



Clinical trial results:

A Randomized, Double-blind, 52-week, Placebo Controlled Efficacy and Safety Study of Dupilumab, in Patients with Bilateral Nasal Polyposis on a Background Therapy with Intranasal Corticosteroids

Summary

EudraCT number	2015-001314-10
Trial protocol	SE PT ES BE
Global end of trial date	16 November 2018

Results information

Result version number	v1 (current)
This version publication date	29 November 2019
First version publication date	29 November 2019

Trial information

Trial identification

Sponsor protocol code	EFC14280
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Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT02898454
WHO universal trial number (UTN)	U1111-1170-7180

Notes:

Sponsors

Sponsor organisation name	Sanofi
Sponsor organisation address	1 avenue Pierre Brossolette, Chilly-Mazarin, France, 91380
Public contact	Trial Transparency Team, Sanofi aventis recherche & développement, Contact-US@sanofi.com
Scientific contact	Trial Transparency Team, Sanofi aventis recherche & développement, Contact-US@sanofi.com

Notes:

Paediatric regulatory details

Is trial part of an agreed paediatric investigation plan (PIP)	No
Does article 45 of REGULATION (EC) No 1901/2006 apply to this trial?	No
Does article 46 of REGULATION (EC) No 1901/2006 apply to this trial?	No

Notes:

Results analysis stage

Analysis stage	Final
Date of interim/final analysis	01 February 2019
Is this the analysis of the primary completion data?	No
Global end of trial reached?	Yes
Global end of trial date	16 November 2018
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To evaluate the efficacy of dupilumab 300 milligram (mg) every 2 weeks (q2w) compared to placebo on a background of mometasone furoate nasal spray (MFNS) in reducing nasal congestion (NC)/obstruction severity and endoscopic nasal polyposis score (NPS) in subjects with bilateral nasal polyposis (NP). In addition for Japanese subjects, reduction in computed tomography (CT) scan opacification of the sinuses was a co-primary objective.

Protection of trial subjects:

Subjects were fully informed of all pertinent aspects of the clinical trial as well as the possibility to discontinue at any time in language and terms appropriate for the subject and considering the local culture. During the course of the trial, subjects were provided with individual subject cards indicating the nature of the trial the subject is participating, contact details and any information needed in the event of a medical emergency.

Collected personal data and human biological samples were processed in compliance with the Sanofi-Aventis Group Personal Data Protection Charter ensuring that the Group abides by the laws governing personal data protection in force in all countries in which it operates.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	28 November 2016
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	Yes

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Argentina: 36
Country: Number of subjects enrolled	Australia: 29
Country: Number of subjects enrolled	Canada: 34
Country: Number of subjects enrolled	Chile: 80
Country: Number of subjects enrolled	Israel: 14
Country: Number of subjects enrolled	Japan: 49
Country: Number of subjects enrolled	Mexico: 21
Country: Number of subjects enrolled	Russian Federation: 21
Country: Number of subjects enrolled	Turkey: 22
Country: Number of subjects enrolled	United States: 55
Country: Number of subjects enrolled	Portugal: 34
Country: Number of subjects enrolled	Spain: 21
Country: Number of subjects enrolled	Sweden: 5
Country: Number of subjects enrolled	Belgium: 27

Worldwide total number of subjects	448
EEA total number of subjects	87

Notes:

Subjects enrolled per age group	
In utero	0
Preterm newborn - gestational age < 37 wk	0
Newborns (0-27 days)	0
Infants and toddlers (28 days-23 months)	0
Children (2-11 years)	0
Adolescents (12-17 years)	0
Adults (18-64 years)	367
From 65 to 84 years	81
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

Study subjects were involved in the study from 28 November 2016 to 16 November 2018 at 117 centres in 14 countries. A total of 806 subjects were screened, of which 448 subjects were enrolled and randomised to receive dupilumab 300 mg or placebo. A total of 358 subjects had screen failures due to failure to meet inclusion criteria.

Pre-assignment

Screening details:

Randomisation was stratified according to asthma and/or non-steroidal anti-inflammatory drug exacerbated respiratory disease (NSAID-ERD) history (yes/no), prior nasal polyps (NP) surgery (yes or not), and country.

Period 1

Period 1 title	Overall study (overall period)
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Double blind
Roles blinded	Subject, Investigator, Carer, Assessor

Arms

Are arms mutually exclusive?	Yes
Arm title	Placebo

Arm description:

Placebo (for dupilumab), 1 subcutaneous (SC) injection q2w from Day 1 of Week 0 up to Week 52 added to background therapy of intranasal MFNS at stable dose.

Arm type	Placebo
Investigational medicinal product name	Placebo (matched to dupilumab 300 mg)
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection in pre-filled syringe
Routes of administration	Subcutaneous use

Dosage and administration details:

2 millilitre (mL), SC injection, q2w using a prefilled syringe for 52 weeks.

Arm title	Dupilumab 300 mg q2w Then q4w
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Arm description:

Dupilumab 300 mg SC injection q2w from Day 1 of Week 0 up to Week 24 and then 300 mg every 4 weeks (q4w) until Week 52 added to background therapy of intranasal MFNS at stable dose. After Week 24, dupilumab administration was alternated with matched placebo injection every other week up to Week 50.

Arm type	Experimental
Investigational medicinal product name	Dupilumab
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection in pre-filled syringe
Routes of administration	Subcutaneous use

Dosage and administration details:

2 mL, SC injection q2w using a prefilled syringe for 24 weeks and then q4w until 52 weeks.

Arm title	Dupilumab 300 mg q2w
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Arm description:

Dupilumab 300 mg SC injection q2w from Day 1 of Week 0 up to Week 52 added to background therapy of intranasal MFNS at stable dose.

Arm type	Experimental
Investigational medicinal product name	Dupilumab
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection in pre-filled syringe
Routes of administration	Subcutaneous use

Dosage and administration details:

2 mL, SC injection once q2w using a prefilled syringe for 52 weeks.

Number of subjects in period 1	Placebo	Dupilumab 300 mg q2w Then q4w	Dupilumab 300 mg q2w
Started	153	145	150
Intent-to-Treat (ITT) Population	153	145	150
Treated	152	145	150
Completed	136	140	144
Not completed	17	5	6
Consent withdrawn by subject	6	3	3
Adverse Event	4	1	2
Lost to follow-up	1	-	-
Did Not Met Eligibility Criteria	1	-	-
Protocol deviation	1	-	1
Lack of efficacy	4	1	-

Baseline characteristics

Reporting groups

Reporting group title	Placebo
Reporting group description: Placebo (for dupilumab), 1 subcutaneous (SC) injection q2w from Day 1 of Week 0 up to Week 52 added to background therapy of intranasal MFNS at stable dose.	
Reporting group title	Dupilumab 300 mg q2w Then q4w
Reporting group description: Dupilumab 300 mg SC injection q2w from Day 1 of Week 0 up to Week 24 and then 300 mg every 4 weeks (q4w) until Week 52 added to background therapy of intranasal MFNS at stable dose. After Week 24, dupilumab administration was alternated with matched placebo injection every other week up to Week 50.	
Reporting group title	Dupilumab 300 mg q2w
Reporting group description: Dupilumab 300 mg SC injection q2w from Day 1 of Week 0 up to Week 52 added to background therapy of intranasal MFNS at stable dose.	

Reporting group values	Placebo	Dupilumab 300 mg q2w Then q4w	Dupilumab 300 mg q2w
Number of subjects	153	145	150
Age categorical Units: Subjects			

Age continuous Units: years arithmetic mean standard deviation	51.67 ± 12.66	52.28 ± 12.87	51.91 ± 11.88
Gender categorical Units: Subjects			
Female	58	58	53
Male	95	87	97
Ethnicity Units: Subjects			
Hispanic or Latino	40	42	50
Not Hispanic or Latino	113	102	100
Unknown or Not Reported	0	1	0
Race Units: Subjects			
Caucasian/White	128	120	124
Black/of African descent	3	2	2
Asian/Oriental	18	19	17
American Indian or Alaska Native	3	2	7
Native Hawaiian or Other Pacific Islander	0	1	0
Multiple	1	1	0
Nasal Congestion/Obstruction (NC) Symptom Severity Score			
NC symptom severity was assessed by the subjects on a scale of 0 to 3, where 0 = no symptoms, 1 = mild symptoms, 2 = moderate symptoms and 3 = severe symptoms, with higher scores indicated more severity.			
Units: score on a scale			

arithmetic mean	2.38	2.44	2.48
standard deviation	± 0.54	± 0.59	± 0.62
Nasal Polyp Score (NPS)			
NPS was the sum of right and left nostril scores, as evaluated by means of nasal endoscopy. For each nostril, NPS was graded based on polyp size from 0 to 4 (0 = no polyps to 4 = large polyps causing complete obstruction of the inferior nasal cavity), with a lower score indicating smaller-sized polyps. Total NPS was the sum of right and left nostril scores and ranges from 0 (no polyps) to 8 (large polyps), with higher score representing more severe disease. In placebo and dupilumab 300 mg q2w arms, 152 and 149 subjects were only involved in the evaluation of the specified baseline measure.			
Units: score on a scale			
arithmetic mean	5.96	6.29	6.07
standard deviation	± 1.21	± 1.20	± 1.22

Reporting group values	Total		
Number of subjects	448		
Age categorical			
Units: Subjects			

Age continuous			
Units: years			
arithmetic mean			
standard deviation	-		
Gender categorical			
Units: Subjects			
Female	169		
Male	279		
Ethnicity			
Units: Subjects			
Hispanic or Latino	132		
Not Hispanic or Latino	315		
Unknown or Not Reported	1		
Race			
Units: Subjects			
Caucasian/White	372		
Black/of African descent	7		
Asian/Oriental	54		
American Indian or Alaska Native	12		
Native Hawaiian or Other Pacific Islander	1		
Multiple	2		
Nasal Congestion/Obstruction (NC) Symptom Severity Score			
NC symptom severity was assessed by the subjects on a scale of 0 to 3, where 0 = no symptoms, 1 = mild symptoms, 2 = moderate symptoms and 3 = severe symptoms, with higher scores indicated more severity.			
Units: score on a scale			
arithmetic mean			
standard deviation	-		
Nasal Polyp Score (NPS)			
NPS was the sum of right and left nostril scores, as evaluated by means of nasal endoscopy. For each nostril, NPS was graded based on polyp size from 0 to 4 (0 = no polyps to 4 = large polyps causing complete obstruction of the inferior nasal cavity), with a lower score indicating smaller-sized polyps. Total NPS was the sum of right and left nostril scores and ranges from 0 (no polyps) to 8 (large polyps), with higher score representing more severe disease. In placebo and dupilumab 300 mg q2w arms, 152 and 149 subjects were only involved in the evaluation of the specified baseline measure.			

Units: score on a scale			
arithmetic mean			
standard deviation	-		

End points

End points reporting groups

Reporting group title	Placebo
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Reporting group description:

Placebo (for dupilumab), 1 subcutaneous (SC) injection q2w from Day 1 of Week 0 up to Week 52 added to background therapy of intranasal MFNS at stable dose.

Reporting group title	Dupilumab 300 mg q2w Then q4w
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Reporting group description:

Dupilumab 300 mg SC injection q2w from Day 1 of Week 0 up to Week 24 and then 300 mg every 4 weeks (q4w) until Week 52 added to background therapy of intranasal MFNS at stable dose. After Week 24, dupilumab administration was alternated with matched placebo injection every other week up to Week 50.

Reporting group title	Dupilumab 300 mg q2w
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Reporting group description:

Dupilumab 300 mg SC injection q2w from Day 1 of Week 0 up to Week 52 added to background therapy of intranasal MFNS at stable dose.

Subject analysis set title	Dupilumab 300 mg (24 Weeks Pooled Arm)
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Subject analysis set type	Intention-to-treat
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Subject analysis set description:

Pooled arm consisted of all subjects from both dupilumab treatment arms up to 24 weeks as both arms to this time point used the 300 mg q2w regimen.

Subject analysis set title	Dupilumab 300 mg q2w Then q4w
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Subject analysis set type	Sub-group analysis
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Subject analysis set description:

Dupilumab 300 mg SC injection q2w from Day 1 of Week 0 up to Week 24 and then 300 mg q4w until Week 52 added to background therapy of intranasal MFNS at stable dose. After Week 24, dupilumab administration was alternated with matched placebo injection every other week up to Week 50. One subject randomised to dupilumab 300 mg q2w arm received 1 dose of placebo and was therefore counted in the 300 mg q2w then q4w arm.

Subject analysis set title	Dupilumab 300 mg q2w Then q4w
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Subject analysis set type	Sub-group analysis
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Subject analysis set description:

Dupilumab 300 mg SC injection q2w from Day 1 of Week 0 up to Week 24 and then 300 mg q4w until Week 52 added to background therapy of intranasal MFNS at stable dose. After Week 24, dupilumab administration was alternated with matched placebo injection every other week up to Week 50. Two subjects randomised to placebo arm accidentally received 1 dose of dupilumab 300 mg and therefore counted in the 300 mg q2w then q4w arm. Similarly one subject randomised to the dupilumab 300 mg q2w arm received 1 dose of placebo and was therefore counted in the 300 mg q2w then q4w arm.

Subject analysis set title	Dupilumab 300 mg (Pooled Arm)
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Subject analysis set type	Intention-to-treat
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Subject analysis set description:

Pooled arm consisted of all subjects who either received Dupilumab 300 mg SC injection q2w from Day 1 of Week 0 up to Week 52 or Dupilumab 300 mg SC injection q2w from Day 1 of Week 0 up to Week 24 and then 300 mg q4w until Week 52, added to background therapy of intranasal MFNS at stable dose.

Primary: Change From Baseline at Week 24 in Nasal Congestion/Obstruction Symptom Severity Score

End point title	Change From Baseline at Week 24 in Nasal Congestion/Obstruction Symptom Severity Score ^[1]
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End point description:

NC symptom severity was assessed by the subjects on a daily basis from Visit 1 and throughout the study using an e-diary on a scale of 0 to 3, where 0 = no symptoms, 1 = mild symptoms, 2 = moderate symptoms and 3 = severe symptoms, with higher scores indicated more severity. Least squares (LS) means and standard error (SE) were obtained from Analysis of covariance (ANCOVA) model described in Statistical Analysis Overview. All subjects randomised to receive Dupilumab had been on 300 mg q2w

regimen until Week 24 and analysed as a pooled population for Week 24 assessments. The analysis was performed on intent-to-treat (ITT) population which included all randomised subjects who were analysed according to the treatment group allocated by randomisation. Data for this end point was planned to be analysed for the combined population of subjects who received Dupilumab.

End point type	Primary
End point timeframe:	
Baseline, Week 24	

Notes:

[1] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.

Justification: Analysis was performed on pooled dupilumab arm.

End point values	Placebo	Dupilumab 300 mg (24 Weeks Pooled Arm)		
Subject group type	Reporting group	Subject analysis set		
Number of subjects analysed	153	295		
Units: score on a scale				
least squares mean (standard error)	-0.38 (± 0.07)	-1.25 (± 0.06)		

Statistical analyses

Statistical analysis title	Dupilumab 300 mg (Pooled Arm) versus Placebo
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Statistical analysis description:

Data was analysed using a hybrid method of the worst-observation carried forward (WOCF) and multiple imputation (MI). The imputed completed data were analysed by fitting ANCOVA model with the corresponding baseline, treatment group, asthma/NASID-ERD status, prior surgery history, and regions as covariates. Statistical inference obtained from all imputed data was combined using Rubin's rule.

Comparison groups	Placebo v Dupilumab 300 mg (24 Weeks Pooled Arm)
Number of subjects included in analysis	448
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.0001
Method	ANCOVA
Parameter estimate	LS mean difference
Point estimate	-0.87
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.03
upper limit	-0.71

Primary: Change From Baseline at Week 24 in Nasal Polyp Score

End point title	Change From Baseline at Week 24 in Nasal Polyp Score ^[2]
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End point description:

NPS: sum of right, left nostril scores, evaluated by nasal endoscopy. For each nostril, NPS was graded based on polyp size from 0 = no polyps to 4 = large polyps causing complete obstruction of inferior nasal cavity; lower score = smaller sized polyps. Total NPS: sum of right and left nostril scores, ranges from 0 (no polyps) to 8 (large polyps), higher score = more severe disease. NPS was assessed by centralised, blinded, independent review of the nasal endoscopy video recordings. LS means and SE were obtained from ANCOVA model described in Statistical Analysis Overview. All subjects randomised

to receive Dupilumab had been on 300 mg q2w regimen until Week 24 and analysed as a pooled population for Week 24 assessments. Analysis was performed on ITT population. Here, 'number of subjects analysed' = subjects evaluable for this end point. Data for this end point measure was planned to be analysed for the combined population of subjects who received Dupilumab.

End point type	Primary
End point timeframe:	
Baseline, Week 24	

Notes:

[2] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.

Justification: Analysis was performed on pooled dupilumab arm.

End point values	Placebo	Dupilumab 300 mg (24 Weeks Pooled Arm)		
Subject group type	Reporting group	Subject analysis set		
Number of subjects analysed	152	294		
Units: score on a scale				
least squares mean (standard error)	0.10 (\pm 0.14)	-1.71 (\pm 0.11)		

Statistical analyses

Statistical analysis title	Dupilumab 300 mg (Pooled Arm) versus Placebo
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Statistical analysis description:

Data was analysed using a hybrid method of the WOCF and MI. The imputed completed data were analysed by fitting an ANCOVA model with corresponding baseline value, treatment group, asthma/NSAID-ERD status, prior surgery history, and regions as covariates. Statistical inference obtained from all imputed data was combined using Rubin's rule.

Comparison groups	Placebo v Dupilumab 300 mg (24 Weeks Pooled Arm)
Number of subjects included in analysis	446
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.0001
Method	ANCOVA
Parameter estimate	LS mean difference
Point estimate	-1.8
Confidence interval	
level	95 %
sides	2-sided
lower limit	-2.1
upper limit	-1.51

Secondary: Change From Baseline at Week 24 in Opacification of Sinuses Measured by Lund Mackay (LMK) Score

End point title	Change From Baseline at Week 24 in Opacification of Sinuses Measured by Lund Mackay (LMK) Score ^[3]
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End point description:

The LMK scoring system rated each of both the left and right frontal, maxillary, sphenoid, ostiomeatal complex, anterior ethmoid and posterior ethmoid sinuses using following grading: 0 = normal, 1 = partial opacification, 2 = total opacification. The total score was the sum of scores from each side and ranges from 0 (normal) to 24 (more opacified); higher score indicated more severe disease. LS means

and SE were obtained from ANCOVA model described in Statistical Analysis Overview. NOTE: For Japan regulatory submission only, this endpoint is not included as a secondary end point and is instead one of the co-primary end points. All subjects randomised to receive Dupilumab had been on 300 mg q2w regimen until Week 24 and analysed as a pooled population for Week 24 assessments. Analysis was performed on ITT population. Here, 'number of subjects analysed' = subjects evaluable for this end point.

End point type	Secondary
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End point timeframe:

Baseline, Week 24

Notes:

[3] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period. Justification: Analysis was performed on pooled dupilumab arm.

End point values	Placebo	Dupilumab 300 mg (24 Weeks Pooled Arm)		
Subject group type	Reporting group	Subject analysis set		
Number of subjects analysed	150	289		
Units: score on a scale				
least squares mean (standard error)	-0.09 (± 0.31)	-5.21 (± 0.24)		

Statistical analyses

Statistical analysis title	Dupilumab 300 mg (Pooled Arm) versus Placebo
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Statistical analysis description:

Data were analysed using a hybrid method of the WOCF and MI. The imputed completed data were analysed by fitting an ANCOVA model with corresponding baseline, treatment group, asthma/NSAID-ERD status, prior surgery history, and regions as covariates. Statistical inference obtained from all imputed data was combined using Rubin's rule.

Comparison groups	Placebo v Dupilumab 300 mg (24 Weeks Pooled Arm)
Number of subjects included in analysis	439
Analysis specification	Pre-specified
Analysis type	superiority ^[4]
P-value	< 0.0001 ^[5]
Method	ANCOVA
Parameter estimate	LS mean difference
Point estimate	-5.13
Confidence interval	
level	95 %
sides	2-sided
lower limit	-5.8
upper limit	-4.46

Notes:

[4] - Hierarchical testing procedure was used to control type I error. For regions outside of Japan, this first secondary endpoint was not tested unless both co-primary endpoints were significant at the 0.05 level. Hierarchical testing continued only when previous endpoint was statistically significant. For Japan submission, LMK was instead a co-primary endpoint which also had to be met before secondary endpoints were tested in the hierarchy. Last endpoint in hierarchy is Week 52 SNOT-22.

[5] - Threshold for significance at 0.05 level.

Secondary: Change From Baseline at Week 24 in Total Symptom Score (TSS)

End point title	Change From Baseline at Week 24 in Total Symptom Score (TSS) ^[6]
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End point description:

The TSS was the sum of subject-assessed nasal symptom scores for NC/obstruction, decreased/loss of sense of smell, and rhinorrhea (anterior/posterior nasal discharge), each accessed on 0-3 categorical scale (where 0 = no symptoms, 1 = mild symptoms, 2 = moderate symptoms and 3 = severe symptoms). Total score ranged from 0 (no symptoms) to 9 (severe symptoms). Higher score indicated more severe symptoms. LS means and SE were obtained from ANCOVA model described in Statistical Analysis Overview. All subjects randomised to receive Dupilumab had been on 300 mg q2w regimen until Week 24 and analysed as a pooled population for Week 24 assessments. Analysis was performed on ITT population. Data for this end point was planned to be analysed for the combined population of subjects who received Dupilumab.

End point type	Secondary
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End point timeframe:

Baseline, Week 24

Notes:

[6] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.

Justification: Analysis was performed on pooled dupilumab arm.

End point values	Placebo	Dupilumab 300 mg (24 Weeks Pooled Arm)		
Subject group type	Reporting group	Subject analysis set		
Number of subjects analysed	153	295		
Units: score on a scale				
least squares mean (standard error)	-1.00 (± 0.20)	-3.45 (± 0.15)		

Statistical analyses

Statistical analysis title	Dupilumab 300 mg (Pooled Arm) versus Placebo
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Statistical analysis description:

Data were analysed using a hybrid method of the WOCF and MI. The imputed completed data were analysed by fitting an ANCOVA model with corresponding baseline value, treatment group, asthma/NSAID-ERD status, prior surgery history, and regions as covariates. Statistical inference obtained from all imputed data was combined using Rubin's rule.

Comparison groups	Placebo v Dupilumab 300 mg (24 Weeks Pooled Arm)
Number of subjects included in analysis	448
Analysis specification	Pre-specified
Analysis type	superiority ^[7]
P-value	< 0.0001 ^[8]
Method	ANCOVA
Parameter estimate	LS mean difference
Point estimate	-2.44
Confidence interval	
level	95 %
sides	2-sided
lower limit	-2.87
upper limit	-2.02

Notes:

[7] - Testing according to the hierarchical testing procedure (only performed if previous end points were statistically significant).

[8] - Threshold for significance at 0.05 level.

Secondary: Change From Baseline at Week 24 in the University of Pennsylvania Smell Identification Test (UPSIT) Score

End point title	Change From Baseline at Week 24 in the University of Pennsylvania Smell Identification Test (UPSIT) Score ^[9]
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End point description:

The UPSIT was a 40-item test to measure the individual's ability to detect odors. Total score ranges from 0 (anosmia) to 40 (normal sense of smell), lower score indicated severe smell loss. LS means and SE were obtained from ANCOVA model described in Statistical Analysis Overview. All subjects randomised to receive Dupilumab had been on 300 mg q2w regimen until Week 24 and analysed as a pooled population for Week 24 assessments. Analysis was performed on ITT population. Here, 'number of subjects analysed' = subjects evaluable for this end point. Data for this end point was planned to be analysed for the combined population of subjects who received Dupilumab.

End point type	Secondary
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End point timeframe:

Baseline, Week 24

Notes:

[9] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period. Justification: Analysis was performed on pooled dupilumab arm.

End point values	Placebo	Dupilumab 300 mg (24 Weeks Pooled Arm)		
Subject group type	Reporting group	Subject analysis set		
Number of subjects analysed	150	287		
Units: score on a scale				
least squares mean (standard error)	-0.81 (± 0.71)	9.71 (± 0.56)		

Statistical analyses

Statistical analysis title	Dupilumab 300 mg (Pooled Arm) versus Placebo
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Statistical analysis description:

Data were analysed using a hybrid method of the WOCF and MI. The imputed completed data were analysed by fitting an ANCOVA model with corresponding baseline value, treatment group, asthma/NSAID-ERD status, prior surgery history, and regions as covariates. Statistical inference obtained from all imputed data was combined using Rubin's rule.

Comparison groups	Placebo v Dupilumab 300 mg (24 Weeks Pooled Arm)
Number of subjects included in analysis	437
Analysis specification	Pre-specified
Analysis type	superiority ^[10]
P-value	< 0.0001 ^[11]
Method	ANCOVA
Parameter estimate	LS mean difference
Point estimate	10.52
Confidence interval	
level	95 %
sides	2-sided
lower limit	8.98
upper limit	12.07

Notes:

[10] - Testing according to the hierarchical testing procedure (only performed if previous end points were statistically significant).

[11] - Threshold for significance at 0.05 level.

Secondary: Change From Baseline at Week 24 in Severity of Decreased/Loss of Smell as Assessed by Subject Daily

End point title	Change From Baseline at Week 24 in Severity of Decreased/Loss of Smell as Assessed by Subject Daily ^[12]
End point description:	
The severity of decreased/loss of sense of smell was reported by the subjects using a 0 to 3 categorical scale (where 0 = no symptoms, 1 = mild symptoms, 2 = moderate symptoms and 3 = severe symptoms), higher score indicated more severe symptoms. LS means and SE were obtained from ANCOVA model described in Statistical Analysis Overview. All subjects randomised to receive dupilumab had been on 300 mg q2w regimen until Week 24 and analysed as a pooled population for Week 24 assessments. Analysis was performed on ITT population. Data for this end point was planned to be analysed for the combined population of subjects who received Dupilumab.	
End point type	Secondary
End point timeframe:	
Baseline, Week 24	
Notes:	
[12] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.	
Justification: Analysis was performed on pooled dupilumab arm.	

End point values	Placebo	Dupilumab 300 mg (24 Weeks Pooled Arm)		
Subject group type	Reporting group	Subject analysis set		
Number of subjects analysed	153	295		
Units: score on a scale				
least squares mean (standard error)	-0.23 (± 0.08)	-1.21 (± 0.06)		

Statistical analyses

Statistical analysis title	Dupilumab 300 mg (Pooled Arm) versus Placebo
Statistical analysis description:	
Data were analysed using a hybrid method of the WOCF and MI. The imputed completed data were analysed by fitting an ANCOVA model with corresponding baseline value, treatment group, asthma/NSAID-ERD status, prior surgery history, and regions as covariates. Statistical inference obtained from all imputed data was combined using Rubin's rule.	
Comparison groups	Placebo v Dupilumab 300 mg (24 Weeks Pooled Arm)
Number of subjects included in analysis	448
Analysis specification	Pre-specified
Analysis type	superiority ^[13]
P-value	< 0.0001 ^[14]
Method	ANCOVA
Parameter estimate	LS mean difference
Point estimate	-0.98
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.15
upper limit	-0.81

Notes:

[13] - Testing according to the hierarchical testing procedure (only performed if previous end points were statistically significant).

[14] - Threshold for significance at 0.05 level.

Secondary: Change From Baseline at Week 24 in 22-item Sino-nasal Outcome Test

(SNOT-22) Scores

End point title	Change From Baseline at Week 24 in 22-item Sino-nasal Outcome Test (SNOT-22) Scores ^[15]
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End point description:

The SNOT-22 is a validated questionnaire was used to assess the impact of chronic rhinosinusitis phenotype with nasal polyps (CRSwNP) on health-related quality of life (HRQoL). It is a 22 item questionnaire with each item assigned a score ranging from 0 (no problem) to 5 (problem as bad as it can be). The total score may range from 0 (no disease) to 110 (worst disease), lower scores representing better health related quality of life. LS means and SE were obtained from ANCOVA model described in Statistical Analysis Overview. All subjects randomised to receive dupilumab had been on 300 mg q2w regimen until Week 24 and analysed as a pooled population for Week 24 assessments. Analysis was performed on ITT population. Here, 'number of subjects analysed' = subjects evaluable for this end point. Data for this end point was planned to be analysed for the combined population of subjects who received Dupilumab.

End point type	Secondary
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End point timeframe:

Baseline, Week 24

Notes:

[15] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.

Justification: Analysis was performed on pooled dupilumab arm.

End point values	Placebo	Dupilumab 300 mg (24 Weeks Pooled Arm)		
Subject group type	Reporting group	Subject analysis set		
Number of subjects analysed	152	292		
Units: score on a scale				
least squares mean (standard error)	-10.40 (\pm 1.61)	-27.77 (\pm 1.26)		

Statistical analyses

Statistical analysis title	Dupilumab 300 mg (Pooled Arm) versus Placebo
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Statistical analysis description:

Data were analysed using a hybrid method of the WOCF and MI. The imputed completed data were analysed by fitting an ANCOVA model with corresponding baseline value, treatment group, asthma/NSAID-ERD status, prior surgery history, and regions as covariates. Statistical inference obtained from all imputed data was combined using Rubin's rule.

Comparison groups	Placebo v Dupilumab 300 mg (24 Weeks Pooled Arm)
Number of subjects included in analysis	444
Analysis specification	Pre-specified
Analysis type	superiority ^[16]
P-value	< 0.0001 ^[17]
Method	ANCOVA
Parameter estimate	LS mean difference
Point estimate	-17.36
Confidence interval	
level	95 %
sides	2-sided
lower limit	-20.87
upper limit	-13.85

Notes:

[16] - Testing according to the hierarchical testing procedure (only performed if previous end points were statistically significant).

[17] - Threshold for significance at 0.05 level.

Secondary: Change From Baseline at Week 52 in Nasal Polyp Score

End point title	Change From Baseline at Week 52 in Nasal Polyp Score
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End point description:

NPS was the sum of right and left nostril scores, as evaluated by means of nasal endoscopy. For each nostril, NPS was graded based on polyp size from 0 to 4 (0 = no polyps to 4 = large polyps causing complete obstruction of the inferior nasal cavity), with a lower score indicating smaller-sized polyps. Total NPS was the sum of right and left nostril scores and ranges from 0 (no polyp) to 8 (large polyp), with highest score representing more severe disease. NPS was assessed by centralised, blinded, independent review of the nasal endoscopy video recordings. Data were analysed using a hybrid method of the WOCF and MI. LS means and SE were obtained from ANCOVA model described in Statistical Analysis Overview. Analysis was performed on ITT population. Here, "number of subjects analysed"= subjects evaluable for this end point.

End point type	Secondary
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End point timeframe:

Baseline, Week 52

End point values	Placebo	Dupilumab 300 mg q2w Then q4w	Dupilumab 300 mg q2w	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	152	145	149	
Units: score on a scale				
least squares mean (standard error)	0.16 (± 0.15)	-2.05 (± 0.15)	-2.24 (± 0.15)	

Statistical analyses

Statistical analysis title	Dupilumab 300 mg q2w Then q4w versus Placebo
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Statistical analysis description:

Data were analysed using a hybrid method of the WOCF and MI. The imputed completed data were analysed by fitting an ANCOVA model with corresponding baseline, treatment group, asthma/NSAID-ERD status, prior surgery history, and regions as covariates. Statistical inference obtained from all imputed data was combined using Rubin's rule.

Comparison groups	Dupilumab 300 mg q2w Then q4w v Placebo
Number of subjects included in analysis	297
Analysis specification	Pre-specified
Analysis type	superiority ^[18]
P-value	< 0.0001 ^[19]
Method	ANCOVA
Parameter estimate	LS mean difference
Point estimate	-2.21
Confidence interval	
level	95 %
sides	2-sided
lower limit	-2.59
upper limit	-1.83

Notes:

[18] - Testing according to the hierarchical testing procedure (only performed if previous end points were statistically significant).

[19] - Threshold for significance at 0.05 level.

Statistical analysis title	Dupilumab 300 mg q2w versus Placebo
Statistical analysis description:	
Data were analysed using a hybrid method of the WOCF and MI. The imputed completed data were analysed by fitting an ANCOVA model with corresponding baseline, treatment group, asthma/NSAID-ERD status, prior surgery history, and regions as covariates. Statistical inference obtained from all imputed data was combined using Rubin's rule.	
Comparison groups	Dupilumab 300 mg q2w v Placebo
Number of subjects included in analysis	301
Analysis specification	Pre-specified
Analysis type	superiority ^[20]
P-value	< 0.0001 ^[21]
Method	ANCOVA
Parameter estimate	LS mean difference
Point estimate	-2.41
Confidence interval	
level	95 %
sides	2-sided
lower limit	-2.78
upper limit	-2.03

Notes:

[20] - Testing according to the hierarchical testing procedure (only performed if previous end points were statistically significant).

[21] - Threshold for significance at 0.05 level.

Secondary: Change From Baseline at Week 52 in Nasal Congestion/Obstruction Symptom Severity Score

End point title	Change From Baseline at Week 52 in Nasal Congestion/Obstruction Symptom Severity Score
End point description:	
NC symptom severity was assessed by the subjects on a daily basis from Visit 1 and throughout the study using an e-diary on a scale of 0 to 3, where 0 = no symptoms, 1 = mild symptoms, 2 = moderate symptoms and 3 = severe symptoms, with higher scores indicated more severity. LS means and SE were obtained from ANCOVA model described in Statistical Analysis Overview. Analysis was performed on ITT population.	
End point type	Secondary
End point timeframe:	
Baseline, Week 52	

End point values	Placebo	Dupilumab 300 mg q2w Then q4w	Dupilumab 300 mg q2w	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	153	145	150	
Units: score on a scale				
least squares mean (standard error)	-0.37 (± 0.08)	-1.48 (± 0.08)	-1.36 (± 0.07)	

Statistical analyses

Statistical analysis title	Dupilumab 300 mg q2w Then q4w versus Placebo
Statistical analysis description:	
Data were analysed using a hybrid method of the WOCF and MI. The imputed completed data were analysed by fitting an ANCOVA model with corresponding baseline, treatment group, asthma/NSAID-ERD status, prior surgery history, and regions as covariates. Statistical inference obtained from all imputed data was combined using Rubin's rule.	
Comparison groups	Dupilumab 300 mg q2w Then q4w v Placebo
Number of subjects included in analysis	298
Analysis specification	Pre-specified
Analysis type	superiority ^[22]
P-value	< 0.0001 ^[23]
Method	ANCOVA
Parameter estimate	LS mean difference
Point estimate	-1.11
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.3
upper limit	-0.92

Notes:

[22] - Testing according to the hierarchical testing procedure (only performed if previous end points were statistically significant).

[23] - Threshold for significance at 0.05 level.

Statistical analysis title	Dupilumab 300 mg q2w versus Placebo
Statistical analysis description:	
Data were analysed using a hybrid method of the WOCF and MI. The imputed completed data were analysed by fitting an ANCOVA model with corresponding baseline, treatment group, asthma/NSAID-ERD status, prior surgery history, and regions as covariates. Statistical inference obtained from all imputed data was combined using Rubin's rule.	
Comparison groups	Dupilumab 300 mg q2w v Placebo
Number of subjects included in analysis	303
Analysis specification	Pre-specified
Analysis type	superiority ^[24]
P-value	< 0.0001 ^[25]
Method	ANCOVA
Parameter estimate	LS mean difference
Point estimate	-0.99
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.18
upper limit	-0.8

Notes:

[24] - Testing according to the hierarchical testing procedure (only performed if previous end points were statistically significant).

[25] - Threshold for significance at 0.05 level.

Secondary: Change From Baseline at Week 52 in 22-item Sino-nasal Outcome Test Scores

End point title	Change From Baseline at Week 52 in 22-item Sino-nasal Outcome Test Scores
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End point description:

The SNOT-22 is a validated questionnaire that was used to assess the impact of CRSwNP on HRQoL. It is a 22 item questionnaire with each item assigned a score ranging from 0 (no problem) to 5 (problem as bad as it can be). The total score may range from 0 (no disease) to 110 (worst disease), lower scores representing better health related quality of life. LS means and SE were obtained from ANCOVA model described in Statistical Analysis Overview. Analysis was performed on ITT population. Here, 'number of subjects analysed' = subjects evaluable for this end point.

End point type	Secondary
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End point timeframe:

Baseline, Week 52

End point values	Placebo	Dupilumab 300 mg q2w Then q4w	Dupilumab 300 mg q2w	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	152	145	147	
Units: score on a scale				
least squares mean (standard error)	-9.06 (\pm 1.61)	-30.42 (\pm 1.65)	-29.79 (\pm 1.64)	

Statistical analyses

Statistical analysis title	Dupilumab 300 mg q2w Then q4w versus Placebo
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Statistical analysis description:

Data were analysed using a hybrid method of the WOCF and MI. The imputed completed data were analysed by fitting an ANCOVA model with corresponding baseline, treatment group, asthma/NSAID-ERD status, prior surgery history, and regions as covariates. Statistical inference obtained from all imputed data was combined using Rubin's rule.

Comparison groups	Dupilumab 300 mg q2w Then q4w v Placebo
Number of subjects included in analysis	297
Analysis specification	Pre-specified
Analysis type	superiority ^[26]
P-value	< 0.0001 ^[27]
Method	ANCOVA
Parameter estimate	LS mean difference
Point estimate	-21.36
Confidence interval	
level	95 %
sides	2-sided
lower limit	-25.45
upper limit	-17.27

Notes:

[26] - Testing according to the hierarchical testing procedure (only performed if previous end points were statistically significant).

[27] - Threshold for significance at 0.05 level.

Statistical analysis title	Dupilumab 300 mg q2w versus Placebo
Statistical analysis description:	
Data were analysed using a hybrid method of the WOCF and MI. The imputed completed data were analysed by fitting an ANCOVA model with corresponding baseline, treatment group, asthma/NSAID-ERD status, prior surgery history, and regions as covariates. Statistical inference obtained from all imputed data was combined using Rubin's rule.	
Comparison groups	Dupilumab 300 mg q2w v Placebo
Number of subjects included in analysis	299
Analysis specification	Pre-specified
Analysis type	superiority ^[28]
P-value	< 0.0001 ^[29]
Method	ANCOVA
Parameter estimate	LS mean difference
Point estimate	-20.73
Confidence interval	
level	95 %
sides	2-sided
lower limit	-24.81
upper limit	-16.65

Notes:

[28] - Testing according to the hierarchical testing procedure (only performed if previous end points were statistically significant).

[29] - Threshold for significance at 0.05 level.

Secondary: Rescue Treatment Use: Estimate of Percentage of Subjects With Greater than or Equal to (\geq) 1 Event by Week 52 Obtained Using Kaplan-Meier Method

End point title	Rescue Treatment Use: Estimate of Percentage of Subjects With Greater than or Equal to (\geq) 1 Event by Week 52 Obtained Using Kaplan-Meier Method ^[30]
End point description:	
Rescue treatment was defined as usage of systemic corticosteroids (SCS) or NP surgery (actual or planned) during the treatment period. Rescue treatment included:	
<ul style="list-style-type: none">• SCS: betamethasone, deflazacort, dexamethasone sodium phosphate, hydrocortisone, meprednisone, methylprednisolone, methylprednisolone sodium succinate, prednisolone, prednisolone sodium succinate, prednisone, stelamin, triamcinolone, and triamcinolone acetonide.• Sino-nasal surgery for nasal polyps when there was worsening of signs and/or symptoms during the study.	
Estimate of percentage of subjects with event by Week 24 was obtained using Kaplan-Meier method. Analysis was performed on ITT population. Data for this end point was planned to be collected and analysed for the pooled population of subjects receiving Dupilumab.	
End point type	Secondary
End point timeframe:	
Baseline up to 52 weeks	

Notes:

[30] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.

Justification: Analysis was performed on pooled dupilumab arm.

End point values	Placebo	Dupilumab 300 mg (Pooled Arm)		
Subject group type	Reporting group	Subject analysis set		
Number of subjects analysed	153	295		
Units: percentage of subjects with event				
number (confidence interval 95%)				
SCS treatment	42.5 (34.5 to 50.2)	13.1 (9.0 to 18.0)		
NP surgery	28.3 (21.2 to 35.7)	5.5 (2.9 to 9.4)		

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline at Week 52 in Total Symptom Score

End point title	Change From Baseline at Week 52 in Total Symptom Score
End point description:	
<p>The TSS was the sum of subject-assessed nasal symptom scores for NC/obstruction, decreased/loss of sense of smell, and rhinorrhea (anterior/posterior nasal discharge), each accessed on 0-3 categorical scale (where 0 = no symptoms, 1 = mild symptoms, 2 = moderate symptoms and 3 = severe symptoms). Total score ranged from 0 (no symptoms) to 9 (severe symptoms). Higher score indicated more severe symptoms. Data was analysed using a hybrid method of the WOCF and MI. The imputed completed data were analysed by fitting an ANCOVA model with corresponding baseline value, treatment group, asthma/NSAID-ERD status, prior surgery history, and regions as covariates. Analysis was performed on ITT population.</p>	
End point type	Secondary
End point timeframe:	
Baseline, Week 52	

End point values	Placebo	Dupilumab 300 mg q2w Then q4w	Dupilumab 300 mg q2w	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	153	145	150	
Units: score on a scale				
least squares mean (standard error)	-0.93 (± 0.20)	-4.17 (± 0.20)	-3.79 (± 0.20)	

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline at Week 52 in the University of Pennsylvania Smell Identification Test Score

End point title	Change From Baseline at Week 52 in the University of Pennsylvania Smell Identification Test Score
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End point description:

The UPSIT was a 40-item test to measure the individual's ability to detect odors. Total score ranges from 0 (anosmia) to 40 (normal sense of smell), lower score indicated severe smell loss. Data was analysed using a hybrid method of the WOCF and MI. The imputed completed data were analysed by fitting an ANCOVA model with corresponding baseline value, treatment group, asthma/NSAID-ERD status, prior surgery history, and regions as covariates. Analysis was performed on ITT population. Here, 'number of subjects analysed' = subjects evaluable for this end point.

End point type	Secondary
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End point timeframe:

Baseline, Week 52

End point values	Placebo	Dupilumab 300 mg q2w Then q4w	Dupilumab 300 mg q2w	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	150	142	145	
Units: score on a scale				
least squares mean (standard error)	-0.78 (± 0.71)	9.99 (± 0.73)	9.53 (± 0.72)	

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline at Week 52 in Severity of Decreased/Loss of Smell

End point title	Change From Baseline at Week 52 in Severity of Decreased/Loss of Smell
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End point description:

The severity of decreased/loss of sense of smell was reported by the subjects using a 0 to 3 categorical scale (where 0 = no symptoms, 1 = mild symptoms, 2 = moderate symptoms and 3 = severe symptoms), higher score indicated more severe symptoms. Data was analysed using a hybrid method of the WOCF and MI. The imputed completed data were analysed by fitting an ANCOVA model with corresponding baseline value, treatment group, asthma/NSAID-ERD status, prior surgery history, and regions as covariates. Analysis was performed on ITT population.

End point type	Secondary
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End point timeframe:

Baseline, Week 52

End point values	Placebo	Dupilumab 300 mg q2w Then q4w	Dupilumab 300 mg q2w	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	153	145	150	
Units: score on a scale				
least squares mean (standard error)	-0.18 (± 0.09)	-1.49 (± 0.09)	-1.29 (± 0.08)	

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline at Week 52 in Opacification of Sinuses Measured by Lund-Mackay Score

End point title	Change From Baseline at Week 52 in Opacification of Sinuses Measured by Lund-Mackay Score
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End point description:

The LMK scoring system rated each of both the left and right frontal, maxillary, sphenoid, ostiomeatal complex, anterior ethmoid and posterior ethmoid sinuses using following grading: 0 = normal, 1 = partial opacification, 2 = total opacification. The total score was the sum of scores from each side and ranges from 0 (normal) to 24 (more opacified); higher score indicated more severe disease. Data was analysed using a hybrid method of the WOCF and MI. The imputed completed data were analysed by fitting an ANCOVA model with corresponding baseline value, treatment group, asthma/NSAID-ERD status, prior surgery history, and regions as covariates. Analysis was performed on ITT population. Here, 'number of subjects analysed' = subjects evaluable for this end point.

End point type	Secondary
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End point timeframe:

Baseline, Week 52

End point values	Placebo	Dupilumab 300 mg q2w Then q4w	Dupilumab 300 mg q2w	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	150	140	149	
Units: score on a scale				
least squares mean (standard error)	0.11 (± 0.37)	-5.60 (± 0.37)	-6.83 (± 0.37)	

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline at Week 24 in Visual Analogue Scale (VAS) for Rhinosinusitis

End point title	Change From Baseline at Week 24 in Visual Analogue Scale (VAS) for Rhinosinusitis ^[31]
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End point description:

The VAS for rhinosinusitis was used to evaluate the total disease severity. Subjects were asked to indicate on a 10 centimetres VAS the answer to the question, "How troublesome are your symptoms of your rhinosinusitis?" The range of VAS was from 0 (not troublesome) to 10 (worst thinkable troublesome), where higher score indicated worse thinkable troublesome. Data was analysed using a hybrid method of WOCF and MI. The imputed completed data were analysed by fitting an ANCOVA model with corresponding baseline value, treatment group, asthma/NSAID-ERD status, prior surgery history, and regions as covariates. All subjects randomised to receive Dupilumab had been on 300 mg

q2w regimen until Week 24 and analysed as a pooled population for Week 24 assessments. Analysis was performed on ITT population. Here, 'number of subjects analysed' = subjects evaluable for this end point. Data for this end point was planned to be analysed for the combined population of subjects who received Dupilumab.

End point type	Secondary
End point timeframe:	
Baseline, Week 24	

Notes:

[31] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.

Justification: Analysis was performed on pooled dupilumab arm.

End point values	Placebo	Dupilumab 300 mg (24 Weeks Pooled Arm)		
Subject group type	Reporting group	Subject analysis set		
Number of subjects analysed	150	289		
Units: centimeters				
least squares mean (standard error)	-1.39 (± 0.24)	-4.32 (± 0.19)		

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline at Week 52 in Visual Analogue Scale for Rhinosinusitis

End point title	Change From Baseline at Week 52 in Visual Analogue Scale for Rhinosinusitis
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End point description:

The VAS for rhinosinusitis was used to evaluate the total disease severity. The subjects were asked to indicate on a 10 centimetres VAS the answer to the question, "How troublesome are your symptoms of your rhinosinusitis?" The range of the VAS was from 0 (not troublesome) to 10 (worse thinkable troublesome), where higher score indicated worse thinkable troublesome. Data was analysed using a hybrid method of the WOCF and MI. The imputed completed data were analysed by fitting an ANCOVA model with corresponding baseline value, treatment group, asthma/NSAID-ERD status, prior surgery history, and regions as covariates. Analysis was performed on ITT population. Here, 'number of subjects analysed' = subjects evaluable for this end point.

End point type	Secondary
End point timeframe:	
Baseline, Week 52	

End point values	Placebo	Dupilumab 300 mg q2w Then q4w	Dupilumab 300 mg q2w	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	150	143	146	
Units: centimetres				
least squares mean (standard error)	-0.93 (± 0.26)	-4.39 (± 0.26)	-4.74 (± 0.26)	

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline at Week 24 in Nasal Peak Inspiratory Flow (NPIF)

End point title	Change From Baseline at Week 24 in Nasal Peak Inspiratory Flow (NPIF) ^[32]
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End point description:

NPIF evaluation represented a physiologic measure of the air flow through both nasal cavities during forced inspiration expressed in litres per minute. Higher NPIF values were indicative of better nasal air flow. Data was analysed using a hybrid method of the WOCF and MI. The imputed completed data were analysed by fitting an ANCOVA model with corresponding baseline value, treatment group, asthma/NSAID-ERD status, prior surgery history, and regions as covariates. All subjects randomised to receive Dupilumab had been on 300 mg q2w regimen until Week 24 and analysed as a pooled population for Week 24 assessments. Analysis was performed on ITT population. Data for this end point was planned to be analysed for the combined population of subjects who received dupilumab.

End point type	Secondary
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End point timeframe:

Baseline, Week 24

Notes:

[32] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.

Justification: Analysis was performed on pooled dupilumab arm.

End point values	Placebo	Dupilumab 300 mg (24 Weeks Pooled Arm)		
Subject group type	Reporting group	Subject analysis set		
Number of subjects analysed	153	295		
Units: litres per minute				
least squares mean (standard error)	18.65 (± 3.95)	55.29 (± 3.08)		

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline at Week 24 in Rhinorrhea Daily Symptom Score

End point title	Change From Baseline at Week 24 in Rhinorrhea Daily Symptom Score ^[33]
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End point description:

Rhinorrhea was reported by the subjects using a 0 to 3 categorical scale (where 0 = no symptoms, 1 = mild symptoms, 2 = moderate symptoms and 3 = severe symptoms), where higher scores indicated more severe symptoms. Data was analysed using a hybrid method of the WOCF and MI. The imputed completed data were analysed by fitting an ANCOVA model with corresponding baseline value, treatment group, asthma/NSAID-ERD status, prior surgery history, and regions as covariates. All subjects randomised to receive Dupilumab had been on 300 mg q2w regimen until Week 24 and analysed as a pooled population for Week 24 assessments. Analysis was performed on ITT population.

Data for this end point was planned to be analysed for the combined population of subjects who received Dupilumab.

End point type	Secondary
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End point timeframe:

Baseline, Week 24

Notes:

[33] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.

Justification: Analysis was performed on pooled dupilumab arm.

End point values	Placebo	Dupilumab 300 mg (24 Weeks Pooled Arm)		
Subject group type	Reporting group	Subject analysis set		
Number of subjects analysed	153	295		
Units: score on a scale				
least squares mean (standard error)	-0.40 (\pm 0.07)	-0.99 (\pm 0.05)		

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline at Week 52 in Rhinorrhea Daily Symptom Score

End point title	Change From Baseline at Week 52 in Rhinorrhea Daily Symptom Score
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End point description:

Rhinorrhea was reported by the subjects using a 0 to 3 categorical scale (where 0 = no symptoms, 1 = mild symptoms, 2 = moderate symptoms and 3 = severe symptoms), where higher scores indicated more severe symptoms. Data was analysed using a hybrid method of the WOCF and MI. The imputed completed data were analysed by fitting an ANCOVA model with corresponding baseline value, treatment group, asthma/NSAID-ERD status, prior surgery history, and regions as covariates. Analysis was performed on ITT population.

End point type	Secondary
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End point timeframe:

Baseline, Week 52

End point values	Placebo	Dupilumab 300 mg q2w Then q4w	Dupilumab 300 mg q2w	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	153	145	150	
Units: score on a scale				
least squares mean (standard error)	-0.35 (\pm 0.07)	-1.19 (\pm 0.07)	-1.15 (\pm 0.07)	

Statistical analyses

No statistical analyses for this end point

Secondary: Mean Total Systemic Corticosteroids Rescue Dose Prescribed During Treatment Period

End point title	Mean Total Systemic Corticosteroids Rescue Dose Prescribed During Treatment Period
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End point description:

SCS included: Betamethasone, deflazacort, dexamethasone, dexamethasone sodium phosphate, hydrocortisone, meprednisone, methylprednisolone, methylprednisolone sodium succinate, prednisolone, prednisolone sodium succinate, prednisone, stelamin, triamcinolone, and triamcinolone acetonide. For every subject, the total dose was calculated as (prescribed total daily dose*duration of SCS use). Then, mean of the total dose of 64 subjects (placebo group), 17 subjects (dupilumab 300 mg q2w then q4w) and 22 subjects (dupilumab 300 mg q2w) was derived. The analysis was performed on ITT population. Here, "number of subjects analysed" = subjects evaluable for this end point.

End point type	Secondary
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End point timeframe:

Baseline to Week 52

End point values	Placebo	Dupilumab 300 mg q2w Then q4w	Dupilumab 300 mg q2w	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	64	17	22	
Units: milligrams				
arithmetic mean (standard deviation)	547.56 (± 665.40)	282.38 (± 243.15)	389.68 (± 502.61)	

Statistical analyses

No statistical analyses for this end point

Secondary: Total Systemic Corticosteroids Rescue Intake Duration: Average Duration Per Subject

End point title	Total Systemic Corticosteroids Rescue Intake Duration: Average Duration Per Subject
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End point description:

Rescue treatment was defined as usage of SCS or NP surgery (actual or planned) during the treatment period. SCS Rescue intake duration was defined as the duration (in days) from start of SCS rescue medication till the end of SCS rescue treatment. Analysis was performed on ITT population. Here, 'number of subjects analysed' = subjects evaluable for this end point.

End point type	Secondary
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End point timeframe:

Baseline to Week 52

End point values	Placebo	Dupilumab 300 mg q2w Then q4w	Dupilumab 300 mg q2w	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	64	17	22	
Units: days				
arithmetic mean (standard deviation)	19.58 (\pm 17.67)	10.71 (\pm 9.00)	23.23 (\pm 55.23)	

Statistical analyses

No statistical analyses for this end point

Secondary: Changed From Baseline at Week 24 in Forced Expiratory Volume in 1 Second (FEV1) for Subjects With Asthma

End point title	Changed From Baseline at Week 24 in Forced Expiratory Volume in 1 Second (FEV1) for Subjects With Asthma ^[34]
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End point description:

FEV1 was the volume of air exhaled in the first second of a forced expiration as measured by spirometer. Data was analysed using a hybrid method of the WOCF and MI. The imputed completed data were analysed by fitting an ANCOVA model with corresponding baseline value, treatment group, prior surgery history, and regions as covariates. All subjects randomised to receive Dupilumab had been on 300 mg q2w regimen until Week 24 and analysed as a pooled population for Week 24 assessments. Analysis was performed on a subset of subjects which included all randomised subjects with asthma and had available data for this end point. Data for this end point was planned to be analysed for the combined population of subjects who received Dupilumab.

End point type	Secondary
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End point timeframe:

Baseline, Week 24

Notes:

[34] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.

Justification: Analysis was performed on pooled dupilumab arm.

End point values	Placebo	Dupilumab 300 mg (24 Weeks Pooled Arm)		
Subject group type	Reporting group	Subject analysis set		
Number of subjects analysed	90	176		
Units: litres				
least squares mean (standard error)	-0.05 (\pm 0.05)	0.17 (\pm 0.04)		

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline at Week 52 in Forced Expiratory Volume in 1 Second for Subjects With Asthma

End point title	Change From Baseline at Week 52 in Forced Expiratory Volume in 1 Second for Subjects With Asthma
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End point description:

FEV1 was the volume of air exhaled in the first second of a forced expiration as measured by spirometer. Data was analysed using a hybrid method of the WOCF and MI. The imputed completed data were analysed by fitting an ANCOVA model with corresponding baseline value, treatment group, prior surgery history, and regions as covariates. Analysis was performed on a subset of subjects which included all randomised subjects with asthma and had available data for this end point.

End point type	Secondary
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End point timeframe:

Baseline, Week 52

End point values	Placebo	Dupilumab 300 mg q2w Then q4w	Dupilumab 300 mg q2w	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	90	91	85	
Units: litres				
least squares mean (standard error)	-0.18 (± 0.05)	0.10 (± 0.05)	0.06 (± 0.05)	

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline at Week 24 in Asthma Control Questionnaire-6 (ACQ-6) for Subjects With Asthma

End point title	Change From Baseline at Week 24 in Asthma Control Questionnaire-6 (ACQ-6) for Subjects With Asthma ^[35]
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End point description:

ACQ-6: 6 questions to assess common asthma symptoms (woken by asthma, symptoms on waking, activity limitation, shortness of breath, wheezing, puffs/inhalations use). Subjects respond to asthma symptom questions on 7-point scale (range 0 = no impairment to 6 = maximum impairment. ACQ-6 score was mean of all 6 questions scores; range 0 (totally controlled) to 6 (severely uncontrolled), higher scores = low asthma control. Data analysed using hybrid method of WOCF and MI. The imputed completed data analysed by an ANCOVA model with corresponding baseline value, treatment, asthma status, prior surgery history and regions as covariates. All subjects randomised to receive Dupilumab had been on 300 mg q2w regimen until Week 24; analysed as pooled population for Week 24 assessments. Analysis performed on subset of subjects included all randomised subjects with asthma, had available data for this end point. Data was planned to be analysed for combined population of subjects who received Dupilumab.

End point type	Secondary
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End point timeframe:

Baseline, Week 24

Notes:

[35] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.

Justification: Analysis was performed on pooled dupilumab arm.

End point values	Placebo	Dupilumab 300 mg (24 Weeks Pooled Arm)		
Subject group type	Reporting group	Subject analysis set		
Number of subjects analysed	90	171		
Units: score on a scale				
least squares mean (standard error)	0.08 (± 0.09)	-0.78 (± 0.07)		

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline at Week 52 in Asthma Control Questionnaire-6 for Subjects With Asthma

End point title	Change From Baseline at Week 52 in Asthma Control Questionnaire-6 for Subjects With Asthma
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End point description:

ACQ-6 had 6 questions which assessed the most common asthma symptoms (woken by asthma, symptoms on waking, activity limitation, shortness of breath, wheezing, puffs/inhalations use). Subjects were asked to recall how their asthma had been during the previous week and to respond to the symptom questions on a 7-point scale ranged from 0 = no impairment to 6 = maximum impairment. The ACQ-6 score was the mean of the scores of all 6 questions and therefore, ranged from 0 (totally controlled) to 6 (severely uncontrolled), with higher scores indicated lower asthma control. Data were analysed using a hybrid method of the WOCF and MI. The imputed completed data were analysed by fitting an ANCOVA model with corresponding baseline value, treatment, asthma status, prior surgery history, and regions as covariates. Analysis was performed on a subset of subjects which included all randomised subjects with Asthma and had available data for this end point.

End point type	Secondary
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End point timeframe:

Baseline, Week 52

End point values	Placebo	Dupilumab 300 mg q2w Then q4w	Dupilumab 300 mg q2w	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	90	89	82	
Units: score on a scale				
least squares mean (standard error)	0.12 (± 0.10)	-0.76 (± 0.10)	-0.83 (± 0.10)	

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline at Week 24 in Nasal Congestion/Obstruction Symptom Severity Score: Subgroup of Subjects With Asthma

End point title	Change From Baseline at Week 24 in Nasal Congestion/Obstruction Symptom Severity Score: Subgroup of Subjects With Asthma ^[36]
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End point description:

NC symptom severity was assessed by the subjects on a daily basis from Visit 1 and throughout the study using an e-diary on a scale of 0 to 3, where 0 = no symptoms, 1 = mild symptoms, 2 = moderate symptoms and 3 = severe symptoms, with higher scores indicated more severity. Data were analysed using a hybrid method of the WOCF and MI. The imputed completed data were analysed by fitting ANCOVA model with corresponding baseline, treatment group, prior surgery history, and regions as covariates. All subjects randomised to receive Dupilumab had been on 300 mg q2w regimen until Week 24 and analysed as a pooled population for Week 24 assessments. Analysis was performed on a subset of subjects which included all randomised subjects with asthma.

End point type	Secondary
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End point timeframe:

Baseline, Week 24

Notes:

[36] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.

Justification: Analysis was performed on pooled dupilumab arm.

End point values	Placebo	Dupilumab 300 mg (24 Weeks Pooled Arm)		
Subject group type	Reporting group	Subject analysis set		
Number of subjects analysed	91	176		
Units: score on a scale				
least squares mean (standard error)	-0.39 (± 0.09)	-1.36 (± 0.07)		

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline at Week 52 in Nasal Congestion/Obstruction Symptom Severity Score: Subgroup of Subjects With Asthma

End point title	Change From Baseline at Week 52 in Nasal Congestion/Obstruction Symptom Severity Score: Subgroup of Subjects With Asthma
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End point description:

NC symptom severity was assessed by the subjects on a daily basis from Visit 1 and throughout the study using an e-diary on a scale of 0 to 3, where 0 = no symptoms, 1 = mild symptoms, 2 = moderate symptoms and 3 = severe symptoms, with higher scores indicated more severity. Data were analysed using a hybrid method of the WOCF and MI. The imputed completed data were analysed by fitting ANCOVA model with corresponding baseline, treatment group, prior surgery history, and regions as covariates. Analysis was performed on a subset of subjects which included all randomised subjects with asthma.

End point type	Secondary
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End point timeframe:

Baseline, Week 52

End point values	Placebo	Dupilumab 300 mg q2w Then q4w	Dupilumab 300 mg q2w	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	91	91	85	
Units: score on a scale				
least squares mean (standard error)	-0.34 (± 0.09)	-1.51 (± 0.09)	-1.44 (± 0.09)	

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline at Week 24 in Nasal Congestion/Obstruction Symptom Severity Score: Subgroup of Subjects With Prior Nasal Polyp Surgery

End point title	Change From Baseline at Week 24 in Nasal Congestion/Obstruction Symptom Severity Score: Subgroup of Subjects With Prior Nasal Polyp Surgery ^[37]
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End point description:

NC symptom severity was assessed by the subjects on a daily basis from Visit 1 and throughout the study using an e-diary on a scale of 0 to 3, where 0 = no symptoms, 1 = mild symptoms, 2 = moderate symptoms and 3 = severe symptoms, with higher scores indicated more severity. Data were analysed using a hybrid method of the WOCF and MI. The imputed completed data were analysed by fitting ANCOVA model with corresponding baseline, treatment group, prior surgery history, and regions as covariates. All subjects randomised to receive dupilumab had been on 300 mg q2w regimen until Week 24 and analysed as a pooled population for Week 24 assessments. Analysis was performed on a subset of subjects which included all randomised subjects with prior NP surgery history.

End point type	Secondary
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End point timeframe:

Baseline, Week 24

Notes:

[37] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.

Justification: Analysis was performed on pooled dupilumab arm.

End point values	Placebo	Dupilumab 300 mg (24 Weeks Pooled Arm)		
Subject group type	Reporting group	Subject analysis set		
Number of subjects analysed	88	173		
Units: score on a scale				
least squares mean (standard error)	-0.27 (± 0.10)	-1.30 (± 0.08)		

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline at Week 52 in Nasal Congestion/Obstruction Symptom Severity Score: Subgroup of Subjects With Prior Nasal Polyp Surgery

End point title	Change From Baseline at Week 52 in Nasal Congestion/Obstruction Symptom Severity Score: Subgroup of Subjects With Prior Nasal Polyp Surgery
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End point description:

NC symptom severity was assessed by the subjects on a daily basis from Visit 1 and throughout the study using an e-diary on a scale of 0 to 3, where 0 = no symptoms, 1 = mild symptoms, 2 = moderate symptoms and 3 = severe symptoms, with higher scores indicated more severity. Data were analysed using a hybrid method of the WOCF and MI. The imputed completed data were analysed by fitting an ANCOVA model with corresponding baseline, treatment group, asthma/NSAID-ERD status, and regions as covariates. Analysis was performed on a subset of subjects which included all randomised subjects with prior NP surgery history.

End point type	Secondary
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End point timeframe:

Baseline, Week 52

End point values	Placebo	Dupilumab 300 mg q2w Then q4w	Dupilumab 300 mg q2w	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	88	85	88	
Units: score on a scale				
least squares mean (standard error)	-0.25 (± 0.10)	-1.54 (± 0.10)	-1.35 (± 0.09)	

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline at Week 24 in Nasal Polyp Score: Subgroup of Subjects With Asthma

End point title	Change From Baseline at Week 24 in Nasal Polyp Score: Subgroup of Subjects With Asthma ^[38]
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End point description:

NPS was the sum of right and left nostril scores, as evaluated by means of nasal endoscopy. For each nostril, NPS was graded from 0 to 4 (0 = no polyps to 4 = large polyps causing complete obstruction of the inferior nasal cavity), with a lower score indicating smaller-sized polyps. Total NPS was the sum of right and left nostril scores and ranges from 0 (no polyp) to 8 (large polyp), with highest score representing more severe disease. NPS was assessed by centralised, blinded, independent review of the nasal endoscopy video recordings. Data were analysed using a hybrid method of the WOCF and MI. LS mean and SE were obtained from ANCOVA model. All subjects randomised to receive Dupilumab had been on 300 mg q2w regimen until Week 24 and analysed as a pooled population for Week 24 assessments. Analysis was performed on a subset of subjects which included all randomised subjects with asthma and had available data for this end point.

End point type	Secondary
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End point timeframe:

Baseline, Week 24

Notes:

[38] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.

Justification: Analysis was performed on pooled dupilumab arm.

End point values	Placebo	Dupilumab 300 mg (24 Weeks Pooled Arm)		
Subject group type	Reporting group	Subject analysis set		
Number of subjects analysed	90	176		
Units: score on a scale				
least squares mean (standard error)	0.13 (± 0.17)	-1.88 (± 0.13)		

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline at Week 52 in Nasal Polyp Score: Subgroup of Subjects With Asthma

End point title	Change From Baseline at Week 52 in Nasal Polyp Score: Subgroup of Subjects With Asthma
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End point description:

NPS was the sum of right and left nostril scores, as evaluated by means of nasal endoscopy. For each nostril, NPS was graded from 0 to 4 (0 = no polyps to 4 = large polyps causing complete obstruction of the inferior nasal cavity), with a lower score indicating smaller-sized polyps. Total NPS was the sum of right and left nostril scores and ranges from 0 (no polyp) to 8 (large polyp), with highest score representing more severe disease. NPS was assessed by centralised, blinded, independent review of the nasal endoscopy video recordings. Data were analysed using a hybrid method of the WOCF and MI. LS mean and SE were obtained from ANCOVA model. Analysis was performed on a subset of subjects which included all randomised subjects with asthma and had available data for this end point.

End point type	Secondary
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End point timeframe:

Baseline, Week 52

End point values	Placebo	Dupilumab 300 mg q2w Then q4w	Dupilumab 300 mg q2w	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	90	91	85	
Units: score on a scale				
least squares mean (standard error)	0.29 (± 0.20)	-2.25 (± 0.20)	-2.34 (± 0.20)	

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline at Week 24 in Nasal Polyp Score: Subgroup of Subjects With Prior Nasal Polyp Surgery

End point title	Change From Baseline at Week 24 in Nasal Polyp Score: Subgroup of Subjects With Prior Nasal Polyp Surgery ^[39]
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End point description:

NPS was the sum of right and left nostril scores, as evaluated by means of nasal endoscopy. For each nostril, NPS was graded from 0 to 4 (0 = no polyps to 4 = large polyps causing complete obstruction of

the inferior nasal cavity), with a lower score indicating smaller-sized polyps. Total NPS was the sum of right and left nostril scores and ranges from 0 (no polyp) to 8 (large polyp), with highest score representing more severe disease. NPS was assessed by centralised, blinded, independent review of the nasal endoscopy video recordings. Data were analysed using a hybrid method of the WOCF and MI. LS mean and SE were obtained from ANCOVA model. All subjects randomised to receive Dupilumab had been on 300 mg q2w regimen until Week 24 and analysed as a pooled population for Week 24 assessments. Analysis was performed on a subset of subjects which included all randomised subjects with prior NP surgery history and had available data for this end point.

End point type	Secondary
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End point timeframe:

Baseline, Week 24

Notes:

[39] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.

Justification: Analysis was performed on pooled dupilumab arm.

End point values	Placebo	Dupilumab 300 mg (24 Weeks Pooled Arm)		
Subject group type	Reporting group	Subject analysis set		
Number of subjects analysed	88	172		
Units: score on a scale				
least squares mean (standard error)	0.22 (± 0.19)	-1.73 (± 0.15)		

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline at Week 52 in Nasal Polyp Score: Subgroup of Subjects With Prior Nasal Polyp Surgery

End point title	Change From Baseline at Week 52 in Nasal Polyp Score: Subgroup of Subjects With Prior Nasal Polyp Surgery
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End point description:

NPS was the sum of right and left nostril scores, as evaluated by means of nasal endoscopy. For each nostril, NPS was graded from 0 to 4 (0 = no polyps to 4 = large polyps causing complete obstruction of the inferior nasal cavity), with a lower score indicating smaller-sized polyps. Total NPS was the sum of right and left nostril scores and ranges from 0 (no polyp) to 8 (large polyp), with highest score representing more severe disease. NPS was assessed by centralised, blinded, independent review of the nasal endoscopy video recordings. Data were analysed using a hybrid method of the WOCF and MI. LS mean and SE were obtained from ANCOVA model. Analysis was performed on a subset of subjects which included all randomised subjects with prior NP surgery history and had available data for this end point.

End point type	Secondary
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End point timeframe:

Baseline, Week 52

End point values	Placebo	Dupilumab 300 mg q2w Then q4w	Dupilumab 300 mg q2w	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	88	85	87	
Units: score on a scale				
least squares mean (standard error)	0.21 (± 0.21)	-2.22 (± 0.22)	-2.56 (± 0.21)	

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline at Week 24 in Opacification of Sinuses Measured by Lund Mackay Score: Subgroup of Subjects With Asthma

End point title	Change From Baseline at Week 24 in Opacification of Sinuses Measured by Lund Mackay Score: Subgroup of Subjects With Asthma ^[40]
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End point description:

The LMK scoring system rated each of both the left and right frontal, maxillary, sphenoid, ostiomeatal complex, anterior ethmoid and posterior ethmoid sinuses using following grading: 0 = normal, 1 = partial opacification, 2 = total opacification. The total score was the sum of scores from each side and ranges from 0 (normal) to 24 (more opacified); higher score indicated more severe disease. Data was analysed using a hybrid method of the WOCF and MI. The imputed completed data were analysed by fitting an ANCOVA model with corresponding baseline value, treatment group, asthma/NSAID-ERD status, prior surgery history, and regions as covariates. All subjects randomised to receive dupilumab had been on 300 mg q2w regimen until Week 24 and analysed as a pooled population for Week 24 assessments. Analysis was performed on a subset of subjects which included all randomised subjects with asthma and had available data for end point.

End point type	Secondary
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End point timeframe:

Baseline, Week 24

Notes:

[40] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.

Justification: Analysis was performed on pooled dupilumab arm.

End point values	Placebo	Dupilumab 300 mg (24 Weeks Pooled Arm)		
Subject group type	Reporting group	Subject analysis set		
Number of subjects analysed	89	174		
Units: score on a scale				
least squares mean (standard error)	-0.33 (± 0.40)	-5.86 (± 0.31)		

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline at Week 52 in Opacification of Sinuses Measured by Lund Mackay Score: Subgroup of Subjects With Asthma

End point title	Change From Baseline at Week 52 in Opacification of Sinuses
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End point description:

The LMK scoring system rated each of both the left and right frontal, maxillary, sphenoid, ostiomeatal complex, anterior ethmoid and posterior ethmoid sinuses using following grading: 0 = normal, 1 = partial opacification, 2 = total opacification. The total score was the sum of scores from each side and ranges from 0 (normal) to 24 (more opacified); higher score indicated more severe disease. Data was analysed using a hybrid method of the WOCF and MI. The imputed completed data were analysed by fitting an ANCOVA model with corresponding baseline value, treatment group, asthma/NSAID-ERD status, prior surgery history, and regions as covariates. Analysis was performed on a subset of subjects which included all randomised subjects with asthma and had available data for this end point.

End point type	Secondary
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End point timeframe:

Baseline, Week 52

End point values	Placebo	Dupilumab 300 mg q2w Then q4w	Dupilumab 300 mg q2w	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	89	89	85	
Units: score on a scale				
least squares mean (standard error)	-0.20 (± 0.46)	-6.23 (± 0.45)	-7.22 (± 0.47)	

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline at Week 24 in Opacification of Sinuses Measured by Lund Mackay Score: Subgroup of Subjects With Prior Nasal Surgery

End point title	Change From Baseline at Week 24 in Opacification of Sinuses Measured by Lund Mackay Score: Subgroup of Subjects With Prior Nasal Surgery ^[41]
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End point description:

The LMK scoring system rated each of both the left and right frontal, maxillary, sphenoid, ostiomeatal complex, anterior ethmoid and posterior ethmoid sinuses using following grading: 0 = normal, 1 = partial opacification, 2 = total opacification. The total score was the sum of scores from each side and ranges from 0 (normal) to 24 (more opacified); higher score indicated more severe disease. Data were analysed using a hybrid method of the WOCF and MI. The imputed completed data were analysed by fitting an ANCOVA model with corresponding baseline, treatment group, asthma/NSAID-ERD status, and regions as covariates. All subjects randomised to receive Dupilumab had been on 300 mg q2w regimen until Week 24 and analysed as a pooled population for Week 24 assessments. Analysis was performed on a subset of subjects which included all randomised subjects with prior NP surgery history and had available data for this end point.

End point type	Secondary
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End point timeframe:

Baseline, Week 24

Notes:

[41] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.

Justification: Analysis was performed on pooled dupilumab arm.

End point values	Placebo	Dupilumab 300 mg (24 Weeks Pooled Arm)		
Subject group type	Reporting group	Subject analysis set		
Number of subjects analysed	85	169		
Units: score on a scale				
least squares mean (standard error)	-0.10 (± 0.42)	-5.42 (± 0.33)		

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline at Week 52 in Opacification of Sinuses Measured by Lund Mackay Score: Subgroup of Subjects With Prior Nasal Polyp Surgery

End point title	Change From Baseline at Week 52 in Opacification of Sinuses Measured by Lund Mackay Score: Subgroup of Subjects With Prior Nasal Polyp Surgery
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End point description:

The LMK scoring system rated each of both the left and right frontal, maxillary, sphenoid, ostiomeatal complex, anterior ethmoid and posterior ethmoid sinuses using following grading: 0 = normal, 1 = partial opacification, 2 = total opacification. The total score was the sum of scores from each side and ranges from 0 (normal) to 24 (more opacified); higher score indicated more severe disease. Data were analysed using a hybrid method of the WOCF and MI. The imputed completed data were analysed by fitting an ANCOVA model with corresponding baseline, treatment group, asthma/NSAID-ERD status, and regions as covariates. Analysis was performed on a subset of subjects which included all randomised subjects with prior NP surgery history and had available data for this end point.

End point type	Secondary
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End point timeframe:

Baseline, Week 52

End point values	Placebo	Dupilumab 300 mg q2w Then q4w	Dupilumab 300 mg q2w	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	85	82	87	
Units: score on a scale				
least squares mean (standard error)	-0.06 (± 0.50)	-6.01 (± 0.50)	-7.45 (± 0.49)	

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Subjects With Treatment-emergent Adverse Events (TEAEs), Serious Adverse Events (SAEs) and TEAEs Leading to Treatment Discontinuation

End point title	Number of Subjects With Treatment-emergent Adverse Events (TEAEs), Serious Adverse Events (SAEs) and TEAEs Leading to Treatment Discontinuation ^[42]
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End point description:

An Adverse Event (AE) was defined as any untoward medical occurrence that did not necessarily have to have a causal relationship with the study treatment. TEAEs were defined as AEs that developed or worsened in grade or became serious during TEAE period which was defined as the period from the time of first dose of drug until 84 days following the last administration of drug. SAE was defined as any untoward medical occurrence that at any dose: results in death, is life-threatening, requires inpatient hospitalisation or prolongation of existing hospitalisation, results in persistent or significant disability/incapacity, is a congenital anomaly/birth defect, is a medically important event. Analysis was performed on safety population which included all subjects who received at least 1 dose or part of a dose of the investigational medicinal product (IMP), analysed according to the treatment actually received.

End point type	Secondary
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End point timeframe:

Baseline up to 84 days after last dose of study drug (up to 64 weeks)

Notes:

[42] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.

Justification: Dupilumab 300 mg q2w Then q4w arm is included in the form of subject analysis set.

End point values	Placebo	Dupilumab 300 mg q2w	Dupilumab 300 mg q2w Then q4w	
Subject group type	Reporting group	Reporting group	Subject analysis set	
Number of subjects analysed	150	149	148	
Units: subjects				
number (not applicable)				
Any TEAE	138	125	134	
Any treatment emergent SAE	16	8	12	
Any TEAE leading to death	0	0	1	
TEAE leading to treatment discontinuation	17	6	2	

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline at Week 24 in European Quality of Life 5 Dimension Scale (EQ-5D) Visual Analog Scale Score

End point title	Change From Baseline at Week 24 in European Quality of Life 5 Dimension Scale (EQ-5D) Visual Analog Scale Score ^[43]
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End point description:

The EQ-5D was a standardized HRQoL questionnaire consisting of EQ-5D descriptive system and EQ VAS. The EQ-5D descriptive system comprised of 5 dimensions: mobility, self-care, usual activities, pain/discomfort and anxiety/depression. Each dimension had 5 levels: no problems, slight problems, moderate problems, severe problems, and extreme problems. EQ VAS recorded the subject's self-rated health on a vertical VAS that allowed them to indicate their health state that can range from 0 (worst imaginable) to 100 (best imaginable). All subjects randomised to receive Dupilumab had been on 300 mg q2w regimen until Week 24 and analysed as a pooled population for Week 24 assessments. Analysis was performed on ITT population. Here, 'number of subjects analysed' = subjects evaluable for this end point. Data for this end point planned to be analysed for the combined population of subjects who received Dupilumab.

End point type	Secondary
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End point timeframe:

Baseline, Week 24

Notes:

[43] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.

Justification: Analysis was performed on pooled dupilumab arm.

End point values	Placebo	Dupilumab 300 mg (24 Weeks Pooled Arm)		
Subject group type	Reporting group	Subject analysis set		
Number of subjects analysed	151	289		
Units: score on a scale				
least squares mean (standard error)	3.91 (\pm 1.50)	10.83 (\pm 1.16)		

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline at Week 52 in European Quality of Life 5 Dimension Scale Visual Analog Scale Score

End point title	Change From Baseline at Week 52 in European Quality of Life 5 Dimension Scale Visual Analog Scale Score
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End point description:

The EQ-5D was a standardized HRQoL questionnaire consisting of EQ-5D descriptive system and EQ VAS. The EQ-5D descriptive system comprised of 5 dimensions: mobility, self-care, usual activities, pain/discomfort and anxiety/depression. Each dimension had 5 levels: no problems, slight problems, moderate problems, severe problems, and extreme problems. EQ VAS recorded the subject's self-rated health on a vertical VAS that allowed them to indicate their health state that can range from 0 (worst imaginable) to 100 (best imaginable). Analysis was performed on ITT population. Here, 'number of subjects analysed' = subjects evaluable for this end point.

End point type	Secondary
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End point timeframe:

Baseline, Week 52

End point values	Placebo	Dupilumab 300 mg q2w Then q4w	Dupilumab 300 mg q2w	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	151	143	146	
Units: score on a scale				
least squares mean (standard error)	1.38 (\pm 1.60)	11.98 (\pm 1.63)	13.14 (\pm 1.62)	

Statistical analyses

No statistical analyses for this end point

Secondary: Functional Dupilumab Concentration in Serum

End point title	Functional Dupilumab Concentration in Serum ^[44]
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End point description:

Analysis performed on pharmacokinetics population which included all subjects who received at least 1 dose of IMP with at least 1 evaluable functional dupilumab concentration result. Here, 'n' = number of subjects with available data for each time point. Data for this end point was not planned to be collected and analysed for placebo. One subject randomised to dupilumab 300 mg q2w arm received 1 dose of placebo and was therefore counted in the 300 mg q2w then q4w arm.

End point type	Secondary
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End point timeframe:

Baseline, Week 2, Week 4, Week 16, Week 24, Week 40, End of treatment (Week 52), End of study (Week 64)

Notes:

[44] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.

Justification: This endpoint is not analysed for placebo.

End point values	Dupilumab 300 mg q2w	Dupilumab 300 mg q2w Then q4w		
Subject group type	Reporting group	Subject analysis set		
Number of subjects analysed	149	146		
Units: nanogram/millilitre				
arithmetic mean (standard deviation)				
Baseline (n = 146, 145)	0.00 (± 0.00)	0.00 (± 0.00)		
Week 2 (n = 146, 143)	22285.67 (± 8459.01)	21545.79 (± 9120.36)		
Week 4 (n = 144, 144)	37326.31 (± 14226.12)	33760.62 (± 16419.72)		
Week 16 (n = 141, 143)	74382.04 (± 33118.68)	70503.07 (± 31234.86)		
Week 24 (n = 143, 144)	79890.06 (± 35361.97)	75929.41 (± 35466.00)		
Week 40 (n = 138, 141)	80526.37 (± 34048.41)	21052.06 (± 18588.68)		
Week 52 (n = 135, 141)	75872.58 (± 34127.85)	17276.13 (± 16353.20)		
Week 64 (n = 135, 139)	851.30 (± 2682.21)	53.60 (± 160.53)		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Subjects With Treatment-Emergent And Treatment-Boosted Anti-drug Antibodies (ADA) Response

End point title	Number of Subjects With Treatment-Emergent And Treatment-Boosted Anti-drug Antibodies (ADA) Response ^[45]
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End point description:

ADA response were categorised as: treatment emergent and treatment boosted response. 1) Treatment emergent was defined as a positive response in the ADA assay post first dose, when baseline results are negative or missing. 2) Treatment boosted was defined as: an ADA positive response in the assay post first dose that is greater-than or equal to 4-fold over baseline titer levels, when baseline results are positive. The analysis was performed on ADA population which included subjects who received at least 1 dose of IMP with at least one evaluable ADA serum sample that was assayed successfully in the ADA assay (either 'ADA negative' or 'ADA positive') following the first dose of the study medication. Two subjects randomised to placebo arm accidentally received 1 dose of dupilumab 300 mg and therefore counted in the 300 mg q2w then q4w arm. One subject randomised to the dupilumab 300 mg q2w arm

received 1 dose of placebo and was therefore counted in the 300 mg q2w then q4w arm.

End point type	Secondary
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End point timeframe:

Baseline to Week 52

Notes:

[45] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.

Justification: Dupilumab 300 mg q2w Then q4w arm is included in the form of subject analysis set.

End point values	Placebo	Dupilumab 300 mg q2w	Dupilumab 300 mg q2w Then q4w	
Subject group type	Reporting group	Reporting group	Subject analysis set	
Number of subjects analysed	149	148	148	
Units: subjects				
number (not applicable)				
With treatment-emergent ADA	6	8	18	
With treatment-boosted ADA	1	0	0	

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

All AEs were collected from signature of the informed consent form up to 64 weeks regardless of seriousness or relationship to investigational product.

Adverse event reporting additional description:

Reported AEs were TEAEs that developed/worsened during the 'on treatment period' (defined as the period from the time of first dose of drug until 84 days following the last administration of drug).

Analysis was performed on safety population.

Assessment type	Systematic
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Dictionary used

Dictionary name	MedDRA
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Dictionary version	21.0
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Reporting groups

Reporting group title	Placebo
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Reporting group description:

Placebo (for dupilumab), 1 SC injection q2w from Day 1 of Week 0 up to Week 52 added to background therapy of intranasal MFNS at stable dose. Two subjects randomised to this arm received 1 dose of dupilumab were included in Dupilumab 300 mg q2w then q4w arm.

Reporting group title	Dupilumab 300 mg q2w Then q4w
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Reporting group description:

Dupilumab 300 mg SC injection q2w from Day 1 of Week 0 up to Week 24 and then 300 mg q4w until Week 52 added to background therapy of intranasal MFNS at stable dose. After Week 24, Dupilumab administration was alternated with matched placebo injection every other week up to Week 50.

Reporting group title	Dupilumab 300 mg q2w
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Reporting group description:

Dupilumab 300 mg SC injection q2w from Day 1 of Week 0 up to Week 52 added to background therapy of intranasal MFNS at stable dose. One subject randomised to this arm received 1 dose of Placebo were included in Dupilumab 300 mg q2w then q4w arm.

Serious adverse events	Placebo	Dupilumab 300 mg q2w Then q4w	Dupilumab 300 mg q2w
Total subjects affected by serious adverse events			
subjects affected / exposed	16 / 150 (10.67%)	12 / 148 (8.11%)	8 / 149 (5.37%)
number of deaths (all causes)	0	1	0
number of deaths resulting from adverse events			
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Nasal Neoplasm Benign			
subjects affected / exposed	0 / 150 (0.00%)	0 / 148 (0.00%)	1 / 149 (0.67%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Vascular disorders			
Peripheral Arterial Occlusive Disease			

subjects affected / exposed	1 / 150 (0.67%)	0 / 148 (0.00%)	0 / 149 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
General disorders and administration site conditions			
Pyrexia			
subjects affected / exposed	0 / 150 (0.00%)	1 / 148 (0.68%)	0 / 149 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Immune system disorders			
Eosinophilic Granulomatosis With Polyangiitis			
subjects affected / exposed	0 / 150 (0.00%)	1 / 148 (0.68%)	0 / 149 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Social circumstances			
Miscarriage Of Partner			
subjects affected / exposed	1 / 150 (0.67%)	0 / 148 (0.00%)	0 / 149 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory, thoracic and mediastinal disorders			
Asthmatic Crisis			
subjects affected / exposed	0 / 150 (0.00%)	1 / 148 (0.68%)	0 / 149 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Chronic Rhinosinusitis With Nasal Polyps			
subjects affected / exposed	1 / 150 (0.67%)	0 / 148 (0.00%)	0 / 149 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nasal Polyps			
subjects affected / exposed	3 / 150 (2.00%)	1 / 148 (0.68%)	0 / 149 (0.00%)
occurrences causally related to treatment / all	0 / 3	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Investigations			
Weight Decreased			

subjects affected / exposed	1 / 150 (0.67%)	0 / 148 (0.00%)	0 / 149 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Injury, poisoning and procedural complications			
Facial Bones Fracture			
subjects affected / exposed	2 / 150 (1.33%)	0 / 148 (0.00%)	0 / 149 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Fall			
subjects affected / exposed	0 / 150 (0.00%)	1 / 148 (0.68%)	0 / 149 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Femur Fracture			
subjects affected / exposed	0 / 150 (0.00%)	0 / 148 (0.00%)	1 / 149 (0.67%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hand Fracture			
subjects affected / exposed	1 / 150 (0.67%)	0 / 148 (0.00%)	0 / 149 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Humerus Fracture			
subjects affected / exposed	1 / 150 (0.67%)	0 / 148 (0.00%)	0 / 149 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Open Globe Injury			
subjects affected / exposed	0 / 150 (0.00%)	1 / 148 (0.68%)	0 / 149 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Traumatic Intracranial Haemorrhage			
subjects affected / exposed	0 / 150 (0.00%)	1 / 148 (0.68%)	0 / 149 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 1	0 / 0
Upper Limb Fracture			

subjects affected / exposed	0 / 150 (0.00%)	1 / 148 (0.68%)	0 / 149 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nervous system disorders			
Syncope			
subjects affected / exposed	1 / 150 (0.67%)	0 / 148 (0.00%)	0 / 149 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Temporal Lobe Epilepsy			
subjects affected / exposed	1 / 150 (0.67%)	0 / 148 (0.00%)	0 / 149 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Blood and lymphatic system disorders			
Eosinophilia			
subjects affected / exposed	0 / 150 (0.00%)	0 / 148 (0.00%)	1 / 149 (0.67%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Ear and labyrinth disorders			
Deafness Neurosensory			
subjects affected / exposed	1 / 150 (0.67%)	0 / 148 (0.00%)	0 / 149 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Vestibular Disorder			
subjects affected / exposed	1 / 150 (0.67%)	0 / 148 (0.00%)	0 / 149 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Eye disorders			
Retinal Vein Thrombosis			
subjects affected / exposed	0 / 150 (0.00%)	0 / 148 (0.00%)	1 / 149 (0.67%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal disorders			
Abdominal Pain			

subjects affected / exposed	1 / 150 (0.67%)	0 / 148 (0.00%)	0 / 149 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Abdominal Pain Upper			
subjects affected / exposed	0 / 150 (0.00%)	1 / 148 (0.68%)	0 / 149 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal Angiectasia			
subjects affected / exposed	0 / 150 (0.00%)	0 / 148 (0.00%)	1 / 149 (0.67%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Oesophageal Perforation			
subjects affected / exposed	0 / 150 (0.00%)	0 / 148 (0.00%)	1 / 149 (0.67%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pancreatitis			
subjects affected / exposed	0 / 150 (0.00%)	1 / 148 (0.68%)	0 / 149 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hepatobiliary disorders			
Cholelithiasis			
subjects affected / exposed	1 / 150 (0.67%)	0 / 148 (0.00%)	0 / 149 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Renal and urinary disorders			
Acute Kidney Injury			
subjects affected / exposed	0 / 150 (0.00%)	1 / 148 (0.68%)	0 / 149 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Musculoskeletal and connective tissue disorders			
Back Pain			
subjects affected / exposed	0 / 150 (0.00%)	1 / 148 (0.68%)	0 / 149 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Osteoarthritis			
subjects affected / exposed	0 / 150 (0.00%)	0 / 148 (0.00%)	1 / 149 (0.67%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infections and infestations			
Appendicitis			
subjects affected / exposed	0 / 150 (0.00%)	0 / 148 (0.00%)	1 / 149 (0.67%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Chronic Sinusitis			
subjects affected / exposed	1 / 150 (0.67%)	0 / 148 (0.00%)	0 / 149 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Corneal Abscess			
subjects affected / exposed	0 / 150 (0.00%)	1 / 148 (0.68%)	0 / 149 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Diverticulitis			
subjects affected / exposed	0 / 150 (0.00%)	1 / 148 (0.68%)	0 / 149 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infectious Pleural Effusion			
subjects affected / exposed	0 / 150 (0.00%)	0 / 148 (0.00%)	1 / 149 (0.67%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumonia			
subjects affected / exposed	0 / 150 (0.00%)	1 / 148 (0.68%)	0 / 149 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Septic Shock			
subjects affected / exposed	0 / 150 (0.00%)	0 / 148 (0.00%)	1 / 149 (0.67%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Wound Infection			

subjects affected / exposed	1 / 150 (0.67%)	0 / 148 (0.00%)	0 / 149 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Frequency threshold for reporting non-serious adverse events: 5 %

Non-serious adverse events	Placebo	Dupilumab 300 mg q2w Then q4w	Dupilumab 300 mg q2w
Total subjects affected by non-serious adverse events			
subjects affected / exposed	111 / 150 (74.00%)	95 / 148 (64.19%)	90 / 149 (60.40%)
Injury, poisoning and procedural complications			
Accidental Overdose			
subjects affected / exposed	11 / 150 (7.33%)	12 / 148 (8.11%)	5 / 149 (3.36%)
occurrences (all)	12	13	5
Nervous system disorders			
Headache			
subjects affected / exposed	18 / 150 (12.00%)	17 / 148 (11.49%)	14 / 149 (9.40%)
occurrences (all)	31	32	17
General disorders and administration site conditions			
Injection Site Erythema			
subjects affected / exposed	11 / 150 (7.33%)	10 / 148 (6.76%)	11 / 149 (7.38%)
occurrences (all)	28	26	25
Injection Site Reaction			
subjects affected / exposed	3 / 150 (2.00%)	8 / 148 (5.41%)	5 / 149 (3.36%)
occurrences (all)	4	24	15
Respiratory, thoracic and mediastinal disorders			
Asthma			
subjects affected / exposed	20 / 150 (13.33%)	15 / 148 (10.14%)	8 / 149 (5.37%)
occurrences (all)	31	23	11
Cough			
subjects affected / exposed	8 / 150 (5.33%)	9 / 148 (6.08%)	9 / 149 (6.04%)
occurrences (all)	11	10	13
Epistaxis			
subjects affected / exposed	20 / 150 (13.33%)	8 / 148 (5.41%)	13 / 149 (8.72%)
occurrences (all)	22	10	16
Nasal Polyps			

subjects affected / exposed occurrences (all)	26 / 150 (17.33%) 51	20 / 148 (13.51%) 20	9 / 149 (6.04%) 14
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	2 / 150 (1.33%)	12 / 148 (8.11%)	7 / 149 (4.70%)
occurrences (all)	2	12	9
Back Pain			
subjects affected / exposed	10 / 150 (6.67%)	5 / 148 (3.38%)	8 / 149 (5.37%)
occurrences (all)	11	6	11
Infections and infestations			
Acute Sinusitis			
subjects affected / exposed	16 / 150 (10.67%)	5 / 148 (3.38%)	5 / 149 (3.36%)
occurrences (all)	18	5	8
Bronchitis			
subjects affected / exposed	8 / 150 (5.33%)	9 / 148 (6.08%)	9 / 149 (6.04%)
occurrences (all)	13	10	10
Nasopharyngitis			
subjects affected / exposed	38 / 150 (25.33%)	31 / 148 (20.95%)	33 / 149 (22.15%)
occurrences (all)	48	53	50
Sinusitis			
subjects affected / exposed	17 / 150 (11.33%)	14 / 148 (9.46%)	9 / 149 (6.04%)
occurrences (all)	29	19	9
Upper Respiratory Tract Infection			
subjects affected / exposed	20 / 150 (13.33%)	8 / 148 (5.41%)	10 / 149 (6.71%)
occurrences (all)	23	9	13

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
17 May 2017	<ul style="list-style-type: none">- Reworded for clarity the procedures to be performed at permanent treatment discontinuation. In addition, added the assessment of rhinorrhea anterior and posterior following early treatment discontinuation to support total symptom score analysis.- Permitted 1 retest of dynamic laboratory tests (i.e., those subject to variability) during screening at the discretion of the Investigator.- Clarified that the analysis of the proportion of subjects who used SCS was to include all SCSs (not just oral corticosteroid)- EQ-5D from exploratory endpoint to secondary efficacy endpoint- Clarified that CT scan was mandatory unless not approved by local ethics committee or institutional review board- Intranasal decongestants added to list of prohibited medications except as needed for nasal endoscopy procedure- Permitted study procedures to be performed over 3 days, if necessary, as long as within the visit window- Deleted the requirement for male birth control (to be consistent with most current safety information)- Correction of typographical and other minor changes

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported