Clinical trial results:
A Randomized, Double-Blind, Placebo-Controlled Study to Investigate the Efficacy and Safety of Dupilumab in Pediatric Patients With Active Eosinophilic Esophagitis

Summary

EudraCT number	2019-003078-24
Trial protocol	Outside EU/EEA
Global end of trial date	14 May 2024

Results information

Result version number	v1 (current)
This version publication date	28 November 2024
First version publication date	28 November 2024

Trial information

Trial identification

Sponsor protocol code	R668-EE-1877

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT04394351
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)	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	14 May 2024
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	14 May 2024
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The Primary objective is to demonstrate the efficacy of dupilumab treatment compared with placebo in pediatric participants with active eosinophilic esophagitis (EoE) based on histologic improvement meeting validated histologic criteria.

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	01 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	Canada: 1
Country: Number of subjects enrolled	United States: 101
Worldwide total number of subjects	102
EEA total number of subjects	0

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)	4
Children (2-11 years)	98
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: -

Pre-assignment

Screening details:

This study consisted of 3 parts: Part A (double-blind 16-week treatment period), Part B (36-week extended active treatment period) and Part C (open-label extension period of up to 108 weeks).

Period 1

Period 1 title	Part A (16 weeks)
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Double blind
Roles blinded	Investigator, Monitor, Carer, Data analyst, Assessor, Subject

Arms

Are arms mutually exclusive?	Yes
Arm title	Part A: Pooled Placebo

Arm description:

Participants who received subcutaneous (SC) injection of placebo matched to higher exposure dupilumab or lower exposure dupilumab in Part A. Lower exposure dupilumab regimen were exposures approximating those in adolescents and adults receiving 300 mg dupilumab Q2W). Higher exposure dupilumab regimen were exposures approximating those in adolescents and adults receiving 300 mg dupilumab QW.

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

Dosage and administration details:

Matching formulation and regimen (depending on the weight tier) as dupilumab without the active substance

Arm title	Part A: Dupilumab Low Dose

Arm description:

Participants received subcutaneous (SC) injection of lower exposure dupilumab in Part A. Lower exposure dupilumab regimen were exposures approximating those in adolescents and adults receiving 300 mg dupilumab Q2W)

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

Dosage and administration details:

Part A consists of a 16-week double-blind treatment period. Patients will be randomized to receive dupilumab or placebo subcutaneous (SC) administration at tiered dosing regimens based on body weight

Arm title	Part A: Dupilumab High Dose

Arm description:

Participants received subcutaneous (SC) injection of higher exposure dupilumab in Part A. Higher exposure dupilumab regimen were exposures approximating those in adolescents and adults receiving 300 mg dupilumab QW

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

Dosage and administration details:

Part A consists of a 16-week double-blind treatment period. Patients will be randomized to receive dupilumab or placebo subcutaneous (SC) administration at tiered dosing regimens based on body weight

Number of subjects in period 1	Part A: Pooled Placebo	Part A: Dupilumab Low Dose	Part A: Dupilumab High Dose
Started	34	31	37
Completed	33	29	37
Not completed	1	2	0
Physician decision	-	1	-
Consent withdrawn by subject	-	1	-
Adverse event, non-fatal	1	-	-

Period 2

Period 2 title	Part B (36 weeks)
Is this the baseline period?	No
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	Part B: Placebo to Dupilumab Low Dose

Arm description:

Participants who received subcutaneous (SC) injection of placebo in Part A and received lower exposure dupilumab in Part B. Lower exposure dupilumab regimen were exposures approximating those in adolescents and adults receiving 300 mg dupilumab Q2W)

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

Dosage and administration details:

Part B consists of a 36-week extended active treatment period. All patients to receive subcutaneous (SC) administration at tiered dosing regimens based on body weight

Arm title	Part B: Placebo to Dupilumab High Dose

Arm description:

Participants who received subcutaneous (SC) injection of placebo in Part A and received higher exposure

dupilumab in Part B. Higher exposure dupilumab regimen were exposures approximating those in adolescents and adults receiving 300 mg dupilumab QW

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

Dosage and administration details:

Part B consists of a 36-week extended active treatment period. All patients to receive subcutaneous (SC) administration at tiered dosing regimens based on body weight

Arm title	Part B: Dupilumab Low Dose to Dupilumab Low Dose

Arm description:

Participants received subcutaneous (SC) injection of lower exposure dupilumab in Parts A and B. Lower exposure dupilumab regimen were exposures approximating those in adolescents and adults receiving 300 mg dupilumab Q2W)

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

Dosage and administration details:

Part B consists of a 36-week extended active treatment period. All patients to receive subcutaneous (SC) administration at tiered dosing regimens based on body weight

Arm title	Part B: Dupilumab High Dose to Dupilumab High Dose

Arm description:

Participants received subcutaneous (SC) injection of higher exposure dupilumab in Parts A and B. Higher exposure dupilumab regimen were exposures approximating those in adolescents and adults receiving 300 mg dupilumab QW.

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

Dosage and administration details:

Part B consists of a 36-week extended active treatment period. All patients to receive subcutaneous (SC) administration at tiered dosing regimens based on body weight

Number of subjects in period 2[1]	Part B: Placebo to Dupilumab Low Dose	Part B: Placebo to Dupilumab High Dose	Part B: Dupilumab Low Dose to Dupilumab Low Dose
Started	14	18	29
Completed	14	18	29
Not completed	0	0	0
Adverse event, non-fatal	-	-	-

Number of subjects in period 2[1]	Part B: Dupilumab High Dose to Dupilumab High

	Dose
Started	37
Completed	36
Not completed	1
Adverse event, non-fatal	1

Notes:

[1] - The number of subjects starting the period is not consistent with the number completing the preceding period. It is expected the number of subjects starting the subsequent period will be the same as the number completing the preceding period.
Justification: Part A participants transitioned to Part B

Period 3

Period 3 title	Part C: Dupilumab (Up to Wk108+12Wk F/U)
Is this the baseline period?	No
Allocation method	Non-randomised - controlled
Blinding used	Not blinded

Blinding implementation details:

Part C: Dupilumab (Up to Wk 108+12 Wk Follow-Up)

Arms

Arm title	Part C: Dupilumab

Arm description:

Participants who completed Part A and B were eligible to enroll in Part C and receive Dupilumab extended active treatment

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

Dosage and administration details:

Part C consists of up to 108-week open-label extension period. All patients will receive higher exposure dupilumab subcutaneous (SC) administration at tiered dosing regimens based on body weight. No matching placebo administered in Part C.

Number of subjects in period 3[2]	Part C: Dupilumab
Started	61
Completed	8
Not completed	53
Physician decision	3
Consent withdrawn by subject	16
Other	32
Protocol deviation	2

Notes:

[2] - The number of subjects starting the period is not consistent with the number completing the preceding period. It is expected the number of subjects starting the subsequent period will be the same as the number completing the preceding period.

Justification: Part B participants transitioned to Part C

Baseline characteristics

Reporting groups	
Reporting group title	Part A: Pooled Placebo
Reporting group description:	
Participants who received subcutaneous (SC) injection of placebo matched to higher exposure dupilumab or lower exposure dupilumab in Part A. Lower exposure dupilumab regimen were exposures approximating those in adolescents and adults receiving 300 mg dupilumab Q2W). Higher exposure dupilumab regimen were exposures approximating those in adolescents and adults receiving 300 mg dupilumab QW.	
Reporting group title	Part A: Dupilumab Low Dose
Reporting group description:	
Participants received subcutaneous (SC) injection of lower exposure dupilumab in Part A. Lower exposure dupilumab regimen were exposures approximating those in adolescents and adults receiving 300 mg dupilumab Q2W)	
Reporting group title	Part A: Dupilumab High Dose
Reporting group description:	
Participants received subcutaneous (SC) injection of higher exposure dupilumab in Part A. Higher exposure dupilumab regimen were exposures approximating those in adolescents and adults receiving 300 mg dupilumab QW	

Reporting group values	Part A: Pooled Placebo	Part A: Dupilumab Low Dose	Part A: Dupilumab High Dose
Number of subjects	34	31	37
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	7.2	7.2	6.8
standard deviation	± 3.03	± 3.07	± 3.11
Sex: Female, Male Units: participants			
Female	9	6	9
Male	25	25	28
Ethnicity (NIH/OMB) Units: Subjects			
Hispanic or Latino	3	2	2
Not Hispanic or Latino	30	29	33
Unknown or Not Reported	1	0	2
Race (NIH/OMB) Units: Subjects			

American Indian or Alaska Native	0	0	0
Asian	0	1	1
Native Hawaiian or Other Pacific Islander	0	0	0
Black or African American	3	4	4
White	30	22	32
More than one race	0	0	0
Unknown or Not Reported	0	0	0
Other	1	4	0

Reporting group values	Total		
Number of subjects	102		
Age categorical			
Units: Subjects			
In utero	0		
Preterm newborn infants (gestational age < 37 wks)	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)	0		
From 65-84 years	0		
85 years and over	0		
Age Continuous			
Units: years			
arithmetic mean			
standard deviation	-		
Sex: Female, Male			
Units: participants			
Female	24		
Male	78		
Ethnicity (NIH/OMB)			
Units: Subjects			
Hispanic or Latino	7		
Not Hispanic or Latino	92		
Unknown or Not Reported	3		
Race (NIH/OMB)			
Units: Subjects			
American Indian or Alaska Native	0		
Asian	2		
Native Hawaiian or Other Pacific Islander	0		
Black or African American	11		
White	84		
More than one race	0		
Unknown or Not Reported	0		
Other	5		

End points reporting groups

Reporting group title	Part A: Pooled Placebo
Reporting group description:	
Participants who received subcutaneous (SC) injection of placebo matched to higher exposure dupilumab or lower exposure dupilumab in Part A. Lower exposure dupilumab regimen were exposures approximating those in adolescents and adults receiving 300 mg dupilumab Q2W). Higher exposure dupilumab regimen were exposures approximating those in adolescents and adults receiving 300 mg dupilumab QW.	
Reporting group title	Part A: Dupilumab Low Dose
Reporting group description:	
Participants received subcutaneous (SC) injection of lower exposure dupilumab in Part A. Lower exposure dupilumab regimen were exposures approximating those in adolescents and adults receiving 300 mg dupilumab Q2W)	
Reporting group title	Part A: Dupilumab High Dose
Reporting group description:	
Participants received subcutaneous (SC) injection of higher exposure dupilumab in Part A. Higher exposure dupilumab regimen were exposures approximating those in adolescents and adults receiving 300 mg dupilumab QW	
Reporting group title	Part B: Placebo to Dupilumab Low Dose
Reporting group description:	
Participants who received subcutaneous (SC) injection of placebo in Part A and received lower exposure dupilumab in Part B. Lower exposure dupilumab regimen were exposures approximating those in adolescents and adults receiving 300 mg dupilumab Q2W)	
Reporting group title	Part B: Placebo to Dupilumab High Dose
Reporting group description:	
Participants who received subcutaneous (SC) injection of placebo in Part A and received higher exposure dupilumab in Part B. Higher exposure dupilumab regimen were exposures approximating those in adolescents and adults receiving 300 mg dupilumab QW	
Reporting group title	Part B: Dupilumab Low Dose to Dupilumab Low Dose
Reporting group description:	
Participants received subcutaneous (SC) injection of lower exposure dupilumab in Parts A and B. Lower exposure dupilumab regimen were exposures approximating those in adolescents and adults receiving 300 mg dupilumab Q2W)	
Reporting group title	Part B: Dupilumab High Dose to Dupilumab High Dose
Reporting group description:	
Participants received subcutaneous (SC) injection of higher exposure dupilumab in Parts A and B. Higher exposure dupilumab regimen were exposures approximating those in adolescents and adults receiving 300 mg dupilumab QW.	
Reporting group title	Part C: Dupilumab
Reporting group description:	
Participants who completed Part A and B were eligible to enroll in Part C and receive Dupilumab extended active treatment	
Subject analysis set title	Part A: Pooled Placebo
Subject analysis set type	Per protocol
Subject analysis set description:	
Participants who received subcutaneous (SC) injection of placebo matched to higher exposure dupilumab or lower exposure dupilumab in Part A. Lower exposure dupilumab regimen were exposures approximating those in adolescents and adults receiving 300 mg dupilumab Q2W). Higher exposure dupilumab regimen were exposures approximating those in adolescents and adults receiving 300 mg dupilumab QW.	
Subject analysis set title	Part A: Dupilumab Low Dose
Subject analysis set type	Per protocol
Subject analysis set description:	
Participants received subcutaneous (SC) injection of lower exposure dupilumab in Part A. Lower exposure dupilumab regimen were exposures approximating those in adolescents and adults receiving	

300 mg dupilumab Q2W

Subject analysis set title	Part A: Dupilumab High Dose
Subject analysis set type	Per protocol

Subject analysis set description:

Participants received subcutaneous (SC) injection of higher exposure dupilumab in Part A. Higher exposure dupilumab regimen were exposures approximating those in adolescents and adults receiving 300 mg dupilumab QW

Subject analysis set title	Part B: Placebo to Dupilumab Low Dose
Subject analysis set type	Per protocol

Subject analysis set description:

Participants who received subcutaneous (SC) injection of placebo in Part A and received lower exposure dupilumab in Part B. Lower exposure dupilumab regimen were exposures approximating those in adolescents and adults receiving 300 mg dupilumab Q2W

Subject analysis set title	Part B: Placebo to Dupilumab High Dose
Subject analysis set type	Per protocol

Subject analysis set description:

Participants who received subcutaneous (SC) injection of placebo in Part A and received higher exposure dupilumab in Part B. Higher exposure dupilumab regimen were exposures approximating those in adolescents and adults receiving 300 mg dupilumab QW

Subject analysis set title	Part B: Dupilumab Low Dose to Dupilumab Low Dose
Subject analysis set type	Per protocol

Subject analysis set description:

Participants received subcutaneous (SC) injection of lower exposure dupilumab in Parts A and B. Lower exposure dupilumab regimen were exposures approximating those in adolescents and adults receiving 300 mg dupilumab Q2W

Subject analysis set title	Part B: Dupilumab High Dose to Dupilumab High Dose
Subject analysis set type	Per protocol

Subject analysis set description:

Participants received subcutaneous (SC) injection of higher exposure dupilumab in Parts A and B. Higher exposure dupilumab regimen were exposures approximating those in adolescents and adults receiving 300 mg dupilumab QW.

Subject analysis set title	Part C: Dupilumab
Subject analysis set type	Per protocol

Subject analysis set description:

Participants who completed Part A or B were eligible to enroll in Part C and receive Dupilumab extended active treatment

Subject analysis set title	Part C: Dupilumab
Subject analysis set type	Sub-group analysis

Subject analysis set description:

Participants received Dupilumab; Anti-Drug Antibody Analysis Set (AAS): The Part C AAS included all participants who received any amount of study drug in Part C and had at least 1 non-missing ADA result following the first dose of study drug. Analysis was based on treatment received.

Primary: Part A: Percentage of Participants Achieving Peak Esophageal Intraepithelial Eosinophil Count of Less Than or Equal to (≤) 6 Eosinophils/High Power Field (eos/hpf) at Week 16

End point title	Part A: Percentage of Participants Achieving Peak Esophageal Intraepithelial Eosinophil Count of Less Than or Equal to (≤) 6 Eosinophils/High Power Field (eos/hpf) at Week 16

End point description:

Peak esophageal intraepithelial eosinophil count was measured from esophageal biopsies. A total of at least 9 mucosal pinch biopsies were collected from 3 esophageal regions: 3 proximal, 3 mid, and 3 distal. The peak esophageal intraepithelial eosinophil count at each visit was the maximum of the quantities of eosinophils in the most inflamed hpfs across the 3 regions. If the quantity of eosinophils was missing for 1 or 2 esophageal regions, the peak eosinophil count was the maximum of the quantities of eosinophils from the region(s) where eosinophil quantities were available. Analysis was performed on Part A FAS which included all randomized participants in Part A.

End point type	Primary

End point timeframe:
At Week 16

End point values	Part A: Pooled Placebo	Part A: Dupilumab Low Dose	Part A: Dupilumab High Dose	
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	
Number of subjects analysed	34	31	37	
Units: percentage of participants				
number (confidence interval 95%)	2.9 (0.07 to 15.33)	58.1 (39.08 to 75.45)	67.6 (50.21 to 81.99)	

Statistical analyses

Statistical analysis title	A: Dupilumab Low Dose vs A: Pooled Placebo
Comparison groups	Part A: Pooled Placebo v Part A: Dupilumab Low Dose
Number of subjects included in analysis	65
Analysis specification	Pre-specified
Analysis type	
P-value	< 0.0001
Method	Cochran-Mantel-Haenszel
Parameter estimate	Odds ratio (OR)
Point estimate	46.7
Confidence interval	
level	95 %
sides	2-sided
lower limit	5.47
upper limit	399.54

Statistical analysis title	A: Dupilumab High Dose vs A: Pooled Placebo
Comparison groups	Part A: Pooled Placebo v Part A: Dupilumab High Dose
Number of subjects included in analysis	71
Analysis specification	Pre-specified
Analysis type	
P-value	< 0.0001
Method	Cochran-Mantel-Haenszel
Parameter estimate	Odds ratio (OR)
Point estimate	53.8
Confidence interval	
level	95 %
sides	2-sided
lower limit	7.37
upper limit	392.82

Secondary: Part A: Percentage of Participants Achieving Peak Esophageal Intraepithelial Eosinophil Count of <15 Eosinophils/High Power Field at Week 16

End point title	Part A: Percentage of Participants Achieving Peak Esophageal Intraepithelial Eosinophil Count of <15 Eosinophils/High Power Field at Week 16

End point description:

Peak esophageal intraepithelial eosinophil count was measured from esophageal biopsies. A total of at least 9 mucosal pinch biopsies were collected from 3 esophageal regions: 3 proximal, 3 mid, and 3 distal. The peak esophageal intraepithelial eosinophil count at each visit was the maximum of the quantities of eosinophils in the most inflamed hpfs across the 3 regions. If the quantity of eosinophils was missing for 1 or 2 esophageal regions, the peak eosinophil count was the maximum of the quantities of eosinophils from the region(s) where eosinophil quantities were available.

End point type	Secondary

End point timeframe:

At Week 16

End point values	Part A: Pooled Placebo	Part A: Dupilumab Low Dose	Part A: Dupilumab High Dose	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	34	31	37	
Units: percentage of participants				
number (confidence interval 95%)	2.9 (0.07 to 15.33)	67.7 (48.63 to 83.32)	83.8 (67.99 to 93.81)	

Statistical analyses

Statistical analysis title	A: Dupilumab Low Dose vs A: Pooled Placebo
Comparison groups	Part A: Pooled Placebo v Part A: Dupilumab Low Dose
Number of subjects included in analysis	65
Analysis specification	Pre-specified
Analysis type	
P-value	< 0.0001 [1]
Method	Cochran-Mantel-Haenszel
Parameter estimate	Odds ratio (OR)
Point estimate	55.3
Confidence interval	
level	95 %
sides	2-sided
lower limit	7.45
upper limit	410.23

Notes:

[1] - P-value is not adjusted for multiple comparisons

Statistical analysis title	A: Dupilumab High Dose vs A: Pooled Placebo

Comparison groups	Part A: Pooled Placebo v Part A: Dupilumab High Dose
Number of subjects included in analysis	71
Analysis specification	Pre-specified
Analysis type	
P-value	< 0.0001
Method	Cochran-Mantel-Haenszel
Parameter estimate	Odds ratio (OR)
Point estimate	178
Confidence interval	
level	95 %
sides	2-sided
lower limit	18.84
upper limit	1682.4

Secondary: Part A: Percent Change From Baseline in Peak Esophageal Intraepithelial Eosinophil Count at Week 16

End point title	Part A: Percent Change From Baseline in Peak Esophageal Intraepithelial Eosinophil Count at Week 16

End point description:

Peak esophageal intraepithelial eosinophil count was measured from esophageal biopsies. A total of at least 9 mucosal pinch biopsies were collected from 3 esophageal regions: 3 proximal, 3 mid, and 3 distal. The peak esophageal intraepithelial eosinophil count at each visit was the maximum of the quantities of eosinophils in the most inflamed hpfs across the 3 regions. If the quantity of eosinophils was missing for 1 or 2 esophageal regions, the peak eosinophil count was the maximum of the quantities of eosinophils from the region(s) where eosinophil quantities were available. Least squared (LS) mean and standard error (SE) from analysis of covariance (ANCOVA) model with Baseline measurement as covariate and the treatment, baseline weight group strata as fixed factors.

End point type	Secondary

End point timeframe:

Baseline, Week 16

End point values	Part A: Pooled Placebo	Part A: Dupilumab Low Dose	Part A: Dupilumab High Dose	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	34	31	37	
Units: percent change				
least squares mean (standard error)	20.98 (± 12.23)	-77.93 (± 12.89)	-86.09 (± 11.84)	

Statistical analyses

Statistical analysis title	A: Dupilumab Low Dose vs A: Pooled Placebo
Comparison groups	Part A: Pooled Placebo v Part A: Dupilumab Low Dose

Number of subjects included in analysis	65
Analysis specification	Pre-specified
Analysis type	
P-value	< 0.0001 [2]
Method	ANCOVA
Parameter estimate	LS mean difference
Point estimate	-98.92
Confidence interval	
level	95 %
sides	2-sided
lower limit	-132.463
upper limit	-65.37

Notes:

[2] - P-value is not adjusted for multiple comparisons

Statistical analysis title	A: Dupilumab High Dose vs A: Pooled Placebo
Comparison groups	Part A: Pooled Placebo v Part A: Dupilumab High Dose
Number of subjects included in analysis	71
Analysis specification	Pre-specified
Analysis type	
P-value	< 0.0001
Method	ANCOVA
Parameter estimate	LS mean difference
Point estimate	-107.07
Confidence interval	
level	95 %
sides	2-sided
lower limit	-139.249
upper limit	-74.9

Secondary: Part A: Change From Baseline in Mean Eosinophilic Esophagitis Histology Scoring System (EoE-HSS) Grade Score at Week 16

End point title	Part A: Change From Baseline in Mean Eosinophilic Esophagitis Histology Scoring System (EoE-HSS) Grade Score at Week 16

End point description:

EoE-HSS is a validated histologic scoring system that measures other histological abnormalities in addition to density of eosinophilic infiltration. Severity (grade) and extent (stage) of abnormalities will be scored using a 4-point scale (0 normal; 3 maximum change). Higher total score indicated greater severity & extent of histological abnormalities. For each of 3 esophageal regions (proximal, mid, and distal), the ratio of the sum of assigned score for each evaluated feature divided by maximum possible score (maximum value is 24) was calculated. The mean grade scores summed over the 3 regions was the final score used in primary analysis, the mean grade score ranged from 0 to 3, with higher score indicating more severe.

End point type	Secondary

End point timeframe:

Baseline, Week 16

End point values	Part A: Pooled Placebo	Part A: Dupilumab Low Dose	Part A: Dupilumab High Dose	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	34	31	37	
Units: Score on a scale				
least squares mean (standard error)	0.023 (± 0.0498)	-0.757 (± 0.0524)	-0.879 (± 0.0481)	

Statistical analyses

Statistical analysis title	A: Dupilumab High Dose vs A: Pooled Placebo
Comparison groups	Part A: Pooled Placebo v Part A: Dupilumab High Dose
Number of subjects included in analysis	71
Analysis specification	Pre-specified
Analysis type	
P-value	< 0.0001
Method	ANCOVA
Parameter estimate	LS mean difference
Point estimate	-0.902
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.0325
upper limit	-0.7714

Statistical analysis title	A: Dupilumab Low Dose vs A: Pooled Placebo
Comparison groups	Part A: Pooled Placebo v Part A: Dupilumab Low Dose
Number of subjects included in analysis	65
Analysis specification	Pre-specified
Analysis type	
P-value	< 0.0001 [3]
Method	ANCOVA
Parameter estimate	LS mean difference
Point estimate	-0.78
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.917
upper limit	-0.644

Notes:

[3] - P-value is not adjusted for multiple comparisons

Secondary: Part A: Normalized Enrichment Score (NES) for the Relative Change From Baseline in the Type 2 Inflammation Signature (T2INF) at Week 16

End point title	Part A: Normalized Enrichment Score (NES) for the Relative Change From Baseline in the Type 2 Inflammation Signature (T2INF) at Week 16

End point description:

A Normalized Enrichment Score (NES) is a way to generate a single numerical value to represent a complex gene expression signature. Changes in NES score represented the overall changes in the expression of that molecular phenotype. The NESs calculated for T2INF reflect the expression at Week 16 relative to Baseline of the pre-specified gene set as a way to evaluate normalization of type 2 inflammation with treatment. For each subject, an NES of 0 indicates no change from baseline, a negative score shows a reduction in disease score (more like normal) and positive score shows worsening (more active disease). NES does not have a minimum/maximum score. Analysis was performed on Part A FAS which included all randomized participants in Part A. Here, 'overall number of participants analyzed' = participants with available data for this outcome measure.

End point type	Secondary

End point timeframe:

Baseline, Week 16

End point values	Part A: Pooled Placebo	Part A: Dupilumab Low Dose	Part A: Dupilumab High Dose	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	21	15	24	
Units: Score on a scale				
median (full range (min-max))	0.340 (-1.84 to 1.65)	-1.930 (-2.00 to -1.39)	-1.895 (-2.03 to -1.61)	

Statistical analyses

Statistical analysis title	A: Dupilumab Low Dose vs A: Pooled Placebo
Comparison groups	Part A: Pooled Placebo v Part A: Dupilumab Low Dose
Number of subjects included in analysis	36
Analysis specification	Pre-specified
Analysis type	
P-value	< 0.0001 [4]
Method	Wilcoxon rank-sum test
Parameter estimate	Hodges-Lehmann estimator
Point estimate	-2.19
Confidence interval	
level	95 %
sides	2-sided
lower limit	-2.45
upper limit	-1.82

Notes:

[4] - P-value is not adjusted for multiple comparisons

Statistical analysis title	A: Dupilumab High Dose vs A: Pooled Placebo
Comparison groups	Part A: Pooled Placebo v Part A: Dupilumab High Dose

Number of subjects included in analysis	45
Analysis specification	Pre-specified
Analysis type	
P-value	< 0.0001
Method	Wilcoxon rank-sum test
Parameter estimate	Hodges-Lehmann estimator
Point estimate	-2.22
Confidence interval	
level	95 %
sides	2-sided
lower limit	-2.44
upper limit	-1.95

Secondary: Part A: Change From Baseline in Mean Eosinophilic Esophagitis Histology Scoring System (EoE-HSS) Stage Score at Week 16

End point title	Part A: Change From Baseline in Mean Eosinophilic Esophagitis Histology Scoring System (EoE-HSS) Stage Score at Week 16

End point description:

EoE-HSS is a validated histologic scoring system that measures other histological abnormalities in addition to density of eosinophilic infiltration. Severity (grade) and extent (stage) of abnormalities will be scored using a 4-point scale (0 normal; 3 maximum change). Higher total score indicated greater severity & extent of histological abnormalities. For each of 3 esophageal regions (proximal, mid, and distal), the ratio of the sum of assigned score for each evaluated feature divided by maximum possible score (maximum value is 24) was calculated. The mean stage scores summed over the 3 regions was the final score used in primary analysis, the mean stage score ranged from 0 to 3, with higher score indicating more severe.

End point type	Secondary

End point timeframe:

Baseline, Week 16

End point values	Part A: Pooled Placebo	Part A: Dupilumab Low Dose	Part A: Dupilumab High Dose	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	34	31	37	
Units: Score on a scale				
least squares mean (standard error)	0.048 (± 0.0482)	-0.721 (± 0.0507)	-0.835 (± 0.0466)	

Statistical analyses

Statistical analysis title	A: Dupilumab Low Dose vs A: Pooled Placebo
Comparison groups	Part A: Pooled Placebo v Part A: Dupilumab Low Dose

Number of subjects included in analysis	65
Analysis specification	Pre-specified
Analysis type	
P-value	< 0.0001 [5]
Method	ANCOVA
Parameter estimate	LS mean difference
Point estimate	-0.769
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.9013
upper limit	-0.6362

Notes:

[5] - P-value is not adjusted for multiple comparisons

Statistical analysis title	A: Dupilumab High Dose vs A: Pooled Placebo
Comparison groups	Part A: Pooled Placebo v Part A: Dupilumab High Dose
Number of subjects included in analysis	71
Analysis specification	Pre-specified
Analysis type	
P-value	< 0.0001
Method	ANCOVA
Parameter estimate	LS mean difference
Point estimate	-0.883
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.0095
upper limit	-0.7568

Secondary: Part A: Normalized Enrichment Score (NES) for the Relative Change From Baseline in the Eosinophilic Esophagitis (EoE) Diagnostic Panel (EDP) at Week 16

End point title	Part A: Normalized Enrichment Score (NES) for the Relative Change From Baseline in the Eosinophilic Esophagitis (EoE) Diagnostic Panel (EDP) at Week 16

End point description:

A Normalized Enrichment Score (NES) is a way to generate a single numerical value to represent a complex gene expression signature. Changes in NES score represented the overall changes in the expression of that molecular phenotype. The NESs calculated for the EDP reflect the expression at Week 16 relative to Baseline of a gene set that is differentially expressed between esophageal biopsies from EoE participants compared to healthy controls as a way to evaluate normalization of the molecular pathology. For each subject, an NES of 0 indicates no change from baseline, a negative score shows a reduction in disease score (more like normal) and positive score shows worsening (more active disease). NES does not have minimum/maximum score. Analysis was performed on Part A FAS which included all randomized participants in Part A. Here, 'overall number of participants analyzed' = participants with available data for this outcome measure.

End point type	Secondary

End point timeframe:

Baseline, Week 16

End point values	Part A: Pooled Placebo	Part A: Dupilumab Low Dose	Part A: Dupilumab High Dose	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	21	15	24	
Units: Score on a scale				
median (full range (min-max))	0.180 (-2.53 to 2.39)	-2.710 (-2.84 to -0.80)	-2.630 (-2.85 to -2.25)	

Statistical analyses

Statistical analysis title	A: Dupilumab Low Dose vs A: Pooled Placebo
Comparison groups	Part A: Pooled Placebo v Part A: Dupilumab Low Dose
Number of subjects included in analysis	36
Analysis specification	Pre-specified
Analysis type	
P-value	< 0.0001 [6]
Method	Wilcoxon rank-sum test
Parameter estimate	Hodges-Lehmann estimator
Point estimate	-2.7
Confidence interval	
level	95 %
sides	2-sided
lower limit	-3.31
upper limit	-1.62

Notes:

[6] - P-value is not adjusted for multiple comparisons

Statistical analysis title	A: Dupilumab High Dose vs A: Pooled Placebo
Comparison groups	Part A: Pooled Placebo v Part A: Dupilumab High Dose
Number of subjects included in analysis	45
Analysis specification	Pre-specified
Analysis type	
P-value	< 0.0001
Method	Wilcoxon rank-sum test
Parameter estimate	Hodges-Lehmann estimator
Point estimate	-2.84
Confidence interval	
level	95 %
sides	2-sided
lower limit	-3.35
upper limit	-1.96

Secondary: Part A: Absolute Change From Baseline in EoE Endoscopic Reference Total Score (EoE-EREFS) at Week 16

End point title	Part A: Absolute Change From Baseline in EoE Endoscopic Reference Total Score (EoE-EREFS) at Week 16

End point description:

The EoE-EREFS is a validated endoscopic scoring system for inflammatory and remodeling features of EoE including edema, rings, exudates, furrows, and stricture. The score was assessed in the proximal and distal esophageal regions with each region scored from 0 to 9 with total scores ranging from 0 to 18. Higher scores indicate worse endoscopic inflammatory and remodeling findings.

End point type	Secondary

End point timeframe:

Baseline, Week 16

End point values	Part A: Pooled Placebo	Part A: Dupilumab Low Dose	Part A: Dupilumab High Dose	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	34	31	37	
Units: score on a scale				
least squares mean (standard error)	0.3 (± 0.45)	-3.0 (± 0.48)	-3.5 (± 0.42)	

Statistical analyses

Statistical analysis title	A: Dupilumab Low Dose vs A: Pooled Placebo
Comparison groups	Part A: Pooled Placebo v Part A: Dupilumab Low Dose
Number of subjects included in analysis	65
Analysis specification	Pre-specified
Analysis type	
P-value	< 0.0001 [7]
Method	ANCOVA
Parameter estimate	LS mean difference
Point estimate	-3.3
Confidence interval	
level	95 %
sides	2-sided
lower limit	-4.59
upper limit	-2.1

Notes:

[7] - P-value is not adjusted for multiple comparisons

Statistical analysis title	A: Dupilumab High Dose vs A: Pooled Placebo
Comparison groups	Part A: Pooled Placebo v Part A: Dupilumab High Dose

Number of subjects included in analysis	71
Analysis specification	Pre-specified
Analysis type	
P-value	< 0.0001
Method	ANCOVA
Parameter estimate	LS mean difference
Point estimate	-3.8
Confidence interval	
level	95 %
sides	2-sided
lower limit	-4.94
upper limit	-2.63

Secondary: Part A: Number of Sign-free Days During the 14-day Period Preceding Week 16 as Measured by the PESQ-C (for participants aged ≥1 to <12 years)

End point title	Part A: Number of Sign-free Days During the 14-day Period Preceding Week 16 as Measured by the PESQ-C (for participants aged ≥1 to <12 years)

End point description:

PESQ-C is a novel, observer-reported outcome measure intended to be completed independently by caregivers of all pediatric EoE participants in the study. The PESQ-C measures the signs of EoE observed by the caregiver, including stomach pain, heartburn, acid reflux, regurgitation, vomiting, food refusal, and trouble swallowing food. WOCF approach was used for imputing the missing data due to rescue treatment/AE/lack of efficacy, and the multiple imputations approach was used for the missing data due to other reasons. LS mean SE derived from ANCOVA model.

End point type	Secondary

End point timeframe:

Week 16

End point values	Part A: Pooled Placebo	Part A: Dupilumab Low Dose	Part A: Dupilumab High Dose	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	34	31	37	
Units: sign-free days				
least squares mean (standard error)	8.93 (± 0.756)	8.93 (± 0.840)	10.38 (± 0.735)	

Statistical analyses

Statistical analysis title	A: Dupilumab Low Dose vs A: Pooled Placebo
Comparison groups	Part A: Pooled Placebo v Part A: Dupilumab Low Dose

Number of subjects included in analysis	65
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.9965 [8]
Method	ANCOVA
Parameter estimate	LS mean difference
Point estimate	0
Confidence interval	
level	95 %
sides	2-sided
lower limit	-2.107
upper limit	2.117

Notes:

[8] - P-value is not adjusted for multiple comparisons

Statistical analysis title	A: Dupilumab High Dose vs A: Pooled Placebo
Comparison groups	Part A: Pooled Placebo v Part A: Dupilumab High Dose
Number of subjects included in analysis	71
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.1507 [9]
Method	ANCOVA
Parameter estimate	LS mean difference
Point estimate	1.45
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.527
upper limit	3.422

Notes:

[9] - P-value is not adjusted for multiple comparisons

Secondary: Part A: Change From Baseline in the Proportion of Days With 1 or More EoE Signs as Measured by Pediatric EoE Sign/Symptom Questionnaire - Caregiver Version (PESQ-C) at Week 16 (for Participants Aged ≥1 to <12 Years)

End point title	Part A: Change From Baseline in the Proportion of Days With 1 or More EoE Signs as Measured by Pediatric EoE Sign/Symptom Questionnaire - Caregiver Version (PESQ-C) at Week 16 (for Participants Aged ≥1 to <12 Years)

End point description:

PESQ-C is a novel, observer-reported outcome measure intended to be completed independently by caregivers of all pediatric EoE participants in the study. PESQ-C measures the signs of EoE observed by the caregiver, including stomach pain, heartburn, acid reflux, regurgitation, vomiting, food refusal, and trouble swallowing food. Data from a 14-day period preceding the baseline visit and a 14-day period preceding week 16 will be used to calculate the proportion of days with 1 or more EoE symptoms.

End point type	Secondary

End point timeframe:

Baseline, Week 16

End point values	Part A: Pooled Placebo	Part A: Dupilumab Low Dose	Part A: Dupilumab High Dose	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	34	31	37	
Units: proportion of days				
least squares mean (standard error)	-0.17 (± 0.054)	-0.18 (± 0.060)	-0.28 (± 0.052)	

Statistical analyses

Statistical analysis title	A: Dupilumab Low Dose vs A: Pooled Placebo
Comparison groups	Part A: Pooled Placebo v Part A: Dupilumab Low Dose
Number of subjects included in analysis	65
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.9533 [10]
Method	ANCOVA
Parameter estimate	LS mean difference
Point estimate	0
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.155
upper limit	0.146

Notes:

[10] - P-value is not adjusted for multiple comparisons

Statistical analysis title	A: Dupilumab High Dose vs A: Pooled Placebo
Comparison groups	Part A: Pooled Placebo v Part A: Dupilumab High Dose
Number of subjects included in analysis	71
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.1526
Method	ANCOVA
Parameter estimate	LS mean difference
Point estimate	-0.1
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.244
upper limit	0.038

Secondary: Part A: Change From Baseline in the Proportion of Total Segments Within a Day (Night, Morning, Afternoon, Evening) With 1 or More EoE Signs as Measured by the PESQ-C at Week 16

End point title	Part A: Change From Baseline in the Proportion of Total Segments Within a Day (Night, Morning, Afternoon, Evening)

	With 1 or More EoE Signs as Measured by the PESQ-C at Week 16

End point description:

PESQ-C is a novel, observer-reported outcome measure intended to be completed independently by caregivers of all pediatric EoE participants in the study. The PESQ-C measured the occurrence of signs of EoE and was completed once daily via an electronic diary. Data from a 14-day period preceding the baseline visit and a 14-day period preceding week 16 will be used to calculate the total time segments within a day (night, morning, afternoon, evening) with 1 or more EoE symptoms.

End point type	Secondary

End point timeframe:

Baseline, Week 16

End point values	Part A: Pooled Placebo	Part A: Dupilumab Low Dose	Part A: Dupilumab High Dose	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	34	31	37	
Units: proportion of segments				
least squares mean (standard error)	-0.11 (± 0.032)	-0.09 (± 0.036)	-0.16 (± 0.031)	

Statistical analyses

Statistical analysis title	A: Dupilumab Low Dose vs A: Pooled Placebo
Comparison groups	Part A: Pooled Placebo v Part A: Dupilumab Low Dose
Number of subjects included in analysis	65
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.6361 [11]
Method	ANCOVA
Parameter estimate	LS mean difference
Point estimate	0.02
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.069
upper limit	0.112

Notes:

[11] - P-value is not adjusted for multiple comparisons

Statistical analysis title	A: Dupilumab High Dose vs A: Pooled Placebo
Comparison groups	Part A: Pooled Placebo v Part A: Dupilumab High Dose

Number of subjects included in analysis	71
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.2064 [12]
Method	ANCOVA
Parameter estimate	LS mean difference
Point estimate	-0.05
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.139
upper limit	0.03

Notes:

[12] - P-value is not adjusted for multiple comparisons

Secondary: Part A: Change From Baseline in the Proportion of Days With 1 or More EoE Signs by Pediatric EoE Sign/Symptom Questionnaire - Participant Version (PESQ-P) (for participants aged ≥8 to <12 years) at Week 16

End point title	Part A: Change From Baseline in the Proportion of Days With 1 or More EoE Signs by Pediatric EoE Sign/Symptom Questionnaire - Participant Version (PESQ-P) (for participants aged ≥8 to <12 years) at Week 16

End point description:

The PESQ-P was a participant-reported outcome measure intended to be completed independently by participants ≥8 to <12 years of age. The PESQ-P measured occurrence of signs of EoE and was completed once daily via an electronic diary. Data from a 14-day period preceding the baseline visit and a 14-day period preceding week 16 will be used to calculate the proportion of days with 1 or more EoE symptoms.

End point type	Secondary

End point timeframe:

Baseline, Week 16

End point values	Part A: Pooled Placebo	Part A: Dupilumab Low Dose	Part A: Dupilumab High Dose	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	17	19	17	
Units: proportion of days				
least squares mean (standard error)	-0.26 (± 0.068)	-0.16 (± 0.067)	-0.13 (± 0.077)	

Statistical analyses

Statistical analysis title	A: Dupilumab Low Dose vs A: Pooled Placebo
Comparison groups	Part A: Pooled Placebo v Part A: Dupilumab Low Dose

Number of subjects included in analysis	36
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.2975 [13]
Method	ANCOVA
Parameter estimate	LS mean difference
Point estimate	0.1
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.088
upper limit	0.286

Notes:

[13] - P-value is not adjusted for multiple comparisons

Statistical analysis title	A: Dupilumab High Dose vs A: Pooled Placebo
Comparison groups	Part A: Pooled Placebo v Part A: Dupilumab High Dose
Number of subjects included in analysis	34
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.2086 [14]
Method	ANCOVA
Parameter estimate	LS mean difference
Point estimate	0.13
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.072
upper limit	0.33

Notes:

[14] - P-value is not adjusted for multiple comparisons

Secondary: Part A: Number of Symptom-free Days During the 14-day Period Preceding Week 16 as Measured by the PESQ-P (for Participants Aged ≥8 to <12 Years)

End point title	Part A: Number of Symptom-free Days During the 14-day Period Preceding Week 16 as Measured by the PESQ-P (for Participants Aged ≥8 to <12 Years)

End point description:

The PESQ-P was a participant-reported outcome measure intended to be completed independently by EoE participants ≥8 to <12 years of age. The PESQ-P measures the signs of EoE, including stomach pain, heartburn, acid reflux, regurgitation, vomiting, food refusal, and trouble swallowing food. The PESQ-P score was calculated based on the daily responses over a 14-day period (i.e., the 14 days prior to the baseline visit and the week 16 visit). The score ranges from 0 to 1. WOCF approach was used for imputing the missing data due to rescue treatment/AE/lack of efficacy, and the multiple imputations approach was used for the missing data due to other reasons. LS Mean SE from ANCOVA.

End point type	Secondary

End point timeframe:

Week 16

End point values	Part A: Pooled Placebo	Part A: Dupilumab Low Dose	Part A: Dupilumab High Dose	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	17	19	17	
Units: sign-free days				
least squares mean (standard error)	10.49 (± 0.953)	9.13 (± 0.936)	8.69 (± 1.081)	

Statistical analyses

Statistical analysis title	A: Dupilumab Low Dose vs A: Pooled Placebo
Comparison groups	Part A: Pooled Placebo v Part A: Dupilumab Low Dose
Number of subjects included in analysis	36
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.3098 [15]
Method	ANCOVA
Parameter estimate	LS mean difference
Point estimate	-1.36
Confidence interval	
level	95 %
sides	2-sided
lower limit	-3.972
upper limit	1.26

Notes:

[15] - P-value is not adjusted for multiple comparisons

Statistical analysis title	A: Dupilumab High Dose vs A: Pooled Placebo
Comparison groups	Part A: Pooled Placebo v Part A: Dupilumab High Dose
Number of subjects included in analysis	34
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.2085 [16]
Method	ANCOVA
Parameter estimate	LS mean difference
Point estimate	-1.8
Confidence interval	
level	95 %
sides	2-sided
lower limit	-4.615
upper limit	1.007

Notes:

[16] - P-value is not adjusted for multiple comparisons

Secondary: Part A: Change From Baseline in the Proportion of Total Segments Within a Day (Night, Morning, Afternoon, Evening) With 1 or More EoE Signs as Measured by the PESQ-P (for Participants Aged ≥8 to <12 Years) at Week 16

End point title	Part A: Change From Baseline in the Proportion of Total Segments Within a Day (Night, Morning, Afternoon, Evening)

	With 1 or More EoE Signs as Measured by the PESQ-P (for Participants Aged ≥8 to <12 Years) at Week 16

End point description:

The PESQ-P was a participant-reported outcome measure intended to be completed independently by EoE participants ≥8 to <12 years of age. The PESQ-P measured the occurrence of signs of EoE and was completed once daily via an electronic diary. Data from a 14-day period preceding the baseline visit and a 14-day period preceding week 16 will be used to calculate the total time segments within a day (night, morning, afternoon, evening) with 1 or more EoE symptoms.

End point type	Secondary

End point timeframe:

Baseline, Week 16

End point values	Part A: Pooled Placebo	Part A: Dupilumab Low Dose	Part A: Dupilumab High Dose	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	17	19	17	
Units: proportion of segments				
least squares mean (standard error)	-0.15 (± 0.040)	-0.08 (± 0.039)	-0.08 (± 0.045)	

Statistical analyses

Statistical analysis title	A: Dupilumab Low Dose vs A: Pooled Placebo
Comparison groups	Part A: Pooled Placebo v Part A: Dupilumab Low Dose
Number of subjects included in analysis	36
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.1939 [17]
Method	ANCOVA
Parameter estimate	LS mean difference
Point estimate	0.07
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.037
upper limit	0.181

Notes:

[17] - P-value is not adjusted for multiple comparisons

Statistical analysis title	A: Dupilumab High Dose vs A: Pooled Placebo
Comparison groups	Part A: Pooled Placebo v Part A: Dupilumab High Dose

Number of subjects included in analysis	34
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.236 [18]
Method	ANCOVA
Parameter estimate	LS mean difference
Point estimate	0.07
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.046
upper limit	0.186

Notes:

[18] - P-value is not adjusted for multiple comparisons

Secondary: Part A: Concentration of Functional Dupilumab in Serum at Baseline, Week 4 and 16

End point title	Part A: Concentration of Functional Dupilumab in Serum at Baseline, Week 4 and 16[19]

End point description:

Concentration of functional dupilumab in serum at Baseline, Week 4 and 16 was reported in this outcome measure.

End point type	Secondary

End point timeframe:

Baseline, Week 4 and 16

Notes:

[19] - 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 who received dupilumab were included in the analysis of this endpoint.

End point values	Part A: Dupilumab Low Dose	Part A: Dupilumab High Dose		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	28	36		
Units: milligrams per liter (mg/L)				
arithmetic mean (standard deviation)				
Baseline	0 (± 0)	0 (± 0)		
Week 4	40.6 (± 11.2)	75.7 (± 25.7)		
Week 16	86.0 (± 29.2)	163 (± 60.8)		

Statistical analyses

No statistical analyses for this end point

Secondary: Part A: Change From Baseline in Total Score as Measured by the Pediatric Eosinophilic Esophagitis Symptom Score (PEESS) Version 2.0 Caregiver Version (PEESSv2.0-C) at Week 16

End point title	Part A: Change From Baseline in Total Score as Measured by the Pediatric Eosinophilic Esophagitis Symptom Score (PEESS)

	Version 2.0 Caregiver Version (PEESSv2.0-C) at Week 16

End point description:

The PEESSv2.0-C is a caregiver-reported outcome measure that assesses the frequency and severity of EoE symptoms among pediatric participants. The PEESSv2.0-C consists of 20 items and has a one-month recall period. Each item had a 0-4 scale, which was transformed to 0-100 as follows: 0 = 0, 1 = 25, 2 = 50, 3 = 75, 4 = 100. The mean total PEESSv2.0 score was computed as the sum of all the item scores over the number of items answered. The total PEESSv2.0-C score ranges from 0 to 100 where higher scores indicate greater symptom burden among pediatric EoE participants. Values after first rescue treatment use were set to missing (censoring). WOCF approach was used for imputing the missing data due to rescue treatment/AE/lack of efficacy, and the MI approach was used for the missing data due to other reasons. LS mean SE from ANCOVA model.

End point type	Secondary

End point timeframe:

Baseline, Week 16

End point values	Part A: Pooled Placebo	Part A: Dupilumab Low Dose	Part A: Dupilumab High Dose	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	34	31	37	
Units: score on a scale				
least squares mean (standard error)	-11.83 (± 2.909)	-10.10 (± 2.785)	-19.86 (± 2.577)	

Statistical analyses

No statistical analyses for this end point

Secondary: Part B: Percentage of Participants Achieving Peak Esophageal Intraepithelial Eosinophil Count of <15 Eosinophils/High Power Field at Week 52

End point title	Part B: Percentage of Participants Achieving Peak Esophageal Intraepithelial Eosinophil Count of <15 Eosinophils/High Power Field at Week 52

End point description:

Peak esophageal intraepithelial eosinophil count was measured from esophageal biopsies. A total of at least 9 mucosal pinch biopsies were collected from 3 esophageal regions: 3 proximal, 3 mid, and 3 distal. The peak esophageal intraepithelial eosinophil count at each visit was the maximum of the quantities of eosinophils in the most inflamed hpfs across the 3 regions. If the quantity of eosinophils was missing for 1 or 2 esophageal regions, the peak eosinophil count was the maximum of the quantities of eosinophils from the region(s) where eosinophil quantities were available.

End point type	Secondary

End point timeframe:

At Week 52

End point values	Part B: Placebo to Dupilumab Low Dose	Part B: Placebo to Dupilumab High Dose	Part B: Dupilumab Low Dose to Dupilumab Low Dose	Part B: Dupilumab High Dose to Dupilumab High Dose
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	14	17	29	35
Units: percentage of participants				
number (not applicable)	92.9	64.7	69.0	85.7

Statistical analyses

No statistical analyses for this end point

Secondary: Part B: Percentage of Participants Achieving Peak Esophageal Intraepithelial Eosinophil Count of ≤6 Eosinophils/High Power Field at Week 52

End point title	Part B: Percentage of Participants Achieving Peak Esophageal Intraepithelial Eosinophil Count of ≤6 Eosinophils/High Power Field at Week 52

End point description:

Peak esophageal intraepithelial eosinophil count was measured from esophageal biopsies. A total of at least 9 mucosal pinch biopsies were collected from 3 esophageal regions: 3 proximal, 3 mid, and 3 distal. The peak esophageal intraepithelial eosinophil count at each visit was the maximum of the quantities of eosinophils in the most inflamed hpfs across the 3 regions. If the quantity of eosinophils was missing for 1 or 2 esophageal regions, the peak eosinophil count was the maximum of the quantities of eosinophils from the region(s) where eosinophil quantities were available.

End point type	Secondary

End point timeframe:

At Week 52

End point values	Part B: Placebo to Dupilumab Low Dose	Part B: Placebo to Dupilumab High Dose	Part B: Dupilumab Low Dose to Dupilumab Low Dose	Part B: Dupilumab High Dose to Dupilumab High Dose
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	14	17	29	35
Units: percentage of participants				
number (not applicable)	92.9	52.9	65.5	62.9

Statistical analyses

No statistical analyses for this end point

Secondary: Part B: Change From Baseline in Mean Eosinophilic Esophagitis Histology Scoring System (EoE-HSS) Grade Score at Week 52

End point title	Part B: Change From Baseline in Mean Eosinophilic Esophagitis Histology Scoring System (EoE-HSS) Grade Score at Week 52

End point description:

EoE-HSS is a validated histologic scoring system that measures other histological abnormalities in addition to density of eosinophilic infiltration. Severity (grade) and extent (stage) of abnormalities will be scored using a 4-point scale (0 normal; 3 maximum change). Higher total score indicated greater severity & extent of histological abnormalities. For each of 3 esophageal regions (proximal, mid, and distal), the ratio of the sum of assigned score for each evaluated feature divided by maximum possible score (maximum value is 24) was calculated. The mean grade scores summed over the 3 regions was the final score used in primary analysis, the mean grade score ranged from 0 to 3, with higher score indicating more severe.

End point type	Secondary

End point timeframe:

Baseline, Week 52

End point values	Part B: Placebo to Dupilumab Low Dose	Part B: Placebo to Dupilumab High Dose	Part B: Dupilumab Low Dose to Dupilumab Low Dose	Part B: Dupilumab High Dose to Dupilumab High Dose
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	14	17	29	35
Units: Score on a scale				
arithmetic mean (standard deviation)	-0.804 (± 0.3099)	-0.885 (± 0.2962)	-0.773 (± 0.3374)	-0.967 (± 0.3920)

Statistical analyses

No statistical analyses for this end point

Secondary: Part B: Percent Change From Baseline in Peak Esophageal Intraepithelial Eosinophil Count at Week 52

End point title	Part B: Percent Change From Baseline in Peak Esophageal Intraepithelial Eosinophil Count at Week 52

End point description:

Peak esophageal intraepithelial eosinophil count was measured from esophageal biopsies. A total of at least 9 mucosal pinch biopsies were collected from 3 esophageal regions: 3 proximal, 3 mid, and 3 distal. The peak esophageal intraepithelial eosinophil count at each visit was the maximum of the quantities of eosinophils in the most inflamed hpfs across the 3 regions. If the quantity of eosinophils was missing for 1 or 2 esophageal regions, the peak eosinophil count was the maximum of the quantities of eosinophils from the region(s) where eosinophil quantities were available.

End point type	Secondary

End point timeframe:

Baseline, Week 52

End point values	Part B: Placebo to Dupilumab Low Dose	Part B: Placebo to Dupilumab High Dose	Part B: Dupilumab Low Dose to Dupilumab Low Dose	Part B: Dupilumab High Dose to Dupilumab High Dose
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	14	17	29	35
Units: percent change				
arithmetic mean (standard deviation)	-92.72 (± 19.229)	-76.83 (± 41.228)	-85.41 (± 22.851)	-90.97 (± 14.482)

Statistical analyses

No statistical analyses for this end point

Secondary: Part B: Change From Baseline in Mean Eosinophilic Esophagitis Histology Scoring System (EoE-HSS) Stage Score at Week 52

End point title	Part B: Change From Baseline in Mean Eosinophilic Esophagitis Histology Scoring System (EoE-HSS) Stage Score at Week 52

End point description:

EoE-HSS is a validated histologic scoring system that measures other histological abnormalities in addition to density of eosinophilic infiltration. Severity (grade) and extent (stage) of abnormalities will be scored using a 4-point scale (0 normal; 3 maximum change). Higher total score indicated greater severity & extent of histological abnormalities. For each of 3 esophageal regions (proximal, mid, and distal), the ratio of the sum of assigned score for each evaluated feature divided by maximum possible score (maximum value is 24) was calculated. The mean stage scores summed over the 3 regions was the final score used in primary analysis, the mean stage score ranged from 0 to 3, with higher score indicating more severe.

End point type	Secondary

End point timeframe:

Baseline, Week 52

End point values	Part B: Placebo to Dupilumab Low Dose	Part B: Placebo to Dupilumab High Dose	Part B: Dupilumab Low Dose to Dupilumab Low Dose	Part B: Dupilumab High Dose to Dupilumab High Dose
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	14	17	29	35
Units: Score on a scale				
arithmetic mean (standard deviation)	-0.767 (± 0.3114)	-0.855 (± 0.3485)	-0.784 (± 0.3183)	-0.892 (± 0.3181)

Statistical analyses

No statistical analyses for this end point

Secondary: Part B: Absolute Change From Baseline in EoE Endoscopic Reference Total Score (EoE-EREFS) at Week 52

End point title	Part B: Absolute Change From Baseline in EoE Endoscopic Reference Total Score (EoE-EREFS) at Week 52

End point description:

The EoE-EREFS is a validated endoscopic scoring system for inflammatory and remodeling features of EoE including edema, rings, exudates, furrows, and stricture. The score was assessed in the proximal and distal esophageal regions with each region scored from 0 to 9 with total scores possibly ranging from 0 to 18. Higher scores indicate worse endoscopic inflammatory and remodeling findings.

End point type	Secondary

End point timeframe:

Baseline, Week 52

End point values	Part B: Placebo to Dupilumab Low Dose	Part B: Placebo to Dupilumab High Dose	Part B: Dupilumab Low Dose to Dupilumab Low Dose	Part B: Dupilumab High Dose to Dupilumab High Dose
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	11	14	22	30
Units: score on a scale				
arithmetic mean (standard deviation)	-5.82 (± 1.722)	-3.64 (± 3.342)	-4.50 (± 3.203)	-4.77 (± 3.081)

Statistical analyses

No statistical analyses for this end point

Secondary: Part B: Change From Baseline in the Proportion of Days With 1 or More EoE Signs Measured by Pediatric EoE Sign/Symptom Questionnaire - Caregiver Version (PESQ-C) at Week 52

End point title	Part B: Change From Baseline in the Proportion of Days With 1 or More EoE Signs Measured by Pediatric EoE Sign/Symptom Questionnaire - Caregiver Version (PESQ-C) at Week 52

End point description:

PESQ-C is a novel, observer-reported outcome measure intended to be completed independently by caregivers of all pediatric EoE participants in the study. Data from a 14-day period preceding the baseline visit and a 14-day period preceding week 16 will be used to calculate the proportion of days with 1 or more EoE symptoms.

End point type	Secondary

End point timeframe:

Baseline, Week 52

End point values	Part B: Placebo to Dupilumab Low Dose	Part B: Placebo to Dupilumab High Dose	Part B: Dupilumab Low Dose to Dupilumab Low Dose	Part B: Dupilumab High Dose to Dupilumab High Dose
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	6	9	18	27
Units: proportion of days				

arithmetic mean (standard deviation)	-0.20 (± 0.373)	-0.47 (± 0.395)	-0.49 (± 0.339)	-0.30 (± 0.299)

Statistical analyses

No statistical analyses for this end point

Secondary: Part B: Change From Baseline in the Proportion of Total Segments Within a Day (Night, Morning, Afternoon, Evening) With 1 or More EoE Signs as Measured by the PESQ-C at Week 52

End point title	Part B: Change From Baseline in the Proportion of Total Segments Within a Day (Night, Morning, Afternoon, Evening) With 1 or More EoE Signs as Measured by the PESQ-C at Week 52

End point description:

PESQ-C is a novel, observer-reported outcome measure intended to be completed independently by caregivers of all pediatric EoE participants in the study. The PESQ-C measured the occurrence of signs of EoE and was completed once daily via an electronic diary. Data from a 14-day period preceding the baseline visit and a 14-day period preceding week 16 will be used to calculate the total time segments within a day (night, morning, afternoon, evening) with 1 or more EoE symptoms.

End point type	Secondary

End point timeframe:

Baseline, Week 52

End point values	Part B: Placebo to Dupilumab Low Dose	Part B: Placebo to Dupilumab High Dose	Part B: Dupilumab Low Dose to Dupilumab Low Dose	Part B: Dupilumab High Dose to Dupilumab High Dose
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	6	9	18	27
Units: proportion of segments				
arithmetic mean (standard deviation)	-0.03 (± 0.249)	-0.24 (± 0.221)	-0.26 (± 0.250)	-0.17 (± 0.187)

Statistical analyses

No statistical analyses for this end point

Secondary: Part B: Number of Sign-free Days During the 14-day Period Preceding Week 52 as Measured by the PESQ-C (for Participants Aged ≥1 to <12 Years)

End point title	Part B: Number of Sign-free Days During the 14-day Period Preceding Week 52 as Measured by the PESQ-C (for Participants Aged ≥1 to <12 Years)

End point description:

PESQ-C is a novel, observer-reported outcome measure intended to be completed independently by caregivers of all pediatric EoE participants in the study.

End point type	Secondary

End point timeframe:
Week 52

End point values	Part B: Placebo to Dupilumab Low Dose	Part B: Placebo to Dupilumab High Dose	Part B: Dupilumab Low Dose to Dupilumab Low Dose	Part B: Dupilumab High Dose to Dupilumab High Dose
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	6	9	18	27
Units: sign-free days				
arithmetic mean (standard deviation)	11.58 (± 3.968)	12.10 (± 4.652)	11.35 (± 3.947)	12.13 (± 4.053)

Statistical analyses

No statistical analyses for this end point

Secondary: Part B: Change From Baseline in the Proportion of Days With 1 or More EoE Signs by Pediatric EoE Sign/Symptom Questionnaire - Participant Version (PESQ-P) (for Participants Aged ≥8 to <12 Years) at Week 52

End point title	Part B: Change From Baseline in the Proportion of Days With 1 or More EoE Signs by Pediatric EoE Sign/Symptom Questionnaire - Participant Version (PESQ-P) (for Participants Aged ≥8 to <12 Years) at Week 52

End point description:

The PESQ-P was a participant-reported outcome measure intended to be completed independently by participants ≥8 to <12 years of age. The PESQ-P measured occurrence of signs of EoE and was completed once daily via an electronic diary. Data from a 14-day period preceding the baseline visit and a 14-day period preceding week 16 will be used to calculate the proportion of days with 1 or more EoE symptoms.

End point type	Secondary

End point timeframe:
Baseline, Week 52

End point values	Part B: Placebo to Dupilumab Low Dose	Part B: Placebo to Dupilumab High Dose	Part B: Dupilumab Low Dose to Dupilumab Low Dose	Part B: Dupilumab High Dose to Dupilumab High Dose
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	3	6	11	12
Units: proportion of days				
arithmetic mean (standard deviation)	-0.33 (± 0.322)	-0.43 (± 0.369)	-0.42 (± 0.400)	-0.26 (± 0.396)

Statistical analyses

No statistical analyses for this end point

Secondary: Part B: Number of Symptom-free Days During the 14-day Period Preceding Week 52 as Measured by the PESQ-P (for Participants Aged ≥8 to <12 Years)

End point title	Part B: Number of Symptom-free Days During the 14-day Period Preceding Week 52 as Measured by the PESQ-P (for Participants Aged ≥8 to <12 Years)

End point description:

The PESQ-P was a participant-reported outcome measure intended to be completed independently by participants ≥8 to <12 years of age. The PESQ-P measures the signs of EoE, including stomach pain, heartburn, acid reflux, regurgitation, vomiting, food refusal, and trouble swallowing food.

End point type	Secondary

End point timeframe:

Week 52

End point values	Part B: Placebo to Dupilumab Low Dose	Part B: Placebo to Dupilumab High Dose	Part B: Dupilumab Low Dose to Dupilumab Low Dose	Part B: Dupilumab High Dose to Dupilumab High Dose
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	3	6	11	12
Units: sign-free days				
arithmetic mean (standard deviation)	9.33 (± 8.083)	11.67 (± 5.715)	10.64 (± 4.943)	13.63 (± 0.874)

Statistical analyses

No statistical analyses for this end point

Secondary: Part B: Change From Baseline in the Proportion of Total Segments Within a Day (Night, Morning, Afternoon, Evening) With 1 or More EoE Signs as Measured by the PESQ-P (for Participants Aged ≥8 to <12 Years) at Week 52

End point title	Part B: Change From Baseline in the Proportion of Total Segments Within a Day (Night, Morning, Afternoon, Evening) With 1 or More EoE Signs as Measured by the PESQ-P (for Participants Aged ≥8 to <12 Years) at Week 52

End point description:

The PESQ-P was a participant-reported outcome measure intended to be completed independently by EoE participants ≥8 to <12 years of age. The PESQ-P measured the occurrence of signs of EoE and was completed once daily via an electronic diary. Data from a 14-day period preceding the baseline visit and a 14-day period preceding week 16 will be used to calculate the total time segments within a day (night, morning, afternoon, evening) with 1 or more EoE symptoms.

End point type	Secondary

End point timeframe:

Baseline, Week 52

End point values	Part B: Placebo to Dupilumab Low Dose	Part B: Placebo to Dupilumab High Dose	Part B: Dupilumab Low Dose to Dupilumab Low Dose	Part B: Dupilumab High Dose to Dupilumab High Dose
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	3	6	11	12
Units: proportion of segments				
arithmetic mean (standard deviation)	-0.17 (± 0.164)	-0.26 (± 0.269)	-0.21 (± 0.293)	-0.16 (± 0.284)

Statistical analyses

No statistical analyses for this end point

Secondary: Part B: Normalized Enrichment Score (NES) for the Relative Change From Baseline in the Type 2 Inflammation Signature (T2INF) at Week 52

End point title	Part B: Normalized Enrichment Score (NES) for the Relative Change From Baseline in the Type 2 Inflammation Signature (T2INF) at Week 52

End point description:

A Normalized Enrichment Score (NES) is a way to generate a single numerical value to represent a complex gene expression signature. Changes in NES score represented the overall changes in the expression of that molecular phenotype. The NESs calculated for T2INF reflect the expression at Week 16 relative to Baseline of the pre-specified gene set as a way to evaluate normalization of type 2 inflammation with treatment. For each subject, an NES of 0 indicates no change from baseline, a negative score shows a reduction in disease score (more like normal) and positive score shows worsening (more active disease). NES does not have minimum/maximum score. Analysis was performed on Part B SAF which included all participants who received at least 1 dose of Part B study drug. Here, 'overall number of participants analyzed' = participants with available data for this outcome measure

End point type	Secondary

End point timeframe:

Baseline, Week 52

End point values	Part B: Placebo to Dupilumab Low Dose	Part B: Placebo to Dupilumab High Dose	Part B: Dupilumab Low Dose to Dupilumab Low Dose	Part B: Dupilumab High Dose to Dupilumab High Dose
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	8	12	16	21
Units: Score on a scale				
median (inter-quartile range (Q1-Q3))	-1.960 (-2.000 to -1.895)	-1.965 (-1.995 to -1.765)	-1.920 (-1.965 to -1.865)	-1.920 (-1.930 to -1.850)

Statistical analyses

No statistical analyses for this end point

Secondary: Part B: Normalized Enrichment Score (NES) for the Relative Change From Baseline in the EoE Diagnostic Panel (EDP) at Week 52

End point title	Part B: Normalized Enrichment Score (NES) for the Relative Change From Baseline in the EoE Diagnostic Panel (EDP) at Week 52

End point description:

A Normalized Enrichment Score (NES) is a way to generate a single numerical value to represent a complex gene expression signature. Changes in NES score represented the overall changes in the expression of that molecular phenotype. The NESs calculated for the EDP reflect the expression at Week 16 relative to Baseline of a gene set that is differentially expressed between esophageal biopsies from EoE participants compared to healthy controls as a way to evaluate normalization of the molecular pathology. For each subject, an NES of 0 indicates no change from baseline, a negative score shows a reduction in disease score (more like normal) and positive score shows worsening (more active disease). NES does not have minimum/maximum score.

End point type	Secondary

End point timeframe:

Baseline, Week 52

End point values	Part B: Placebo to Dupilumab Low Dose	Part B: Placebo to Dupilumab High Dose	Part B: Dupilumab Low Dose to Dupilumab Low Dose	Part B: Dupilumab High Dose to Dupilumab High Dose
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	8	12	16	21
Units: NES				
number (not applicable)	-2.715	-2.615	-2.625	-2.670

Statistical analyses

No statistical analyses for this end point

Secondary: Part B: Change From Baseline in Body Weight for Age Percentile at Week 52

End point title	Part B: Change From Baseline in Body Weight for Age Percentile at Week 52

End point description:

Body weight for age percentile was calculated based on the growth charts from the Centers for Disease Control and Prevention (CDC) for ages 0 to 20 years (for ages 2 to <12 years) and World Health Organization (WHO) growth charts for ages 0 to <2 years (for ages 1 to <2 years). These charts included a set of smoothed percentiles along with CDC LMS (Lambda-Mu-Sigma) parameters to allow the calculation of percentiles.

End point type	Secondary

End point timeframe:

Baseline, Week 52

End point values	Part B: Placebo to Dupilumab Low Dose	Part B: Placebo to Dupilumab High Dose	Part B: Dupilumab Low Dose to Dupilumab Low Dose	Part B: Dupilumab High Dose to Dupilumab High Dose
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	14	16	29	35
Units: Percentile				
arithmetic mean (standard deviation)	-0.02 (± 13.893)	5.48 (± 12.644)	4.75 (± 11.968)	5.96 (± 11.519)

Statistical analyses

No statistical analyses for this end point

Secondary: Part B: Change from Baseline in Body Mass Index (BMI) for Age Z-score for Participants ≥2 Years of Age at Week 52

End point title	Part B: Change from Baseline in Body Mass Index (BMI) for Age Z-score for Participants ≥2 Years of Age at Week 52

End point description:

BMI for age z-score indicates how much higher or lower a participant's BMI for age is relative to a reference growth chart (based on the growth charts from Centers for Disease Control and Prevention [CDC] for ages 0 to 20 years [for ages 2 to <12 years]). An increase in the mean change in BMI for age z-score (ie, increase in the standard deviation [SD] from the reference growth chart) indicates an increase in BMI for age relative to the reference.

End point type	Secondary

End point timeframe:

Baseline, Week 52

End point values	Part B: Placebo to Dupilumab Low Dose	Part B: Placebo to Dupilumab High Dose	Part B: Dupilumab Low Dose to Dupilumab Low Dose	Part B: Dupilumab High Dose to Dupilumab High Dose
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	14	15	27	32
Units: z-score				
arithmetic mean (standard deviation)	-0.0206 (± 0.54625)	0.0687 (± 0.47605)	-0.0549 (± 0.88582)	0.0987 (± 0.72329)

Statistical analyses

No statistical analyses for this end point

Secondary: Part B: Change From Baseline in Weight for Age Z-score at Week 52

End point title	Part B: Change From Baseline in Weight for Age Z-score at Week 52

End point description:

Weight for age z-score indicates how much higher or lower a participant's weight for age is relative to a reference growth chart (based on the growth charts from CDC for ages 0 to 20 years [for ages 2 to <12 years] and World Health Organization (WHO) growth charts for ages 0 to <2 years [for ages 1 to <2 years]). An increase in the mean change in weight for age z-score (increase in the SD from the reference growth chart) indicates an increase in weight for age relative to the reference.

End point type	Secondary

End point timeframe:

Baseline, Week 52

End point values	Part B: Placebo to Dupilumab Low Dose	Part B: Placebo to Dupilumab High Dose	Part B: Dupilumab Low Dose to Dupilumab Low Dose	Part B: Dupilumab High Dose to Dupilumab High Dose
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	14	16	29	35
Units: z-score				
arithmetic mean (standard deviation)	0.0640 (± 0.46264)	0.2016 (± 0.39446)	0.1445 (± 0.40310)	0.2049 (± 0.40305)

Statistical analyses

No statistical analyses for this end point

Secondary: Part B: Change From Baseline in Body Weight From Height Z-score at Week 52

End point title	Part B: Change From Baseline in Body Weight From Height Z-score at Week 52

End point description:

Weight for height z-score indicates how much higher or lower a participant's weight for height is relative to a reference growth chart (based on the growth charts from CDC for ages 0 to 20 years [for ages 2 to <12 years] and WHO growth charts for ages 0 to <2 years [for ages 1 to <2 years]). An increase in the mean change in weight for height z-score (increase in the SD from the reference growth chart) indicates an increase in weight for height relative to the reference.

End point type	Secondary

End point timeframe:

Baseline, Week 52

End point values	Part B: Placebo to Dupilumab Low Dose	Part B: Placebo to Dupilumab High Dose	Part B: Dupilumab Low Dose to Dupilumab Low Dose	Part B: Dupilumab High Dose to Dupilumab High Dose
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	2	3	9	12
Units: z-score				
arithmetic mean (standard deviation)	0.0962 (± 0.48902)	-0.0100 (± 0.51706)	-0.2700 (± 1.04895)	-0.0151 (± 0.67968)

Statistical analyses

No statistical analyses for this end point

Secondary: Part B: Concentration of Functional Dupilumab in Serum at Week 32 and 52

End point title	Part B: Concentration of Functional Dupilumab in Serum at Week 32 and 52

End point description:

Concentration of functional dupilumab in serum at Week 32 and 52 was reported in this outcome measure.

End point type	Secondary

End point timeframe:

Week 32 and 52

End point values	Part B: Placebo to Dupilumab Low Dose	Part B: Placebo to Dupilumab High Dose	Part B: Dupilumab Low Dose to Dupilumab Low Dose	Part B: Dupilumab High Dose to Dupilumab High Dose
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	14	18	29	37
Units: mg/L				
arithmetic mean (standard deviation)				
Week 32	105 (± 49.8)	142 (± 48.5)	99.0 (± 42.8)	186 (± 59.5)
Week 52	101 (± 44.3)	149 (± 59.1)	83.0 (± 33.2)	179 (± 75.3)

Statistical analyses

No statistical analyses for this end point

Secondary: Part A: Number of Participants With Treatment-Emergent Adverse Events (TEAEs), Serious TEAEs, Adverse Events of Special Interest (AESIs) and TEAEs Leading to Permanent Discontinuation of Study Drug

End point title	Part A: Number of Participants With Treatment-Emergent Adverse Events (TEAEs), Serious TEAEs, Adverse Events of Special Interest (AESIs) and TEAEs Leading to Permanent

	Discontinuation of Study Drug

End point description:

An adverse event (AE) was defined as any untoward medical occurrence in a participant or clinical investigation patient administered with a pharmaceutical product and which does not necessarily have to have a causal relationship with this treatment. A serious AE was any untoward medical occurrence that at any dose resulted in death, life-threatening, initial or prolonged inpatient hospitalization, persistent or significant disability/incapacity, congenital anomaly/birth defect, or a medically important event. The term TEAE is defined as AEs starting or worsening after the first intake of the study drug. TEAEs include both Serious TEAEs and non-serious TEAEs. An AESI was defined as one of scientific and medical concern specific to the Sponsor's product or program, for which ongoing monitoring and rapid communication by the Investigator to the Sponsor was appropriate.

End point type	Secondary

End point timeframe:

From Baseline up to Week 16 in Part A

End point values	Part A: Pooled Placebo	Part A: Dupilumab Low Dose	Part A: Dupilumab High Dose	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	34	30	37	
Units: Participants				
Participants with any TEAE	31	26	27	
Participants with any Serious TEAE	0	1	2	
Participants with any AESI	1	1	2	
Any TEAE leading to discontinuation of study drug	2	0	0	

Statistical analyses

No statistical analyses for this end point

Secondary: Part B: Number of Participants With Treatment-Emergent Adverse Events (TEAEs), Serious TEAEs, Adverse Events of Special Interest (AESIs) and TEAEs Leading to Permanent Discontinuation of Study Drug

End point title	Part B: Number of Participants With Treatment-Emergent Adverse Events (TEAEs), Serious TEAEs, Adverse Events of Special Interest (AESIs) and TEAEs Leading to Permanent Discontinuation of Study Drug

End point description:

An AE was defined as any untoward medical occurrence in a participant or clinical investigation patient administered with a pharmaceutical product and which does not necessarily have to have a causal relationship with this treatment. A serious AE was any untoward medical occurrence that at any dose resulted in death, life-threatening, initial or prolonged inpatient hospitalization, persistent or significant disability/incapacity, congenital anomaly/birth defect, or a medically important event. The term TEAE is defined as AEs starting or worsening after the first intake of the study drug. TEAEs include both Serious TEAEs and non-serious TEAEs. An AESI was defined as one of scientific and medical concern specific to the Sponsor's product or program, for which ongoing monitoring and rapid communication by the Investigator to the Sponsor was appropriate.

End point type	Secondary

End point timeframe:

From Week 16 up to Week 52 in Part B

End point values	Part B: Placebo to Dupilumab Low Dose	Part B: Placebo to Dupilumab High Dose	Part B: Dupilumab Low Dose to Dupilumab Low Dose	Part B: Dupilumab High Dose to Dupilumab High Dose
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	14	18	29	37
Units: Participants				
Participants with any TEAE	14	15	28	34
Participants with any Serious TEAE	1	0	3	2
Participants with any AESI	0	1	3	4
Any TEAE leading to discontinuation of study drug	0	0	0	1

Statistical analyses

No statistical analyses for this end point

Secondary: Part A: Number of Participants With Positive Treatment-emergent Antidrug Antibodies (ADA) Response

End point title	Part A: Number of Participants With Positive Treatment-emergent Antidrug Antibodies (ADA) Response

End point description:

Treatment-emergent ADA was defined as a negative result or missing result at baseline with at least one positive post baseline result in the ADA assay. Samples positive in the dupilumab ADA assay were characterized for ADA titers (low, moderate and high). The low treatment-emergent ADA titer as defined as titer level <1000, moderate as 1000 to 10000 and high as >10000.

End point type	Secondary

End point timeframe:

From Baseline up to Week 16 in Part A

End point values	Part A: Pooled Placebo	Part A: Dupilumab Low Dose	Part A: Dupilumab High Dose	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	25	26	31	
Units: Participants	1	0	1	

Statistical analyses

No statistical analyses for this end point

Secondary: Part A: Number of Participants With Positive Treatment-emergent Antidrug Antibodies (ADA) by Maximum Titer Category

End point title	Part A: Number of Participants With Positive Treatment-emergent Antidrug Antibodies (ADA) by Maximum Titer Category

End point description:

Treatment-emergent ADA was defined as a negative result or missing result at baseline with at least one positive post baseline result in the ADA assay. Samples positive in the dupilumab ADA assay were characterized for ADA titers (low, moderate and high). The low treatment-emergent ADA titer as defined as titer level <1000, moderate as 1000 to 10000 and high as >10000.

End point type	Secondary

End point timeframe:

From Baseline up to Week 16 in Part A

End point values	Part A: Pooled Placebo	Part A: Dupilumab Low Dose	Part A: Dupilumab High Dose	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	1	0[20]	1	
Units: Participants				
Treatment-emergent ADA Titer: Low	1		1	
Treatment-emergent ADA Titer: Moderate	0		0	
Treatment-emergent ADA Titer: High	0		0	

Notes:

[20] - Number of participants analyzed of 0 = none had positive TE ADA response to measure titer level.

Statistical analyses

No statistical analyses for this end point

Secondary: Part B: Number of Participants With Positive Treatment-emergent Antidrug Antibodies (ADA) Response and Titer

End point title	Part B: Number of Participants With Positive Treatment-emergent Antidrug Antibodies (ADA) Response and Titer

End point description:

Treatment-emergent ADA was defined as a negative result or missing result at baseline with at least one positive post baseline result in the ADA assay. Samples positive in the dupilumab ADA assay were characterized for ADA titers (low, moderate and high). The low treatment-emergent ADA titer as defined as titer level <1000, moderate as 1000 to 10000 and high as >10000.

No patient exhibited a treatment-emergent ADA response in Part B and titer was not reported.

End point type	Secondary

End point timeframe:

From Week 16 up to Week 52 in Part B

End point values	Part B: Placebo to Dupilumab Low Dose	Part B: Placebo to Dupilumab High Dose	Part B: Dupilumab Low Dose to Dupilumab Low Dose	Part B: Dupilumab High Dose to Dupilumab High Dose
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	14	18	29	37
Units: Participants	0	0	0	0

Statistical analyses

No statistical analyses for this end point

Secondary: Part C: Percent change in peak esophageal intraepithelial eosinophil count (eos/hpf) from Baseline to Week 160

End point title	Part C: Percent change in peak esophageal intraepithelial eosinophil count (eos/hpf) from Baseline to Week 160

End point description:

End point type	Secondary

End point timeframe:

Baseline to Week 160

End point values	Part C: Dupilumab			
Subject group type	Reporting group			
Number of subjects analysed	0[21]			
Units: Percentage of change				
number (not applicable)				

Notes:

[21] - No data was collected for this endpoint.

Statistical analyses

No statistical analyses for this end point

Secondary: Part C: Percentage of participants achieving peak esophageal intraepithelial eosinophil count of <15 eos/hpf At Week 160

End point title	Part C: Percentage of participants achieving peak esophageal intraepithelial eosinophil count of <15 eos/hpf At Week 160

End point description:

End point type	Secondary

End point timeframe:

At Week 160

End point values	Part C: Dupilumab			
Subject group type	Reporting group			
Number of subjects analysed	0[22]			
Units: Percentage				
number (not applicable)				

Notes:

[22] - No data was collected for this endpoint.

Statistical analyses

No statistical analyses for this end point

Secondary: Part C: Percentage of participants achieving peak esophageal intraepithelial eosinophil count of <15 eos/hpf At Week 100

End point title	Part C: Percentage of participants achieving peak esophageal intraepithelial eosinophil count of <15 eos/hpf At Week 100

End point description:

End point type	Secondary

End point timeframe:

At Week 100

End point values	Part C: Dupilumab			
Subject group type	Reporting group			
Number of subjects analysed	41			
Units: Percentage of participants				
number (not applicable)	92.7			

Statistical analyses

No statistical analyses for this end point

Secondary: Part C: Percentage of participants achieving peak esophageal intraepithelial eosinophil count of ≤6 eos/hpf (400×) At Week 100

End point title	Part C: Percentage of participants achieving peak esophageal intraepithelial eosinophil count of ≤6 eos/hpf (400×) At Week 100

End point description:

End point type	Secondary

End point timeframe:

At Week 100

End point values	Part C: Dupilumab			
Subject group type	Reporting group			
Number of subjects analysed	41			
Units: Percentage of participants				
number (not applicable)	70.7			

Statistical analyses

No statistical analyses for this end point

Secondary: Part C: Percentage of participants achieving peak esophageal intraepithelial eosinophil count of ≤6 eos/hpf (400×) at Week 160

End point title	Part C: Percentage of participants achieving peak esophageal intraepithelial eosinophil count of ≤6 eos/hpf (400×) at Week 160

End point description:

End point type	Secondary

End point timeframe:

At Week 160

End point values	Part C: Dupilumab			
Subject group type	Reporting group			
Number of subjects analysed	0[23]			
Units: Percentage of participants				
number (not applicable)				

Notes:

[23] - No data was collected for this endpoint

Statistical analyses

No statistical analyses for this end point

Secondary: Part C: Absolute change in mean EoE-HSS from Baseline to Week 100

End point title	Part C: Absolute change in mean EoE-HSS from Baseline to Week 100

End point description:

End point type	Secondary

End point timeframe:

Baseline to Week 100

End point values	Part C: Dupilumab			
Subject group type	Reporting group			
Number of subjects analysed	61			
Units: Score on a scale				
arithmetic mean (standard deviation)				
EoE-HSS Grade Score	1.213 (± 0.3720)			
EoE-HSS Stage Score	1.232 (± 0.3526)			

Statistical analyses

No statistical analyses for this end point

Secondary: Part C: Percent change in peak esophageal intraepithelial eosinophil count (eos/hpf) from Baseline to Week 100

End point title	Part C: Percent change in peak esophageal intraepithelial eosinophil count (eos/hpf) from Baseline to Week 100

End point description:

End point type	Secondary

End point timeframe:

Baseline to Week 100

End point values	Part C: Dupilumab			
Subject group type	Reporting group			
Number of subjects analysed	41			
Units: Percentage of change				
arithmetic mean (standard deviation)	-91.50 (± 13.348)			

Statistical analyses

No statistical analyses for this end point

Secondary: Part C: Absolute change in mean EoE-HSS from Baseline to Week 160

End point title	Part C: Absolute change in mean EoE-HSS from Baseline to Week 160

End point description:

End point type	Secondary

End point timeframe:

Baseline to Week 160

End point values	Part C: Dupilumab			
Subject group type	Reporting group			
Number of subjects analysed	0[24]			
Units: Score on a scale				
arithmetic mean (standard deviation)	()			

Notes:

[24] - No data was collected for this endpoint.

Statistical analyses

No statistical analyses for this end point

Secondary: Part C: NES for the relative change in the type 2 inflammation transcriptome signature Baseline to Week 100

End point title	Part C: NES for the relative change in the type 2 inflammation transcriptome signature Baseline to Week 100

End point description:

End point type	Secondary

End point timeframe:

Baseline to Week 100

End point values	Part C: Dupilumab			
Subject group type	Reporting group			
Number of subjects analysed	39			
Units: Score on a scale				
number (not applicable)	-1.970			

Statistical analyses

No statistical analyses for this end point

Secondary: Part C: NES for the relative change in the EDP transcriptome signature from Baseline to Week 100

End point title	Part C: NES for the relative change in the EDP transcriptome signature from Baseline to Week 100

End point description:

A Normalized Enrichment Score (NES) is a way to generate a single numerical value to represent a complex gene expression signature. Changes in NES score represented the overall changes in the

expression of that molecular phenotype. The NESs calculated for the EDP reflect the expression at Week 16 relative to Baseline of a gene set that is differentially expressed between esophageal biopsies from EoE participants compared to healthy controls as a way to evaluate normalization of the molecular pathology. For each subject, an NES of 0 indicates no change from baseline, a negative score shows a reduction in disease score (more like normal) and positive score shows worsening (more active disease). NES does not have minimum/maximum score.

End point type	Secondary

End point timeframe:

Baseline to Week 100

End point values	Part C: Dupilumab			
Subject group type	Reporting group			
Number of subjects analysed	39			
Units: Score on a scale				
median (inter-quartile range (Q1-Q3))	-2.720 (-2.800 to -2.510)			

Statistical analyses

No statistical analyses for this end point

Secondary: Part C: Absolute change in EoE-EREFS from Baseline to Week 160

End point title	Part C: Absolute change in EoE-EREFS from Baseline to Week 160

End point description:

End point type	Secondary

End point timeframe:

Baseline to Week 160

End point values	Part C: Dupilumab			
Subject group type	Reporting group			
Number of subjects analysed	0[25]			
Units: Score on a scale				
arithmetic mean (standard deviation)	()			

Notes:

[25] - No data was collected for this endpoint.

Statistical analyses

No statistical analyses for this end point

Secondary: Part C: Absolute change in EoE-EREFS from Baseline to Week 100

End point title	Part C: Absolute change in EoE-EREFS from Baseline to Week

	100

End point description:

End point type	Secondary

End point timeframe:

Baseline to Week 100

End point values	Part C: Dupilumab			
Subject group type	Reporting group			
Number of subjects analysed	32			
Units: Score on a scale				
arithmetic mean (standard deviation)	-5.34 (± 2.535)			

Statistical analyses

No statistical analyses for this end point

Secondary: Part C: NES for the relative change in the EDP transcriptome signature from Baseline to Week 160

End point title	Part C: NES for the relative change in the EDP transcriptome signature from Baseline to Week 160

End point description:

End point type	Secondary

End point timeframe:

Baseline to Week 160

End point values	Part C: Dupilumab			
Subject group type	Reporting group			
Number of subjects analysed	0[26]			
Units: Score on a scale				
number (not applicable)				

Notes:

[26] - No data collected for this endpoint

Statistical analyses

No statistical analyses for this end point

Secondary: Part C: Change in total score as measured by the PEESSv2.0- caregiver version questionnaire from Baseline to Week 160

End point title	Part C: Change in total score as measured by the PEESSv2.0-

	caregiver version questionnaire from Baseline to Week 160

End point description:

End point type	Secondary

End point timeframe:

Baseline to Week 160

End point values	Part C: Dupilumab			
Subject group type	Reporting group			
Number of subjects analysed	0[27]			
Units: Score on a scale				
number (not applicable)				

Notes:

[27] - No data was collected for this endpoint.

Statistical analyses

No statistical analyses for this end point

Secondary: Part C: Incidence of TEAEs Up to Week 160

End point title	Part C: Incidence of TEAEs Up to Week 160

End point description:

End point type	Secondary

End point timeframe:

Up to Week 160

End point values	Part C: Dupilumab			
Subject group type	Reporting group			
Number of subjects analysed	61			
Units: Events				
number (not applicable)	86.9			

Statistical analyses

No statistical analyses for this end point

Secondary: Part C: Percentage of participants (with food elimination diet regimens at baseline) that have a re-introduction of a previously eliminated food group from Baseline by Week 100

End point title	Part C: Percentage of participants (with food elimination diet regimens at baseline) that have a re-introduction of a

	previously eliminated food group from Baseline by Week 100

End point description:

End point type	Secondary

End point timeframe:

Baseline by Week 100

End point values	Part C: Dupilumab			
Subject group type	Reporting group			
Number of subjects analysed	61			
Units: Percentage of participants				
number (not applicable)	14.8			

Statistical analyses

No statistical analyses for this end point

Secondary: Part C: Change in body weight for age percentile from Baseline up to Week 160

End point title	Part C: Change in body weight for age percentile from Baseline up to Week 160

End point description:

End point type	Secondary

End point timeframe:

Baseline up to Week 160

End point values	Part C: Dupilumab			
Subject group type	Reporting group			
Number of subjects analysed	0[28]			
Units: kilograms (kg)				
number (not applicable)				

Notes:

[28] - No data was collected for this endpoint

Statistical analyses

No statistical analyses for this end point

Secondary: Part C: Percentage of participants (with food elimination diet regimens at baseline) that have a re-introduction of a previously eliminated food group from Baseline by Week 160

End point title	Part C: Percentage of participants (with food elimination diet regimens at baseline) that have a re-introduction of a previously eliminated food group from Baseline by Week 160

End point description:

End point type	Secondary

End point timeframe:

Baseline by Week 160

End point values	Part C: Dupilumab			
Subject group type	Reporting group			
Number of subjects analysed	0[29]			
Units: Percentage of participants				
number (not applicable)				

Notes:

[29] - No data was collected for this endpoint

Statistical analyses

No statistical analyses for this end point

Secondary: Part C: NES for the relative change in the type 2 inflammation transcriptome signature from Baseline to Week 160

End point title	Part C: NES for the relative change in the type 2 inflammation transcriptome signature from Baseline to Week 160

End point description:

End point type	Secondary

End point timeframe:

Baseline to Week 160

End point values	Part C: Dupilumab			
Subject group type	Reporting group			
Number of subjects analysed	0[30]			
Units: Score on a scale				
number (not applicable)				

Notes:

[30] - No data was collected for this endpoint

Statistical analyses

No statistical analyses for this end point

Secondary: Part C: Change in weight for height z-score from Baseline up to Week 160

End point title	Part C: Change in weight for height z-score from Baseline up to Week 160

End point description:

End point type	Secondary

End point timeframe:

Baseline up to Week 160

End point values	Part C: Dupilumab			
Subject group type	Reporting group			
Number of subjects analysed	0[31]			
Units: z-score				
arithmetic mean (standard deviation)	()			

Notes:

[31] - No data was collected for this endpoint

Statistical analyses

No statistical analyses for this end point

Secondary: Part C: Change in body mass index for age z-score from Baseline to up to Week 160

End point title	Part C: Change in body mass index for age z-score from Baseline to up to Week 160

End point description:

End point type	Secondary

End point timeframe:

Baseline to up to Week 160

End point values	Part C: Dupilumab			
Subject group type	Reporting group			
Number of subjects analysed	0[32]			
Units: z-score				
arithmetic mean (standard deviation)	()			

Notes:

[32] - No data was collected for this endpoint

Statistical analyses

No statistical analyses for this end point

Secondary: Part C: Change in weight for age z-score from Baseline up to Week 160

End point title	Part C: Change in weight for age z-score from Baseline up to Week 160

End point description:

End point type	Secondary

End point timeframe:

Baseline up to Week 160

End point values	Part C: Dupilumab			
Subject group type	Reporting group			
Number of subjects analysed	0[33]			
Units: z-score				
arithmetic mean (standard deviation)	()			

Notes:

[33] - No data was collected for this endpoint

Statistical analyses

No statistical analyses for this end point

Secondary: Part C: Incidence of treatment-emergent SAEs Up to Week 160

End point title	Part C: Incidence of treatment-emergent SAEs Up to Week 160

End point description:

End point type	Secondary

End point timeframe:

Up to Week 160

End point values	Part C: Dupilumab			
Subject group type	Reporting group			
Number of subjects analysed	61			
Units: Events				
number (not applicable)	4.9			

Statistical analyses

No statistical analyses for this end point

Secondary: Part C: Incidence of treatment-emergent AESIs Up to Week 160

End point title	Part C: Incidence of treatment-emergent AESIs Up to Week 160

End point description:

End point type	Secondary

End point timeframe:
Up to Week 160

End point values	Part C: Dupilumab			
Subject group type	Reporting group			
Number of subjects analysed	61			
Units: Events				
number (not applicable)	9.8			

Statistical analyses

No statistical analyses for this end point

Secondary: Part C: Concentration of functional dupilumab in serum up to Week 160

End point title	Part C: Concentration of functional dupilumab in serum up to Week 160

End point description:

End point type	Secondary

End point timeframe:
Baseline to end of study, Up to Week 160

End point values	Part A: Pooled Placebo	Part A: Dupilumab Low Dose	Part A: Dupilumab High Dose	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	0[34]	0[35]	0[36]	
Units: mg/L				
arithmetic mean (standard deviation)	()	()	()	

Notes:
[34] - No data was collected for this endpoint
[35] - No data was collected for this endpoint
[36] - No data was collected for this endpoint

Statistical analyses

No statistical analyses for this end point

Secondary: Part C: Incidence of TEAEs leading to permanent discontinuation of study treatment Up to Week 160

End point title	Part C: Incidence of TEAEs leading to permanent discontinuation of study treatment Up to Week 160

End point description:

End point type	Secondary

End point timeframe:

Up to Week 160

End point values	Part C: Dupilumab			
Subject group type	Reporting group			
Number of subjects analysed	61			
Units: Events				
number (not applicable)	0			

Statistical analyses

No statistical analyses for this end point

Secondary: Part C: Number of Participants with treatment-emergent ADA responses and titer Up to Week 160

End point title	Part C: Number of Participants with treatment-emergent ADA responses and titer Up to Week 160

End point description:

Anti-Drug Antibody Analysis Set (AAS): The Part C AAS included all participants who received any amount of study drug in Part C and had at least 1 non-missing ADA result following the first dose of study drug. Analysis was based on treatment received.

End point type	Secondary

End point timeframe:

Up to Week 160

End point values	Part C: Dupilumab			
Subject group type	Subject analysis set			
Number of subjects analysed	39			
Units: Participants				
number (not applicable)	0			

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

From signing of the informed consent through week 160 + 12 week follow-up

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	27.0

Reporting groups

Reporting group title	Part A: Pooled Placebo

Reporting group description:

Participants who received subcutaneous (SC) injection of placebo matched to higher exposure dupilumab or lower exposure dupilumab in Part A. Lower exposure dupilumab regimen were exposures approximating those in adolescents and adults receiving 300 mg dupilumab Q2W). Higher exposure dupilumab regimen were exposures approximating those in adolescents and adults receiving 300 mg dupilumab QW.

Reporting group title	Part A: Dupilumab High Dose

Reporting group description:

Participants received subcutaneous (SC) injection of higher exposure dupilumab in Part A. Higher exposure dupilumab regimen were exposures approximating those in adolescents and adults receiving 300 mg dupilumab QW

Reporting group title	Part C: Dupilumab

Reporting group description:

Participants who completed Part A or B were eligible to enroll in Part C and receive Dupilumab extended active treatment

Reporting group title	Part B: Placebo to Dupilumab High Dose

Reporting group description:

Participants who received subcutaneous (SC) injection of placebo in Part A and received higher exposure dupilumab in Part B. Higher exposure dupilumab regimen were exposures approximating those in adolescents and adults receiving 300 mg dupilumab QW

Reporting group title	Part B: Dupilumab Low Dose to Dupilumab Low Dose

Reporting group description:

Participants received subcutaneous (SC) injection of lower exposure dupilumab in Parts A and B. Lower exposure dupilumab regimen were exposures approximating those in adolescents and adults receiving 300 mg dupilumab Q2W

Reporting group title	Part B: Dupilumab High Dose to Dupilumab High Dose

Reporting group description:

Participants received subcutaneous (SC) injection of higher exposure dupilumab in Parts A and B. Higher exposure dupilumab regimen were exposures approximating those in adolescents and adults receiving 300 mg dupilumab QW.

Reporting group title	Part A: Dupilumab Low Dose

Reporting group description:

Participants received subcutaneous (SC) injection of lower exposure dupilumab in Part A. Lower exposure dupilumab regimen were exposures approximating those in adolescents and adults receiving 300 mg dupilumab Q2W

Reporting group title	Part B: Placebo to Dupilumab Low Dose

Reporting group description:

Participants who received subcutaneous (SC) injection of placebo in Part A and received lower exposure dupilumab in Part B. Lower exposure dupilumab regimen were exposures approximating those in adolescents and adults receiving 300 mg dupilumab Q2W

Serious adverse events	Part A: Pooled Placebo	Part A: Dupilumab High Dose	Part C: Dupilumab
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 34 (0.00%)	2 / 37 (5.41%)	3 / 61 (4.92%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events			
Investigations			
Endoscopy gastrointestinal			
subjects affected / exposed	0 / 34 (0.00%)	0 / 37 (0.00%)	1 / 61 (1.64%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Injury, poisoning and procedural complications			
Procedural pain			
subjects affected / exposed	0 / 34 (0.00%)	1 / 37 (2.70%)	0 / 61 (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
Post procedural haemorrhage			
subjects affected / exposed	0 / 34 (0.00%)	0 / 37 (0.00%)	0 / 61 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac disorders			
Cardiac arrest			
subjects affected / exposed	0 / 34 (0.00%)	0 / 37 (0.00%)	1 / 61 (1.64%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Blood and lymphatic system disorders			
Leukocytosis			
subjects affected / exposed	0 / 34 (0.00%)	0 / 37 (0.00%)	0 / 61 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
General disorders and administration site conditions			
Pyrexia			
subjects affected / exposed	0 / 34 (0.00%)	0 / 37 (0.00%)	0 / 61 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal disorders			

Oesophageal food impaction			
subjects affected / exposed	0 / 34 (0.00%)	0 / 37 (0.00%)	1 / 61 (1.64%)
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			
Sleep apnoea syndrome			
subjects affected / exposed	0 / 34 (0.00%)	0 / 37 (0.00%)	0 / 61 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Throat tightness			
subjects affected / exposed	0 / 34 (0.00%)	0 / 37 (0.00%)	0 / 61 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Obstructive sleep apnoea syndrome			
subjects affected / exposed	0 / 34 (0.00%)	1 / 37 (2.70%)	0 / 61 (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
Asthma			
subjects affected / exposed	0 / 34 (0.00%)	0 / 37 (0.00%)	0 / 61 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Renal and urinary disorders			
Nephrolithiasis			
subjects affected / exposed	0 / 34 (0.00%)	1 / 37 (2.70%)	0 / 61 (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
Infections and infestations			
HCoV-OC43 infection			
subjects affected / exposed	0 / 34 (0.00%)	0 / 37 (0.00%)	0 / 61 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Perirectal abscess			

subjects affected / exposed	0 / 34 (0.00%)	0 / 37 (0.00%)	1 / 61 (1.64%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Serious adverse events	Part B: Placebo to Dupilumab High Dose	Part B: Dupilumab Low Dose to Dupilumab Low Dose	Part B: Dupilumab High Dose to Dupilumab High Dose
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 18 (0.00%)	2 / 29 (6.90%)	2 / 37 (5.41%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events			
Investigations			
Endoscopy gastrointestinal			
subjects affected / exposed	0 / 18 (0.00%)	0 / 29 (0.00%)	0 / 37 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Injury, poisoning and procedural complications			
Procedural pain			
subjects affected / exposed	0 / 18 (0.00%)	0 / 29 (0.00%)	0 / 37 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Post procedural haemorrhage			
subjects affected / exposed	0 / 18 (0.00%)	0 / 29 (0.00%)	1 / 37 (2.70%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac disorders			
Cardiac arrest			
subjects affected / exposed	0 / 18 (0.00%)	0 / 29 (0.00%)	0 / 37 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Blood and lymphatic system disorders			
Leukocytosis			
subjects affected / exposed	0 / 18 (0.00%)	0 / 29 (0.00%)	0 / 37 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
General disorders and administration site conditions			

Pyrexia			
subjects affected / exposed	0 / 18 (0.00%)	0 / 29 (0.00%)	0 / 37 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal disorders			
Oesophageal food impaction			
subjects affected / exposed	0 / 18 (0.00%)	0 / 29 (0.00%)	0 / 37 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory, thoracic and mediastinal disorders			
Sleep apnoea syndrome			
subjects affected / exposed	0 / 18 (0.00%)	0 / 29 (0.00%)	1 / 37 (2.70%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Throat tightness			
subjects affected / exposed	0 / 18 (0.00%)	1 / 29 (3.45%)	0 / 37 (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
Obstructive sleep apnoea syndrome			
subjects affected / exposed	0 / 18 (0.00%)	0 / 29 (0.00%)	0 / 37 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Asthma			
subjects affected / exposed	0 / 18 (0.00%)	0 / 29 (0.00%)	1 / 37 (2.70%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Renal and urinary disorders			
Nephrolithiasis			
subjects affected / exposed	0 / 18 (0.00%)	0 / 29 (0.00%)	0 / 37 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infections and infestations			
HCoV-OC43 infection			

subjects affected / exposed	0 / 18 (0.00%)	1 / 29 (3.45%)	0 / 37 (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
Perirectal abscess			
subjects affected / exposed	0 / 18 (0.00%)	0 / 29 (0.00%)	0 / 37 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Serious adverse events	Part A: Dupilumab Low Dose	Part B: Placebo to Dupilumab Low Dose	
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 30 (0.00%)	1 / 14 (7.14%)	
number of deaths (all causes)	0	0	
number of deaths resulting from adverse events			
Investigations			
Endoscopy gastrointestinal			
subjects affected / exposed	0 / 30 (0.00%)	0 / 14 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Injury, poisoning and procedural complications			
Procedural pain			
subjects affected / exposed	0 / 30 (0.00%)	0 / 14 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Post procedural haemorrhage			
subjects affected / exposed	0 / 30 (0.00%)	0 / 14 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac disorders			
Cardiac arrest			
subjects affected / exposed	0 / 30 (0.00%)	0 / 14 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Blood and lymphatic system disorders			
Leukocytosis			

subjects affected / exposed	0 / 30 (0.00%)	1 / 14 (7.14%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
General disorders and administration site conditions			
Pyrexia			
subjects affected / exposed	0 / 30 (0.00%)	1 / 14 (7.14%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal disorders			
Oesophageal food impaction			
subjects affected / exposed	0 / 30 (0.00%)	0 / 14 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory, thoracic and mediastinal disorders			
Sleep apnoea syndrome			
subjects affected / exposed	0 / 30 (0.00%)	0 / 14 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Throat tightness			
subjects affected / exposed	0 / 30 (0.00%)	0 / 14 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Obstructive sleep apnoea syndrome			
subjects affected / exposed	0 / 30 (0.00%)	0 / 14 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Asthma			
subjects affected / exposed	0 / 30 (0.00%)	0 / 14 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Renal and urinary disorders			
Nephrolithiasis			

subjects affected / exposed	0 / 30 (0.00%)	0 / 14 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infections and infestations			
HCoV-OC43 infection			
subjects affected / exposed	0 / 30 (0.00%)	0 / 14 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Perirectal abscess			
subjects affected / exposed	0 / 30 (0.00%)	0 / 14 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

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

Non-serious adverse events	Part A: Pooled Placebo	Part A: Dupilumab High Dose	Part C: Dupilumab
Total subjects affected by non-serious adverse events			
subjects affected / exposed	28 / 34 (82.35%)	26 / 37 (70.27%)	52 / 61 (85.25%)
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Skin papilloma			
subjects affected / exposed	0 / 34 (0.00%)	0 / 37 (0.00%)	0 / 61 (0.00%)
occurrences (all)	0	0	0
Vascular disorders			
Flushing			
subjects affected / exposed	0 / 34 (0.00%)	0 / 37 (0.00%)	1 / 61 (1.64%)
occurrences (all)	0	0	1
General disorders and administration site conditions			
Injection site reaction			
subjects affected / exposed	7 / 34 (20.59%)	4 / 37 (10.81%)	5 / 61 (8.20%)
occurrences (all)	8	11	32
Injection site erythema			
subjects affected / exposed	1 / 34 (2.94%)	4 / 37 (10.81%)	2 / 61 (3.28%)
occurrences (all)	1	8	2
Pyrexia			

subjects affected / exposed	1 / 34 (2.94%)	2 / 37 (5.41%)	11 / 61 (18.03%)
occurrences (all)	1	2	18
Fatigue			
subjects affected / exposed	0 / 34 (0.00%)	2 / 37 (5.41%)	0 / 61 (0.00%)
occurrences (all)	0	2	0
Injection site pain			
subjects affected / exposed	0 / 34 (0.00%)	0 / 37 (0.00%)	3 / 61 (4.92%)
occurrences (all)	0	0	5
Injection site haemorrhage			
subjects affected / exposed	1 / 34 (2.94%)	1 / 37 (2.70%)	1 / 61 (1.64%)
occurrences (all)	1	1	2
Injection site swelling			
subjects affected / exposed	1 / 34 (2.94%)	1 / 37 (2.70%)	0 / 61 (0.00%)
occurrences (all)	1	1	0
Chest pain			
subjects affected / exposed	0 / 34 (0.00%)	0 / 37 (0.00%)	1 / 61 (1.64%)
occurrences (all)	0	0	1
Malaise			
subjects affected / exposed	0 / 34 (0.00%)	0 / 37 (0.00%)	0 / 61 (0.00%)
occurrences (all)	0	0	0
Injection site induration			
subjects affected / exposed	0 / 34 (0.00%)	0 / 37 (0.00%)	0 / 61 (0.00%)
occurrences (all)	0	0	0
Injection site inflammation			
subjects affected / exposed	0 / 34 (0.00%)	1 / 37 (2.70%)	0 / 61 (0.00%)
occurrences (all)	0	1	0
Injection site oedema			
subjects affected / exposed	0 / 34 (0.00%)	1 / 37 (2.70%)	1 / 61 (1.64%)
occurrences (all)	0	4	1
Influenza like illness			
subjects affected / exposed	0 / 34 (0.00%)	0 / 37 (0.00%)	1 / 61 (1.64%)
occurrences (all)	0	0	1
Vessel puncture site pain			
subjects affected / exposed	0 / 34 (0.00%)	0 / 37 (0.00%)	0 / 61 (0.00%)
occurrences (all)	0	0	0
Injection site mass			

subjects affected / exposed	1 / 34 (2.94%)	1 / 37 (2.70%)	2 / 61 (3.28%)
occurrences (all)	1	1	11
Injection site bruising			
subjects affected / exposed	1 / 34 (2.94%)	0 / 37 (0.00%)	1 / 61 (1.64%)
occurrences (all)	1	0	1
Immune system disorders			
Seasonal allergy			
subjects affected / exposed	2 / 34 (5.88%)	0 / 37 (0.00%)	4 / 61 (6.56%)
occurrences (all)	2	0	5
Food allergy			
subjects affected / exposed	0 / 34 (0.00%)	0 / 37 (0.00%)	2 / 61 (3.28%)
occurrences (all)	0	0	2
Immunisation reaction			
subjects affected / exposed	0 / 34 (0.00%)	0 / 37 (0.00%)	0 / 61 (0.00%)
occurrences (all)	0	0	0
Anaphylactic reaction			
subjects affected / exposed	0 / 34 (0.00%)	1 / 37 (2.70%)	1 / 61 (1.64%)
occurrences (all)	0	1	1
Reproductive system and breast disorders			
Genital rash			
subjects affected / exposed	0 / 34 (0.00%)	0 / 37 (0.00%)	0 / 61 (0.00%)
occurrences (all)	0	0	0
Genital pain			
subjects affected / exposed	0 / 34 (0.00%)	0 / 37 (0.00%)	0 / 61 (0.00%)
occurrences (all)	0	0	0
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	2 / 34 (5.88%)	1 / 37 (2.70%)	8 / 61 (13.11%)
occurrences (all)	2	2	11
Rhinitis allergic			
subjects affected / exposed	3 / 34 (8.82%)	1 / 37 (2.70%)	0 / 61 (0.00%)
occurrences (all)	3	1	0
Asthma			
subjects affected / exposed	1 / 34 (2.94%)	0 / 37 (0.00%)	2 / 61 (3.28%)
occurrences (all)	1	0	2
Oropharyngeal pain			

subjects affected / exposed	1 / 34 (2.94%)	0 / 37 (0.00%)	6 / 61 (9.84%)
occurrences (all)	1	0	6
Epistaxis			
subjects affected / exposed	0 / 34 (0.00%)	1 / 37 (2.70%)	3 / 61 (4.92%)
occurrences (all)	0	1	4
Wheezing			
subjects affected / exposed	1 / 34 (2.94%)	0 / 37 (0.00%)	0 / 61 (0.00%)
occurrences (all)	1	0	0
Bronchial hyperreactivity			
subjects affected / exposed	0 / 34 (0.00%)	0 / 37 (0.00%)	0 / 61 (0.00%)
occurrences (all)	0	0	0
Upper-airway cough syndrome			
subjects affected / exposed	1 / 34 (2.94%)	1 / 37 (2.70%)	2 / 61 (3.28%)
occurrences (all)	1	1	2
Laryngospasm			
subjects affected / exposed	0 / 34 (0.00%)	1 / 37 (2.70%)	0 / 61 (0.00%)
occurrences (all)	0	1	0
Nasal congestion			
subjects affected / exposed	0 / 34 (0.00%)	0 / 37 (0.00%)	1 / 61 (1.64%)
occurrences (all)	0	0	1
Oropharyngeal cobble stone mucosa			
subjects affected / exposed	0 / 34 (0.00%)	0 / 37 (0.00%)	1 / 61 (1.64%)
occurrences (all)	0	0	1
Rhinorrhoea			
subjects affected / exposed	0 / 34 (0.00%)	0 / 37 (0.00%)	3 / 61 (4.92%)
occurrences (all)	0	0	4
Productive cough			
subjects affected / exposed	0 / 34 (0.00%)	0 / 37 (0.00%)	1 / 61 (1.64%)
occurrences (all)	0	0	1
Throat irritation			
subjects affected / exposed	0 / 34 (0.00%)	0 / 37 (0.00%)	1 / 61 (1.64%)
occurrences (all)	0	0	1
Throat tightness			
subjects affected / exposed	0 / 34 (0.00%)	0 / 37 (0.00%)	1 / 61 (1.64%)
occurrences (all)	0	0	1
Psychiatric disorders			

Fear of injection			
subjects affected / exposed	2 / 34 (5.88%)	0 / 37 (0.00%)	0 / 61 (0.00%)
occurrences (all)	9	0	0
Insomnia			
subjects affected / exposed	2 / 34 (5.88%)	0 / 37 (0.00%)	0 / 61 (0.00%)
occurrences (all)	2	0	0
Enuresis			
subjects affected / exposed	0 / 34 (0.00%)	0 / 37 (0.00%)	0 / 61 (0.00%)
occurrences (all)	0	0	0
Encopresis			
subjects affected / exposed	0 / 34 (0.00%)	0 / 37 (0.00%)	1 / 61 (1.64%)
occurrences (all)	0	0	1
Attention deficit hyperactivity disorder			
subjects affected / exposed	0 / 34 (0.00%)	0 / 37 (0.00%)	3 / 61 (4.92%)
occurrences (all)	0	0	3
Investigations			
Hepatic enzyme increased			
subjects affected / exposed	0 / 34 (0.00%)	0 / 37 (0.00%)	0 / 61 (0.00%)
occurrences (all)	0	0	0
Blood potassium increased			
subjects affected / exposed	0 / 34 (0.00%)	0 / 37 (0.00%)	0 / 61 (0.00%)
occurrences (all)	0	0	0
Aspartate aminotransferase increased			
subjects affected / exposed	0 / 34 (0.00%)	0 / 37 (0.00%)	0 / 61 (0.00%)
occurrences (all)	0	0	0
Alanine aminotransferase increased			
subjects affected / exposed	0 / 34 (0.00%)	0 / 37 (0.00%)	0 / 61 (0.00%)
occurrences (all)	0	0	0
Neutrophil count decreased			
subjects affected / exposed	0 / 34 (0.00%)	0 / 37 (0.00%)	0 / 61 (0.00%)
occurrences (all)	0	0	0
Blood alkaline phosphatase increased			
subjects affected / exposed	0 / 34 (0.00%)	0 / 37 (0.00%)	1 / 61 (1.64%)
occurrences (all)	0	0	1
Blood parathyroid hormone increased			

subjects affected / exposed	0 / 34 (0.00%)	0 / 37 (0.00%)	1 / 61 (1.64%)
occurrences (all)	0	0	2
Serum ferritin decreased			
subjects affected / exposed	0 / 34 (0.00%)	0 / 37 (0.00%)	1 / 61 (1.64%)
occurrences (all)	0	0	1
Injury, poisoning and procedural complications			
Arthropod bite			
subjects affected / exposed	0 / 34 (0.00%)	1 / 37 (2.70%)	0 / 61 (0.00%)
occurrences (all)	0	2	0
Ligament sprain			
subjects affected / exposed	1 / 34 (2.94%)	0 / 37 (0.00%)	1 / 61 (1.64%)
occurrences (all)	1	0	2
Arthropod sting			
subjects affected / exposed	0 / 34 (0.00%)	1 / 37 (2.70%)	2 / 61 (3.28%)
occurrences (all)	0	1	2
Face injury			
subjects affected / exposed	0 / 34 (0.00%)	0 / 37 (0.00%)	2 / 61 (3.28%)
occurrences (all)	0	0	2
Wrist fracture			
subjects affected / exposed	0 / 34 (0.00%)	1 / 37 (2.70%)	0 / 61 (0.00%)
occurrences (all)	0	1	0
Sunburn			
subjects affected / exposed	0 / 34 (0.00%)	0 / 37 (0.00%)	1 / 61 (1.64%)
occurrences (all)	0	0	1
Gas poisoning			
subjects affected / exposed	0 / 34 (0.00%)	0 / 37 (0.00%)	0 / 61 (0.00%)
occurrences (all)	0	0	0
Nasal injury			
subjects affected / exposed	0 / 34 (0.00%)	0 / 37 (0.00%)	0 / 61 (0.00%)
occurrences (all)	0	0	0
Foot fracture			
subjects affected / exposed	0 / 34 (0.00%)	0 / 37 (0.00%)	1 / 61 (1.64%)
occurrences (all)	0	0	1
Animal bite			

subjects affected / exposed	0 / 34 (0.00%)	0 / 37 (0.00%)	1 / 61 (1.64%)
occurrences (all)	0	0	1
Hand fracture			
subjects affected / exposed	0 / 34 (0.00%)	0 / 37 (0.00%)	1 / 61 (1.64%)
occurrences (all)	0	0	1
Joint injury			
subjects affected / exposed	0 / 34 (0.00%)	0 / 37 (0.00%)	2 / 61 (3.28%)
occurrences (all)	0	0	2
Limb injury			
subjects affected / exposed	0 / 34 (0.00%)	1 / 37 (2.70%)	0 / 61 (0.00%)
occurrences (all)	0	1	0
Ligament rupture			
subjects affected / exposed	1 / 34 (2.94%)	0 / 37 (0.00%)	1 / 61 (1.64%)
occurrences (all)	1	0	1
Nervous system disorders			
Dizziness			
subjects affected / exposed	2 / 34 (5.88%)	1 / 37 (2.70%)	1 / 61 (1.64%)
occurrences (all)	2	1	1
Headache			
subjects affected / exposed	1 / 34 (2.94%)	2 / 37 (5.41%)	6 / 61 (9.84%)
occurrences (all)	1	2	9
Lethargy			
subjects affected / exposed	0 / 34 (0.00%)	0 / 37 (0.00%)	0 / 61 (0.00%)
occurrences (all)	0	0	0
Ear and labyrinth disorders			
Otorrhoea			
subjects affected / exposed	1 / 34 (2.94%)	0 / 37 (0.00%)	0 / 61 (0.00%)
occurrences (all)	1	0	0
Ear pain			
subjects affected / exposed	0 / 34 (0.00%)	0 / 37 (0.00%)	1 / 61 (1.64%)
occurrences (all)	0	0	1
Motion sickness			
subjects affected / exposed	1 / 34 (2.94%)	0 / 37 (0.00%)	3 / 61 (4.92%)
occurrences (all)	5	0	3
Eye disorders			

Eye swelling			
subjects affected / exposed	1 / 34 (2.94%)	0 / 37 (0.00%)	0 / 61 (0.00%)
occurrences (all)	1	0	0
Ocular hyperaemia			
subjects affected / exposed	0 / 34 (0.00%)	0 / 37 (0.00%)	0 / 61 (0.00%)
occurrences (all)	0	0	0
Eye pruritus			
subjects affected / exposed	0 / 34 (0.00%)	0 / 37 (0.00%)	1 / 61 (1.64%)
occurrences (all)	0	0	2
Dry eye			
subjects affected / exposed	0 / 34 (0.00%)	1 / 37 (2.70%)	0 / 61 (0.00%)
occurrences (all)	0	1	0
Conjunctivitis allergic			
subjects affected / exposed	1 / 34 (2.94%)	0 / 37 (0.00%)	0 / 61 (0.00%)
occurrences (all)	1	0	0
Astigmatism			
subjects affected / exposed	0 / 34 (0.00%)	0 / 37 (0.00%)	1 / 61 (1.64%)
occurrences (all)	0	0	1
Gastrointestinal disorders			
Vomiting			
subjects affected / exposed	6 / 34 (17.65%)	3 / 37 (8.11%)	11 / 61 (18.03%)
occurrences (all)	15	7	24
Abdominal pain			
subjects affected / exposed	3 / 34 (8.82%)	1 / 37 (2.70%)	3 / 61 (4.92%)
occurrences (all)	3	1	3
Constipation			
subjects affected / exposed	2 / 34 (5.88%)	2 / 37 (5.41%)	3 / 61 (4.92%)
occurrences (all)	2	2	3
Abdominal pain upper			
subjects affected / exposed	0 / 34 (0.00%)	1 / 37 (2.70%)	2 / 61 (3.28%)
occurrences (all)	0	2	2
Gastrooesophageal reflux disease			
subjects affected / exposed	0 / 34 (0.00%)	0 / 37 (0.00%)	5 / 61 (8.20%)
occurrences (all)	0	0	5
Nausea			

subjects affected / exposed	0 / 34 (0.00%)	2 / 37 (5.41%)	2 / 61 (3.28%)
occurrences (all)	0	3	3
Diarrhoea			
subjects affected / exposed	1 / 34 (2.94%)	2 / 37 (5.41%)	1 / 61 (1.64%)
occurrences (all)	1	2	1
Eosinophilic oesophagitis			
subjects affected / exposed	1 / 34 (2.94%)	0 / 37 (0.00%)	0 / 61 (0.00%)
occurrences (all)	1	0	0
Oral pain			
subjects affected / exposed	1 / 34 (2.94%)	0 / 37 (0.00%)	0 / 61 (0.00%)
occurrences (all)	1	0	0
Oral discomfort			
subjects affected / exposed	0 / 34 (0.00%)	0 / 37 (0.00%)	0 / 61 (0.00%)
occurrences (all)	0	0	0
Dysphagia			
subjects affected / exposed	0 / 34 (0.00%)	0 / 37 (0.00%)	1 / 61 (1.64%)
occurrences (all)	0	0	1
Lip blister			
subjects affected / exposed	0 / 34 (0.00%)	0 / 37 (0.00%)	0 / 61 (0.00%)
occurrences (all)	0	0	0
Dyspepsia			
subjects affected / exposed	0 / 34 (0.00%)	0 / 37 (0.00%)	0 / 61 (0.00%)
occurrences (all)	0	0	0
Abdominal discomfort			
subjects affected / exposed	0 / 34 (0.00%)	0 / 37 (0.00%)	1 / 61 (1.64%)
occurrences (all)	0	0	1
Faeces hard			
subjects affected / exposed	0 / 34 (0.00%)	0 / 37 (0.00%)	1 / 61 (1.64%)
occurrences (all)	0	0	1
Flatulence			
subjects affected / exposed	0 / 34 (0.00%)	0 / 37 (0.00%)	1 / 61 (1.64%)
occurrences (all)	0	0	1
Skin and subcutaneous tissue disorders			
Rash			
subjects affected / exposed	2 / 34 (5.88%)	3 / 37 (8.11%)	5 / 61 (8.20%)
occurrences (all)	2	4	5

Eczema			
subjects affected / exposed	1 / 34 (2.94%)	0 / 37 (0.00%)	3 / 61 (4.92%)
occurrences (all)	2	0	3
Urticaria			
subjects affected / exposed	2 / 34 (5.88%)	1 / 37 (2.70%)	2 / 61 (3.28%)
occurrences (all)	2	3	2
Dry skin			
subjects affected / exposed	2 / 34 (5.88%)	1 / 37 (2.70%)	3 / 61 (4.92%)
occurrences (all)	2	1	3
Rash papular			
subjects affected / exposed	1 / 34 (2.94%)	0 / 37 (0.00%)	0 / 61 (0.00%)
occurrences (all)	1	0	0
Dermatitis			
subjects affected / exposed	0 / 34 (0.00%)	1 / 37 (2.70%)	3 / 61 (4.92%)
occurrences (all)	0	1	3
Hand dermatitis			
subjects affected / exposed	0 / 34 (0.00%)	0 / 37 (0.00%)	0 / 61 (0.00%)
occurrences (all)	0	0	0
Keratosis pilaris			
subjects affected / exposed	0 / 34 (0.00%)	0 / 37 (0.00%)	0 / 61 (0.00%)
occurrences (all)	0	0	0
Perioral dermatitis			
subjects affected / exposed	0 / 34 (0.00%)	0 / 37 (0.00%)	0 / 61 (0.00%)
occurrences (all)	0	0	0
Petechiae			
subjects affected / exposed	0 / 34 (0.00%)	0 / 37 (0.00%)	0 / 61 (0.00%)
occurrences (all)	0	0	0
Pruritus			
subjects affected / exposed	0 / 34 (0.00%)	0 / 37 (0.00%)	2 / 61 (3.28%)
occurrences (all)	0	0	2
Skin lesion			
subjects affected / exposed	0 / 34 (0.00%)	0 / 37 (0.00%)	0 / 61 (0.00%)
occurrences (all)	0	0	0
Rash erythematous			
subjects affected / exposed	0 / 34 (0.00%)	0 / 37 (0.00%)	0 / 61 (0.00%)
occurrences (all)	0	0	0

Erythema			
subjects affected / exposed	0 / 34 (0.00%)	0 / 37 (0.00%)	2 / 61 (3.28%)
occurrences (all)	0	0	2
Macule			
subjects affected / exposed	0 / 34 (0.00%)	0 / 37 (0.00%)	2 / 61 (3.28%)
occurrences (all)	0	0	2
Rash macular			
subjects affected / exposed	0 / 34 (0.00%)	0 / 37 (0.00%)	1 / 61 (1.64%)
occurrences (all)	0	0	1
Acne			
subjects affected / exposed	0 / 34 (0.00%)	0 / 37 (0.00%)	1 / 61 (1.64%)
occurrences (all)	0	0	1
Dermatitis contact			
subjects affected / exposed	0 / 34 (0.00%)	0 / 37 (0.00%)	2 / 61 (3.28%)
occurrences (all)	0	0	2
Musculoskeletal and connective tissue disorders			
Tendon pain			
subjects affected / exposed	0 / 34 (0.00%)	0 / 37 (0.00%)	0 / 61 (0.00%)
occurrences (all)	0	0	0
Musculoskeletal discomfort			
subjects affected / exposed	0 / 34 (0.00%)	0 / 37 (0.00%)	0 / 61 (0.00%)
occurrences (all)	0	0	0
Pain in extremity			
subjects affected / exposed	1 / 34 (2.94%)	0 / 37 (0.00%)	4 / 61 (6.56%)
occurrences (all)	1	0	4
Arthralgia			
subjects affected / exposed	1 / 34 (2.94%)	0 / 37 (0.00%)	2 / 61 (3.28%)
occurrences (all)	1	0	3
Back pain			
subjects affected / exposed	0 / 34 (0.00%)	0 / 37 (0.00%)	3 / 61 (4.92%)
occurrences (all)	0	0	3
Myalgia			
subjects affected / exposed	0 / 34 (0.00%)	0 / 37 (0.00%)	1 / 61 (1.64%)
occurrences (all)	0	0	1
Infections and infestations			

Sinusitis			
subjects affected / exposed	3 / 34 (8.82%)	0 / 37 (0.00%)	1 / 61 (1.64%)
occurrences (all)	3	0	1
Upper respiratory tract infection			
subjects affected / exposed	3 / 34 (8.82%)	0 / 37 (0.00%)	8 / 61 (13.11%)
occurrences (all)	3	0	8
Ear infection			
subjects affected / exposed	2 / 34 (5.88%)	0 / 37 (0.00%)	5 / 61 (8.20%)
occurrences (all)	3	0	5
Molluscum contagiosum			
subjects affected / exposed	2 / 34 (5.88%)	0 / 37 (0.00%)	1 / 61 (1.64%)
occurrences (all)	2	0	1
COVID-19			
subjects affected / exposed	0 / 34 (0.00%)	6 / 37 (16.22%)	5 / 61 (8.20%)
occurrences (all)	0	6	6
Viral upper respiratory tract infection			
subjects affected / exposed	2 / 34 (5.88%)	0 / 37 (0.00%)	3 / 61 (4.92%)
occurrences (all)	2	0	4
Gastroenteritis viral			
subjects affected / exposed	1 / 34 (2.94%)	4 / 37 (10.81%)	5 / 61 (8.20%)
occurrences (all)	1	4	7
Nasopharyngitis			
subjects affected / exposed	2 / 34 (5.88%)	2 / 37 (5.41%)	4 / 61 (6.56%)
occurrences (all)	2	2	4
Respiratory tract infection viral			
subjects affected / exposed	1 / 34 (2.94%)	1 / 37 (2.70%)	2 / 61 (3.28%)
occurrences (all)	2	1	2
Hordeolum			
subjects affected / exposed	1 / 34 (2.94%)	0 / 37 (0.00%)	2 / 61 (3.28%)
occurrences (all)	4	0	3
Beta haemolytic streptococcal infection			
subjects affected / exposed	0 / 34 (0.00%)	0 / 37 (0.00%)	0 / 61 (0.00%)
occurrences (all)	0	0	0
Conjunctivitis			

subjects affected / exposed	0 / 34 (0.00%)	0 / 37 (0.00%)	4 / 61 (6.56%)
occurrences (all)	0	0	5
Croup infectious			
subjects affected / exposed	0 / 34 (0.00%)	1 / 37 (2.70%)	4 / 61 (6.56%)
occurrences (all)	0	1	4
Ear infection viral			
subjects affected / exposed	0 / 34 (0.00%)	0 / 37 (0.00%)	0 / 61 (0.00%)
occurrences (all)	0	0	0
Influenza			
subjects affected / exposed	0 / 34 (0.00%)	1 / 37 (2.70%)	3 / 61 (4.92%)
occurrences (all)	0	1	3
Gastrointestinal viral infection			
subjects affected / exposed	0 / 34 (0.00%)	0 / 37 (0.00%)	1 / 61 (1.64%)
occurrences (all)	0	0	1
Groin infection			
subjects affected / exposed	0 / 34 (0.00%)	0 / 37 (0.00%)	0 / 61 (0.00%)
occurrences (all)	0	0	0
Impetigo			
subjects affected / exposed	0 / 34 (0.00%)	0 / 37 (0.00%)	0 / 61 (0.00%)
occurrences (all)	0	0	0
Eye infection			
subjects affected / exposed	0 / 34 (0.00%)	0 / 37 (0.00%)	0 / 61 (0.00%)
occurrences (all)	0	0	0
Otitis media			
subjects affected / exposed	0 / 34 (0.00%)	0 / 37 (0.00%)	2 / 61 (3.28%)
occurrences (all)	0	0	2
Pharyngitis			
subjects affected / exposed	0 / 34 (0.00%)	0 / 37 (0.00%)	2 / 61 (3.28%)
occurrences (all)	0	0	4
Pharyngitis streptococcal			
subjects affected / exposed	0 / 34 (0.00%)	0 / 37 (0.00%)	13 / 61 (21.31%)
occurrences (all)	0	0	15
Urinary tract infection			
subjects affected / exposed	0 / 34 (0.00%)	0 / 37 (0.00%)	0 / 61 (0.00%)
occurrences (all)	0	0	0
Stoma site infection			

subjects affected / exposed	0 / 34 (0.00%)	0 / 37 (0.00%)	0 / 61 (0.00%)
occurrences (all)	0	0	0
Tonsillitis			
subjects affected / exposed	0 / 34 (0.00%)	0 / 37 (0.00%)	0 / 61 (0.00%)
occurrences (all)	0	0	0
Rhinitis			
subjects affected / exposed	0 / 34 (0.00%)	0 / 37 (0.00%)	1 / 61 (1.64%)
occurrences (all)	0	0	1
Viral infection			
subjects affected / exposed	0 / 34 (0.00%)	0 / 37 (0.00%)	0 / 61 (0.00%)
occurrences (all)	0	0	0
Pneumonia			
subjects affected / exposed	0 / 34 (0.00%)	0 / 37 (0.00%)	1 / 61 (1.64%)
occurrences (all)	0	0	1
Paronychia			
subjects affected / exposed	0 / 34 (0.00%)	0 / 37 (0.00%)	1 / 61 (1.64%)
occurrences (all)	0	0	1
Gastroenteritis			
subjects affected / exposed	0 / 34 (0.00%)	0 / 37 (0.00%)	2 / 61 (3.28%)
occurrences (all)	0	0	2
Cellulitis			
subjects affected / exposed	0 / 34 (0.00%)	0 / 37 (0.00%)	2 / 61 (3.28%)
occurrences (all)	0	0	2
Metabolism and nutrition disorders			
Iron deficiency			
subjects affected / exposed	0 / 34 (0.00%)	0 / 37 (0.00%)	0 / 61 (0.00%)
occurrences (all)	0	0	0
Decreased appetite			
subjects affected / exposed	0 / 34 (0.00%)	0 / 37 (0.00%)	0 / 61 (0.00%)
occurrences (all)	0	0	0

Non-serious adverse events	Part B: Placebo to Dupilumab High Dose	Part B: Dupilumab Low Dose to Dupilumab Low Dose	Part B: Dupilumab High Dose to Dupilumab High Dose
Total subjects affected by non-serious adverse events			
subjects affected / exposed	16 / 18 (88.89%)	27 / 29 (93.10%)	31 / 37 (83.78%)
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			

Skin papilloma			
subjects affected / exposed	1 / 18 (5.56%)	0 / 29 (0.00%)	1 / 37 (2.70%)
occurrences (all)	2	0	1
Vascular disorders			
Flushing			
subjects affected / exposed	0 / 18 (0.00%)	0 / 29 (0.00%)	0 / 37 (0.00%)
occurrences (all)	0	0	0
General disorders and administration site conditions			
Injection site reaction			
subjects affected / exposed	5 / 18 (27.78%)	4 / 29 (13.79%)	5 / 37 (13.51%)
occurrences (all)	21	17	18
Injection site erythema			
subjects affected / exposed	2 / 18 (11.11%)	0 / 29 (0.00%)	0 / 37 (0.00%)
occurrences (all)	2	0	0
Pyrexia			
subjects affected / exposed	2 / 18 (11.11%)	3 / 29 (10.34%)	6 / 37 (16.22%)
occurrences (all)	4	3	7
Fatigue			
subjects affected / exposed	3 / 18 (16.67%)	1 / 29 (3.45%)	0 / 37 (0.00%)
occurrences (all)	3	1	0
Injection site pain			
subjects affected / exposed	1 / 18 (5.56%)	1 / 29 (3.45%)	1 / 37 (2.70%)
occurrences (all)	1	3	1
Injection site haemorrhage			
subjects affected / exposed	0 / 18 (0.00%)	0 / 29 (0.00%)	2 / 37 (5.41%)
occurrences (all)	0	0	2
Injection site swelling			
subjects affected / exposed	0 / 18 (0.00%)	0 / 29 (0.00%)	2 / 37 (5.41%)
occurrences (all)	0	0	2
Chest pain			
subjects affected / exposed	0 / 18 (0.00%)	0 / 29 (0.00%)	3 / 37 (8.11%)
occurrences (all)	0	0	3
Malaise			
subjects affected / exposed	1 / 18 (5.56%)	0 / 29 (0.00%)	1 / 37 (2.70%)
occurrences (all)	1	0	1
Injection site induration			

subjects affected / exposed	1 / 18 (5.56%)	0 / 29 (0.00%)	0 / 37 (0.00%)
occurrences (all)	1	0	0
Injection site inflammation			
subjects affected / exposed	0 / 18 (0.00%)	2 / 29 (6.90%)	1 / 37 (2.70%)
occurrences (all)	0	4	1
Injection site oedema			
subjects affected / exposed	1 / 18 (5.56%)	1 / 29 (3.45%)	1 / 37 (2.70%)
occurrences (all)	1	1	1
Influenza like illness			
subjects affected / exposed	0 / 18 (0.00%)	0 / 29 (0.00%)	0 / 37 (0.00%)
occurrences (all)	0	0	0
Vessel puncture site pain			
subjects affected / exposed	1 / 18 (5.56%)	0 / 29 (0.00%)	0 / 37 (0.00%)
occurrences (all)	1	0	0
Injection site mass			
subjects affected / exposed	0 / 18 (0.00%)	0 / 29 (0.00%)	1 / 37 (2.70%)
occurrences (all)	0	0	2
Injection site bruising			
subjects affected / exposed	0 / 18 (0.00%)	0 / 29 (0.00%)	0 / 37 (0.00%)
occurrences (all)	0	0	0
Immune system disorders			
Seasonal allergy			
subjects affected / exposed	1 / 18 (5.56%)	4 / 29 (13.79%)	2 / 37 (5.41%)
occurrences (all)	1	4	2
Food allergy			
subjects affected / exposed	2 / 18 (11.11%)	0 / 29 (0.00%)	1 / 37 (2.70%)
occurrences (all)	2	0	1
Immunisation reaction			
subjects affected / exposed	1 / 18 (5.56%)	1 / 29 (3.45%)	0 / 37 (0.00%)
occurrences (all)	1	1	0
Anaphylactic reaction			
subjects affected / exposed	0 / 18 (0.00%)	2 / 29 (6.90%)	0 / 37 (0.00%)
occurrences (all)	0	2	0
Reproductive system and breast disorders			

Genital rash			
subjects affected / exposed	0 / 18 (0.00%)	0 / 29 (0.00%)	0 / 37 (0.00%)
occurrences (all)	0	0	0
Genital pain			
subjects affected / exposed	0 / 18 (0.00%)	0 / 29 (0.00%)	0 / 37 (0.00%)
occurrences (all)	0	0	0
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	5 / 18 (27.78%)	4 / 29 (13.79%)	5 / 37 (13.51%)
occurrences (all)	7	4	6
Rhinitis allergic			
subjects affected / exposed	0 / 18 (0.00%)	3 / 29 (10.34%)	2 / 37 (5.41%)
occurrences (all)	0	4	2
Asthma			
subjects affected / exposed	0 / 18 (0.00%)	5 / 29 (17.24%)	3 / 37 (8.11%)
occurrences (all)	0	6	3
Oropharyngeal pain			
subjects affected / exposed	2 / 18 (11.11%)	1 / 29 (3.45%)	2 / 37 (5.41%)
occurrences (all)	2	1	3
Epistaxis			
subjects affected / exposed	1 / 18 (5.56%)	0 / 29 (0.00%)	1 / 37 (2.70%)
occurrences (all)	2	0	2
Wheezing			
subjects affected / exposed	1 / 18 (5.56%)	0 / 29 (0.00%)	0 / 37 (0.00%)
occurrences (all)	1	0	0
Bronchial hyperreactivity			
subjects affected / exposed	1 / 18 (5.56%)	0 / 29 (0.00%)	0 / 37 (0.00%)
occurrences (all)	1	0	0
Upper-airway cough syndrome			
subjects affected / exposed	1 / 18 (5.56%)	0 / 29 (0.00%)	2 / 37 (5.41%)
occurrences (all)	1	0	2
Laryngospasm			
subjects affected / exposed	0 / 18 (0.00%)	0 / 29 (0.00%)	0 / 37 (0.00%)
occurrences (all)	0	0	0
Nasal congestion			

subjects affected / exposed	1 / 18 (5.56%)	1 / 29 (3.45%)	4 / 37 (10.81%)
occurrences (all)	1	1	4
Oropharyngeal cobble stone mucosa			
subjects affected / exposed	0 / 18 (0.00%)	0 / 29 (0.00%)	0 / 37 (0.00%)
occurrences (all)	0	0	0
Rhinorrhoea			
subjects affected / exposed	2 / 18 (11.11%)	0 / 29 (0.00%)	1 / 37 (2.70%)
occurrences (all)	2	0	2
Productive cough			
subjects affected / exposed	0 / 18 (0.00%)	0 / 29 (0.00%)	1 / 37 (2.70%)
occurrences (all)	0	0	1
Throat irritation			
subjects affected / exposed	1 / 18 (5.56%)	0 / 29 (0.00%)	0 / 37 (0.00%)
occurrences (all)	1	0	0
Throat tightness			
subjects affected / exposed	0 / 18 (0.00%)	0 / 29 (0.00%)	0 / 37 (0.00%)
occurrences (all)	0	0	0
Psychiatric disorders			
Fear of injection			
subjects affected / exposed	0 / 18 (0.00%)	0 / 29 (0.00%)	0 / 37 (0.00%)
occurrences (all)	0	0	0
Insomnia			
subjects affected / exposed	0 / 18 (0.00%)	2 / 29 (6.90%)	0 / 37 (0.00%)
occurrences (all)	0	2	0
Enuresis			
subjects affected / exposed	1 / 18 (5.56%)	0 / 29 (0.00%)	0 / 37 (0.00%)
occurrences (all)	1	0	0
Encopresis			
subjects affected / exposed	0 / 18 (0.00%)	0 / 29 (0.00%)	0 / 37 (0.00%)
occurrences (all)	0	0	0
Attention deficit hyperactivity disorder			
subjects affected / exposed	0 / 18 (0.00%)	1 / 29 (3.45%)	1 / 37 (2.70%)
occurrences (all)	0	1	1
Investigations			

Hepatic enzyme increased			
subjects affected / exposed	1 / 18 (5.56%)	0 / 29 (0.00%)	0 / 37 (0.00%)
occurrences (all)	1	0	0
Blood potassium increased			
subjects affected / exposed	0 / 18 (0.00%)	0 / 29 (0.00%)	0 / 37 (0.00%)
occurrences (all)	0	0	0
Aspartate aminotransferase increased			
subjects affected / exposed	0 / 18 (0.00%)	0 / 29 (0.00%)	0 / 37 (0.00%)
occurrences (all)	0	0	0
Alanine aminotransferase increased			
subjects affected / exposed	0 / 18 (0.00%)	0 / 29 (0.00%)	0 / 37 (0.00%)
occurrences (all)	0	0	0
Neutrophil count decreased			
subjects affected / exposed	1 / 18 (5.56%)	0 / 29 (0.00%)	0 / 37 (0.00%)
occurrences (all)	1	0	0
Blood alkaline phosphatase increased			
subjects affected / exposed	0 / 18 (0.00%)	0 / 29 (0.00%)	0 / 37 (0.00%)
occurrences (all)	0	0	0
Blood parathyroid hormone increased			
subjects affected / exposed	0 / 18 (0.00%)	0 / 29 (0.00%)	0 / 37 (0.00%)
occurrences (all)	0	0	0
Serum ferritin decreased			
subjects affected / exposed	0 / 18 (0.00%)	0 / 29 (0.00%)	0 / 37 (0.00%)
occurrences (all)	0	0	0
Injury, poisoning and procedural complications			
Arthropod bite			
subjects affected / exposed	1 / 18 (5.56%)	0 / 29 (0.00%)	2 / 37 (5.41%)
occurrences (all)	1	0	2
Ligament sprain			
subjects affected / exposed	0 / 18 (0.00%)	1 / 29 (3.45%)	0 / 37 (0.00%)
occurrences (all)	0	1	0
Arthropod sting			
subjects affected / exposed	0 / 18 (0.00%)	0 / 29 (0.00%)	1 / 37 (2.70%)
occurrences (all)	0	0	1
Face injury			

subjects affected / exposed	0 / 18 (0.00%)	2 / 29 (6.90%)	0 / 37 (0.00%)
occurrences (all)	0	2	0
Wrist fracture			
subjects affected / exposed	1 / 18 (5.56%)	1 / 29 (3.45%)	0 / 37 (0.00%)
occurrences (all)	1	1	0
Sunburn			
subjects affected / exposed	1 / 18 (5.56%)	0 / 29 (0.00%)	0 / 37 (0.00%)
occurrences (all)	1	0	0
Gas poisoning			
subjects affected / exposed	1 / 18 (5.56%)	0 / 29 (0.00%)	0 / 37 (0.00%)
occurrences (all)	1	0	0
Nasal injury			
subjects affected / exposed	1 / 18 (5.56%)	0 / 29 (0.00%)	0 / 37 (0.00%)
occurrences (all)	1	0	0
Foot fracture			
subjects affected / exposed	0 / 18 (0.00%)	0 / 29 (0.00%)	1 / 37 (2.70%)
occurrences (all)	0	0	1
Animal bite			
subjects affected / exposed	0 / 18 (0.00%)	1 / 29 (3.45%)	0 / 37 (0.00%)
occurrences (all)	0	1	0
Hand fracture			
subjects affected / exposed	0 / 18 (0.00%)	0 / 29 (0.00%)	0 / 37 (0.00%)
occurrences (all)	0	0	0
Joint injury			
subjects affected / exposed	0 / 18 (0.00%)	1 / 29 (3.45%)	1 / 37 (2.70%)
occurrences (all)	0	1	1
Limb injury			
subjects affected / exposed	0 / 18 (0.00%)	0 / 29 (0.00%)	2 / 37 (5.41%)
occurrences (all)	0	0	2
Ligament rupture			
subjects affected / exposed	0 / 18 (0.00%)	0 / 29 (0.00%)	0 / 37 (0.00%)
occurrences (all)	0	0	0
Nervous system disorders			
Dizziness			
subjects affected / exposed	0 / 18 (0.00%)	0 / 29 (0.00%)	0 / 37 (0.00%)
occurrences (all)	0	0	0

Headache			
subjects affected / exposed	4 / 18 (22.22%)	3 / 29 (10.34%)	4 / 37 (10.81%)
occurrences (all)	4	5	4
Lethargy			
subjects affected / exposed	1 / 18 (5.56%)	0 / 29 (0.00%)	0 / 37 (0.00%)
occurrences (all)	1	0	0
Ear and labyrinth disorders			
Otorrhoea			
subjects affected / exposed	1 / 18 (5.56%)	0 / 29 (0.00%)	0 / 37 (0.00%)
occurrences (all)	1	0	0
Ear pain			
subjects affected / exposed	1 / 18 (5.56%)	0 / 29 (0.00%)	1 / 37 (2.70%)
occurrences (all)	1	0	1
Motion sickness			
subjects affected / exposed	0 / 18 (0.00%)	0 / 29 (0.00%)	0 / 37 (0.00%)
occurrences (all)	0	0	0
Eye disorders			
Eye swelling			
subjects affected / exposed	0 / 18 (0.00%)	3 / 29 (10.34%)	0 / 37 (0.00%)
occurrences (all)	0	3	0
Ocular hyperaemia			
subjects affected / exposed	0 / 18 (0.00%)	4 / 29 (13.79%)	0 / 37 (0.00%)
occurrences (all)	0	7	0
Eye pruritus			
subjects affected / exposed	0 / 18 (0.00%)	1 / 29 (3.45%)	0 / 37 (0.00%)
occurrences (all)	0	1	0
Dry eye			
subjects affected / exposed	1 / 18 (5.56%)	0 / 29 (0.00%)	0 / 37 (0.00%)
occurrences (all)	1	0	0
Conjunctivitis allergic			
subjects affected / exposed	1 / 18 (5.56%)	0 / 29 (0.00%)	0 / 37 (0.00%)
occurrences (all)	1	0	0
Astigmatism			
subjects affected / exposed	0 / 18 (0.00%)	0 / 29 (0.00%)	0 / 37 (0.00%)
occurrences (all)	0	0	0
Gastrointestinal disorders			

Vomiting			
subjects affected / exposed	2 / 18 (11.11%)	3 / 29 (10.34%)	5 / 37 (13.51%)
occurrences (all)	2	6	7
Abdominal pain			
subjects affected / exposed	2 / 18 (11.11%)	3 / 29 (10.34%)	4 / 37 (10.81%)
occurrences (all)	3	3	4
Constipation			
subjects affected / exposed	0 / 18 (0.00%)	2 / 29 (6.90%)	1 / 37 (2.70%)
occurrences (all)	0	2	1
Abdominal pain upper			
subjects affected / exposed	0 / 18 (0.00%)	3 / 29 (10.34%)	2 / 37 (5.41%)
occurrences (all)	0	3	2
Gastrooesophageal reflux disease			
subjects affected / exposed	1 / 18 (5.56%)	1 / 29 (3.45%)	1 / 37 (2.70%)
occurrences (all)	1	2	1
Nausea			
subjects affected / exposed	2 / 18 (11.11%)	2 / 29 (6.90%)	1 / 37 (2.70%)
occurrences (all)	2	2	1
Diarrhoea			
subjects affected / exposed	3 / 18 (16.67%)	3 / 29 (10.34%)	3 / 37 (8.11%)
occurrences (all)	9	3	3
Eosinophilic oesophagitis			
subjects affected / exposed	0 / 18 (0.00%)	1 / 29 (3.45%)	1 / 37 (2.70%)
occurrences (all)	0	1	1
Oral pain			
subjects affected / exposed	0 / 18 (0.00%)	0 / 29 (0.00%)	0 / 37 (0.00%)
occurrences (all)	0	0	0
Oral discomfort			
subjects affected / exposed	1 / 18 (5.56%)	0 / 29 (0.00%)	0 / 37 (0.00%)
occurrences (all)	1	0	0
Dysphagia			
subjects affected / exposed	0 / 18 (0.00%)	2 / 29 (6.90%)	1 / 37 (2.70%)
occurrences (all)	0	3	1
Lip blister			
subjects affected / exposed	1 / 18 (5.56%)	0 / 29 (0.00%)	0 / 37 (0.00%)
occurrences (all)	1	0	0

Dyspepsia			
subjects affected / exposed	2 / 18 (11.11%)	1 / 29 (3.45%)	0 / 37 (0.00%)
occurrences (all)	2	1	0
Abdominal discomfort			
subjects affected / exposed	1 / 18 (5.56%)	0 / 29 (0.00%)	0 / 37 (0.00%)
occurrences (all)	1	0	0
Faeces hard			
subjects affected / exposed	0 / 18 (0.00%)	0 / 29 (0.00%)	0 / 37 (0.00%)
occurrences (all)	0	0	0
Flatulence			
subjects affected / exposed	0 / 18 (0.00%)	1 / 29 (3.45%)	0 / 37 (0.00%)
occurrences (all)	0	1	0
Skin and subcutaneous tissue disorders			
Rash			
subjects affected / exposed	2 / 18 (11.11%)	1 / 29 (3.45%)	4 / 37 (10.81%)
occurrences (all)	4	2	7
Eczema			
subjects affected / exposed	2 / 18 (11.11%)	2 / 29 (6.90%)	0 / 37 (0.00%)
occurrences (all)	2	2	0
Urticaria			
subjects affected / exposed	0 / 18 (0.00%)	2 / 29 (6.90%)	1 / 37 (2.70%)
occurrences (all)	0	2	2
Dry skin			
subjects affected / exposed	0 / 18 (0.00%)	0 / 29 (0.00%)	1 / 37 (2.70%)
occurrences (all)	0	0	1
Rash papular			
subjects affected / exposed	0 / 18 (0.00%)	0 / 29 (0.00%)	2 / 37 (5.41%)
occurrences (all)	0	0	3
Dermatitis			
subjects affected / exposed	0 / 18 (0.00%)	1 / 29 (3.45%)	0 / 37 (0.00%)
occurrences (all)	0	1	0
Hand dermatitis			
subjects affected / exposed	1 / 18 (5.56%)	0 / 29 (0.00%)	0 / 37 (0.00%)
occurrences (all)	1	0	0
Keratosis pilaris			

subjects affected / exposed	1 / 18 (5.56%)	0 / 29 (0.00%)	1 / 37 (2.70%)
occurrences (all)	1	0	1
Perioral dermatitis			
subjects affected / exposed	0 / 18 (0.00%)	0 / 29 (0.00%)	0 / 37 (0.00%)
occurrences (all)	0	0	0
Petechiae			
subjects affected / exposed	0 / 18 (0.00%)	0 / 29 (0.00%)	0 / 37 (0.00%)
occurrences (all)	0	0	0
Pruritus			
subjects affected / exposed	1 / 18 (5.56%)	0 / 29 (0.00%)	0 / 37 (0.00%)
occurrences (all)	1	0	0
Skin lesion			
subjects affected / exposed	1 / 18 (5.56%)	1 / 29 (3.45%)	0 / 37 (0.00%)
occurrences (all)	1	2	0
Rash erythematous			
subjects affected / exposed	1 / 18 (5.56%)	0 / 29 (0.00%)	0 / 37 (0.00%)
occurrences (all)	1	0	0
Erythema			
subjects affected / exposed	0 / 18 (0.00%)	1 / 29 (3.45%)	1 / 37 (2.70%)
occurrences (all)	0	1	1
Macule			
subjects affected / exposed	0 / 18 (0.00%)	0 / 29 (0.00%)	0 / 37 (0.00%)
occurrences (all)	0	0	0
Rash macular			
subjects affected / exposed	0 / 18 (0.00%)	0 / 29 (0.00%)	0 / 37 (0.00%)
occurrences (all)	0	0	0
Acne			
subjects affected / exposed	0 / 18 (0.00%)	0 / 29 (0.00%)	0 / 37 (0.00%)
occurrences (all)	0	0	0
Dermatitis contact			
subjects affected / exposed	0 / 18 (0.00%)	0 / 29 (0.00%)	1 / 37 (2.70%)
occurrences (all)	0	0	1
Musculoskeletal and connective tissue disorders			
Tendon pain			

subjects affected / exposed	0 / 18 (0.00%)	0 / 29 (0.00%)	0 / 37 (0.00%)
occurrences (all)	0	0	0
Musculoskeletal discomfort			
subjects affected / exposed	1 / 18 (5.56%)	0 / 29 (0.00%)	0 / 37 (0.00%)
occurrences (all)	1	0	0
Pain in extremity			
subjects affected / exposed	3 / 18 (16.67%)	0 / 29 (0.00%)	2 / 37 (5.41%)
occurrences (all)	3	0	3
Arthralgia			
subjects affected / exposed	1 / 18 (5.56%)	0 / 29 (0.00%)	1 / 37 (2.70%)
occurrences (all)	2	0	1
Back pain			
subjects affected / exposed	0 / 18 (0.00%)	0 / 29 (0.00%)	0 / 37 (0.00%)
occurrences (all)	0	0	0
Myalgia			
subjects affected / exposed	0 / 18 (0.00%)	2 / 29 (6.90%)	0 / 37 (0.00%)
occurrences (all)	0	4	0
Infections and infestations			
Sinusitis			
subjects affected / exposed	1 / 18 (5.56%)	1 / 29 (3.45%)	0 / 37 (0.00%)
occurrences (all)	1	1	0
Upper respiratory tract infection			
subjects affected / exposed	1 / 18 (5.56%)	8 / 29 (27.59%)	2 / 37 (5.41%)
occurrences (all)	1	9	2
Ear infection			
subjects affected / exposed	1 / 18 (5.56%)	1 / 29 (3.45%)	2 / 37 (5.41%)
occurrences (all)	1	1	2
Molluscum contagiosum			
subjects affected / exposed	0 / 18 (0.00%)	0 / 29 (0.00%)	0 / 37 (0.00%)
occurrences (all)	0	0	0
COVID-19			
subjects affected / exposed	6 / 18 (33.33%)	7 / 29 (24.14%)	11 / 37 (29.73%)
occurrences (all)	7	7	11
Viral upper respiratory tract infection			
subjects affected / exposed	1 / 18 (5.56%)	4 / 29 (13.79%)	1 / 37 (2.70%)
occurrences (all)	1	4	1

Gastroenteritis viral			
subjects affected / exposed	1 / 18 (5.56%)	1 / 29 (3.45%)	2 / 37 (5.41%)
occurrences (all)	1	1	2
Nasopharyngitis			
subjects affected / exposed	1 / 18 (5.56%)	1 / 29 (3.45%)	3 / 37 (8.11%)
occurrences (all)	1	1	6
Respiratory tract infection viral			
subjects affected / exposed	1 / 18 (5.56%)	1 / 29 (3.45%)	1 / 37 (2.70%)
occurrences (all)	3	1	1
Hordeolum			
subjects affected / exposed	0 / 18 (0.00%)	1 / 29 (3.45%)	0 / 37 (0.00%)
occurrences (all)	0	1	0
Beta haemolytic streptococcal infection			
subjects affected / exposed	1 / 18 (5.56%)	0 / 29 (0.00%)	0 / 37 (0.00%)
occurrences (all)	1	0	0
Conjunctivitis			
subjects affected / exposed	2 / 18 (11.11%)	4 / 29 (13.79%)	2 / 37 (5.41%)
occurrences (all)	2	4	2
Croup infectious			
subjects affected / exposed	1 / 18 (5.56%)	1 / 29 (3.45%)	2 / 37 (5.41%)
occurrences (all)	1	1	2
Ear infection viral			
subjects affected / exposed	1 / 18 (5.56%)	0 / 29 (0.00%)	0 / 37 (0.00%)
occurrences (all)	1	0	0
Influenza			
subjects affected / exposed	1 / 18 (5.56%)	4 / 29 (13.79%)	4 / 37 (10.81%)
occurrences (all)	1	4	4
Gastrointestinal viral infection			
subjects affected / exposed	1 / 18 (5.56%)	2 / 29 (6.90%)	1 / 37 (2.70%)
occurrences (all)	1	2	1
Groin infection			
subjects affected / exposed	1 / 18 (5.56%)	0 / 29 (0.00%)	0 / 37 (0.00%)
occurrences (all)	1	0	0
Impetigo			

subjects affected / exposed	0 / 18 (0.00%)	0 / 29 (0.00%)	0 / 37 (0.00%)
occurrences (all)	0	0	0
Eye infection			
subjects affected / exposed	0 / 18 (0.00%)	2 / 29 (6.90%)	0 / 37 (0.00%)
occurrences (all)	0	2	0
Otitis media			
subjects affected / exposed	1 / 18 (5.56%)	0 / 29 (0.00%)	3 / 37 (8.11%)
occurrences (all)	1	0	3
Pharyngitis			
subjects affected / exposed	1 / 18 (5.56%)	1 / 29 (3.45%)	0 / 37 (0.00%)
occurrences (all)	1	1	0
Pharyngitis streptococcal			
subjects affected / exposed	1 / 18 (5.56%)	2 / 29 (6.90%)	0 / 37 (0.00%)
occurrences (all)	2	2	0
Urinary tract infection			
subjects affected / exposed	0 / 18 (0.00%)	0 / 29 (0.00%)	2 / 37 (5.41%)
occurrences (all)	0	0	2
Stoma site infection			
subjects affected / exposed	1 / 18 (5.56%)	0 / 29 (0.00%)	0 / 37 (0.00%)
occurrences (all)	1	0	0
Tonsillitis			
subjects affected / exposed	1 / 18 (5.56%)	0 / 29 (0.00%)	0 / 37 (0.00%)
occurrences (all)	1	0	0
Rhinitis			
subjects affected / exposed	2 / 18 (11.11%)	0 / 29 (0.00%)	0 / 37 (0.00%)
occurrences (all)	3	0	0
Viral infection			
subjects affected / exposed	1 / 18 (5.56%)	0 / 29 (0.00%)	0 / 37 (0.00%)
occurrences (all)	1	0	0
Pneumonia			
subjects affected / exposed	0 / 18 (0.00%)	0 / 29 (0.00%)	2 / 37 (5.41%)
occurrences (all)	0	0	2
Paronychia			
subjects affected / exposed	0 / 18 (0.00%)	0 / 29 (0.00%)	0 / 37 (0.00%)
occurrences (all)	0	0	0
Gastroenteritis			

subjects affected / exposed	0 / 18 (0.00%)	1 / 29 (3.45%)	1 / 37 (2.70%)
occurrences (all)	0	1	1
Cellulitis			
subjects affected / exposed	0 / 18 (0.00%)	0 / 29 (0.00%)	1 / 37 (2.70%)
occurrences (all)	0	0	1
Metabolism and nutrition disorders			
Iron deficiency			
subjects affected / exposed	0 / 18 (0.00%)	0 / 29 (0.00%)	0 / 37 (0.00%)
occurrences (all)	0	0	0
Decreased appetite			
subjects affected / exposed	1 / 18 (5.56%)	0 / 29 (0.00%)	0 / 37 (0.00%)
occurrences (all)	1	0	0

Non-serious adverse events	Part A: Dupilumab Low Dose	Part B: Placebo to Dupilumab Low Dose	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	24 / 30 (80.00%)	14 / 14 (100.00%)	
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Skin papilloma			
subjects affected / exposed	0 / 30 (0.00%)	0 / 14 (0.00%)	
occurrences (all)	0	0	
Vascular disorders			
Flushing			
subjects affected / exposed	0 / 30 (0.00%)	0 / 14 (0.00%)	
occurrences (all)	0	0	
General disorders and administration site conditions			
Injection site reaction			
subjects affected / exposed	4 / 30 (13.33%)	4 / 14 (28.57%)	
occurrences (all)	11	34	
Injection site erythema			
subjects affected / exposed	1 / 30 (3.33%)	1 / 14 (7.14%)	
occurrences (all)	2	1	
Pyrexia			
subjects affected / exposed	0 / 30 (0.00%)	3 / 14 (21.43%)	
occurrences (all)	0	3	
Fatigue			

subjects affected / exposed	0 / 30 (0.00%)	0 / 14 (0.00%)		
occurrences (all)	0	0		
Injection site pain				
subjects affected / exposed	3 / 30 (10.00%)	3 / 14 (21.43%)		
occurrences (all)	3	6		
Injection site haemorrhage				
subjects affected / exposed	0 / 30 (0.00%)	1 / 14 (7.14%)		
occurrences (all)	0	1		
Injection site swelling				
subjects affected / exposed	0 / 30 (0.00%)	1 / 14 (7.14%)		
occurrences (all)	0	1		
Chest pain				
subjects affected / exposed	0 / 30 (0.00%)	0 / 14 (0.00%)		
occurrences (all)	0	0		
Malaise				
subjects affected / exposed	0 / 30 (0.00%)	0 / 14 (0.00%)		
occurrences (all)	0	0		
Injection site induration				
subjects affected / exposed	0 / 30 (0.00%)	0 / 14 (0.00%)		
occurrences (all)	0	0		
Injection site inflammation				
subjects affected / exposed	0 / 30 (0.00%)	0 / 14 (0.00%)		
occurrences (all)	0	0		
Injection site oedema				
subjects affected / exposed	0 / 30 (0.00%)	0 / 14 (0.00%)		
occurrences (all)	0	0		
Influenza like illness				
subjects affected / exposed	1 / 30 (3.33%)	1 / 14 (7.14%)		
occurrences (all)	1	1		
Vessel puncture site pain				
subjects affected / exposed	0 / 30 (0.00%)	0 / 14 (0.00%)		
occurrences (all)	0	0		
Injection site mass				
subjects affected / exposed	0 / 30 (0.00%)	0 / 14 (0.00%)		
occurrences (all)	0	0		
Injection site bruising				

subjects affected / exposed	0 / 30 (0.00%)	0 / 14 (0.00%)	
occurrences (all)	0	0	
Immune system disorders			
Seasonal allergy			
subjects affected / exposed	1 / 30 (3.33%)	1 / 14 (7.14%)	
occurrences (all)	1	1	
Food allergy			
subjects affected / exposed	0 / 30 (0.00%)	0 / 14 (0.00%)	
occurrences (all)	0	0	
Immunisation reaction			
subjects affected / exposed	0 / 30 (0.00%)	0 / 14 (0.00%)	
occurrences (all)	0	0	
Anaphylactic reaction			
subjects affected / exposed	1 / 30 (3.33%)	0 / 14 (0.00%)	
occurrences (all)	1	0	
Reproductive system and breast disorders			
Genital rash			
subjects affected / exposed	0 / 30 (0.00%)	1 / 14 (7.14%)	
occurrences (all)	0	1	
Genital pain			
subjects affected / exposed	0 / 30 (0.00%)	1 / 14 (7.14%)	
occurrences (all)	0	1	
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	2 / 30 (6.67%)	1 / 14 (7.14%)	
occurrences (all)	2	1	
Rhinitis allergic			
subjects affected / exposed	2 / 30 (6.67%)	0 / 14 (0.00%)	
occurrences (all)	2	0	
Asthma			
subjects affected / exposed	0 / 30 (0.00%)	1 / 14 (7.14%)	
occurrences (all)	0	1	
Oropharyngeal pain			
subjects affected / exposed	1 / 30 (3.33%)	2 / 14 (14.29%)	
occurrences (all)	1	2	
Epistaxis			

subjects affected / exposed	0 / 30 (0.00%)	1 / 14 (7.14%)	
occurrences (all)	0	1	
Wheezing			
subjects affected / exposed	0 / 30 (0.00%)	0 / 14 (0.00%)	
occurrences (all)	0	0	
Bronchial hyperreactivity			
subjects affected / exposed	0 / 30 (0.00%)	0 / 14 (0.00%)	
occurrences (all)	0	0	
Upper-airway cough syndrome			
subjects affected / exposed	0 / 30 (0.00%)	0 / 14 (0.00%)	
occurrences (all)	0	0	
Laryngospasm			
subjects affected / exposed	0 / 30 (0.00%)	1 / 14 (7.14%)	
occurrences (all)	0	1	
Nasal congestion			
subjects affected / exposed	1 / 30 (3.33%)	1 / 14 (7.14%)	
occurrences (all)	1	1	
Oropharyngeal cobble stone mucosa			
subjects affected / exposed	0 / 30 (0.00%)	1 / 14 (7.14%)	
occurrences (all)	0	1	
Rhinorrhoea			
subjects affected / exposed	1 / 30 (3.33%)	2 / 14 (14.29%)	
occurrences (all)	1	3	
Productive cough			
subjects affected / exposed	0 / 30 (0.00%)	0 / 14 (0.00%)	
occurrences (all)	0	0	
Throat irritation			
subjects affected / exposed	0 / 30 (0.00%)	0 / 14 (0.00%)	
occurrences (all)	0	0	
Throat tightness			
subjects affected / exposed	0 / 30 (0.00%)	0 / 14 (0.00%)	
occurrences (all)	0	0	
Psychiatric disorders			
Fear of injection			
subjects affected / exposed	1 / 30 (3.33%)	0 / 14 (0.00%)	
occurrences (all)	1	0	

Insomnia			
subjects affected / exposed	1 / 30 (3.33%)	1 / 14 (7.14%)	
occurrences (all)	1	1	
Enuresis			
subjects affected / exposed	0 / 30 (0.00%)	0 / 14 (0.00%)	
occurrences (all)	0	0	
Encopresis			
subjects affected / exposed	0 / 30 (0.00%)	0 / 14 (0.00%)	
occurrences (all)	0	0	
Attention deficit hyperactivity disorder			
subjects affected / exposed	0 / 30 (0.00%)	0 / 14 (0.00%)	
occurrences (all)	0	0	
Investigations			
Hepatic enzyme increased			
subjects affected / exposed	0 / 30 (0.00%)	0 / 14 (0.00%)	
occurrences (all)	0	0	
Blood potassium increased			
subjects affected / exposed	0 / 30 (0.00%)	1 / 14 (7.14%)	
occurrences (all)	0	1	
Aspartate aminotransferase increased			
subjects affected / exposed	0 / 30 (0.00%)	1 / 14 (7.14%)	
occurrences (all)	0	1	
Alanine aminotransferase increased			
subjects affected / exposed	0 / 30 (0.00%)	1 / 14 (7.14%)	
occurrences (all)	0	1	
Neutrophil count decreased			
subjects affected / exposed	0 / 30 (0.00%)	0 / 14 (0.00%)	
occurrences (all)	0	0	
Blood alkaline phosphatase increased			
subjects affected / exposed	0 / 30 (0.00%)	0 / 14 (0.00%)	
occurrences (all)	0	0	
Blood parathyroid hormone increased			
subjects affected / exposed	0 / 30 (0.00%)	0 / 14 (0.00%)	
occurrences (all)	0	0	
Serum ferritin decreased			

subjects affected / exposed	0 / 30 (0.00%)	0 / 14 (0.00%)	
occurrences (all)	0	0	
Injury, poisoning and procedural complications			
Arthropod bite			
subjects affected / exposed	0 / 30 (0.00%)	0 / 14 (0.00%)	
occurrences (all)	0	0	
Ligament sprain			
subjects affected / exposed	0 / 30 (0.00%)	1 / 14 (7.14%)	
occurrences (all)	0	1	
Arthropod sting			
subjects affected / exposed	0 / 30 (0.00%)	1 / 14 (7.14%)	
occurrences (all)	0	1	
Face injury			
subjects affected / exposed	0 / 30 (0.00%)	0 / 14 (0.00%)	
occurrences (all)	0	0	
Wrist fracture			
subjects affected / exposed	0 / 30 (0.00%)	0 / 14 (0.00%)	
occurrences (all)	0	0	
Sunburn			
subjects affected / exposed	0 / 30 (0.00%)	0 / 14 (0.00%)	
occurrences (all)	0	0	
Gas poisoning			
subjects affected / exposed	0 / 30 (0.00%)	0 / 14 (0.00%)	
occurrences (all)	0	0	
Nasal injury			
subjects affected / exposed	0 / 30 (0.00%)	0 / 14 (0.00%)	
occurrences (all)	0	0	
Foot fracture			
subjects affected / exposed	0 / 30 (0.00%)	0 / 14 (0.00%)	
occurrences (all)	0	0	
Animal bite			
subjects affected / exposed	0 / 30 (0.00%)	0 / 14 (0.00%)	
occurrences (all)	0	0	
Hand fracture			

subjects affected / exposed	0 / 30 (0.00%)	0 / 14 (0.00%)	
occurrences (all)	0	0	
Joint injury			
subjects affected / exposed	0 / 30 (0.00%)	0 / 14 (0.00%)	
occurrences (all)	0	0	
Limb injury			
subjects affected / exposed	0 / 30 (0.00%)	0 / 14 (0.00%)	
occurrences (all)	0	0	
Ligament rupture			
subjects affected / exposed	0 / 30 (0.00%)	0 / 14 (0.00%)	
occurrences (all)	0	0	
Nervous system disorders			
Dizziness			
subjects affected / exposed	1 / 30 (3.33%)	0 / 14 (0.00%)	
occurrences (all)	2	0	
Headache			
subjects affected / exposed	4 / 30 (13.33%)	0 / 14 (0.00%)	
occurrences (all)	5	0	
Lethargy			
subjects affected / exposed	0 / 30 (0.00%)	0 / 14 (0.00%)	
occurrences (all)	0	0	
Ear and labyrinth disorders			
Otorrhoea			
subjects affected / exposed	0 / 30 (0.00%)	0 / 14 (0.00%)	
occurrences (all)	0	0	
Ear pain			
subjects affected / exposed	0 / 30 (0.00%)	0 / 14 (0.00%)	
occurrences (all)	0	0	
Motion sickness			
subjects affected / exposed	0 / 30 (0.00%)	0 / 14 (0.00%)	
occurrences (all)	0	0	
Eye disorders			
Eye swelling			
subjects affected / exposed	2 / 30 (6.67%)	0 / 14 (0.00%)	
occurrences (all)	2	0	
Ocular hyperaemia			

subjects affected / exposed	0 / 30 (0.00%)	0 / 14 (0.00%)	
occurrences (all)	0	0	
Eye pruritus			
subjects affected / exposed	0 / 30 (0.00%)	1 / 14 (7.14%)	
occurrences (all)	0	1	
Dry eye			
subjects affected / exposed	0 / 30 (0.00%)	0 / 14 (0.00%)	
occurrences (all)	0	0	
Conjunctivitis allergic			
subjects affected / exposed	0 / 30 (0.00%)	1 / 14 (7.14%)	
occurrences (all)	0	1	
Astigmatism			
subjects affected / exposed	0 / 30 (0.00%)	0 / 14 (0.00%)	
occurrences (all)	0	0	
Gastrointestinal disorders			
Vomiting			
subjects affected / exposed	1 / 30 (3.33%)	0 / 14 (0.00%)	
occurrences (all)	1	0	
Abdominal pain			
subjects affected / exposed	1 / 30 (3.33%)	1 / 14 (7.14%)	
occurrences (all)	1	1	
Constipation			
subjects affected / exposed	0 / 30 (0.00%)	0 / 14 (0.00%)	
occurrences (all)	0	0	
Abdominal pain upper			
subjects affected / exposed	2 / 30 (6.67%)	1 / 14 (7.14%)	
occurrences (all)	2	1	
Gastrooesophageal reflux disease			
subjects affected / exposed	2 / 30 (6.67%)	0 / 14 (0.00%)	
occurrences (all)	2	0	
Nausea			
subjects affected / exposed	3 / 30 (10.00%)	1 / 14 (7.14%)	
occurrences (all)	3	1	
Diarrhoea			
subjects affected / exposed	2 / 30 (6.67%)	1 / 14 (7.14%)	
occurrences (all)	3	2	

Eosinophilic oesophagitis			
subjects affected / exposed	0 / 30 (0.00%)	2 / 14 (14.29%)	
occurrences (all)	0	2	
Oral pain			
subjects affected / exposed	0 / 30 (0.00%)	1 / 14 (7.14%)	
occurrences (all)	0	1	
Oral discomfort			
subjects affected / exposed	0 / 30 (0.00%)	0 / 14 (0.00%)	
occurrences (all)	0	0	
Dysphagia			
subjects affected / exposed	0 / 30 (0.00%)	1 / 14 (7.14%)	
occurrences (all)	0	1	
Lip blister			
subjects affected / exposed	0 / 30 (0.00%)	0 / 14 (0.00%)	
occurrences (all)	0	0	
Dyspepsia			
subjects affected / exposed	0 / 30 (0.00%)	0 / 14 (0.00%)	
occurrences (all)	0	0	
Abdominal discomfort			
subjects affected / exposed	0 / 30 (0.00%)	0 / 14 (0.00%)	
occurrences (all)	0	0	
Faeces hard			
subjects affected / exposed	0 / 30 (0.00%)	0 / 14 (0.00%)	
occurrences (all)	0	0	
Flatulence			
subjects affected / exposed	0 / 30 (0.00%)	0 / 14 (0.00%)	
occurrences (all)	0	0	
Skin and subcutaneous tissue disorders			
Rash			
subjects affected / exposed	3 / 30 (10.00%)	2 / 14 (14.29%)	
occurrences (all)	3	4	
Eczema			
subjects affected / exposed	2 / 30 (6.67%)	0 / 14 (0.00%)	
occurrences (all)	2	0	
Urticaria			

subjects affected / exposed	2 / 30 (6.67%)	3 / 14 (21.43%)		
occurrences (all)	2	3		
Dry skin				
subjects affected / exposed	1 / 30 (3.33%)	0 / 14 (0.00%)		
occurrences (all)	1	0		
Rash papular				
subjects affected / exposed	0 / 30 (0.00%)	0 / 14 (0.00%)		
occurrences (all)	0	0		
Dermatitis				
subjects affected / exposed	0 / 30 (0.00%)	1 / 14 (7.14%)		
occurrences (all)	0	1		
Hand dermatitis				
subjects affected / exposed	0 / 30 (0.00%)	0 / 14 (0.00%)		
occurrences (all)	0	0		
Keratosis pilaris				
subjects affected / exposed	0 / 30 (0.00%)	0 / 14 (0.00%)		
occurrences (all)	0	0		
Perioral dermatitis				
subjects affected / exposed	1 / 30 (3.33%)	1 / 14 (7.14%)		
occurrences (all)	1	1		
Petechiae				
subjects affected / exposed	0 / 30 (0.00%)	1 / 14 (7.14%)		
occurrences (all)	0	1		
Pruritus				
subjects affected / exposed	0 / 30 (0.00%)	0 / 14 (0.00%)		
occurrences (all)	0	0		
Skin lesion				
subjects affected / exposed	0 / 30 (0.00%)	0 / 14 (0.00%)		
occurrences (all)	0	0		
Rash erythematous				
subjects affected / exposed	1 / 30 (3.33%)	0 / 14 (0.00%)		
occurrences (all)	1	0		
Erythema				
subjects affected / exposed	1 / 30 (3.33%)	0 / 14 (0.00%)		
occurrences (all)	1	0		
Macule				

subjects affected / exposed	0 / 30 (0.00%)	0 / 14 (0.00%)	
occurrences (all)	0	0	
Rash macular			
subjects affected / exposed	0 / 30 (0.00%)	0 / 14 (0.00%)	
occurrences (all)	0	0	
Acne			
subjects affected / exposed	0 / 30 (0.00%)	0 / 14 (0.00%)	
occurrences (all)	0	0	
Dermatitis contact			
subjects affected / exposed	0 / 30 (0.00%)	0 / 14 (0.00%)	
occurrences (all)	0	0	
Musculoskeletal and connective tissue disorders			
Tendon pain			
subjects affected / exposed	0 / 30 (0.00%)	1 / 14 (7.14%)	
occurrences (all)	0	1	
Musculoskeletal discomfort			
subjects affected / exposed	0 / 30 (0.00%)	0 / 14 (0.00%)	
occurrences (all)	0	0	
Pain in extremity			
subjects affected / exposed	0 / 30 (0.00%)	1 / 14 (7.14%)	
occurrences (all)	0	1	
Arthralgia			
subjects affected / exposed	0 / 30 (0.00%)	0 / 14 (0.00%)	
occurrences (all)	0	0	
Back pain			
subjects affected / exposed	0 / 30 (0.00%)	0 / 14 (0.00%)	
occurrences (all)	0	0	
Myalgia			
subjects affected / exposed	0 / 30 (0.00%)	0 / 14 (0.00%)	
occurrences (all)	0	0	
Infections and infestations			
Sinusitis			
subjects affected / exposed	1 / 30 (3.33%)	1 / 14 (7.14%)	
occurrences (all)	1	1	
Upper respiratory tract infection			

subjects affected / exposed	1 / 30 (3.33%)	2 / 14 (14.29%)		
occurrences (all)	1	2		
Ear infection				
subjects affected / exposed	0 / 30 (0.00%)	1 / 14 (7.14%)		
occurrences (all)	0	1		
Molluscum contagiosum				
subjects affected / exposed	0 / 30 (0.00%)	0 / 14 (0.00%)		
occurrences (all)	0	0		
COVID-19				
subjects affected / exposed	9 / 30 (30.00%)	3 / 14 (21.43%)		
occurrences (all)	9	3		
Viral upper respiratory tract infection				
subjects affected / exposed	0 / 30 (0.00%)	0 / 14 (0.00%)		
occurrences (all)	0	0		
Gastroenteritis viral				
subjects affected / exposed	0 / 30 (0.00%)	0 / 14 (0.00%)		
occurrences (all)	0	0		
Nasopharyngitis				
subjects affected / exposed	1 / 30 (3.33%)	0 / 14 (0.00%)		
occurrences (all)	1	0		
Respiratory tract infection viral				
subjects affected / exposed	0 / 30 (0.00%)	1 / 14 (7.14%)		
occurrences (all)	0	1		
Hordeolum				
subjects affected / exposed	0 / 30 (0.00%)	1 / 14 (7.14%)		
occurrences (all)	0	3		
Beta haemolytic streptococcal infection				
subjects affected / exposed	0 / 30 (0.00%)	0 / 14 (0.00%)		
occurrences (all)	0	0		
Conjunctivitis				
subjects affected / exposed	1 / 30 (3.33%)	0 / 14 (0.00%)		
occurrences (all)	1	0		
Croup infectious				
subjects affected / exposed	0 / 30 (0.00%)	0 / 14 (0.00%)		
occurrences (all)	0	0		

Ear infection viral				
subjects affected / exposed	0 / 30 (0.00%)	0 / 14 (0.00%)		
occurrences (all)	0	0		
Influenza				
subjects affected / exposed	0 / 30 (0.00%)	4 / 14 (28.57%)		
occurrences (all)	0	4		
Gastrointestinal viral infection				
subjects affected / exposed	1 / 30 (3.33%)	1 / 14 (7.14%)		
occurrences (all)	1	1		
Groin infection				
subjects affected / exposed	0 / 30 (0.00%)	0 / 14 (0.00%)		
occurrences (all)	0	0		
Impetigo				
subjects affected / exposed	0 / 30 (0.00%)	1 / 14 (7.14%)		
occurrences (all)	0	1		
Eye infection				
subjects affected / exposed	0 / 30 (0.00%)	0 / 14 (0.00%)		
occurrences (all)	0	0		
Otitis media				
subjects affected / exposed	1 / 30 (3.33%)	0 / 14 (0.00%)		
occurrences (all)	1	0		
Pharyngitis				
subjects affected / exposed	0 / 30 (0.00%)	0 / 14 (0.00%)		
occurrences (all)	0	0		
Pharyngitis streptococcal				
subjects affected / exposed	0 / 30 (0.00%)	2 / 14 (14.29%)		
occurrences (all)	0	2		
Urinary tract infection				
subjects affected / exposed	0 / 30 (0.00%)	0 / 14 (0.00%)		
occurrences (all)	0	0		
Stoma site infection				
subjects affected / exposed	0 / 30 (0.00%)	0 / 14 (0.00%)		
occurrences (all)	0	0		
Tonsillitis				
subjects affected / exposed	0 / 30 (0.00%)	0 / 14 (0.00%)		
occurrences (all)	0	0		

Rhinitis			
subjects affected / exposed	0 / 30 (0.00%)	0 / 14 (0.00%)	
occurrences (all)	0	0	
Viral infection			
subjects affected / exposed	0 / 30 (0.00%)	0 / 14 (0.00%)	
occurrences (all)	0	0	
Pneumonia			
subjects affected / exposed	0 / 30 (0.00%)	0 / 14 (0.00%)	
occurrences (all)	0	0	
Paronychia			
subjects affected / exposed	0 / 30 (0.00%)	0 / 14 (0.00%)	
occurrences (all)	0	0	
Gastroenteritis			
subjects affected / exposed	0 / 30 (0.00%)	0 / 14 (0.00%)	
occurrences (all)	0	0	
Cellulitis			
subjects affected / exposed	0 / 30 (0.00%)	0 / 14 (0.00%)	
occurrences (all)	0	0	
Metabolism and nutrition disorders			
Iron deficiency			
subjects affected / exposed	0 / 30 (0.00%)	1 / 14 (7.14%)	
occurrences (all)	0	1	
Decreased appetite			
subjects affected / exposed	0 / 30 (0.00%)	0 / 14 (0.00%)	
occurrences (all)	0	0	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
07 April 2020	Added the PEESSv2.0- caregiver version questionnaire as a secondary endpoint; Changed the PESQ-Caregiver and PESQ-Patient questionnaires to secondary endpoints; Clarifications; Added endpoints; Updated inclusion criteria
18 November 2020	Added additional treatment arm to evaluate a lower exposure of dupilumab; clariifications and updated language.
13 June 2021	Included an exit interview; added symptom/sign-free days based on the PESQ-P or PESQ-C as a secondary endpoint
03 August 2022	Added long-term extension period; Clarifications and editorial corrections

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

Limitations of the trial such as small numbers of subjects analysed or technical problems leading to unreliable data.

14May2024 - All participants met criteria defined in the protocol as reasons for treatment completion prior to reaching week 160. The study was not ended prematurely due to safety reasons.

Notes: