Clinical trial results:
One year study to evaluate the long-term safety and tolerability of dupilumab in pediatric patients with asthma who participated in a previous dupilumab asthma clinical study

Summary

EudraCT number	2017-003317-25
Trial protocol	Outside EU/EEA LT HU PL IT ES
Global end of trial date	01 April 2025

Results information

Result version number	v1
This version publication date	23 October 2025
First version publication date	23 October 2025

Trial information

Trial identification

Sponsor protocol code	LTS14424

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT03560466
WHO universal trial number (UTN)	U1111-1200-1757

Notes:

Sponsors

Sponsor organisation name	Sanofi aventis recherche & développement
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)	Yes
EMA paediatric investigation plan number(s)	EMEA-001501-PIP02-13
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?	Yes

Notes:

Results analysis stage

Analysis stage	Final
Date of interim/final analysis	29 April 2025
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	01 April 2025
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

Main study: To evaluate the long-term safety and tolerability of dupilumab in pediatric participants with asthma who participated in a previous dupilumab asthma clinical study EFC14153 (2016-001607-23). Japan sub-study: To evaluate the efficacy of dupilumab in children 6 to <12 years of age with uncontrolled persistent asthma in the Japan sub-study.

Protection of trial subjects:

The study was conducted by investigators experienced in the treatment of pediatric participants. The parent(s) or guardian(s) as well as the children were fully informed of all pertinent aspects of the clinical trial as well as the possibility to discontinue at any time. In addition to the consent form for the parent(s)/guardian(s), an assent form in child-appropriate language was provided and explained to the child. Repeated invasive procedures were minimized. The number of blood samples as well as the amount of blood drawn were adjusted according to age and weight. A topical anesthesia may have been used to minimize distress and discomfort.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	21 June 2018
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: 54
Country: Number of subjects enrolled	Australia: 1
Country: Number of subjects enrolled	Brazil: 19
Country: Number of subjects enrolled	Canada: 4
Country: Number of subjects enrolled	Chile: 29
Country: Number of subjects enrolled	Colombia: 7
Country: Number of subjects enrolled	Hungary: 25
Country: Number of subjects enrolled	Italy: 6
Country: Number of subjects enrolled	Japan: 13
Country: Number of subjects enrolled	Lithuania: 17
Country: Number of subjects enrolled	Mexico: 55
Country: Number of subjects enrolled	Poland: 23
Country: Number of subjects enrolled	Russian Federation: 10
Country: Number of subjects enrolled	South Africa: 12
Country: Number of subjects enrolled	Spain: 1
Country: Number of subjects enrolled	Türkiye: 7

Country: Number of subjects enrolled	Ukraine: 51
Country: Number of subjects enrolled	United States: 44
Worldwide total number of subjects	378
EEA total number of subjects	72

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)	378
Adolescents (12-17 years)	0
Adults (18-64 years)	0
From 65 to 84 years	0
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

The main study was conducted at 70 centers in 17 countries, and the sub-study was conducted at 11 centers in Japan. 365 participants who rolled over from parent study EFC14153 were enrolled in the main study and 13 participants (not included in parent study EFC14153) were enrolled in Japan sub-study.

Pre-assignment

Screening details:

All participants received dupilumab dose based on body weight in the main study and Japan sub-study. As pre-specified in the protocol and statistical analysis plan (SAP), the results are presented by study and treatment group, regardless of the dose regimen.

Period 1

Period 1 title	Overall Study (overall period)
Is this the baseline period?	Yes
Allocation method	Not applicable
Blinding used	Not blinded

Arms

Are arms mutually exclusive?	Yes
Arm title	Main Study: Placebo-Dupilumab

Arm description:

Participants who received placebo matched to dupilumab in the parent study EFC14153 received dupilumab for 52 weeks in the main study as follows:
- 100 milligrams (mg) once every 2 weeks (q2w) as a subcutaneous (SC) injection or 300 mg once every 4 weeks (q4w) as an SC injection for participants with body weight ≤30 kilograms (kg).
- 200 mg q2w as an SC injection for participants with body weight >30 kg.
Participants also received a stable-dose background therapy of medium-dose inhaled corticosteroids (ICS) with a second controller medication (i.e., long-acting beta-2 agonists [LABA], long-acting muscarinic antagonists [LAMA], leukotriene receptor antagonists [LTRA] or methylxanthines) or high-dose ICS alone or high-dose ICS with second controller medication. Albuterol/salbutamol or levalbuterol/levosalbutamol was given as reliever medication as instructed by Investigator.

Arm type	Experimental
Investigational medicinal product name	Dupilumab
Investigational medicinal product code	SAR231893
Other name	Dupixent, REGN668
Pharmaceutical forms	Solution for injection in pre-filled syringe
Routes of administration	Subcutaneous use

Dosage and administration details:

Dupilumab was administered as an SC injection at a dose 100 mg q2w or 300mg q4w for participants with body weight ≤30 kg and 200 mg q2w for participants with body weight >30 kg for 52 weeks.

Arm title	Main Study: Dupilumab-Dupilumab

Arm description:

Participants who received dupilumab in the parent study EFC14153 received dupilumab for 52 weeks in the main study as follows:
- 100 mg q2w as an SC injection or 300 mg q4w as an SC injection for participants with body weight ≤30 kg.
- 200 mg q2w as an SC injection for participants with body weight >30 kg.
Participants also received a stable-dose background therapy of medium-dose ICS with a second controller medication (i.e., LABA, LAMA, LTRA or methylxanthines) or high-dose ICS alone or high-dose ICS with second controller medication. Albuterol/salbutamol or levalbuterol/levosalbutamol was given as reliever medication as instructed by Investigator.

Arm type	Experimental

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

Dosage and administration details:

Dupilumab was administered as an SC injection at a dose 100 mg q2w or 300mg q4w for participants with body weight ≤30 kg and 200 mg q2w for participants with body weight >30 kg for 52 weeks.

Arm title	Japan Sub-study: Dupilumab

Arm description:

Participants received dupilumab for 52 weeks in the Japan sub-study as follows:
- 100 mg q2w as an SC injection or 300 mg q4w as an SC injection for participants with body weight ≥15 kg and ≤30 kg.
- 200 mg q2w as an SC injection for participants with body weight >30 kg.
Participants also received a stable-dose background therapy of medium-dose ICS with a second controller medication (i.e., LABA, LAMA, LTRA or methylxanthines) or high-dose ICS alone or high-dose ICS with second controller medication. Albuterol/salbutamol or levalbuterol/levosalbutamol was given as reliever medication as instructed by Investigator.

Arm type	Experimental
Investigational medicinal product name	Dupilumab
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Routes of administration	Subcutaneous use

Dosage and administration details:

Dupilumab was administered as an SC injection at a dose 100 mg q2w or 300 mg q4w for participants with body weight ≥15 kg and ≤30 kg and 200 mg q2w for participants with body weight >30 kg for 52 weeks.

Number of subjects in period 1	Main Study: Placebo-Dupilumab	Main Study: Dupilumab-Dupilumab	Japan Sub-study: Dupilumab
Started	125	240	13
Completed	118	228	12
Not completed	7	12	1
Adverse event, non-fatal	1	2	-
Unspecified	6	8	1
Poor compliance to protocol	-	2	-

Baseline characteristics

Reporting groups

Reporting group title	Main Study: Placebo-Dupilumab

Reporting group description:

Participants who received placebo matched to dupilumab in the parent study EFC14153 received dupilumab for 52 weeks in the main study as follows:
- 100 milligrams (mg) once every 2 weeks (q2w) as a subcutaneous (SC) injection or 300 mg once every 4 weeks (q4w) as an SC injection for participants with body weight ≤30 kilograms (kg).
- 200 mg q2w as an SC injection for participants with body weight >30 kg.
Participants also received a stable-dose background therapy of medium-dose inhaled corticosteroids (ICS) with a second controller medication (i.e., long-acting beta-2 agonists [LABA], long-acting muscarinic antagonists [LAMA], leukotriene receptor antagonists [LTRA] or methylxanthines) or high-dose ICS alone or high-dose ICS with second controller medication. Albuterol/salbutamol or levalbuterol/levosalbutamol was given as reliever medication as instructed by Investigator.

Reporting group title	Main Study: Dupilumab-Dupilumab

Reporting group description:

Participants who received dupilumab in the parent study EFC14153 received dupilumab for 52 weeks in the main study as follows:
- 100 mg q2w as an SC injection or 300 mg q4w as an SC injection for participants with body weight ≤30 kg.
- 200 mg q2w as an SC injection for participants with body weight >30 kg.
Participants also received a stable-dose background therapy of medium-dose ICS with a second controller medication (i.e., LABA, LAMA, LTRA or methylxanthines) or high-dose ICS alone or high-dose ICS with second controller medication. Albuterol/salbutamol or levalbuterol/levosalbutamol was given as reliever medication as instructed by Investigator.

Reporting group title	Japan Sub-study: Dupilumab

Reporting group description:

Participants received dupilumab for 52 weeks in the Japan sub-study as follows:
- 100 mg q2w as an SC injection or 300 mg q4w as an SC injection for participants with body weight ≥15 kg and ≤30 kg.
- 200 mg q2w as an SC injection for participants with body weight >30 kg.
Participants also received a stable-dose background therapy of medium-dose ICS with a second controller medication (i.e., LABA, LAMA, LTRA or methylxanthines) or high-dose ICS alone or high-dose ICS with second controller medication. Albuterol/salbutamol or levalbuterol/levosalbutamol was given as reliever medication as instructed by Investigator.

Reporting group values	Main Study: Placebo-Dupilumab	Main Study: Dupilumab-Dupilumab	Japan Sub-study: Dupilumab
Number of subjects	125	240	13
Age Categorical Units: Participants			
Age Continuous Units: years			
arithmetic mean	9.9	9.9	9.69
standard deviation	± 1.6	± 1.7	± 1.11
Gender Categorical Units: Participants			
Female	46	85	4
Male	79	155	9
Race Units: Subjects			
Caucasian/White	111	215	0
Black/of African Descent	6	9	0

Asian	0	1	13
American Indian or Alaska Native	0	1	0
Other	8	14	0

Reporting group values	Total		
Number of subjects	378		
Age Categorical Units: Participants			
Age Continuous Units: years arithmetic mean standard deviation	- -		
Gender Categorical Units: Participants			
Female	135		
Male	243		
Race Units: Subjects			
Caucasian/White	326		
Black/of African Descent	15		
Asian	14		
American Indian or Alaska Native	1		
Other	22		

End points

End points reporting groups

Reporting group title	Main Study: Placebo-Dupilumab

Reporting group description:

Participants who received placebo matched to dupilumab in the parent study EFC14153 received dupilumab for 52 weeks in the main study as follows:
- 100 milligrams (mg) once every 2 weeks (q2w) as a subcutaneous (SC) injection or 300 mg once every 4 weeks (q4w) as an SC injection for participants with body weight ≤30 kilograms (kg).
- 200 mg q2w as an SC injection for participants with body weight >30 kg.
Participants also received a stable-dose background therapy of medium-dose inhaled corticosteroids (ICS) with a second controller medication (i.e., long-acting beta-2 agonists [LABA], long-acting muscarinic antagonists [LAMA], leukotriene receptor antagonists [LTRA] or methylxanthines) or high-dose ICS alone or high-dose ICS with second controller medication. Albuterol/salbutamol or levalbuterol/levosalbutamol was given as reliever medication as instructed by Investigator.

Reporting group title	Main Study: Dupilumab-Dupilumab

Reporting group description:

Participants who received dupilumab in the parent study EFC14153 received dupilumab for 52 weeks in the main study as follows:
- 100 mg q2w as an SC injection or 300 mg q4w as an SC injection for participants with body weight ≤30 kg.
- 200 mg q2w as an SC injection for participants with body weight >30 kg.
Participants also received a stable-dose background therapy of medium-dose ICS with a second controller medication (i.e., LABA, LAMA, LTRA or methylxanthines) or high-dose ICS alone or high-dose ICS with second controller medication. Albuterol/salbutamol or levalbuterol/levosalbutamol was given as reliever medication as instructed by Investigator.

Reporting group title	Japan Sub-study: Dupilumab

Reporting group description:

Participants received dupilumab for 52 weeks in the Japan sub-study as follows:
- 100 mg q2w as an SC injection or 300 mg q4w as an SC injection for participants with body weight ≥15 kg and ≤30 kg.
- 200 mg q2w as an SC injection for participants with body weight >30 kg.
Participants also received a stable-dose background therapy of medium-dose ICS with a second controller medication (i.e., LABA, LAMA, LTRA or methylxanthines) or high-dose ICS alone or high-dose ICS with second controller medication. Albuterol/salbutamol or levalbuterol/levosalbutamol was given as reliever medication as instructed by Investigator.

Subject analysis set title	Main Study: Dupilumab 100 mg q2w
Subject analysis set type	Per protocol

Subject analysis set description:

All participants from the main study who received dupilumab 100 mg q2w were included in this arm.

Subject analysis set title	Main Study: Dupilumab 200 mg q2w
Subject analysis set type	Per protocol

Subject analysis set description:

All participants from the main study who received dupilumab 200 mg q2w were included in this arm.

Subject analysis set title	Main Study: Dupilumab 300 mg q4w
Subject analysis set type	Per protocol

Subject analysis set description:

All participants from the main study who received dupilumab 300 mg q4w were included in this arm.

Subject analysis set title	Japan Sub-study: Dupilumab 100 mg q2w
Subject analysis set type	Per protocol

Subject analysis set description:

All participants from the Japan sub-study who received dupilumab 100 mg q2w were included in this arm.

Subject analysis set title	Japan Sub-study: Dupilumab 200 mg q2w
Subject analysis set type	Per protocol

Subject analysis set description:

All participants from the Japan sub-study who received dupilumab 200 mg q2w were included in this arm.

Subject analysis set title	Japan Sub-study: Dupilumab 300 mg q4w
Subject analysis set type	Per protocol

Subject analysis set description:

All participants from the Japan sub-study who received dupilumab 300 mg q4w were included in this arm.

Primary: Main Study: Number of Participants With Any Treatment-Emergent Adverse Events (TEAEs)

End point title	Main Study: Number of Participants With Any Treatment-Emergent Adverse Events (TEAEs)[1][2]

End point description:

An adverse event (AE) was any untoward medical occurrence in a participant or clinical investigation participant administered a pharmaceutical product and which did not necessarily have to have a causal relationship with this treatment. TEAEs were AEs that developed or worsened or became serious during the TEAE period. Safety population included all participants exposed to at least 1 dose or part of a dose of the study treatment during current study regardless of the amount of treatment administered.

End point type	Primary

End point timeframe:

From first dose of study treatment (Day 1) up to 112 days post last dose of study treatment, approximately 64 weeks

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: As the endpoint is descriptive in nature, no statistical analysis is provided.

[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: Only participants in the Main study arms were analyzed in this endpoint.

End point values	Main Study: Placebo-Dupilumab	Main Study: Dupilumab-Dupilumab		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	125	240		
Units: participants	85	147		

Statistical analyses

No statistical analyses for this end point

Primary: Japan Sub-study: Change From Baseline to Week 12 in Pre-Bronchodilator Percent Predicted Forced Expiratory Volume in 1 Second (FEV1)

End point title	Japan Sub-study: Change From Baseline to Week 12 in Pre-Bronchodilator Percent Predicted Forced Expiratory Volume in 1 Second (FEV1)[3][4]

End point description:

FEV1 was the volume of air (in liters) exhaled from the lungs in the first second of a forced expiration as measured by spirometer. Spirometry was performed after a wash out period of bronchodilators according to their action duration. Baseline was defined as the last available measurement prior to the first study treatment dose if the participant was treated, or the last available value up to enrollment if the participant was not exposed to study treatment in the current study. Intent-to-treat (ITT) population included all participants in the enrolled population in the current study.

End point type	Primary

End point timeframe:

Baseline (Day 1) to Week 12

Notes:

[3] - 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: As the endpoint is descriptive in nature, no statistical analysis is provided.

[4] - 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: Only participants in the Japan sub-study arms were analyzed in this endpoint.

End point values	Japan Sub-study: Dupilumab			
Subject group type	Reporting group			
Number of subjects analysed	13			
Units: percent predicted FEV1				
arithmetic mean (standard deviation)	7.08 (± 6.78)			

Statistical analyses

No statistical analyses for this end point

Secondary: Japan Sub-study: Number of Participants With Any Treatment-Emergent Adverse Events

End point title	Japan Sub-study: Number of Participants With Any Treatment-Emergent Adverse Events[5]

End point description:

An AE was any untoward medical occurrence in a participant or clinical investigation participant administered a pharmaceutical product and which did not necessarily have to have a causal relationship with this treatment. TEAEs were AEs that developed or worsened or became serious during the TEAE period. Safety population included all enrolled participants who took at least 1 dose of study treatment in the current study, regardless of the amount of treatment administered.

End point type	Secondary

End point timeframe:

From first dose of study treatment (Day 1) up to 112 days post last dose of study treatment, approximately 64 weeks

Notes:

[5] - 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: Only participants in the Japan sub-study arms were analyzed in this endpoint.

End point values	Japan Sub-study: Dupilumab			
Subject group type	Reporting group			
Number of subjects analysed	13			
Units: participants	13			

Statistical analyses

No statistical analyses for this end point

Secondary: Annualized Rate of Severe Asthma Exacerbation Events During the 52-

Week Treatment Period

End point title	Annualized Rate of Severe Asthma Exacerbation Events During the 52-Week Treatment Period

End point description:

A severe exacerbation event during study was defined as a deterioration of asthma requiring use of systemic corticosteroid (SCS) for ≥3 days or hospitalization/emergency room visit because of asthma, requiring SCS. Annualized severe exacerbation event rate was defined as total number of events that occurred during 52-week treatment period divided by total number of participant-years followed in 52-week treatment period. Main study: safety population included all participants exposed to at least 1 dose or part of a dose of study treatment during current study regardless of amount of treatment administered. Sub-study: ITT population included all participants in enrolled population in the current study.

End point type	Secondary

End point timeframe:

Up to Week 52

End point values	Main Study: Placebo-Dupilumab	Main Study: Dupilumab-Dupilumab	Japan Sub-study: Dupilumab	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	125	240	13	
Units: exacerbations per participant-years				
number (not applicable)	0.114	0.120	0.462	

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in Pre-Bronchodilator Percent Predicted Forced Expiratory Volume in 1 Second Over Time

End point title	Change From Baseline in Pre-Bronchodilator Percent Predicted Forced Expiratory Volume in 1 Second Over Time

End point description:

FEV1 was volume of air (in liters) exhaled from the lungs in first second of a forced expiration as measured by spirometer. Spirometry was performed after a wash out period of bronchodilators according to their action duration. Baseline (main study): original baseline of parent study EFC14153. Baseline (sub-study): last available measurement prior to first study treatment dose if participant was treated, or last available value up to enrollment if participant was not exposed to study treatment in current study. Main study: safety population included all participants exposed to at least 1 dose or part of a dose of study treatment during current study regardless of amount of treatment administered. Sub-study: ITT population included all participants in enrolled population in current study. Only participants with data collected are reported. n=number of participants with data collected at specified timepoints. 99999=no data as there were no participants analyzed for that timepoint.

End point type	Secondary

End point timeframe:

Baseline (Day 1) and Weeks 2, 4 (Japan sub-study), 8, 12, 24, 52 and 64

End point values	Main Study: Placebo-Dupilumab	Main Study: Dupilumab-Dupilumab	Japan Sub-study: Dupilumab	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	122	231	13	
Units: percent predicted FEV1				
arithmetic mean (standard deviation)				
Week 2 (n=122, 231, 12)	8.06 (± 15.71)	11.03 (± 18.74)	7.50 (± 9.29)	
Week 4 (n=0, 0, 13)	99999 (± 99999)	99999 (± 99999)	7.00 (± 7.12)	
Week 8 (n=120, 222, 13)	7.93 (± 14.88)	12.47 (± 18.60)	6.31 (± 8.97)	
Week 12 (n=118, 226, 13)	8.31 (± 14.70)	10.95 (± 17.33)	7.08 (± 6.78)	
Week 24 (n=118, 219, 13)	8.37 (± 15.48)	11.23 (± 18.24)	4.08 (± 8.75)	
Week 52 (n=116, 212, 11)	8.81 (± 16.18)	12.19 (± 17.88)	6.73 (± 8.09)	
Week 64 (n=112, 212, 12)	7.98 (± 17.14)	10.67 (± 17.19)	1.17 (± 8.03)	

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in Absolute Forced Expiratory Volume in 1 Second Over Time

End point title	Change From Baseline in Absolute Forced Expiratory Volume in 1 Second Over Time

End point description:

FEV1 was volume of air (in liters) exhaled from the lungs in first second of a forced expiration as measured by spirometer. Spirometry was performed after a wash out period of bronchodilators according to their action duration. Baseline (main study): original baseline of parent study EFC14153. Baseline (sub-study): last available measurement prior to first study treatment dose if participant was treated, or last available value up to enrollment if participant was not exposed to study treatment in current study. Main study: safety population included all participants exposed to at least 1 dose or part of a dose of study treatment during current study regardless of amount of treatment administered. Sub-study: ITT population included all participants in enrolled population in current study. Only participants with data collected are reported. n=number of participants with data collected at specified timepoints. 99999=no data as there were no participants analyzed for that timepoint.

End point type	Secondary

End point timeframe:

Baseline (Day 1) and Weeks 2, 4 (Japan sub-study), 8, 12, 24, 52 and 64

End point values	Main Study: Placebo-Dupilumab	Main Study: Dupilumab-Dupilumab	Japan Sub-study: Dupilumab	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	122	231	13	
Units: liter				
arithmetic mean (standard deviation)				
Week 2 (n=122, 231, 12)	0.36 (± 0.32)	0.42 (± 0.38)	0.13 (± 0.15)	

Week 4 (n=0, 0, 13)	99999 (± 99999)	99999 (± 99999)	0.13 (± 0.13)	
Week 8 (n=120, 222, 13)	0.38 (± 0.32)	0.47 (± 0.39)	0.12 (± 0.15)	
Week 12 (n=118, 226, 13)	0.41 (± 0.31)	0.45 (± 0.36)	0.17 (± 0.13)	
Week 24 (n=118, 219, 13)	0.46 (± 0.35)	0.51 (± 0.39)	0.15 (± 0.15)	
Week 52 (n=116, 212, 11)	0.62 (± 0.41)	0.66 (± 0.41)	0.34 (± 0.21)	
Week 64 (n=112, 212, 12)	0.66 (± 0.45)	0.70 (± 0.44)	0.25 (± 0.14)	

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in Forced Vital Capacity (FVC) Over Time

End point title	Change From Baseline in Forced Vital Capacity (FVC) Over Time

End point description:

FVC was defined as volume of air (in liters) that could be forcibly blown out after full inspiration in upright position as measured by spirometer. Spirometry was performed after wash out period of bronchodilators according to their action duration. Baseline(main study):original baseline of parent study EFC14153. Baseline(sub-study): last available measurement prior to first study treatment dose if participant was treated or last available value up to enrollment if participant was not exposed to study treatment in current study. Main study: safety population=all participants exposed to at least 1 dose or part of a dose of study treatment during current study regardless of amount of treatment administered. Sub-study: ITT population=all participants in enrolled population in current study. Only participants with data collected are reported. n=number of participants with data collected at specified timepoints. 99999=no data as there were no participants analyzed for that timepoint.

End point type	Secondary

End point timeframe:

Baseline (Day 1) and Weeks 2, 4 (Japan sub-study), 8, 12, 24, 52 and 64

End point values	Main Study: Placebo-Dupilumab	Main Study: Dupilumab-Dupilumab	Japan Sub-study: Dupilumab	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	122	231	13	
Units: liter				
arithmetic mean (standard deviation)				
Week 2 (n=122, 231, 12)	0.35 (± 0.29)	0.38 (± 0.38)	0.11 (± 0.15)	
Week 4 (n=0, 0, 13)	99999 (± 99999)	99999 (± 99999)	0.09 (± 0.12)	
Week 8 (n=120, 222, 13)	0.37 (± 0.30)	0.45 (± 0.42)	0.11 (± 0.14)	
Week 12 (n=118, 226, 13)	0.40 (± 0.30)	0.43 (± 0.39)	0.12 (± 0.11)	
Week 24 (n=118, 219, 13)	0.47 (± 0.36)	0.50 (± 0.40)	0.17 (± 0.15)	
Week 52 (n=116, 212, 11)	0.68 (± 0.42)	0.70 (± 0.45)	0.36 (± 0.22)	
Week 64 (n=112, 212, 12)	0.74 (± 0.49)	0.75 (± 0.48)	0.41 (± 0.24)	

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in Forced Expiratory Flow [FEF] 25% to 75% Over Time

End point title	Change From Baseline in Forced Expiratory Flow [FEF] 25% to 75% Over Time

End point description:

FEF:amount of air which can be forcibly exhaled from lungs in first second of forced exhalation.FEF 25-75%:mean FEF between 25% and 75% of FVC,FVC:volume of air that could be forcibly blown out after full inspiration in upright position. Spirometry was performed after wash out period of bronchodilators. Baseline(main study):original baseline of parent study. Baseline(sub-study): last available measurement prior to first study treatment dose if participant was treated or last available value up to enrollment if participant was not exposed to study treatment in current study. Main study:safety population=all participants exposed to at least 1 dose or part of dose of study treatment during current regardless of amount of treatment administered. Sub-study:ITT population=all participants in enrolled population in current study.n=number of participants with data collected at specified timepoints.99999=no data as there were no participants analyzed for that timepoint.

End point type	Secondary

End point timeframe:

Baseline (Day 1) and Weeks 2, 4 (Japan sub-study), 8, 12, 24, 52 and 64

End point values	Main Study: Placebo-Dupilumab	Main Study: Dupilumab-Dupilumab	Japan Sub-study: Dupilumab	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	122	231	13	
Units: liter per second				
arithmetic mean (standard deviation)				
Week 2 (n=122, 231, 12)	0.49 (± 0.63)	0.58 (± 0.66)	0.21 (± 0.26)	
Week 4 (n=0, 0, 13)	99999 (± 99999)	99999 (± 99999)	0.25 (± 0.23)	
Week 8 (n=120, 222, 13)	0.48 (± 0.60)	0.62 (± 0.63)	0.15 (± 0.30)	
Week 12 (n=118, 226, 13)	0.54 (± 0.60)	0.59 (± 0.61)	0.29 (± 0.31)	
Week 24 (n=118, 219, 13)	0.58 (± 0.68)	0.66 (± 0.65)	0.15 (± 0.37)	
Week 52 (n=116, 212, 11)	0.73 (± 0.75)	0.77 (± 0.67)	0.40 (± 0.46)	
Week 64 (n=112, 212, 12)	0.77 (± 0.78)	0.79 (± 0.70)	0.11 (± 0.34)	

Statistical analyses

No statistical analyses for this end point

Secondary: Main Study: Change From Baseline in Percent Predicted Forced Vital Capacity Over Time

End point title	Main Study: Change From Baseline in Percent Predicted Forced Vital Capacity Over Time[6]

End point description:

FVC was defined as volume of air (in liters) that could be forcibly blown out after full inspiration in upright position as measured by spirometer. Spirometry was performed after wash out period of bronchodilators according to their action duration. Baseline was defined as the original baseline of parent study EFC14153. Safety population included all participants exposed to at least 1 dose or part of a dose of study treatment during current study regardless of amount of treatment administered. Only participants with data collected are reported. n=number of participants with data collected at specified

timepoints.

End point type	Secondary

End point timeframe:

Baseline (Day 1) and Weeks 2, 8, 12, 24, 52 and 64

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: Only participants in the Main study arms were analyzed in this endpoint.

End point values	Main Study: Placebo-Dupilumab	Main Study: Dupilumab-Dupilumab		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	122	231		
Units: percent predicted FVC				
arithmetic mean (standard deviation)				
Week 2 (n=122, 231)	2.98 (± 12.91)	5.02 (± 16.33)		
Week 8 (n=120, 222)	2.88 (± 12.17)	6.64 (± 17.42)		
Week 12 (n=118, 226)	3.23 (± 12.49)	5.03 (± 16.45)		
Week 24 (n=118, 219)	3.19 (± 13.35)	5.28 (± 16.20)		
Week 52 (n=116, 212)	3.74 (± 13.10)	6.43 (± 16.40)		
Week 64 (n=112, 212)	3.13 (± 15.14)	4.83 (± 16.09)		

Statistical analyses

No statistical analyses for this end point

Secondary: Japan Sub-study: Change From Baseline in Asthma Control Questionnaire-Interviewer Administered, 7-Question Version (ACQ-7-IA) Over Time

End point title	Japan Sub-study: Change From Baseline in Asthma Control Questionnaire-Interviewer Administered, 7-Question Version (ACQ-7-IA) Over Time[7]

End point description:

ACQ-7-IA had 7 questions with first 5 items of ACQ-7 addressing most common asthma symptoms:frequency in past week awoken by asthma during night,severity of asthma symptoms in morning,limitation of daily activities due to asthma,shortness of breath due to asthma, wheeze; 2 questions on short-acting bronchodilator use and predicted bronchodilator use of FEV1.Participants/parents/guardians recalled child's previous week asthma and responded to questions on 7-point scale: 0=no impairment, 6=maximum impairment. Global ACQ-7-IA score: mean of 7 questions; ranged 0(totally controlled) to 6(severely uncontrolled).Higher scores=lower asthma control. Baseline:last available measurement prior to first study treatment dose if participant was treated or last available value up to enrollment if participant was not exposed to study treatment in current study.ITT population=all participants in enrolled population in current study.n=number of participants with data collected at specified timepoints.

End point type	Secondary

End point timeframe:

Baseline (Day 1) and Weeks 2, 4, 8, 12, 24, 36, 52 and 64

Notes:

[7] - 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: Only participants in the Japan sub-study arms were analyzed in this endpoint.

End point values	Japan Sub-study: Dupilumab			
Subject group type	Reporting group			
Number of subjects analysed	13			
Units: score on a scale				
arithmetic mean (standard deviation)				
Week 2 (n=13)	-0.65 (± 0.64)			
Week 4 (n=13)	-0.68 (± 0.75)			
Week 8 (n=13)	-0.84 (± 0.59)			
Week 12 (n=13)	-1.03 (± 0.66)			
Week 24 (n=13)	-0.96 (± 0.61)			
Week 36 (n=13)	-1.01 (± 0.47)			
Week 52 (n=13)	-1.21 (± 0.37)			
Week 64 (n=12)	-0.99 (± 0.52)			

Statistical analyses

No statistical analyses for this end point

Secondary: Japan Sub-study: Change From Baseline in Asthma Control Questionnaire-Interviewer Administered, 5-Question Version (ACQ-5-IA) Over Time

End point title	Japan Sub-study: Change From Baseline in Asthma Control Questionnaire-Interviewer Administered, 5-Question Version (ACQ-5-IA) Over Time[8]

End point description:

The ACQ-5-IA had 5 questions addressing most common asthma symptoms: frequency in past week awoken by asthma during night, severity of asthma symptoms in morning, limitation of daily activities due to asthma, shortness of breath due to asthma and wheeze. Participants/parents/guardians recalled the child's previous week asthma and responded to symptom and bronchodilator use questions on a 7-point scale: 0=no impairment, 6=maximum impairment. Global ACQ-5-IA score was mean of 5 questions ranging from 0 (totally controlled) to 6 (severely uncontrolled). Higher score indicated lower asthma control. Baseline: last available measurement prior to first study treatment dose if participant was treated, or last available value up to enrollment if participant was not exposed to study treatment in current study. ITT population included all participants in enrolled population in current study. n=number of participants with data collected at specified timepoints.

End point type	Secondary

End point timeframe:

Baseline (Day 1) and Weeks 2, 4, 8, 12, 24, 36, 52 and 64

Notes:

[8] - 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: Only participants in the Japan sub-study arms were analyzed in this endpoint.

End point values	Japan Sub-study: Dupilumab			
Subject group type	Reporting group			
Number of subjects analysed	13			
Units: score on a scale				
arithmetic mean (standard deviation)				
Week 2 (n=13)	-0.68 (± 0.87)			
Week 4 (n=13)	-0.75 (± 1.06)			
Week 8 (n=13)	-0.92 (± 0.82)			

Week 12 (n=13)	-1.20 (± 0.84)			
Week 24 (n=13)	-1.15 (± 0.68)			
Week 36 (n=13)	-1.25 (± 0.54)			
Week 52 (n=13)	-1.49 (± 0.54)			
Week 64 (n=12)	-1.28 (± 0.59)			

Statistical analyses

No statistical analyses for this end point

Secondary: Serum Concentrations of Dupilumab

End point title	Serum Concentrations of Dupilumab

End point description:

Blood samples were collected at the specified timepoints for determination of functional dupilumab concentration in serum. Pharmacokinetic population (main and sub-study) included all the participants in the safety population with at least 1 non-missing and evaluable pre-dose serum concentration value after the first dose of dupilumab in the current study. Only participants with data collected are reported. n=number of participants with data collected at specified timepoints. As pre-specified in the SAP, serum concentration is presented by dose regimen for main and sub-study.

End point type	Secondary

End point timeframe:

Weeks 12, 24, 52 and 64

End point values	Main Study: Dupilumab 100 mg q2w	Main Study: Dupilumab 200 mg q2w	Main Study: Dupilumab 300 mg q4w	Japan Sub-study: Dupilumab 100 mg q2w
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	52	299	16	3
Units: nanogram per milliliter				
arithmetic mean (standard deviation)				
Week 12 (n=52, 296, 6, 3, 7, 3)	60740.38 (± 23885.77)	80450.15 (± 39865.24)	79600.00 (± 25509.84)	38600.00 (± 20850.18)
Week 24 (n=38, 293, 12, 3, 6, 3)	64201.03 (± 22890.02)	81849.66 (± 42824.93)	80675.00 (± 26921.27)	41300.00 (± 22138.65)
Week 52 (n=27, 299, 16, 3, 7, 3)	52808.85 (± 21526.05)	71910.74 (± 42290.54)	81289.94 (± 31957.07)	41000.00 (± 23157.94)
Week 64 (n=28, 298, 16, 3, 6, 3)	1884.04 (± 9763.01)	3391.86 (± 16196.36)	184.69 (± 582.75)	39.00 (± 0.00)

End point values	Japan Sub-study: Dupilumab 200 mg q2w	Japan Sub-study: Dupilumab 300 mg q4w		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	7	3		
Units: nanogram per milliliter				
arithmetic mean (standard deviation)				

Week 12 (n=52, 296, 6, 3, 7, 3)	79128.57 (± 24513.31)	53066.67 (± 18569.96)		
Week 24 (n=38, 293, 12, 3, 6, 3)	98316.67 (± 18066.81)	55166.67 (± 14558.96)		
Week 52 (n=27, 299, 16, 3, 7, 3)	91128.57 (± 28739.33)	59300.00 (± 18107.46)		
Week 64 (n=28, 298, 16, 3, 6, 3)	39.00 (± 0.00)	39.00 (± 0.00)		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Participants With Anti-Drug Antibodies (ADAs) Against Dupilumab

End point title	Number of Participants With Anti-Drug Antibodies (ADAs) Against Dupilumab

End point description:

ADA positive was defined as either treatment-boosted or treatment-emergent response in the ADA assay. Treatment-boosted response was defined as a positive response in the ADA assay post first dose in the current study that was greater than or equal to 4-fold of the baseline titer levels, when baseline results were positive. Treatment-emergent response was defined as a positive response in the ADA assay post first dose in the current study, when baseline results were negative or missing. Baseline (main study): original baseline of parent study EFC14153. Baseline (sub-study): last available measurement prior to first study treatment dose if participant was treated, or last available value up to enrollment if participant was not exposed to study treatment in current study. ADA population (main and sub-study) included all the participants in the safety population with at least 1 non-missing ADA result following the first dose of dupilumab in the current study.

End point type	Secondary

End point timeframe:

From first dose of study treatment (Day 1) to Week 64

End point values	Main Study: Placebo-Dupilumab	Main Study: Dupilumab-Dupilumab	Japan Sub-study: Dupilumab	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	124	239	13	
Units: participants				
Treatment-boosted ADA Response	1	0	0	
Treatment-emergent ADA Response	10	7	2	

Statistical analyses

No statistical analyses for this end point

Secondary: Main Study: Percent Change From Baseline in Blood Eosinophil Count at Week 64

End point title	Main Study: Percent Change From Baseline in Blood Eosinophil Count at Week 64[9]

End point description:

Blood samples were collected at specified timepoints to assess percent change from baseline in eosinophil count. Baseline was defined as the original baseline of parent study EFC14153. Safety population included all participants exposed to at least 1 dose or part of a dose of the study treatment during current study regardless of the amount of treatment administered. Only participants with data collected are reported.

End point type	Secondary

End point timeframe:

Baseline (Day 1) to Week 64

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: Only participants in the Main study arms were analyzed in this endpoint.

End point values	Main Study: Placebo-Dupilumab	Main Study: Dupilumab-Dupilumab		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	103	186		
Units: percent change				
arithmetic mean (standard deviation)	34.528 (± 207.067)	29.769 (± 323.837)		

Statistical analyses

No statistical analyses for this end point

Secondary: Percent Change From Baseline in Total Immunoglobulin (Ig) E in Serum at Week 64

End point title	Percent Change From Baseline in Total Immunoglobulin (Ig) E in Serum at Week 64

End point description:

Blood samples were collected at specified timepoints to assess percent change from baseline in total IgE in serum. Baseline (main study): the original baseline of parent study EFC14153. Baseline (sub-study): last available measurement prior to first study treatment dose if participant was treated, or last available value up to enrollment if participant was not exposed to study treatment in current study. Main study: safety population included all participants exposed to at least 1 dose or part of a dose of the study treatment during current study regardless of the amount of treatment administered. Sub-study: safety population included all enrolled participants who took at least 1 dose of study treatment in the current study, regardless of the amount of treatment administered. Only participants with data collected are reported.

End point type	Secondary

End point timeframe:

Baseline (Day 1) to Week 64

End point values	Main Study: Placebo-Dupilumab	Main Study: Dupilumab-Dupilumab	Japan Sub-study: Dupilumab	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	113	219	12	
Units: percent change				
median (inter-quartile range (Q1-Q3))	-76.9 (-85.2 to	-86.8 (-91.4 to	-75.0 (-81.1 to	

-63.4)	-77.3)	-70.0)

Statistical analyses

No statistical analyses for this end point

Secondary: Japan Sub-study: Change From Baseline in Fractional Exhaled Nitric Oxide (FeNO) at Week 64

End point title	Japan Sub-study: Change From Baseline in Fractional Exhaled Nitric Oxide (FeNO) at Week 64[10]

End point description:

FeNO was analyzed using a NIOX instrument or similar analyzer using a flow rate of 50 milliliter per second. FeNO assessment was conducted prior to spirometry and following a fast of ≥1 hour. Baseline was defined as the last available measurement prior to first study treatment dose if participant was treated, or last available value up to enrollment if participant was not exposed to study treatment in the current study. Safety population included all enrolled participants who took at least 1 dose of study treatment in the current study, regardless of the amount of treatment administered. Only participants with data collected are reported.

End point type	Secondary

End point timeframe:

Baseline (Day 1) to Week 64

Notes:

[10] - 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: Only participants in the Japan sub-study arms were analyzed in this endpoint.

End point values	Japan Sub-study: Dupilumab			
Subject group type	Reporting group			
Number of subjects analysed	12			
Units: parts per billion				
arithmetic mean (standard deviation)	-8.3 (± 27.5)			

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

AEs: From first dose of study treatment (Day 1) up to 112 days post last dose of study treatment, approximately 64 weeks for main study and sub-study each. Deaths: From first dose of study treatment (Day 1) up to end of follow-up, approximately 353 weeks.

Adverse event reporting additional description:

Analysis was performed on safety population. As pre-specified in the protocol and SAP, the results are presented by study and treatment group, regardless of the dose regimen.

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	27.1

Reporting groups

Reporting group title	Main Study: Placebo-Dupilumab

Reporting group description:

Participants who received placebo matched to dupilumab in the parent study EFC14153 received dupilumab for 52 weeks in the main study as follows: - 100 mg q2w as an SC injection or 300 mg q4w as an SC injection for participants with body weight ≤30 kg. - 200 mg q2w as an SC injection for participants with body weight >30 kg. Participants also received a stable-dose background therapy of medium-dose ICS with a second controller medication (i.e., LABA, LAMA, LTRA or methylxanthines) or high-dose ICS alone or high-dose ICS with second controller medication. Albuterol/salbutamol or levalbuterol/levosalbutamol was given as reliever medication as instructed by Investigator.

Reporting group title	Japan Sub-study: Dupilumab

Reporting group description:

Participants received dupilumab for 52 weeks in the Japan sub-study as follows: - 100 mg q2w as an SC injection or 300 mg q4w as an SC injection for participants with body weight ≥15 kg and ≤30 kg. - 200 mg q2w as an SC injection for participants with body weight >30 kg. Participants also received a stable-dose background therapy of medium-dose ICS with a second controller medication (i.e., LABA, LAMA, LTRA or methylxanthines) or high-dose ICS alone or high-dose ICS with second controller medication. Albuterol/salbutamol or levalbuterol/levosalbutamol was given as reliever medication as instructed by Investigator.

Reporting group title	Main Study: Dupilumab-Dupilumab

Reporting group description:

Participants who received dupilumab in the parent study EFC14153 received dupilumab for 52 weeks in the main study as follows: - 100 mg q2w as an SC injection or 300 mg q4w as an SC injection for participants with body weight ≤30 kg. - 200 mg q2w as an SC injection for participants with body weight >30 kg. Participants also received a stable-dose background therapy of medium-dose ICS with a second controller medication (i.e., LABA, LAMA, LTRA or methylxanthines) or high-dose ICS alone or high-dose ICS with second controller medication. Albuterol/salbutamol or levalbuterol/levosalbutamol was given as reliever medication as instructed by Investigator.

Serious adverse events	Main Study: Placebo-Dupilumab	Japan Sub-study: Dupilumab	Main Study: Dupilumab-Dupilumab
Total subjects affected by serious adverse events			
subjects affected / exposed	1 / 125 (0.80%)	4 / 13 (30.77%)	6 / 240 (2.50%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events	0	0	0
Injury, poisoning and procedural complications			

Radius Fracture			
subjects affected / exposed	0 / 125 (0.00%)	0 / 13 (0.00%)	1 / 240 (0.42%)
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			
Constipation			
subjects affected / exposed	0 / 125 (0.00%)	0 / 13 (0.00%)	1 / 240 (0.42%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory, thoracic and mediastinal disorders			
Asthma			
subjects affected / exposed	0 / 125 (0.00%)	2 / 13 (15.38%)	0 / 240 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 5	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Atelectasis			
subjects affected / exposed	0 / 125 (0.00%)	0 / 13 (0.00%)	1 / 240 (0.42%)
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			
Bronchitis			
subjects affected / exposed	0 / 125 (0.00%)	1 / 13 (7.69%)	0 / 240 (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
Complicated Appendicitis			
subjects affected / exposed	0 / 125 (0.00%)	0 / 13 (0.00%)	1 / 240 (0.42%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Influenza			
subjects affected / exposed	0 / 125 (0.00%)	1 / 13 (7.69%)	0 / 240 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumonia			

subjects affected / exposed	1 / 125 (0.80%)	0 / 13 (0.00%)	0 / 240 (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
Pulmonary Tuberculosis			
subjects affected / exposed	0 / 125 (0.00%)	0 / 13 (0.00%)	1 / 240 (0.42%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Upper Respiratory Tract Infection			
subjects affected / exposed	0 / 125 (0.00%)	0 / 13 (0.00%)	1 / 240 (0.42%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
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	Main Study: Placebo-Dupilumab	Japan Sub-study: Dupilumab	Main Study: Dupilumab-Dupilumab
Total subjects affected by non-serious adverse events			
subjects affected / exposed	63 / 125 (50.40%)	13 / 13 (100.00%)	108 / 240 (45.00%)
Injury, poisoning and procedural complications			
Accidental Overdose			
subjects affected / exposed	2 / 125 (1.60%)	1 / 13 (7.69%)	5 / 240 (2.08%)
occurrences (all)	2	1	5
Contusion			
subjects affected / exposed	2 / 125 (1.60%)	1 / 13 (7.69%)	2 / 240 (0.83%)
occurrences (all)	2	1	2
Eyelid Injury			
subjects affected / exposed	0 / 125 (0.00%)	1 / 13 (7.69%)	0 / 240 (0.00%)
occurrences (all)	0	1	0
Scratch			
subjects affected / exposed	0 / 125 (0.00%)	1 / 13 (7.69%)	1 / 240 (0.42%)
occurrences (all)	0	1	2
Wrist Fracture			
subjects affected / exposed	0 / 125 (0.00%)	1 / 13 (7.69%)	0 / 240 (0.00%)
occurrences (all)	0	1	0
Ligament Sprain			

subjects affected / exposed	2 / 125 (1.60%)	1 / 13 (7.69%)	3 / 240 (1.25%)
occurrences (all)	2	1	3
Nervous system disorders			
Tension Headache			
subjects affected / exposed	0 / 125 (0.00%)	2 / 13 (15.38%)	0 / 240 (0.00%)
occurrences (all)	0	2	0
Headache			
subjects affected / exposed	3 / 125 (2.40%)	1 / 13 (7.69%)	8 / 240 (3.33%)
occurrences (all)	4	1	15
Blood and lymphatic system disorders			
Eosinophilia			
subjects affected / exposed	7 / 125 (5.60%)	1 / 13 (7.69%)	8 / 240 (3.33%)
occurrences (all)	8	1	8
General disorders and administration site conditions			
Injection Site Erythema			
subjects affected / exposed	3 / 125 (2.40%)	1 / 13 (7.69%)	7 / 240 (2.92%)
occurrences (all)	6	4	11
Injection Site Induration			
subjects affected / exposed	0 / 125 (0.00%)	1 / 13 (7.69%)	1 / 240 (0.42%)
occurrences (all)	0	1	2
Injection Site Reaction			
subjects affected / exposed	9 / 125 (7.20%)	0 / 13 (0.00%)	8 / 240 (3.33%)
occurrences (all)	73	0	46
Pyrexia			
subjects affected / exposed	3 / 125 (2.40%)	6 / 13 (46.15%)	5 / 240 (2.08%)
occurrences (all)	3	7	5
Gastrointestinal disorders			
Constipation			
subjects affected / exposed	1 / 125 (0.80%)	1 / 13 (7.69%)	0 / 240 (0.00%)
occurrences (all)	1	1	0
Dental Caries			
subjects affected / exposed	0 / 125 (0.00%)	1 / 13 (7.69%)	1 / 240 (0.42%)
occurrences (all)	0	2	1
Vomiting			
subjects affected / exposed	1 / 125 (0.80%)	1 / 13 (7.69%)	5 / 240 (2.08%)
occurrences (all)	1	1	7

Enterocolitis			
subjects affected / exposed	0 / 125 (0.00%)	1 / 13 (7.69%)	0 / 240 (0.00%)
occurrences (all)	0	1	0
Diarrhoea			
subjects affected / exposed	7 / 125 (5.60%)	2 / 13 (15.38%)	10 / 240 (4.17%)
occurrences (all)	7	3	10
Respiratory, thoracic and mediastinal disorders			
Rhinitis Allergic			
subjects affected / exposed	9 / 125 (7.20%)	1 / 13 (7.69%)	7 / 240 (2.92%)
occurrences (all)	9	1	10
Skin and subcutaneous tissue disorders			
Acne			
subjects affected / exposed	0 / 125 (0.00%)	2 / 13 (15.38%)	3 / 240 (1.25%)
occurrences (all)	0	2	3
Dermatitis Contact			
subjects affected / exposed	2 / 125 (1.60%)	1 / 13 (7.69%)	3 / 240 (1.25%)
occurrences (all)	2	1	3
Miliaria			
subjects affected / exposed	0 / 125 (0.00%)	1 / 13 (7.69%)	1 / 240 (0.42%)
occurrences (all)	0	1	1
Eczema			
subjects affected / exposed	0 / 125 (0.00%)	2 / 13 (15.38%)	0 / 240 (0.00%)
occurrences (all)	0	2	0
Psychiatric disorders			
Insomnia			
subjects affected / exposed	0 / 125 (0.00%)	1 / 13 (7.69%)	1 / 240 (0.42%)
occurrences (all)	0	1	1
Musculoskeletal and connective tissue disorders			
Osteochondrosis			
subjects affected / exposed	0 / 125 (0.00%)	1 / 13 (7.69%)	0 / 240 (0.00%)
occurrences (all)	0	1	0
Arthralgia			
subjects affected / exposed	1 / 125 (0.80%)	2 / 13 (15.38%)	2 / 240 (0.83%)
occurrences (all)	1	2	2
Infections and infestations			

Hordeolum			
subjects affected / exposed	0 / 125 (0.00%)	1 / 13 (7.69%)	2 / 240 (0.83%)
occurrences (all)	0	1	2
Herpes Zoster			
subjects affected / exposed	0 / 125 (0.00%)	1 / 13 (7.69%)	0 / 240 (0.00%)
occurrences (all)	0	1	0
Covid-19			
subjects affected / exposed	1 / 125 (0.80%)	2 / 13 (15.38%)	3 / 240 (1.25%)
occurrences (all)	1	2	3
Bronchitis			
subjects affected / exposed	5 / 125 (4.00%)	3 / 13 (23.08%)	7 / 240 (2.92%)
occurrences (all)	6	4	10
Oral Herpes			
subjects affected / exposed	1 / 125 (0.80%)	1 / 13 (7.69%)	0 / 240 (0.00%)
occurrences (all)	1	2	0
Nasopharyngitis			
subjects affected / exposed	12 / 125 (9.60%)	5 / 13 (38.46%)	21 / 240 (8.75%)
occurrences (all)	17	12	25
Lower Respiratory Tract Infection			
subjects affected / exposed	0 / 125 (0.00%)	1 / 13 (7.69%)	0 / 240 (0.00%)
occurrences (all)	0	1	0
Pharyngitis			
subjects affected / exposed	12 / 125 (9.60%)	5 / 13 (38.46%)	15 / 240 (6.25%)
occurrences (all)	13	7	16
Influenza			
subjects affected / exposed	7 / 125 (5.60%)	5 / 13 (38.46%)	13 / 240 (5.42%)
occurrences (all)	9	8	16
Sinusitis			
subjects affected / exposed	3 / 125 (2.40%)	1 / 13 (7.69%)	5 / 240 (2.08%)
occurrences (all)	5	1	6
Viral Upper Respiratory Tract Infection			
subjects affected / exposed	6 / 125 (4.80%)	1 / 13 (7.69%)	9 / 240 (3.75%)
occurrences (all)	7	2	12
Upper Respiratory Tract Infection			

subjects affected / exposed	5 / 125 (4.00%)	2 / 13 (15.38%)	19 / 240 (7.92%)
occurrences (all)	7	6	28
Tonsillitis			
subjects affected / exposed	3 / 125 (2.40%)	1 / 13 (7.69%)	6 / 240 (2.50%)
occurrences (all)	3	1	6

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
09 July 2018	Changed study sample size due to the increase in the sample size of EFC14153 (parent study of the LTS14424), removed secondary safety endpoint, removed optional pharmacogenetic informed consent/assent form mention, changed pregnancy outcome follow-up period, added LAMA and ultra LABA (vilanterol) withhold period before spirometry, included the total volume of blood collected at a single visit, corrected the information that data for current study Visit (V) 1 coming from end of treatment (EOT) visit from parent study would not be reported in current study electronic case report form.
12 December 2019	Changed dupilumab dose for children with body weight ≤30 kg from 100 mg q2w to 300 mg q4w, removed immunoglobulins as other secondary endpoints, clarified when an asthma exacerbation was to be reported as AE, added relatedness to study treatment in the adverse event of special interest anaphylactic reaction and systemic allergic reaction, clarified that hepatitis serologies were not repeated for determining participants' eligibility in the current study, changed study sample size, updated analysis populations according to the dose regimen, updated retention of study documents in study sites from 15 to 25 years.
15 April 2020	Allowed later entrance in current study for EFC14153 participants who were not able to perform the EFC14153 EOT visit onsite to rollover at V28/EOT, or to receive last study treatment doses in parent study EFC14153 due to the coronavirus disease 2019 pandemic, removed the monthly 300 mg dose specific analysis set, allowed at home administration of 300 mg monthly doses from the second administration onwards (following first 300 mg administered onsite).

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported