Clinical trial results:
A Randomized, Double-Blind, Placebo-Controlled, Parallel-Group Study to Evaluate the Efficacy and Safety of Dupilumab in Patients with Allergic Bronchopulmonary Aspergillosis

Summary

EudraCT number	2019-002619-24
Trial protocol	DE HU GB NL BG FR PL RO
Global end of trial date	09 February 2024

Results information

Result version number	v1 (current)
This version publication date	21 February 2025
First version publication date	21 February 2025

Trial information

Trial identification

Sponsor protocol code	R668-ABPA-1923

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT04442269
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Regeneron Pharmaceuticals, Inc.
Sponsor organisation address	777 Old Saw Mill River Road, Tarrytown, NY, United States, 10591
Public contact	Clinical Trials Administrator, Regeneron Pharmaceuticals, Inc., 001 844-734-6643, clinicaltrials@regeneron.com
Scientific contact	Clinical Trials Administrator, Regeneron Pharmaceuticals, Inc., 001 844-734-6643, clinicaltrials@regeneron.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	09 February 2024
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	09 February 2024
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The primary objective of the study was to evaluate the efficacy of dupilumab on lung function in participants with Allergic Bronchopulmonary Aspergillosis (ABPA).

Protection of trial subjects:

It is the responsibility of both the sponsor and the investigator(s) to ensure that this clinical study will be conducted in accordance with the ethical principles that have their origin in the Declaration of Helsinki, and that are consistent with the ICH guidelines for GCP and applicable regulatory requirements.

Background therapy: -	
Evidence for comparator: -	
Actual start date of recruitment	15 September 2020
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	Bulgaria: 3
Country: Number of subjects enrolled	France: 15
Country: Number of subjects enrolled	Germany: 4
Country: Number of subjects enrolled	Hungary: 1
Country: Number of subjects enrolled	Japan: 5
Country: Number of subjects enrolled	Netherlands: 6
Country: Number of subjects enrolled	Poland: 3
Country: Number of subjects enrolled	Romania: 6
Country: Number of subjects enrolled	United Kingdom: 6
Country: Number of subjects enrolled	United States: 13
Worldwide total number of subjects	62
EEA total number of subjects	38

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)	43
From 65 to 84 years	18
85 years and over	1

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

A total of 62 participants were randomized in a 1:1 randomization ratio (35 participants were assigned to the dupilumab group and 27 participants to the placebo group).

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, Monitor, Carer, Data analyst, Assessor

Arms

Are arms mutually exclusive?	Yes
Arm title	Placebo

Arm description:

Matching dupilumab without active substance

Arm type	Placebo
Investigational medicinal product name	placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection/infusion
Routes of administration	Subcutaneous use

Dosage and administration details:

Matching dupilumab without active substance

Arm title	Dupilumab 300 mg Q2W

Arm description:

Subcutaneous (SC) dose every two weeks (Q2W)

Arm type	Experimental
Investigational medicinal product name	dupilumab
Investigational medicinal product code	REGN668
Other name	Dupixent
Pharmaceutical forms	Solution for injection/infusion
Routes of administration	Subcutaneous use

Dosage and administration details:

300 milligrams (mg) every 2 weeks (Q2W)

Number of subjects in period 1	Placebo	Dupilumab 300 mg Q2W
Started	27	35
Completed	20	29
Not completed	7	6
Adverse event, serious fatal	-	1

Consent withdrawn by subject	3	2
Adverse event, non-fatal	1	-
Decision by the Investigator/Sponsor	1	1
Protocol Deviation	-	1
Travel Limitations	1	1
Lost to follow-up	1	-

Baseline characteristics

Reporting groups	
Reporting group title	Placebo
Reporting group description:	
Matching dupilumab without active substance	
Reporting group title	Dupilumab 300 mg Q2W
Reporting group description:	
Subcutaneous (SC) dose every two weeks (Q2W)	

Reporting group values	Placebo	Dupilumab 300 mg Q2W	Total
Number of subjects	27	35	62
Age categorical			
Units: Subjects			
In utero			
Preterm newborn infants (gestational age < 37 wks)			
Newborns (0-27 days)			
Infants and toddlers (28 days-23 months)			
Children (2-11 years)			
Adolescents (12-17 years)			
Adults (18-64 years)			
From 65-84 years			
85 years and over			
Age Continuous			
Units: years			
arithmetic mean	57.1	61.2	
standard deviation	± 14.38	± 8.62	-
Sex: Female, Male			
Units: Participants			
Female	17	22	39
Male	10	13	23
Ethnicity (NIH/OMB)			
Units: Subjects			
Hispanic or Latino	2	4	6
Not Hispanic or Latino	24	29	53
Unknown or Not Reported	1	2	3
Race/Ethnicity, Customized			
Units: Subjects			
White	25	28	53
Asian	1	4	5
Other	0	1	1
Not Reported	1	2	3

End points

End points reporting groups	
Reporting group title	Placebo
Reporting group description: Matching dupilumab without active substance	
Reporting group title	Dupilumab 300 mg Q2W
Reporting group description: Subcutaneous (SC) dose every two weeks (Q2W)	

Primary: Change from baseline in pre-bronchodilator forced expiratory volume in 1 second (FEV1) compared to placebo	
End point title	Change from baseline in pre-bronchodilator forced expiratory volume in 1 second (FEV1) compared to placebo
End point description: Randomized participants with available data for analysis in the statistical model	
End point type	Primary
End point timeframe: At Week 24	

End point values	Placebo	Dupilumab 300 mg Q2W		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	26	34		
Units: Liters				
least squares mean (standard error)	0.002 (± 0.0558)	0.203 (± 0.0482)		

Statistical analyses

Statistical analysis title	Placebo, Dupilumab 300 mg Q2W
Comparison groups	Placebo v Dupilumab 300 mg Q2W
Number of subjects included in analysis	60
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.0022
Method	Repeated Measures Mixed Models Analysis
Parameter estimate	Least Squares Mean Difference
Point estimate	0.201
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.0768
upper limit	0.3256

Secondary: Annualized rate of Allergic Bronchopulmonary Aspergillosis (ABPA)-related exacerbations

End point title	Annualized rate of Allergic Bronchopulmonary Aspergillosis (ABPA)-related exacerbations

End point description:

Defined as severe respiratory exacerbations that are associated with a doubling of serum total Immunoglobulin E (IgE) from the prior pre-exacerbation value.

The full analysis set (FAS) includes all randomized participants. It is based on the treatment allocated as randomized.

Adjusted Rate: Negative Binomial Regression Model
Unadjusted Rate: (Number of events)/(number of participant years)

End point type	Secondary

End point timeframe:

Over the 24 to 52 Week Treatment Period

End point values	Placebo	Dupilumab 300 mg Q2W		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	27	35		
Units: Events per person-year				
number (not applicable)				
Adjusted Rate	99999	99999		
Unadjusted Rate	0	0		

Statistical analyses

No statistical analyses for this end point

Secondary: Annualized rate of severe respiratory exacerbations

End point title	Annualized rate of severe respiratory exacerbations

End point description:

Defined as new onset of symptoms or clinical worsening of respiratory symptoms requiring systemic corticosteroid treatment for ≥3 consecutive days; for participants who are on maintenance systemic corticosteroids, at least double the dose of maintenance systemic corticosteroids for ≥3 consecutive days (with or without antibiotic therapy if indicated)

The full analysis set (FAS) includes all randomized participants. It is based on the treatment allocated as randomized.

Adjusted Rate: Negative Binomial Regression Model
Unadjusted Rate: (Number of events)/(number of participant years)

End point type	Secondary

End point timeframe:

Over the 24 to 52 Week Treatment Period

End point values	Placebo	Dupilumab 300 mg Q2W		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	27	35		
Units: Events per person year				
number (not applicable)				
Adjusted Rate	1.551	0.695		
Unadjusted Rate	0.943	0.545		

Statistical analyses

No statistical analyses for this end point

Secondary: Annualized rate of severe respiratory exacerbations requiring either hospitalization or observation for >24 hours in an ED/urgent care facility

End point title	Annualized rate of severe respiratory exacerbations requiring either hospitalization or observation for >24 hours in an ED/urgent care facility

End point description:

Annualized rate of severe respiratory exacerbations requiring either hospitalization or observation for >24 hours in an emergency department/urgent care facility (events per person-year)
The full analysis set (FAS) includes all randomized participants. It is based on the treatment allocated as randomized.

Adjusted Rate: Negative Binomial Regression Model
Unadjusted Rate: (Number of events)/(number of participant years)

End point type	Secondary

End point timeframe:

Over the 24 to 52 Week Treatment Period

End point values	Placebo	Dupilumab 300 mg Q2W		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	27	35		
Units: Events per person year				
number (not applicable)				
Adjusted Rate	99999	99999		
Unadjusted Rate	0.041	0.128		

Statistical analyses

No statistical analyses for this end point

Secondary: Change from baseline in Asthma Control Questionnaire (ACQ)-5 Score

End point title	Change from baseline in Asthma Control Questionnaire (ACQ)-5 Score

End point description:

ACQ is completed by participant to measure both the adequacy of asthma control and change in asthma control, which occurs either spontaneously or as a result of treatment. The ACQ-5 score is the mean of the first 5 questions, between 0 (totally controlled) and 6 (severely uncontrolled). A higher score indicates lower asthma control. Participants with a score below 1.0 reflect adequately controlled asthma and participants with scores above 1.0 reflect inadequately controlled asthma. The optimal cut-point score of 1.50 should be used to be confident that a participant has inadequately controlled asthma.

Randomized participants with a baseline measurement and at least one post-baseline measurement at the post-baseline time point of interest

End point type	Secondary

End point timeframe:

Over the 24 to 52 Week Treatment Period

End point values	Placebo	Dupilumab 300 mg Q2W		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	27	35		
Units: ACQ-5 Score				
arithmetic mean (standard deviation)				
Week 24 (n=23,32)	-1.10 (± 1.102)	-1.24 (± 1.081)		
Week 36 (n=22,29)	-0.81 (± 0.878)	-1.15 (± 1.208)		
Week 44 (n=20,26)	-0.87 (± 1.233)	-1.01 (± 1.359)		
Week 52 (n=16,27)	-0.84 (± 1.183)	-1.29 (± 1.241)		

Statistical analyses

No statistical analyses for this end point

Secondary: Change from baseline in St. George’s Respiratory Questionnaire (SGRQ) total score

End point title	Change from baseline in St. George’s Respiratory Questionnaire (SGRQ) total score

End point description:

SGRQ will be completed by the participant to measure and quantify health status in adult participants with chronic airflow limitation. Total score ranges from 0 to 100. Scores by dimension are calculated for three domains: Symptoms, Activity, and Impacts (Psychosocial). Lower score indicates better Quality of Life (QoL).

Randomized participants with a baseline measurement and at least one post-baseline measurement at the post-baseline time point of interest

End point type	Secondary

End point timeframe:

Over the 24 to 52 Week Treatment Period

End point values	Placebo	Dupilumab 300 mg Q2W		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	27	35		
Units: SGRQ Total Score				
arithmetic mean (standard deviation)				
Week 12 (n=22,34)	-9.463 (± 16.3993)	-17.956 (± 14.6184)		
Week 24 (n=22,31)	-7.626 (± 14.5412)	-23.079 (± 15.9104)		
Week 36 (n=21,29)	-8.796 (± 16.4257)	-20.178 (± 15.5266)		
Week 52 (n=19,28)	-8.938 (± 15.3127)	-25.309 (± 20.1035)		

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of participants achieving a reduction in the SGRQ total score of 4 points or greater from baseline

End point title	Percentage of participants achieving a reduction in the SGRQ total score of 4 points or greater from baseline

End point description:

SGRQ will be completed by the participants to measure and quantify health status in adult participants with chronic airflow limitation. Total score ranges from 0 to 100. Scores by dimension are calculated for three domains: Symptoms, Activity, and Impacts (Psychosocial). Lower score indicates better Quality of Life (QoL).

Participants must have both the baseline and at least one post-baseline measurement at the given post-baseline time point to be included in the calculation of the proportion at the given post-baseline time point.

End point type	Secondary

End point timeframe:

Up to 52 Weeks

End point values	Placebo	Dupilumab 300 mg Q2W		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	27	35		
Units: Percent				
number (confidence interval 95%)				
Week 12 (n=22,34)	50.0 (30.72 to 69.28)	85.3 (69.87 to 93.55)		
Week 24 (n=22,31)	63.6 (42.95 to 80.27)	87.1 (71.15 to 94.87)		
Week 36 (n=21,29)	57.1 (36.55 to 75.53)	86.2 (69.44 to 94.50)		

Week 52 (n=19,28)	68.4 (46.01 to 84.64)	89.3 (72.80 to 96.29)		

Statistical analyses

No statistical analyses for this end point

Secondary: Percent change from baseline in total IgE in serum

End point title	Percent change from baseline in total IgE in serum

End point description:

Randomized participants with a baseline measurement and at least one post-baseline measurement at the post-baseline time point of interest

End point type	Secondary

End point timeframe:

Over the 24 to 52 Week Treatment Period

End point values	Placebo	Dupilumab 300 mg Q2W		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	27	35		
Units: Percentage of change				
arithmetic mean (standard deviation)				
Week 24 (n=24,32)	-0.665 (± 40.2236)	-47.245 (± 19.4110)		
Week 36 (n=22,29)	-5.945 (± 27.6767)	-57.752 (± 18.0812)		
Week 52 (n=21,28)	-2.767 (± 42.8914)	-62.175 (± 17.0285)		

Statistical analyses

No statistical analyses for this end point

Secondary: Percent change from baseline in A fumigatus-specific IgE in serum

End point title	Percent change from baseline in A fumigatus-specific IgE in serum

End point description:

Randomized participants with a baseline measurement and at least one post-baseline measurement at the post-baseline time point of interest

End point type	Secondary

End point timeframe:

Over the 24 to 52 Week Treatment Period

End point values	Placebo	Dupilumab 300 mg Q2W		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	27	35		
Units: Percentage of change				
arithmetic mean (standard deviation)				
Week 24 (n=23,32)	0.099 (± 39.7612)	-39.859 (± 25.3095)		
Week 36 (n=21,30)	6.766 (± 39.9041)	-45.654 (± 26.7915)		
Week 52 (n=21,27)	12.618 (± 94.6306)	-49.126 (± 30.6790)		

Statistical analyses

No statistical analyses for this end point

Secondary: Absolute change from baseline in fractional exhaled nitric oxide (FeNO)

End point title	Absolute change from baseline in fractional exhaled nitric oxide (FeNO)

End point description:

Randomized participants with a baseline measurement and at least one post-baseline measurement at the post-baseline time point of interest

End point type	Secondary

End point timeframe:

Over the 24 to 52 Week Treatment Period

End point values	Placebo	Dupilumab 300 mg Q2W		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	27	35		
Units: ppb				
arithmetic mean (standard deviation)				
Week 24 (n=20,26)	-4.80 (± 23.521)	-22.04 (± 38.410)		
Week 36 (n=18,29)	3.11 (± 20.571)	-21.48 (± 40.538)		
Week 44 (n=21,28)	1.38 (± 21.896)	-19.18 (± 37.122)		
Week 52 (n=19,26)	-4.79 (± 27.634)	-19.04 (± 35.471)		

Statistical analyses

No statistical analyses for this end point

Secondary: Percent change from baseline in fractional exhaled nitric oxide (FeNO)

End point title	Percent change from baseline in fractional exhaled nitric oxide (FeNO)

End point description:

Randomized participants with a baseline measurement and at least one post-baseline measurement at the post-baseline time point of interest

End point type	Secondary

End point timeframe:

Over the 24 to 52 Week Treatment Period

End point values	Placebo	Dupilumab 300 mg Q2W		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	27	35		
Units: Percentage of change				
arithmetic mean (standard deviation)				
Week 24 (n=20,26)	1.67 (± 44.069)	-29.91 (± 32.527)		
Week 36 (n=18,29)	19.80 (± 44.053)	-24.56 (± 43.975)		
Week 44 (n=21,28)	15.43 (± 54.887)	-19.83 (± 48.308)		
Week 52 (n=19,26)	2.55 (± 56.506)	-20.35 (± 48.100)		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Participants with treatment-emergent adverse events (TEAEs) from baseline

End point title	Number of Participants with treatment-emergent adverse events (TEAEs) from baseline

End point description:

The safety analysis set (SAF) includes all randomized participants who received any study drug; it is based on the treatment received

End point type	Secondary

End point timeframe:

Through the end of the 52 Week Treatment Period

End point values	Placebo	Dupilumab 300 mg Q2W		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	27	35		
Units: Participants with TEAEs	22	30		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Participants with treatment-emergent anti-drug antibody (ADA) responses and titer over time

End point title	Number of Participants with treatment-emergent anti-drug antibody (ADA) responses and titer over time

End point description:

TE = Treatment-Emergent
TB = Treatment-Boosted

The Pharmacokinetic Analysis Set (PKAS) includes all randomized participants who received any study drug and who had at least one non-missing drug concentration result following the first dose of study drug. The PKAS is based on the treatment received rather than as randomized.

End point type	Secondary

End point timeframe:

Up to 64 Weeks

End point values	Placebo	Dupilumab 300 mg Q2W		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	25	34		
Units: Participants				
TE & TB Max Titer Category Low (<1,000)	0	1		
TE & TB Max Category Moderate (1,000-10,000)	0	0		
TE & TB Max Category High (>10,000)	0	0		

Statistical analyses

No statistical analyses for this end point

Secondary: Concentrations of functional dupilumab in serum by treatment regimen

End point title	Concentrations of functional dupilumab in serum by treatment regimen[1]

End point description:

Includes all randomized participants who received dupilumab and who had at least one non-missing dupilumab result following the first dose. The PKAS is based on the treatment received rather than as randomized.

End point type	Secondary

End point timeframe:

Up to 64 Weeks

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: Information not reported for placebo arm.

End point values	Dupilumab 300 mg Q2W			
Subject group type	Reporting group			
Number of subjects analysed	34			
Units: mg/L				
arithmetic mean (standard deviation)				
Week 0 (n=33)	0 (± 0)			
Week 12 (n=31)	63.8 (± 35.4)			
Week 24 (n=33)	86.5 (± 53.6)			
Week 52 (n=32)	82.2 (± 55.4)			
Week 64 (n=29)	1.67 (± 4.38)			

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information	
Timeframe for reporting adverse events: From Day 1 to EOS (End Of Study) visit ~(up to 64 weeks)	
Assessment type	Systematic
Dictionary used	
Dictionary name	MedDRA
Dictionary version	26.1
Reporting groups	
Reporting group title	Dupilumab 300 mg Q2W
Reporting group description: Subcutaneous (SC) dose every two weeks (Q2W)	
Reporting group title	Placebo
Reporting group description: Matching dupilumab without active substance	

Serious adverse events	Dupilumab 300 mg Q2W	Placebo	
Total subjects affected by serious adverse events			
subjects affected / exposed	3 / 35 (8.57%)	5 / 27 (18.52%)	
number of deaths (all causes)	1	1	
number of deaths resulting from adverse events			
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Pancreatic carcinoma metastatic			
subjects affected / exposed	0 / 35 (0.00%)	1 / 27 (3.70%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Oesophageal carcinoma			
subjects affected / exposed	0 / 35 (0.00%)	1 / 27 (3.70%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Injury, poisoning and procedural complications			
Pelvic fracture			
subjects affected / exposed	0 / 35 (0.00%)	1 / 27 (3.70%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Congenital, familial and genetic disorders			

Trisomy 16			
subjects affected / exposed	0 / 35 (0.00%)	1 / 27 (3.70%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vascular disorders			
Deep vein thrombosis			
subjects affected / exposed	1 / 35 (2.86%)	0 / 27 (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			
Abortion spontaneous			
subjects affected / exposed	0 / 35 (0.00%)	1 / 27 (3.70%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory, thoracic and mediastinal disorders			
Asthma			
subjects affected / exposed	1 / 35 (2.86%)	0 / 27 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory disorder			
subjects affected / exposed	1 / 35 (2.86%)	0 / 27 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Haemoptysis			
subjects affected / exposed	1 / 35 (2.86%)	0 / 27 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Renal and urinary disorders			
Nephrotic syndrome			
subjects affected / exposed	1 / 35 (2.86%)	0 / 27 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Infections and infestations			
Influenza			

subjects affected / exposed	2 / 35 (5.71%)	0 / 27 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Pneumonia			
subjects affected / exposed	0 / 35 (0.00%)	1 / 27 (3.70%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Lower respiratory tract infection			
subjects affected / exposed	0 / 35 (0.00%)	1 / 27 (3.70%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Bronchopulmonary aspergillosis allergic			
subjects affected / exposed	0 / 35 (0.00%)	1 / 27 (3.70%)	
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 / 35 (2.86%)	0 / 27 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumonia bacterial			
subjects affected / exposed	2 / 35 (5.71%)	0 / 27 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	

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

Non-serious adverse events	Dupilumab 300 mg Q2W	Placebo	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	29 / 35 (82.86%)	19 / 27 (70.37%)	
Nervous system disorders			
Headache			
subjects affected / exposed	6 / 35 (17.14%)	2 / 27 (7.41%)	
occurrences (all)	15	3	
General disorders and administration			

site conditions			
Injection site erythema			
subjects affected / exposed	4 / 35 (11.43%)	0 / 27 (0.00%)	
occurrences (all)	35	0	
Injection site pain			
subjects affected / exposed	3 / 35 (8.57%)	1 / 27 (3.70%)	
occurrences (all)	3	1	
Pyrexia			
subjects affected / exposed	2 / 35 (5.71%)	0 / 27 (0.00%)	
occurrences (all)	3	0	
Malaise			
subjects affected / exposed	2 / 35 (5.71%)	0 / 27 (0.00%)	
occurrences (all)	2	0	
Influenza like illness			
subjects affected / exposed	2 / 35 (5.71%)	0 / 27 (0.00%)	
occurrences (all)	2	0	
Asthenia			
subjects affected / exposed	2 / 35 (5.71%)	3 / 27 (11.11%)	
occurrences (all)	2	9	
Injection site swelling			
subjects affected / exposed	3 / 35 (8.57%)	0 / 27 (0.00%)	
occurrences (all)	6	0	
Eye disorders			
Blepharitis			
subjects affected / exposed	2 / 35 (5.71%)	0 / 27 (0.00%)	
occurrences (all)	2	0	
Gastrointestinal disorders			
Abdominal pain upper			
subjects affected / exposed	1 / 35 (2.86%)	2 / 27 (7.41%)	
occurrences (all)	1	2	
Gastrooesophageal reflux disease			
subjects affected / exposed	2 / 35 (5.71%)	1 / 27 (3.70%)	
occurrences (all)	2	1	
Constipation			
subjects affected / exposed	2 / 35 (5.71%)	0 / 27 (0.00%)	
occurrences (all)	2	0	
Nausea			

subjects affected / exposed	3 / 35 (8.57%)	0 / 27 (0.00%)	
occurrences (all)	3	0	
Respiratory, thoracic and mediastinal disorders			
Respiratory disorder			
subjects affected / exposed	4 / 35 (11.43%)	9 / 27 (33.33%)	
occurrences (all)	4	22	
Cough			
subjects affected / exposed	4 / 35 (11.43%)	1 / 27 (3.70%)	
occurrences (all)	6	1	
Asthma			
subjects affected / exposed	4 / 35 (11.43%)	3 / 27 (11.11%)	
occurrences (all)	5	4	
Musculoskeletal and connective tissue disorders			
Myalgia			
subjects affected / exposed	3 / 35 (8.57%)	0 / 27 (0.00%)	
occurrences (all)	3	0	
Back pain			
subjects affected / exposed	3 / 35 (8.57%)	0 / 27 (0.00%)	
occurrences (all)	3	0	
Arthralgia			
subjects affected / exposed	8 / 35 (22.86%)	0 / 27 (0.00%)	
occurrences (all)	15	0	
Infections and infestations			
Acute sinusitis			
subjects affected / exposed	2 / 35 (5.71%)	2 / 27 (7.41%)	
occurrences (all)	2	2	
Urinary tract infection			
subjects affected / exposed	4 / 35 (11.43%)	0 / 27 (0.00%)	
occurrences (all)	6	0	
Upper respiratory tract infection			
subjects affected / exposed	4 / 35 (11.43%)	1 / 27 (3.70%)	
occurrences (all)	6	1	
COVID-19			
subjects affected / exposed	6 / 35 (17.14%)	3 / 27 (11.11%)	
occurrences (all)	6	3	
Pneumonia			

subjects affected / exposed	2 / 35 (5.71%)	1 / 27 (3.70%)	
occurrences (all)	3	1	
Respiratory tract infection			
subjects affected / exposed	2 / 35 (5.71%)	0 / 27 (0.00%)	
occurrences (all)	2	0	
Rhinitis			
subjects affected / exposed	2 / 35 (5.71%)	0 / 27 (0.00%)	
occurrences (all)	2	0	
Sinusitis			
subjects affected / exposed	2 / 35 (5.71%)	1 / 27 (3.70%)	
occurrences (all)	2	1	
Tooth infection			
subjects affected / exposed	2 / 35 (5.71%)	0 / 27 (0.00%)	
occurrences (all)	3	0	
Viral upper respiratory tract infection			
subjects affected / exposed	2 / 35 (5.71%)	1 / 27 (3.70%)	
occurrences (all)	2	2	
Respiratory tract infection bacterial			
subjects affected / exposed	0 / 35 (0.00%)	3 / 27 (11.11%)	
occurrences (all)	0	3	
Lower respiratory tract infection			
subjects affected / exposed	2 / 35 (5.71%)	2 / 27 (7.41%)	
occurrences (all)	2	3	
Cystitis			
subjects affected / exposed	2 / 35 (5.71%)	0 / 27 (0.00%)	
occurrences (all)	3	0	
Conjunctivitis			
subjects affected / exposed	2 / 35 (5.71%)	0 / 27 (0.00%)	
occurrences (all)	3	0	
Bronchopulmonary aspergillosis allergic			
subjects affected / exposed	2 / 35 (5.71%)	0 / 27 (0.00%)	
occurrences (all)	5	0	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
29 January 2020	Language updates
11 February 2021	The purpose of this protocol amendment was to: update inclusion and exclusion criteria; add provisions to protect patient safety and data integrity during the COVID-19 pandemic; and for minor clarifications, editorial corrections and consistency.
02 February 2023	The purpose of this protocol amendment was to modify study phase, number of participants to be enrolled, study schedule, treatment period, and endpoints. This was due to difficulty in reaching study enrollment goal during the COVID-19 pandemic and low prevalence of ABPA.
24 March 2023	The purpose of this amendment was to modify the study phase.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported