Clinical trial results:
A Phase 3, Randomized, 3-Part Study to Investigate the Efficacy and Safety of Dupilumab in Adult and Adolescent Patients with Eosinophilic Esophagitis (EoE)

Summary

EudraCT number	2018-000844-25
Trial protocol	DE FR SE GB NL PT BE IT ES
Global end of trial date	07 June 2022

Results information

Result version number	v1 (current)
This version publication date	22 December 2022
First version publication date	22 December 2022

Trial information

Trial identification

Sponsor protocol code	R668-EE-1774

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT03633617
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Regeneron Pharmaceuticals, Inc.
Sponsor organisation address	777 Old Saw Mill River Rd., Tarrytown, NY, United States, 10591
Public contact	Clinical Trials Administrator, Regeneron Pharmaceuticals, Inc., 001 8447346643, clinicaltrials@regeneron.com
Scientific contact	Clinical Trials Administrator, Regeneron Pharmaceuticals, Inc., 001 8447346643, 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-PIP04-19
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	07 June 2022
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	07 June 2022
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The primary objectives of the study by study part are:

Part A: To determine the treatment effect of dupilumab compared with placebo in adult and adolescent patients with EoE after 24 weeks of treatment as assessed by histological and clinical measures and to inform/confirm the final sample size determination for Part B. (Participants enrolled in Part A may not participate in Part B)
Part B: To demonstrate the efficacy of dupilumab treatment compared with placebo in adult and adolescent patients with EoE after 24 weeks of treatment as assessed by histological and clinical measures.
Part C: To assess the safety and efficacy of dupilumab treatment in adult and adolescent patients with EoE after up to 52 weeks of treatment as assessed by histological and clinical measures.

Protection of trial subjects:

It is the responsibility of both the sponsor and the investigators 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 International Council for Harmonisation (ICH) guidelines for Good Clinical Practice (GCP) and applicable regulatory requirements.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	24 September 2018
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	Yes

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Australia: 10
Country: Number of subjects enrolled	Belgium: 3
Country: Number of subjects enrolled	Canada: 9
Country: Number of subjects enrolled	Germany: 3
Country: Number of subjects enrolled	Spain: 9
Country: Number of subjects enrolled	France: 1
Country: Number of subjects enrolled	United Kingdom: 2
Country: Number of subjects enrolled	Italy: 7
Country: Number of subjects enrolled	Netherlands: 4
Country: Number of subjects enrolled	Sweden: 1
Country: Number of subjects enrolled	United States: 272
Worldwide total number of subjects	321
EEA total number of subjects	28

Notes:

Subjects enrolled per age group	
In utero	0
Preterm newborn - gestational age < 37 wk	0
Newborns (0-27 days)	0
Infants and toddlers (28 days-23 months)	0
Children (2-11 years)	0
Adolescents (12-17 years)	99
Adults (18-64 years)	220
From 65 to 84 years	2
85 years and over	0

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

Part A (24-week double-blind treatment period [DBTP]):157 participants screened, 81 randomized and received at least 1 dose of study drug; Part B (24-week DBTP): 462 participants screened, 240 randomized, 239 received treatment (1 participant randomized to placebo did not meet eligibility criteria and was discontinued prior to being treated).

Period 1

Period 1 title	Double-blind, placebo-controlled
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Double blind
Roles blinded	Subject, Investigator, Data analyst, Assessor, Monitor

Arms

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

Arm description:

Participants received placebo matching dupilumab subcutaneously (SC) during Part A (24-week DBTP). At end of week 24 visit (one-week after last dose of study drug during DBTP), eligible participants from Part A entered into 28-week extended treatment (Part C) and 12-week follow-up. Participants who did not enter into Part C, entered follow-up period.

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

Dosage and administration details:

Placebo matching dupilumab

Arm title	Part A: Dupilumab 300 mg QW

Arm description:

Participants received dupilumab 300 milligrams (mg) SC once per week (QW) during Part A (24-week DBTP). At end of week 24 visit (one-week after last dose of study drug during DBTP), eligible participants from Part A entered into 28-week extended treatment (Part C) and 12-week follow-up. Participants who did not enter into Part C, entered follow-up period.

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

Dosage and administration details:

Dupilumab 300 mg delivered subcutaneously (SC) once weekly (QW)

Arm title	Part B: Placebo

Arm description:

Participants received placebo matching dupilumab SC during Part B (24-week DBTP). At end of week 24 visit (one-week after last dose of study drug during DBTP), eligible participants from Part B entered into 28-week extended treatment (Part C) and 12-week follow-up. Participants who did not enter into Part C, entered follow-up period.

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

Dosage and administration details:

Placebo matching dupilumab

Arm title	Part B: Dupilumab 300 mg Q2W

Arm description:

Participants received dupilumab 300 mg once every 2 weeks (Q2W) SC during Part B (24-week DBTP). At end of week 24 visit (one-week after last dose of study drug during DBTP), eligible participants from Part B entered into 28-week extended treatment (Part C) and 12-week follow-up. Participants who did not enter into Part C, entered follow-up period.

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

Dosage and administration details:

Dupilumab 300 mg delivered subcutaneously (SC) once every 2 weeks (Q2W); a SC injection of placebo was delivered in between dupilumab doses to maintain injection frequency between groups.

Arm title	Part B: Dupilumab 300 mg QW

Arm description:

Participants received dupilumab 300 mg SC once per week (QW) during Part B (24-week DBTP). At end of week 24 visit (one-week after last dose of study drug during DBTP), eligible participants from Part B entered into 28-week extended treatment (Part C) and 12-week follow-up. Participants who did not enter into Part C, entered follow-up period.

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

Dosage and administration details:

Dupilumab 300 mg delivered subcutaneously (SC) once weekly (QW)

Number of subjects in period 1	Part A: Placebo	Part A: Dupilumab 300 mg QW	Part B: Placebo
Started	39	42	79
Completed week 24 (Part A ; Part B)	37	40	74
Completed	37	40	74
Not completed	2	2	5
COVID-19 Restrictions	-	-	1
Consent withdrawn by subject	-	1	1
Physician decision	-	-	-
Adverse event, non-fatal	-	1	2

Unconfirmed early termination visit	1	-	-
Pregnancy	1	-	-
Lost to follow-up	-	-	-
Randomized, but no study drug (did not qualify)	-	-	1

Number of subjects in period 1	Part B: Dupilumab 300 mg Q2W	Part B: Dupilumab 300 mg QW
Started	81	80
Completed week 24 (Part A ; Part B)	79	75
Completed	79	75
Not completed	2	5
COVID-19 Restrictions	-	-
Consent withdrawn by subject	-	2
Physician decision	-	1
Adverse event, non-fatal	2	1
Unconfirmed early termination visit	-	-
Pregnancy	-	-
Lost to follow-up	-	1
Randomized, but no study drug (did not qualify)	-	-

Period 2

Period 2 title	Extended active treatment & follow-up
Is this the baseline period?	No
Allocation method	Randomised - controlled
Blinding used	Double blind
Roles blinded	Subject, Investigator, Monitor, Data analyst, Assessor

Blinding implementation details:

Only participants entering Part C from Part B were blinded to treatment regimen in Part C.

Arms

Are arms mutually exclusive?	Yes
Arm title	Part A/C: Placebo / Dupilumab 300 mg QW

Arm description:

Participants randomized to placebo in Part A, received dupilumab 300 mg QW for 28-week extended treatment (Part C) followed by 12-week follow-up. Participants who did not enter into Part C, entered follow-up.

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

Dosage and administration details:

Dupilumab 300 mg delivered subcutaneously (SC) once weekly (QW)

Arm title	Part A/C: Dupilumab 300 mg QW / Dupilumab 300 mg QW

Arm description:

Participants randomized to dupilumab 300 mg QW in Part A continued to receive the same regimen for 28-week extended treatment (Part C) followed by 12-week follow-up. Participants who did not enter into Part C, entered follow-up.

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

Dosage and administration details:

Dupilumab 300 mg delivered subcutaneously (SC) once weekly (QW)

Arm title	Part B/C: Placebo / Dupilumab 300 mg Q2W

Arm description:

Participants randomized to placebo in Part B were re-randomized in a 1:1 ratio to receive dupilumab 300 mg Q2W for 28-week extended treatment (Part C) followed by 12-week follow-up. Participants who did not enter into Part C, entered follow-up.

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

Dosage and administration details:

Dupilumab 300 mg delivered subcutaneously (SC) once every 2 weeks (Q2W); a SC injection of placebo was delivered in between dupilumab doses to maintain injection frequency between groups.

Arm title	Part B/C: Placebo / Dupilumab 300 mg QW

Arm description:

Participants randomized to placebo in Part B were re-randomized in a 1:1 ratio to receive dupilumab 300 mg QW for 28-week extended treatment (Part C) followed by 12-week follow-up. Participants who did not enter into Part C, entered follow-up.

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

Dosage and administration details:

Dupilumab 300 mg delivered subcutaneously (SC) once weekly (QW)

Arm title	Part B/C: Dupilumab 300 mg Q2W / Dupilumab 300 mg Q2W

Arm description:

Participants randomized to dupilumab 300 mg Q2W in Part B continued to receive the same regimen for 28-week extended treatment (Part C) followed by 12-week follow-up. Participants who did not enter into Part C, entered follow-up.

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

Dosage and administration details:

Dupilumab 300 mg delivered subcutaneously (SC) once every 2 weeks (Q2W); a SC injection of placebo

was delivered in between dupilumab doses to maintain injection frequency between groups.

Arm title	Part B/C: Dupilumab 300 mg QW / Dupilumab 300 mg QW

Arm description:

Participants randomized to dupilumab 300 mg QW during Part B, continued to receive the same regimen for 28-week extended treatment (Part C) followed by 12-week follow-up. Participants who did not enter into Part C, entered follow-up.

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

Dosage and administration details:

Dupilumab 300 mg delivered subcutaneously (SC) once weekly (QW)

Number of subjects in period 2[1]	Part A/C: Placebo / Dupilumab 300 mg QW	Part A/C: Dupilumab 300 mg QW / Dupilumab 300 mg QW	Part B/C: Placebo / Dupilumab 300 mg Q2W
Started	37	40	37
Completed week 52 treatment (Part C)	32	38	34
Completed	30	35	33
Not completed	7	5	4
Consent withdrawn by subject	2	2	-
Physician decision	-	-	1
Adverse event, non-fatal	1	-	1
Pregnancy	-	-	-
COVID-19 related	1	-	-
Lost to follow-up	3	3	1
Lack of efficacy	-	-	1
Protocol deviation	-	-	-

Number of subjects in period 2[1]	Part B/C: Placebo / Dupilumab 300 mg QW	Part B/C: Dupilumab 300 mg Q2W / Dupilumab 300 mg Q2W	Part B/C: Dupilumab 300 mg QW / Dupilumab 300 mg QW
Started	37	79	74
Completed week 52 treatment (Part C)	36	74	65
Completed	36	67	64
Not completed	1	12	10
Consent withdrawn by subject	1	1	6
Physician decision	-	-	1

Adverse event, non-fatal	-	-	-
Pregnancy	-	1	-
COVID-19 related	-	-	-
Lost to follow-up	-	7	2
Lack of efficacy	-	-	-
Protocol deviation	-	3	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: One participant's week 24 visit in Part A was delayed due to COVID-19; afterwards, participant moved to Part C

Baseline characteristics

Reporting groups	
Reporting group title	Part A: Placebo
Reporting group description:	
Participants received placebo matching dupilumab subcutaneously (SC) during Part A (24-week DBTP). At end of week 24 visit (one-week after last dose of study drug during DBTP), eligible participants from Part A entered into 28-week extended treatment (Part C) and 12-week follow-up. Participants who did not enter into Part C, entered follow-up period.	
Reporting group title	Part A: Dupilumab 300 mg QW
Reporting group description:	
Participants received dupilumab 300 milligrams (mg) SC once per week (QW) during Part A (24-week DBTP). At end of week 24 visit (one-week after last dose of study drug during DBTP), eligible participants from Part A entered into 28-week extended treatment (Part C) and 12-week follow-up. Participants who did not enter into Part C, entered follow-up period.	
Reporting group title	Part B: Placebo
Reporting group description:	
Participants received placebo matching dupilumab SC during Part B (24-week DBTP). At end of week 24 visit (one-week after last dose of study drug during DBTP), eligible participants from Part B entered into 28-week extended treatment (Part C) and 12-week follow-up. Participants who did not enter into Part C, entered follow-up period.	
Reporting group title	Part B: Dupilumab 300 mg Q2W
Reporting group description:	
Participants received dupilumab 300 mg once every 2 weeks (Q2W) SC during Part B (24-week DBTP). At end of week 24 visit (one-week after last dose of study drug during DBTP), eligible participants from Part B entered into 28-week extended treatment (Part C) and 12-week follow-up. Participants who did not enter into Part C, entered follow-up period.	
Reporting group title	Part B: Dupilumab 300 mg QW
Reporting group description:	
Participants received dupilumab 300 mg SC once per week (QW) during Part B (24-week DBTP). At end of week 24 visit (one-week after last dose of study drug during DBTP), eligible participants from Part B entered into 28-week extended treatment (Part C) and 12-week follow-up. Participants who did not enter into Part C, entered follow-up period.	

Reporting group values	Part A: Placebo	Part A: Dupilumab 300 mg QW	Part B: Placebo
Number of subjects	39	42	79
Age Categorical			
Age			
Units: Participants			
≥ 12 to < 18 years old	9	11	26
≥ 18 to < 40 years old	22	13	38
≥ 40 to < 65 years old	8	18	15
≥ 65 years old	0	0	0
Sex: Female, Male Units: Participants			
Female	18	14	21
Male	21	28	58
Ethnicity (NIH/OMB) Units: Subjects			
Hispanic or Latino	1	4	5
Not Hispanic or Latino	38	38	74
Unknown or Not Reported	0	0	0
Race/Ethnicity, Customized			

Race			
Units: Subjects			
White	37	41	72
Black or African American	1	1	3
Asian	0	0	1
Other	1	0	2
Not reported	0	0	1
Dysphagia Symptom Questionnaire (DSQ) Total Score			
The DSQ is used to measure the frequency and intensity of dysphagia. DSQ scores can range from 0 to 84, with a lower score indicating less-frequent or less-severe dysphagia.			
Units: Score on a Scale			
arithmetic mean	35.1	32.2	36.1
standard deviation	± 12.11	± 12.66	± 10.55
Peak Eosinophils (eos) Count of Three Regions per High-power Field (/hpf)			
Units: Eosinophils/high-power field (eos/hpf)			
arithmetic mean	96.5	82.6	84.3
standard deviation	± 54.69	± 41.02	± 41.20
Eosinophilic Esophagitis (EoE) Histological Grade Calculated Mean Score (0 - 3)			
Severity (grade) and extent (stage) of esophageal abnormalities were scored by blinded, central pathologists using a 4-point scale (0 normal; 3 maximum change) for eight features: eosinophil density, basal zone hyperplasia, eosinophil abscesses, eosinophil surface layering, dilated intercellular spaces, surface epithelial alteration, dyskeratotic epithelial cells and lamina propria fibrosis (absent/present). Higher score indicates greater severity and extent of histological abnormalities.			
Units: Score on a Scale			
arithmetic mean	1.324	1.260	1.226
standard deviation	± 0.4676	± 0.4088	± 0.3996
Eosinophilic Esophagitis (EoE) Histological Stage Calculated Mean Score (0 - 3)			
Severity (grade) and extent (stage) of esophageal abnormalities were scored by blinded, central pathologists using a 4-point scale (0 normal; 3 maximum change) for eight features: eosinophil density, basal zone hyperplasia, eosinophil abscesses, eosinophil surface layering, dilated intercellular spaces, surface epithelial alteration, dyskeratotic epithelial cells and lamina propria fibrosis (absent/present). Higher score indicates greater severity and extent of histological abnormalities.			
Units: Score on a Scale			
arithmetic mean	1.376	1.299	1.216
standard deviation	± 0.3972	± 0.3334	± 0.3608

Reporting group values	Part B: Dupilumab 300 mg Q2W	Part B: Dupilumab 300 mg QW	Total
Number of subjects	81	80	321
Age Categorical			
Age			
Units: Participants			
≥ 12 to < 18 years old	27	26	99
≥ 18 to < 40 years old	35	38	146
≥ 40 to < 65 years old	18	15	74
≥ 65 years old	1	1	2
Sex: Female, Male			
Units: Participants			
Female	36	30	119
Male	45	50	202

Ethnicity (NIH/OMB) Units: Subjects			
Hispanic or Latino	3	5	18
Not Hispanic or Latino	77	75	302
Unknown or Not Reported	1	0	1
Race/Ethnicity, Customized			
Race			
Units: Subjects			
White	74	71	295
Black or African American	3	2	10
Asian	1	3	5
Other	2	3	8
Not reported	1	1	3
Dysphagia Symptom Questionnaire (DSQ) Total Score			
The DSQ is used to measure the frequency and intensity of dysphagia. DSQ scores can range from 0 to 84, with a lower score indicating less-frequent or less-severe dysphagia.			
Units: Score on a Scale			
arithmetic mean	35.6	38.4	
standard deviation	± 12.24	± 10.70	-
Peak Eosinophils (eos) Count of Three Regions per High-power Field (/hpf) Units: Eosinophils/high-power field (eos/hpf)			
arithmetic mean	87.7	89.2	
standard deviation	± 49.37	± 46.67	-
Eosinophilic Esophagitis (EoE) Histological Grade Calculated Mean Score (0 - 3)			
Severity (grade) and extent (stage) of esophageal abnormalities were scored by blinded, central pathologists using a 4-point scale (0 normal; 3 maximum change) for eight features: eosinophil density, basal zone hyperplasia, eosinophil abscesses, eosinophil surface layering, dilated intercellular spaces, surface epithelial alteration, dyskeratotic epithelial cells and lamina propria fibrosis (absent/present). Higher score indicates greater severity and extent of histological abnormalities.			
Units: Score on a Scale			
arithmetic mean	1.245	1.305	
standard deviation	± 0.3721	± 0.3882	-
Eosinophilic Esophagitis (EoE) Histological Stage Calculated Mean Score (0 - 3)			
Severity (grade) and extent (stage) of esophageal abnormalities were scored by blinded, central pathologists using a 4-point scale (0 normal; 3 maximum change) for eight features: eosinophil density, basal zone hyperplasia, eosinophil abscesses, eosinophil surface layering, dilated intercellular spaces, surface epithelial alteration, dyskeratotic epithelial cells and lamina propria fibrosis (absent/present). Higher score indicates greater severity and extent of histological abnormalities.			
Units: Score on a Scale			
arithmetic mean	1.248	1.294	
standard deviation	± 0.3182	± 0.3256	-

End points

End points reporting groups

Reporting group title	Part A: Placebo
Reporting group description:	
Participants received placebo matching dupilumab subcutaneously (SC) during Part A (24-week DBTP). At end of week 24 visit (one-week after last dose of study drug during DBTP), eligible participants from Part A entered into 28-week extended treatment (Part C) and 12-week follow-up. Participants who did not enter into Part C, entered follow-up period.	
Reporting group title	Part A: Dupilumab 300 mg QW
Reporting group description:	
Participants received dupilumab 300 milligrams (mg) SC once per week (QW) during Part A (24-week DBTP). At end of week 24 visit (one-week after last dose of study drug during DBTP), eligible participants from Part A entered into 28-week extended treatment (Part C) and 12-week follow-up. Participants who did not enter into Part C, entered follow-up period.	
Reporting group title	Part B: Placebo
Reporting group description:	
Participants received placebo matching dupilumab SC during Part B (24-week DBTP). At end of week 24 visit (one-week after last dose of study drug during DBTP), eligible participants from Part B entered into 28-week extended treatment (Part C) and 12-week follow-up. Participants who did not enter into Part C, entered follow-up period.	
Reporting group title	Part B: Dupilumab 300 mg Q2W
Reporting group description:	
Participants received dupilumab 300 mg once every 2 weeks (Q2W) SC during Part B (24-week DBTP). At end of week 24 visit (one-week after last dose of study drug during DBTP), eligible participants from Part B entered into 28-week extended treatment (Part C) and 12-week follow-up. Participants who did not enter into Part C, entered follow-up period.	
Reporting group title	Part B: Dupilumab 300 mg QW
Reporting group description:	
Participants received dupilumab 300 mg SC once per week (QW) during Part B (24-week DBTP). At end of week 24 visit (one-week after last dose of study drug during DBTP), eligible participants from Part B entered into 28-week extended treatment (Part C) and 12-week follow-up. Participants who did not enter into Part C, entered follow-up period.	
Reporting group title	Part A/C: Placebo / Dupilumab 300 mg QW
Reporting group description:	
Participants randomized to placebo in Part A, received dupilumab 300 mg QW for 28-week extended treatment (Part C) followed by 12-week follow-up. Participants who did not enter into Part C, entered follow-up.	
Reporting group title	Part A/C: Dupilumab 300 mg QW / Dupilumab 300 mg QW
Reporting group description:	
Participants randomized to dupilumab 300 mg QW in Part A continued to receive the same regimen for 28-week extended treatment (Part C) followed by 12-week follow-up. Participants who did not enter into Part C, entered follow-up.	
Reporting group title	Part B/C: Placebo / Dupilumab 300 mg Q2W
Reporting group description:	
Participants randomized to placebo in Part B were re-randomized in a 1:1 ratio to receive dupilumab 300 mg Q2W for 28-week extended treatment (Part C) followed by 12-week follow-up. Participants who did not enter into Part C, entered follow-up.	
Reporting group title	Part B/C: Placebo / Dupilumab 300 mg QW
Reporting group description:	
Participants randomized to placebo in Part B were re-randomized in a 1:1 ratio to receive dupilumab 300 mg QW for 28-week extended treatment (Part C) followed by 12-week follow-up. Participants who did not enter into Part C, entered follow-up.	
Reporting group title	Part B/C: Dupilumab 300 mg Q2W / Dupilumab 300 mg Q2W
Reporting group description:	
Participants randomized to dupilumab 300 mg Q2W in Part B continued to receive the same regimen for 28-week extended treatment (Part C) followed by 12-week follow-up. Participants who did not enter into Part C, entered follow-up.	

Reporting group title	Part B/C: Dupilumab 300 mg QW / Dupilumab 300 mg QW

Reporting group description:

Participants randomized to dupilumab 300 mg QW during Part B, continued to receive the same regimen for 28-week extended treatment (Part C) followed by 12-week follow-up. Participants who did not enter into Part C, entered follow-up.

Primary: Percentage of participants achieving peak esophageal intraepithelial eosinophil count of ≤6 eosinophils per high-power field (eos/hpf) in all three regions at week 24

End point title	Percentage of participants achieving peak esophageal intraepithelial eosinophil count of ≤6 eosinophils per high-power field (eos/hpf) in all three regions at week 24

End point description:

Esophageal intraepithelial eosinophil count obtained by esophageal endoscopy with biopsies (all 3 esophageal regions: proximal, mid, and distal). Part A Full Analysis Set (FAS): All participants randomized to Part A (Participants considered non-responder after rescue treatment use and multiple imputation (MI) method for missing due to COVID-19; Participants considered non-responder for missing not due to COVID-19); Part B FAS: All participants randomized to Part B (Participants considered non-responder after rescue treatment use or missing not due to COVID-19 and MI method for missing or dosing interruption due to COVID-19)

End point type	Primary

End point timeframe:

At week 24

End point values	Part A: Placebo	Part A: Dupilumab 300 mg QW	Part B: Placebo	Part B: Dupilumab 300 mg Q2W
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	39	42	79	81
Units: Percentage of Participants				
number (confidence interval 95%)	5.1 (0.63 to 17.32)	59.5 (43.28 to 74.37)	6.3 (2.09 to 14.16)	60.5 (49.01 to 71.19)

End point values	Part B: Dupilumab 300 mg QW			
Subject group type	Reporting group			
Number of subjects analysed	80			
Units: Percentage of Participants				
number (confidence interval 95%)	58.8 (47.18 to 69.65)			

Statistical analyses

Statistical analysis title	Part A: Placebo, Part A: Dupilumab 300 mg SC QW

Statistical analysis description:

Difference is dupilumab minus placebo

Comparison groups	Part A: Placebo v Part A: Dupilumab 300 mg QW
Number of subjects included in analysis	81
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.0001
Method	Cochran-Mantel-Haenszel
Parameter estimate	Difference in proportion
Point estimate	55.3
Confidence interval	
level	95 %
sides	2-sided
lower limit	39.58
upper limit	71.04

Statistical analysis title	Part B: Placebo, Part B: Dupilumab 300 mg SC Q2W
Statistical analysis description: Difference is dupilumab minus placebo	
Comparison groups	Part B: Placebo v Part B: Dupilumab 300 mg Q2W
Number of subjects included in analysis	160
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.0001
Method	Cochran-Mantel-Haenszel
Parameter estimate	Difference in proportion
Point estimate	56
Confidence interval	
level	95 %
sides	2-sided
lower limit	43.44
upper limit	68.54

Statistical analysis title	Part B: Placebo, Part B: Dupilumab 300 mg SC QW
Statistical analysis description: Difference is dupilumab minus placebo	
Comparison groups	Part B: Placebo v Part B: Dupilumab 300 mg QW
Number of subjects included in analysis	159
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.0001
Method	Cochran-Mantel-Haenszel
Parameter estimate	Difference in proportion
Point estimate	53.5

Confidence interval	
level	95 %
sides	2-sided
lower limit	41.2
upper limit	65.79

Primary: Absolute change from baseline in Dysphagia Symptom Questionnaire (DSQ) total score at week 24

End point title	Absolute change from baseline in Dysphagia Symptom Questionnaire (DSQ) total score at week 24

End point description:

The DSQ is used to measure the frequency and intensity of dysphagia. DSQ scores can range from 0 to 84, with a lower score indicating less-frequent or less-severe dysphagia. Part A Full Analysis Set (FAS): All participant randomized to Part A (MI method for missing data or data set to missing after rescue treatment use); Part B FAS: All participants randomized to Part B (MI method for missing data or data set to missing after rescue treatment use)

End point type	Primary

End point timeframe:

Baseline and week 24

End point values	Part A: Placebo	Part A: Dupilumab 300 mg QW	Part B: Placebo	Part B: Dupilumab 300 mg Q2W
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	39	42	79	81
Units: Score on a Scale				
least squares mean (confidence interval 95%)	-9.60 (-15.056 to -4.136)	-21.92 (-26.870 to -16.967)	-13.86 (-17.605 to -10.120)	-14.37 (-18.018 to -10.723)

End point values	Part B: Dupilumab 300 mg QW			
Subject group type	Reporting group			
Number of subjects analysed	80			
Units: Score on a Scale				
least squares mean (confidence interval 95%)	-23.78 (-27.427 to -20.131)			

Statistical analyses

Statistical analysis title	Part A: Placebo, Part A: Dupilumab 300 mg SC QW

Statistical analysis description:

Dupilumab group vs. Placebo

Comparison groups	Part A: Placebo v Part A: Dupilumab 300 mg QW
Number of subjects included in analysis	81
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.0004
Method	ANCOVA
Parameter estimate	LS Mean Difference
Point estimate	-12.32
Confidence interval	
level	95 %
sides	2-sided
lower limit	-19.107
upper limit	-5.537

Statistical analysis title	Part B: Placebo, Part B: Dupilumab 300 mg SC QW
Statistical analysis description: Dupilumab group vs. Placebo	
Comparison groups	Part B: Placebo v Part B: Dupilumab 300 mg QW
Number of subjects included in analysis	159
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.0001
Method	ANCOVA
Parameter estimate	LS Mean Difference
Point estimate	-9.92
Confidence interval	
level	95 %
sides	2-sided
lower limit	-14.811
upper limit	-5.022

Statistical analysis title	Part B: Placebo, Part B: Dupilumab 300 mg SC Q2W
Statistical analysis description: Dupilumab group vs. Placebo	
Comparison groups	Part B: Placebo v Part B: Dupilumab 300 mg Q2W
Number of subjects included in analysis	160
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.8393
Method	ANCOVA
Parameter estimate	LS Mean Difference
Point estimate	-0.51

Confidence interval	
level	95 %
sides	2-sided
lower limit	-5.423
upper limit	4.406

Secondary: Percent change from baseline in peak esophageal intraepithelial eosinophil count (eos/hpf) in all three regions at week 24

End point title	Percent change from baseline in peak esophageal intraepithelial eosinophil count (eos/hpf) in all three regions at week 24

End point description:

Esophageal intraepithelial eosinophil count obtained by esophageal endoscopy with biopsies (all 3 esophageal regions: proximal, mid, and distal). A greater esophageal intraepithelial eosinophil count from baseline indicates worsening disease. Part A FAS (Worst-observation carried forward [WOCF]-MI method with WOCF for rescue treatment use and missing not due to COVID-19; MI method for missing due to COVID-19); Part B FAS (WOCF-MI method with WOCF for rescue treatment use and missing not due to COVID-19 and MI method for missing or dosing interruption due to COVID-19)

End point type	Secondary

End point timeframe:

Baseline and week 24

End point values	Part A: Placebo	Part A: Dupilumab 300 mg QW	Part B: Placebo	Part B: Dupilumab 300 mg Q2W
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	39	42	79	81
Units: Percentage of Change				
least squares mean (confidence interval 95%)	-2.98 (-17.886 to 11.921)	-71.24 (-84.863 to -57.613)	8.38 (-11.677 to 28.433)	-70.84 (-87.095 to -54.585)

End point values	Part B: Dupilumab 300 mg QW			
Subject group type	Reporting group			
Number of subjects analysed	80			
Units: Percentage of Change				
least squares mean (confidence interval 95%)	-80.24 (-96.589 to -63.895)			

Statistical analyses

Statistical analysis title	Part A: Placebo; Part A: Dupilumab 300 mg QW

Statistical analysis description:

Dupilumab 300 mg QW vs Placebo

Comparison groups	Part A: Placebo v Part A: Dupilumab 300 mg QW
Number of subjects included in analysis	81
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.0001
Method	ANCOVA
Parameter estimate	LS Mean Difference
Point estimate	-68.26
Confidence interval	
level	95 %
sides	2-sided
lower limit	-86.896
upper limit	-49.615

Statistical analysis title	Part B: Placebo, Part B: Dupilumab 300 mg SC QW
Statistical analysis description: Dupilumab 300 mg QW vs Placebo	
Comparison groups	Part B: Placebo v Part B: Dupilumab 300 mg QW
Number of subjects included in analysis	159
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.0001
Method	ANCOVA
Parameter estimate	LS Mean Difference
Point estimate	-88.62
Confidence interval	
level	95 %
sides	2-sided
lower limit	-112.194
upper limit	-65.046

Statistical analysis title	Part B: Placebo, Part B: Dupilumab 300 mg SC Q2W
Statistical analysis description: Dupilumab 300 mg Q2W vs Placebo	
Comparison groups	Part B: Placebo v Part B: Dupilumab 300 mg Q2W
Number of subjects included in analysis	160
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.0001
Method	ANCOVA
Parameter estimate	LS Mean Difference
Point estimate	-79.22

Confidence interval	
level	95 %
sides	2-sided
lower limit	-103.098
upper limit	-55.338

Secondary: Percent change from baseline in DSQ total score at week 24

End point title	Percent change from baseline in DSQ total score at week 24

End point description:

The DSQ is used to measure the frequency and intensity of dysphagia. DSQ scores can range from 0 to 84, with a lower score indicating less-frequent or less-severe dysphagia. Part A FAS (MI method for missing data or data set to missing after rescue treatment use); Part B FAS (MI method for missing data or data set to missing after rescue treatment use)

End point type	Secondary

End point timeframe:

Baseline and week 24

End point values	Part A: Placebo	Part A: Dupilumab 300 mg QW	Part B: Placebo	Part B: Dupilumab 300 mg Q2W
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	39	42	79	81
Units: Percentage of Change				
least squares mean (confidence interval 95%)	-31.68 (-47.545 to -15.818)	-69.17 (-83.578 to -54.752)	-41.43 (-51.749 to -31.116)	-45.78 (-55.658 to -35.904)

End point values	Part B: Dupilumab 300 mg QW			
Subject group type	Reporting group			
Number of subjects analysed	80			
Units: Percentage of Change				
least squares mean (confidence interval 95%)	-64.32 (-74.267 to 54.382)			

Statistical analyses

Statistical analysis title	Part A: Placebo, Part A: Dupilumab 300 mg SC QW

Statistical analysis description:

Dupilumab 300 mg QW vs Placebo

Comparison groups	Part A: Placebo v Part A: Dupilumab 300 mg QW

Number of subjects included in analysis	81
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.0002
Method	ANCOVA
Parameter estimate	LS Mean Difference
Point estimate	-37.48
Confidence interval	
level	95 %
sides	2-sided
lower limit	-57.222
upper limit	-17.745

Statistical analysis title	Part B: Placebo, Part B: Dupilumab 300 mg SC Q2W
Statistical analysis description: Dupilumab 300 mg Q2W vs Placebo	
Comparison groups	Part B: Placebo v Part B: Dupilumab 300 mg Q2W
Number of subjects included in analysis	160
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.5243
Method	ANCOVA
Parameter estimate	LS Mean Difference
Point estimate	-4.35
Confidence interval	
level	95 %
sides	2-sided
lower limit	-17.734
upper limit	9.038

Statistical analysis title	Part B: Placebo, Part B: Dupilumab 300 mg SC QW
Statistical analysis description: Dupilumab 300 mg QW vs Placebo	
Comparison groups	Part B: Placebo v Part B: Dupilumab 300 mg QW
Number of subjects included in analysis	159
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.0008
Method	ANCOVA
Parameter estimate	LS Mean Difference
Point estimate	-22.89
Confidence interval	
level	95 %
sides	2-sided
lower limit	-36.272
upper limit	-9.513

Secondary: Absolute change from baseline in Eosinophilic Esophagitis Histology Scoring System (EoEHSS) mean Grade score at week 24

End point title	Absolute change from baseline in Eosinophilic Esophagitis Histology Scoring System (EoEHSS) mean Grade score at week 24

End point description:

Severity (grade) and extent (stage) of esophageal abnormalities were scored by blinded, central pathologists using a 4-point scale (0 normal; 3 maximum change) for eight features: eosinophil density, basal zone hyperplasia, eosinophil abscesses, eosinophil surface layering, dilated intercellular spaces, surface epithelial alteration, dyskeratotic epithelial cells and lamina propria fibrosis (absent/present). Higher score indicates greater severity and extent of histological abnormalities. Part A FAS (WOCF-MI method with WOCF for rescue treatment use and missing not due to COVID-19; MI method for missing due to COVID-19); Part B FAS (WOCF-MI method with WOCF for rescue treatment use and missing not due to COVID-19 and MI method for missing or dosing interruption due to COVID-19)

End point type	Secondary

End point timeframe:

Baseline and week 24

End point values	Part A: Placebo	Part A: Dupilumab 300 mg QW	Part B: Placebo	Part B: Dupilumab 300 mg Q2W
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	39	42	79	81
Units: Score on a Scale				
least squares mean (confidence interval 95%)	-0.001 (-0.1166 to 0.1139)	-0.761 (-0.8732 to -0.6484)	-0.148 (-0.2379 to -0.0584)	-0.814 (-0.8958 to -0.7317)

End point values	Part B: Dupilumab 300 mg QW			
Subject group type	Reporting group			
Number of subjects analysed	80			
Units: Score on a Scale				
least squares mean (confidence interval 95%)	-0.830 (-0.9136 to -0.7463)			

Statistical analyses

Statistical analysis title	Part A: Placebo, Part A: Dupilumab 300 mg SC QW

Statistical analysis description:

Dupilumab 300 mg QW vs Placebo

Comparison groups	Part A: Placebo v Part A: Dupilumab 300 mg QW

Number of subjects included in analysis	81
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.0001
Method	ANCOVA
Parameter estimate	LS Mean Difference
Point estimate	-0.759
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.9061
upper limit	-0.6127

Statistical analysis title	Part B: Placebo, Part B: Dupilumab 300 mg SC QW
Statistical analysis description: Dupilumab 300 mg QW vs Placebo	
Comparison groups	Part B: Placebo v Part B: Dupilumab 300 mg QW
Number of subjects included in analysis	159
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.0001
Method	ANCOVA
Parameter estimate	LS Mean Difference
Point estimate	-0.682
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.7929
upper limit	-0.5707

Statistical analysis title	Part B: Placebo, Part B: Dupilumab 300 mg SC Q2W
Statistical analysis description: Dupilumab 300 mg Q2W vs Placebo	
Comparison groups	Part B: Placebo v Part B: Dupilumab 300 mg Q2W
Number of subjects included in analysis	160
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.0001
Method	ANCOVA
Parameter estimate	LS Mean Difference
Point estimate	-0.666
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.7773
upper limit	-0.5538

Secondary: Absolute change from baseline in EoEHSS mean Stage score at week 24

End point title	Absolute change from baseline in EoEHSS mean Stage score at week 24

End point description:

Severity (grade) and extent (stage) of esophageal abnormalities were scored by blinded, central pathologists using a 4-point scale (0 normal; 3 maximum change) for eight features: eosinophil density, basal zone hyperplasia, eosinophil abscesses, eosinophil surface layering, dilated intercellular spaces, surface epithelial alteration, dyskeratotic epithelial cells and lamina propria fibrosis (absent/present). Higher score indicates greater severity and extent of histological abnormalities. Part A FAS (WOCF-MI method with WOCF for rescue treatment use and missing not due to COVID-19; MI method for missing due to COVID-19); Part B FAS (WOCF-MI Method with WOCF for Rescue Treatment Use and Missing Not Due to COVID-19 and MI Method for Missing or Dosing Interruption Due to COVID-19)

End point type	Secondary

End point timeframe:

Baseline and week 24

End point values	Part A: Placebo	Part A: Dupilumab 300 mg QW	Part B: Placebo	Part B: Dupilumab 300 mg Q2W
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	39	42	79	81
Units: Score on a Scale				
least squares mean (confidence interval 95%)	-0.012 (-0.1243 to 0.0995)	-0.753 (-0.8627 to -0.6441)	-0.132 (-0.2179 to -0.0464)	-0.793 (-0.8713 to -0.7144)

End point values	Part B: Dupilumab 300 mg QW			
Subject group type	Reporting group			
Number of subjects analysed	80			
Units: Score on a Scale				
least squares mean (confidence interval 95%)	-0.804 (-0.8839 to -0.7237)			

Statistical analyses

Statistical analysis title	Part A: Placebo, Part A: Dupilumab 300 mg SC QW

Statistical analysis description:

Dupilumab 300 mg QW vs Placebo

Comparison groups	Part A: Placebo v Part A: Dupilumab 300 mg QW

Number of subjects included in analysis	81
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.0001
Method	ANCOVA
Parameter estimate	LS Mean Difference
Point estimate	-0.741
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.8842
upper limit	-0.5978

Statistical analysis title	Part B: Placebo, Part B: Dupilumab 300 mg SC QW
Statistical analysis description: Dupilumab 300 mg QW vs Placebo	
Comparison groups	Part B: Placebo v Part B: Dupilumab 300 mg QW
Number of subjects included in analysis	159
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.0001
Method	ANCOVA
Parameter estimate	LS Mean Difference
Point estimate	-0.672
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.7778
upper limit	-0.5655

Statistical analysis title	Part B: Placebo, Part B: Dupilumab 300 mg SC Q2W
Statistical analysis description: Dupilumab 300 mg Q2W vs Placebo	
Comparison groups	Part B: Placebo v Part B: Dupilumab 300 mg Q2W
Number of subjects included in analysis	160
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.0001
Method	ANCOVA
Parameter estimate	LS Mean Difference
Point estimate	-0.661
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.7674
upper limit	-0.554

Secondary: Absolute change from baseline in EoE Endoscopic Reference total Score (EoE-EREFS) at week 24

End point title	Absolute change from baseline in EoE Endoscopic Reference total Score (EoE-EREFS) at week 24

End point description:

EoE esophageal characteristics analyzed based on the EoE-EREFS, a scoring system for inflammatory and remodeling features of disease. The overall total score ranges from 0 to 18 with higher number indicating worse disease. Part A FAS (WOCF-MI method with WOCF for rescue treatment use and missing not due to COVID-19; MI method for missing due to COVID-19); Part B FAS (WOCF-MI Method with WOCF for Rescue Treatment Use and Missing Not Due to COVID-19 and MI Method for Missing or Dosing Interruption Due to COVID-19)

End point type	Secondary

End point timeframe:

Baseline and week 24

End point values	Part A: Placebo	Part A: Dupilumab 300 mg QW	Part B: Placebo	Part B: Dupilumab 300 mg Q2W
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	39	42	79	81
Units: Score on a Scale				
least squares mean (confidence interval 95%)	-0.3 (-1.11 to 0.50)	-3.2 (-3.98 to -2.38)	-0.6 (-1.37 to 0.12)	-4.6 (-5.24 to -3.89)

End point values	Part B: Dupilumab 300 mg QW			
Subject group type	Reporting group			
Number of subjects analysed	80			
Units: Score on a Scale				
least squares mean (confidence interval 95%)	-4.5 (-5.17 to -3.77)			

Statistical analyses

Statistical analysis title	Part A: Placebo, Part A: Dupilumab 300 mg SC QW

Statistical analysis description:

Dupilumab 300 mg QW vs Placebo

Comparison groups	Part A: Placebo v Part A: Dupilumab 300 mg QW

Number of subjects included in analysis	81
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.0001
Method	ANCOVA
Parameter estimate	LS Mean Difference
Point estimate	-2.9
Confidence interval	
level	95 %
sides	2-sided
lower limit	-3.91
upper limit	-1.84

Statistical analysis title	Part B: Placebo, Part B: Dupilumab 300 mg SC QW
Statistical analysis description: Dupilumab 300 mg QW vs Placebo	
Comparison groups	Part B: Placebo v Part B: Dupilumab 300 mg QW
Number of subjects included in analysis	159
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.0001
Method	ANCOVA
Parameter estimate	LS Mean Difference
Point estimate	-3.8
Confidence interval	
level	95 %
sides	2-sided
lower limit	-4.77
upper limit	-2.93

Statistical analysis title	Part B: Placebo, Part B: Dupilumab 300 mg SC Q2W
Statistical analysis description: Dupilumab 300 mg Q2W vs Placebo	
Comparison groups	Part B: Placebo v Part B: Dupilumab 300 mg Q2W
Number of subjects included in analysis	160
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.0001
Method	ANCOVA
Parameter estimate	LS Mean Difference
Point estimate	-3.9
Confidence interval	
level	95 %
sides	2-sided
lower limit	-4.86
upper limit	-3.02

Secondary: Percentage of participants achieving peak esophageal intraepithelial eosinophil count of <15 eos/hpf in all three regions at week 24

End point title	Percentage of participants achieving peak esophageal intraepithelial eosinophil count of <15 eos/hpf in all three regions at week 24

End point description:

Esophageal intraepithelial eosinophil count obtained by esophageal endoscopy with biopsies (all 3 esophageal regions: proximal, mid, and distal). Part A FAS (Participants considered non-responder after rescue treatment use and MI method for missing due to COVID-19; Participants considered non-responder for missing not due to COVID-19); Part B FAS (Participants considered non-responder after rescue treatment use or missing not due to COVID-19 and MI method for missing or dosing interruption due to COVID-19).

End point type	Secondary

End point timeframe:

At week 24

End point values	Part A: Placebo	Part A: Dupilumab 300 mg QW	Part B: Placebo	Part B: Dupilumab 300 mg Q2W
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	39	42	79	81
Units: Percentage of Participants				
number (confidence interval 95%)	7.7 (1.62 to 20.87)	64.3 (48.03 to 78.45)	7.6 (2.84 to 15.80)	79.0 (68.54 to 87.27)

End point values	Part B: Dupilumab 300 mg QW			
Subject group type	Reporting group			
Number of subjects analysed	80			
Units: Percentage of Participants				
number (confidence interval 95%)	82.5 (72.38 to 90.09)			

Statistical analyses

Statistical analysis title	Part A: Placebo, Part A: Dupilumab 300 mg SC QW

Statistical analysis description:

Difference is Dupilumab minus Placebo

Comparison groups	Part A: Placebo v Part A: Dupilumab 300 mg QW

Number of subjects included in analysis	81
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.0001
Method	Cochran-Mantel-Haenszel
Parameter estimate	Difference in proportion
Point estimate	57.5
Confidence interval	
level	95 %
sides	2-sided
lower limit	41.69
upper limit	73.33

Statistical analysis title	Part B: Placebo, Part B: Dupilumab 300 mg SC QW
Statistical analysis description: Difference is Dupilumab minus Placebo	
Comparison groups	Part B: Placebo v Part B: Dupilumab 300 mg QW
Number of subjects included in analysis	159
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.0001
Method	Cochran-Mantel-Haenszel
Parameter estimate	Difference in proportion
Point estimate	74.9
Confidence interval	
level	95 %
sides	2-sided
lower limit	64.25
upper limit	85.5

Statistical analysis title	Part B: Placebo, Part B: Dupilumab 300 mg SC Q2W
Statistical analysis description: Difference is Dupilumab minus Placebo	
Comparison groups	Part B: Placebo v Part B: Dupilumab 300 mg Q2W
Number of subjects included in analysis	160
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.0001
Method	Cochran-Mantel-Haenszel
Parameter estimate	Difference in proportion
Point estimate	72.4
Confidence interval	
level	95 %
sides	2-sided
lower limit	61.05
upper limit	83.7

Secondary: Normalized Enrichment Score (NES) for the relative change from baseline in EoE Diagnostic Panel (EDP) at week 24

End point title	Normalized Enrichment Score (NES) for the relative change from baseline in EoE Diagnostic Panel (EDP) at week 24

End point description:

NES reflects the degree to which the activity level of a set of disease transcripts is overrepresented at the extremes (top or bottom) of the entire ranked list of transcripts within a sample and is normalized by accounting for the number of transcripts in the set. A NES of 0 indicates no change from baseline, a negative score reflects a reduction in the disease score (more like normal) and a positive score reflects worsening (more active disease). Part A FAS (Participants with NES Score in Part A; Last observation carried forward [LOCF] method with data set to missing after rescue treatment use); Part B FAS (Participants with NES Score in Part B; LOCF method with data set to missing after rescue treatment use)

End point type	Secondary

End point timeframe:

Baseline and week 24

End point values	Part A: Placebo	Part A: Dupilumab 300 mg QW	Part B: Placebo	Part B: Dupilumab 300 mg Q2W
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	29	31	41	44
Units: Score on a Scale				
median (not applicable)	-0.160 (± 99999)	-2.660 (± 99999)	-0.730 (± 99999)	-2.675 (± 99999)

End point values	Part B: Dupilumab 300 mg QW			
Subject group type	Reporting group			
Number of subjects analysed	40			
Units: Score on a Scale				
median (not applicable)	-2.665 (± 99999)			

Statistical analyses

Statistical analysis title	Part B:Placebo, Part B:Dupilumab 300 mg SC Q2W

Statistical analysis description:

Median Difference is Dupilumab minus Placebo

Comparison groups	Part B: Placebo v Part B: Dupilumab 300 mg Q2W

Number of subjects included in analysis	85
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.0001
Method	Wilcoxon rank-sum test
Parameter estimate	Hodges-Lehmann estimator
Point estimate	-1.84
Confidence interval	
level	95 %
sides	2-sided
lower limit	-2.42
upper limit	-1.11

Statistical analysis title	Part A: Placebo, Part A: Dupilumab 300 mg SC QW
Statistical analysis description: Median Difference is Dupilumab minus Placebo	
Comparison groups	Part A: Placebo v Part A: Dupilumab 300 mg QW
Number of subjects included in analysis	60
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.0001
Method	Wilcoxon rank-sum test
Parameter estimate	Hodges-Lehmann estimator
Point estimate	-2.25
Confidence interval	
level	95 %
sides	2-sided
lower limit	-2.72
upper limit	-1.73

Statistical analysis title	Part B: Placebo, Part B: Dupilumab 300 mg SC QW
Statistical analysis description: Median Difference is Dupilumab minus Placebo	
Comparison groups	Part B: Placebo v Part B: Dupilumab 300 mg QW
Number of subjects included in analysis	81
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.0001
Method	Wilcoxon rank-sum test
Parameter estimate	Hodges-Lehmann estimator
Point estimate	-1.85
Confidence interval	
level	95 %
sides	2-sided
lower limit	-2.44
upper limit	-1.15

Secondary: NES for the relative change from baseline in type 2 inflammation signature at week 24

End point title	NES for the relative change from baseline in type 2 inflammation signature at week 24

End point description:

NES reflects the degree to which the activity level of a set of disease transcripts is overrepresented at the extremes (top or bottom) of the entire ranked list of transcripts within a sample and is normalized by accounting for the number of transcripts in the set. A NES of 0 indicates no change from baseline, a negative score reflects a reduction in the disease score (more like normal) and a positive score reflects worsening (more active disease). Part A FAS (Participants with NES Score in Part A; LOCF Method with data set to missing after rescue treatment use); Part B FAS (Participants with NES Score in Part B; LOCF method with data set to missing after rescue treatment use)

End point type	Secondary

End point timeframe:

Baseline and week 24

End point values	Part A: Placebo	Part A: Dupilumab 300 mg QW	Part B: Placebo	Part B: Dupilumab 300 mg Q2W
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	29	31	41	44
Units: Score on a Scale				
median (not applicable)	-0.320 (± 99999)	-1.970 (± 99999)	-0.640 (± 99999)	-1.950 (± 99999)

End point values	Part B: Dupilumab 300 mg QW			
Subject group type	Reporting group			
Number of subjects analysed	40			
Units: Score on a Scale				
median (not applicable)	-1.930 (± 99999)			

Statistical analyses

Statistical analysis title	Part A: Placebo, Part A: Dupilumab 300 mg SC QW

Statistical analysis description:

Median Difference is Dupilumab minus Placebo

Comparison groups	Part A: Placebo v Part A: Dupilumab 300 mg QW

Number of subjects included in analysis	60
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.0001
Method	Wilcoxon rank-sum test
Parameter estimate	Hodges-Lehmann estimator
Point estimate	-1.59
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.74
upper limit	-1.27

Statistical analysis title	Part B: Placebo, Part B: Dupilumab 300 mg SC QW
Statistical analysis description: Median Difference is Dupilumab minus Placebo	
Comparison groups	Part B: Placebo v Part B: Dupilumab 300 mg QW
Number of subjects included in analysis	81
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.0001
Method	Wilcoxon rank-sum test
Parameter estimate	Hodges-Lehmann estimator
Point estimate	-1.275
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.82
upper limit	-1.07

Statistical analysis title	Part B:Placebo, Part B:Dupilumab 300 mg SC Q2W
Statistical analysis description: Median Difference is Dupilumab minus Placebo	
Comparison groups	Part B: Placebo v Part B: Dupilumab 300 mg Q2W
Number of subjects included in analysis	85
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.0001
Method	Wilcoxon rank-sum test
Parameter estimate	Hodges-Lehmann estimator
Point estimate	-1.255
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.73
upper limit	-1.05

Secondary: Percentage of participants achieving peak esophageal intraepithelial eosinophil count of ≤1 eos/hpf in all three regions at week 24

End point title	Percentage of participants achieving peak esophageal intraepithelial eosinophil count of ≤1 eos/hpf in all three regions at week 24

End point description:

Esophageal intraepithelial eosinophil count obtained by esophageal endoscopy with biopsies (all 3 esophageal regions: proximal, mid, and distal). Part A FAS (Participants considered non-responder after rescue treatment use and MI method for missing due to COVID-19; Participants considered non-responder for missing not due to COVID-19); Part B FAS (Participants considered non-responder after rescue treatment use or missing not due to COVID-19 and MI method for missing or dosing interruption due to COVID-19)

End point type	Secondary

End point timeframe:

At week 24

End point values	Part A: Placebo	Part A: Dupilumab 300 mg QW	Part B: Placebo	Part B: Dupilumab 300 mg Q2W
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	39	42	79	81
Units: Percentage of Participants				
number (confidence interval 95%)	0.0 (0.00 to 9.03)	21.4 (10.30 to 36.81)	1.3 (0.03 to 6.85)	27.2 (17.87 to 38.19)

End point values	Part B: Dupilumab 300 mg QW			
Subject group type	Reporting group			
Number of subjects analysed	80			
Units: Percentage of Participants				
number (confidence interval 95%)	28.8 (19.18 to 39.95)			

Statistical analyses

Statistical analysis title	Part A: Placebo, Part A: Dupilumab 300 mg SC QW

Statistical analysis description:

Difference is Dupilumab minus Placebo

Comparison groups	Part A: Placebo v Part A: Dupilumab 300 mg QW

Number of subjects included in analysis	81
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.0017
Method	Cochran-Mantel-Haenszel
Parameter estimate	Difference in proportion
Point estimate	21.9
Confidence interval	
level	95 %
sides	2-sided
lower limit	9.42
upper limit	34.38

Statistical analysis title	Part B: Placebo, Part B: Dupilumab 300 mg SC QW
Statistical analysis description: Difference is Dupilumab minus Placebo	
Comparison groups	Part B: Placebo v Part B: Dupilumab 300 mg QW
Number of subjects included in analysis	159
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.0001
Method	Cochran-Mantel-Haenszel
Parameter estimate	Difference in proportion
Point estimate	28.9
Confidence interval	
level	95 %
sides	2-sided
lower limit	18.36
upper limit	39.46

Statistical analysis title	Part B: Placebo, Part B: Dupilumab 300 mg SC Q2W
Statistical analysis description: Difference is Dupilumab minus Placebo	
Comparison groups	Part B: Placebo v Part B: Dupilumab 300 mg Q2W
Number of subjects included in analysis	160
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.0001
Method	Cochran-Mantel-Haenszel
Parameter estimate	Difference in proportion
Point estimate	27.6
Confidence interval	
level	95 %
sides	2-sided
lower limit	17.2
upper limit	38.09

Secondary: Absolute change from baseline in health-related quality of life (QOL) average score as measured by EoE Impact Questionnaire (EoE-IQ) at week 24

End point title	Absolute change from baseline in health-related quality of life (QOL) average score as measured by EoE Impact Questionnaire (EoE-IQ) at week 24

End point description:

The EoE-IQ measures impact of EoE on emotional, social, work & school, & sleep aspects. Participants were asked to respond to 11 questions based on experience living with EoE during past 7 days. Response to each item is on a 5-point scale (1=Not at all [impacted] 2=A little, 3=Somewhat, 4=Quite a bit, 5=Extremely [impacted]). The average score is the sum of non-missing responses divided by the number of items with non-missing responses. The average score can range from 1 to 5; a higher score is indicative of a more negative impact. Part A FAS (MI method with data set to missing after rescue treatment use); Part B FAS (MI method with data set to missing after rescue treatment use)

End point type	Secondary

End point timeframe:

Baseline and week 24

End point values	Part A: Placebo	Part A: Dupilumab 300 mg QW	Part B: Placebo	Part B: Dupilumab 300 mg Q2W
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	39	42	79	81
Units: Score on a Scale				
least squares mean (confidence interval 95%)	-0.246 (-0.4659 to -0.0266)	-0.614 (-0.8140 to -0.4149)	-0.578 (-0.6977 to -0.4585)	-0.593 (-0.7152 to -0.4706)

End point values	Part B: Dupilumab 300 mg QW			
Subject group type	Reporting group			
Number of subjects analysed	80			
Units: Score on a Scale				
least squares mean (confidence interval 95%)	-0.887 (-1.0050 to -0.7685)			

Statistical analyses

Statistical analysis title	Part A: Placebo, Part A: Dupilumab 300 mg SC QW

Statistical analysis description:

Dupilumab group vs Placebo

Comparison groups	Part A: Placebo v Part A: Dupilumab 300 mg QW

Number of subjects included in analysis	81
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.0077
Method	ANCOVA
Parameter estimate	LS Mean Difference
Point estimate	-0.368
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.6388
upper limit	-0.0975

Statistical analysis title	Part B: Placebo, Part B: Dupilumab 300 mg SC QW
Statistical analysis description: Dupilumab group vs. Placebo	
Comparison groups	Part B: Placebo v Part B: Dupilumab 300 mg QW
Number of subjects included in analysis	159
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.0002
Method	ANCOVA
Parameter estimate	LS Mean Difference
Point estimate	-0.309
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.4703
upper limit	-0.1471

Statistical analysis title	Part B: Placebo, Part B: Dupilumab 300 mg SC Q2W
Statistical analysis description: Dupilumab group vs Placebo	
Comparison groups	Part B: Placebo v Part B: Dupilumab 300 mg Q2W
Number of subjects included in analysis	160
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.8586
Method	ANCOVA
Parameter estimate	LS Mean Difference
Point estimate	-0.015
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.1782
upper limit	0.1485

Secondary: Absolute change from baseline in Severity of EoE symptoms other than dysphagia as measured by EoE Symptom Questionnaire (EoE-SQ) at week 24

End point title	Absolute change from baseline in Severity of EoE symptoms other than dysphagia as measured by EoE Symptom Questionnaire (EoE-SQ) at week 24

End point description:

The EoE-SQ asks about symptoms that participants with EoE may have (chest pain, stomach pain, burning feeling in chest, food or liquid coming back up into throat, throwing up) during the past 7 days. Response to the severity of each symptom based on the worst experience in the past 7 days is on a scale of 0 to 10 (higher is worse). The EoE-SQ severity score is calculated as the sum of the severity scores from questions 1 to 3 (chest pain, stomach pain, burning feeling in chest), which could range from 0 to 30; a higher score is indicative of more severe symptoms. Part A FAS (MI method with data set to missing after rescue treatment use); Part B FAS (MI method with data set to missing after rescue treatment use)

End point type	Secondary

End point timeframe:

Baseline and week 24

End point values	Part A: Placebo	Part A: Dupilumab 300 mg QW	Part B: Placebo	Part B: Dupilumab 300 mg Q2W
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	39	42	79	81
Units: Score on a Scale				
least squares mean (confidence interval 95%)	-3.9 (-5.46 to -2.31)	-5.8 (-7.24 to -4.44)	-4.0 (-5.16 to -2.80)	-4.5 (-5.59 to -3.32)

End point values	Part B: Dupilumab 300 mg QW			
Subject group type	Reporting group			
Number of subjects analysed	80			
Units: Score on a Scale				
least squares mean (confidence interval 95%)	-5.4 (-6.60 to -4.27)			

Statistical analyses

Statistical analysis title	Part A: Placebo, Part A: Dupilumab 300 mg SC QW

Statistical analysis description:

Dupilumab group vs. Placebo

Comparison groups	Part A: Placebo v Part A: Dupilumab 300 mg QW

Number of subjects included in analysis	81
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.0467
Method	ANCOVA
Parameter estimate	LS Mean Difference
Point estimate	-2
Confidence interval	
level	95 %
sides	2-sided
lower limit	-3.87
upper limit	-0.03

Statistical analysis title	Part B: Placebo, Part B: Dupilumab 300 mg SC Q2W
Statistical analysis description: Dupilumab group vs. Placebo	
Comparison groups	Part B: Placebo v Part B: Dupilumab 300 mg Q2W
Number of subjects included in analysis	160
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.5469
Method	ANCOVA
Parameter estimate	LS Mean Difference
Point estimate	-0.5
Confidence interval	
level	95 %
sides	2-sided
lower limit	-2.03
upper limit	1.08

Statistical analysis title	Part B: Placebo, Part B: Dupilumab 300 mg SC QW
Statistical analysis description: Dupilumab group vs. Placebo	
Comparison groups	Part B: Placebo v Part B: Dupilumab 300 mg QW
Number of subjects included in analysis	159
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.0718
Method	ANCOVA
Parameter estimate	LS Mean Difference
Point estimate	-1.5
Confidence interval	
level	95 %
sides	2-sided
lower limit	-3
upper limit	0.13

Secondary: Absolute change from baseline in Frequency of EoE symptoms other than dysphagia as measured by EoE-SQ at week 24

End point title	Absolute change from baseline in Frequency of EoE symptoms other than dysphagia as measured by EoE-SQ at week 24

End point description:

The EoE-SQ asks about symptoms that participants with EoE may have (chest pain, stomach pain, burning feeling in chest, food or liquid coming back up into throat, throwing up) during the past 7 days. Response to the frequency of each symptom is on a 5-point scale (1 = 'Never', 2 = 'One day', 3 = ' 2-6 days', 4 = 'Once a day', 5 = 'More than once a day'). The EoE-SQ frequency score is calculated as the sum of the frequency scores from the 5 items which could range from 5 to 25; a higher score is indicative of higher frequency of symptoms. Part A FAS (MI method with data set to missing after rescue treatment use); Part B FAS (MI method with data set to missing after rescue treatment use)

End point type	Secondary

End point timeframe:

Baseline and week 24

End point values	Part A: Placebo	Part A: Dupilumab 300 mg QW	Part B: Placebo	Part B: Dupilumab 300 mg Q2W
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	39	42	79	81
Units: Score on a Scale				
least squares mean (confidence interval 95%)	-1.7 (-2.67 to -0.71)	-3.4 (-4.29 to -2.53)	-2.6 (-3.25 to -1.87)	-3.0 (-3.69 to -2.36)

End point values	Part B: Dupilumab 300 mg QW			
Subject group type	Reporting group			
Number of subjects analysed	80			
Units: Score on a Scale				
least squares mean (confidence interval 95%)	-3.9 (-4.61 to -3.25)			

Statistical analyses

Statistical analysis title	Part A: Placebo, Part A: Dupilumab 300 mg SC QW

Statistical analysis description:

Dupilumab group vs. Placebo

Comparison groups	Part A: Placebo v Part A: Dupilumab 300 mg QW

Number of subjects included in analysis	81
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.0051
Method	ANCOVA
Parameter estimate	LS Mean Difference
Point estimate	-1.7
Confidence interval	
level	95 %
sides	2-sided
lower limit	-2.93
upper limit	-0.52

Statistical analysis title	Part B: Placebo, Part B: Dupilumab 300 mg SC QW
Statistical analysis description: Dupilumab group vs. Placebo	
Comparison groups	Part B: Placebo v Part B: Dupilumab 300 mg QW
Number of subjects included in analysis	159
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.0037
Method	ANCOVA
Parameter estimate	LS Mean Difference
Point estimate	-1.4
Confidence interval	
level	95 %
sides	2-sided
lower limit	-2.3
upper limit	0.45

Statistical analysis title	Part B: Placebo, Part B: Dupilumab 300 mg SC Q2W
Statistical analysis description: Dupilumab group vs. Placebo	
Comparison groups	Part B: Placebo v Part B: Dupilumab 300 mg Q2W
Number of subjects included in analysis	160
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.3152
Method	ANCOVA
Parameter estimate	LS Mean Difference
Point estimate	-0.5
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.38
upper limit	0.44

Secondary: Percentage of participants who received rescue medication during the 24-week double-blind, placebo-controlled treatment period

End point title	Percentage of participants who received rescue medication during the 24-week double-blind, placebo-controlled treatment period

End point description:

End point type	Secondary

End point timeframe:

At week 24

End point values	Part A: Placebo	Part A: Dupilumab 300 mg QW	Part B: Placebo	Part B: Dupilumab 300 mg Q2W
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	39	42	79	81
Units: Percentage of Participants				
number (confidence interval 95%)	12.8 (4.30 to 27.43)	0.0 (0.00 to 8.41)	2.5 (0.31 to 8.85)	1.2 (0.03 to 6.69)

End point values	Part B: Dupilumab 300 mg QW			
Subject group type	Reporting group			
Number of subjects analysed	80			
Units: Percentage of Participants				
number (confidence interval 95%)	2.5 (0.30 to 8.74)			

Statistical analyses

Statistical analysis title	Part A: Placebo, Part A: Dupilumab 300 mg SC QW

Statistical analysis description:

Difference is Dupilumab minus Placebo

Comparison groups	Part A: Placebo v Part A: Dupilumab 300 mg QW
Number of subjects included in analysis	81
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.017
Method	Cochran-Mantel-Haenszel
Parameter estimate	Difference in proportion
Point estimate	-12.7

Confidence interval	
level	95 %
sides	2-sided
lower limit	-23.21
upper limit	-2.26

Statistical analysis title	Part B: Placebo, Part B: Dupilumab 300 mg SC Q2W
Statistical analysis description: Difference is Dupilumab minus Placebo	
Comparison groups	Part B: Placebo v Part B: Dupilumab 300 mg Q2W
Number of subjects included in analysis	160
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.5493
Method	Cochran-Mantel-Haenszel
Parameter estimate	Difference in proportion
Point estimate	-1.3
Confidence interval	
level	95 %
sides	2-sided
lower limit	-5.51
upper limit	2.93

Statistical analysis title	Part B: Placebo, Part B: Dupilumab 300 mg SC QW
Statistical analysis description: Difference is Dupilumab minus Placebo	
Comparison groups	Part B: Placebo v Part B: Dupilumab 300 mg QW
Number of subjects included in analysis	159
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.9887
Method	Cochran-Mantel-Haenszel
Parameter estimate	Difference in proportion
Point estimate	0
Confidence interval	
level	95 %
sides	2-sided
lower limit	-4.9
upper limit	5.02

Secondary: Concentration of functional dupilumab in serum at week 24

End point title	Concentration of functional dupilumab in serum at week 24

End point description:

The PK analysis set (PKAS) for Part A included all randomized participants who received any study drug

and who had at least one non-missing drug concentration result following the first dose of study drug in the corresponding study part. The PKAS for Part B included all randomized participants who received any study drug and who had at least one non-missing drug concentration result following the first dose of study drug in the corresponding study part.

End point type	Secondary

End point timeframe:

Up to week 24

End point values	Part A: Placebo	Part A: Dupilumab 300 mg QW	Part B: Placebo	Part B: Dupilumab 300 mg Q2W
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	39	42	76	79
Units: milligrams per liter (mg/L)				
arithmetic mean (standard deviation)				
Week 0 (n=38,41,75,77,73)	0 (± 0)	0 (± 0)	0.00553 (± 0.0479)	0 (± 0)
Week 12 (n=37,42,72,67,65)	0 (± 0)	187 (± 63.3)	0.00118 (± 0.0100)	70.2 (± 37.7)
Week 24 (n=33,36,67,68,63)	0 (± 0)	197 (± 71.8)	0 (± 0)	72.1 (± 46.6)

End point values	Part B: Dupilumab 300 mg QW			
Subject group type	Reporting group			
Number of subjects analysed	76			
Units: milligrams per liter (mg/L)				
arithmetic mean (standard deviation)				
Week 0 (n=38,41,75,77,73)	0 (± 0)			
Week 12 (n=37,42,72,67,65)	162 (± 83.7)			
Week 24 (n=33,36,67,68,63)	189 (± 98.8)			

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of participants achieving peak esophageal intraepithelial eosinophil count of ≤6 eosinophils per high-power field (eos/hpf) in all three regions at week 52

End point title	Percentage of participants achieving peak esophageal intraepithelial eosinophil count of ≤6 eosinophils per high-power field (eos/hpf) in all three regions at week 52

End point description:

Esophageal intraepithelial eosinophil count obtained by esophageal endoscopy with biopsies (all 3 esophageal regions: proximal, mid, and distal). Part C safety analysis set (SAF): All participants who were randomized in Part A/B, entered Part C, and received any study drug in Part C.

End point type	Secondary

End point timeframe:

At week 52

End point values	Part A/C: Placebo / Dupilumab 300 mg QW	Part A/C: Dupilumab 300 mg QW / Dupilumab 300 mg QW	Part B/C: Placebo / Dupilumab 300 mg Q2W	Part B/C: Placebo / Dupilumab 300 mg QW
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	30	34	32	37
Units: Percentage of Participants				
number (not applicable)	60.0	55.9	71.9	67.6

End point values	Part B/C: Dupilumab 300 mg Q2W / Dupilumab 300 mg Q2W	Part B/C: Dupilumab 300 mg QW / Dupilumab 300 mg QW		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	73	65		
Units: Percentage of Participants				
number (not applicable)	74.0	84.6		

Statistical analyses

No statistical analyses for this end point

Secondary: Absolute change in DSQ total score at week 52

End point title	Absolute change in DSQ total score at week 52

End point description:

The DSQ is used to measure the frequency and intensity of dysphagia. DSQ scores can range from 0 to 84, with a lower score indicating less-frequent or less-severe dysphagia. Part C safety analysis set (SAF): All participants who were randomized in Part A/B, entered Part C, and received any study drug in Part C.

End point type	Secondary

End point timeframe:

Baseline (of previous study part) and week 52

End point values	Part A/C: Placebo / Dupilumab 300 mg QW	Part A/C: Dupilumab 300 mg QW / Dupilumab 300 mg QW	Part B/C: Placebo / Dupilumab 300 mg Q2W	Part B/C: Placebo / Dupilumab 300 mg QW
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	23	29	27	24
Units: Score on a Scale				
arithmetic mean (standard deviation)	-21.71 (± 17.143)	-23.44 (± 16.149)	-23.69 (± 13.737)	-27.25 (± 11.457)

End point values	Part B/C: Dupilumab 300 mg Q2W / Dupilumab 300 mg Q2W	Part B/C: Dupilumab 300 mg QW / Dupilumab 300 mg QW		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	52	54		
Units: Score on a Scale				
arithmetic mean (standard deviation)	-20.87 (± 16.387)	-30.26 (± 15.389)		

Statistical analyses

No statistical analyses for this end point

Secondary: Percent change in DSQ total score at week 52

End point title	Percent change in DSQ total score at week 52

End point description:

The DSQ is used to measure the frequency and intensity of dysphagia. DSQ scores can range from 0 to 84, with a lower score indicating less-frequent or less-severe dysphagia. Part C safety analysis set (SAF): All participants who were randomized in Part A/B, entered Part C, and received any study drug in Part C.

End point type	Secondary

End point timeframe:

Baseline (of previous study part) and week 52

End point values	Part A/C: Placebo / Dupilumab 300 mg QW	Part A/C: Dupilumab 300 mg QW / Dupilumab 300 mg QW	Part B/C: Placebo / Dupilumab 300 mg Q2W	Part B/C: Placebo / Dupilumab 300 mg QW
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	23	29	27	24
Units: Percentage of Change				
arithmetic mean (standard deviation)	-65.87 (± 49.705)	-75.93 (± 36.892)	-71.01 (± 37.256)	-78.13 (± 31.003)

End point values	Part B/C: Dupilumab 300 mg Q2W / Dupilumab 300 mg Q2W	Part B/C: Dupilumab 300 mg QW / Dupilumab 300 mg QW		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	52	54		
Units: Percentage of Change				
arithmetic mean (standard deviation)	-61.19 (± 44.447)	-80.74 (± 32.866)		

Statistical analyses

No statistical analyses for this end point

Secondary: Absolute change in EoE-EREFS total score at week 52

End point title	Absolute change in EoE-EREFS total score at week 52

End point description:

EoE esophageal characteristics analyzed based on the EoE-EREFS, a scoring system for inflammatory and remodeling features of disease. The overall total score ranges from 0 to 18 with higher number indicating worse disease. Part C safety analysis set (SAF): All participants who were randomized in Part A/B, entered Part C, and received any study drug in Part C.

End point type	Secondary

End point timeframe:

Baseline (of previous study part) and week 52

End point values	Part A/C: Placebo / Dupilumab 300 mg QW	Part A/C: Dupilumab 300 mg QW / Dupilumab 300 mg QW	Part B/C: Placebo / Dupilumab 300 mg Q2W	Part B/C: Placebo / Dupilumab 300 mg QW
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	30	35	31	37
Units: Score on a Scale				
arithmetic mean (standard deviation)	-3.9 (± 2.74)	-4.1 (± 3.37)	-4.3 (± 3.21)	-6.1 (± 3.60)

End point values	Part B/C: Dupilumab 300 mg Q2W / Dupilumab 300 mg Q2W	Part B/C: Dupilumab 300 mg QW / Dupilumab 300 mg QW		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	73	63		
Units: Score on a Scale				
arithmetic mean (standard deviation)	-5.2 (± 3.40)	-5.3 (± 2.85)		

Statistical analyses

No statistical analyses for this end point

Secondary: Percent change in peak esophageal intraepithelial eosinophil count (eos/hpf) in all three regions at week 52

End point title	Percent change in peak esophageal intraepithelial eosinophil count (eos/hpf) in all three regions at week 52

End point description:

Esophageal intraepithelial eosinophil count obtained by esophageal endoscopy with biopsies (all 3 esophageal regions: proximal, mid, and distal). A greater esophageal intraepithelial eosinophil count from baseline indicates worsening disease. Part C safety analysis set (SAF): All participants who were randomized in Part A/B, entered Part C, and received any study drug in Part C.

End point type	Secondary

End point timeframe:

Baseline (of previous study part) and week 52

End point values	Part A/C: Placebo / Dupilumab 300 mg QW	Part A/C: Dupilumab 300 mg QW / Dupilumab 300 mg QW	Part B/C: Placebo / Dupilumab 300 mg Q2W	Part B/C: Placebo / Dupilumab 300 mg QW
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	30	34	32	37
Units: Percentage of Change				
arithmetic mean (standard deviation)	-83.76 (± 24.996)	-88.59 (± 13.506)	-91.20 (± 13.037)	-84.21 (± 42.169)

End point values	Part B/C: Dupilumab 300 mg Q2W / Dupilumab 300 mg Q2W	Part B/C: Dupilumab 300 mg QW / Dupilumab 300 mg QW		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	73	65		
Units: Percentage of Change				
arithmetic mean (standard deviation)	-84.78 (± 40.973)	-95.85 (± 4.037)		

Statistical analyses

No statistical analyses for this end point

Secondary: Absolute change in EoEHSS mean Grade score at week 52

End point title	Absolute change in EoEHSS mean Grade score at week 52

End point description:

Severity (grade) and extent (stage) of esophageal abnormalities were scored by blinded, central pathologists using a 4-point scale (0 normal; 3 maximum change) for eight features: eosinophil density, basal zone hyperplasia, eosinophil abscesses, eosinophil surface layering, dilated intercellular spaces, surface epithelial alteration, dyskeratotic epithelial cells and lamina propria fibrosis (absent/present). Higher score indicates greater severity and extent of histological abnormalities. Part C safety analysis set (SAF): All participants who were randomized in Part A/B, entered Part C, and received any study drug in Part C.

End point type	Secondary

End point timeframe:

Baseline (of previous study part) and week 52

End point values	Part A/C: Placebo / Dupilumab 300 mg QW	Part A/C: Dupilumab 300 mg QW / Dupilumab 300 mg QW	Part B/C: Placebo / Dupilumab 300 mg Q2W	Part B/C: Placebo / Dupilumab 300 mg QW
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	30	34	32	37
Units: Score on a Scale				
arithmetic mean (standard deviation)	-0.873 (± 0.5506)	-0.873 (± 0.3537)	-0.779 (± 0.4292)	-0.906 (± 0.3936)

End point values	Part B/C: Dupilumab 300 mg Q2W / Dupilumab 300 mg Q2W	Part B/C: Dupilumab 300 mg QW / Dupilumab 300 mg QW		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	73	65		
Units: Score on a Scale				
arithmetic mean (standard deviation)	-0.838 (± 0.4039)	-0.968 (± 0.4293)		

Statistical analyses

No statistical analyses for this end point

Secondary: Absolute change in EoEHSS mean Stage score at week 52

End point title	Absolute change in EoEHSS mean Stage score at week 52

End point description:

Severity (grade) and extent (stage) of esophageal abnormalities were scored by blinded, central pathologists using a 4-point scale (0 normal; 3 maximum change) for eight features: eosinophil density, basal zone hyperplasia, eosinophil abscesses, eosinophil surface layering, dilated intercellular spaces, surface epithelial alteration, dyskeratotic epithelial cells and lamina propria fibrosis (absent/present).

Higher score indicates greater severity and extent of histological abnormalities. Part C safety analysis set (SAF): All participants who were randomized in Part A/B, entered Part C, and received any study drug in Part C.

End point type	Secondary

End point timeframe:

Baseline (of previous study part) and week 52

End point values	Part A/C: Placebo / Dupilumab 300 mg QW	Part A/C: Dupilumab 300 mg QW / Dupilumab 300 mg QW	Part B/C: Placebo / Dupilumab 300 mg Q2W	Part B/C: Placebo / Dupilumab 300 mg QW
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	30	34	32	37
Units: Score on a Scale				
arithmetic mean (standard deviation)	-0.874 (± 0.4630)	-0.891 (± 0.2770)	-0.710 (± 0.3783)	-0.871 (± 0.3510)

End point values	Part B/C: Dupilumab 300 mg Q2W / Dupilumab 300 mg Q2W	Part B/C: Dupilumab 300 mg QW / Dupilumab 300 mg QW		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	73	65		
Units: Score on a Scale				
arithmetic mean (standard deviation)	-0.809 (± 0.3434)	-0.932 (± 0.3730)		

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of participants achieving peak esophageal intraepithelial eosinophil count of <15 eos/hpf in all three regions at week 52

End point title	Percentage of participants achieving peak esophageal intraepithelial eosinophil count of <15 eos/hpf in all three regions at week 52

End point description:

Esophageal intraepithelial eosinophil count obtained by esophageal endoscopy with biopsies (all 3 esophageal regions: proximal, mid, and distal). Part C safety analysis set (SAF): All participants who were randomized in Part A/B, entered Part C, and received any study drug in Part C.

End point type	Secondary

End point timeframe:

At week 52

End point values	Part A/C: Placebo / Dupilumab 300 mg QW	Part A/C: Dupilumab 300 mg QW / Dupilumab 300 mg QW	Part B/C: Placebo / Dupilumab 300 mg Q2W	Part B/C: Placebo / Dupilumab 300 mg QW
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	30	34	32	37
Units: Percentage of Participants				
number (not applicable)	70.0	82.4	87.5	78.4

End point values	Part B/C: Dupilumab 300 mg Q2W / Dupilumab 300 mg Q2W	Part B/C: Dupilumab 300 mg QW / Dupilumab 300 mg QW		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	73	65		
Units: Percentage of Participants				
number (not applicable)	83.6	100		

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of participants achieving peak esophageal intraepithelial eosinophil count of ≤1 eos/hpf in all three regions at week 52

End point title	Percentage of participants achieving peak esophageal intraepithelial eosinophil count of ≤1 eos/hpf in all three regions at week 52

End point description:

Esophageal intraepithelial eosinophil count obtained by esophageal endoscopy with biopsies (all 3 esophageal regions: proximal, mid, and distal). Part C safety analysis set (SAF): All participants who were randomized in Part A/B, entered Part C, and received any study drug in Part C.

End point type	Secondary

End point timeframe:

At week 52

End point values	Part A/C: Placebo / Dupilumab 300 mg QW	Part A/C: Dupilumab 300 mg QW / Dupilumab 300 mg QW	Part B/C: Placebo / Dupilumab 300 mg Q2W	Part B/C: Placebo / Dupilumab 300 mg QW
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	30	34	32	37
Units: Percentage of Participants				
number (not applicable)	26.7	29.4	40.6	16.2

End point values	Part B/C: Dupilumab 300 mg Q2W / Dupilumab 300 mg Q2W	Part B/C: Dupilumab 300 mg QW / Dupilumab 300 mg QW		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	73	65		
Units: Percentage of Participants				
number (not applicable)	31.5	30.8		

Statistical analyses

No statistical analyses for this end point

Secondary: Absolute change in health-related QOL average score as measured by EoE-IQ at week 52

End point title	Absolute change in health-related QOL average score as measured by EoE-IQ at week 52

End point description:

The EoE-IQ measures impact of EoE on emotional, social, work & school, & sleep aspects. Participants were asked to respond to 11 questions based on experience living with EoE during past 7 days. Response to each item is on a 5-point scale (1=Not at all [impacted] 2=A little, 3=Somewhat, 4=Quite a bit, 5=Extremely [impacted]). The average score is the sum of non-missing responses divided by the number of items with non-missing responses. The average score can range from 1 to 5; a higher score is indicative of a more negative impact. Part C safety analysis set (SAF): All participants who were randomized in Part A/B, entered Part C, and received any study drug in Part C.

End point type	Secondary

End point timeframe:

Baseline (of previous study part) and week 52

End point values	Part A/C: Placebo / Dupilumab 300 mg QW	Part A/C: Dupilumab 300 mg QW / Dupilumab 300 mg QW	Part B/C: Placebo / Dupilumab 300 mg Q2W	Part B/C: Placebo / Dupilumab 300 mg QW
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	27	27	31	35
Units: Score on a Scale				
arithmetic mean (standard deviation)	-0.954 (± 0.6690)	-0.911 (± 0.6344)	-1.021 (± 0.7169)	-0.858 (± 0.6360)

End point values	Part B/C: Dupilumab 300 mg Q2W / Dupilumab 300 mg Q2W	Part B/C: Dupilumab 300 mg QW / Dupilumab 300 mg QW		

Subject group type	Reporting group	Reporting group		
Number of subjects analysed	67	56		
Units: Score on a Scale				
arithmetic mean (standard deviation)	-0.773 (± 0.6217)	-0.935 (± 0.6883)		

Statistical analyses

No statistical analyses for this end point

Secondary: Absolute change from baseline in Severity of EoE symptoms other than dysphagia as measured by EoE-SQ at week 52

End point title	Absolute change from baseline in Severity of EoE symptoms other than dysphagia as measured by EoE-SQ at week 52

End point description:

The EoE-SQ asks about symptoms that participants with EoE may have (chest pain, stomach pain, burning feeling in chest, food or liquid coming back up into throat, throwing up) during the past 7 days. Response to the severity of each symptom based on the worst experience in the past 7 days is on a scale of 0 to 10 (higher is worse). The EoE-SQ severity score is calculated as the sum of the severity scores from questions 1 to 3 (chest pain, stomach pain, burning feeling in chest), which could range from 0 to 30; a higher score is indicative of more severe symptoms. Part C safety analysis set (SAF): All participants who were randomized in Part A/B, entered Part C, and received any study drug in Part C.

End point type	Secondary

End point timeframe:

Baseline (of previous study part) and week 52

End point values	Part A/C: Placebo / Dupilumab 300 mg QW	Part A/C: Dupilumab 300 mg QW / Dupilumab 300 mg QW	Part B/C: Placebo / Dupilumab 300 mg Q2W	Part B/C: Placebo / Dupilumab 300 mg QW
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	27	27	32	35
Units: Score on a Scale				
arithmetic mean (standard deviation)	-7.2 (± 6.46)	-5.9 (± 6.80)	-6.2 (± 6.42)	-5.9 (± 6.47)

End point values	Part B/C: Dupilumab 300 mg Q2W / Dupilumab 300 mg Q2W	Part B/C: Dupilumab 300 mg QW / Dupilumab 300 mg QW		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	68	57		
Units: Score on a Scale				
arithmetic mean (standard deviation)	-4.7 (± 5.99)	-6.4 (± 6.86)		

Statistical analyses

No statistical analyses for this end point

Secondary: Absolute change from baseline in Frequency of EoE symptoms other than dysphagia as measured by EoE-SQ at week 52

End point title	Absolute change from baseline in Frequency of EoE symptoms other than dysphagia as measured by EoE-SQ at week 52

End point description:

The EoE-SQ asks about symptoms that participants with EoE may have (chest pain, stomach pain, burning feeling in chest, food or liquid coming back up into throat, throwing up) during the past 7 days. Response to the frequency of each symptom is on a 5-point scale (1 = 'Never', 2 = 'One day', 3 = ' 2-6 days', 4 = 'Once a day', 5 = 'More than once a day'). The EoE-SQ frequency score is calculated as the sum of the frequency scores from the 5 items which could range from 5 to 25; a higher score is indicative of higher frequency of symptoms. Part C safety analysis set (SAF): All participants who were randomized in Part A/B, entered Part C, and received any study drug in Part C.

End point type	Secondary

End point timeframe:

Baseline (of previous study part) and week 52

End point values	Part A/C: Placebo / Dupilumab 300 mg QW	Part A/C: Dupilumab 300 mg QW / Dupilumab 300 mg QW	Part B/C: Placebo / Dupilumab 300 mg Q2W	Part B/C: Placebo / Dupilumab 300 mg QW
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	27	27	32	35
Units: Score on a Scale				
arithmetic mean (standard deviation)	-4.3 (± 3.78)	-3.2 (± 3.50)	-4.0 (± 3.54)	-3.8 (± 3.62)

End point values	Part B/C: Dupilumab 300 mg Q2W / Dupilumab 300 mg Q2W	Part B/C: Dupilumab 300 mg QW / Dupilumab 300 mg QW		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	68	57		
Units: Score on a Scale				
arithmetic mean (standard deviation)	-3.6 (± 3.45)	-4.7 (± 4.03)		

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of participants who received rescue medication during the 28-week extended active treatment period

End point title	Percentage of participants who received rescue medication during the 28-week extended active treatment period

End point description:

End point type	Secondary

End point timeframe:

Baseline (of Part C) to week 28

End point values	Part A/C: Placebo / Dupilumab 300 mg QW	Part A/C: Dupilumab 300 mg QW / Dupilumab 300 mg QW	Part B/C: Placebo / Dupilumab 300 mg Q2W	Part B/C: Placebo / Dupilumab 300 mg QW
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	37	40	37	37
Units: Percentage of Participants				
number (not applicable)	8.1	0	2.7	2.7

End point values	Part B/C: Dupilumab 300 mg Q2W / Dupilumab 300 mg Q2W	Part B/C: Dupilumab 300 mg QW / Dupilumab 300 mg QW		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	79	74		
Units: Percentage of Participants				
number (not applicable)	0	1.4		

Statistical analyses

No statistical analyses for this end point

Secondary: NES for the relative change from baseline in EoE Diagnostic Panel (EDP) at week 52

End point title	NES for the relative change from baseline in EoE Diagnostic Panel (EDP) at week 52

End point description:

NES reflects the degree to which the activity level of a set of disease transcripts is overrepresented at the extremes (top or bottom) of the entire ranked list of transcripts within a sample and is normalized by accounting for the number of transcripts in the set. An NES of 0 indicates no change from baseline, a negative score reflects a reduction in the disease score (more like normal) and a positive score reflects worsening (more active disease). Part C safety analysis set (SAF): All participants who were randomized in Part A/B, entered Part C, and received any study drug in Part C.

End point type	Secondary

End point timeframe:

Baseline (of previous study part) and week 52

End point values	Part A/C: Placebo / Dupilumab 300 mg QW	Part A/C: Dupilumab 300 mg QW / Dupilumab 300 mg QW	Part B/C: Placebo / Dupilumab 300 mg Q2W	Part B/C: Placebo / Dupilumab 300 mg QW
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	27	30	17	24
Units: Score on a Scale				
median (full range (min-max))	-2.580 (-2.87 to -0.45)	-2.670 (-2.83 to -1.09)	-2.28 (-2.8 to -0.8)	-2.62 (-2.9 to -2.1)

End point values	Part B/C: Dupilumab 300 mg Q2W / Dupilumab 300 mg Q2W	Part B/C: Dupilumab 300 mg QW / Dupilumab 300 mg QW		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	60	49		
Units: Score on a Scale				
median (full range (min-max))	-2.64 (-2.9 to 1.2)	-2.69 (-2.9 to -0.6)		

Statistical analyses

No statistical analyses for this end point

Secondary: NES for the relative change in type 2 inflammation signature at week 52

End point title	NES for the relative change in type 2 inflammation signature at week 52

End point description:

NES reflects the degree to which the activity level of a set of disease transcripts is overrepresented at the extremes (top or bottom) of the entire ranked list of transcripts within a sample and is normalized by accounting for the number of transcripts in the set. An NES of 0 indicates no change from baseline, a negative score reflects a reduction in the disease score (more like normal) and a positive score reflects worsening (more active disease). Part C safety analysis set (SAF): All participants who were randomized in Part A/B, entered Part C, and received any study drug in Part C.

End point type	Secondary

End point timeframe:

Baseline (of previous study part) and week 52

End point values	Part A/C: Placebo / Dupilumab 300 mg QW	Part A/C: Dupilumab 300 mg QW / Dupilumab 300 mg QW	Part B/C: Placebo / Dupilumab 300 mg Q2W	Part B/C: Placebo / Dupilumab 300 mg QW
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	27	30	17	24
Units: Score on a Scale				
median (full range (min-max))	-1.940 (-2.11 to -0.42)	-1.970 (-2.07 to -0.95)	-1.76 (-2.1 to -1.0)	-1.96 (-2.1 to -1.5)

End point values	Part B/C: Dupilumab 300 mg Q2W / Dupilumab 300 mg Q2W	Part B/C: Dupilumab 300 mg QW / Dupilumab 300 mg QW		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	60	49		
Units: Score on a Scale				
median (full range (min-max))	-1.95 (-2.1 to 0.3)	-1.97 (-2.2 to -0.7)		

Statistical analyses

No statistical analyses for this end point

Secondary: Concentration of functional dupilumab in serum at week 52

End point title	Concentration of functional dupilumab in serum at week 52

End point description:

The PK analysis set (PKAS) for Part A and Part C included all randomized participants who received any study drug and who had at least one non-missing drug concentration result following the first dose of study drug in the corresponding study part. The PKAS for Part B and Part C included all randomized participants who received any study drug and who had at least one non-missing drug concentration result following the first dose of study drug in the corresponding study part.

End point type	Secondary

End point timeframe:

Baseline (of Part C) up to week 52

End point values	Part A/C: Placebo / Dupilumab 300 mg QW	Part A/C: Dupilumab 300 mg QW / Dupilumab 300 mg QW	Part B/C: Placebo / Dupilumab 300 mg Q2W	Part B/C: Placebo / Dupilumab 300 mg QW
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	34	38	36	37
Units: milligrams per liter (mg/L)				
arithmetic mean (standard deviation)				
Week 24 (n=32,36,35,37,73,64)	0 (± 0)	193 (± 71.4)	0 (± 0)	1.21 (± 7.33)
Week 32 (n=28,24,31,35,71,58)	101 (± 44.6)	205 (± 76.8)	46.0 (± 33.1)	124 (± 56.7)
Week 52 (n=30,37,33,37,73,66)	137 (± 81.6)	152 (± 70.2)	58.6 (± 36.5)	151 (± 96.0)

End point values	Part B/C: Dupilumab 300 mg Q2W / Dupilumab 300 mg Q2W	Part B/C: Dupilumab 300 mg QW / Dupilumab 300 mg QW		

Subject group type	Reporting group	Reporting group		
Number of subjects analysed	77	69		
Units: milligrams per liter (mg/L)				
arithmetic mean (standard deviation)				
Week 24 (n=32,36,35,37,73,64)	74.6 (± 45.5)	199 (± 92.7)		
Week 32 (n=28,24,31,35,71,58)	74.0 (± 42.0)	195 (± 94.6)		
Week 52 (n=30,37,33,37,73,66)	68.9 (± 45.7)	176 (± 120)		

Statistical analyses

No statistical analyses for this end point

Secondary: Incidence of treatment-emergent anti-drug antibody (ADA) response

End point title	Incidence of treatment-emergent anti-drug antibody (ADA) response

End point description:

Number of treatment-emergent ADA responses to dupilumab reported. The ADA analysis set (AAS) for Part A and Part C included all participants who received any study drug and had at least one non-missing ADA result from the dupilumab ADA assay after first dose of the study drug in the corresponding study part (participants analyzed according to treatment actually received). The AAS for Part B and Part C included all participants who received any study drug and had at least one non-missing ADA result from the dupilumab ADA assay after first dose of the study drug in the corresponding study part (participants analyzed according to treatment actually received)..

End point type	Secondary

End point timeframe:

Baseline (of previous study part) up to week 52

End point values	Part A: Placebo	Part A/C: Placebo / Dupilumab 300 mg QW	Part A: Dupilumab 300 mg QW	Part A/C: Dupilumab 300 mg QW / Dupilumab 300 mg QW
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	39	35	42	39
Units: Events				
number (not applicable)	0	4	0	1

End point values	Part B: Placebo	Part B/C: Placebo / Dupilumab 300 mg Q2W	Part B: Dupilumab 300 mg Q2W	Part B/C: Placebo / Dupilumab 300 mg QW
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	77	36	77	37
Units: Events				
number (not applicable)	0	1	2	0

End point values	Part B: Dupilumab 300 mg QW	Part B/C: Dupilumab 300 mg Q2W / Dupilumab 300 mg Q2W	Part B/C: Dupilumab 300 mg QW / Dupilumab 300 mg QW	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	76	77	69	
Units: Events				
number (not applicable)	1	5	0	

Statistical analyses

No statistical analyses for this end point

Adverse events information

Timeframe for reporting adverse events:

From day of first dose up to 12 weeks after end of treatment visit

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	25.0

Reporting groups

Reporting group title	Part A: Placebo

Reporting group description:

Participants received placebo matching dupilumab SC during Part A (24-week DBTP). At end of week 24 visit (one-week after last dose of study drug during DBTP), eligible participants from Part A entered into 28-week extended treatment (Part C) and 12-week follow-up. Participants who did not enter into Part C, entered follow-up period.

Reporting group title	Part B: Placebo

Reporting group description:

Participants received placebo matching dupilumab SC during Part B (24-week DBTP). At end of week 24 visit (one-week after last dose of study drug during DBTP), eligible participants from Part B entered into 28-week extended treatment (Part C) and 12-week follow-up. Participants who did not enter into Part C, entered follow-up period.

Reporting group title	Part B: Dupilumab 300 mg Q2W

Reporting group description:

Participants received dupilumab 300 mg Q2W SC during Part B (24-week DBTP). At end of week 24 visit (one-week after last dose of study drug during DBTP), eligible participants from Part B entered into 28-week extended treatment (Part C) and 12-week follow-up. Participants who did not enter into Part C, entered follow-up period.

Reporting group title	Part A: Dupilumab 300 mg QW

Reporting group description:

Participants received dupilumab 300 mg SC QW during Part A (24-week DBTP). At end of week 24 visit (one-week after last dose of study drug during DBTP), eligible participants from Part A entered into 28-week extended treatment (Part C) and 12-week follow-up. Participants who did not enter into Part C, entered follow-up period.

Reporting group title	Part B: Dupilumab 300 mg QW

Reporting group description:

Participants received dupilumab 300 mg SC QW during Part B (24-week DBTP). At end of week 24 visit (one-week after last dose of study drug during DBTP), eligible participants from Part B entered into 28-week extended treatment (Part C) and 12-week follow-up. Participants who did not enter into Part C, entered follow-up period.

Reporting group title	Part C: Dupilumab 300 mg Q2W (placebo in Part B)

Reporting group description:

Participants randomized to placebo in Part B were re-randomized in a 1:1 ratio to receive dupilumab 300 mg Q2W for 28-week extended treatment (Part C) followed by 12-week follow-up. Participants who did not enter into Part C, entered follow-up.

Reporting group title	Part C: Dupilumab 300 mg QW (placebo in Part A or B)

Reporting group description:

Participants randomized to placebo in Part A, received dupilumab 300 mg QW for 28-week extended treatment (Part C) followed by 12-week follow-up. Participants who did not enter into Part C, entered follow-up. Participants randomized to placebo in Part B were re-randomized in a 1:1 ratio to receive dupilumab 300 mg Q2W for 28-week extended treatment (Part C) followed by 12-week follow-up. Participants who did not enter into Part C, entered follow-up.

Reporting group title	Part C: Dupilumab 300 mg Q2W (Part B regimen continued)

Reporting group description:

Participants randomized to dupilumab 300 mg Q2W in Part B continued to receive the same regimen for 28-week extended treatment (Part C) followed by 12-week follow-up. Participants who did not enter into Part C, entered follow-up.

Reporting group title	Part C: Dupilumab 300 mg QW (Part A or B regimen continued)

Reporting group description:

Participants randomized to dupilumab 300 mg QW in Part A continued to receive the same regimen for 28-week extended treatment (Part C) followed by 12-week follow-up. Participants who did not enter into Part C, entered follow-up. Participants randomized to dupilumab 300 mg QW during Part B, continued to receive the same regimen for 28-week extended treatment (Part C) followed by 12-week follow-up. Participants who did not enter into Part C, entered follow-up.

Serious adverse events	Part A: Placebo	Part B: Placebo	Part B: Dupilumab 300 mg Q2W
Total subjects affected by serious adverse events			
subjects affected / exposed	2 / 39 (5.13%)	1 / 78 (1.28%)	2 / 81 (2.47%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events			
Investigations			
Blood creatine phosphokinase abnormal			
subjects affected / exposed	0 / 39 (0.00%)	0 / 78 (0.00%)	0 / 81 (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
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Breast cancer			
subjects affected / exposed	0 / 39 (0.00%)	0 / 78 (0.00%)	0 / 81 (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			
Open globe injury			
subjects affected / exposed	0 / 39 (0.00%)	0 / 78 (0.00%)	0 / 81 (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
Pregnancy, puerperium and perinatal conditions			
Abortion spontaneous			
subjects affected / exposed	1 / 39 (2.56%)	0 / 78 (0.00%)	0 / 81 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
General disorders and administration site conditions			
Chest pain			

subjects affected / exposed	0 / 39 (0.00%)	0 / 78 (0.00%)	0 / 81 (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
Systemic inflammatory response syndrome			
subjects affected / exposed	0 / 39 (0.00%)	0 / 78 (0.00%)	0 / 81 (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			
Abdominal pain			
subjects affected / exposed	0 / 39 (0.00%)	0 / 78 (0.00%)	0 / 81 (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
Diarrhoea			
subjects affected / exposed	0 / 39 (0.00%)	0 / 78 (0.00%)	0 / 81 (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
Rectal tenesmus			
subjects affected / exposed	0 / 39 (0.00%)	0 / 78 (0.00%)	0 / 81 (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
Vomiting			
subjects affected / exposed	0 / 39 (0.00%)	0 / 78 (0.00%)	0 / 81 (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
Reproductive system and breast disorders			
Uterine polyp			
subjects affected / exposed	0 / 39 (0.00%)	0 / 78 (0.00%)	0 / 81 (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
Psychiatric disorders			
Suicidal ideation			

subjects affected / exposed	1 / 39 (2.56%)	0 / 78 (0.00%)	2 / 81 (2.47%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Depression suicidal			
subjects affected / exposed	0 / 39 (0.00%)	0 / 78 (0.00%)	0 / 81 (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
Mental status changes			
subjects affected / exposed	0 / 39 (0.00%)	1 / 78 (1.28%)	0 / 81 (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
Generalised anxiety disorder			
subjects affected / exposed	0 / 39 (0.00%)	0 / 78 (0.00%)	0 / 81 (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
Substance use disorder			
subjects affected / exposed	0 / 39 (0.00%)	0 / 78 (0.00%)	0 / 81 (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			
Campylobacter colitis			
subjects affected / exposed	0 / 39 (0.00%)	0 / 78 (0.00%)	0 / 81 (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
Pneumonia aspiration			
subjects affected / exposed	0 / 39 (0.00%)	0 / 78 (0.00%)	0 / 81 (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
Cellulitis			
subjects affected / exposed	0 / 39 (0.00%)	0 / 78 (0.00%)	0 / 81 (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
Enterocolitis infectious			

subjects affected / exposed	0 / 39 (0.00%)	0 / 78 (0.00%)	0 / 81 (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
Pneumonia mycoplasmal			
subjects affected / exposed	0 / 39 (0.00%)	0 / 78 (0.00%)	0 / 81 (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 300 mg QW	Part B: Dupilumab 300 mg QW	Part C: Dupilumab 300 mg Q2W (placebo in Part B)
Total subjects affected by serious adverse events			
subjects affected / exposed	2 / 42 (4.76%)	5 / 80 (6.25%)	1 / 37 (2.70%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events			
Investigations			
Blood creatine phosphokinase abnormal			
subjects affected / exposed	0 / 42 (0.00%)	1 / 80 (1.25%)	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
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Breast cancer			
subjects affected / exposed	0 / 42 (0.00%)	1 / 80 (1.25%)	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
Injury, poisoning and procedural complications			
Open globe injury			
subjects affected / exposed	0 / 42 (0.00%)	0 / 80 (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
Pregnancy, puerperium and perinatal conditions			
Abortion spontaneous			
subjects affected / exposed	0 / 42 (0.00%)	0 / 80 (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			
Chest pain			
subjects affected / exposed	0 / 42 (0.00%)	0 / 80 (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
Systemic inflammatory response syndrome			
subjects affected / exposed	0 / 42 (0.00%)	0 / 80 (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			
Abdominal pain			
subjects affected / exposed	1 / 42 (2.38%)	0 / 80 (0.00%)	0 / 37 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Diarrhoea			
subjects affected / exposed	0 / 42 (0.00%)	0 / 80 (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
Rectal tenesmus			
subjects affected / exposed	0 / 42 (0.00%)	0 / 80 (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
Vomiting			
subjects affected / exposed	0 / 42 (0.00%)	0 / 80 (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
Reproductive system and breast disorders			
Uterine polyp			
subjects affected / exposed	1 / 42 (2.38%)	0 / 80 (0.00%)	0 / 37 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Psychiatric disorders			
Suicidal ideation			

subjects affected / exposed	0 / 42 (0.00%)	0 / 80 (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
Depression suicidal			
subjects affected / exposed	0 / 42 (0.00%)	1 / 80 (1.25%)	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
Mental status changes			
subjects affected / exposed	0 / 42 (0.00%)	0 / 80 (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
Generalised anxiety disorder			
subjects affected / exposed	0 / 42 (0.00%)	0 / 80 (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
Substance use disorder			
subjects affected / exposed	0 / 42 (0.00%)	0 / 80 (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			
Campylobacter colitis			
subjects affected / exposed	0 / 42 (0.00%)	1 / 80 (1.25%)	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
Pneumonia aspiration			
subjects affected / exposed	0 / 42 (0.00%)	1 / 80 (1.25%)	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
Cellulitis			
subjects affected / exposed	0 / 42 (0.00%)	0 / 80 (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
Enterocolitis infectious			

subjects affected / exposed	0 / 42 (0.00%)	0 / 80 (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
Pneumonia mycoplasmal			
subjects affected / exposed	0 / 42 (0.00%)	0 / 80 (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 C: Dupilumab 300 mg QW (placebo in Part A or B)	Part C: Dupilumab 300 mg Q2W (Part B regimen continued)	Part C: Dupilumab 300 mg QW (Part A or B regimen continued)
Total subjects affected by serious adverse events			
subjects affected / exposed	3 / 74 (4.05%)	1 / 79 (1.27%)	4 / 114 (3.51%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events			
Investigations			
Blood creatine phosphokinase abnormal			
subjects affected / exposed	0 / 74 (0.00%)	0 / 79 (0.00%)	0 / 114 (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
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Breast cancer			
subjects affected / exposed	0 / 74 (0.00%)	0 / 79 (0.00%)	0 / 114 (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			
Open globe injury			
subjects affected / exposed	0 / 74 (0.00%)	0 / 79 (0.00%)	0 / 114 (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
Pregnancy, puerperium and perinatal conditions			
Abortion spontaneous			
subjects affected / exposed	0 / 74 (0.00%)	0 / 79 (0.00%)	0 / 114 (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			
Chest pain			
subjects affected / exposed	0 / 74 (0.00%)	0 / 79 (0.00%)	1 / 114 (0.88%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Systemic inflammatory response syndrome			
subjects affected / exposed	1 / 74 (1.35%)	0 / 79 (0.00%)	0 / 114 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal disorders			
Abdominal pain			
subjects affected / exposed	0 / 74 (0.00%)	0 / 79 (0.00%)	0 / 114 (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
Diarrhoea			
subjects affected / exposed	0 / 74 (0.00%)	0 / 79 (0.00%)	1 / 114 (0.88%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Rectal tenesmus			
subjects affected / exposed	0 / 74 (0.00%)	0 / 79 (0.00%)	1 / 114 (0.88%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Vomiting			
subjects affected / exposed	1 / 74 (1.35%)	0 / 79 (0.00%)	0 / 114 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Reproductive system and breast disorders			
Uterine polyp			
subjects affected / exposed	0 / 74 (0.00%)	0 / 79 (0.00%)	0 / 114 (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
Psychiatric disorders			
Suicidal ideation			

subjects affected / exposed	0 / 74 (0.00%)	0 / 79 (0.00%)	0 / 114 (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
Depression suicidal			
subjects affected / exposed	0 / 74 (0.00%)	0 / 79 (0.00%)	0 / 114 (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
Mental status changes			
subjects affected / exposed	0 / 74 (0.00%)	0 / 79 (0.00%)	0 / 114 (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
Generalised anxiety disorder			
subjects affected / exposed	0 / 74 (0.00%)	1 / 79 (1.27%)	0 / 114 (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
Substance use disorder			
subjects affected / exposed	0 / 74 (0.00%)	1 / 79 (1.27%)	0 / 114 (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			
Campylobacter colitis			
subjects affected / exposed	0 / 74 (0.00%)	0 / 79 (0.00%)	0 / 114 (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
Pneumonia aspiration			
subjects affected / exposed	0 / 74 (0.00%)	0 / 79 (0.00%)	0 / 114 (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
Cellulitis			
subjects affected / exposed	1 / 74 (1.35%)	0 / 79 (0.00%)	0 / 114 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Enterocolitis infectious			

subjects affected / exposed	0 / 74 (0.00%)	0 / 79 (0.00%)	1 / 114 (0.88%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumonia mycoplasmal			
subjects affected / exposed	0 / 74 (0.00%)	0 / 79 (0.00%)	1 / 114 (0.88%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

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

Non-serious adverse events	Part A: Placebo	Part B: Placebo	Part B: Dupilumab 300 mg Q2W
Total subjects affected by non-serious adverse events			
subjects affected / exposed	28 / 39 (71.79%)	41 / 78 (52.56%)	57 / 81 (70.37%)
Investigations			
Blood creatine phosphokinase increased			
subjects affected / exposed	2 / 39 (5.13%)	1 / 78 (1.28%)	1 / 81 (1.23%)
occurrences (all)	2	1	1
Injury, poisoning and procedural complications			
Vaccination complication			
subjects affected / exposed	0 / 39 (0.00%)	0 / 78 (0.00%)	0 / 81 (0.00%)
occurrences (all)	0	0	0
Vascular disorders			
Hypertension			
subjects affected / exposed	0 / 39 (0.00%)	1 / 78 (1.28%)	1 / 81 (1.23%)
occurrences (all)	0	1	1
Nervous system disorders			
Headache			
subjects affected / exposed	4 / 39 (10.26%)	9 / 78 (11.54%)	5 / 81 (6.17%)
occurrences (all)	11	28	10
General disorders and administration site conditions			
Injection site erythema			
subjects affected / exposed	6 / 39 (15.38%)	9 / 78 (11.54%)	18 / 81 (22.22%)
occurrences (all)	22	42	93
Injection site reaction			

subjects affected / exposed	5 / 39 (12.82%)	16 / 78 (20.51%)	18 / 81 (22.22%)
occurrences (all)	19	69	75
Injection site pain			
subjects affected / exposed	3 / 39 (7.69%)	4 / 78 (5.13%)	10 / 81 (12.35%)
occurrences (all)	6	21	45
Injection site oedema			
subjects affected / exposed	2 / 39 (5.13%)	3 / 78 (3.85%)	4 / 81 (4.94%)
occurrences (all)	2	7	4
Injection site pruritus			
subjects affected / exposed	2 / 39 (5.13%)	3 / 78 (3.85%)	1 / 81 (1.23%)
occurrences (all)	2	5	6
Injection site bruising			
subjects affected / exposed	1 / 39 (2.56%)	0 / 78 (0.00%)	6 / 81 (7.41%)
occurrences (all)	2	0	7
Injection site swelling			
subjects affected / exposed	1 / 39 (2.56%)	2 / 78 (2.56%)	7 / 81 (8.64%)
occurrences (all)	5	10	12
Pyrexia			
subjects affected / exposed	1 / 39 (2.56%)	1 / 78 (1.28%)	3 / 81 (3.70%)
occurrences (all)	1	1	3
Fatigue			
subjects affected / exposed	0 / 39 (0.00%)	4 / 78 (5.13%)	2 / 81 (2.47%)
occurrences (all)	0	20	2
Injection site urticaria			
subjects affected / exposed	0 / 39 (0.00%)	2 / 78 (2.56%)	6 / 81 (7.41%)
occurrences (all)	0	4	9
Immune system disorders			
Food allergy			
subjects affected / exposed	0 / 39 (0.00%)	0 / 78 (0.00%)	1 / 81 (1.23%)
occurrences (all)	0	0	1
Gastrointestinal disorders			
Nausea			
subjects affected / exposed	3 / 39 (7.69%)	7 / 78 (8.97%)	4 / 81 (4.94%)
occurrences (all)	4	7	4
Abdominal pain			

subjects affected / exposed	2 / 39 (5.13%)	4 / 78 (5.13%)	2 / 81 (2.47%)
occurrences (all)	3	4	2
Diarrhoea			
subjects affected / exposed	2 / 39 (5.13%)	8 / 78 (10.26%)	3 / 81 (3.70%)
occurrences (all)	2	12	4
Dysphagia			
subjects affected / exposed	2 / 39 (5.13%)	0 / 78 (0.00%)	1 / 81 (1.23%)
occurrences (all)	2	0	1
Vomiting			
subjects affected / exposed	1 / 39 (2.56%)	4 / 78 (5.13%)	3 / 81 (3.70%)
occurrences (all)	1	6	5
Dyspepsia			
subjects affected / exposed	0 / 39 (0.00%)	4 / 78 (5.13%)	2 / 81 (2.47%)
occurrences (all)	0	9	2
Eosinophilic oesophagitis			
subjects affected / exposed	0 / 39 (0.00%)	0 / 78 (0.00%)	0 / 81 (0.00%)
occurrences (all)	0	0	0
Respiratory, thoracic and mediastinal disorders			
Oropharyngeal pain			
subjects affected / exposed	2 / 39 (5.13%)	6 / 78 (7.69%)	5 / 81 (6.17%)
occurrences (all)	2	7	6
Rhinitis allergic			
subjects affected / exposed	2 / 39 (5.13%)	2 / 78 (2.56%)	1 / 81 (1.23%)
occurrences (all)	2	2	1
Rhinorrhoea			
subjects affected / exposed	0 / 39 (0.00%)	0 / 78 (0.00%)	0 / 81 (0.00%)
occurrences (all)	0	0	0
Skin and subcutaneous tissue disorders			
Dermatitis atopic			
subjects affected / exposed	4 / 39 (10.26%)	1 / 78 (1.28%)	0 / 81 (0.00%)
occurrences (all)	5	1	0
Rash			
subjects affected / exposed	4 / 39 (10.26%)	0 / 78 (0.00%)	4 / 81 (4.94%)
occurrences (all)	4	0	4
Acne			

subjects affected / exposed	1 / 39 (2.56%)	3 / 78 (3.85%)	2 / 81 (2.47%)
occurrences (all)	1	3	3
Psychiatric disorders			
Anxiety			
subjects affected / exposed	0 / 39 (0.00%)	1 / 78 (1.28%)	2 / 81 (2.47%)
occurrences (all)	0	1	2
Infections and infestations			
Nasopharyngitis			
subjects affected / exposed	4 / 39 (10.26%)	3 / 78 (3.85%)	4 / 81 (4.94%)
occurrences (all)	4	4	5
Sinusitis			
subjects affected / exposed	2 / 39 (5.13%)	0 / 78 (0.00%)	0 / 81 (0.00%)
occurrences (all)	2	0	0
COVID-19			
subjects affected / exposed	1 / 39 (2.56%)	0 / 78 (0.00%)	5 / 81 (6.17%)
occurrences (all)	1	0	5
Upper respiratory tract infection			
subjects affected / exposed	0 / 39 (0.00%)	2 / 78 (2.56%)	2 / 81 (2.47%)
occurrences (all)	0	2	2

Non-serious adverse events	Part A: Dupilumab 300 mg QW	Part B: Dupilumab 300 mg QW	Part C: Dupilumab 300 mg Q2W (placebo in Part B)
Total subjects affected by non-serious adverse events			
subjects affected / exposed	26 / 42 (61.90%)	50 / 80 (62.50%)	19 / 37 (51.35%)
Investigations			
Blood creatine phosphokinase increased			
subjects affected / exposed	0 / 42 (0.00%)	3 / 80 (3.75%)	4 / 37 (10.81%)
occurrences (all)	0	3	6
Injury, poisoning and procedural complications			
Vaccination complication			
subjects affected / exposed	0 / 42 (0.00%)	2 / 80 (2.50%)	0 / 37 (0.00%)
occurrences (all)	0	2	0
Vascular disorders			
Hypertension			
subjects affected / exposed	1 / 42 (2.38%)	4 / 80 (5.00%)	0 / 37 (0.00%)
occurrences (all)	1	5	0
Nervous system disorders			

Headache			
subjects affected / exposed	2 / 42 (4.76%)	7 / 80 (8.75%)	2 / 37 (5.41%)
occurrences (all)	7	8	6
General disorders and administration site conditions			
Injection site erythema			
subjects affected / exposed	4 / 42 (9.52%)	8 / 80 (10.00%)	2 / 37 (5.41%)
occurrences (all)	12	25	32
Injection site reaction			
subjects affected / exposed	9 / 42 (21.43%)	16 / 80 (20.00%)	3 / 37 (8.11%)
occurrences (all)	45	84	4
Injection site pain			
subjects affected / exposed	5 / 42 (11.90%)	7 / 80 (8.75%)	4 / 37 (10.81%)
occurrences (all)	9	39	34
Injection site oedema			
subjects affected / exposed	2 / 42 (4.76%)	0 / 80 (0.00%)	0 / 37 (0.00%)
occurrences (all)	7	0	0
Injection site pruritus			
subjects affected / exposed	1 / 42 (2.38%)	4 / 80 (5.00%)	1 / 37 (2.70%)
occurrences (all)	1	5	6
Injection site bruising			
subjects affected / exposed	1 / 42 (2.38%)	0 / 80 (0.00%)	1 / 37 (2.70%)
occurrences (all)	2	0	4
Injection site swelling			
subjects affected / exposed	5 / 42 (11.90%)	10 / 80 (12.50%)	4 / 37 (10.81%)
occurrences (all)	7	25	4
Pyrexia			
subjects affected / exposed	2 / 42 (4.76%)	5 / 80 (6.25%)	0 / 37 (0.00%)
occurrences (all)	2	5	0
Fatigue			
subjects affected / exposed	1 / 42 (2.38%)	5 / 80 (6.25%)	1 / 37 (2.70%)
occurrences (all)	1	5	1
Injection site urticaria			
subjects affected / exposed	0 / 42 (0.00%)	0 / 80 (0.00%)	0 / 37 (0.00%)
occurrences (all)	0	0	0
Immune system disorders			

Food allergy			
subjects affected / exposed	0 / 42 (0.00%)	0 / 80 (0.00%)	2 / 37 (5.41%)
occurrences (all)	0	0	2
Gastrointestinal disorders			
Nausea			
subjects affected / exposed	1 / 42 (2.38%)	5 / 80 (6.25%)	2 / 37 (5.41%)
occurrences (all)	2	5	3
Abdominal pain			
subjects affected / exposed	1 / 42 (2.38%)	4 / 80 (5.00%)	0 / 37 (0.00%)
occurrences (all)	1	4	0
Diarrhoea			
subjects affected / exposed	2 / 42 (4.76%)	1 / 80 (1.25%)	2 / 37 (5.41%)
occurrences (all)	2	1	2
Dysphagia			
subjects affected / exposed	0 / 42 (0.00%)	2 / 80 (2.50%)	1 / 37 (2.70%)
occurrences (all)	0	2	1
Vomiting			
subjects affected / exposed	2 / 42 (4.76%)	3 / 80 (3.75%)	1 / 37 (2.70%)
occurrences (all)	2	3	1
Dyspepsia			
subjects affected / exposed	0 / 42 (0.00%)	0 / 80 (0.00%)	0 / 37 (0.00%)
occurrences (all)	0	0	0
Eosinophilic oesophagitis			
subjects affected / exposed	0 / 42 (0.00%)	0 / 80 (0.00%)	4 / 37 (10.81%)
occurrences (all)	0	0	4
Respiratory, thoracic and mediastinal disorders			
Oropharyngeal pain			
subjects affected / exposed	0 / 42 (0.00%)	4 / 80 (5.00%)	0 / 37 (0.00%)
occurrences (all)	0	4	0
Rhinitis allergic			
subjects affected / exposed	1 / 42 (2.38%)	2 / 80 (2.50%)	0 / 37 (0.00%)
occurrences (all)	1	2	0
Rhinorrhoea			
subjects affected / exposed	3 / 42 (7.14%)	0 / 80 (0.00%)	0 / 37 (0.00%)
occurrences (all)	3	0	0
Skin and subcutaneous tissue disorders			

Dermatitis atopic			
subjects affected / exposed	0 / 42 (0.00%)	0 / 80 (0.00%)	0 / 37 (0.00%)
occurrences (all)	0	0	0
Rash			
subjects affected / exposed	0 / 42 (0.00%)	3 / 80 (3.75%)	1 / 37 (2.70%)
occurrences (all)	0	3	1
Acne			
subjects affected / exposed	0 / 42 (0.00%)	0 / 80 (0.00%)	2 / 37 (5.41%)
occurrences (all)	0	0	2
Psychiatric disorders			
Anxiety			
subjects affected / exposed	0 / 42 (0.00%)	3 / 80 (3.75%)	1 / 37 (2.70%)
occurrences (all)	0	3	1
Infections and infestations			
Nasopharyngitis			
subjects affected / exposed	5 / 42 (11.90%)	2 / 80 (2.50%)	2 / 37 (5.41%)
occurrences (all)	6	2	2
Sinusitis			
subjects affected / exposed	1 / 42 (2.38%)	4 / 80 (5.00%)	0 / 37 (0.00%)
occurrences (all)	1	5	0
COVID-19			
subjects affected / exposed	0 / 42 (0.00%)	4 / 80 (5.00%)	1 / 37 (2.70%)
occurrences (all)	0	4	1
Upper respiratory tract infection			
subjects affected / exposed	4 / 42 (9.52%)	3 / 80 (3.75%)	0 / 37 (0.00%)
occurrences (all)	4	4	0

Non-serious adverse events	Part C: Dupilumab 300 mg QW (placebo in Part A or B)	Part C: Dupilumab 300 mg Q2W (Part B regimen continued)	Part C: Dupilumab 300 mg QW (Part A or B regimen continued)
Total subjects affected by non-serious adverse events			
subjects affected / exposed	44 / 74 (59.46%)	47 / 79 (59.49%)	62 / 114 (54.39%)
Investigations			
Blood creatine phosphokinase increased			
subjects affected / exposed	3 / 74 (4.05%)	2 / 79 (2.53%)	2 / 114 (1.75%)
occurrences (all)	3	2	3
Injury, poisoning and procedural complications			

Vaccination complication			
subjects affected / exposed	1 / 74 (1.35%)	4 / 79 (5.06%)	2 / 114 (1.75%)
occurrences (all)	1	4	2
Vascular disorders			
Hypertension			
subjects affected / exposed	0 / 74 (0.00%)	1 / 79 (1.27%)	2 / 114 (1.75%)
occurrences (all)	0	1	2
Nervous system disorders			
Headache			
subjects affected / exposed	4 / 74 (5.41%)	4 / 79 (5.06%)	5 / 114 (4.39%)
occurrences (all)	9	6	8
General disorders and administration site conditions			
Injection site erythema			
subjects affected / exposed	6 / 74 (8.11%)	6 / 79 (7.59%)	10 / 114 (8.77%)
occurrences (all)	13	36	21
Injection site reaction			
subjects affected / exposed	12 / 74 (16.22%)	14 / 79 (17.72%)	14 / 114 (12.28%)
occurrences (all)	40	50	101
Injection site pain			
subjects affected / exposed	6 / 74 (8.11%)	6 / 79 (7.59%)	9 / 114 (7.89%)
occurrences (all)	7	66	45
Injection site oedema			
subjects affected / exposed	3 / 74 (4.05%)	3 / 79 (3.80%)	3 / 114 (2.63%)
occurrences (all)	12	12	8
Injection site pruritus			
subjects affected / exposed	1 / 74 (1.35%)	3 / 79 (3.80%)	0 / 114 (0.00%)
occurrences (all)	1	8	0
Injection site bruising			
subjects affected / exposed	4 / 74 (5.41%)	1 / 79 (1.27%)	3 / 114 (2.63%)
occurrences (all)	4	4	3
Injection site swelling			
subjects affected / exposed	0 / 74 (0.00%)	2 / 79 (2.53%)	4 / 114 (3.51%)
occurrences (all)	0	4	27
Pyrexia			
subjects affected / exposed	0 / 74 (0.00%)	1 / 79 (1.27%)	2 / 114 (1.75%)
occurrences (all)	0	1	2

Fatigue			
subjects affected / exposed	1 / 74 (1.35%)	1 / 79 (1.27%)	2 / 114 (1.75%)
occurrences (all)	1	1	2
Injection site urticaria			
subjects affected / exposed	0 / 74 (0.00%)	2 / 79 (2.53%)	0 / 114 (0.00%)
occurrences (all)	0	5	0
Immune system disorders			
Food allergy			
subjects affected / exposed	0 / 74 (0.00%)	1 / 79 (1.27%)	2 / 114 (1.75%)
occurrences (all)	0	1	2
Gastrointestinal disorders			
Nausea			
subjects affected / exposed	1 / 74 (1.35%)	2 / 79 (2.53%)	4 / 114 (3.51%)
occurrences (all)	1	2	4
Abdominal pain			
subjects affected / exposed	0 / 74 (0.00%)	2 / 79 (2.53%)	4 / 114 (3.51%)
occurrences (all)	0	2	4
Diarrhoea			
subjects affected / exposed	2 / 74 (2.70%)	2 / 79 (2.53%)	0 / 114 (0.00%)
occurrences (all)	2	2	0
Dysphagia			
subjects affected / exposed	1 / 74 (1.35%)	4 / 79 (5.06%)	4 / 114 (3.51%)
occurrences (all)	2	4	4
Vomiting			
subjects affected / exposed	3 / 74 (4.05%)	2 / 79 (2.53%)	4 / 114 (3.51%)
occurrences (all)	4	2	4
Dyspepsia			
subjects affected / exposed	4 / 74 (5.41%)	2 / 79 (2.53%)	4 / 114 (3.51%)
occurrences (all)	6	2	6
Eosinophilic oesophagitis			
subjects affected / exposed	0 / 74 (0.00%)	0 / 79 (0.00%)	0 / 114 (0.00%)
occurrences (all)	0	0	0
Respiratory, thoracic and mediastinal disorders			
Oropharyngeal pain			
subjects affected / exposed	0 / 74 (0.00%)	2 / 79 (2.53%)	1 / 114 (0.88%)
occurrences (all)	0	2	1

Rhinitis allergic			
subjects affected / exposed	3 / 74 (4.05%)	0 / 79 (0.00%)	1 / 114 (0.88%)
occurrences (all)	3	0	1
Rhinorrhoea			
subjects affected / exposed	0 / 74 (0.00%)	0 / 79 (0.00%)	1 / 114 (0.88%)
occurrences (all)	0	0	1
Skin and subcutaneous tissue disorders			
Dermatitis atopic			
subjects affected / exposed	1 / 74 (1.35%)	1 / 79 (1.27%)	2 / 114 (1.75%)
occurrences (all)	1	1	2
Rash			
subjects affected / exposed	0 / 74 (0.00%)	2 / 79 (2.53%)	7 / 114 (6.14%)
occurrences (all)	0	2	9
Acne			
subjects affected / exposed	4 / 74 (5.41%)	2 / 79 (2.53%)	2 / 114 (1.75%)
occurrences (all)	4	2	2
Psychiatric disorders			
Anxiety			
subjects affected / exposed	4 / 74 (5.41%)	1 / 79 (1.27%)	4 / 114 (3.51%)
occurrences (all)	4	1	5
Infections and infestations			
Nasopharyngitis			
subjects affected / exposed	7 / 74 (9.46%)	2 / 79 (2.53%)	5 / 114 (4.39%)
occurrences (all)	8	3	6
Sinusitis			
subjects affected / exposed	2 / 74 (2.70%)	2 / 79 (2.53%)	1 / 114 (0.88%)
occurrences (all)	2	2	1
COVID-19			
subjects affected / exposed	7 / 74 (9.46%)	8 / 79 (10.13%)	10 / 114 (8.77%)
occurrences (all)	7	8	10
Upper respiratory tract infection			
subjects affected / exposed	2 / 74 (2.70%)	0 / 79 (0.00%)	6 / 114 (5.26%)
occurrences (all)	2	0	7

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
04 October 2018	Added an exclusion criterion: known systemic hypersensitivity to dupilumab or the excipients of the drug product; Exclusion Criterion # 26: replaced serum creatinine threshold with estimated glomerular filtration rate (eGFR); Exclusion Criterion #27: replaced the example for severe renal conditions of "patients on dialysis" with "severe nephrotic syndrome"; Exclusion Criterion #33: Added clarification that the reliability of sexual abstinence needs to be evaluated in relation to the duration of the clinical trial and the preferred and usual lifestyle of the patient based on Clinical Trial Facilitation Group guideline on contraception; Clarified criteria for resumption of treatment after study drug has been temporarily discontinued because of a severe laboratory abnormality.
18 April 2019	Per Health Authority request, changed Part C from open-label to a design with added placebo SC injections alternating with dupilumab 300 mg Q2W doses in order to mask the dosing regimen for Part B patients during this extended active treatment phase of the study; Added a per protocol set to the defined efficacy analysis sets to assess the overall robustness of the analysis results. Added that any re-estimation of sample size for Part B will be documented in the Part B SAP before its database lock. If the re-estimated sample size requires an increase of the planned sample size in Part B by more than 86 total patients (25%), it will also be documented in a protocol amendment so as to inform Has, ECs, and investigators; Added a substudy which may be performed at select sites and a secondary endpoint to the study for the endolumenal functional lumen imaging probe (EndoFLIP) procedure to measure esophageal distensibility during the esophagogastroscopy procedures at selected sites in approximately 150 adult patients; Added additional secondary endpoints for proportion of patients who receive rescue medications or procedures during the 24-week placebo-controlled treatment period and absolute change in EoE Stage Score from the EoEHSS from baseline to week 24.
10 March 2020	The purpose of this amendment was to add transcriptome sequencing for analyzing RNA expression of eosinophilic esophagitis (EoE) and type 2 inflammation to the study secondary objectives and endpoints, and to add the European Quality of Life 5-dimension 3-level (EQ-5D3L) Questionnaire to collect general health status of EoE patients. Additionally, the Eosinophilic Esophagitis-Endoscopic Reference Score (EoE-EREFS) procedure for Part B patients was revised to allow for centralized reading and scoring. Other minor changes were made to align with regulatory authority feedback and for general clarification.
16 April 2020	The purpose of this protocol amendment was to protect patient safety and data integrity during the COVID-19 pandemic by allowing for certain study procedures to occur at delayed time points and/or outside of the clinic environment. All temporary mechanisms utilized, and deviations from planned study procedures are to be documented as being related to COVID-19 and will remain in effect only for the duration of the public health emergency.
05 November 2020	The purpose of this protocol amendment was to adjust the sample size for Part B based on the results of Part A of the study, and to add an additional database lock after all patients in Part A complete study week 52 of Part C. Other changes were made for clarification and consistency

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? Yes

Date	Interruption	Restart date
27 March 2020	Enrollment was halted due to operational challenges associated with measures in place to limit the spread of the COVID-19 pandemic.	01 June 2020

Notes:

Limitations and caveats

None reported