (-0.17, 0.07)
P-value vs. placebo [a]		0.4123

[a] Derived from MMRM model with change from baseline in AM asthma symptom score values up to Week 52 as the response variable, and treatment, age, baseline weight group, region, baseline eosinophil level, baseline FeNO level, baseline ICS dose level, visit, treatment by-visit interaction, baseline AM asthma symptom score value and baseline-by-visit interaction as covariates.

Type 2 inflammatory asthma phenotype population is defined as the randomized patients with baseline blood eosinophils >= 0.15 Giga/L or baseline FeNO >= 20 ppb.

PGM=PRODOPS/SAR231893/EFC14153/CSR/REPORT/PGM/eff_mmrm_i_t_aded.sas OUT=REPORT/OUTPUT/eff_asam_chg_a52_t2e3_t_x.rtf (27NOV2020 - 2:53)

Project Code / Study Number / Analysis: SAR231893 / EFC14153 / CSR

16.2.6 Efficacy response data

16.2.6.15 AM asthma symptom score

16.2.6.15.4 Change from baseline in AM asthma symptom score over time (MMRM including measurements up to Week 52) - Type 2 inflammatory asthma phenotype population and baseline blood eosinophils >=0.3 Giga/L population

	Type 2 inflammatory asthma phenotype population	
AM asthma symptom score	**Placebo (N=114)**	**Dupilumab (N=236)**
Week 20		
Change from baseline		
Number of patients in the model	110	228
LS Mean (SE) [a]	-0.42 (0.05)	-0.53 (0.04)
LS Mean Diff vs. placebo (95% CI) [a]		-0.10 (-0.22, 0.01)
P-value vs. placebo [a]		0.0852
Week 24		
Change from baseline		
Number of patients in the model	110	228
LS Mean (SE) [a]	-0.46 (0.05)	-0.56 (0.04)
LS Mean Diff vs. placebo (95% CI) [a]		-0.10 (-0.22, 0.02)
P-value vs. placebo [a]		0.1059

[a] Derived from MMRM model with change from baseline in AM asthma symptom score values up to Week 52 as the response variable, and treatment, age, baseline weight group, region, baseline eosinophil level, baseline FeNO level, baseline ICS dose level, visit, treatment by-visit interaction, baseline AM asthma symptom score value and baseline-by-visit interaction as covariates.

Type 2 inflammatory asthma phenotype population is defined as the randomized patients with baseline blood eosinophils >= 0.15 Giga/L or baseline FeNO >= 20 ppb.

PGM=PRODOPS/SAR231893/EFC14153/CSR/REPORT/PGM/eff_mmrm_i_t_aded.sas OUT=REPORT/OUTPUT/eff_asam_chg_a52_t2e3_t_x.rtf (27NOV2020 - 2:53)

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

Project Code / Study Number / Analysis: SAR231893 / EFC14153 / CSR

16.2.6 Efficacy response data

16.2.6.15 AM asthma symptom score

16.2.6.15.4 Change from baseline in AM asthma symptom score over time (MMRM including measurements up to Week 52) - Type 2 inflammatory asthma phenotype population and baseline blood eosinophils >=0.3 Giga/L population

	Type 2 inflammatory asthma phenotype population	
AM asthma symptom score	**Placebo (N=114)**	**Dupilumab (N=236)**
Week 28		
Change from baseline		
Number of patients in the model	110	228
LS Mean (SE) [a]	-0.48 (0.05)	-0.55 (0.04)
LS Mean Diff vs. placebo (95% CI) [a]		-0.06 (-0.18, 0.06)
P-value vs. placebo [a]		0.3128
Week 32		
Change from baseline		
Number of patients in the model	110	228
LS Mean (SE) [a]	-0.51 (0.05)	-0.55 (0.04)
LS Mean Diff vs. placebo (95% CI) [a]		-0.04 (-0.17, 0.08)
P-value vs. placebo [a]		0.4845

[a] Derived from MMRM model with change from baseline in AM asthma symptom score values up to Week 52 as the response variable, and treatment, age, baseline weight group, region, baseline eosinophil level, baseline FeNO level, baseline ICS dose level, visit, treatment by-visit interaction, baseline AM asthma symptom score value and baseline-by-visit interaction as covariates.

Type 2 inflammatory asthma phenotype population is defined as the randomized patients with baseline blood eosinophils >= 0.15 Giga/L or baseline FeNO >= 20 ppb.

PGM=PRODOPS/SAR231893/EFC14153/CSR/REPORT/PGM/eff_mmrm_i_t_aded.sas OUT=REPORT/OUTPUT/eff_asam_chg_a52_t2e3_t_x.rtf (27NOV2020 - 2:53)

Project Code / Study Number / Analysis: SAR231893 / EFC14153 / CSR

16.2.6 Efficacy response data

16.2.6.15 AM asthma symptom score

16.2.6.15.4 Change from baseline in AM asthma symptom score over time (MMRM including measurements up to Week 52) - Type 2 inflammatory asthma phenotype population and baseline blood eosinophils >=0.3 Giga/L population

	Type 2 inflammatory asthma phenotype population	
AM asthma symptom score	**Placebo (N=114)**	**Dupilumab (N=236)**
Week 36		
Change from baseline		
Number of patients in the model	110	228
LS Mean (SE) [a]	-0.48 (0.05)	-0.56 (0.04)
LS Mean Diff vs. placebo (95% CI) [a]		-0.08 (-0.20, 0.04)
P-value vs. placebo [a]		0.2106
Week 40		
Change from baseline		
Number of patients in the model	110	228
LS Mean (SE) [a]	-0.47 (0.05)	-0.59 (0.04)
LS Mean Diff vs. placebo (95% CI) [a]		-0.12 (-0.24, -0.00)
P-value vs. placebo [a]		0.0455

[a] Derived from MMRM model with change from baseline in AM asthma symptom score values up to Week 52 as the response variable, and treatment, age, baseline weight group, region, baseline eosinophil level, baseline FeNO level, baseline ICS dose level, visit, treatment by-visit interaction, baseline AM asthma symptom score value and baseline-by-visit interaction as covariates.

Type 2 inflammatory asthma phenotype population is defined as the randomized patients with baseline blood eosinophils >= 0.15 Giga/L or baseline FeNO >= 20 ppb.

PGM=PRODOPS/SAR231893/EFC14153/CSR/REPORT/PGM/eff_mmrm_i_t_aded.sas OUT=REPORT/OUTPUT/eff_asam_chg_a52_t2e3_t_x.rtf (27NOV2020 - 2:53)

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

Project Code / Study Number / Analysis: SAR231893 / EFC14153 / CSR

16.2.6 Efficacy response data

16.2.6.15 AM asthma symptom score

16.2.6.15.4 Change from baseline in AM asthma symptom score over time (MMRM including measurements up to Week 52) - Type 2 inflammatory asthma phenotype population and baseline blood eosinophils >=0.3 Giga/L population

	Type 2 inflammatory asthma phenotype population	
AM asthma symptom score	**Placebo (N=114)**	**Dupilumab (N=236)**
Week 44		
Change from baseline		
Number of patients in the model	110	228
LS Mean (SE) [a]	-0.48 (0.05)	-0.61 (0.04)
LS Mean Diff vs. placebo (95% CI) [a]		-0.13 (-0.25, -0.01)
P-value vs. placebo [a]		0.0388
Week 48		
Change from baseline		
Number of patients in the model	110	228
LS Mean (SE) [a]	-0.47 (0.05)	-0.61 (0.04)
LS Mean Diff vs. placebo (95% CI) [a]		-0.14 (-0.25, -0.02)
P-value vs. placebo [a]		0.0198

[a] Derived from MMRM model with change from baseline in AM asthma symptom score values up to Week 52 as the response variable, and treatment, age, baseline weight group, region, baseline eosinophil level, baseline FeNO level, baseline ICS dose level, visit, treatment by-visit interaction, baseline AM asthma symptom score value and baseline-by-visit interaction as covariates.

Type 2 inflammatory asthma phenotype population is defined as the randomized patients with baseline blood eosinophils >= 0.15 Giga/L or baseline FeNO >= 20 ppb.

PGM=PRODOPS/SAR231893/EFC14153/CSR/REPORT/PGM/eff_mmrm_i_t_aded.sas OUT=REPORT/OUTPUT/eff_asam_chg_a52_t2e3_t_x.rtf (27NOV2020 - 2:53)

Project Code / Study Number / Analysis: SAR231893 / EFC14153 / CSR

16.2.6 Efficacy response data

16.2.6.15 AM asthma symptom score

16.2.6.15.4 Change from baseline in AM asthma symptom score over time (MMRM including measurements up to Week 52) - Type 2 inflammatory asthma phenotype population and baseline blood eosinophils >=0.3 Giga/L population

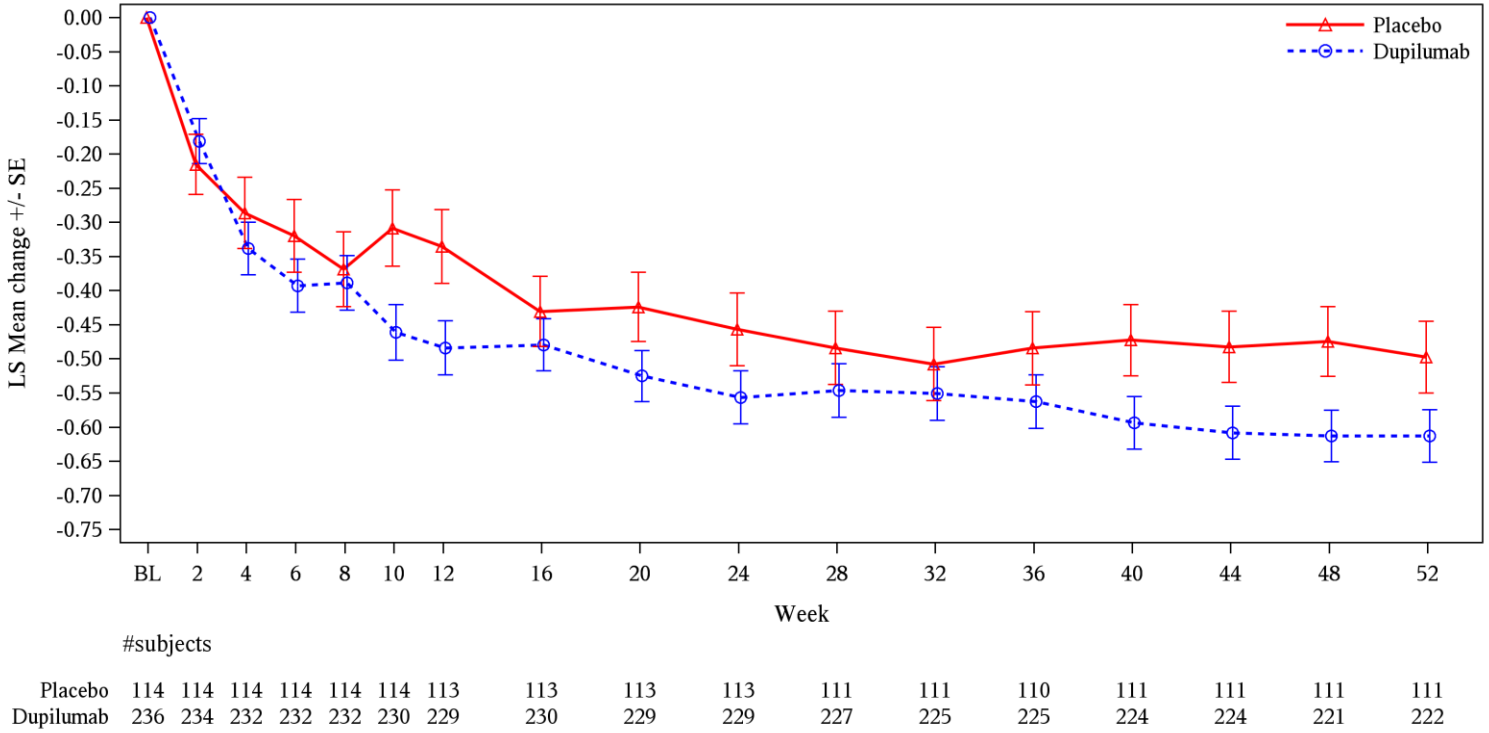
	Type 2 inflammatory asthma phenotype population	
AM asthma symptom score	**Placebo (N=114)**	**Dupilumab (N=236)**
Week 52		
Change from baseline		
Number of patients in the model	110	228
LS Mean (SE) [a]	-0.50 (0.05)	-0.61 (0.04)
LS Mean Diff vs. placebo (95% CI) [a]		-0.12 (-0.23, 0.00)
P-value vs. placebo [a]		0.0582

[a] Derived from MMRM model with change from baseline in AM asthma symptom score values up to Week 52 as the response variable, and treatment, age, baseline weight group, region, baseline eosinophil level, baseline FeNO level, baseline ICS dose level, visit, treatment by-visit interaction, baseline AM asthma symptom score value and baseline-by-visit interaction as covariates.

Type 2 inflammatory asthma phenotype population is defined as the randomized patients with baseline blood eosinophils >= 0.15 Giga/L or baseline FeNO >= 20 ppb.

PGM=PRODOPS/SAR231893/EFC14153/CSR/REPORT/PGM/eff_mmrm_i_t_aded.sas OUT=REPORT/OUTPUT/eff_asam_chg_a52_t2e3_t_x.rtf (27NOV2020 - 2:53)

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen
Project Code / Study Number / Analysis: SAR231893 / EFC14153 / CSR
16.2.6 Efficacy response data
16.2.6.15 AM asthma symptom score
16.2.6.15.5 Plot of LS mean change from baseline in AM asthma symptom score over time (MMRM including measurements up to Week 52) - Type 2 inflammatory asthma phenotype population



BL=Baseline
Type 2 inflammatory asthma phenotype population is defined as the randomized patients with baseline blood eosinophils >= 0.15 Giga/L or baseline FeNO >= 20 ppb.
PGM=PRODOPS/SAR231893/EFC14153/CSR/REPORT/PGM/eff_mmrm_i_g_intext_aded.sas OUT=REPORT/OUTPUT/eff_asam_chg_a52_t2_g_x.rtf (27NOV2020 - 2:51)

16.2.6 Efficacy response data

16.2.6.16 PM asthma symptom score

16.2.6.16.1 Summary of PM asthma symptom score over time - Type 2 inflammatory asthma phenotype population and baseline blood eosinophils >=0.3 Giga/L population

	Type 2 inflammatory asthma phenotype population	
PM asthma symptom score	**Placebo (N=114)**	**Dupilumab (N=236)**
Baseline		
Value		
Number	114	236
Mean (SD)	0.92 (0.72)	0.92 (0.77)
Median	0.93	1.00
Q1 : Q3	0.29 : 1.43	0.29 : 1.29
Min : Max	0.0 : 2.6	0.0 : 3.0
Week 2		
Value		
Number	114	234
Mean (SD)	0.76 (0.70)	0.80 (0.72)
Median	0.64	0.64
Q1 : Q3	0.21 : 1.21	0.10 : 1.15
Min : Max	0.0 : 2.9	0.0 : 3.0

Type 2 inflammatory asthma phenotype population is defined as the randomized patients with baseline blood eosinophils >= 0.15 Giga/L or baseline FeNO >= 20 ppb.
PGM=PRODOPS/SAR231893/EFC14153/CSR/REPORT/PGM/eff_sum_vis_i_t.sas OUT=REPORT/OUTPUT/eff_sum_aspm_t2e3_t_x.rtf (27NOV2020 - 6:43)

Project Code / Study Number / Analysis: SAR231893 / EFC14153 / CSR

16.2.6 Efficacy response data

16.2.6.16 PM asthma symptom score

16.2.6.16.1 Summary of PM asthma symptom score over time - Type 2 inflammatory asthma phenotype population and baseline blood eosinophils >=0.3 Giga/L population

	Type 2 inflammatory asthma phenotype population	
PM asthma symptom score	**Placebo (N=114)**	**Dupilumab (N=236)**
Change from baseline		
Number	114	234
Mean (SD)	-0.16 (0.50)	-0.12 (0.48)
Median	-0.09	0.00
Q1 : Q3	-0.36 : 0.14	-0.36 : 0.07
Min : Max	-2.0 : 0.8	-2.1 : 1.5
Percent change from baseline		
Number	95	194
Mean (SD)	-16.79 (69.88)	-0.85 (106.32)
Median	-21.54	-11.25
Q1 : Q3	-62.50 : 7.69	-50.00 : 7.14
Min : Max	-100.0 : 315.4	-100.0 : 700.0

Type 2 inflammatory asthma phenotype population is defined as the randomized patients with baseline blood eosinophils >= 0.15 Giga/L or baseline FeNO >= 20 ppb.

PGM=PRODOPS/SAR231893/EFC14153/CSR/REPORT/PGM/eff_sum_vis_i_t.sas OUT=REPORT/OUTPUT/eff_sum_aspm_t2e3_t_x.rtf (27NOV2020 - 6:43)

Project Code / Study Number / Analysis: SAR231893 / EFC14153 / CSR

16.2.6 Efficacy response data

16.2.6.16 PM asthma symptom score

16.2.6.16.1 Summary of PM asthma symptom score over time - Type 2 inflammatory asthma phenotype population and baseline blood eosinophils >=0.3 Giga/L population

	Type 2 inflammatory asthma phenotype population	
PM asthma symptom score	**Placebo (N=114)**	**Dupilumab (N=236)**
Week 4		
Value		
Number	114	233
Mean (SD)	0.68 (0.69)	0.64 (0.66)
Median	0.45	0.43
Q1 : Q3	0.08 : 1.13	0.08 : 1.00
Min : Max	0.0 : 2.9	0.0 : 3.0
Change from baseline		
Number	114	233
Mean (SD)	-0.25 (0.60)	-0.28 (0.65)
Median	-0.14	-0.14
Q1 : Q3	-0.57 : 0.07	-0.57 : 0.00
Min : Max	-2.1 : 1.3	-3.0 : 2.1

Type 2 inflammatory asthma phenotype population is defined as the randomized patients with baseline blood eosinophils >= 0.15 Giga/L or baseline FeNO >= 20 ppb.

PGM=PRODOPS/SAR231893/EFC14153/CSR/REPORT/PGM/eff_sum_vis_i_t.sas OUT=REPORT/OUTPUT/eff_sum_aspm_t2e3_t_x.rtf (27NOV2020 - 6:43)

16.2.6 Efficacy response data

16.2.6.16 PM asthma symptom score

16.2.6.16.1 Summary of PM asthma symptom score over time - Type 2 inflammatory asthma phenotype population and baseline blood eosinophils >=0.3 Giga/L population

	Type 2 inflammatory asthma phenotype population	
PM asthma symptom score	**Placebo (N=114)**	**Dupilumab (N=236)**
Percent change from baseline		
Number	95	194
Mean (SD)	-23.25 (80.98)	-17.68 (104.54)
Median	-33.33	-33.49
Q1 : Q3	-77.27 : 0.00	-75.00 : 0.00
Min : Max	-100.0 : 500.0	-100.0 : 734.6
Week 6		
Value		
Number	114	232
Mean (SD)	0.67 (0.72)	0.56 (0.64)
Median	0.40	0.33
Q1 : Q3	0.00 : 1.00	0.00 : 1.00
Min : Max	0.0 : 2.9	0.0 : 3.0

Type 2 inflammatory asthma phenotype population is defined as the randomized patients with baseline blood eosinophils >= 0.15 Giga/L or baseline FeNO >= 20 ppb.
PGM=PRODOPS/SAR231893/EFC14153/CSR/REPORT/PGM/eff_sum_vis_i_t.sas OUT=REPORT/OUTPUT/eff_sum_aspm_t2e3_t_x.rtf (27NOV2020 - 6:43)

Project Code / Study Number / Analysis: SAR231893 / EFC14153 / CSR

16.2.6 Efficacy response data

16.2.6.16 PM asthma symptom score

16.2.6.16.1 Summary of PM asthma symptom score over time - Type 2 inflammatory asthma phenotype population and baseline blood eosinophils >=0.3 Giga/L population

	Type 2 inflammatory asthma phenotype population	
PM asthma symptom score	**Placebo (N=114)**	**Dupilumab (N=236)**
Change from baseline		
Number	114	232
Mean (SD)	-0.25 (0.63)	-0.36 (0.67)
Median	-0.16	-0.14
Q1 : Q3	-0.57 : 0.00	-0.72 : 0.00
Min : Max	-2.1 : 1.9	-3.0 : 1.3
Percent change from baseline		
Number	95	193
Mean (SD)	-25.44 (77.59)	-31.90 (95.13)
Median	-30.00	-50.00
Q1 : Q3	-91.03 : 0.00	-87.50 : 0.00
Min : Max	-100.0 : 450.0	-100.0 : 900.0

Type 2 inflammatory asthma phenotype population is defined as the randomized patients with baseline blood eosinophils >= 0.15 Giga/L or baseline FeNO >= 20 ppb.

PGM=PRODOPS/SAR231893/EFC14153/CSR/REPORT/PGM/eff_sum_vis_i_t.sas OUT=REPORT/OUTPUT/eff_sum_aspm_t2e3_t_x.rtf (27NOV2020 - 6:43)

16.2.6 Efficacy response data

16.2.6.16 PM asthma symptom score

16.2.6.16.1 Summary of PM asthma symptom score over time - Type 2 inflammatory asthma phenotype population and baseline blood eosinophils >=0.3 Giga/L population

	Type 2 inflammatory asthma phenotype population	
PM asthma symptom score	**Placebo (N=114)**	**Dupilumab (N=236)**
Week 8		
Value		
Number	114	231
Mean (SD)	0.60 (0.70)	0.54 (0.66)
Median	0.29	0.21
Q1 : Q3	0.00 : 1.07	0.00 : 1.00
Min : Max	0.0 : 2.6	0.0 : 3.1
Change from baseline		
Number	114	231
Mean (SD)	-0.32 (0.65)	-0.38 (0.70)
Median	-0.21	-0.24
Q1 : Q3	-0.79 : 0.00	-0.77 : 0.00
Min : Max	-2.1 : 2.1	-3.0 : 1.8

Type 2 inflammatory asthma phenotype population is defined as the randomized patients with baseline blood eosinophils >= 0.15 Giga/L or baseline FeNO >= 20 ppb.

PGM=PRODOPS/SAR231893/EFC14153/CSR/REPORT/PGM/eff_sum_vis_i_t.sas OUT=REPORT/OUTPUT/eff_sum_aspm_t2e3_t_x.rtf (27NOV2020 - 6:43)

Project Code / Study Number / Analysis: SAR231893 / EFC14153 / CSR

16.2.6 Efficacy response data

16.2.6.16 PM asthma symptom score

16.2.6.16.1 Summary of PM asthma symptom score over time - Type 2 inflammatory asthma phenotype population and baseline blood eosinophils >=0.3 Giga/L population

	Type 2 inflammatory asthma phenotype population	
PM asthma symptom score	**Placebo (N=114)**	**Dupilumab (N=236)**
Percent change from baseline		
Number	95	192
Mean (SD)	-25.50 (132.23)	-30.81 (118.06)
Median	-46.15	-50.00
Q1 : Q3	-100.00 : 0.00	-100.00 : 0.00
Min : Max	-100.0 : 928.6	-100.0 : 869.2
Week 10		
Value		
Number	113	230
Mean (SD)	0.62 (0.72)	0.49 (0.68)
Median	0.36	0.17
Q1 : Q3	0.00 : 1.00	0.00 : 0.86
Min : Max	0.0 : 2.8	0.0 : 3.1

Type 2 inflammatory asthma phenotype population is defined as the randomized patients with baseline blood eosinophils >= 0.15 Giga/L or baseline FeNO >= 20 ppb.

PGM=PRODOPS/SAR231893/EFC14153/CSR/REPORT/PGM/eff_sum_vis_i_t.sas OUT=REPORT/OUTPUT/eff_sum_aspm_t2e3_t_x.rtf (27NOV2020 - 6:43)

Project Code / Study Number / Analysis: SAR231893 / EFC14153 / CSR

16.2.6 Efficacy response data

16.2.6.16 PM asthma symptom score

16.2.6.16.1 Summary of PM asthma symptom score over time - Type 2 inflammatory asthma phenotype population and baseline blood eosinophils >=0.3 Giga/L population

	Type 2 inflammatory asthma phenotype population	
PM asthma symptom score	**Placebo (N=114)**	**Dupilumab (N=236)**
Change from baseline		
Number	113	230
Mean (SD)	-0.29 (0.63)	-0.44 (0.71)
Median	-0.14	-0.26
Q1 : Q3	-0.64 : 0.00	-0.79 : 0.00
Min : Max	-2.1 : 1.9	-3.0 : 2.6
Percent change from baseline		
Number	94	192
Mean (SD)	-30.98 (86.08)	-38.57 (152.16)
Median	-40.45	-66.67
Q1 : Q3	-95.80 : 0.00	-100.00 : -7.14
Min : Max	-100.0 : 542.9	-100.0 : 1838.5

Type 2 inflammatory asthma phenotype population is defined as the randomized patients with baseline blood eosinophils >= 0.15 Giga/L or baseline FeNO >= 20 ppb.

PGM=PRODOPS/SAR231893/EFC14153/CSR/REPORT/PGM/eff_sum_vis_i_t.sas OUT=REPORT/OUTPUT/eff_sum_aspm_t2e3_t_x.rtf (27NOV2020 - 6:43)

Project Code / Study Number / Analysis: SAR231893 / EFC14153 / CSR

16.2.6 Efficacy response data

16.2.6.16 PM asthma symptom score

16.2.6.16.1 Summary of PM asthma symptom score over time - Type 2 inflammatory asthma phenotype population and baseline blood eosinophils >=0.3 Giga/L population

	Type 2 inflammatory asthma phenotype population	
PM asthma symptom score	**Placebo (N=114)**	**Dupilumab (N=236)**
Week 12		
Value		
Number	113	231
Mean (SD)	0.62 (0.70)	0.49 (0.69)
Median	0.29	0.14
Q1 : Q3	0.00 : 1.00	0.00 : 0.92
Min : Max	0.0 : 2.9	0.0 : 3.0
Change from baseline		
Number	113	231
Mean (SD)	-0.29 (0.65)	-0.43 (0.72)
Median	-0.21	-0.27
Q1 : Q3	-0.71 : 0.00	-0.85 : 0.00
Min : Max	-2.1 : 1.8	-3.0 : 2.0

Type 2 inflammatory asthma phenotype population is defined as the randomized patients with baseline blood eosinophils >= 0.15 Giga/L or baseline FeNO >= 20 ppb.

PGM=PRODOPS/SAR231893/EFC14153/CSR/REPORT/PGM/eff_sum_vis_i_t.sas OUT=REPORT/OUTPUT/eff_sum_aspm_t2e3_t_x.rtf (27NOV2020 - 6:43)

Project Code / Study Number / Analysis: SAR231893 / EFC14153 / CSR

16.2.6 Efficacy response data

16.2.6.16 PM asthma symptom score

16.2.6.16.1 Summary of PM asthma symptom score over time - Type 2 inflammatory asthma phenotype population and baseline blood eosinophils >=0.3 Giga/L population

	Type 2 inflammatory asthma phenotype population	
PM asthma symptom score	**Placebo (N=114)**	**Dupilumab (N=236)**
Percent change from baseline		
Number	94	192
Mean (SD)	-28.56 (118.30)	-37.53 (127.37)
Median	-50.00	-75.00
Q1 : Q3	-100.00 : -3.57	-100.00 : 0.00
Min : Max	-100.0 : 881.8	-100.0 : 1250.0
Week 16		
Value		
Number	113	230
Mean (SD)	0.52 (0.66)	0.50 (0.68)
Median	0.18	0.15
Q1 : Q3	0.00 : 0.96	0.00 : 0.96
Min : Max	0.0 : 3.0	0.0 : 3.0

Type 2 inflammatory asthma phenotype population is defined as the randomized patients with baseline blood eosinophils >= 0.15 Giga/L or baseline FeNO >= 20 ppb.
PGM=PRODOPS/SAR231893/EFC14153/CSR/REPORT/PGM/eff_sum_vis_i_t.sas OUT=REPORT/OUTPUT/eff_sum_aspm_t2e3_t_x.rtf (27NOV2020 - 6:43)

Project Code / Study Number / Analysis: SAR231893 / EFC14153 / CSR

16.2.6 Efficacy response data

16.2.6.16 PM asthma symptom score

16.2.6.16.1 Summary of PM asthma symptom score over time - Type 2 inflammatory asthma phenotype population and baseline blood eosinophils >=0.3 Giga/L population

	Type 2 inflammatory asthma phenotype population	
PM asthma symptom score	**Placebo (N=114)**	**Dupilumab (N=236)**
Change from baseline		
Number	113	230
Mean (SD)	-0.40 (0.63)	-0.42 (0.71)
Median	-0.20	-0.26
Q1 : Q3	-0.75 : 0.00	-0.85 : 0.00
Min : Max	-2.4 : 1.5	-3.0 : 1.9
Percent change from baseline		
Number	94	191
Mean (SD)	-44.23 (60.77)	-38.03 (109.78)
Median	-53.17	-72.00
Q1 : Q3	-100.00 : -3.85	-100.00 : -2.08
Min : Max	-100.0 : 285.7	-100.0 : 1000.0

Type 2 inflammatory asthma phenotype population is defined as the randomized patients with baseline blood eosinophils >= 0.15 Giga/L or baseline FeNO >= 20 ppb.

PGM=PRODOPS/SAR231893/EFC14153/CSR/REPORT/PGM/eff_sum_vis_i_t.sas OUT=REPORT/OUTPUT/eff_sum_aspm_t2e3_t_x.rtf (27NOV2020 - 6:43)

Project Code / Study Number / Analysis: SAR231893 / EFC14153 / CSR

16.2.6 Efficacy response data

16.2.6.16 PM asthma symptom score

16.2.6.16.1 Summary of PM asthma symptom score over time - Type 2 inflammatory asthma phenotype population and baseline blood eosinophils >=0.3 Giga/L population

	Type 2 inflammatory asthma phenotype population	
PM asthma symptom score	**Placebo (N=114)**	**Dupilumab (N=236)**
Week 20		
Value		
Number	113	229
Mean (SD)	0.51 (0.63)	0.44 (0.63)
Median	0.24	0.09
Q1 : Q3	0.00 : 1.00	0.00 : 0.89
Min : Max	0.0 : 3.0	0.0 : 3.0
Change from baseline		
Number	113	229
Mean (SD)	-0.40 (0.65)	-0.49 (0.71)
Median	-0.23	-0.29
Q1 : Q3	-0.84 : 0.00	-0.96 : 0.00
Min : Max	-2.1 : 0.9	-3.0 : 1.4

Type 2 inflammatory asthma phenotype population is defined as the randomized patients with baseline blood eosinophils >= 0.15 Giga/L or baseline FeNO >= 20 ppb.

PGM=PRODOPS/SAR231893/EFC14153/CSR/REPORT/PGM/eff_sum_vis_i_t.sas OUT=REPORT/OUTPUT/eff_sum_aspm_t2e3_t_x.rtf (27NOV2020 - 6:43)

16.2.6 Efficacy response data

16.2.6.16 PM asthma symptom score

16.2.6.16.1 Summary of PM asthma symptom score over time - Type 2 inflammatory asthma phenotype population and baseline blood eosinophils >=0.3 Giga/L population

	Type 2 inflammatory asthma phenotype population	
PM asthma symptom score	**Placebo (N=114)**	**Dupilumab (N=236)**
Percent change from baseline		
Number	94	192
Mean (SD)	-44.25 (59.35)	-43.56 (94.07)
Median	-55.90	-78.39
Q1 : Q3	-100.00 : -1.92	-100.00 : -4.22
Min : Max	-100.0 : 223.1	-100.0 : 707.7
Week 24		
Value		
Number	113	229
Mean (SD)	0.48 (0.62)	0.41 (0.63)
Median	0.17	0.08
Q1 : Q3	0.00 : 0.92	0.00 : 0.71
Min : Max	0.0 : 3.0	0.0 : 3.0

Type 2 inflammatory asthma phenotype population is defined as the randomized patients with baseline blood eosinophils >= 0.15 Giga/L or baseline FeNO >= 20 ppb.
PGM=PRODOPS/SAR231893/EFC14153/CSR/REPORT/PGM/eff_sum_vis_i_t.sas OUT=REPORT/OUTPUT/eff_sum_aspm_t2e3_t_x.rtf (27NOV2020 - 6:43)

Project Code / Study Number / Analysis: SAR231893 / EFC14153 / CSR

16.2.6 Efficacy response data

16.2.6.16 PM asthma symptom score

16.2.6.16.1 Summary of PM asthma symptom score over time - Type 2 inflammatory asthma phenotype population and baseline blood eosinophils >=0.3 Giga/L population

	Type 2 inflammatory asthma phenotype population	
PM asthma symptom score	**Placebo (N=114)**	**Dupilumab (N=236)**
Change from baseline		
Number	113	229
Mean (SD)	-0.43 (0.66)	-0.52 (0.73)
Median	-0.26	-0.29
Q1 : Q3	-0.86 : 0.00	-1.00 : 0.00
Min : Max	-2.1 : 1.6	-3.0 : 1.3
Percent change from baseline		
Number	94	192
Mean (SD)	-45.13 (59.33)	-48.11 (81.42)
Median	-50.00	-86.36
Q1 : Q3	-100.00 : -5.77	-100.00 : -11.70
Min : Max	-100.0 : 191.7	-100.0 : 463.9

Type 2 inflammatory asthma phenotype population is defined as the randomized patients with baseline blood eosinophils >= 0.15 Giga/L or baseline FeNO >= 20 ppb.

PGM=PRODOPS/SAR231893/EFC14153/CSR/REPORT/PGM/eff_sum_vis_i_t.sas OUT=REPORT/OUTPUT/eff_sum_aspm_t2e3_t_x.rtf (27NOV2020 - 6:43)

Project Code / Study Number / Analysis: SAR231893 / EFC14153 / CSR

16.2.6 Efficacy response data

16.2.6.16 PM asthma symptom score

16.2.6.16.1 Summary of PM asthma symptom score over time - Type 2 inflammatory asthma phenotype population and baseline blood eosinophils >=0.3 Giga/L population

	Type 2 inflammatory asthma phenotype population	
PM asthma symptom score	**Placebo (N=114)**	**Dupilumab (N=236)**
Week 28		
Value		
Number	111	227
Mean (SD)	0.44 (0.60)	0.39 (0.65)
Median	0.08	0.05
Q1 : Q3	0.00 : 0.96	0.00 : 0.60
Min : Max	0.0 : 3.0	0.0 : 3.1
Change from baseline		
Number	111	227
Mean (SD)	-0.46 (0.71)	-0.53 (0.76)
Median	-0.29	-0.33
Q1 : Q3	-1.00 : 0.00	-1.00 : 0.00
Min : Max	-2.3 : 1.6	-3.0 : 2.4

Type 2 inflammatory asthma phenotype population is defined as the randomized patients with baseline blood eosinophils >= 0.15 Giga/L or baseline FeNO >= 20 ppb.

PGM=PRODOPS/SAR231893/EFC14153/CSR/REPORT/PGM/eff_sum_vis_i_t.sas OUT=REPORT/OUTPUT/eff_sum_aspm_t2e3_t_x.rtf (27NOV2020 - 6:43)

16.2.6 Efficacy response data

16.2.6.16 PM asthma symptom score

16.2.6.16.1 Summary of PM asthma symptom score over time - Type 2 inflammatory asthma phenotype population and baseline blood eosinophils >=0.3 Giga/L population

	Type 2 inflammatory asthma phenotype population	
PM asthma symptom score	**Placebo (N=114)**	**Dupilumab (N=236)**
Percent change from baseline		
Number	92	190
Mean (SD)	-46.71 (95.79)	-44.98 (128.65)
Median	-68.53	-89.88
Q1 : Q3	-100.00 : -12.73	-100.00 : -12.50
Min : Max	-100.0 : 730.8	-100.0 : 1219.2
Week 32		
Value		
Number	111	226
Mean (SD)	0.42 (0.58)	0.40 (0.63)
Median	0.09	0.04
Q1 : Q3	0.00 : 0.89	0.00 : 0.78
Min : Max	0.0 : 3.0	0.0 : 3.0

Type 2 inflammatory asthma phenotype population is defined as the randomized patients with baseline blood eosinophils >= 0.15 Giga/L or baseline FeNO >= 20 ppb.
PGM=PRODOPS/SAR231893/EFC14153/CSR/REPORT/PGM/eff_sum_vis_i_t.sas OUT=REPORT/OUTPUT/eff_sum_aspm_t2e3_t_x.rtf (27NOV2020 - 6:43)

Project Code / Study Number / Analysis: SAR231893 / EFC14153 / CSR

16.2.6 Efficacy response data

16.2.6.16 PM asthma symptom score

16.2.6.16.1 Summary of PM asthma symptom score over time - Type 2 inflammatory asthma phenotype population and baseline blood eosinophils >=0.3 Giga/L population

	Type 2 inflammatory asthma phenotype population	
PM asthma symptom score	**Placebo (N=114)**	**Dupilumab (N=236)**
Change from baseline		
Number	111	226
Mean (SD)	-0.49 (0.72)	-0.53 (0.76)
Median	-0.32	-0.29
Q1 : Q3	-1.00 : 0.00	-1.00 : 0.00
Min : Max	-2.4 : 1.7	-3.0 : 1.7
Percent change from baseline		
Number	92	189
Mean (SD)	-51.96 (73.67)	-45.35 (89.45)
Median	-80.61	-87.50
Q1 : Q3	-100.00 : -17.63	-100.00 : -5.00
Min : Max	-100.0 : 433.3	-100.0 : 600.0

Type 2 inflammatory asthma phenotype population is defined as the randomized patients with baseline blood eosinophils >= 0.15 Giga/L or baseline FeNO >= 20 ppb.

PGM=PRODOPS/SAR231893/EFC14153/CSR/REPORT/PGM/eff_sum_vis_i_t.sas OUT=REPORT/OUTPUT/eff_sum_aspm_t2e3_t_x.rtf (27NOV2020 - 6:43)

16.2.6 Efficacy response data

16.2.6.16 PM asthma symptom score

16.2.6.16.1 Summary of PM asthma symptom score over time - Type 2 inflammatory asthma phenotype population and baseline blood eosinophils >=0.3 Giga/L population

	Type 2 inflammatory asthma phenotype population	
PM asthma symptom score	**Placebo (N=114)**	**Dupilumab (N=236)**
Week 36		
Value		
Number	110	226
Mean (SD)	0.44 (0.59)	0.39 (0.63)
Median	0.11	0.04
Q1 : Q3	0.00 : 0.92	0.00 : 0.61
Min : Max	0.0 : 3.0	0.0 : 3.1
Change from baseline		
Number	110	226
Mean (SD)	-0.46 (0.72)	-0.55 (0.75)
Median	-0.30	-0.30
Q1 : Q3	-1.00 : 0.00	-1.00 : 0.00
Min : Max	-2.4 : 1.6	-3.0 : 2.6

Type 2 inflammatory asthma phenotype population is defined as the randomized patients with baseline blood eosinophils >= 0.15 Giga/L or baseline FeNO >= 20 ppb.
PGM=PRODOPS/SAR231893/EFC14153/CSR/REPORT/PGM/eff_sum_vis_i_t.sas OUT=REPORT/OUTPUT/eff_sum_aspm_t2e3_t_x.rtf (27NOV2020 - 6:43)

Project Code / Study Number / Analysis: SAR231893 / EFC14153 / CSR

16.2.6 Efficacy response data

16.2.6.16 PM asthma symptom score

16.2.6.16.1 Summary of PM asthma symptom score over time - Type 2 inflammatory asthma phenotype population and baseline blood eosinophils >=0.3 Giga/L population

	Type 2 inflammatory asthma phenotype population	
PM asthma symptom score	**Placebo (N=114)**	**Dupilumab (N=236)**
Percent change from baseline		
Number	91	190
Mean (SD)	-50.08 (74.06)	-49.23 (101.63)
Median	-73.26	-90.58
Q1 : Q3	-100.00 : -4.89	-100.00 : -12.50
Min : Max	-100.0 : 477.8	-100.0 : 896.2
Week 40		
Value		
Number	111	224
Mean (SD)	0.47 (0.63)	0.35 (0.61)
Median	0.08	0.00
Q1 : Q3	0.00 : 1.00	0.00 : 0.51
Min : Max	0.0 : 3.0	0.0 : 3.0

Type 2 inflammatory asthma phenotype population is defined as the randomized patients with baseline blood eosinophils >= 0.15 Giga/L or baseline FeNO >= 20 ppb.
PGM=PRODOPS/SAR231893/EFC14153/CSR/REPORT/PGM/eff_sum_vis_i_t.sas OUT=REPORT/OUTPUT/eff_sum_aspm_t2e3_t_x.rtf (27NOV2020 - 6:43)

Project Code / Study Number / Analysis: SAR231893 / EFC14153 / CSR

16.2.6 Efficacy response data

16.2.6.16 PM asthma symptom score

16.2.6.16.1 Summary of PM asthma symptom score over time - Type 2 inflammatory asthma phenotype population and baseline blood eosinophils >=0.3 Giga/L population

	Type 2 inflammatory asthma phenotype population	
PM asthma symptom score	**Placebo (N=114)**	**Dupilumab (N=236)**
Change from baseline		
Number	111	224
Mean (SD)	-0.44 (0.71)	-0.58 (0.77)
Median	-0.29	-0.32
Q1 : Q3	-1.00 : 0.00	-1.00 : 0.00
Min : Max	-2.1 : 2.0	-3.0 : 1.8
Percent change from baseline		
Number	92	188
Mean (SD)	-50.38 (54.32)	-54.13 (112.45)
Median	-69.62	-97.15
Q1 : Q3	-100.00 : 0.00	-100.00 : -25.79
Min : Max	-100.0 : 94.4	-100.0 : 1125.0

Type 2 inflammatory asthma phenotype population is defined as the randomized patients with baseline blood eosinophils >= 0.15 Giga/L or baseline FeNO >= 20 ppb.

PGM=PRODOPS/SAR231893/EFC14153/CSR/REPORT/PGM/eff_sum_vis_i_t.sas OUT=REPORT/OUTPUT/eff_sum_aspm_t2e3_t_x.rtf (27NOV2020 - 6:43)

Project Code / Study Number / Analysis: SAR231893 / EFC14153 / CSR

16.2.6 Efficacy response data

16.2.6.16 PM asthma symptom score

16.2.6.16.1 Summary of PM asthma symptom score over time - Type 2 inflammatory asthma phenotype population and baseline blood eosinophils >=0.3 Giga/L population

	Type 2 inflammatory asthma phenotype population	
PM asthma symptom score	**Placebo (N=114)**	**Dupilumab (N=236)**
Week 44		
Value		
Number	111	223
Mean (SD)	0.46 (0.60)	0.35 (0.61)
Median	0.11	0.00
Q1 : Q3	0.00 : 1.00	0.00 : 0.40
Min : Max	0.0 : 3.0	0.0 : 3.0
Change from baseline		
Number	111	223
Mean (SD)	-0.45 (0.70)	-0.58 (0.78)
Median	-0.25	-0.43
Q1 : Q3	-1.00 : 0.00	-1.00 : 0.00
Min : Max	-2.4 : 1.2	-3.0 : 2.0

Type 2 inflammatory asthma phenotype population is defined as the randomized patients with baseline blood eosinophils >= 0.15 Giga/L or baseline FeNO >= 20 ppb.

PGM=PRODOPS/SAR231893/EFC14153/CSR/REPORT/PGM/eff_sum_vis_i_t.sas OUT=REPORT/OUTPUT/eff_sum_aspm_t2e3_t_x.rtf (27NOV2020 - 6:43)

16.2.6 Efficacy response data

16.2.6.16 PM asthma symptom score

16.2.6.16.1 Summary of PM asthma symptom score over time - Type 2 inflammatory asthma phenotype population and baseline blood eosinophils >=0.3 Giga/L population

	Type 2 inflammatory asthma phenotype population	
PM asthma symptom score	**Placebo (N=114)**	**Dupilumab (N=236)**
Percent change from baseline		
Number	92	187
Mean (SD)	-49.17 (69.87)	-55.68 (81.36)
Median	-76.63	-92.86
Q1 : Q3	-100.00 : -11.06	-100.00 : -12.50
Min : Max	-100.0 : 411.1	-100.0 : 716.7
Week 48		
Value		
Number	111	222
Mean (SD)	0.43 (0.57)	0.34 (0.61)
Median	0.14	0.00
Q1 : Q3	0.00 : 1.00	0.00 : 0.43
Min : Max	0.0 : 3.0	0.0 : 3.0

Type 2 inflammatory asthma phenotype population is defined as the randomized patients with baseline blood eosinophils >= 0.15 Giga/L or baseline FeNO >= 20 ppb.
PGM=PRODOPS/SAR231893/EFC14153/CSR/REPORT/PGM/eff_sum_vis_i_t.sas OUT=REPORT/OUTPUT/eff_sum_aspm_t2e3_t_x.rtf (27NOV2020 - 6:43)

Project Code / Study Number / Analysis: SAR231893 / EFC14153 / CSR

16.2.6 Efficacy response data

16.2.6.16 PM asthma symptom score

16.2.6.16.1 Summary of PM asthma symptom score over time - Type 2 inflammatory asthma phenotype population and baseline blood eosinophils >=0.3 Giga/L population

	Type 2 inflammatory asthma phenotype population	
PM asthma symptom score	**Placebo (N=114)**	**Dupilumab (N=236)**
Change from baseline		
Number	111	222
Mean (SD)	-0.47 (0.66)	-0.59 (0.78)
Median	-0.31	-0.43
Q1 : Q3	-0.96 : 0.00	-1.00 : 0.00
Min : Max	-2.4 : 0.9	-3.0 : 2.7
Percent change from baseline		
Number	92	186
Mean (SD)	-51.14 (65.72)	-55.41 (94.46)
Median	-73.86	-97.99
Q1 : Q3	-100.00 : -11.25	-100.00 : -12.50
Min : Max	-100.0 : 343.5	-100.0 : 950.0

Type 2 inflammatory asthma phenotype population is defined as the randomized patients with baseline blood eosinophils >= 0.15 Giga/L or baseline FeNO >= 20 ppb.

PGM=PRODOPS/SAR231893/EFC14153/CSR/REPORT/PGM/eff_sum_vis_i_t.sas OUT=REPORT/OUTPUT/eff_sum_aspm_t2e3_t_x.rtf (27NOV2020 - 6:43)

Project Code / Study Number / Analysis: SAR231893 / EFC14153 / CSR

16.2.6 Efficacy response data

16.2.6.16 PM asthma symptom score

16.2.6.16.1 Summary of PM asthma symptom score over time - Type 2 inflammatory asthma phenotype population and baseline blood eosinophils >=0.3 Giga/L population

	Type 2 inflammatory asthma phenotype population	
PM asthma symptom score	**Placebo (N=114)**	**Dupilumab (N=236)**
Week 52		
Value		
Number	111	222
Mean (SD)	0.42 (0.60)	0.34 (0.61)
Median	0.00	0.00
Q1 : Q3	0.00 : 0.96	0.00 : 0.46
Min : Max	0.0 : 3.0	0.0 : 3.5
Change from baseline		
Number	111	222
Mean (SD)	-0.48 (0.65)	-0.59 (0.79)
Median	-0.33	-0.41
Q1 : Q3	-1.00 : 0.00	-1.00 : 0.00
Min : Max	-2.4 : 0.9	-3.0 : 3.2

Type 2 inflammatory asthma phenotype population is defined as the randomized patients with baseline blood eosinophils >= 0.15 Giga/L or baseline FeNO >= 20 ppb.

PGM=PRODOPS/SAR231893/EFC14153/CSR/REPORT/PGM/eff_sum_vis_i_t.sas OUT=REPORT/OUTPUT/eff_sum_aspm_t2e3_t_x.rtf (27NOV2020 - 6:43)

16.2.6 Efficacy response data

16.2.6.16 PM asthma symptom score

16.2.6.16.1 Summary of PM asthma symptom score over time - Type 2 inflammatory asthma phenotype population and baseline blood eosinophils >=0.3 Giga/L population

	Type 2 inflammatory asthma phenotype population	
PM asthma symptom score	**Placebo (N=114)**	**Dupilumab (N=236)**
Percent change from baseline		
Number	92	186
Mean (SD)	-57.01 (51.63)	-54.99 (108.18)
Median	-89.40	-100.00
Q1 : Q3	-100.00 : -13.34	-100.00 : -30.43
Min : Max	-100.0 : 90.5	-100.0 : 1125.0
Week 56		
Value		
Number	39	78
Mean (SD)	0.53 (0.75)	0.36 (0.66)
Median	0.00	0.00
Q1 : Q3	0.00 : 1.00	0.00 : 0.50
Min : Max	0.0 : 2.7	0.0 : 3.0

Type 2 inflammatory asthma phenotype population is defined as the randomized patients with baseline blood eosinophils >= 0.15 Giga/L or baseline FeNO >= 20 ppb.
PGM=PRODOPS/SAR231893/EFC14153/CSR/REPORT/PGM/eff_sum_vis_i_t.sas OUT=REPORT/OUTPUT/eff_sum_aspm_t2e3_t_x.rtf (27NOV2020 - 6:43)

Project Code / Study Number / Analysis: SAR231893 / EFC14153 / CSR

16.2.6 Efficacy response data

16.2.6.16 PM asthma symptom score

16.2.6.16.1 Summary of PM asthma symptom score over time - Type 2 inflammatory asthma phenotype population and baseline blood eosinophils >=0.3 Giga/L population

	Type 2 inflammatory asthma phenotype population	
PM asthma symptom score	**Placebo (N=114)**	**Dupilumab (N=236)**
Change from baseline		
Number	39	78
Mean (SD)	-0.40 (0.81)	-0.56 (0.88)
Median	-0.38	-0.43
Q1 : Q3	-0.86 : 0.00	-1.14 : 0.00
Min : Max	-2.6 : 1.4	-3.0 : 3.0
Percent change from baseline		
Number	32	66
Mean (SD)	-32.42 (104.78)	-46.01 (177.66)
Median	-83.61	-100.00
Q1 : Q3	-100.00 : 0.00	-100.00 : -29.41
Min : Max	-100.0 : 366.7	-100.0 : 1300.0

Type 2 inflammatory asthma phenotype population is defined as the randomized patients with baseline blood eosinophils >= 0.15 Giga/L or baseline FeNO >= 20 ppb.

PGM=PRODOPS/SAR231893/EFC14153/CSR/REPORT/PGM/eff_sum_vis_i_t.sas OUT=REPORT/OUTPUT/eff_sum_aspm_t2e3_t_x.rtf (27NOV2020 - 6:43)

Project Code / Study Number / Analysis: SAR231893 / EFC14153 / CSR

16.2.6 Efficacy response data

16.2.6.16 PM asthma symptom score

16.2.6.16.1 Summary of PM asthma symptom score over time - Type 2 inflammatory asthma phenotype population and baseline blood eosinophils >=0.3 Giga/L population

	Type 2 inflammatory asthma phenotype population	
PM asthma symptom score	**Placebo (N=114)**	**Dupilumab (N=236)**
Week 60		
Value		
Number	3	14
Mean (SD)	1.03 (1.71)	0.29 (0.58)
Median	0.09	0.00
Q1 : Q3	0.00 : 3.00	0.00 : 0.13
Min : Max	0.0 : 3.0	0.0 : 1.8
Change from baseline		
Number	3	14
Mean (SD)	-0.06 (0.93)	-0.80 (0.76)
Median	-0.43	-0.71
Q1 : Q3	-0.75 : 1.00	-1.33 : -0.04
Min : Max	-0.7 : 1.0	-2.0 : 0.0

Type 2 inflammatory asthma phenotype population is defined as the randomized patients with baseline blood eosinophils >= 0.15 Giga/L or baseline FeNO >= 20 ppb.

PGM=PRODOPS/SAR231893/EFC14153/CSR/REPORT/PGM/eff_sum_vis_i_t.sas OUT=REPORT/OUTPUT/eff_sum_aspm_t2e3_t_x.rtf (27NOV2020 - 6:43)

16.2.6 Efficacy response data

16.2.6.16 PM asthma symptom score

16.2.6.16.1 Summary of PM asthma symptom score over time - Type 2 inflammatory asthma phenotype population and baseline blood eosinophils >=0.3 Giga/L population

	Type 2 inflammatory asthma phenotype population	
PM asthma symptom score	**Placebo (N=114)**	**Dupilumab (N=236)**
Percent change from baseline		
Number	3	12
Mean (SD)	-46.52 (83.75)	-75.91 (40.46)
Median	-89.57	-100.00
Q1 : Q3	-100.00 : 50.00	-100.00 : -57.75
Min : Max	-100.0 : 50.0	-100.0 : 0.0
Week 64		
Value		
Number	2	14
Mean (SD)	0.83 (0.25)	0.44 (0.66)
Median	0.83	0.00
Q1 : Q3	0.65 : 1.00	0.00 : 1.00
Min : Max	0.7 : 1.0	0.0 : 1.9

Type 2 inflammatory asthma phenotype population is defined as the randomized patients with baseline blood eosinophils >= 0.15 Giga/L or baseline FeNO >= 20 ppb.
PGM=PRODOPS/SAR231893/EFC14153/CSR/REPORT/PGM/eff_sum_vis_i_t.sas OUT=REPORT/OUTPUT/eff_sum_aspm_t2e3_t_x.rtf (27NOV2020 - 6:43)

Project Code / Study Number / Analysis: SAR231893 / EFC14153 / CSR

16.2.6 Efficacy response data

16.2.6.16 PM asthma symptom score

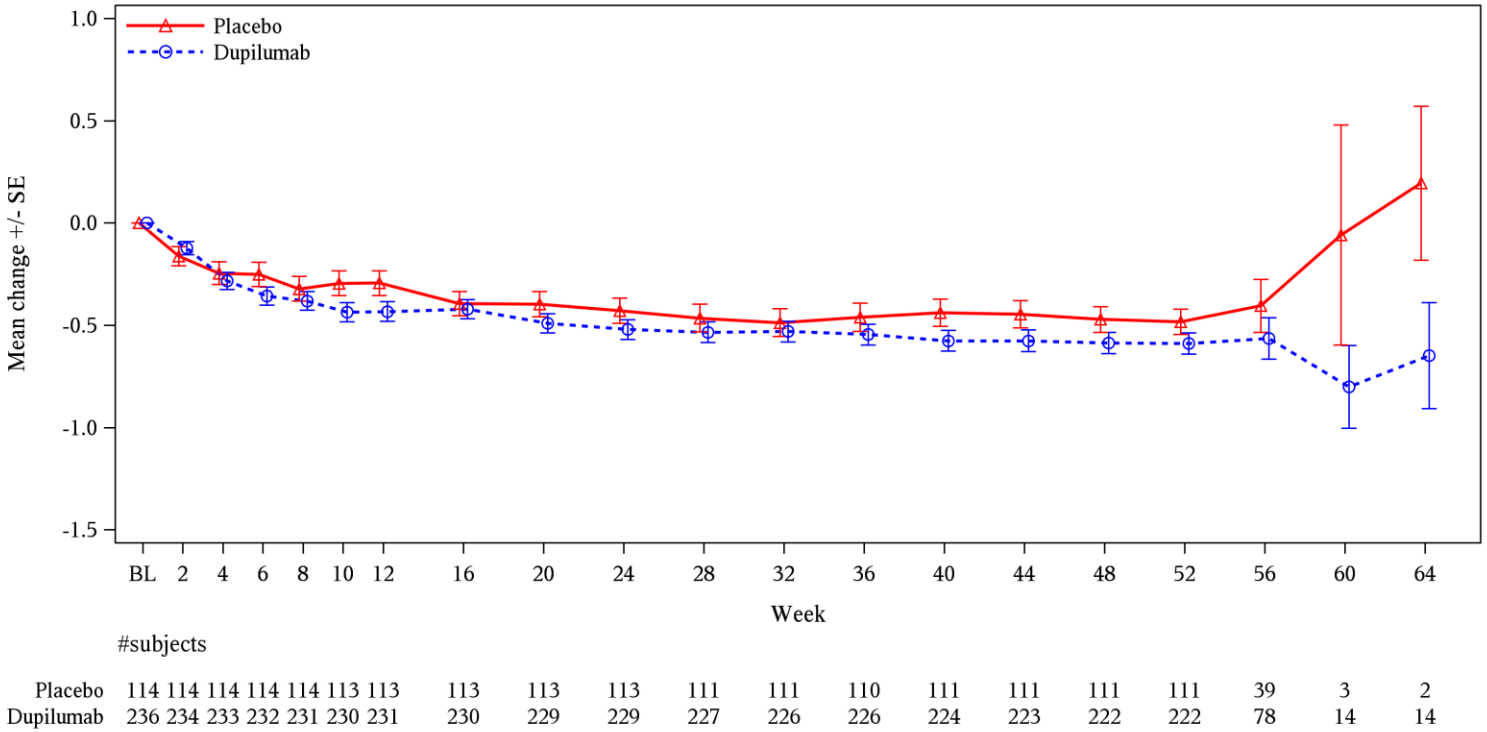
16.2.6.16.1 Summary of PM asthma symptom score over time - Type 2 inflammatory asthma phenotype population and baseline blood eosinophils >=0.3 Giga/L population

	Type 2 inflammatory asthma phenotype population	
PM asthma symptom score	**Placebo (N=114)**	**Dupilumab (N=236)**
Change from baseline		
Number	2	14
Mean (SD)	0.20 (0.53)	-0.65 (0.97)
Median	0.20	-0.47
Q1 : Q3	-0.18 : 0.57	-1.33 : 0.00
Min : Max	-0.2 : 0.6	-2.0 : 1.6
Percent change from baseline		
Number	2	12
Mean (SD)	55.80 (109.65)	-72.35 (41.30)
Median	55.80	-100.00
Q1 : Q3	-21.74 : 133.33	-100.00 : -38.67
Min : Max	-21.7 : 133.3	-100.0 : 1.5

Type 2 inflammatory asthma phenotype population is defined as the randomized patients with baseline blood eosinophils >= 0.15 Giga/L or baseline FeNO >= 20 ppb.

PGM=PRODOPS/SAR231893/EFC14153/CSR/REPORT/PGM/eff_sum_vis_i_t.sas OUT=REPORT/OUTPUT/eff_sum_aspm_t2e3_t_x.rtf (27NOV2020 - 6:43)

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen
Project Code / Study Number / Analysis: SAR231893 / EFC14153 / CSR
16.2.6 Efficacy response data
16.2.6.16 PM asthma symptom score
16.2.6.16.2 Plot of mean change from baseline in PM asthma symptom score over time - Type 2 inflammatory asthma phenotype population



#subjects

	BL	2	4	6	8	10	12	16	20	24	28	32	36	40	44	48	52	56	60	64
Placebo	114	114	114	114	114	113	113	113	113	113	111	111	110	111	111	111	111	39	3	2
Dupilumab	236	234	233	232	231	230	231	230	229	229	227	226	226	224	223	222	222	78	14	14

BL=Baseline
Type 2 inflammatory asthma phenotype population is defined as the randomized patients with baseline blood eosinophils >= 0.15 Giga/L or baseline FeNO >= 20 ppb.
PGM=PRODOPS/SAR231893/EFC14153/CSR/REPORT/PGM/eff_sum_vis_i_g.sas OUT=REPORT/OUTPUT/eff_sum_aspm_t2_g_x.rtf (27NOV2020 - 6:37)

16.2.6 Efficacy response data

16.2.6.16 PM asthma symptom score

16.2.6.16.4 Change from baseline in PM asthma symptom score over time (MMRM including measurements up to Week 52) - Type 2 inflammatory asthma phenotype population and baseline blood eosinophils >=0.3 Giga/L population

	Type 2 inflammatory asthma phenotype population	
PM asthma symptom score	**Placebo (N=114)**	**Dupilumab (N=236)**
Baseline		
Value		
Number	114	236
Mean (SD)	0.92 (0.72)	0.92 (0.77)
Median	0.93	1.00
Q1 : Q3	0.29 : 1.43	0.29 : 1.29
Min : Max	0.0 : 2.6	0.0 : 3.0
Week 2		
Change from baseline		
Number of patients in the model	110	228
LS Mean (SE) [a]	-0.17 (0.05)	-0.13 (0.03)
LS Mean Diff vs. placebo (95% CI) [a]		0.04 (-0.06, 0.14)
P-value vs. placebo [a]		0.4174

[a] Derived from MMRM model with change from baseline in PM asthma symptom score values up to Week 52 as the response variable, and treatment, age, baseline weight group, region, baseline eosinophil level, baseline FeNO level, baseline ICS dose level, visit, treatment by-visit interaction, baseline PM asthma symptom score value and baseline-by-visit interaction as covariates.

Type 2 inflammatory asthma phenotype population is defined as the randomized patients with baseline blood eosinophils >= 0.15 Giga/L or baseline FeNO >= 20 ppb.

PGM=PRODOPS/SAR231893/EFC14153/CSR/REPORT/PGM/eff_mmrm_i_t_aded.sas OUT=REPORT/OUTPUT/eff_aspm_chg_a52_t2e3_t_x.rtf (27NOV2020 - 2:59)

Project Code / Study Number / Analysis: SAR231893 / EFC14153 / CSR

16.2.6 Efficacy response data

16.2.6.16 PM asthma symptom score

16.2.6.16.4 Change from baseline in PM asthma symptom score over time (MMRM including measurements up to Week 52) - Type 2 inflammatory asthma phenotype population and baseline blood eosinophils >=0.3 Giga/L population

	Type 2 inflammatory asthma phenotype population	
PM asthma symptom score	**Placebo (N=114)**	**Dupilumab (N=236)**
Week 4		
Change from baseline		
Number of patients in the model	110	228
LS Mean (SE) [a]	-0.25 (0.05)	-0.29 (0.04)
LS Mean Diff vs. placebo (95% CI) [a]		-0.04 (-0.16, 0.09)
P-value vs. placebo [a]		0.5498
Week 6		
Change from baseline		
Number of patients in the model	110	228
LS Mean (SE) [a]	-0.26 (0.06)	-0.37 (0.04)
LS Mean Diff vs. placebo (95% CI) [a]		-0.12 (-0.24, 0.01)
P-value vs. placebo [a]		0.0735

[a] Derived from MMRM model with change from baseline in PM asthma symptom score values up to Week 52 as the response variable, and treatment, age, baseline weight group, region, baseline eosinophil level, baseline FeNO level, baseline ICS dose level, visit, treatment by-visit interaction, baseline PM asthma symptom score value and baseline-by-visit interaction as covariates.

Type 2 inflammatory asthma phenotype population is defined as the randomized patients with baseline blood eosinophils >= 0.15 Giga/L or baseline FeNO >= 20 ppb.

PGM=PRODOPS/SAR231893/EFC14153/CSR/REPORT/PGM/eff_mmrm_i_t_aded.sas OUT=REPORT/OUTPUT/eff_aspm_chg_a52_t2e3_t_x.rtf (27NOV2020 - 2:59)

Project Code / Study Number / Analysis: SAR231893 / EFC14153 / CSR

16.2.6 Efficacy response data

16.2.6.16 PM asthma symptom score

16.2.6.16.4 Change from baseline in PM asthma symptom score over time (MMRM including measurements up to Week 52) - Type 2 inflammatory asthma phenotype population and baseline blood eosinophils >=0.3 Giga/L population

	Type 2 inflammatory asthma phenotype population	
PM asthma symptom score	**Placebo (N=114)**	**Dupilumab (N=236)**
Week 8		
Change from baseline		
Number of patients in the model	110	228
LS Mean (SE) [a]	-0.33 (0.06)	-0.40 (0.04)
LS Mean Diff vs. placebo (95% CI) [a]		-0.08 (-0.21, 0.05)
P-value vs. placebo [a]		0.2513
Week 10		
Change from baseline		
Number of patients in the model	110	228
LS Mean (SE) [a]	-0.30 (0.06)	-0.45 (0.04)
LS Mean Diff vs. placebo (95% CI) [a]		-0.15 (-0.29, -0.02)
P-value vs. placebo [a]		0.0241

[a] Derived from MMRM model with change from baseline in PM asthma symptom score values up to Week 52 as the response variable, and treatment, age, baseline weight group, region, baseline eosinophil level, baseline FeNO level, baseline ICS dose level, visit, treatment by-visit interaction, baseline PM asthma symptom score value and baseline-by-visit interaction as covariates.

Type 2 inflammatory asthma phenotype population is defined as the randomized patients with baseline blood eosinophils >= 0.15 Giga/L or baseline FeNO >= 20 ppb.

PGM=PRODOPS/SAR231893/EFC14153/CSR/REPORT/PGM/eff_mmrm_i_t_aded.sas OUT=REPORT/OUTPUT/eff_aspm_chg_a52_t2e3_t_x.rtf (27NOV2020 - 2:59)

Project Code / Study Number / Analysis: SAR231893 / EFC14153 / CSR

16.2.6 Efficacy response data

16.2.6.16 PM asthma symptom score

16.2.6.16.4 Change from baseline in PM asthma symptom score over time (MMRM including measurements up to Week 52) - Type 2 inflammatory asthma phenotype population and baseline blood eosinophils >=0.3 Giga/L population

	Type 2 inflammatory asthma phenotype population	
PM asthma symptom score	**Placebo (N=114)**	**Dupilumab (N=236)**
Week 12		
Change from baseline		
Number of patients in the model	110	228
LS Mean (SE) [a]	-0.30 (0.06)	-0.45 (0.04)
LS Mean Diff vs. placebo (95% CI) [a]		-0.15 (-0.29, -0.02)
P-value vs. placebo [a]		0.0270
Week 16		
Change from baseline		
Number of patients in the model	110	228
LS Mean (SE) [a]	-0.40 (0.06)	-0.44 (0.04)
LS Mean Diff vs. placebo (95% CI) [a]		-0.04 (-0.17, 0.10)
P-value vs. placebo [a]		0.5922

[a] Derived from MMRM model with change from baseline in PM asthma symptom score values up to Week 52 as the response variable, and treatment, age, baseline weight group, region, baseline eosinophil level, baseline FeNO level, baseline ICS dose level, visit, treatment by-visit interaction, baseline PM asthma symptom score value and baseline-by-visit interaction as covariates.

Type 2 inflammatory asthma phenotype population is defined as the randomized patients with baseline blood eosinophils >= 0.15 Giga/L or baseline FeNO >= 20 ppb.

PGM=PRODOPS/SAR231893/EFC14153/CSR/REPORT/PGM/eff_mmrm_i_t_aded.sas OUT=REPORT/OUTPUT/eff_aspm_chg_a52_t2e3_t_x.rtf (27NOV2020 - 2:59)

Project Code / Study Number / Analysis: SAR231893 / EFC14153 / CSR

16.2.6 Efficacy response data

16.2.6.16 PM asthma symptom score

16.2.6.16.4 Change from baseline in PM asthma symptom score over time (MMRM including measurements up to Week 52) - Type 2 inflammatory asthma phenotype population and baseline blood eosinophils >=0.3 Giga/L population

	Type 2 inflammatory asthma phenotype population	
PM asthma symptom score	**Placebo (N=114)**	**Dupilumab (N=236)**
Week 20		
Change from baseline		
Number of patients in the model	110	228
LS Mean (SE) [a]	-0.41 (0.06)	-0.50 (0.04)
LS Mean Diff vs. placebo (95% CI) [a]		-0.09 (-0.22, 0.03)
P-value vs. placebo [a]		0.1533
Week 24		
Change from baseline		
Number of patients in the model	110	228
LS Mean (SE) [a]	-0.44 (0.06)	-0.53 (0.04)
LS Mean Diff vs. placebo (95% CI) [a]		-0.09 (-0.22, 0.04)
P-value vs. placebo [a]		0.1673

[a] Derived from MMRM model with change from baseline in PM asthma symptom score values up to Week 52 as the response variable, and treatment, age, baseline weight group, region, baseline eosinophil level, baseline FeNO level, baseline ICS dose level, visit, treatment by-visit interaction, baseline PM asthma symptom score value and baseline-by-visit interaction as covariates.

Type 2 inflammatory asthma phenotype population is defined as the randomized patients with baseline blood eosinophils >= 0.15 Giga/L or baseline FeNO >= 20 ppb.

PGM=PRODOPS/SAR231893/EFC14153/CSR/REPORT/PGM/eff_mmrm_i_t_aded.sas OUT=REPORT/OUTPUT/eff_aspm_chg_a52_t2e3_t_x.rtf (27NOV2020 - 2:59)

Project Code / Study Number / Analysis: SAR231893 / EFC14153 / CSR

16.2.6 Efficacy response data

16.2.6.16 PM asthma symptom score

16.2.6.16.4 Change from baseline in PM asthma symptom score over time (MMRM including measurements up to Week 52) - Type 2 inflammatory asthma phenotype population and baseline blood eosinophils >=0.3 Giga/L population

	Type 2 inflammatory asthma phenotype population	
PM asthma symptom score	**Placebo (N=114)**	**Dupilumab (N=236)**
Week 28		
Change from baseline		
Number of patients in the model	110	228
LS Mean (SE) [a]	-0.48 (0.06)	-0.55 (0.04)
LS Mean Diff vs. placebo (95% CI) [a]		-0.07 (-0.20, 0.06)
P-value vs. placebo [a]		0.3103
Week 32		
Change from baseline		
Number of patients in the model	110	228
LS Mean (SE) [a]	-0.51 (0.06)	-0.54 (0.04)
LS Mean Diff vs. placebo (95% CI) [a]		-0.04 (-0.17, 0.09)
P-value vs. placebo [a]		0.5678

[a] Derived from MMRM model with change from baseline in PM asthma symptom score values up to Week 52 as the response variable, and treatment, age, baseline weight group, region, baseline eosinophil level, baseline FeNO level, baseline ICS dose level, visit, treatment by-visit interaction, baseline PM asthma symptom score value and baseline-by-visit interaction as covariates.

Type 2 inflammatory asthma phenotype population is defined as the randomized patients with baseline blood eosinophils >= 0.15 Giga/L or baseline FeNO >= 20 ppb.

PGM=PRODOPS/SAR231893/EFC14153/CSR/REPORT/PGM/eff_mmrm_i_t_aded.sas OUT=REPORT/OUTPUT/eff_aspm_chg_a52_t2e3_t_x.rtf (27NOV2020 - 2:59)

Project Code / Study Number / Analysis: SAR231893 / EFC14153 / CSR

16.2.6 Efficacy response data

16.2.6.16 PM asthma symptom score

16.2.6.16.4 Change from baseline in PM asthma symptom score over time (MMRM including measurements up to Week 52) - Type 2 inflammatory asthma phenotype population and baseline blood eosinophils >=0.3 Giga/L population

	Type 2 inflammatory asthma phenotype population	
PM asthma symptom score	**Placebo (N=114)**	**Dupilumab (N=236)**
Week 36		
Change from baseline		
Number of patients in the model	110	228
LS Mean (SE) [a]	-0.47 (0.06)	-0.55 (0.04)
LS Mean Diff vs. placebo (95% CI) [a]		-0.08 (-0.21, 0.05)
P-value vs. placebo [a]		0.2052
Week 40		
Change from baseline		
Number of patients in the model	110	228
LS Mean (SE) [a]	-0.46 (0.06)	-0.58 (0.04)
LS Mean Diff vs. placebo (95% CI) [a]		-0.13 (-0.25, 0.00)
P-value vs. placebo [a]		0.0528

[a] Derived from MMRM model with change from baseline in PM asthma symptom score values up to Week 52 as the response variable, and treatment, age, baseline weight group, region, baseline eosinophil level, baseline FeNO level, baseline ICS dose level, visit, treatment by-visit interaction, baseline PM asthma symptom score value and baseline-by-visit interaction as covariates.

Type 2 inflammatory asthma phenotype population is defined as the randomized patients with baseline blood eosinophils >= 0.15 Giga/L or baseline FeNO >= 20 ppb.

PGM=PRODOPS/SAR231893/EFC14153/CSR/REPORT/PGM/eff_mmrm_i_t_aded.sas OUT=REPORT/OUTPUT/eff_aspm_chg_a52_t2e3_t_x.rtf (27NOV2020 - 2:59)

Project Code / Study Number / Analysis: SAR231893 / EFC14153 / CSR

16.2.6 Efficacy response data

16.2.6.16 PM asthma symptom score

16.2.6.16.4 Change from baseline in PM asthma symptom score over time (MMRM including measurements up to Week 52) - Type 2 inflammatory asthma phenotype population and baseline blood eosinophils >=0.3 Giga/L population

	Type 2 inflammatory asthma phenotype population	
PM asthma symptom score	**Placebo (N=114)**	**Dupilumab (N=236)**
Week 44		
Change from baseline		
Number of patients in the model	110	228
LS Mean (SE) [a]	-0.47 (0.06)	-0.59 (0.04)
LS Mean Diff vs. placebo (95% CI) [a]		-0.12 (-0.25, 0.01)
P-value vs. placebo [a]		0.0648
Week 48		
Change from baseline		
Number of patients in the model	110	228
LS Mean (SE) [a]	-0.49 (0.05)	-0.59 (0.04)
LS Mean Diff vs. placebo (95% CI) [a]		-0.10 (-0.23, 0.02)
P-value vs. placebo [a]		0.1096

[a] Derived from MMRM model with change from baseline in PM asthma symptom score values up to Week 52 as the response variable, and treatment, age, baseline weight group, region, baseline eosinophil level, baseline FeNO level, baseline ICS dose level, visit, treatment by-visit interaction, baseline PM asthma symptom score value and baseline-by-visit interaction as covariates.

Type 2 inflammatory asthma phenotype population is defined as the randomized patients with baseline blood eosinophils >= 0.15 Giga/L or baseline FeNO >= 20 ppb.

PGM=PRODOPS/SAR231893/EFC14153/CSR/REPORT/PGM/eff_mmrm_i_t_aded.sas OUT=REPORT/OUTPUT/eff_aspm_chg_a52_t2e3_t_x.rtf (27NOV2020 - 2:59)

Project Code / Study Number / Analysis: SAR231893 / EFC14153 / CSR

16.2.6 Efficacy response data

16.2.6.16 PM asthma symptom score

16.2.6.16.4 Change from baseline in PM asthma symptom score over time (MMRM including measurements up to Week 52) - Type 2 inflammatory asthma phenotype population and baseline blood eosinophils >=0.3 Giga/L population

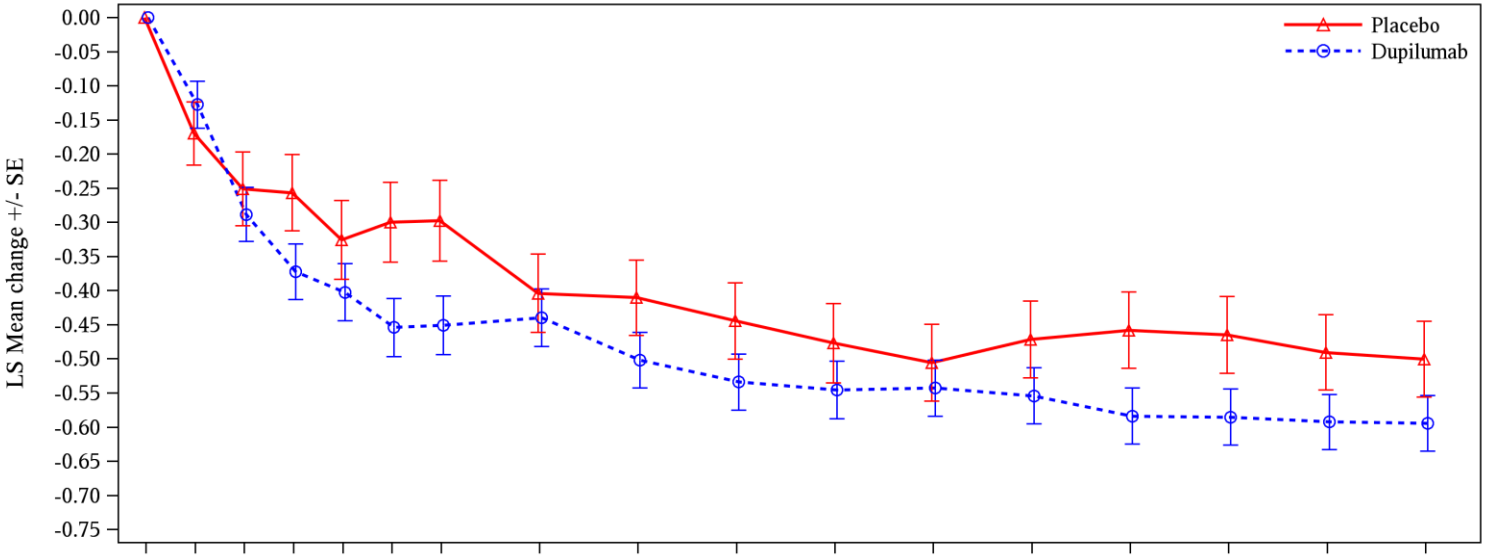
	Type 2 inflammatory asthma phenotype population	
PM asthma symptom score	**Placebo (N=114)**	**Dupilumab (N=236)**
Week 52		
Change from baseline		
Number of patients in the model	110	228
LS Mean (SE) [a]	-0.50 (0.06)	-0.59 (0.04)
LS Mean Diff vs. placebo (95% CI) [a]		-0.09 (-0.22, 0.03)
P-value vs. placebo [a]		0.1463

[a] Derived from MMRM model with change from baseline in PM asthma symptom score values up to Week 52 as the response variable, and treatment, age, baseline weight group, region, baseline eosinophil level, baseline FeNO level, baseline ICS dose level, visit, treatment by-visit interaction, baseline PM asthma symptom score value and baseline-by-visit interaction as covariates.

Type 2 inflammatory asthma phenotype population is defined as the randomized patients with baseline blood eosinophils >= 0.15 Giga/L or baseline FeNO >= 20 ppb.

PGM=PRODOPS/SAR231893/EFC14153/CSR/REPORT/PGM/eff_mmrm_i_t_aded.sas OUT=REPORT/OUTPUT/eff_aspm_chg_a52_t2e3_t_x.rtf (27NOV2020 - 2:59)

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen
Project Code / Study Number / Analysis: SAR231893 / EFC14153 / CSR
16.2.6 Efficacy response data
16.2.6.16 PM asthma symptom score
16.2.6.16.5 Plot of LS mean change from baseline in PM asthma symptom score over time (MMRM including measurements up to Week 52) - Type 2 inflammatory asthma phenotype population



#subjects

	BL	2	4	6	8	10	12	16	20	24	28	32	36	40	44	48	52
Placebo	114	114	114	114	114	113	113	113	113	113	111	111	110	111	111	111	111
Dupilumab	236	234	233	232	231	230	231	230	229	229	227	226	226	224	223	222	222

BL=Baseline
Type 2 inflammatory asthma phenotype population is defined as the randomized patients with baseline blood eosinophils >= 0.15 Giga/L or baseline FeNO >= 20 ppb.
PGM=PRODOPS/SAR231893/EFC14153/CSR/REPORT/PGM/eff_mmrm_i_g_intext_aded.sas OUT=REPORT/OUTPUT/eff_aspm_chg_a52_t2_g_x.rtf (27NOV2020 - 2:58)

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

Project Code / Study Number / Analysis: SAR231893 / EFC14153 / CSR

16.2.6 Efficacy response data

16.2.6.17 Number of nocturnal awakenings

16.2.6.17.1 Summary of number of nocturnal awakenings over time - Type 2 inflammatory asthma phenotype population and baseline blood eosinophils >=0.3 Giga/L population

	Type 2 inflammatory asthma phenotype population	
Number of nocturnal awakenings	**Placebo (N=114)**	**Dupilumab (N=236)**
Baseline		
Value		
Number	114	236
Mean (SD)	0.32 (0.45)	0.39 (0.68)
Median	0.14	0.14
Q1 : Q3	0.00 : 0.50	0.00 : 0.43
Min : Max	0.0 : 2.5	0.0 : 4.4
Week 2		
Value		
Number	114	234
Mean (SD)	0.22 (0.38)	0.26 (0.53)
Median	0.00	0.00
Q1 : Q3	0.00 : 0.29	0.00 : 0.25
Min : Max	0.0 : 2.0	0.0 : 3.9

Type 2 inflammatory asthma phenotype population is defined as the randomized patients with baseline blood eosinophils >= 0.15 Giga/L or baseline FeNO >= 20 ppb.

PGM=PRODOPS/SAR231893/EFC14153/CSR/REPORT/PGM/eff_sum_vis_i_t.sas OUT=REPORT/OUTPUT/eff_sum_awakens_t2e3_t_x.rtf (27NOV2020 - 6:43)

Project Code / Study Number / Analysis: SAR231893 / EFC14153 / CSR

16.2.6 Efficacy response data

16.2.6.17 Number of nocturnal awakenings

16.2.6.17.1 Summary of number of nocturnal awakenings over time - Type 2 inflammatory asthma phenotype population and baseline blood eosinophils >=0.3 Giga/L population

	Type 2 inflammatory asthma phenotype population	
Number of nocturnal awakenings	**Placebo (N=114)**	**Dupilumab (N=236)**
Change from baseline		
Number	114	234
Mean (SD)	-0.10 (0.38)	-0.13 (0.43)
Median	0.00	0.00
Q1 : Q3	-0.17 : 0.00	-0.14 : 0.00
Min : Max	-2.5 : 0.6	-3.9 : 1.1
Percent change from baseline		
Number	61	126
Mean (SD)	-31.43 (85.54)	-38.90 (68.54)
Median	-50.00	-50.00
Q1 : Q3	-100.00 : 0.00	-100.00 : 0.00
Min : Max	-100.0 : 315.4	-100.0 : 350.0

Type 2 inflammatory asthma phenotype population is defined as the randomized patients with baseline blood eosinophils >= 0.15 Giga/L or baseline FeNO >= 20 ppb.
PGM=PRODOPS/SAR231893/EFC14153/CSR/REPORT/PGM/eff_sum_vis_i_t.sas OUT=REPORT/OUTPUT/eff_sum_awakens_t2e3_t_x.rtf (27NOV2020 - 6:43)

16.2.6 Efficacy response data

16.2.6.17 Number of nocturnal awakenings

16.2.6.17.1 Summary of number of nocturnal awakenings over time - Type 2 inflammatory asthma phenotype population and baseline blood eosinophils >=0.3 Giga/L population

	Type 2 inflammatory asthma phenotype population	
Number of nocturnal awakenings	**Placebo (N=114)**	**Dupilumab (N=236)**
Week 4		
Value		
Number	114	232
Mean (SD)	0.20 (0.37)	0.18 (0.44)
Median	0.00	0.00
Q1 : Q3	0.00 : 0.23	0.00 : 0.14
Min : Max	0.0 : 2.0	0.0 : 3.0
Change from baseline		
Number	114	232
Mean (SD)	-0.13 (0.43)	-0.22 (0.58)
Median	0.00	0.00
Q1 : Q3	-0.26 : 0.00	-0.29 : 0.00
Min : Max	-2.5 : 0.7	-4.4 : 0.9

Type 2 inflammatory asthma phenotype population is defined as the randomized patients with baseline blood eosinophils >= 0.15 Giga/L or baseline FeNO >= 20 ppb.
PGM=PRODOPS/SAR231893/EFC14153/CSR/REPORT/PGM/eff_sum_vis_i_t.sas OUT=REPORT/OUTPUT/eff_sum_awakens_t2e3_t_x.rtf (27NOV2020 - 6:43)

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

Project Code / Study Number / Analysis: SAR231893 / EFC14153 / CSR

16.2.6 Efficacy response data

16.2.6.17 Number of nocturnal awakenings

16.2.6.17.1 Summary of number of nocturnal awakenings over time - Type 2 inflammatory asthma phenotype population and baseline blood eosinophils >=0.3 Giga/L population

	Type 2 inflammatory asthma phenotype population	
Number of nocturnal awakenings	**Placebo (N=114)**	**Dupilumab (N=236)**
Percent change from baseline		
Number	61	125
Mean (SD)	-53.60 (65.58)	-49.56 (89.00)
Median	-87.50	-89.29
Q1 : Q3	-100.00 : -14.29	-100.00 : -30.00
Min : Max	-100.0 : 200.0	-100.0 : 546.2
Week 6		
Value		
Number	114	232
Mean (SD)	0.18 (0.35)	0.15 (0.42)
Median	0.00	0.00
Q1 : Q3	0.00 : 0.15	0.00 : 0.08
Min : Max	0.0 : 1.5	0.0 : 3.1

Type 2 inflammatory asthma phenotype population is defined as the randomized patients with baseline blood eosinophils >= 0.15 Giga/L or baseline FeNO >= 20 ppb.

PGM=PRODOPS/SAR231893/EFC14153/CSR/REPORT/PGM/eff_sum_vis_i_t.sas OUT=REPORT/OUTPUT/eff_sum_awakens_t2e3_t_x.rtf (27NOV2020 - 6:43)

16.2.6 Efficacy response data

16.2.6.17 Number of nocturnal awakenings

16.2.6.17.1 Summary of number of nocturnal awakenings over time - Type 2 inflammatory asthma phenotype population and baseline blood eosinophils >=0.3 Giga/L population

	Type 2 inflammatory asthma phenotype population	
Number of nocturnal awakenings	**Placebo (N=114)**	**Dupilumab (N=236)**
Change from baseline		
Number	114	232
Mean (SD)	-0.14 (0.44)	-0.24 (0.58)
Median	0.00	0.00
Q1 : Q3	-0.29 : 0.00	-0.29 : 0.00
Min : Max	-2.3 : 1.4	-4.4 : 1.0
Percent change from baseline		
Number	61	125
Mean (SD)	-51.82 (83.55)	-65.94 (70.21)
Median	-91.07	-100.00
Q1 : Q3	-100.00 : -22.22	-100.00 : -50.00
Min : Max	-100.0 : 250.0	-100.0 : 490.9

Type 2 inflammatory asthma phenotype population is defined as the randomized patients with baseline blood eosinophils >= 0.15 Giga/L or baseline FeNO >= 20 ppb.
PGM=PRODOPS/SAR231893/EFC14153/CSR/REPORT/PGM/eff_sum_vis_i_t.sas OUT=REPORT/OUTPUT/eff_sum_awakens_t2e3_t_x.rtf (27NOV2020 - 6:43)

16.2.6 Efficacy response data

16.2.6.17 Number of nocturnal awakenings

16.2.6.17.1 Summary of number of nocturnal awakenings over time - Type 2 inflammatory asthma phenotype population and baseline blood eosinophils >=0.3 Giga/L population

	Type 2 inflammatory asthma phenotype population	
Number of nocturnal awakenings	**Placebo (N=114)**	**Dupilumab (N=236)**
Week 8		
Value		
Number	114	232
Mean (SD)	0.15 (0.34)	0.18 (0.53)
Median	0.00	0.00
Q1 : Q3	0.00 : 0.09	0.00 : 0.08
Min : Max	0.0 : 1.6	0.0 : 4.7
Change from baseline		
Number	114	232
Mean (SD)	-0.17 (0.44)	-0.21 (0.69)
Median	0.00	0.00
Q1 : Q3	-0.29 : 0.00	-0.29 : 0.00
Min : Max	-2.5 : 1.1	-4.4 : 3.8

Type 2 inflammatory asthma phenotype population is defined as the randomized patients with baseline blood eosinophils >= 0.15 Giga/L or baseline FeNO >= 20 ppb.
PGM=PRODOPS/SAR231893/EFC14153/CSR/REPORT/PGM/eff_sum_vis_i_t.sas OUT=REPORT/OUTPUT/eff_sum_awakens_t2e3_t_x.rtf (27NOV2020 - 6:43)

16.2.6 Efficacy response data

16.2.6.17 Number of nocturnal awakenings

16.2.6.17.1 Summary of number of nocturnal awakenings over time - Type 2 inflammatory asthma phenotype population and baseline blood eosinophils >=0.3 Giga/L population

	Type 2 inflammatory asthma phenotype population	
Number of nocturnal awakenings	**Placebo (N=114)**	**Dupilumab (N=236)**
Percent change from baseline		
Number	61	125
Mean (SD)	-62.62 (61.95)	-50.59 (123.25)
Median	-100.00	-100.00
Q1 : Q3	-100.00 : -40.00	-100.00 : -48.57
Min : Max	-100.0 : 225.0	-100.0 : 677.8
Week 10		
Value		
Number	114	230
Mean (SD)	0.21 (0.40)	0.15 (0.46)
Median	0.00	0.00
Q1 : Q3	0.00 : 0.22	0.00 : 0.00
Min : Max	0.0 : 2.0	0.0 : 3.2

Type 2 inflammatory asthma phenotype population is defined as the randomized patients with baseline blood eosinophils >= 0.15 Giga/L or baseline FeNO >= 20 ppb.
PGM=PRODOPS/SAR231893/EFC14153/CSR/REPORT/PGM/eff_sum_vis_i_t.sas OUT=REPORT/OUTPUT/eff_sum_awakens_t2e3_t_x.rtf (27NOV2020 - 6:43)

16.2.6 Efficacy response data

16.2.6.17 Number of nocturnal awakenings

16.2.6.17.1 Summary of number of nocturnal awakenings over time - Type 2 inflammatory asthma phenotype population and baseline blood eosinophils >=0.3 Giga/L population

	Type 2 inflammatory asthma phenotype population	
Number of nocturnal awakenings	**Placebo (N=114)**	**Dupilumab (N=236)**
Change from baseline		
Number	114	230
Mean (SD)	-0.12 (0.45)	-0.25 (0.57)
Median	0.00	0.00
Q1 : Q3	-0.21 : 0.00	-0.33 : 0.00
Min : Max	-2.2 : 1.4	-4.4 : 2.0
Percent change from baseline		
Number	61	124
Mean (SD)	-27.75 (135.70)	-66.76 (69.28)
Median	-100.00	-100.00
Q1 : Q3	-100.00 : 0.00	-100.00 : -58.33
Min : Max	-100.0 : 500.0	-100.0 : 250.0

Type 2 inflammatory asthma phenotype population is defined as the randomized patients with baseline blood eosinophils >= 0.15 Giga/L or baseline FeNO >= 20 ppb.
PGM=PRODOPS/SAR231893/EFC14153/CSR/REPORT/PGM/eff_sum_vis_i_t.sas OUT=REPORT/OUTPUT/eff_sum_awakens_t2e3_t_x.rtf (27NOV2020 - 6:43)

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

Project Code / Study Number / Analysis: SAR231893 / EFC14153 / CSR

16.2.6 Efficacy response data

16.2.6.17 Number of nocturnal awakenings

16.2.6.17.1 Summary of number of nocturnal awakenings over time - Type 2 inflammatory asthma phenotype population and baseline blood eosinophils >=0.3 Giga/L population

	Type 2 inflammatory asthma phenotype population	
Number of nocturnal awakenings	**Placebo (N=114)**	**Dupilumab (N=236)**
Week 12		
Value		
Number	113	229
Mean (SD)	0.18 (0.36)	0.13 (0.44)
Median	0.00	0.00
Q1 : Q3	0.00 : 0.23	0.00 : 0.00
Min : Max	0.0 : 1.9	0.0 : 3.4
Change from baseline		
Number	113	229
Mean (SD)	-0.14 (0.38)	-0.26 (0.62)
Median	0.00	0.00
Q1 : Q3	-0.21 : 0.00	-0.29 : 0.00
Min : Max	-2.2 : 1.1	-4.4 : 1.7

Type 2 inflammatory asthma phenotype population is defined as the randomized patients with baseline blood eosinophils >= 0.15 Giga/L or baseline FeNO >= 20 ppb.

PGM=PRODOPS/SAR231893/EFC14153/CSR/REPORT/PGM/eff_sum_vis_i_t.sas OUT=REPORT/OUTPUT/eff_sum_awakens_t2e3_t_x.rtf (27NOV2020 - 6:43)

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

Project Code / Study Number / Analysis: SAR231893 / EFC14153 / CSR

16.2.6 Efficacy response data

16.2.6.17 Number of nocturnal awakenings

16.2.6.17.1 Summary of number of nocturnal awakenings over time - Type 2 inflammatory asthma phenotype population and baseline blood eosinophils >=0.3 Giga/L population

	Type 2 inflammatory asthma phenotype population	
Number of nocturnal awakenings	**Placebo (N=114)**	**Dupilumab (N=236)**
Percent change from baseline		
Number	60	123
Mean (SD)	-53.19 (73.90)	-63.56 (99.67)
Median	-85.71	-100.00
Q1 : Q3	-100.00 : -20.83	-100.00 : -62.50
Min : Max	-100.0 : 375.0	-100.0 : 600.0
Week 16		
Value		
Number	113	230
Mean (SD)	0.13 (0.34)	0.12 (0.37)
Median	0.00	0.00
Q1 : Q3	0.00 : 0.08	0.00 : 0.04
Min : Max	0.0 : 2.7	0.0 : 2.7

Type 2 inflammatory asthma phenotype population is defined as the randomized patients with baseline blood eosinophils >= 0.15 Giga/L or baseline FeNO >= 20 ppb.

PGM=PRODOPS/SAR231893/EFC14153/CSR/REPORT/PGM/eff_sum_vis_i_t.sas OUT=REPORT/OUTPUT/eff_sum_awakens_t2e3_t_x.rtf (27NOV2020 - 6:43)

16.2.6 Efficacy response data

16.2.6.17 Number of nocturnal awakenings

16.2.6.17.1 Summary of number of nocturnal awakenings over time - Type 2 inflammatory asthma phenotype population and baseline blood eosinophils >=0.3 Giga/L population

	Type 2 inflammatory asthma phenotype population	
Number of nocturnal awakenings	**Placebo (N=114)**	**Dupilumab (N=236)**
Change from baseline		
Number	113	230
Mean (SD)	-0.19 (0.39)	-0.27 (0.58)
Median	0.00	0.00
Q1 : Q3	-0.29 : 0.00	-0.33 : 0.00
Min : Max	-1.9 : 1.2	-4.4 : 0.8
Percent change from baseline		
Number	60	123
Mean (SD)	-63.36 (60.34)	-69.29 (64.49)
Median	-95.83	-100.00
Q1 : Q3	-100.00 : -34.52	-100.00 : -59.62
Min : Max	-100.0 : 224.1	-100.0 : 421.7

Type 2 inflammatory asthma phenotype population is defined as the randomized patients with baseline blood eosinophils >= 0.15 Giga/L or baseline FeNO >= 20 ppb.
PGM=PRODOPS/SAR231893/EFC14153/CSR/REPORT/PGM/eff_sum_vis_i_t.sas OUT=REPORT/OUTPUT/eff_sum_awakens_t2e3_t_x.rtf (27NOV2020 - 6:43)

16.2.6 Efficacy response data

16.2.6.17 Number of nocturnal awakenings

16.2.6.17.1 Summary of number of nocturnal awakenings over time - Type 2 inflammatory asthma phenotype population and baseline blood eosinophils >=0.3 Giga/L population

	Type 2 inflammatory asthma phenotype population	
Number of nocturnal awakenings	**Placebo (N=114)**	**Dupilumab (N=236)**
Week 20		
Value		
Number	113	229
Mean (SD)	0.14 (0.33)	0.10 (0.30)
Median	0.00	0.00
Q1 : Q3	0.00 : 0.10	0.00 : 0.04
Min : Max	0.0 : 2.5	0.0 : 2.3
Change from baseline		
Number	113	229
Mean (SD)	-0.19 (0.43)	-0.30 (0.60)
Median	0.00	0.00
Q1 : Q3	-0.29 : 0.00	-0.43 : 0.00
Min : Max	-2.5 : 0.9	-4.4 : 0.5

Type 2 inflammatory asthma phenotype population is defined as the randomized patients with baseline blood eosinophils >= 0.15 Giga/L or baseline FeNO >= 20 ppb.
PGM=PRODOPS/SAR231893/EFC14153/CSR/REPORT/PGM/eff_sum_vis_i_t.sas OUT=REPORT/OUTPUT/eff_sum_awakens_t2e3_t_x.rtf (27NOV2020 - 6:43)

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

Project Code / Study Number / Analysis: SAR231893 / EFC14153 / CSR

16.2.6 Efficacy response data

16.2.6.17 Number of nocturnal awakenings

16.2.6.17.1 Summary of number of nocturnal awakenings over time - Type 2 inflammatory asthma phenotype population and baseline blood eosinophils >=0.3 Giga/L population

	Type 2 inflammatory asthma phenotype population	
Number of nocturnal awakenings	**Placebo (N=114)**	**Dupilumab (N=236)**
Percent change from baseline		
Number	60	124
Mean (SD)	-64.22 (59.56)	-76.87 (52.84)
Median	-100.00	-100.00
Q1 : Q3	-100.00 : -56.43	-100.00 : -80.64
Min : Max	-100.0 : 159.3	-100.0 : 263.6
Week 24		
Value		
Number	113	229
Mean (SD)	0.13 (0.41)	0.10 (0.35)
Median	0.00	0.00
Q1 : Q3	0.00 : 0.05	0.00 : 0.00
Min : Max	0.0 : 3.3	0.0 : 3.1

Type 2 inflammatory asthma phenotype population is defined as the randomized patients with baseline blood eosinophils >= 0.15 Giga/L or baseline FeNO >= 20 ppb.

PGM=PRODOPS/SAR231893/EFC14153/CSR/REPORT/PGM/eff_sum_vis_i_t.sas OUT=REPORT/OUTPUT/eff_sum_awakens_t2e3_t_x.rtf (27NOV2020 - 6:43)

Project Code / Study Number / Analysis: SAR231893 / EFC14153 / CSR

16.2.6 Efficacy response data

16.2.6.17 Number of nocturnal awakenings

16.2.6.17.1 Summary of number of nocturnal awakenings over time - Type 2 inflammatory asthma phenotype population and baseline blood eosinophils >=0.3 Giga/L population

	Type 2 inflammatory asthma phenotype population	
Number of nocturnal awakenings	**Placebo (N=114)**	**Dupilumab (N=236)**
Change from baseline		
Number	113	229
Mean (SD)	-0.19 (0.51)	-0.29 (0.60)
Median	0.00	0.00
Q1 : Q3	-0.30 : 0.00	-0.40 : 0.00
Min : Max	-2.4 : 3.2	-4.4 : 0.6
Percent change from baseline		
Number	60	124
Mean (SD)	-35.06 (300.52)	-80.38 (42.84)
Median	-96.40	-100.00
Q1 : Q3	-100.00 : -55.49	-100.00 : -84.77
Min : Max	-100.0 : 2233.3	-100.0 : 177.8

Type 2 inflammatory asthma phenotype population is defined as the randomized patients with baseline blood eosinophils >= 0.15 Giga/L or baseline FeNO >= 20 ppb.

PGM=PRODOPS/SAR231893/EFC14153/CSR/REPORT/PGM/eff_sum_vis_i_t.sas OUT=REPORT/OUTPUT/eff_sum_awakens_t2e3_t_x.rtf (27NOV2020 - 6:43)

16.2.6 Efficacy response data

16.2.6.17 Number of nocturnal awakenings

16.2.6.17.1 Summary of number of nocturnal awakenings over time - Type 2 inflammatory asthma phenotype population and baseline blood eosinophils >=0.3 Giga/L population

	Type 2 inflammatory asthma phenotype population	
Number of nocturnal awakenings	**Placebo (N=114)**	**Dupilumab (N=236)**
Week 28		
Value		
Number	111	227
Mean (SD)	0.11 (0.31)	0.11 (0.40)
Median	0.00	0.00
Q1 : Q3	0.00 : 0.00	0.00 : 0.00
Min : Max	0.0 : 2.0	0.0 : 3.6
Change from baseline		
Number	111	227
Mean (SD)	-0.22 (0.45)	-0.28 (0.60)
Median	0.00	0.00
Q1 : Q3	-0.33 : 0.00	-0.35 : 0.00
Min : Max	-2.5 : 1.1	-4.4 : 1.5

Type 2 inflammatory asthma phenotype population is defined as the randomized patients with baseline blood eosinophils >= 0.15 Giga/L or baseline FeNO >= 20 ppb.
PGM=PRODOPS/SAR231893/EFC14153/CSR/REPORT/PGM/eff_sum_vis_i_t.sas OUT=REPORT/OUTPUT/eff_sum_awakens_t2e3_t_x.rtf (27NOV2020 - 6:43)

16.2.6 Efficacy response data

16.2.6.17 Number of nocturnal awakenings

16.2.6.17.1 Summary of number of nocturnal awakenings over time - Type 2 inflammatory asthma phenotype population and baseline blood eosinophils >=0.3 Giga/L population

	Type 2 inflammatory asthma phenotype population	
Number of nocturnal awakenings	**Placebo (N=114)**	**Dupilumab (N=236)**
Percent change from baseline		
Number	59	123
Mean (SD)	-67.84 (106.67)	-68.56 (88.91)
Median	-100.00	-100.00
Q1 : Q3	-100.00 : -76.00	-100.00 : -65.38
Min : Max	-100.0 : 689.5	-100.0 : 733.3
Week 32		
Value		
Number	111	225
Mean (SD)	0.09 (0.28)	0.10 (0.39)
Median	0.00	0.00
Q1 : Q3	0.00 : 0.00	0.00 : 0.00
Min : Max	0.0 : 2.0	0.0 : 4.0

Type 2 inflammatory asthma phenotype population is defined as the randomized patients with baseline blood eosinophils >= 0.15 Giga/L or baseline FeNO >= 20 ppb.
PGM=PRODOPS/SAR231893/EFC14153/CSR/REPORT/PGM/eff_sum_vis_i_t.sas OUT=REPORT/OUTPUT/eff_sum_awakens_t2e3_t_x.rtf (27NOV2020 - 6:43)

16.2.6 Efficacy response data

16.2.6.17 Number of nocturnal awakenings

16.2.6.17.1 Summary of number of nocturnal awakenings over time - Type 2 inflammatory asthma phenotype population and baseline blood eosinophils >=0.3 Giga/L population

	Type 2 inflammatory asthma phenotype population	
Number of nocturnal awakenings	**Placebo (N=114)**	**Dupilumab (N=236)**
Change from baseline		
Number	111	225
Mean (SD)	-0.23 (0.43)	-0.29 (0.61)
Median	0.00	0.00
Q1 : Q3	-0.33 : 0.00	-0.43 : 0.00
Min : Max	-2.5 : 0.5	-4.4 : 0.8
Percent change from baseline		
Number	59	121
Mean (SD)	-74.84 (55.61)	-77.13 (53.81)
Median	-100.00	-100.00
Q1 : Q3	-100.00 : -75.00	-100.00 : -88.46
Min : Max	-100.0 : 194.7	-100.0 : 250.0

Type 2 inflammatory asthma phenotype population is defined as the randomized patients with baseline blood eosinophils >= 0.15 Giga/L or baseline FeNO >= 20 ppb.
PGM=PRODOPS/SAR231893/EFC14153/CSR/REPORT/PGM/eff_sum_vis_i_t.sas OUT=REPORT/OUTPUT/eff_sum_awakens_t2e3_t_x.rtf (27NOV2020 - 6:43)

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

Project Code / Study Number / Analysis: SAR231893 / EFC14153 / CSR

16.2.6 Efficacy response data

16.2.6.17 Number of nocturnal awakenings

16.2.6.17.1 Summary of number of nocturnal awakenings over time - Type 2 inflammatory asthma phenotype population and baseline blood eosinophils >=0.3 Giga/L population

	Type 2 inflammatory asthma phenotype population	
Number of nocturnal awakenings	**Placebo (N=114)**	**Dupilumab (N=236)**
Week 36		
Value		
Number	110	225
Mean (SD)	0.11 (0.32)	0.10 (0.39)
Median	0.00	0.00
Q1 : Q3	0.00 : 0.06	0.00 : 0.00
Min : Max	0.0 : 2.7	0.0 : 3.7
Change from baseline		
Number	110	225
Mean (SD)	-0.22 (0.44)	-0.29 (0.64)
Median	0.00	0.00
Q1 : Q3	-0.33 : 0.00	-0.43 : 0.00
Min : Max	-2.5 : 1.1	-4.4 : 2.8

Type 2 inflammatory asthma phenotype population is defined as the randomized patients with baseline blood eosinophils >= 0.15 Giga/L or baseline FeNO >= 20 ppb.

PGM=PRODOPS/SAR231893/EFC14153/CSR/REPORT/PGM/eff_sum_vis_i_t.sas OUT=REPORT/OUTPUT/eff_sum_awakens_t2e3_t_x.rtf (27NOV2020 - 6:43)

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

Project Code / Study Number / Analysis: SAR231893 / EFC14153 / CSR

16.2.6 Efficacy response data

16.2.6.17 Number of nocturnal awakenings

16.2.6.17.1 Summary of number of nocturnal awakenings over time - Type 2 inflammatory asthma phenotype population and baseline blood eosinophils >=0.3 Giga/L population

	Type 2 inflammatory asthma phenotype population	
Number of nocturnal awakenings	**Placebo (N=114)**	**Dupilumab (N=236)**
Percent change from baseline		
Number	59	122
Mean (SD)	-69.39 (53.65)	-66.45 (143.70)
Median	-100.00	-100.00
Q1 : Q3	-100.00 : -58.00	-100.00 : -94.02
Min : Max	-100.0 : 133.3	-100.0 : 1400.0
Week 40		
Value		
Number	111	224
Mean (SD)	0.10 (0.29)	0.09 (0.35)
Median	0.00	0.00
Q1 : Q3	0.00 : 0.04	0.00 : 0.00
Min : Max	0.0 : 2.2	0.0 : 3.5

Type 2 inflammatory asthma phenotype population is defined as the randomized patients with baseline blood eosinophils >= 0.15 Giga/L or baseline FeNO >= 20 ppb.

PGM=PRODOPS/SAR231893/EFC14153/CSR/REPORT/PGM/eff_sum_vis_i_t.sas OUT=REPORT/OUTPUT/eff_sum_awakens_t2e3_t_x.rtf (27NOV2020 - 6:43)

16.2.6 Efficacy response data

16.2.6.17 Number of nocturnal awakenings

16.2.6.17.1 Summary of number of nocturnal awakenings over time - Type 2 inflammatory asthma phenotype population and baseline blood eosinophils >=0.3 Giga/L population

	Type 2 inflammatory asthma phenotype population	
Number of nocturnal awakenings	**Placebo (N=114)**	**Dupilumab (N=236)**
Change from baseline		
Number	111	224
Mean (SD)	-0.22 (0.44)	-0.31 (0.67)
Median	0.00	0.00
Q1 : Q3	-0.33 : 0.00	-0.43 : 0.00
Min : Max	-2.5 : 0.8	-4.4 : 3.3
Percent change from baseline		
Number	59	122
Mean (SD)	-66.15 (91.00)	-68.35 (161.50)
Median	-100.00	-100.00
Q1 : Q3	-100.00 : -69.75	-100.00 : -89.44
Min : Max	-100.0 : 533.3	-100.0 : 1650.0

Type 2 inflammatory asthma phenotype population is defined as the randomized patients with baseline blood eosinophils >= 0.15 Giga/L or baseline FeNO >= 20 ppb.
PGM=PRODOPS/SAR231893/EFC14153/CSR/REPORT/PGM/eff_sum_vis_i_t.sas OUT=REPORT/OUTPUT/eff_sum_awakens_t2e3_t_x.rtf (27NOV2020 - 6:43)

16.2.6 Efficacy response data

16.2.6.17 Number of nocturnal awakenings

16.2.6.17.1 Summary of number of nocturnal awakenings over time - Type 2 inflammatory asthma phenotype population and baseline blood eosinophils >=0.3 Giga/L population

	Type 2 inflammatory asthma phenotype population	
Number of nocturnal awakenings	**Placebo (N=114)**	**Dupilumab (N=236)**
Week 44		
Value		
Number	111	224
Mean (SD)	0.11 (0.31)	0.08 (0.34)
Median	0.00	0.00
Q1 : Q3	0.00 : 0.04	0.00 : 0.00
Min : Max	0.0 : 2.3	0.0 : 3.3
Change from baseline		
Number	111	224
Mean (SD)	-0.21 (0.43)	-0.31 (0.68)
Median	0.00	-0.03
Q1 : Q3	-0.33 : 0.00	-0.43 : 0.00
Min : Max	-2.5 : 0.7	-4.4 : 3.1

Type 2 inflammatory asthma phenotype population is defined as the randomized patients with baseline blood eosinophils >= 0.15 Giga/L or baseline FeNO >= 20 ppb.
PGM=PRODOPS/SAR231893/EFC14153/CSR/REPORT/PGM/eff_sum_vis_i_t.sas OUT=REPORT/OUTPUT/eff_sum_awakens_t2e3_t_x.rtf (27NOV2020 - 6:43)

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

Project Code / Study Number / Analysis: SAR231893 / EFC14153 / CSR

16.2.6 Efficacy response data

16.2.6.17 Number of nocturnal awakenings

16.2.6.17.1 Summary of number of nocturnal awakenings over time - Type 2 inflammatory asthma phenotype population and baseline blood eosinophils >=0.3 Giga/L population

	Type 2 inflammatory asthma phenotype population	
Number of nocturnal awakenings	**Placebo (N=114)**	**Dupilumab (N=236)**
Percent change from baseline		
Number	59	122
Mean (SD)	-71.35 (60.28)	-69.70 (153.88)
Median	-100.00	-100.00
Q1 : Q3	-100.00 : -68.42	-100.00 : -85.42
Min : Max	-100.0 : 226.7	-100.0 : 1566.7
Week 48		
Value		
Number	111	221
Mean (SD)	0.10 (0.27)	0.06 (0.23)
Median	0.00	0.00
Q1 : Q3	0.00 : 0.07	0.00 : 0.00
Min : Max	0.0 : 2.2	0.0 : 1.9

Type 2 inflammatory asthma phenotype population is defined as the randomized patients with baseline blood eosinophils >= 0.15 Giga/L or baseline FeNO >= 20 ppb.

PGM=PRODOPS/SAR231893/EFC14153/CSR/REPORT/PGM/eff_sum_vis_i_t.sas OUT=REPORT/OUTPUT/eff_sum_awakens_t2e3_t_x.rtf (27NOV2020 - 6:43)

16.2.6 Efficacy response data

16.2.6.17 Number of nocturnal awakenings

16.2.6.17.1 Summary of number of nocturnal awakenings over time - Type 2 inflammatory asthma phenotype population and baseline blood eosinophils >=0.3 Giga/L population

	Type 2 inflammatory asthma phenotype population	
Number of nocturnal awakenings	**Placebo (N=114)**	**Dupilumab (N=236)**
Change from baseline		
Number	111	221
Mean (SD)	-0.22 (0.42)	-0.34 (0.65)
Median	0.00	-0.03
Q1 : Q3	-0.33 : 0.00	-0.43 : 0.00
Min : Max	-2.5 : 0.6	-4.4 : 0.5
Percent change from baseline		
Number	59	119
Mean (SD)	-67.92 (63.42)	-83.52 (49.13)
Median	-100.00	-100.00
Q1 : Q3	-100.00 : -58.82	-100.00 : -97.92
Min : Max	-100.0 : 246.2	-100.0 : 326.1

Type 2 inflammatory asthma phenotype population is defined as the randomized patients with baseline blood eosinophils >= 0.15 Giga/L or baseline FeNO >= 20 ppb.
PGM=PRODOPS/SAR231893/EFC14153/CSR/REPORT/PGM/eff_sum_vis_i_t.sas OUT=REPORT/OUTPUT/eff_sum_awakens_t2e3_t_x.rtf (27NOV2020 - 6:43)

16.2.6 Efficacy response data

16.2.6.17 Number of nocturnal awakenings

16.2.6.17.1 Summary of number of nocturnal awakenings over time - Type 2 inflammatory asthma phenotype population and baseline blood eosinophils >=0.3 Giga/L population

	Type 2 inflammatory asthma phenotype population	
Number of nocturnal awakenings	**Placebo (N=114)**	**Dupilumab (N=236)**
Week 52		
Value		
Number	111	222
Mean (SD)	0.11 (0.31)	0.07 (0.26)
Median	0.00	0.00
Q1 : Q3	0.00 : 0.04	0.00 : 0.00
Min : Max	0.0 : 2.1	0.0 : 2.0
Change from baseline		
Number	111	222
Mean (SD)	-0.22 (0.45)	-0.33 (0.66)
Median	0.00	-0.07
Q1 : Q3	-0.33 : 0.00	-0.43 : 0.00
Min : Max	-2.5 : 1.2	-4.4 : 1.8

Type 2 inflammatory asthma phenotype population is defined as the randomized patients with baseline blood eosinophils >= 0.15 Giga/L or baseline FeNO >= 20 ppb.
PGM=PRODOPS/SAR231893/EFC14153/CSR/REPORT/PGM/eff_sum_vis_i_t.sas OUT=REPORT/OUTPUT/eff_sum_awakens_t2e3_t_x.rtf (27NOV2020 - 6:43)

16.2.6 Efficacy response data

16.2.6.17 Number of nocturnal awakenings

16.2.6.17.1 Summary of number of nocturnal awakenings over time - Type 2 inflammatory asthma phenotype population and baseline blood eosinophils >=0.3 Giga/L population

	Type 2 inflammatory asthma phenotype population	
Number of nocturnal awakenings	**Placebo (N=114)**	**Dupilumab (N=236)**
Percent change from baseline		
Number	59	120
Mean (SD)	-69.93 (61.52)	-79.10 (95.42)
Median	-100.00	-100.00
Q1 : Q3	-100.00 : -60.00	-100.00 : -100.00
Min : Max	-100.0 : 223.1	-100.0 : 900.0
Week 56		
Value		
Number	35	84
Mean (SD)	0.14 (0.40)	0.03 (0.14)
Median	0.00	0.00
Q1 : Q3	0.00 : 0.00	0.00 : 0.00
Min : Max	0.0 : 1.8	0.0 : 1.0

Type 2 inflammatory asthma phenotype population is defined as the randomized patients with baseline blood eosinophils >= 0.15 Giga/L or baseline FeNO >= 20 ppb.
PGM=PRODOPS/SAR231893/EFC14153/CSR/REPORT/PGM/eff_sum_vis_i_t.sas OUT=REPORT/OUTPUT/eff_sum_awakens_t2e3_t_x.rtf (27NOV2020 - 6:43)

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

Project Code / Study Number / Analysis: SAR231893 / EFC14153 / CSR

16.2.6 Efficacy response data

16.2.6.17 Number of nocturnal awakenings

16.2.6.17.1 Summary of number of nocturnal awakenings over time - Type 2 inflammatory asthma phenotype population and baseline blood eosinophils >=0.3 Giga/L population

	Type 2 inflammatory asthma phenotype population	
Number of nocturnal awakenings	**Placebo (N=114)**	**Dupilumab (N=236)**
Change from baseline		
Number	35	84
Mean (SD)	-0.21 (0.45)	-0.23 (0.32)
Median	0.00	-0.14
Q1 : Q3	-0.38 : 0.00	-0.33 : 0.00
Min : Max	-1.3 : 1.1	-1.3 : 0.2
Percent change from baseline		
Number	20	45
Mean (SD)	-36.37 (188.08)	-90.06 (37.75)
Median	-100.00	-100.00
Q1 : Q3	-100.00 : -65.00	-100.00 : -100.00
Min : Max	-100.0 : 740.0	-100.0 : 133.3

Type 2 inflammatory asthma phenotype population is defined as the randomized patients with baseline blood eosinophils >= 0.15 Giga/L or baseline FeNO >= 20 ppb.

PGM=PRODOPS/SAR231893/EFC14153/CSR/REPORT/PGM/eff_sum_vis_i_t.sas OUT=REPORT/OUTPUT/eff_sum_awakens_t2e3_t_x.rtf (27NOV2020 - 6:43)

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

Project Code / Study Number / Analysis: SAR231893 / EFC14153 / CSR

16.2.6 Efficacy response data

16.2.6.17 Number of nocturnal awakenings

16.2.6.17.1 Summary of number of nocturnal awakenings over time - Type 2 inflammatory asthma phenotype population and baseline blood eosinophils >=0.3 Giga/L population

	Type 2 inflammatory asthma phenotype population	
Number of nocturnal awakenings	**Placebo (N=114)**	**Dupilumab (N=236)**
Week 60		
Value		
Number	3	14
Mean (SD)	0.00 (0.00)	0.00 (0.01)
Median	0.00	0.00
Q1 : Q3	0.00 : 0.00	0.00 : 0.00
Min : Max	0.0 : 0.0	0.0 : 0.0
Change from baseline		
Number	3	14
Mean (SD)	-0.44 (0.77)	-0.26 (0.30)
Median	0.00	-0.23
Q1 : Q3	-1.33 : 0.00	-0.33 : 0.00
Min : Max	-1.3 : 0.0	-1.0 : 0.0

Type 2 inflammatory asthma phenotype population is defined as the randomized patients with baseline blood eosinophils >= 0.15 Giga/L or baseline FeNO >= 20 ppb.

PGM=PRODOPS/SAR231893/EFC14153/CSR/REPORT/PGM/eff_sum_vis_i_t.sas OUT=REPORT/OUTPUT/eff_sum_awakens_t2e3_t_x.rtf (27NOV2020 - 6:43)

16.2.6 Efficacy response data

16.2.6.17 Number of nocturnal awakenings

16.2.6.17.1 Summary of number of nocturnal awakenings over time - Type 2 inflammatory asthma phenotype population and baseline blood eosinophils >=0.3 Giga/L population

	Type 2 inflammatory asthma phenotype population	
Number of nocturnal awakenings	**Placebo (N=114)**	**Dupilumab (N=236)**
Percent change from baseline		
Number	1	8
Mean (SD)	-100.00 (NC)	-99.40 (1.68)
Median	-100.00	-100.00
Q1 : Q3	-100.00 : -100.00	-100.00 : -100.00
Min : Max	-100.0 : -100.0	-100.0 : -95.2
Week 64		
Value		
Number	2	14
Mean (SD)	0.38 (0.18)	0.05 (0.18)
Median	0.38	0.00
Q1 : Q3	0.25 : 0.50	0.00 : 0.00
Min : Max	0.3 : 0.5	0.0 : 0.7

Type 2 inflammatory asthma phenotype population is defined as the randomized patients with baseline blood eosinophils >= 0.15 Giga/L or baseline FeNO >= 20 ppb.
PGM=PRODOPS/SAR231893/EFC14153/CSR/REPORT/PGM/eff_sum_vis_i_t.sas OUT=REPORT/OUTPUT/eff_sum_awakens_t2e3_t_x.rtf (27NOV2020 - 6:43)

Project Code / Study Number / Analysis: SAR231893 / EFC14153 / CSR

16.2.6 Efficacy response data

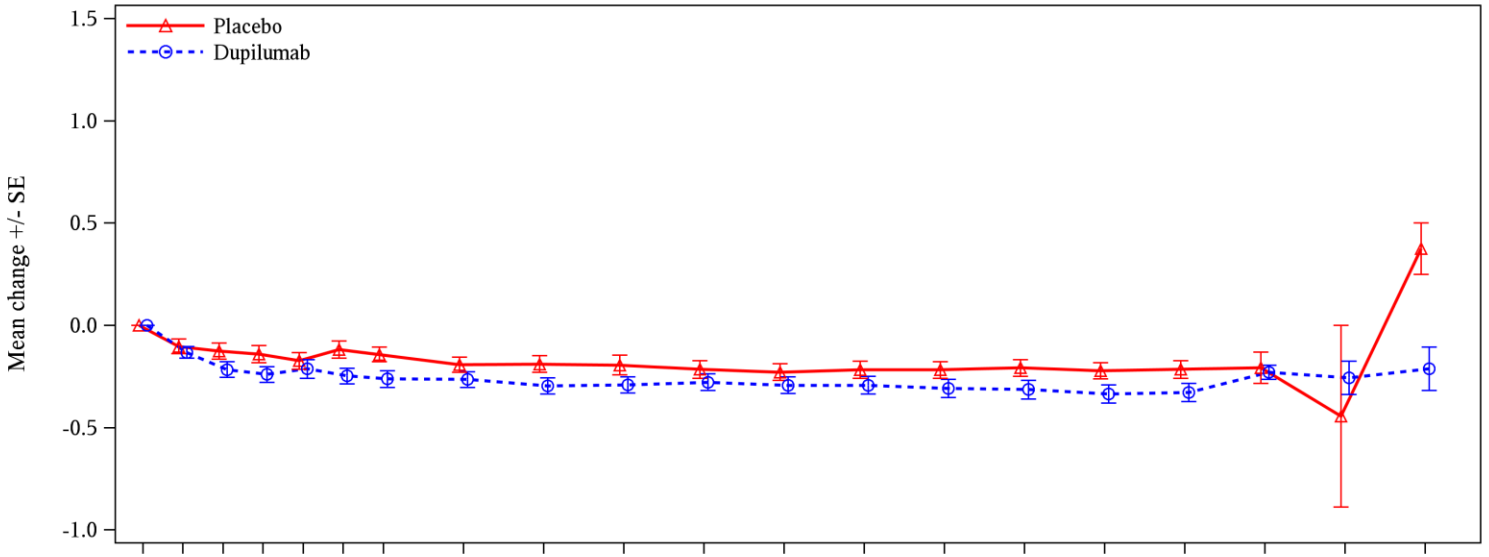
16.2.6.17 Number of nocturnal awakenings

16.2.6.17.1 Summary of number of nocturnal awakenings over time - Type 2 inflammatory asthma phenotype population and baseline blood eosinophils >=0.3 Giga/L population

	Type 2 inflammatory asthma phenotype population	
Number of nocturnal awakenings	**Placebo (N=114)**	**Dupilumab (N=236)**
Change from baseline		
Number	2	14
Mean (SD)	0.38 (0.18)	-0.21 (0.40)
Median	0.38	-0.23
Q1 : Q3	0.25 : 0.50	-0.33 : 0.00
Min : Max	0.3 : 0.5	-1.0 : 0.7
Percent change from baseline		
Number	0	8
Mean (SD)		-100.00 (0.00)
Median		-100.00
Q1 : Q3		-100.00 : -100.00
Min : Max		-100.0 : -100.0

Type 2 inflammatory asthma phenotype population is defined as the randomized patients with baseline blood eosinophils >= 0.15 Giga/L or baseline FeNO >= 20 ppb.
PGM=PRODOPS/SAR231893/EFC14153/CSR/REPORT/PGM/eff_sum_vis_i_t.sas OUT=REPORT/OUTPUT/eff_sum_awakens_t2e3_t_x.rtf (27NOV2020 - 6:43)

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen
Project Code / Study Number / Analysis: SAR231893 / EFC14153 / CSR
16.2.6 Efficacy response data
16.2.6.17 Number of nocturnal awakenings
16.2.6.17.2 Plot of mean change from baseline in number of nocturnal awakenings over time - Type 2 inflammatory asthma phenotype population



#subjects

	BL	2	4	6	8	10	12	16	20	24	28	32	36	40	44	48	52	56	60	64
Placebo	114	114	114	114	114	114	113	113	113	113	111	111	110	111	111	111	111	35	3	2
Dupilumab	236	234	232	232	232	230	229	230	229	229	227	225	225	224	224	221	222	84	14	14

BL=Baseline
Type 2 inflammatory asthma phenotype population is defined as the randomized patients with baseline blood eosinophils >= 0.15 Giga/L or baseline FeNO >= 20 ppb.
PGM=PRODOPS/SAR231893/EFC14153/CSR/REPORT/PGM/eff_sum_vis_i_g.sas OUT=REPORT/OUTPUT/eff_sum_awakens_t2_g_x.rtf (27NOV2020 - 6:37)

Project Code / Study Number / Analysis: SAR231893 / EFC14153 / CSR

16.2.6 Efficacy response data

16.2.6.17 Number of nocturnal awakenings

16.2.6.17.4 Change from baseline in number of nocturnal awakenings over time (MMRM including measurements up to Week 52) - Type 2 inflammatory asthma phenotype population and baseline blood eosinophils >=0.3 Giga/L population

	Type 2 inflammatory asthma phenotype population	
Number of nocturnal awakenings	**Placebo (N=114)**	**Dupilumab (N=236)**
Baseline		
Value		
Number	114	236
Mean (SD)	0.32 (0.45)	0.39 (0.68)
Median	0.14	0.14
Q1 : Q3	0.00 : 0.50	0.00 : 0.43
Min : Max	0.0 : 2.5	0.0 : 4.4
Week 2		
Change from baseline		
Number of patients in the model	110	228
LS Mean (SE) [a]	-0.13 (0.03)	-0.13 (0.02)
LS Mean Diff vs. placebo (95% CI) [a]		-0.00 (-0.08, 0.07)
P-value vs. placebo [a]		0.9465

[a] Derived from MMRM model with change from baseline in number of nocturnal awakenings values up to Week 52 as the response variable, and treatment, age, baseline weight group, region, baseline eosinophil level, baseline FeNO level, baseline ICS dose level, visit, treatment by-visit interaction, baseline number of nocturnal awakenings value and baseline-by-visit interaction as covariates.

Type 2 inflammatory asthma phenotype population is defined as the randomized patients with baseline blood eosinophils >= 0.15 Giga/L or baseline FeNO >= 20 ppb.

PGM=PRODOPS/SAR231893/EFC14153/CSR/REPORT/PGM/eff_mmrm_i_t_aded.sas OUT=REPORT/OUTPUT/eff_awakens_chg_a52_t2e3_t_x.rtf (27NOV2020 - 3:05)

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

Project Code / Study Number / Analysis: SAR231893 / EFC14153 / CSR

16.2.6 Efficacy response data

16.2.6.17 Number of nocturnal awakenings

16.2.6.17.4 Change from baseline in number of nocturnal awakenings over time (MMRM including measurements up to Week 52) - Type 2 inflammatory asthma phenotype population and baseline blood eosinophils >=0.3 Giga/L population

	Type 2 inflammatory asthma phenotype population	
Number of nocturnal awakenings	**Placebo (N=114)**	**Dupilumab (N=236)**
Week 4		
Change from baseline		
Number of patients in the model	110	228
LS Mean (SE) [a]	-0.16 (0.03)	-0.21 (0.03)
LS Mean Diff vs. placebo (95% CI) [a]		-0.05 (-0.13, 0.03)
P-value vs. placebo [a]		0.2023
Week 6		
Change from baseline		
Number of patients in the model	110	228
LS Mean (SE) [a]	-0.18 (0.03)	-0.23 (0.02)
LS Mean Diff vs. placebo (95% CI) [a]		-0.06 (-0.14, 0.02)
P-value vs. placebo [a]		0.1451

[a] Derived from MMRM model with change from baseline in number of nocturnal awakenings values up to Week 52 as the response variable, and treatment, age, baseline weight group, region, baseline eosinophil level, baseline FeNO level, baseline ICS dose level, visit, treatment by-visit interaction, baseline number of nocturnal awakenings value and baseline-by-visit interaction as covariates.

Type 2 inflammatory asthma phenotype population is defined as the randomized patients with baseline blood eosinophils >= 0.15 Giga/L or baseline FeNO >= 20 ppb.

PGM=PRODOPS/SAR231893/EFC14153/CSR/REPORT/PGM/eff_mmrm_i_t_aded.sas OUT=REPORT/OUTPUT/eff_awakens_chg_a52_t2e3_t_x.rtf (27NOV2020 - 3:05)

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

Project Code / Study Number / Analysis: SAR231893 / EFC14153 / CSR

16.2.6 Efficacy response data

16.2.6.17 Number of nocturnal awakenings

16.2.6.17.4 Change from baseline in number of nocturnal awakenings over time (MMRM including measurements up to Week 52) - Type 2 inflammatory asthma phenotype population and baseline blood eosinophils >=0.3 Giga/L population

	Type 2 inflammatory asthma phenotype population	
Number of nocturnal awakenings	**Placebo (N=114)**	**Dupilumab (N=236)**
Week 8		
Change from baseline		
Number of patients in the model	110	228
LS Mean (SE) [a]	-0.21 (0.04)	-0.21 (0.03)
LS Mean Diff vs. placebo (95% CI) [a]		0.00 (-0.10, 0.10)
P-value vs. placebo [a]		0.9584
Week 10		
Change from baseline		
Number of patients in the model	110	228
LS Mean (SE) [a]	-0.15 (0.04)	-0.24 (0.03)
LS Mean Diff vs. placebo (95% CI) [a]		-0.09 (-0.18, -0.01)
P-value vs. placebo [a]		0.0329

[a] Derived from MMRM model with change from baseline in number of nocturnal awakenings values up to Week 52 as the response variable, and treatment, age, baseline weight group, region, baseline eosinophil level, baseline FeNO level, baseline ICS dose level, visit, treatment by-visit interaction, baseline number of nocturnal awakenings value and baseline-by-visit interaction as covariates.

Type 2 inflammatory asthma phenotype population is defined as the randomized patients with baseline blood eosinophils >= 0.15 Giga/L or baseline FeNO >= 20 ppb.

PGM=PRODOPS/SAR231893/EFC14153/CSR/REPORT/PGM/eff_mmrm_i_t_aded.sas OUT=REPORT/OUTPUT/eff_awakens_chg_a52_t2e3_t_x.rtf (27NOV2020 - 3:05)

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

Project Code / Study Number / Analysis: SAR231893 / EFC14153 / CSR

16.2.6 Efficacy response data

16.2.6.17 Number of nocturnal awakenings

16.2.6.17.4 Change from baseline in number of nocturnal awakenings over time (MMRM including measurements up to Week 52) - Type 2 inflammatory asthma phenotype population and baseline blood eosinophils >=0.3 Giga/L population

	Type 2 inflammatory asthma phenotype population	
Number of nocturnal awakenings	**Placebo (N=114)**	**Dupilumab (N=236)**
Week 12		
Change from baseline		
Number of patients in the model	110	228
LS Mean (SE) [a]	-0.17 (0.04)	-0.26 (0.03)
LS Mean Diff vs. placebo (95% CI) [a]		-0.08 (-0.17, -0.00)
P-value vs. placebo [a]		0.0473
Week 16		
Change from baseline		
Number of patients in the model	110	228
LS Mean (SE) [a]	-0.23 (0.03)	-0.27 (0.02)
LS Mean Diff vs. placebo (95% CI) [a]		-0.04 (-0.11, 0.03)
P-value vs. placebo [a]		0.2746

[a] Derived from MMRM model with change from baseline in number of nocturnal awakenings values up to Week 52 as the response variable, and treatment, age, baseline weight group, region, baseline eosinophil level, baseline FeNO level, baseline ICS dose level, visit, treatment by-visit interaction, baseline number of nocturnal awakenings value and baseline-by-visit interaction as covariates.

Type 2 inflammatory asthma phenotype population is defined as the randomized patients with baseline blood eosinophils >= 0.15 Giga/L or baseline FeNO >= 20 ppb.

PGM=PRODOPS/SAR231893/EFC14153/CSR/REPORT/PGM/eff_mmrm_i_t_aded.sas OUT=REPORT/OUTPUT/eff_awakens_chg_a52_t2e3_t_x.rtf (27NOV2020 - 3:05)

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

Project Code / Study Number / Analysis: SAR231893 / EFC14153 / CSR

16.2.6 Efficacy response data

16.2.6.17 Number of nocturnal awakenings

16.2.6.17.4 Change from baseline in number of nocturnal awakenings over time (MMRM including measurements up to Week 52) - Type 2 inflammatory asthma phenotype population and baseline blood eosinophils >=0.3 Giga/L population

	Type 2 inflammatory asthma phenotype population	
Number of nocturnal awakenings	**Placebo (N=114)**	**Dupilumab (N=236)**
Week 20		
Change from baseline		
Number of patients in the model	110	228
LS Mean (SE) [a]	-0.23 (0.03)	-0.29 (0.02)
LS Mean Diff vs. placebo (95% CI) [a]		-0.06 (-0.12, 0.00)
P-value vs. placebo [a]		0.0629
Week 24		
Change from baseline		
Number of patients in the model	110	228
LS Mean (SE) [a]	-0.23 (0.03)	-0.29 (0.02)
LS Mean Diff vs. placebo (95% CI) [a]		-0.06 (-0.14, 0.02)
P-value vs. placebo [a]		0.1635

[a] Derived from MMRM model with change from baseline in number of nocturnal awakenings values up to Week 52 as the response variable, and treatment, age, baseline weight group, region, baseline eosinophil level, baseline FeNO level, baseline ICS dose level, visit, treatment by-visit interaction, baseline number of nocturnal awakenings value and baseline-by-visit interaction as covariates.

Type 2 inflammatory asthma phenotype population is defined as the randomized patients with baseline blood eosinophils >= 0.15 Giga/L or baseline FeNO >= 20 ppb.

PGM=PRODOPS/SAR231893/EFC14153/CSR/REPORT/PGM/eff_mmrm_i_t_aded.sas OUT=REPORT/OUTPUT/eff_awakens_chg_a52_t2e3_t_x.rtf (27NOV2020 - 3:05)

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

Project Code / Study Number / Analysis: SAR231893 / EFC14153 / CSR

16.2.6 Efficacy response data

16.2.6.17 Number of nocturnal awakenings

16.2.6.17.4 Change from baseline in number of nocturnal awakenings over time (MMRM including measurements up to Week 52) - Type 2 inflammatory asthma phenotype population and baseline blood eosinophils >=0.3 Giga/L population

	Type 2 inflammatory asthma phenotype population	
Number of nocturnal awakenings	**Placebo (N=114)**	**Dupilumab (N=236)**
Week 28		
Change from baseline		
Number of patients in the model	110	228
LS Mean (SE) [a]	-0.25 (0.03)	-0.27 (0.02)
LS Mean Diff vs. placebo (95% CI) [a]		-0.03 (-0.10, 0.05)
P-value vs. placebo [a]		0.5131
Week 32		
Change from baseline		
Number of patients in the model	110	228
LS Mean (SE) [a]	-0.27 (0.03)	-0.29 (0.02)
LS Mean Diff vs. placebo (95% CI) [a]		-0.02 (-0.10, 0.05)
P-value vs. placebo [a]		0.5262

[a] Derived from MMRM model with change from baseline in number of nocturnal awakenings values up to Week 52 as the response variable, and treatment, age, baseline weight group, region, baseline eosinophil level, baseline FeNO level, baseline ICS dose level, visit, treatment by-visit interaction, baseline number of nocturnal awakenings value and baseline-by-visit interaction as covariates.

Type 2 inflammatory asthma phenotype population is defined as the randomized patients with baseline blood eosinophils >= 0.15 Giga/L or baseline FeNO >= 20 ppb.

PGM=PRODOPS/SAR231893/EFC14153/CSR/REPORT/PGM/eff_mmrm_i_t_aded.sas OUT=REPORT/OUTPUT/eff_awakens_chg_a52_t2e3_t_x.rtf (27NOV2020 - 3:05)

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

Project Code / Study Number / Analysis: SAR231893 / EFC14153 / CSR

16.2.6 Efficacy response data

16.2.6.17 Number of nocturnal awakenings

16.2.6.17.4 Change from baseline in number of nocturnal awakenings over time (MMRM including measurements up to Week 52) - Type 2 inflammatory asthma phenotype population and baseline blood eosinophils >=0.3 Giga/L population

	Type 2 inflammatory asthma phenotype population	
Number of nocturnal awakenings	**Placebo (N=114)**	**Dupilumab (N=236)**
Week 36		
Change from baseline		
Number of patients in the model	110	228
LS Mean (SE) [a]	-0.25 (0.03)	-0.29 (0.02)
LS Mean Diff vs. placebo (95% CI) [a]		-0.04 (-0.12, 0.04)
P-value vs. placebo [a]		0.3223
Week 40		
Change from baseline		
Number of patients in the model	110	228
LS Mean (SE) [a]	-0.26 (0.03)	-0.30 (0.02)
LS Mean Diff vs. placebo (95% CI) [a]		-0.04 (-0.12, 0.03)
P-value vs. placebo [a]		0.2383

[a] Derived from MMRM model with change from baseline in number of nocturnal awakenings values up to Week 52 as the response variable, and treatment, age, baseline weight group, region, baseline eosinophil level, baseline FeNO level, baseline ICS dose level, visit, treatment by-visit interaction, baseline number of nocturnal awakenings value and baseline-by-visit interaction as covariates.

Type 2 inflammatory asthma phenotype population is defined as the randomized patients with baseline blood eosinophils >= 0.15 Giga/L or baseline FeNO >= 20 ppb.

PGM=PRODOPS/SAR231893/EFC14153/CSR/REPORT/PGM/eff_mmrm_i_t_aded.sas OUT=REPORT/OUTPUT/eff_awakens_chg_a52_t2e3_t_x.rtf (27NOV2020 - 3:05)

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

Project Code / Study Number / Analysis: SAR231893 / EFC14153 / CSR

16.2.6 Efficacy response data

16.2.6.17 Number of nocturnal awakenings

16.2.6.17.4 Change from baseline in number of nocturnal awakenings over time (MMRM including measurements up to Week 52) - Type 2 inflammatory asthma phenotype population and baseline blood eosinophils >=0.3 Giga/L population

	Type 2 inflammatory asthma phenotype population	
Number of nocturnal awakenings	**Placebo (N=114)**	**Dupilumab (N=236)**
Week 44		
Change from baseline		
Number of patients in the model	110	228
LS Mean (SE) [a]	-0.25 (0.03)	-0.31 (0.02)
LS Mean Diff vs. placebo (95% CI) [a]		-0.06 (-0.13, 0.02)
P-value vs. placebo [a]		0.1280
Week 48		
Change from baseline		
Number of patients in the model	110	228
LS Mean (SE) [a]	-0.26 (0.03)	-0.31 (0.02)
LS Mean Diff vs. placebo (95% CI) [a]		-0.05 (-0.11, 0.01)
P-value vs. placebo [a]		0.1183

[a] Derived from MMRM model with change from baseline in number of nocturnal awakenings values up to Week 52 as the response variable, and treatment, age, baseline weight group, region, baseline eosinophil level, baseline FeNO level, baseline ICS dose level, visit, treatment by-visit interaction, baseline number of nocturnal awakenings value and baseline-by-visit interaction as covariates.

Type 2 inflammatory asthma phenotype population is defined as the randomized patients with baseline blood eosinophils >= 0.15 Giga/L or baseline FeNO >= 20 ppb.

PGM=PRODOPS/SAR231893/EFC14153/CSR/REPORT/PGM/eff_mmrm_i_t_aded.sas OUT=REPORT/OUTPUT/eff_awakens_chg_a52_t2e3_t_x.rtf (27NOV2020 - 3:05)

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

Project Code / Study Number / Analysis: SAR231893 / EFC14153 / CSR

16.2.6 Efficacy response data

16.2.6.17 Number of nocturnal awakenings

16.2.6.17.4 Change from baseline in number of nocturnal awakenings over time (MMRM including measurements up to Week 52) - Type 2 inflammatory asthma phenotype population and baseline blood eosinophils >=0.3 Giga/L population

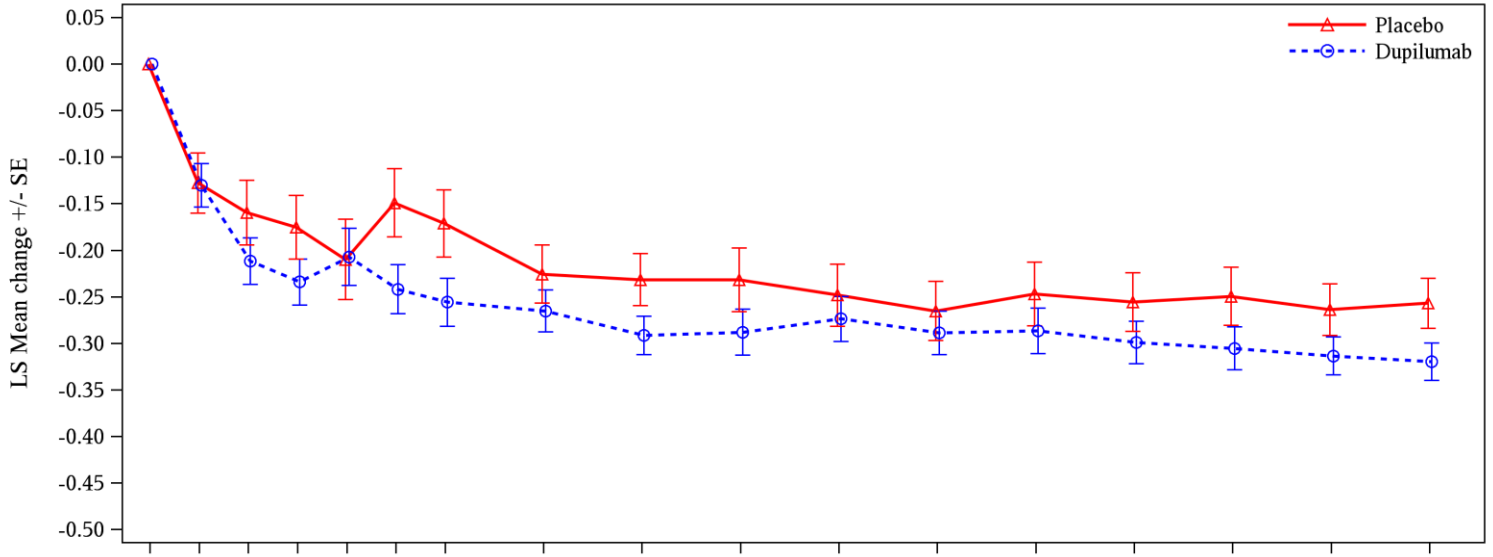
	Type 2 inflammatory asthma phenotype population	
Number of nocturnal awakenings	**Placebo (N=114)**	**Dupilumab (N=236)**
Week 52		
Change from baseline		
Number of patients in the model	110	228
LS Mean (SE) [a]	-0.26 (0.03)	-0.32 (0.02)
LS Mean Diff vs. placebo (95% CI) [a]		-0.06 (-0.12, -0.00)
P-value vs. placebo [a]		0.0445

[a] Derived from MMRM model with change from baseline in number of nocturnal awakenings values up to Week 52 as the response variable, and treatment, age, baseline weight group, region, baseline eosinophil level, baseline FeNO level, baseline ICS dose level, visit, treatment by-visit interaction, baseline number of nocturnal awakenings value and baseline-by-visit interaction as covariates.

Type 2 inflammatory asthma phenotype population is defined as the randomized patients with baseline blood eosinophils >= 0.15 Giga/L or baseline FeNO >= 20 ppb.

PGM=PRODOPS/SAR231893/EFC14153/CSR/REPORT/PGM/eff_mmrm_i_t_aded.sas OUT=REPORT/OUTPUT/eff_awakens_chg_a52_t2e3_t_x.rtf (27NOV2020 - 3:05)

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen
Project Code / Study Number / Analysis: SAR231893 / EFC14153 / CSR
16.2.6 Efficacy response data
16.2.6.17 Number of nocturnal awakenings
16.2.6.17.5 Plot of LS mean change from baseline in number of nocturnal awakenings over time (MMRM including measurements up to Week 52) - Type 2 inflammatory asthma phenotype population



#subjects

	BL	2	4	6	8	10	12	16	20	24	28	32	36	40	44	48	52
Placebo	114	114	114	114	114	114	113	113	113	113	111	111	110	111	111	111	111
Dupilumab	236	234	232	232	232	230	229	230	229	229	227	225	225	224	224	221	222

BL=Baseline
Type 2 inflammatory asthma phenotype population is defined as the randomized patients with baseline blood eosinophils >= 0.15 Giga/L or baseline FeNO >= 20 ppb.
PGM=PRODOPS/SAR231893/EFC14153/CSR/REPORT/PGM/eff_mmrm_i_g_intext_aded.sas OUT=REPORT/OUTPUT/eff_awakens_chg_a52_t2_g_x.rtf (27NOV2020 - 3:05)

Project Code / Study Number / Analysis: SAR231893 / EFC14153 / CSR

16.2.6 Efficacy response data

16.2.6.20 PAQLQ(S)-IA global score

16.2.6.20.1 Summary of PAQLQ(S)-IA global score over time - Type 2 inflammatory asthma phenotype population and baseline blood eosinophils >=0.3 Giga/L population

	Type 2 inflammatory asthma phenotype population	
PAQLQ(S)-IA global score	**Placebo (N=107)**	**Dupilumab (N=211)**
Baseline		
Value		
Number	104	203
Mean (SD)	4.92 (1.13)	4.95 (1.08)
Median	5.11	5.13
Q1 : Q3	4.20 : 5.89	4.26 : 5.70
Min : Max	1.8 : 6.9	1.3 : 6.8
Week 12		
Value		
Number	102	199
Mean (SD)	5.97 (1.00)	6.07 (0.93)
Median	6.30	6.35
Q1 : Q3	5.57 : 6.70	5.70 : 6.78
Min : Max	3.1 : 7.0	2.4 : 7.0

Type 2 inflammatory asthma phenotype population is defined as the randomized patients with baseline blood eosinophils >= 0.15 Giga/L or baseline FeNO >= 20 ppb. Only patients of age >=7 years old at randomization are included in the analysis.

PGM=PRODOPS/SAR231893/EFC14153/CSR/REPORT/PGM/eff_sum_vis_i_t.sas OUT=REPORT/OUTPUT/eff_sum_aqlq_t2e3_t_x.rtf (27NOV2020 - 6:43)

Project Code / Study Number / Analysis: SAR231893 / EFC14153 / CSR

16.2.6 Efficacy response data

16.2.6.20 PAQLQ(S)-IA global score

16.2.6.20.1 Summary of PAQLQ(S)-IA global score over time - Type 2 inflammatory asthma phenotype population and baseline blood eosinophils >=0.3 Giga/L population

	Type 2 inflammatory asthma phenotype population	
PAQLQ(S)-IA global score	**Placebo (N=107)**	**Dupilumab (N=211)**
Change from baseline		
Number	99	191
Mean (SD)	1.06 (1.25)	1.11 (1.03)
Median	0.91	0.96
Q1 : Q3	0.35 : 1.78	0.48 : 1.70
Min : Max	-3.7 : 4.7	-3.1 : 4.3
Percent change from baseline		
Number	99	191
Mean (SD)	28.35 (39.70)	28.07 (37.87)
Median	17.32	18.94
Q1 : Q3	6.34 : 40.78	8.25 : 36.45
Min : Max	-54.2 : 257.1	-56.7 : 322.6

Type 2 inflammatory asthma phenotype population is defined as the randomized patients with baseline blood eosinophils >= 0.15 Giga/L or baseline FeNO >= 20 ppb. Only patients of age >=7 years old at randomization are included in the analysis.

PGM=PRODOPS/SAR231893/EFC14153/CSR/REPORT/PGM/eff_sum_vis_i_t.sas OUT=REPORT/OUTPUT/eff_sum_aqlq_t2e3_t_x.rtf (27NOV2020 - 6:43)

Project Code / Study Number / Analysis: SAR231893 / EFC14153 / CSR

16.2.6 Efficacy response data

16.2.6.20 PAQLQ(S)-IA global score

16.2.6.20.1 Summary of PAQLQ(S)-IA global score over time - Type 2 inflammatory asthma phenotype population and baseline blood eosinophils >=0.3 Giga/L population

	Type 2 inflammatory asthma phenotype population	
PAQLQ(S)-IA global score	**Placebo (N=107)**	**Dupilumab (N=211)**
Week 24		
Value		
Number	100	198
Mean (SD)	6.11 (0.92)	6.28 (0.90)
Median	6.48	6.61
Q1 : Q3	5.74 : 6.83	6.00 : 6.89
Min : Max	3.4 : 7.0	2.0 : 7.0
Change from baseline		
Number	97	191
Mean (SD)	1.16 (1.25)	1.35 (1.15)
Median	1.04	1.30
Q1 : Q3	0.43 : 1.96	0.70 : 2.09
Min : Max	-1.7 : 4.9	-3.4 : 5.6

Type 2 inflammatory asthma phenotype population is defined as the randomized patients with baseline blood eosinophils >= 0.15 Giga/L or baseline FeNO >= 20 ppb. Only patients of age >=7 years old at randomization are included in the analysis.

PGM=PRODOPS/SAR231893/EFC14153/CSR/REPORT/PGM/eff_sum_vis_i_t.sas OUT=REPORT/OUTPUT/eff_sum_aqlq_t2e3_t_x.rtf (27NOV2020 - 6:43)

16.2.6 Efficacy response data

16.2.6.20 PAQLQ(S)-IA global score

16.2.6.20.1 Summary of PAQLQ(S)-IA global score over time - Type 2 inflammatory asthma phenotype population and baseline blood eosinophils >=0.3 Giga/L population

	Type 2 inflammatory asthma phenotype population	
PAQLQ(S)-IA global score	**Placebo (N=107)**	**Dupilumab (N=211)**
Percent change from baseline		
Number	97	191
Mean (SD)	30.87 (42.70)	34.55 (44.40)
Median	21.24	26.40
Q1 : Q3	7.56 : 45.92	11.97 : 45.79
Min : Max	-28.4 : 266.7	-62.4 : 412.9
Week 36		
Value		
Number	102	192
Mean (SD)	6.16 (1.01)	6.44 (0.76)
Median	6.52	6.74
Q1 : Q3	5.91 : 6.83	6.15 : 6.91
Min : Max	2.4 : 7.0	1.4 : 7.0

Type 2 inflammatory asthma phenotype population is defined as the randomized patients with baseline blood eosinophils >= 0.15 Giga/L or baseline FeNO >= 20 ppb. Only patients of age >=7 years old at randomization are included in the analysis.

PGM=PRODOPS/SAR231893/EFC14153/CSR/REPORT/PGM/eff_sum_vis_i_t.sas OUT=REPORT/OUTPUT/eff_sum_aqlq_t2e3_t_x.rtf (27NOV2020 - 6:43)

Project Code / Study Number / Analysis: SAR231893 / EFC14153 / CSR

16.2.6 Efficacy response data

16.2.6.20 PAQLQ(S)-IA global score

16.2.6.20.1 Summary of PAQLQ(S)-IA global score over time - Type 2 inflammatory asthma phenotype population and baseline blood eosinophils >=0.3 Giga/L population

	Type 2 inflammatory asthma phenotype population	
PAQLQ(S)-IA global score	**Placebo (N=107)**	**Dupilumab (N=211)**
Change from baseline		
Number	100	184
Mean (SD)	1.25 (1.37)	1.53 (1.18)
Median	1.07	1.43
Q1 : Q3	0.41 : 2.07	0.83 : 2.17
Min : Max	-2.6 : 5.1	-4.6 : 4.9
Percent change from baseline		
Number	100	184
Mean (SD)	33.56 (46.71)	39.86 (48.36)
Median	20.73	28.09
Q1 : Q3	7.14 : 49.07	14.39 : 51.42
Min : Max	-43.4 : 278.6	-76.3 : 364.5

Type 2 inflammatory asthma phenotype population is defined as the randomized patients with baseline blood eosinophils >= 0.15 Giga/L or baseline FeNO >= 20 ppb. Only patients of age >=7 years old at randomization are included in the analysis.

PGM=PRODOPS/SAR231893/EFC14153/CSR/REPORT/PGM/eff_sum_vis_i_t.sas OUT=REPORT/OUTPUT/eff_sum_aqlq_t2e3_t_x.rtf (27NOV2020 - 6:43)

Project Code / Study Number / Analysis: SAR231893 / EFC14153 / CSR

16.2.6 Efficacy response data

16.2.6.20 PAQLQ(S)-IA global score

16.2.6.20.1 Summary of PAQLQ(S)-IA global score over time - Type 2 inflammatory asthma phenotype population and baseline blood eosinophils >=0.3 Giga/L population

	Type 2 inflammatory asthma phenotype population	
PAQLQ(S)-IA global score	**Placebo (N=107)**	**Dupilumab (N=211)**
Week 52		
Value		
Number	103	191
Mean (SD)	6.18 (0.94)	6.54 (0.66)
Median	6.57	6.78
Q1 : Q3	5.87 : 6.87	6.35 : 6.96
Min : Max	3.1 : 7.0	3.3 : 7.0
Change from baseline		
Number	101	184
Mean (SD)	1.26 (1.28)	1.60 (1.07)
Median	1.22	1.57
Q1 : Q3	0.35 : 2.09	0.80 : 2.33
Min : Max	-2.7 : 4.9	-1.0 : 5.3

Type 2 inflammatory asthma phenotype population is defined as the randomized patients with baseline blood eosinophils >= 0.15 Giga/L or baseline FeNO >= 20 ppb. Only patients of age >=7 years old at randomization are included in the analysis.

PGM=PRODOPS/SAR231893/EFC14153/CSR/REPORT/PGM/eff_sum_vis_i_t.sas OUT=REPORT/OUTPUT/eff_sum_aqlq_t2e3_t_x.rtf (27NOV2020 - 6:43)

Project Code / Study Number / Analysis: SAR231893 / EFC14153 / CSR

16.2.6 Efficacy response data

16.2.6.20 PAQLQ(S)-IA global score

16.2.6.20.1 Summary of PAQLQ(S)-IA global score over time - Type 2 inflammatory asthma phenotype population and baseline blood eosinophils >=0.3 Giga/L population

	Type 2 inflammatory asthma phenotype population	
PAQLQ(S)-IA global score	**Placebo (N=107)**	**Dupilumab (N=211)**
Percent change from baseline		
Number	101	184
Mean (SD)	33.19 (43.81)	40.30 (44.57)
Median	22.40	30.92
Q1 : Q3	6.50 : 52.38	14.02 : 53.43
Min : Max	-43.7 : 266.7	-19.2 : 393.5
Week 64		
Value		
Number	2	15
Mean (SD)	3.48 (0.25)	6.22 (1.48)
Median	3.48	6.70
Q1 : Q3	3.30 : 3.65	6.13 : 6.83
Min : Max	3.3 : 3.7	1.0 : 7.0

Type 2 inflammatory asthma phenotype population is defined as the randomized patients with baseline blood eosinophils >= 0.15 Giga/L or baseline FeNO >= 20 ppb. Only patients of age >=7 years old at randomization are included in the analysis.

PGM=PRODOPS/SAR231893/EFC14153/CSR/REPORT/PGM/eff_sum_vis_i_t.sas OUT=REPORT/OUTPUT/eff_sum_aqlq_t2e3_t_x.rtf (27NOV2020 - 6:43)

Project Code / Study Number / Analysis: SAR231893 / EFC14153 / CSR

16.2.6 Efficacy response data

16.2.6.20 PAQLQ(S)-IA global score

16.2.6.20.1 Summary of PAQLQ(S)-IA global score over time - Type 2 inflammatory asthma phenotype population and baseline blood eosinophils >=0.3 Giga/L population

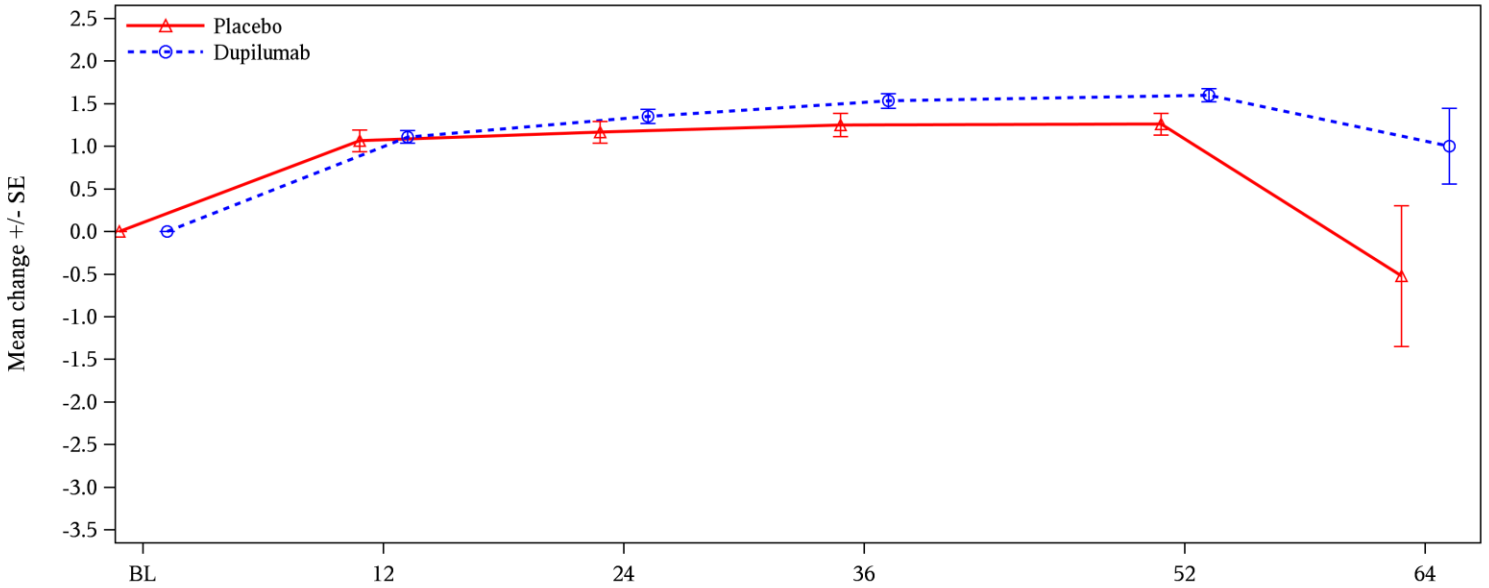
	Type 2 inflammatory asthma phenotype population	
PAQLQ(S)-IA global score	**Placebo (N=107)**	**Dupilumab (N=211)**
Change from baseline		
Number	2	14
Mean (SD)	-0.52 (1.17)	1.00 (1.66)
Median	-0.52	1.50
Q1 : Q3	-1.35 : 0.30	0.52 : 1.96
Min : Max	-1.3 : 0.3	-4.2 : 2.5
Percent change from baseline		
Number	2	14
Mean (SD)	-8.41 (26.23)	21.23 (34.19)
Median	-8.41	29.13
Q1 : Q3	-26.96 : 10.14	9.30 : 40.54
Min : Max	-27.0 : 10.1	-80.8 : 63.0

Type 2 inflammatory asthma phenotype population is defined as the randomized patients with baseline blood eosinophils >= 0.15 Giga/L or baseline FeNO >= 20 ppb. Only patients of age >=7 years old at randomization are included in the analysis.

PGM=PRODOPS/SAR231893/EFC14153/CSR/REPORT/PGM/eff_sum_vis_i_t.sas OUT=REPORT/OUTPUT/eff_sum_aqlq_t2e3_t_x.rtf (27NOV2020 - 6:43)

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen
Project Code / Study Number / Analysis: SAR231893 / EFC14153 / CSR

16.2.6 Efficacy response data
16.2.6.20 PAQLQ(S)-IA global score
16.2.6.20.2 Plot of mean change from baseline in PAQLQ(S)-IA global score over time - Type 2 inflammatory asthma phenotype population



#subjects						
Placebo	104	99	97	100	101	2
Dupilumab	203	191	191	184	184	14

BL=Baseline
Type 2 inflammatory asthma phenotype population is defined as the randomized patients with baseline blood eosinophils >= 0.15 Giga/L or baseline FeNO >= 20 ppb.
Only patients of age >=7 years old at randomization are included in the analysis.
PGM=PRODOPS/SAR231893/EFC14153/CSR/REPORT/PGM/eff_sum_vis_i_g.sas OUT=REPORT/OUTPUT/eff_sum_aqlq_t2_g_x.rtf (27NOV2020 - 6:38)

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

Project Code / Study Number / Analysis: SAR231893 / EFC14153 / CSR

16.2.6 Efficacy response data

16.2.6.20 PAQLQ(S)-IA global score

16.2.6.20.4 Change from baseline in PAQLQ(S)-IA global score over time (MMRM including measurements up to Week 52) - Type 2 inflammatory asthma phenotype population and baseline blood eosinophils >=0.3 Giga/L population

	Type 2 inflammatory asthma phenotype population	
PAQLQ(S)-IA global score	**Placebo (N=107)**	**Dupilumab (N=211)**
Baseline		
Value		
Number	104	203
Mean (SD)	4.92 (1.13)	4.95 (1.08)
Median	5.11	5.13
Q1 : Q3	4.20 : 5.89	4.26 : 5.70
Min : Max	1.8 : 6.9	1.3 : 6.8
Week 12		
Change from baseline		
Number of patients in the model	102	201
LS Mean (SE) [a]	0.97 (0.09)	1.08 (0.07)
LS Mean Diff vs. placebo (95% CI) [a]		0.11 (-0.10, 0.32)
P-value vs. placebo [a]		0.3046

[a] Derived from MMRM model with change from baseline in PAQLQ(S)-IA global score values up to Week 52 as the response variable, and treatment, age, baseline weight group, region, baseline eosinophil level, baseline FeNO level, baseline ICS dose level, visit, treatment by-visit interaction, baseline PAQLQ(S)-IA global score value and baseline-by-visit interaction as covariates.

Type 2 inflammatory asthma phenotype population is defined as the randomized patients with baseline blood eosinophils >= 0.15 Giga/L or baseline FeNO >= 20 ppb. Only patients of age >=7 years old at randomization are included in the analysis.

PGM=PRODOPS/SAR231893/EFC14153/CSR/REPORT/PGM/eff_mmrm_i_t_intext.sas OUT=REPORT/OUTPUT/eff_aqlq_chg_a52_t2e3_t_x.rtf (27NOV2020 - 6:14)

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

Project Code / Study Number / Analysis: SAR231893 / EFC14153 / CSR

16.2.6 Efficacy response data

16.2.6.20 PAQLQ(S)-IA global score

16.2.6.20.4 Change from baseline in PAQLQ(S)-IA global score over time (MMRM including measurements up to Week 52) - Type 2 inflammatory asthma phenotype population and baseline blood eosinophils >=0.3 Giga/L population

	Type 2 inflammatory asthma phenotype population	
PAQLQ(S)-IA global score	**Placebo (N=107)**	**Dupilumab (N=211)**
Week 24		
Change from baseline		
Number of patients in the model	102	201
LS Mean (SE) [a]	1.11 (0.09)	1.30 (0.07)
LS Mean Diff vs. placebo (95% CI) [a]		0.19 (-0.03, 0.40)
P-value vs. placebo [a]		0.0843
Week 36		
Change from baseline		
Number of patients in the model	102	201
LS Mean (SE) [a]	1.15 (0.09)	1.48 (0.07)
LS Mean Diff vs. placebo (95% CI) [a]		0.33 (0.13, 0.53)
P-value vs. placebo [a]		0.0014

[a] Derived from MMRM model with change from baseline in PAQLQ(S)-IA global score values up to Week 52 as the response variable, and treatment, age, baseline weight group, region, baseline eosinophil level, baseline FeNO level, baseline ICS dose level, visit, treatment by-visit interaction, baseline PAQLQ(S)-IA global score value and baseline-by-visit interaction as covariates.

Type 2 inflammatory asthma phenotype population is defined as the randomized patients with baseline blood eosinophils >= 0.15 Giga/L or baseline FeNO >= 20 ppb. Only patients of age >=7 years old at randomization are included in the analysis.

PGM=PRODOPS/SAR231893/EFC14153/CSR/REPORT/PGM/eff_mmrm_i_t_intext.sas OUT=REPORT/OUTPUT/eff_aqlq_chg_a52_t2e3_t_x.rtf (27NOV2020 - 6:14)

Project Code / Study Number / Analysis: SAR231893 / EFC14153 / CSR

16.2.6 Efficacy response data

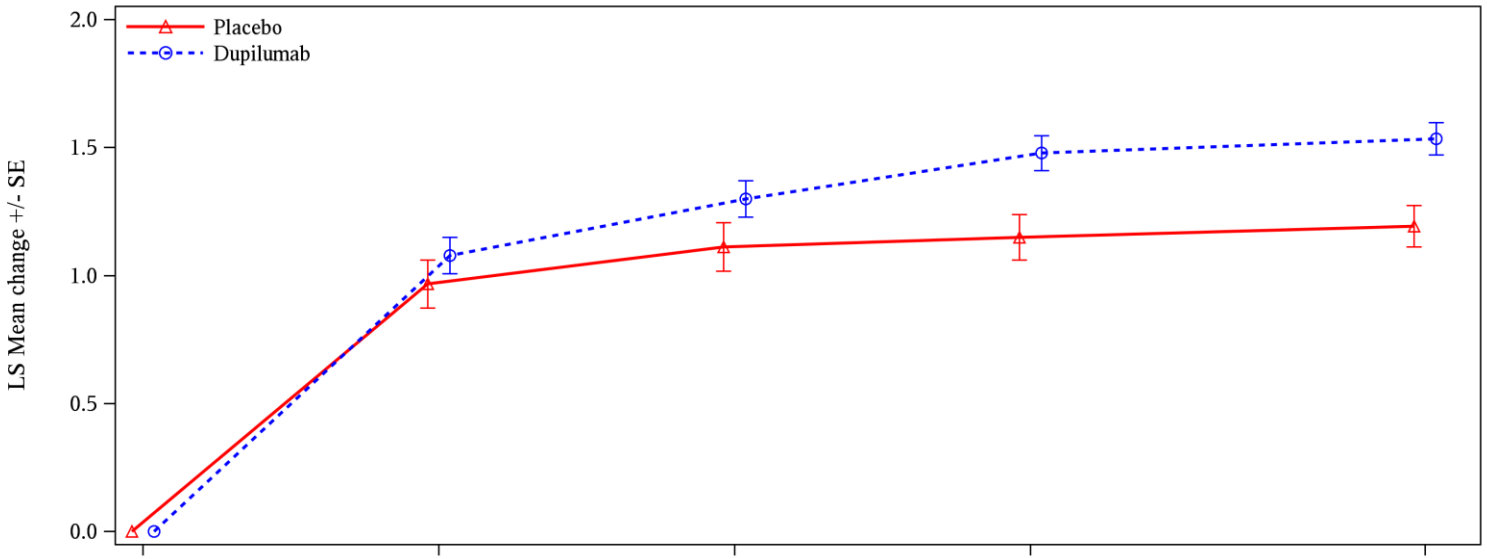
16.2.6.20 PAQLQ(S)-IA global score

16.2.6.20.4 Change from baseline in PAQLQ(S)-IA global score over time (MMRM including measurements up to Week 52) - Type 2 inflammatory asthma phenotype population and baseline blood eosinophils >=0.3 Giga/L population

	Type 2 inflammatory asthma phenotype population	
PAQLQ(S)-IA global score	**Placebo (N=107)**	**Dupilumab (N=211)**
Week 52		
Change from baseline		
Number of patients in the model	102	201
LS Mean (SE) [a]	1.19 (0.08)	1.53 (0.06)
LS Mean Diff vs. placebo (95% CI) [a]		0.34 (0.16, 0.52)
P-value vs. placebo [a]		0.0002

[a] Derived from MMRM model with change from baseline in PAQLQ(S)-IA global score values up to Week 52 as the response variable, and treatment, age, baseline weight group, region, baseline eosinophil level, baseline FeNO level, baseline ICS dose level, visit, treatment by-visit interaction, baseline PAQLQ(S)-IA global score value and baseline-by-visit interaction as covariates.
Type 2 inflammatory asthma phenotype population is defined as the randomized patients with baseline blood eosinophils >= 0.15 Giga/L or baseline FeNO >= 20 ppb. Only patients of age >=7 years old at randomization are included in the analysis.
PGM=PRODOPS/SAR231893/EFC14153/CSR/REPORT/PGM/eff_mmrm_i_t_intext.sas OUT=REPORT/OUTPUT/eff_aqlq_chg_a52_t2e3_t_x.rtf (27NOV2020 - 6:14)

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen
Project Code / Study Number / Analysis: SAR231893 / EFC14153 / CSR
16.2.6 Efficacy response data
16.2.6.20 PAQLQ(S)-IA global score
16.2.6.20.5 Plot of LS mean change from baseline in PAQLQ(S)-IA global score over time (MMRM including measurements up to Week 52) - Type 2 inflammatory asthma phenotype population



#subjects

	BL	12	24	36	52
Placebo	104	99	97	100	101
Dupilumab	203	191	191	184	184

BL=Baseline
Type 2 inflammatory asthma phenotype population is defined as the randomized patients with baseline blood eosinophils >= 0.15 Giga/L or baseline FeNO >= 20 ppb. Only patients of age >=7 years old at randomization are included in the analysis.
PGM=PRODOPS/SAR231893/EFC14153/CSR/REPORT/PGM/eff_mmrm_i_g_intext_adqs.sas OUT=REPORT/OUTPUT/eff_aqlq_chg_a52_t2_g_x.rtf (27NOV2020 - 3:25)

Project Code / Study Number / Analysis: SAR231893 / EFC14153 / CSR_RWE

8 EQ-VAS - ITT type 2 inflammatory asthma phenotype population

8.1 Change from baseline in EQ-VAS up to week 52

EQ-VAS	Placebo (N=87)	Dupilumab (N=181)
Baseline		
Value		
Number	84	180
Mean (SD)	72.92 (17.37)	73.56 (17.45)
Median	75.00	79.00
Q1 : Q3	65.00 : 85.00	62.50 : 85.50
Min : Max	5.0 : 100.0	9.0 : 100.0
Week 24		
Value		
Number	85	174
Mean (SD)	77.38 (15.32)	85.91 (13.13)
Median	80.00	90.00
Q1 : Q3	70.00 : 90.00	80.00 : 95.00
Min : Max	45.0 : 100.0	40.0 : 100.0

[a]Derived from MMRM model with change from baseline in EQ-VAS values up to Week 52 as the response variable, and treatment, baseline weight group, region, age, baseline eosinophil level, baseline FeNO level, baseline ICS dose level, visit, treatment by-visit interaction, baseline EQ-VAS value and baseline-by-visit interaction as covariates.

Type 2 inflammatory asthma phenotype population is defined as the randomized patients with baseline blood eosinophils >= 0.15 Giga/L or baseline FeNO >= 20 ppb. Only patients of age >=8 years old at randomization are included in the analysis.

PGM=DEVOPS/SAR231893/EFC14153/CSR_RWE/REPORT/PGM/eff_mmrm_i_t_intext.sas OUT=REPORT/OUTPUT/eff_eqvas_ger_chg_t2_t_x.rtf (11AUG2021 - 10:33)

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

Project Code / Study Number / Analysis: SAR231893 / EFC14153 / CSR_RWE

8 EQ-VAS - ITT type 2 inflammatory asthma phenotype population

8.1 Change from baseline in EQ-VAS up to week 52

EQ-VAS	Placebo (N=87)	Dupilumab (N=181)
Change from baseline		
Number	82	173
Mean (SD)	4.49 (20.49)	12.02 (19.08)
Median	5.00	10.00
Q1 : Q3	-9.00 : 15.00	0.00 : 20.00
Min : Max	-43.0 : 75.0	-40.0 : 86.0
Number of patients in the model	83	173
LS Mean (SE) [a]	4.05 (1.70)	11.84 (1.28)
LS Mean Diff vs. placebo (95% CI) [a]		7.79 (4.18, 11.40)
P-value vs. placebo [a]		<.001

[a]Derived from MMRM model with change from baseline in EQ-VAS values up to Week 52 as the response variable, and treatment, baseline weight group, region, age, baseline eosinophil level, baseline FeNO level, baseline ICS dose level, visit, treatment by-visit interaction, baseline EQ-VAS value and baseline-by-visit interaction as covariates.

Type 2 inflammatory asthma phenotype population is defined as the randomized patients with baseline blood eosinophils >= 0.15 Giga/L or baseline FeNO >= 20 ppb. Only patients of age >=8 years old at randomization are included in the analysis.

PGM=DEVOPS/SAR231893/EFC14153/CSR_RWE/REPORT/PGM/eff_mmrm_i_t_intext.sas OUT=REPORT/OUTPUT/eff_eqvas_ger_chg_t2_t_x.rtf (11AUG2021 - 10:33)

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

Project Code / Study Number / Analysis: SAR231893 / EFC14153 / CSR_RWE

8 EQ-VAS - ITT type 2 inflammatory asthma phenotype population

8.1 Change from baseline in EQ-VAS up to week 52

EQ-VAS	Placebo (N=87)	Dupilumab (N=181)
Week 52		
Value		
Number	83	170
Mean (SD)	83.28 (14.55)	87.84 (13.34)
Median	85.00	92.00
Q1 : Q3	75.00 : 95.00	85.00 : 96.00
Min : Max	45.0 : 100.0	30.0 : 100.0
Change from baseline		
Number	81	169
Mean (SD)	9.52 (20.85)	15.08 (19.75)
Median	7.00	15.00
Q1 : Q3	-1.00 : 20.00	5.00 : 25.00
Min : Max	-42.0 : 75.0	-40.0 : 90.0

[a]Derived from MMRM model with change from baseline in EQ-VAS values up to Week 52 as the response variable, and treatment, baseline weight group, region, age, baseline eosinophil level, baseline FeNO level, baseline ICS dose level, visit, treatment by-visit interaction, baseline EQ-VAS value and baseline-by-visit interaction as covariates.

Type 2 inflammatory asthma phenotype population is defined as the randomized patients with baseline blood eosinophils >= 0.15 Giga/L or baseline FeNO >= 20 ppb. Only patients of age >=8 years old at randomization are included in the analysis.

PGM=DEVOPS/SAR231893/EFC14153/CSR_RWE/REPORT/PGM/eff_mmrm_i_t_intext.sas OUT=REPORT/OUTPUT/eff_eqvas_ger_chg_t2_t_x.rtf (11AUG2021 - 10:33)

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

Project Code / Study Number / Analysis: SAR231893 / EFC14153 / CSR_RWE

8 EQ-VAS - ITT type 2 inflammatory asthma phenotype population

8.1 Change from baseline in EQ-VAS up to week 52

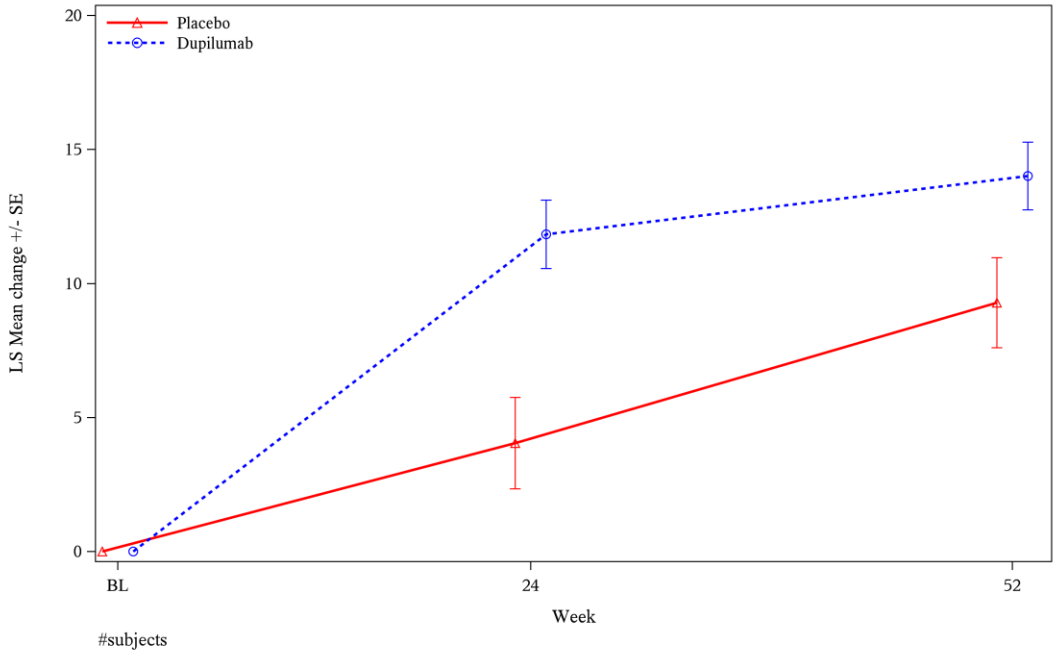
EQ-VAS	Placebo (N=87)	Dupilumab (N=181)
Number of patients in the model	83	173
LS Mean (SE) [a]	9.29 (1.68)	14.02 (1.26)
LS Mean Diff vs. placebo (95% CI) [a]		4.73 (1.18, 8.28)
P-value vs. placebo [a]		0.009

[a]Derived from MMRM model with change from baseline in EQ-VAS values up to Week 52 as the response variable, and treatment, baseline weight group, region, age, baseline eosinophil level, baseline FeNO level, baseline ICS dose level, visit, treatment by-visit interaction, baseline EQ-VAS value and baseline-by-visit interaction as covariates.

Type 2 inflammatory asthma phenotype population is defined as the randomized patients with baseline blood eosinophils >= 0.15 Giga/L or baseline FeNO >= 20 ppb. Only patients of age >=8 years old at randomization are included in the analysis.

PGM=DEVOPS/SAR231893/EFC14153/CSR_RWE/REPORT/PGM/eff_mmrm_i_t_intext.sas OUT=REPORT/OUTPUT/eff_eqvas_ger_chg_t2_t_x.rtf (11AUG2021 - 10:33)

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen
Project Code / Study Number / Analysis: SAR231893 / EFC14153 / CSR_RWE
8 EQ-VAS - ITT type 2 inflammatory asthma phenotype population
8.2 Plot of LS mean change from baseline in EQ-VAS over time (MMRM including measurements up to Week 52)



BL=Baseline
Type 2 inflammatory asthma phenotype population is defined as the randomized patients with baseline blood eosinophils >= 0.15 Giga/L or baseline FeNO >= 20 ppb.
Only patients of age >=8 years old at randomization are included in the analysis.
PGM=DEVOPS/SAR231893/EFC14153/CSR_RWE/REPORT/PGM/eff_mmrm_i_g_adqs.sas OUT=REPORT/OUTPUT/eff_eqvs_ger_chg_a52_t2_g_x.rtf (10AUG2021 - 9:32)

Project Code / Study Number / Analysis: SAR231893 / EFC14153 / CSR_RWE

8 EQ-VAS - ITT type 2 inflammatory asthma phenotype population

8.3 Summary of treatment effect on change from baseline at Week 52

EQ-VAS	Placebo (N=87)	Dupilumab (N=181)
Baseline		
Value		
Number	84	180
Mean (SD)	72.92 (17.37)	73.56 (17.45)
Median	75.00	79.00
Q1 : Q3	65.00 : 85.00	62.50 : 85.50
Min : Max	5.0 : 100.0	9.0 : 100.0
Week 52		
Value		
Number	83	170
Mean (SD)	83.28 (14.55)	87.84 (13.34)
Median	85.00	92.00
Q1 : Q3	75.00 : 95.00	85.00 : 96.00
Min : Max	45.0 : 100.0	30.0 : 100.0
Change from baseline		
Number	81	169
LS Mean (SE)[a]	9.29 (1.68)	14.02 (1.26)
LS Mean Diff (95% CI)[a]	-	4.73 (1.18 to 8.28)
Hedges'g (95% CI)	-	0.293 (0.073 to 0.513)
p-value[a]		0.009

Rücklaufquoten für PRO

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

Project Code / Study Number / Analysis: SAR231893 / EFC14153 / CSR_RWE

2 PRO endpoints

2.1 Response rates of questionnaires by visit for ACQ-5-IA - ITT type 2 inflammatory asthma phenotype population

n(%) of patients with completed ACQ-5-IA	**Placebo (N=114)**	**Dupilumab (N=236)**
Baseline		
Number of patients still remaining in the study	114	236
Number of completed questionnaires received (% in relation to Type 2 inflammatory asthma phenotype population)	114 (100%)	236 (100%)
Number of completed questionnaires (% in relation to Type 2 inflammatory asthma phenotype population still remaining in the study)	114 (100%)	236 (100%)
Week 2		
Number of patients still remaining in the study	114	233
Number of completed questionnaires received (% in relation to Type 2 inflammatory asthma phenotype population)	110 (96.5%)	232 (98.3%)
Number of completed questionnaires (% in relation to Type 2 inflammatory asthma phenotype population still remaining in the study)	110 (96.5%)	232 (99.6%)
Week 4		
Number of patients still remaining in the study	114	233
Number of completed questionnaires received (% in relation to Type 2 inflammatory asthma phenotype population)	110 (96.5%)	226 (95.8%)
Number of completed questionnaires (% in relation to Type 2 inflammatory asthma phenotype population still remaining in the study)	110 (96.5%)	226 (97.0%)
Week 6		
Number of patients still remaining in the study	114	233

The number of patients remaining in the study is determined according to the time windows defined for the parameter in the statistical analysis plan

PGM=DEVOPS/SAR231893/EFC14153/CSR_RWE/REPORT/PGM/eff_pro_quest_ger.sas OUT=REPORT/OUTPUT/eff_pro_quest_acq5_ger_t2_t_x.rtf (12AUG2021 - 16:06)

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

Project Code / Study Number / Analysis: SAR231893 / EFC14153 / CSR_RWE

2 PRO endpoints

2.1 Response rates of questionnaires by visit for ACQ-5-IA - ITT type 2 inflammatory asthma phenotype population

n(%) of patients with completed ACQ-5-IA	**Placebo (N=114)**	**Dupilumab (N=236)**
Number of completed questionnaires received (% in relation to Type 2 inflammatory asthma phenotype population)	113 (99.1%)	229 (97.0%)
Number of completed questionnaires (% in relation to Type 2 inflammatory asthma phenotype population still remaining in the study)	113 (99.1%)	229 (98.3%)
Week 8		
Number of patients still remaining in the study	114	233
Number of completed questionnaires received (% in relation to Type 2 inflammatory asthma phenotype population)	113 (99.1%)	227 (96.2%)
Number of completed questionnaires (% in relation to Type 2 inflammatory asthma phenotype population still remaining in the study)	113 (99.1%)	227 (97.4%)
Week 10		
Number of patients still remaining in the study	113	233
Number of completed questionnaires received (% in relation to Type 2 inflammatory asthma phenotype population)	113 (99.1%)	226 (95.8%)
Number of completed questionnaires (% in relation to Type 2 inflammatory asthma phenotype population still remaining in the study)	113 (100%)	226 (97.0%)
Week 12		
Number of patients still remaining in the study	113	233
Number of completed questionnaires received (% in relation to Type 2 inflammatory asthma phenotype population)	113 (99.1%)	229 (97.0%)

The number of patients remaining in the study is determined according to the time windows defined for the parameter in the statistical analysis plan

PGM=DEVOPS/SAR231893/EFC14153/CSR_RWE/REPORT/PGM/eff_pro_quest_ger.sas OUT=REPORT/OUTPUT/eff_pro_quest_acq5_ger_t2_t_x.rtf (12AUG2021 - 16:06)

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

Project Code / Study Number / Analysis: SAR231893 / EFC14153 / CSR_RWE

2 PRO endpoints

2.1 Response rates of questionnaires by visit for ACQ-5-IA - ITT type 2 inflammatory asthma phenotype population

n(%) of patients with completed ACQ-5-IA	Placebo (N=114)	Dupilumab (N=236)
Number of completed questionnaires (% in relation to Type 2 inflammatory asthma phenotype population still remaining in the study)	113 (100%)	229 (98.3%)
Week 16		
Number of patients still remaining in the study	113	232
Number of completed questionnaires received (% in relation to Type 2 inflammatory asthma phenotype population)	110 (96.5%)	227 (96.2%)
Number of completed questionnaires (% in relation to Type 2 inflammatory asthma phenotype population still remaining in the study)	110 (97.3%)	227 (97.8%)
Week 20		
Number of patients still remaining in the study	113	231
Number of completed questionnaires received (% in relation to Type 2 inflammatory asthma phenotype population)	112 (98.2%)	223 (94.5%)
Number of completed questionnaires (% in relation to Type 2 inflammatory asthma phenotype population still remaining in the study)	112 (99.1%)	223 (96.5%)
Week 24		
Number of patients still remaining in the study	113	230
Number of completed questionnaires received (% in relation to Type 2 inflammatory asthma phenotype population)	112 (98.2%)	228 (96.6%)
Number of completed questionnaires (% in relation to Type 2 inflammatory asthma phenotype population still remaining in the study)	112 (99.1%)	228 (99.1%)

The number of patients remaining in the study is determined according to the time windows defined for the parameter in the statistical analysis plan

PGM=DEVOPS/SAR231893/EFC14153/CSR_RWE/REPORT/PGM/eff_pro_quest_ger.sas OUT=REPORT/OUTPUT/eff_pro_quest_acq5_ger_t2_t_x.rtf (12AUG2021 - 16:06)

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

Project Code / Study Number / Analysis: SAR231893 / EFC14153 / CSR_RWE

2 PRO endpoints

2.1 Response rates of questionnaires by visit for ACQ-5-IA - ITT type 2 inflammatory asthma phenotype population

n(%) of patients with completed ACQ-5-IA	**Placebo (N=114)**	**Dupilumab (N=236)**
Week 28		
Number of patients still remaining in the study	112	229
Number of completed questionnaires received (% in relation to Type 2 inflammatory asthma phenotype population)	112 (98.2%)	225 (95.3%)
Number of completed questionnaires (% in relation to Type 2 inflammatory asthma phenotype population still remaining in the study)	112 (100%)	225 (98.3%)
Week 32		
Number of patients still remaining in the study	112	229
Number of completed questionnaires received (% in relation to Type 2 inflammatory asthma phenotype population)	110 (96.5%)	223 (94.5%)
Number of completed questionnaires (% in relation to Type 2 inflammatory asthma phenotype population still remaining in the study)	110 (98.2%)	223 (97.4%)
Week 36		
Number of patients still remaining in the study	112	229
Number of completed questionnaires received (% in relation to Type 2 inflammatory asthma phenotype population)	111 (97.4%)	218 (92.4%)
Number of completed questionnaires (% in relation to Type 2 inflammatory asthma phenotype population still remaining in the study)	111 (99.1%)	218 (95.2%)
Week 40		
Number of patients still remaining in the study	112	228

The number of patients remaining in the study is determined according to the time windows defined for the parameter in the statistical analysis plan

PGM=DEVOPS/SAR231893/EFC14153/CSR_RWE/REPORT/PGM/eff_pro_quest_ger.sas OUT=REPORT/OUTPUT/eff_pro_quest_acq5_ger_t2_t_x.rtf (12AUG2021 - 16:06)

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

Project Code / Study Number / Analysis: SAR231893 / EFC14153 / CSR_RWE

2 PRO endpoints

2.1 Response rates of questionnaires by visit for ACQ-5-IA - ITT type 2 inflammatory asthma phenotype population

n(%) of patients with completed ACQ-5-IA	**Placebo (N=114)**	**Dupilumab (N=236)**
Number of completed questionnaires received (% in relation to Type 2 inflammatory asthma phenotype population)	106 (93.0%)	220 (93.2%)
Number of completed questionnaires (% in relation to Type 2 inflammatory asthma phenotype population still remaining in the study)	106 (94.6%)	220 (96.5%)
Week 44		
Number of patients still remaining in the study	111	225
Number of completed questionnaires received (% in relation to Type 2 inflammatory asthma phenotype population)	109 (95.6%)	215 (91.1%)
Number of completed questionnaires (% in relation to Type 2 inflammatory asthma phenotype population still remaining in the study)	109 (98.2%)	215 (95.6%)
Week 48		
Number of patients still remaining in the study	111	224
Number of completed questionnaires received (% in relation to Type 2 inflammatory asthma phenotype population)	110 (96.5%)	219 (92.8%)
Number of completed questionnaires (% in relation to Type 2 inflammatory asthma phenotype population still remaining in the study)	110 (99.1%)	219 (97.8%)
Week 52		
Number of patients still remaining in the study	111	224
Number of completed questionnaires received (% in relation to Type 2 inflammatory asthma phenotype population)	110 (96.5%)	222 (94.1%)

The number of patients remaining in the study is determined according to the time windows defined for the parameter in the statistical analysis plan

PGM=DEVOPS/SAR231893/EFC14153/CSR_RWE/REPORT/PGM/eff_pro_quest_ger.sas OUT=REPORT/OUTPUT/eff_pro_quest_acq5_ger_t2_t_x.rtf (12AUG2021 - 16:06)

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

Project Code / Study Number / Analysis: SAR231893 / EFC14153 / CSR_RWE

2 PRO endpoints

2.1 Response rates of questionnaires by visit for ACQ-5-IA - ITT type 2 inflammatory asthma phenotype population

n(%) of patients with completed ACQ-5-IA	**Placebo (N=114)**	**Dupilumab (N=236)**
Number of completed questionnaires (% in relation to Type 2 inflammatory asthma phenotype population still remaining in the study)	110 (99.1%)	222 (99.1%)

The number of patients remaining in the study is determined according to the time windows defined for the parameter in the statistical analysis plan

PGM=DEVOPS/SAR231893/EFC14153/CSR_RWE/REPORT/PGM/eff_pro_quest_ger.sas OUT=REPORT/OUTPUT/eff_pro_quest_acq5_ger_t2_t_x.rtf (12AUG2021 - 16:06)

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

Project Code / Study Number / Analysis: SAR231893 / EFC14153 / CSR_RWE

2 PRO endpoints

2.2 Response rates of questionnaires by visit for PAQLQ(S)-IA global score - ITT type 2 inflammatory asthma phenotype population

n(%) of patients with completed PAQLQ(S)-IA global score	Placebo (N=107)	Dupilumab (N=211)
Baseline		
Number of patients still remaining in the study	107	211
Number of completed questionnaires received (% in relation to Type 2 inflammatory asthma phenotype population)	104 (97.2%)	203 (96.2%)
Number of completed questionnaires (% in relation to Type 2 inflammatory asthma phenotype population still remaining in the study)	104 (97.2%)	203 (96.2%)
Week 12		
Number of patients still remaining in the study	107	209
Number of completed questionnaires received (% in relation to Type 2 inflammatory asthma phenotype population)	102 (95.3%)	199 (94.3%)
Number of completed questionnaires (% in relation to Type 2 inflammatory asthma phenotype population still remaining in the study)	102 (95.3%)	199 (95.2%)
Week 24		
Number of patients still remaining in the study	106	207
Number of completed questionnaires received (% in relation to Type 2 inflammatory asthma phenotype population)	100 (93.5%)	198 (93.8%)
Number of completed questionnaires (% in relation to Type 2 inflammatory asthma phenotype population still remaining in the study)	100 (94.3%)	198 (95.7%)
Week 36		
Number of patients still remaining in the study	105	205

The number of patients remaining in the study is determined according to the time windows defined for the parameter in the statistical analysis plan
Only patients of age >=7 years old at randomization are included in the analysis.
PGM=DEVOPS/SAR231893/EFC14153/CSR_RWE/REPORT/PGM/eff_pro_quest_ger.sas OUT=REPORT/OUTPUT/eff_pro_quest_aqlq_ger_t2_t_x.rtf (12AUG2021 - 16:06)

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

Project Code / Study Number / Analysis: SAR231893 / EFC14153 / CSR_RWE

2 PRO endpoints

2.2 Response rates of questionnaires by visit for PAQLQ(S)-IA global score - ITT type 2 inflammatory asthma phenotype population

n(%) of patients with completed PAQLQ(S)-IA global score	**Placebo (N=107)**	**Dupilumab (N=211)**
Number of completed questionnaires received (% in relation to Type 2 inflammatory asthma phenotype population)	102 (95.3%)	192 (91.0%)
Number of completed questionnaires (% in relation to Type 2 inflammatory asthma phenotype population still remaining in the study)	102 (97.1%)	192 (93.7%)
Week 52		
Number of patients still remaining in the study	104	200
Number of completed questionnaires received (% in relation to Type 2 inflammatory asthma phenotype population)	103 (96.3%)	191 (90.5%)
Number of completed questionnaires (% in relation to Type 2 inflammatory asthma phenotype population still remaining in the study)	103 (99.0%)	191 (95.5%)

The number of patients remaining in the study is determined according to the time windows defined for the parameter in the statistical analysis plan
Only patients of age >=7 years old at randomization are included in the analysis.
PGM=DEVOPS/SAR231893/EFC14153/CSR_RWE/REPORT/PGM/eff_pro_quest_ger.sas OUT=REPORT/OUTPUT/eff_pro_quest_aqlq_ger_t2_t_x.rtf (12AUG2021 - 16:06)

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

Project Code / Study Number / Analysis: SAR231893 / EFC14153 / CSR_RWE

2 PRO endpoints

2.3 Response rates of questionnaires by visit for EQ-VAS - ITT type 2 inflammatory asthma phenotype population

n(%) of patients with completed EQ-VAS	**Placebo (N=87)**	**Dupilumab (N=181)**
Baseline		
Number of patients still remaining in the study	87	181
Number of completed questionnaires received (% in relation to Type 2 inflammatory asthma phenotype population)	84 (96.6%)	180 (99.4%)
Number of completed questionnaires (% in relation to Type 2 inflammatory asthma phenotype population still remaining in the study)	84 (96.6%)	180 (99.4%)
Week 24		
Number of patients still remaining in the study	87	179
Number of completed questionnaires received (% in relation to Type 2 inflammatory asthma phenotype population)	85 (97.7%)	174 (96.1%)
Number of completed questionnaires (% in relation to Type 2 inflammatory asthma phenotype population still remaining in the study)	85 (97.7%)	174 (97.2%)
Week 52		
Number of patients still remaining in the study	85	175
Number of completed questionnaires received (% in relation to Type 2 inflammatory asthma phenotype population)	83 (95.4%)	170 (93.9%)
Number of completed questionnaires (% in relation to Type 2 inflammatory asthma phenotype population still remaining in the study)	83 (97.6%)	170 (97.1%)

The number of patients remaining in the study is determined according to the time windows defined for the parameter in the statistical analysis plan
Only patients of age >=8 years old at randomization are included in the analysis.
PGM=DEVOPS/SAR231893/EFC14153/CSR_RWE/REPORT/PGM/eff_pro_quest_ger.sas OUT=REPORT/OUTPUT/eff_pro_quest_eqvas_ger_t2_t_x.rtf (12AUG2021 - 16:06)

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

Project Code / Study Number / Analysis: SAR231893 / EFC14153 / CSR_RWE

2 PRO endpoints

2.4 Response rates of questionnaires by visit for AM Asthma symptom score - ITT type 2 inflammatory asthma phenotype population

n(%) of patients with completed AM symptom score	Placebo (N=114)	Dupilumab (N=236)
Baseline		
Number of patients still remaining in the study	114	236
Number of completed questionnaires received (% in relation to Type 2 inflammatory asthma phenotype population)	114 (100%)	236 (100%)
Number of completed questionnaires (% in relation to Type 2 inflammatory asthma phenotype population still remaining in the study)	114 (100%)	236 (100%)
Week 2		
Number of patients still remaining in the study	114	234
Number of completed questionnaires received (% in relation to Type 2 inflammatory asthma phenotype population)	114 (100%)	234 (99.2%)
Number of completed questionnaires (% in relation to Type 2 inflammatory asthma phenotype population still remaining in the study)	114 (100%)	234 (100%)
Week 4		
Number of patients still remaining in the study	114	233
Number of completed questionnaires received (% in relation to Type 2 inflammatory asthma phenotype population)	114 (100%)	232 (98.3%)
Number of completed questionnaires (% in relation to Type 2 inflammatory asthma phenotype population still remaining in the study)	114 (100%)	232 (99.6%)
Week 6		
Number of patients still remaining in the study	114	233

The number of patients remaining in the study is determined according to the time windows defined for the parameter in the statistical analysis plan

PGM=DEVOPS/SAR231893/EFC14153/CSR_RWE/REPORT/PGM/eff_pro_quest_ger.sas OUT=REPORT/OUTPUT/eff_pro_quest_scam_ger_t2_t_x.rtf (12AUG2021 - 16:06)

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

Project Code / Study Number / Analysis: SAR231893 / EFC14153 / CSR_RWE

2 PRO endpoints

2.4 Response rates of questionnaires by visit for AM Asthma symptom score - ITT type 2 inflammatory asthma phenotype population

n(%) of patients with completed AM symptom score	Placebo (N=114)	Dupilumab (N=236)
Number of completed questionnaires received (% in relation to Type 2 inflammatory asthma phenotype population)	114 (100%)	232 (98.3%)
Number of completed questionnaires (% in relation to Type 2 inflammatory asthma phenotype population still remaining in the study)	114 (100%)	232 (99.6%)
Week 8		
Number of patients still remaining in the study	114	233
Number of completed questionnaires received (% in relation to Type 2 inflammatory asthma phenotype population)	114 (100%)	232 (98.3%)
Number of completed questionnaires (% in relation to Type 2 inflammatory asthma phenotype population still remaining in the study)	114 (100%)	232 (99.6%)
Week 10		
Number of patients still remaining in the study	114	233
Number of completed questionnaires received (% in relation to Type 2 inflammatory asthma phenotype population)	114 (100%)	230 (97.5%)
Number of completed questionnaires (% in relation to Type 2 inflammatory asthma phenotype population still remaining in the study)	114 (100%)	230 (98.7%)
Week 12		
Number of patients still remaining in the study	113	233
Number of completed questionnaires received (% in relation to Type 2 inflammatory asthma phenotype population)	113 (99.1%)	229 (97.0%)

The number of patients remaining in the study is determined according to the time windows defined for the parameter in the statistical analysis plan

PGM=DEVOPS/SAR231893/EFC14153/CSR_RWE/REPORT/PGM/eff_pro_quest_ger.sas OUT=REPORT/OUTPUT/eff_pro_quest_scam_ger_t2_t_x.rtf (12AUG2021 - 16:06)

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

Project Code / Study Number / Analysis: SAR231893 / EFC14153 / CSR_RWE

2 PRO endpoints

2.4 Response rates of questionnaires by visit for AM Asthma symptom score - ITT type 2 inflammatory asthma phenotype population

n(%) of patients with completed AM symptom score	Placebo (N=114)	Dupilumab (N=236)
Number of completed questionnaires (% in relation to Type 2 inflammatory asthma phenotype population still remaining in the study)	113 (100%)	229 (98.3%)
Week 16		
Number of patients still remaining in the study	113	233
Number of completed questionnaires received (% in relation to Type 2 inflammatory asthma phenotype population)	113 (99.1%)	230 (97.5%)
Number of completed questionnaires (% in relation to Type 2 inflammatory asthma phenotype population still remaining in the study)	113 (100%)	230 (98.7%)
Week 20		
Number of patients still remaining in the study	113	231
Number of completed questionnaires received (% in relation to Type 2 inflammatory asthma phenotype population)	113 (99.1%)	229 (97.0%)
Number of completed questionnaires (% in relation to Type 2 inflammatory asthma phenotype population still remaining in the study)	113 (100%)	229 (99.1%)
Week 24		
Number of patients still remaining in the study	113	230
Number of completed questionnaires received (% in relation to Type 2 inflammatory asthma phenotype population)	113 (99.1%)	229 (97.0%)
Number of completed questionnaires (% in relation to Type 2 inflammatory asthma phenotype population still remaining in the study)	113 (100%)	229 (99.6%)

The number of patients remaining in the study is determined according to the time windows defined for the parameter in the statistical analysis plan

PGM=DEVOPS/SAR231893/EFC14153/CSR_RWE/REPORT/PGM/eff_pro_quest_ger.sas OUT=REPORT/OUTPUT/eff_pro_quest_scam_ger_t2_t_x.rtf (12AUG2021 - 16:06)

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

Project Code / Study Number / Analysis: SAR231893 / EFC14153 / CSR_RWE

2 PRO endpoints

2.4 Response rates of questionnaires by visit for AM Asthma symptom score - ITT type 2 inflammatory asthma phenotype population

n(%) of patients with completed AM symptom score	Placebo (N=114)	Dupilumab (N=236)
Week 28		
Number of patients still remaining in the study	113	230
Number of completed questionnaires received (% in relation to Type 2 inflammatory asthma phenotype population)	111 (97.4%)	227 (96.2%)
Number of completed questionnaires (% in relation to Type 2 inflammatory asthma phenotype population still remaining in the study)	111 (98.2%)	227 (98.7%)
Week 32		
Number of patients still remaining in the study	112	229
Number of completed questionnaires received (% in relation to Type 2 inflammatory asthma phenotype population)	111 (97.4%)	225 (95.3%)
Number of completed questionnaires (% in relation to Type 2 inflammatory asthma phenotype population still remaining in the study)	111 (99.1%)	225 (98.3%)
Week 36		
Number of patients still remaining in the study	112	229
Number of completed questionnaires received (% in relation to Type 2 inflammatory asthma phenotype population)	110 (96.5%)	225 (95.3%)
Number of completed questionnaires (% in relation to Type 2 inflammatory asthma phenotype population still remaining in the study)	110 (98.2%)	225 (98.3%)
Week 40		
Number of patients still remaining in the study	112	228

The number of patients remaining in the study is determined according to the time windows defined for the parameter in the statistical analysis plan

PGM=DEVOPS/SAR231893/EFC14153/CSR_RWE/REPORT/PGM/eff_pro_quest_ger.sas OUT=REPORT/OUTPUT/eff_pro_quest_scam_ger_t2_t_x.rtf (12AUG2021 - 16:06)

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

Project Code / Study Number / Analysis: SAR231893 / EFC14153 / CSR_RWE

2 PRO endpoints

2.4 Response rates of questionnaires by visit for AM Asthma symptom score - ITT type 2 inflammatory asthma phenotype population

n(%) of patients with completed AM symptom score	Placebo (N=114)	Dupilumab (N=236)
Number of completed questionnaires received (% in relation to Type 2 inflammatory asthma phenotype population)	111 (97.4%)	224 (94.9%)
Number of completed questionnaires (% in relation to Type 2 inflammatory asthma phenotype population still remaining in the study)	111 (99.1%)	224 (98.2%)
Week 44		
Number of patients still remaining in the study	111	227
Number of completed questionnaires received (% in relation to Type 2 inflammatory asthma phenotype population)	111 (97.4%)	224 (94.9%)
Number of completed questionnaires (% in relation to Type 2 inflammatory asthma phenotype population still remaining in the study)	111 (100%)	224 (98.7%)
Week 48		
Number of patients still remaining in the study	111	224
Number of completed questionnaires received (% in relation to Type 2 inflammatory asthma phenotype population)	111 (97.4%)	221 (93.6%)
Number of completed questionnaires (% in relation to Type 2 inflammatory asthma phenotype population still remaining in the study)	111 (100%)	221 (98.7%)
Week 52		
Number of patients still remaining in the study	111	224
Number of completed questionnaires received (% in relation to Type 2 inflammatory asthma phenotype population)	111 (97.4%)	222 (94.1%)

The number of patients remaining in the study is determined according to the time windows defined for the parameter in the statistical analysis plan

PGM=DEVOPS/SAR231893/EFC14153/CSR_RWE/REPORT/PGM/eff_pro_quest_ger.sas OUT=REPORT/OUTPUT/eff_pro_quest_scam_ger_t2_t_x.rtf (12AUG2021 - 16:06)

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

Project Code / Study Number / Analysis: SAR231893 / EFC14153 / CSR_RWE

2 PRO endpoints

2.4 Response rates of questionnaires by visit for AM Asthma symptom score - ITT type 2 inflammatory asthma phenotype population

n(%) of patients with completed AM symptom score	**Placebo (N=114)**	**Dupilumab (N=236)**
Number of completed questionnaires (% in relation to Type 2 inflammatory asthma phenotype population still remaining in the study)	111 (100%)	222 (99.1%)

The number of patients remaining in the study is determined according to the time windows defined for the parameter in the statistical analysis plan

PGM=DEVOPS/SAR231893/EFC14153/CSR_RWE/REPORT/PGM/eff_pro_quest_ger.sas OUT=REPORT/OUTPUT/eff_pro_quest_scam_ger_t2_t_x.rtf (12AUG2021 - 16:06)

Project Code / Study Number / Analysis: SAR231893 / EFC14153 / CSR_RWE

2 PRO endpoints

2.5 Response rates of questionnaires by visit for PM Asthma symptom score - ITT type 2 inflammatory asthma phenotype population

n(%) of patients with completed PM symptom score	Placebo (N=114)	Dupilumab (N=236)
Baseline		
Number of patients still remaining in the study	114	236
Number of completed questionnaires received (% in relation to Type 2 inflammatory asthma phenotype population)	114 (100%)	236 (100%)
Number of completed questionnaires (% in relation to Type 2 inflammatory asthma phenotype population still remaining in the study)	114 (100%)	236 (100%)
Week 2		
Number of patients still remaining in the study	114	236
Number of completed questionnaires received (% in relation to Type 2 inflammatory asthma phenotype population)	114 (100%)	234 (99.2%)
Number of completed questionnaires (% in relation to Type 2 inflammatory asthma phenotype population still remaining in the study)	114 (100%)	234 (99.2%)
Week 4		
Number of patients still remaining in the study	114	233
Number of completed questionnaires received (% in relation to Type 2 inflammatory asthma phenotype population)	114 (100%)	233 (98.7%)
Number of completed questionnaires (% in relation to Type 2 inflammatory asthma phenotype population still remaining in the study)	114 (100%)	233 (100%)
Week 6		
Number of patients still remaining in the study	114	233

The number of patients remaining in the study is determined according to the time windows defined for the parameter in the statistical analysis plan
PGM=DEVOPS/SAR231893/EFC14153/CSR_RWE/REPORT/PGM/eff_pro_quest_ger.sas OUT=REPORT/OUTPUT/eff_pro_quest_scam_ger_t2_t_x.rtf (12AUG2021 - 16:06)

Project Code / Study Number / Analysis: SAR231893 / EFC14153 / CSR_RWE

2 PRO endpoints

2.5 Response rates of questionnaires by visit for PM Asthma symptom score - ITT type 2 inflammatory asthma phenotype population

n(%) of patients with completed PM symptom score	Placebo (N=114)	Dupilumab (N=236)
Number of completed questionnaires received (% in relation to Type 2 inflammatory asthma phenotype population)	114 (100%)	232 (98.3%)
Number of completed questionnaires (% in relation to Type 2 inflammatory asthma phenotype population still remaining in the study)	114 (100%)	232 (99.6%)
Week 8		
Number of patients still remaining in the study	114	233
Number of completed questionnaires received (% in relation to Type 2 inflammatory asthma phenotype population)	114 (100%)	231 (97.9%)
Number of completed questionnaires (% in relation to Type 2 inflammatory asthma phenotype population still remaining in the study)	114 (100%)	231 (99.1%)
Week 10		
Number of patients still remaining in the study	114	233
Number of completed questionnaires received (% in relation to Type 2 inflammatory asthma phenotype population)	113 (99.1%)	230 (97.5%)
Number of completed questionnaires (% in relation to Type 2 inflammatory asthma phenotype population still remaining in the study)	113 (99.1%)	230 (98.7%)
Week 12		
Number of patients still remaining in the study	113	233
Number of completed questionnaires received (% in relation to Type 2 inflammatory asthma phenotype population)	113 (99.1%)	231 (97.9%)
Number of completed questionnaires (% in relation to Type 2 inflammatory asthma phenotype population still remaining in the study)	113 (100%)	231 (99.1%)

The number of patients remaining in the study is determined according to the time windows defined for the parameter in the statistical analysis plan
PGM=DEVOPS/SAR231893/EFC14153/CSR_RWE/REPORT/PGM/eff_pro_quest_ger.sas OUT=REPORT/OUTPUT/eff_pro_quest_scam_ger_t2_t_x.rtf (12AUG2021 - 16:06)

Project Code / Study Number / Analysis: SAR231893 / EFC14153 / CSR_RWE

2 PRO endpoints

2.5 Response rates of questionnaires by visit for PM Asthma symptom score - ITT type 2 inflammatory asthma phenotype population

n(%) of patients with completed PM symptom score	Placebo (N=114)	Dupilumab (N=236)
Week 16		
Number of patients still remaining in the study	113	233
Number of completed questionnaires received (% in relation to Type 2 inflammatory asthma phenotype population)	113 (99.1%)	230 (97.5%)
Number of completed questionnaires (% in relation to Type 2 inflammatory asthma phenotype population still remaining in the study)	113 (100%)	230 (98.7%)
Week 20		
Number of patients still remaining in the study	113	231
Number of completed questionnaires received (% in relation to Type 2 inflammatory asthma phenotype population)	113 (99.1%)	229 (97.0%)
Number of completed questionnaires (% in relation to Type 2 inflammatory asthma phenotype population still remaining in the study)	113 (100%)	229 (99.1%)
Week 24		
Number of patients still remaining in the study	113	230
Number of completed questionnaires received (% in relation to Type 2 inflammatory asthma phenotype population)	113 (99.1%)	229 (97.0%)
Number of completed questionnaires (% in relation to Type 2 inflammatory asthma phenotype population still remaining in the study)	113 (100%)	229 (99.6%)
Week 28		
Number of patients still remaining in the study	113	230

The number of patients remaining in the study is determined according to the time windows defined for the parameter in the statistical analysis plan
PGM=DEVOPS/SAR231893/EFC14153/CSR_RWE/REPORT/PGM/eff_pro_quest_ger.sas OUT=REPORT/OUTPUT/eff_pro_quest_scam_ger_t2_t_x.rtf (12AUG2021 - 16:06)

Project Code / Study Number / Analysis: SAR231893 / EFC14153 / CSR_RWE

2 PRO endpoints

2.5 Response rates of questionnaires by visit for PM Asthma symptom score - ITT type 2 inflammatory asthma phenotype population

n(%) of patients with completed PM symptom score	Placebo (N=114)	Dupilumab (N=236)
Number of completed questionnaires received (% in relation to Type 2 inflammatory asthma phenotype population)	111 (97.4%)	227 (96.2%)
Number of completed questionnaires (% in relation to Type 2 inflammatory asthma phenotype population still remaining in the study)	111 (98.2%)	227 (98.7%)
Week 32		
Number of patients still remaining in the study	112	229
Number of completed questionnaires received (% in relation to Type 2 inflammatory asthma phenotype population)	111 (97.4%)	226 (95.8%)
Number of completed questionnaires (% in relation to Type 2 inflammatory asthma phenotype population still remaining in the study)	111 (99.1%)	226 (98.7%)
Week 36		
Number of patients still remaining in the study	112	229
Number of completed questionnaires received (% in relation to Type 2 inflammatory asthma phenotype population)	110 (96.5%)	226 (95.8%)
Number of completed questionnaires (% in relation to Type 2 inflammatory asthma phenotype population still remaining in the study)	110 (98.2%)	226 (98.7%)
Week 40		
Number of patients still remaining in the study	112	228
Number of completed questionnaires received (% in relation to Type 2 inflammatory asthma phenotype population)	111 (97.4%)	224 (94.9%)
Number of completed questionnaires (% in relation to Type 2 inflammatory asthma phenotype population still remaining in the study)	111 (99.1%)	224 (98.2%)

The number of patients remaining in the study is determined according to the time windows defined for the parameter in the statistical analysis plan
PGM=DEVOPS/SAR231893/EFC14153/CSR_RWE/REPORT/PGM/eff_pro_quest_ger.sas OUT=REPORT/OUTPUT/eff_pro_quest_scam_ger_t2_t_x.rtf (12AUG2021 - 16:06)

Project Code / Study Number / Analysis: SAR231893 / EFC14153 / CSR_RWE

2 PRO endpoints

2.5 Response rates of questionnaires by visit for PM Asthma symptom score - ITT type 2 inflammatory asthma phenotype population

n(%) of patients with completed PM symptom score	**Placebo (N=114)**	**Dupilumab (N=236)**
Week 44		
Number of patients still remaining in the study	111	227
Number of completed questionnaires received (% in relation to Type 2 inflammatory asthma phenotype population)	111 (97.4%)	223 (94.5%)
Number of completed questionnaires (% in relation to Type 2 inflammatory asthma phenotype population still remaining in the study)	111 (100%)	223 (98.2%)
Week 48		
Number of patients still remaining in the study	111	224
Number of completed questionnaires received (% in relation to Type 2 inflammatory asthma phenotype population)	111 (97.4%)	222 (94.1%)
Number of completed questionnaires (% in relation to Type 2 inflammatory asthma phenotype population still remaining in the study)	111 (100%)	222 (99.1%)
Week 52		
Number of patients still remaining in the study	111	224
Number of completed questionnaires received (% in relation to Type 2 inflammatory asthma phenotype population)	111 (97.4%)	222 (94.1%)
Number of completed questionnaires (% in relation to Type 2 inflammatory asthma phenotype population still remaining in the study)	111 (100%)	222 (99.1%)

The number of patients remaining in the study is determined according to the time windows defined for the parameter in the statistical analysis plan
PGM=DEVOPS/SAR231893/EFC14153/CSR_RWE/REPORT/PGM/eff_pro_quest_ger.sas OUT=REPORT/OUTPUT/eff_pro_quest_scam_ger_t2_t_x.rtf (12AUG2021 - 16:06)

Ermittlung der für eine Therapie mit Omalizumab in Frage kommenden Population

Project Code / Study Number / Analysis: SAR231893 / EFC14153 / CSR_RWE

4 Eligibility for Omalizumab treatment (using GINA 2015 classification) - Type 2 inflammatory asthma phenotype population and ITT population (using antigen-specific IgE)

	Type 2 inflammatory asthma phenotype population (N=350)			ITT population (N=408)		
n(%)	**Placebo (N=114)**	**Dupilumab (N=236)**	**All (N=350)**	**Placebo (N=135)**	**Dupilumab (N=273)**	**All (N=408)**
a) Baseline IgE>=30 IU/mL and at least one allergen-specific IgE* value >=0.35 IU/ml at Baseline	81 (71.1%)	179 (75.8%)	260 (74.3%)	82 (60.7%)	188 (68.9%)	270 (66.2%)
b) Baseline total IgE (IU/ml) >=200 and <=1300 IU/mL	57 (50.0%)	120 (50.8%)	177 (50.6%)	61 (45.2%)	126 (46.2%)	187 (45.8%)
c) Patients with high ICS dose at baseline AND with a second controller AND (with >=2 severe exa. OR >=1 severe exa. experienced requiring hospitalization or urgent medical care in the the past year)	42 (36.8%)	77 (32.6%)	119 (34.0%)	52 (38.5%)	91 (33.3%)	143 (35.0%)
a) and b) and c)	16 (14.0%)	38 (16.1%)	54 (15.4%)	17 (12.6%)	40 (14.7%)	57 (14.0%)

MedDRA 23.0
*German cockroach, Dog dander, Cat dander, D. pteronyssinus, D. farinae, A. tenuis alternata, A. fumigatus, C. herbarum
PGM=DEVOPS/SAR231893/EFC14153/CSR_RWE/REPORT/PGM/dis_spop_ger_i_t.sas OUT=REPORT/OUTPUT/dis_spop_ger_oma_speca_i_t_x.rtf (19FEB2021 - 16:52)

Project Code / Study Number / Analysis: SAR231893 / EFC14153 / CSR_RWE

6 Eligibility for Omalizumab treatment (using new GINA 2020 classification) - Type 2 inflammatory asthma phenotype population and ITT population (using antigen-specific IgE)

	Type 2 inflammatory asthma phenotype population (N=350)			ITT population (N=408)		
n(%)	**Placebo (N=114)**	**Dupilumab (N=236)**	**All (N=350)**	**Placebo (N=135)**	**Dupilumab (N=273)**	**All (N=408)**
a) Baseline IgE>=30 IU/mL and at least one allergen-specific IgE* value >=0.35 IU/ml at Baseline	81 (71.1%)	180 (76.3%)	261 (74.6%)	82 (60.7%)	189 (69.2%)	271 (66.4%)
b) Baseline total IgE (IU/ml) >=200 and <=1300 IU/mL	57 (50.0%)	120 (50.8%)	177 (50.6%)	61 (45.2%)	126 (46.2%)	187 (45.8%)
c) Patients with high ICS dose at baseline AND with a second controller AND (with >=2 severe exa. OR >=1 severe exa. experienced requiring hospitalization or urgent medical care in the the past year)	77 (67.5%)	161 (68.2%)	238 (68.0%)	77 (57.0%)	161 (59.0%)	238 (58.3%)
a) and b) and c)	33 (28.9%)	76 (32.2%)	109 (31.1%)	33 (24.4%)	76 (27.8%)	109 (26.7%)