Clinical trial results:
A Randomized, Double-Blind, Head-to-Head Comparison of Dupilumab Versus Omalizumab in Severe Chronic Rhinosinusitis with Nasal Polyps (CRSwNP) and Comorbid Asthma Patients

Summary

EudraCT number	2021-000829-27
Trial protocol	FR DE BE CZ FI HU SE ES DK PT PL IT RO
Global end of trial date	27 December 2024

Results information

Result version number	v1 (current)
This version publication date	11 December 2025
First version publication date	11 December 2025

Trial information

Trial identification

Sponsor protocol code	LPS16747

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT04998604
WHO universal trial number (UTN)	U1111-1255-4713

Notes:

Sponsors

Sponsor organisation name	Sanofi-Aventis Recherche & Développement
Sponsor organisation address	82, Avenue Raspail, Gentilly, France, 94250
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	27 January 2025
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	27 December 2024
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To evaluate the efficacy of dupilumab compared to omalizumab in reducing the polyp size and improving sense of smell.

Protection of trial subjects:

Participants 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 participant and considering the local culture. During the course of the trial, participants were provided with individual participant cards indicating the nature of the trial the participant 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	27 September 2021
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	No

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Belgium: 19
Country: Number of subjects enrolled	Canada: 12
Country: Number of subjects enrolled	Czechia: 49
Country: Number of subjects enrolled	Denmark: 9
Country: Number of subjects enrolled	Finland: 10
Country: Number of subjects enrolled	France: 12
Country: Number of subjects enrolled	Germany: 7
Country: Number of subjects enrolled	Hungary: 35
Country: Number of subjects enrolled	Italy: 27
Country: Number of subjects enrolled	Mexico: 6
Country: Number of subjects enrolled	Poland: 64
Country: Number of subjects enrolled	Portugal: 30
Country: Number of subjects enrolled	Romania: 11
Country: Number of subjects enrolled	Spain: 30
Country: Number of subjects enrolled	Sweden: 6
Country: Number of subjects enrolled	United Kingdom: 7
Country: Number of subjects enrolled	United States: 26

Worldwide total number of subjects	360
EEA total number of subjects	309

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)	297
From 65 to 84 years	63
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

The study was conducted at 87 active centers in 17 countries. A total of 819 participants were screened between 27 September 2021 and 25 April 2024, of which 459 participants were screen failures. Screen failures were mainly due to not meeting eligibility criteria.

EE= Eastern European; ROW= Rest of World.

Pre-assignment

Screening details:

A total of 360 participants were randomized in a 1:1 ratio to receive either dupilumab or omalizumab in study. Randomization was stratified by prior surgery for nasal polyp, inhaled corticosteroids (ICS) doses (low versus medium/high dose ICS), presence of aspirin-exacerbated respiratory disease (AERD) and region (EE versus ROW).

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

Arms

Are arms mutually exclusive?	Yes
Arm title	Dupilumab 300 mg Q2W

Arm description:

Participants received dupilumab 300 milligrams (mg) subcutaneous (SC) injection every 2 weeks (Q2W) for 24 weeks.

Arm type	Experimental
Investigational medicinal product name	Dupilumab
Investigational medicinal product code	SAR231893
Other name	Dupixent
Pharmaceutical forms	Solution for injection in pre-filled syringe
Routes of administration	Subcutaneous use

Dosage and administration details:

Dupilumab 300 mg SC injection was administered Q2W for 24 weeks.

Arm title	Omalizumab 75 to 600 mg Q2W/Q4W

Arm description:

Participants received omalizumab 75 to 600 mg SC injection Q2W/every 4 weeks (Q4W) based on their serum immunoglobulin E (IgE) levels and body weight for 24 weeks.

Arm type	Active comparator
Investigational medicinal product name	Omalizumab
Investigational medicinal product code	
Other name	Xolair
Pharmaceutical forms	Solution for injection in pre-filled syringe
Routes of administration	Subcutaneous use

Dosage and administration details:

Omalizumab 75 to 600 mg SC injection was administered Q2W/Q4W based on their serum IgE levels and body weight for 24 weeks.

Number of subjects in period 1	Dupilumab 300 mg Q2W	Omalizumab 75 to 600 mg Q2W/Q4W
Started	181	179
Randomized and Treated	179	173
Completed	174	165
Not completed	7	14
Consent withdrawn by subject	2	4
Adverse event, non-fatal	3	2
Not related to coronavirus disease 2019 pandemic	2	8

Baseline characteristics

Reporting groups	
Reporting group title	Dupilumab 300 mg Q2W
Reporting group description:	
Participants received dupilumab 300 milligrams (mg) subcutaneous (SC) injection every 2 weeks (Q2W) for 24 weeks.	
Reporting group title	Omalizumab 75 to 600 mg Q2W/Q4W
Reporting group description:	
Participants received omalizumab 75 to 600 mg SC injection Q2W/every 4 weeks (Q4W) based on their serum immunoglobulin E (IgE) levels and body weight for 24 weeks.	

Reporting group values	Dupilumab 300 mg Q2W	Omalizumab 75 to 600 mg Q2W/Q4W	Total
Number of subjects	181	179	360
Age Categorical Units: participants			
Age Continuous Units: years			
arithmetic mean	51.0	52.1	
standard deviation	± 13.33	± 12.90	-
Gender Categorical Units: participants			
Female	74	88	162
Male	107	91	198
Race Units: Subjects			
American Indian or Alaska Native	0	2	2
Asian	1	1	2
Black or African American	2	1	3
White	171	170	341
Multiple	0	1	1
Not Reported	6	2	8
Unknown	1	2	3
University of Pennsylvania Smell Identification Test (UPSIT)			
UPSIT: a 40-item test to quantitatively assess human olfactory function and it consisted of 4 booklets, each containing 10 odorants with 1 odorant per page. Participant released odorant by rubbing brown-strip (contained odorant microcapsules) with tip of pencil and to indicate which of 4 words best described odor. Thus, each participant received score out of 40 possible correct answers. Total UPSIT score ranged from 0 (loss of smell/anosmia) to 40 (normal sense of smell/normosmia). Higher scores=better olfactory function. Only those participants with data available at baseline are reported.			
Units: score on a scale arithmetic mean			
standard deviation	±	±	-
Nasal Polyp Score (NPS)			
The NPS was assessed by the independent physician to grade the extent/severity of nasal polyps based on evaluation by nasal endoscopy. The NPS scores for each nostril was graded based on polyp size from 0 (no polyps) to 4 (large polyps causing complete obstruction of the inferior nasal cavity). The total NPS score was calculated as the sum of right and left nostril scores and ranged from 0 (no polyps) to 8 (large polyps). Higher scores indicate more extensive or severe nasal polyps.			
Units: score on a scale			

arithmetic mean	6.11	6.15	
standard deviation	± 1.165	± 1.277	-

Subject analysis sets

Subject analysis set title	Dupilumab 300 mg Q2W
Subject analysis set type	Intention-to-treat

Subject analysis set description:

Participants received dupilumab 300 mg SC injection Q2W for 24 weeks.

Subject analysis set title	Omalizumab 75 to 600 mg Q2W/Q4W
Subject analysis set type	Intention-to-treat

Subject analysis set description:

Participants received omalizumab 75 to 600 mg SC injection Q2W/Q4W based on their serum IgE levels and body weight for 24 weeks.

Reporting group values	Dupilumab 300 mg Q2W	Omalizumab 75 to 600 mg Q2W/Q4W	
Number of subjects	180	175	
Age Categorical Units: participants			
Age Continuous Units: years arithmetic mean standard deviation	±	±	
Gender Categorical Units: participants			
Female Male			
Race Units: Subjects			
American Indian or Alaska Native Asian Black or African American White Multiple Not Reported Unknown			
University of Pennsylvania Smell Identification Test (UPSIT)			
UPSIT: a 40-item test to quantitatively assess human olfactory function and it consisted of 4 booklets, each containing 10 odorants with 1 odorant per page. Participant released odorant by rubbing brown-strip (contained odorant microcapsules) with tip of pencil and to indicate which of 4 words best described odor. Thus, each participant received score out of 40 possible correct answers. Total UPSIT score ranged from 0 (loss of smell/anosmia) to 40 (normal sense of smell/normosmia). Higher scores=better olfactory function. Only those participants with data available at baseline are reported.			
Units: score on a scale arithmetic mean standard deviation	11.1 ± 5.45	11.0 ± 6.13	
Nasal Polyp Score (NPS)			
The NPS was assessed by the independent physician to grade the extent/severity of nasal polyps based on evaluation by nasal endoscopy. The NPS scores for each nostril was graded based on polyp size from 0 (no polyps) to 4 (large polyps causing complete obstruction of the inferior nasal cavity). The total NPS			

score was calculated as the sum of right and left nostril scores and ranged from 0 (no polyps) to 8 (large polyps). Higher scores indicate more extensive or severe nasal polyps.			
Units: score on a scale arithmetic mean standard deviation	± 	± 	

End points

End points reporting groups

Reporting group title	Dupilumab 300 mg Q2W
Reporting group description:	
Participants received dupilumab 300 milligrams (mg) subcutaneous (SC) injection every 2 weeks (Q2W) for 24 weeks.	
Reporting group title	Omalizumab 75 to 600 mg Q2W/Q4W
Reporting group description:	
Participants received omalizumab 75 to 600 mg SC injection Q2W/every 4 weeks (Q4W) based on their serum immunoglobulin E (IgE) levels and body weight for 24 weeks.	
Subject analysis set title	Dupilumab 300 mg Q2W
Subject analysis set type	Intention-to-treat
Subject analysis set description:	
Participants received dupilumab 300 mg SC injection Q2W for 24 weeks.	
Subject analysis set title	Omalizumab 75 to 600 mg Q2W/Q4W
Subject analysis set type	Intention-to-treat
Subject analysis set description:	
Participants received omalizumab 75 to 600 mg SC injection Q2W/Q4W based on their serum IgE levels and body weight for 24 weeks.	

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

End point title	Change From Baseline to Week 24 in Nasal Polyp Score
End point description:	
The NPS was assessed by the independent physician to grade the extent/severity of nasal polyps based on evaluation by nasal endoscopy. The NPS scores for each nostril was graded based on polyp size from 0 (no polyps) to 4 (large polyps causing complete obstruction of the inferior nasal cavity). The total NPS score was calculated as the sum of right and left nostril scores and ranged from 0 (no polyps) to 8 (large polyps). Higher scores indicated more extensive or severe nasal polyps. Negative change from baseline indicated less severity of nasal polyps. Baseline was defined as the last available valid (non-missing) value up to and including the day of first administration of study treatment. The ITT analysis set included all randomized participants. Only participants with data collected at Week 24 are reported.	
End point type	Primary
End point timeframe:	
Baseline (Day 1) and Week 24	

End point values	Dupilumab 300 mg Q2W	Omalizumab 75 to 600 mg Q2W/Q4W		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	172	165		
Units: score on a scale				
least squares mean (confidence interval 95%)	-2.65 (-2.95 to -2.36)	-1.05 (-1.35 to -0.75)		

Statistical analyses

Statistical analysis title	Treatment difference in NPS

Statistical analysis description:

A hierarchical testing procedure was used to control the type-I error and handle multiple secondary endpoint analysis. Testing was performed sequentially in order the endpoints were reported and continued when primary endpoint was statistically significant at 2-sided 0.05.

Comparison groups	Dupilumab 300 mg Q2W v Omalizumab 75 to 600 mg Q2W/Q4W
Number of subjects included in analysis	337
Analysis specification	Pre-specified
Analysis type	superiority[1]
P-value	< 0.001 [2]
Method	ANCOVA
Parameter estimate	Least squares (LS) mean difference
Point estimate	-1.6
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.96
upper limit	-1.25
Variability estimate	Standard error of the mean
Dispersion value	0.182

Notes:

[1] - At each post-baseline visit, each of the imputed complete data was analyzed by fitting an analysis of covariance (ANCOVA) model with the corresponding baseline value, study treatment (dupilumab, omalizumab), prior surgery (yes, no), ICS doses (low, medium/high), presence of AERD (yes, no), region (EE, ROW) as covariates.

[2] - The threshold for statistical significance was 0.05 level.

Primary: Change From Baseline to Week 24 in University of Pennsylvania Smell Identification Test

End point title	Change From Baseline to Week 24 in University of Pennsylvania Smell Identification Test

End point description:

The UPSIT was a 40-item test to quantitatively assess human olfactory function. The UPSIT test consisted of 4 booklets, each containing 10 odorants with 1 odorant per page. The participant was asked to release the odorant by rubbing the brown-strip (contained odorant microcapsules) with the tip of a pencil and to indicate which of 4 words best described the odor. Thus, each participant received a score out of 40 possible correct answers. The total UPSIT score ranged from 0 (loss of smell/anosmia) to 40 (normal sense of smell/normosmia). Higher scores indicated better olfactory function. Positive change from baseline indicated normal olfactory function. Baseline was defined as the last available valid (non-missing) value up to and including the day of first administration of study treatment. The ITT analysis set included all randomized participants. Only participants with data collected at Week 24 are reported.

End point type	Primary

End point timeframe:

Baseline (Day 1) and Week 24

End point values	Dupilumab 300 mg Q2W	Omalizumab 75 to 600 mg Q2W/Q4W		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	173	166		
Units: score on a scale				
least squares mean (confidence interval 95%)	12.7 (11.3 to 14.1)	4.7 (3.2 to 6.1)		

Statistical analyses

Statistical analysis title	Treatment difference in UPSIT

Statistical analysis description:

Testing according to the hierarchical testing procedure (only performed if the previous endpoint was statistically significant).

Comparison groups	Dupilumab 300 mg Q2W v Omalizumab 75 to 600 mg Q2W/Q4W
Number of subjects included in analysis	339
Analysis specification	Pre-specified
Analysis type	superiority[3]
P-value	< 0.001 [4]
Method	ANCOVA
Parameter estimate	LS mean difference
Point estimate	8
Confidence interval	
level	95 %
sides	2-sided
lower limit	6.3
upper limit	9.7
Variability estimate	Standard error of the mean
Dispersion value	0.88

Notes:

[3] - At each post-baseline visit, each of the imputed complete data was analyzed by fitting an ANCOVA model with the corresponding baseline value, study treatment (dupilumab, omalizumab), prior surgery (yes, no), ICS doses (low, medium/high), presence of AERD (yes, no), region (EE, ROW) as covariates.
[4] - The threshold for statistical significance was 0.05 level.

Secondary: Change From Baseline to Week 24 in the Loss of Smell Score of the Chronic Rhinosinusitis With Nasal Polyp (CRSwNP) Nasal Symptom Diary

End point title	Change From Baseline to Week 24 in the Loss of Smell Score of the Chronic Rhinosinusitis With Nasal Polyp (CRSwNP) Nasal Symptom Diary

End point description:

The nasal symptom diary was designed to assess the severity of chronic rhinosinusitis nasal symptoms daily. These symptoms included nasal congestion (NC)/obstruction, loss of smell, anterior rhinorrhea, and posterior rhinorrhea. The severity of loss of smell was scored by participants using a scale ranged from 0 to 3 (where, 0= no symptoms, 1= mild symptoms, 2= moderate symptoms and 3= severe symptoms that were hard to tolerate, caused interference with activities, or daily living). Higher scores indicated greater symptom severity. Negative change from baseline indicated less severe symptom. Baseline value was calculated by averaging the data collected/recorded from Day -6 to Day 1. The ITT analysis set included all randomized participants. Only participants with data collected at Week 24 are reported.

End point type	Secondary

End point timeframe:

Baseline (average of Day -6 to Day 1) and Week 24

End point values	Dupilumab 300 mg Q2W	Omalizumab 75 to 600 mg Q2W/Q4W		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	170	164		
Units: score on a scale				
least squares mean (confidence interval 95%)	-1.55 (-1.71 to -1.38)	-0.74 (-0.90 to -0.57)		

Statistical analyses

Statistical analysis title	Treatment difference in Loss of Smell Score

Statistical analysis description:

Testing according to the hierarchical testing procedure (only performed if the previous endpoint was statistically significant).

Comparison groups	Dupilumab 300 mg Q2W v Omalizumab 75 to 600 mg Q2W/Q4W
Number of subjects included in analysis	334
Analysis specification	Pre-specified
Analysis type	superiority[5]
P-value	< 0.001 [6]
Method	ANCOVA
Parameter estimate	LS mean difference
Point estimate	-0.81
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.01
upper limit	-0.61
Variability estimate	Standard error of the mean
Dispersion value	0.101

Notes:

[5] - Each of the imputed complete data was analyzed by fitting an ANCOVA model with the corresponding baseline value, study treatment (dupilumab, omalizumab), prior surgery (yes, no), ICS doses (low, medium/high), presence of AERD (yes, no), region (EE, ROW) as covariates.
[6] - The threshold for statistical significance was 0.05 level.

Secondary: Change From Baseline to Week 24 in the Nasal Congestion Score of the Chronic Rhinosinusitis With Nasal Polyp Nasal Symptom Diary

End point title	Change From Baseline to Week 24 in the Nasal Congestion Score of the Chronic Rhinosinusitis With Nasal Polyp Nasal Symptom Diary

End point description:

The nasal symptom diary was designed to assess the severity of chronic rhinosinusitis nasal symptoms daily. These symptoms included nasal congestion (NC)/obstruction, loss of smell, anterior rhinorrhea, and posterior rhinorrhea. The severity of nasal congestion was scored by participants using a scale ranged from 0 to 3 (where, 0= no symptoms, 1= mild symptoms, 2= moderate symptoms and 3= severe symptoms that were hard to tolerate, caused interference with activities, or daily living). Higher scores indicated greater symptom severity. Negative change from baseline indicated less severe symptom. Baseline value was calculated by averaging the data collected/recorded from Day -6 to Day 1. The ITT analysis set included all randomized participants. Only participants with data collected at Week 24 are reported.

End point type	Secondary

End point timeframe:

Baseline (average of Day -6 to Day 1) and Week 24

End point values	Dupilumab 300 mg Q2W	Omalizumab 75 to 600 mg Q2W/Q4W		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	170	164		
Units: score on a scale				
least squares mean (confidence interval 95%)	-1.63 (-1.76 to -1.49)	-1.05 (-1.18 to -0.91)		

Statistical analyses

Statistical analysis title	Treatment difference in NC score

Statistical analysis description:

Testing according to the hierarchical testing procedure (only performed if the previous endpoint was statistically significant).

Comparison groups	Dupilumab 300 mg Q2W v Omalizumab 75 to 600 mg Q2W/Q4W
Number of subjects included in analysis	334
Analysis specification	Pre-specified
Analysis type	superiority[7]
P-value	< 0.001 [8]
Method	ANCOVA
Parameter estimate	LS mean difference
Point estimate	-0.58
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.74
upper limit	-0.42
Variability estimate	Standard error of the mean
Dispersion value	0.082

Notes:

[7] - Each of the imputed complete data was analyzed by fitting an ANCOVA model with the corresponding baseline value, study treatment (dupilumab, omalizumab), prior surgery (yes, no), ICS doses (low, medium/high), presence of AERD (yes, no), region (EE, ROW) as covariates.
[8] - The threshold for statistical significance was 0.05 level.

Secondary: Change From Baseline to Week 24 in Total Symptom Score (TSS) Derived From the Chronic Rhinosinusitis With Nasal Polyp Nasal Symptom Diary

End point title	Change From Baseline to Week 24 in Total Symptom Score (TSS) Derived From the Chronic Rhinosinusitis With Nasal Polyp Nasal Symptom Diary

End point description:

The TSS is a composite score consisted of the following symptoms assessed daily in the morning: NC/obstruction, decreased/loss of sense of smell, and rhinorrhea (average of anterior/posterior nasal discharge). Each item was scored on a scale ranged from 0 to 3 (where, 0= no symptoms, 1= mild symptoms, 2= moderate symptoms and 3= severe symptoms that were hard to tolerate, and caused interference with activities, or daily living). Higher score indicated greater symptom severity. The TSS score was calculated by summing the individual symptom score and ranged from 0 (no symptoms) to 9 (severe symptoms). Higher scores on the TSS indicated greater symptom severity. Negative change from baseline indicated less severe symptom. Baseline was calculated by averaging the data

collected/recorded from Day -6 to Day 1. The ITT analysis set included all randomized participants. Only participants with data collected at Week 24 are reported.

End point type	Secondary

End point timeframe:

Baseline (average of Day -6 to Day 1) and Week 24

End point values	Dupilumab 300 mg Q2W	Omalizumab 75 to 600 mg Q2W/Q4W		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	170	164		
Units: score on a scale				
least squares mean (confidence interval 95%)	-4.48 (-4.82 to -4.14)	-2.73 (-3.09 to -2.38)		

Statistical analyses

Statistical analysis title	Treatment difference in TSS

Statistical analysis description:

Testing according to the hierarchical testing procedure (only performed if the previous endpoint was statistically significant).

Comparison groups	Dupilumab 300 mg Q2W v Omalizumab 75 to 600 mg Q2W/Q4W
Number of subjects included in analysis	334
Analysis specification	Pre-specified
Analysis type	superiority[9]
P-value	< 0.001 [10]
Method	ANCOVA
Parameter estimate	LS mean difference
Point estimate	-1.74
Confidence interval	
level	95 %
sides	2-sided
lower limit	-2.15
upper limit	-1.33
Variability estimate	Standard error of the mean
Dispersion value	0.21

Notes:

[9] - Each of the imputed complete data was analyzed by fitting an ANCOVA model with the corresponding baseline value, study treatment (dupilumab, omalizumab), prior surgery (yes, no), ICS doses (low, medium/high), presence of AERD (yes, no), region (EE, ROW) as covariates.
[10] - The threshold for statistical significance was 0.05 level.

Secondary: Change From Baseline to Week 24 in Sino-Nasal Outcome Test 22-Items (SNOT-22) Total Score

End point title	Change From Baseline to Week 24 in Sino-Nasal Outcome Test 22-Items (SNOT-22) Total Score

End point description:

The SNOT-22 is a patient-reported outcome questionnaire designed to assess impact of chronic rhinosinusitis on participants' health-related quality of life. The SNOT-22 consisted of 22 items covering

symptoms, social/emotional impact, productivity, and sleep consequences of chronic rhinosinusitis. Each item was rated on a 6-point Likert scale response option, score ranged from 0 (no problem) to 5 (problem as bad as it can be). The SNOT-22 total score was sum of each item score, and it ranged from 0 (no problem) to 110 (problem as bad as it can be). Higher scores indicated greater rhinosinusitis-related health burden, meaning for this parameter lower score indicated better condition. Negative change from baseline indicated improvement in health-related quality of life. Baseline was defined as last available valid (non-missing) value up to and including day of first administration of study treatment. The ITT analysis set. Only participants with data collected at Week 24 are reported.

End point type	Secondary

End point timeframe:

Baseline (Day 1) and Week 24

End point values	Dupilumab 300 mg Q2W	Omalizumab 75 to 600 mg Q2W/Q4W		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	161	158		
Units: score on a scale				
least squares mean (confidence interval 95%)	-44.6 (-47.9 to -41.3)	-31.9 (-35.2 to -28.5)		

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline to Week 24 in Sino-Nasal Outcome Test 22-Items: Nasal Domain Score

End point title	Change From Baseline to Week 24 in Sino-Nasal Outcome Test 22-Items: Nasal Domain Score

End point description:

SNOT-22:a patient-reported outcome questionnaire designed to assess impact of chronic rhinosinusitis on participants' health-related quality of life (HRQoL). SNOT-22:categorized into 5 domains: Nasal(items 1,2,3,4,5,6,7 and 12); Ear/Facial(items 8,9,10 and 11); Sleep(items 13,14,15 and 16); Function(items 17,18 and 19); Emotion(items 20,21 and 22). Each item of Nasal domain was rated on 6-point Likert scale ranged from 0 (no problem) to 5 (problem as bad as it can be) with higher score=greater rhinosinusitis-related health burden. Total score of Nasal domain was average score of items of nasal domain and ranged from 0 (no problem) to 5 (problem as bad as it can be), where higher score=greater rhinosinusitis-related health burden. Negative change from baseline indicated improvement in HRQoL. Baseline:last available valid (non-missing) value up to and including day of 1st administration of study treatment. ITT analysis set. Only participants with data collected at Week 24 are reported.

End point type	Secondary

End point timeframe:

Baseline (Day 1) and Week 24

End point values	Dupilumab 300 mg Q2W	Omalizumab 75 to 600 mg Q2W/Q4W		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	161	158		
Units: score on a scale				
least squares mean (confidence interval 95%)	-2.4 (-2.6 to -2.2)	-1.6 (-1.8 to -1.4)		

Statistical analyses

No statistical analyses for this end point

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

End point title	Change From Baseline to Week 24 in Nasal Peak Inspiratory Flow (NPIF)

End point description:

The NPIF evaluation represented a physiologic measure of the air flow through both nasal cavities during forced inspiration. The NPIF is the best validated technique for the evaluation of nasal flow through the nose. Participants were issued an NPIF meter and were instructed on the use of the device and written instructions on the use of the NPIF meter was provided. Higher NPIF values were indicative of better nasal air flow. Positive change from baseline indicated better nasal air flow. Baseline was the mean measurement recorded for the 7 days (Day -6 to Day 1) prior to first dose of study treatment. The ITT analysis set included all randomized participants. Only participants with data collected at Week 24 are reported.

End point type	Secondary

End point timeframe:

Baseline (average of Day -6 to Day 1) and Week 24

End point values	Dupilumab 300 mg Q2W	Omalizumab 75 to 600 mg Q2W/Q4W		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	169	163		
Units: Liters per minute				
least squares mean (confidence interval 95%)	68.96 (60.90 to 77.02)	37.69 (29.28 to 46.09)		

Statistical analyses

No statistical analyses for this end point

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

End point title	Change From Baseline to Week 24 in Rhinosinusitis Visual Analogue Scale (Rhinosinusitis VAS)

End point description:

The rhinosinusitis severity VAS was used to evaluate the overall severity of the rhinosinusitis. It is a recommended scale to determine the participant’s disease severity and to guide the treatment for

chronic rhinosinusitis. The participants were asked to answer the following question: "How troublesome are your symptoms of your rhinosinusitis" on a 10-centimeter VAS from 0 (not troublesome) to 10 (worst thinkable troublesome). Higher scores on the VAS score indicated more severe chronic rhinosinusitis. Negative change from baseline indicated less severity of rhinosinusitis. Baseline was defined as the last available valid (non-missing) value up to and including the day of first administration of study treatment. The ITT analysis set included all randomized participants. Only participants with data collected at Week 24 are reported.

End point type	Secondary

End point timeframe:

Baseline (Day 1) and Week 24

End point values	Dupilumab 300 mg Q2W	Omalizumab 75 to 600 mg Q2W/Q4W		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	161	158		
Units: units on a scale				
least squares mean (confidence interval 95%)	-5.43 (-5.96 to -4.90)	-3.56 (-4.11 to -3.01)		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Participants With Treatment-Emergent Adverse Events (TEAEs), Treatment-Emergent Serious Adverse Events (SAEs) and Treatment-Emergent Adverse Events of Special Interest (AESIs)

End point title	Number of Participants With Treatment-Emergent Adverse Events (TEAEs), Treatment-Emergent Serious Adverse Events (SAEs) and Treatment-Emergent Adverse Events of Special Interest (AESIs)

End point description:

An adverse event (AE) was any untoward medical occurrence in a participant or clinical study participant, temporally associated with use of study treatment, whether or not considered related to study treatment. An SAE was defined as any AE that at any dose resulted in death, was life-threatening, required inpatient hospitalization or prolongation of existing hospitalization, resulted in persistent or significant disability/incapacity, was a congenital anomaly/birth defect, or was an important medical event. An AESI was an AE (serious or nonserious) of scientific and medical concern specific to Sponsor's product or program, for which ongoing monitoring and immediate notification by Investigator to Sponsor was required. TEAEs was defined as an AEs that occurred from first administration of study treatment (on Day 1) up to 98 days after last dose of study treatment administration. Safety analysis set included all randomized participants who received at least 1 dose of study treatment.

End point type	Secondary

End point timeframe:

From first dose of study treatment administration (Day 1) up to 98 days after the last dose of study treatment administration (considering the maximum duration of treatment exposure) i.e., up to approximately 329 days

End point values	Dupilumab 300 mg Q2W	Omalizumab 75 to 600 mg Q2W/Q4W		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	179	173		
Units: participants				
Any TEAE	115	116		
Any Serious TEAE	3	7		
Any Treatment-Emergent AESI	4	2		

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Serious AEs and other AEs were collected from first dose of study treatment administration (Day 1) up to 98 days after the last dose of study treatment administration (considering maximum duration of treatment exposure) i.e., up to approximately 329 days.

Adverse event reporting additional description:

Deaths (all causes) were collected from first dose of study treatment (Day 1) up to end of follow-up for death for each participant, i.e., up to approximately 39 months. Analysis was performed on the safety analysis set.

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	27.1

Reporting groups

Reporting group title	Omalizumab 75 to 600 mg Q2W/Q4W

Reporting group description:

Participants received omalizumab 75 to 600 mg SC injection Q2W/Q4W based on their serum IgE levels and body weight for 24 weeks.

Reporting group title	Dupilumab 300 mg Q2W

Reporting group description:

Participants received dupilumab 300 mg SC injection Q2W for 24 weeks.

Serious adverse events	Omalizumab 75 to 600 mg Q2W/Q4W	Dupilumab 300 mg Q2W	
Total subjects affected by serious adverse events			
subjects affected / exposed	7 / 173 (4.05%)	3 / 179 (1.68%)	
number of deaths (all causes)	0	0	
number of deaths resulting from adverse events	0	0	
Injury, poisoning and procedural complications			
Contusion			
subjects affected / exposed	1 / 173 (0.58%)	0 / 179 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vascular disorders			
Granulomatosis With Polyangiitis			
subjects affected / exposed	0 / 173 (0.00%)	1 / 179 (0.56%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac disorders			
Atrial Fibrillation			

subjects affected / exposed	1 / 173 (0.58%)	0 / 179 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pregnancy, puerperium and perinatal conditions			
Pregnancy			
subjects affected / exposed	0 / 173 (0.00%)	1 / 179 (0.56%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Immune system disorders			
Eosinophilic Granulomatosis With Polyangiitis			
subjects affected / exposed	1 / 173 (0.58%)	0 / 179 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal disorders			
Pancreatitis Acute			
subjects affected / exposed	0 / 173 (0.00%)	1 / 179 (0.56%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infections and infestations			
Mycobacterium Avium Complex Infection			
subjects affected / exposed	0 / 173 (0.00%)	1 / 179 (0.56%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Appendicitis			
subjects affected / exposed	1 / 173 (0.58%)	0 / 179 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Neuroborreliosis			
subjects affected / exposed	1 / 173 (0.58%)	0 / 179 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumonia Klebsiella			

subjects affected / exposed	0 / 173 (0.00%)	1 / 179 (0.56%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumonia			
subjects affected / exposed	2 / 173 (1.16%)	0 / 179 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

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

Non-serious adverse events	Omalizumab 75 to 600 mg Q2W/Q4W	Dupilumab 300 mg Q2W	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	53 / 173 (30.64%)	48 / 179 (26.82%)	
Injury, poisoning and procedural complications			
Accidental Overdose			
subjects affected / exposed	21 / 173 (12.14%)	12 / 179 (6.70%)	
occurrences (all)	24	14	
Nervous system disorders			
Headache			
subjects affected / exposed	13 / 173 (7.51%)	10 / 179 (5.59%)	
occurrences (all)	17	12	
Infections and infestations			
Upper Respiratory Tract Infection			
subjects affected / exposed	8 / 173 (4.62%)	10 / 179 (5.59%)	
occurrences (all)	8	12	
Nasopharyngitis			
subjects affected / exposed	20 / 173 (11.56%)	21 / 179 (11.73%)	
occurrences (all)	22	25	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
10 June 2021	Updated the exclusion criteria to exclude participants with infections receiving symptomatic treatment.
14 May 2024	Reduced the sample size due to enrollment challenges and optimization of the targeted participant population to focus on nasal function endpoints while maintaining the favorable benefit-risk of the study.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported