Clinical trial results:
A randomized, double-blind, placebo-controlled, parallel-group study to evaluate the effect of dupilumab on exercise capacity in patients with moderate-to-severe asthma

Summary

EudraCT number	2019-002742-20
Trial protocol	DE GB
Global end of trial date	15 July 2023

Results information

Result version number	v1 (current)
This version publication date	06 April 2024
First version publication date	06 April 2024

Trial information

Trial identification

Sponsor protocol code	R668-AS-1903

Additional study identifiers

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

Notes:

Sponsors

Sponsor organisation name	Regeneron Pharmaceuticals, Inc
Sponsor organisation address	777 Old Saw Mill River Road, Tarrytown, 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	15 July 2023
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	15 July 2023
Was the trial ended prematurely?	Yes

Notes:

General information about the trial

Main objective of the trial:

Determine whether dupilumab treatment improves exercise capacity and physical activities.

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	16 July 2020
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	France: 4
Country: Number of subjects enrolled	Germany: 14
Country: Number of subjects enrolled	Poland: 6
Country: Number of subjects enrolled	Spain: 10
Country: Number of subjects enrolled	United States: 6
Worldwide total number of subjects	40
EEA total number of subjects	34

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)	40

From 65 to 84 years	0
85 years and over	0

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

127 participants screened, 87 screen-fail, 40 participants randomized

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 placebo

Arm type	Placebo
Investigational medicinal product name	Placebo for Dupilumab
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Cutaneous liquid
Routes of administration	Subcutaneous use

Dosage and administration details:

Matching placebo - 600 mg loading dose on study day 1 followed by 300 mg Q2W from weeks 2 to 10

Arm title	dupilumab

Arm description:

A loading dose at the start of the treatment followed by once every two weeks (Q2W).

Arm type	Experimental
Investigational medicinal product name	Dupilumab
Investigational medicinal product code	REGN668
Other name	DUPIXENT
Pharmaceutical forms	Cutaneous liquid
Routes of administration	Subcutaneous use

Dosage and administration details:

600 mg loading dose on study day 1 followed by 300 mg Q2W from weeks 2 to 10

Number of subjects in period 1	Placebo	dupilumab
Started	20	20
Completed	18	20
Not completed	2	0
Adverse event, non-fatal	1	-
Did not complete End of Study follow-up	1	-

Baseline characteristics

Reporting groups	
Reporting group title	Placebo
Reporting group description:	
Matching dupilumab placebo	
Reporting group title	dupilumab
Reporting group description:	
A loading dose at the start of the treatment followed by once every two weeks (Q2W).	

Reporting group values	Placebo	dupilumab	Total
Number of subjects	20	20	40
Age categorical Units: Subjects			
In utero	0	0	0
Preterm newborn infants (gestational age < 37 wks)	0	0	0
Newborns (0-27 days)	0	0	0
Infants and toddlers (28 days-23 months)	0	0	0
Children (2-11 years)	0	0	0
Adolescents (12-17 years)	0	0	0
Adults (18-64 years)	20	20	40
From 65-84 years	0	0	0
85 years and over	0	0	0
Age Continuous Units: Years			
arithmetic mean	46.5	45.3	
standard deviation	± 7.7	± 7.8	-
Sex: Female, Male Units: Participants			
Female	11	8	19
Male	9	12	21
Race (NIH/OMB) Units: Subjects			
American Indian or Alaska Native	0	0	0
Asian	0	0	0
Native Hawaiian or Other Pacific Islander	0	0	0
Black or African American	2	1	3
White	18	19	37
More than one race	0	0	0
Unknown or Not Reported	0	0	0
Ethnicity (NIH/OMB) Units: Subjects			
Hispanic or Latino	1	2	3
Not Hispanic or Latino	19	18	37
Unknown or Not Reported	0	0	0

End points

End points reporting groups

Reporting group title	Placebo
Reporting group description: Matching dupilumab placebo	
Reporting group title	dupilumab
Reporting group description: A loading dose at the start of the treatment followed by once every two weeks (Q2W).	

Primary: Change from baseline to week 12 in constant work rate exercise endurance time

End point title	Change from baseline to week 12 in constant work rate exercise endurance time[1]
End point description: CWRET (Constant Work Rate Exercise Test) will be performed on an electromagnetically-braked cycle ergometer in an exercise physiology laboratory overseen by a trained pulmonologist or medical doctor designee.	
End point type	Primary
End point timeframe: Up to week 12	

Notes:

[1] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: No statistical analyses for this end point

End point values	Placebo	dupilumab		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	17	20		
Units: Minutes				
arithmetic mean (confidence interval 95%)	0.923 (-0.614 to 2.460)	1.742 (-0.054 to 3.538)		

Statistical analyses

No statistical analyses for this end point

Secondary: Change from baseline to week 12 in pre- and post-exercise Forced Expiratory Volume in One Second (FEV1)

End point title	Change from baseline to week 12 in pre- and post-exercise Forced Expiratory Volume in One Second (FEV1)
End point description: Based on spirometry data	
End point type	Secondary
End point timeframe: Up to week 12	

End point values	Placebo	dupilumab		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	20	20		
Units: Liters				
arithmetic mean (confidence interval 95%)				
Pre-exercise	0.2123 (0.0072 to 0.4174)	0.4205 (0.1409 to 0.7000)		
2-min Post-Exercise	0.2550 (-0.2390 to 0.7490)	0.2902 (0.0886 to 0.4919)		
5-min Post-Exercise	0.2416 (0.0238 to 0.4593)	0.4156 (0.1505 to 0.6808)		
10-min Post-Exercise	0.2211 (0.0180 to 0.4243)	0.4613 (0.2167 to 0.7060)		
20-min Post-Exercise	0.2496 (0.0608 to 0.4384)	0.4738 (0.2230 to 0.7245)		

Statistical analyses

No statistical analyses for this end point

Secondary: Change from baseline to week 12 in the mean duration of moderate-to-vigorous physical activity

End point title	Change from baseline to week 12 in the mean duration of moderate-to-vigorous physical activity
End point description:	
Defined as ≥3 METs. Based on accelerometry data	
End point type	Secondary
End point timeframe:	
Up to week 12	

End point values	Placebo	dupilumab		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	15	16		
Units: Minutes				
arithmetic mean (confidence interval 95%)	-11.01 (-30.52 to 8.50)	9.38 (-13.41 to 32.18)		

Statistical analyses

No statistical analyses for this end point

Secondary: Change from baseline to week 12 in average number of steps walked per day

End point title	Change from baseline to week 12 in average number of steps walked per day
End point description:	
Based on accelerometry data	
End point type	Secondary
End point timeframe:	
Up to week 12	

End point values	Placebo	dupilumab		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	15	16		
Units: Steps				
arithmetic mean (confidence interval 95%)	-1066.11 (-2921.32 to 789.10)	925.92 (-691.46 to 2543.30)		

Statistical analyses

No statistical analyses for this end point

Secondary: Change from baseline to week 12 in total energy expenditure

End point title	Change from baseline to week 12 in total energy expenditure
End point description:	
Metabolic equivalents of tasks [METs]. Based on accelerometry data	
End point type	Secondary
End point timeframe:	
Up to week 12	

End point values	Placebo	dupilumab		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	15	16		
Units: METs (metabolic equivalent of task)				
arithmetic mean (confidence interval 95%)	23.40 (-87.37 to 134.17)	59.36 (-15.83 to 134.55)		

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information	
Timeframe for reporting adverse events: Up to 22 weeks	
Assessment type	Systematic
Dictionary used	
Dictionary name	MedDRA
Dictionary version	26.0
Reporting groups	
Reporting group title	Placebo
Reporting group description: Matching dupilumab placebo	
Reporting group title	Dupilumab 300 mg Q2W
Reporting group description: A loading dose at the start of the treatment followed by once every two weeks (Q2W).	

Serious adverse events	Placebo	Dupilumab 300 mg Q2W	
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 20 (0.00%)	0 / 20 (0.00%)	
number of deaths (all causes)	0	0	
number of deaths resulting from adverse events			

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

Non-serious adverse events	Placebo	Dupilumab 300 mg Q2W	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	9 / 20 (45.00%)	3 / 20 (15.00%)	
Injury, poisoning and procedural complications			
Immunisation reaction			
subjects affected / exposed	0 / 20 (0.00%)	1 / 20 (5.00%)	
occurrences (all)	0	1	
Nervous system disorders			
Headache			
subjects affected / exposed	2 / 20 (10.00%)	0 / 20 (0.00%)	
occurrences (all)	3	0	
Syncope			

subjects affected / exposed	1 / 20 (5.00%)	0 / 20 (0.00%)	
occurrences (all)	1	0	
General disorders and administration site conditions			
Injection site erythema			
subjects affected / exposed	0 / 20 (0.00%)	1 / 20 (5.00%)	
occurrences (all)	0	2	
Eye disorders			
Eye discharge			
subjects affected / exposed	1 / 20 (5.00%)	0 / 20 (0.00%)	
occurrences (all)	1	0	
Gastrointestinal disorders			
Food poisoning			
subjects affected / exposed	1 / 20 (5.00%)	0 / 20 (0.00%)	
occurrences (all)	1	0	
Respiratory, thoracic and mediastinal disorders			
Asthma			
subjects affected / exposed	2 / 20 (10.00%)	1 / 20 (5.00%)	
occurrences (all)	2	1	
Cough			
subjects affected / exposed	1 / 20 (5.00%)	1 / 20 (5.00%)	
occurrences (all)	1	1	
Sinus pain			
subjects affected / exposed	0 / 20 (0.00%)	1 / 20 (5.00%)	
occurrences (all)	0	1	
Musculoskeletal and connective tissue disorders			
Back pain			
subjects affected / exposed	1 / 20 (5.00%)	0 / 20 (0.00%)	
occurrences (all)	1	0	
Tendonitis			
subjects affected / exposed	1 / 20 (5.00%)	0 / 20 (0.00%)	
occurrences (all)	1	0	
Sacroiliitis			
subjects affected / exposed	1 / 20 (5.00%)	0 / 20 (0.00%)	
occurrences (all)	1	0	
Infections and infestations			

Rhinitis			
subjects affected / exposed	0 / 20 (0.00%)	1 / 20 (5.00%)	
occurrences (all)	0	1	
Bronchitis			
subjects affected / exposed	1 / 20 (5.00%)	0 / 20 (0.00%)	
occurrences (all)	1	0	
COVID-19			
subjects affected / exposed	3 / 20 (15.00%)	0 / 20 (0.00%)	
occurrences (all)	3	0	
Respiratory tract infection			
subjects affected / exposed	1 / 20 (5.00%)	0 / 20 (0.00%)	
occurrences (all)	1	0	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? No

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported