Clinical trial results:
A multi-center, single-arm study to investigate the pharmacokinetics and safety of dupilumab in male and female participants >=2 years to <12 years of age with uncontrolled chronic spontaneous urticaria (CSU)

Summary

EudraCT number	2022-000260-22
Trial protocol	Outside EU/EEA
Global end of trial date	03 February 2025

Results information

Result version number	v1 (current)
This version publication date	16 August 2025
First version publication date	16 August 2025

Trial information

Trial identification

Sponsor protocol code	PKM16982

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT05526521
WHO universal trial number (UTN)	U1111-1266-5669

Notes:

Sponsors

Sponsor organisation name	Sanofi aventis recherche & développement
Sponsor organisation address	82 Avenue Raspail, Gentilly, France, 94250
Public contact	Trial Transparency Team, Sanofi aventis recherche & développement, Contact-US@sanofi.com
Scientific contact	Trial Transparency Team, Sanofi aventis recherche & développement, Contact-US@sanofi.com

Notes:

Paediatric regulatory details

Is trial part of an agreed paediatric investigation plan (PIP)	Yes
EMA paediatric investigation plan number(s)	EMEA-001501-PIP07-20
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	28 February 2025
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	03 February 2025
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To characterize the serum concentration of dupilumab over time.

Protection of trial subjects:

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

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	25 August 2022
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	No

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Canada: 4
Country: Number of subjects enrolled	Japan: 3
Country: Number of subjects enrolled	United States: 8
Worldwide total number of subjects	15
EEA total number of subjects	0

Notes:

Subjects enrolled per age group

In utero	0
Preterm newborn - gestational age < 37 wk	0
Newborns (0-27 days)	0
Infants and toddlers (28 days-23 months)	0
Children (2-11 years)	15
Adolescents (12-17 years)	0
Adults (18-64 years)	0

From 65 to 84 years	0
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

A total of 23 participants were screened from 25-Aug-2022 to 02-May-2024 of which 8 were screen failures mainly due to not meeting eligibility criteria.

Pre-assignment

Screening details:

A total of 15 participants were enrolled in the study to receive dupilumab at 1 of 4 dose regimens based on the body weight and age.

Period 1

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

Arms

Are arms mutually exclusive?	Yes
Arm title	Dupilumab 200 mg Q4W

Arm description:

Participants received dupilumab 200 milligrams (mg) subcutaneous (SC) injection every 4 weeks (Q4W) with no loading dose in children aged >=2 years to <12 years with body weight >=5 kilograms (kg) and <15 kg from Day 1 up to 24 weeks.

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

Dosage and administration details:

Dupilumab was administered for 24 weeks as specified in the protocol.

Arm title	Dupilumab 300 mg Q4W

Arm description:

Participants received dupilumab 300 mg SC injection Q4W with no loading dose in children aged >=2 years to <6 years with body weight >=15 kg and <30 kg from Day 1 up to 24 weeks.

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

Dosage and administration details:

Dupilumab was administered for 24 weeks as specified in the protocol.

Arm title	Dupilumab 300 mg Q4W, 600 mg Loading Dose

Arm description:

Participants received dupilumab 300 mg SC injection Q4W with an initial 600 mg loading dose in children aged >=6 years to <12 years with body weight >=15 kg and <30 kg from Day 1 up to 24 weeks.

Arm type	Experimental

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

Dosage and administration details:

Dupilumab was administered for 24 weeks as specified in the protocol.

Arm title	Dupilumab 200 mg Q2W, 400 mg Loading Dose

Arm description:

Participants received dupilumab 200 mg SC injection every 2 weeks (Q2W) with an initial 400 mg loading dose in children aged >=2 years to <12 years with body weight >=30 kg and <60 kg from Day 1 up to 24 weeks.

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

Dosage and administration details:

Dupilumab was administered for 24 weeks as specified in the protocol.

Number of subjects in period 1	Dupilumab 200 mg Q4W	Dupilumab 300 mg Q4W	Dupilumab 300 mg Q4W, 600 mg Loading Dose
Started	1	4	2
Completed	1	3	2
Not completed	0	1	0
Consent withdrawn by subject	-	1	-

Number of subjects in period 1	Dupilumab 200 mg Q2W, 400 mg Loading Dose
Started	8
Completed	8
Not completed	0
Consent withdrawn by subject	-

Baseline characteristics

Reporting groups	
Reporting group title	Dupilumab 200 mg Q4W
Reporting group description:	
Participants received dupilumab 200 milligrams (mg) subcutaneous (SC) injection every 4 weeks (Q4W) with no loading dose in children aged >=2 years to <12 years with body weight >=5 kilograms (kg) and <15 kg from Day 1 up to 24 weeks.	
Reporting group title	Dupilumab 300 mg Q4W
Reporting group description:	
Participants received dupilumab 300 mg SC injection Q4W with no loading dose in children aged >=2 years to <6 years with body weight >=15 kg and <30 kg from Day 1 up to 24 weeks.	
Reporting group title	Dupilumab 300 mg Q4W, 600 mg Loading Dose
Reporting group description:	
Participants received dupilumab 300 mg SC injection Q4W with an initial 600 mg loading dose in children aged >=6 years to <12 years with body weight >=15 kg and <30 kg from Day 1 up to 24 weeks.	
Reporting group title	Dupilumab 200 mg Q2W, 400 mg Loading Dose
Reporting group description:	
Participants received dupilumab 200 mg SC injection every 2 weeks (Q2W) with an initial 400 mg loading dose in children aged >=2 years to <12 years with body weight >=30 kg and <60 kg from Day 1 up to 24 weeks.	

Reporting group values	Dupilumab 200 mg Q4W	Dupilumab 300 mg Q4W	Dupilumab 300 mg Q4W, 600 mg Loading Dose
Number of subjects	1	4	2
Age Categorical Units: participants			
>=2 to <6 years	0	4	0
>=6 to 12 years	1	0	2
Sex: Female, Male Units: participants			
Female	1	2	2
Male	0	2	0
Race (NIH/OMB) Units: Subjects			
American Indian or Alaska Native	0	0	0
Asian	1	0	1
Native Hawaiian or Other Pacific Islander	0	0	0
Black or African American	0	0	0
White	0	4	1
More than one race	0	0	0
Unknown or Not Reported	0	0	0

Reporting group values	Dupilumab 200 mg Q2W, 400 mg Loading Dose	Total	
Number of subjects	8	15	
Age Categorical Units: participants			
>=2 to <6 years	0	4	
>=6 to 12 years	8	11	

Sex: Female, Male Units: participants			
Female	6	11	
Male	2	4	
Race (NIH/OMB) Units: Subjects			
American Indian or Alaska Native	0	0	
Asian	2	4	
Native Hawaiian or Other Pacific Islander	0	0	
Black or African American	1	1	
White	4	9	
More than one race	0	0	
Unknown or Not Reported	1	1	

End points

End points reporting groups

Reporting group title	Dupilumab 200 mg Q4W
Reporting group description:	
Participants received dupilumab 200 milligrams (mg) subcutaneous (SC) injection every 4 weeks (Q4W) with no loading dose in children aged >=2 years to <12 years with body weight >=5 kilograms (kg) and <15 kg from Day 1 up to 24 weeks.	
Reporting group title	Dupilumab 300 mg Q4W
Reporting group description:	
Participants received dupilumab 300 mg SC injection Q4W with no loading dose in children aged >=2 years to <6 years with body weight >=15 kg and <30 kg from Day 1 up to 24 weeks.	
Reporting group title	Dupilumab 300 mg Q4W, 600 mg Loading Dose
Reporting group description:	
Participants received dupilumab 300 mg SC injection Q4W with an initial 600 mg loading dose in children aged >=6 years to <12 years with body weight >=15 kg and <30 kg from Day 1 up to 24 weeks.	
Reporting group title	Dupilumab 200 mg Q2W, 400 mg Loading Dose
Reporting group description:	
Participants received dupilumab 200 mg SC injection every 2 weeks (Q2W) with an initial 400 mg loading dose in children aged >=2 years to <12 years with body weight >=30 kg and <60 kg from Day 1 up to 24 weeks.	

Primary: Serum Concentration of Dupilumab at Weeks 12 and 24

End point title	Serum Concentration of Dupilumab at Weeks 12 and 24[1]
End point description:	
Blood samples were collected at specified timepoints to obtain dupilumab concentration. The pharmacokinetic (PK) population included all enrolled and treated participants (safety population) with at least 1 post-baseline PK result. Only those participants with data collected at Weeks 12 or 24 are reported. Here, n= number of participants with data collected for specified categories. 99999=standard deviation (SD) cannot be calculated for 1 participant.	
End point type	Primary
End point timeframe:	
Weeks 12 and 24	

Notes:

[1] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: As the endpoint is descriptive in nature, no statistical analysis have been presented.

End point values	Dupilumab 200 mg Q4W	Dupilumab 300 mg Q4W	Dupilumab 300 mg Q4W, 600 mg Loading Dose	Dupilumab 200 mg Q2W, 400 mg Loading Dose
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	1	3	2	8
Units: nanogram/milliliter				
arithmetic mean (standard deviation)				
Week 12 (n=1,1,2,8)	67700 (± 99999)	105000 (± 99999)	45800 (± 12400)	91600 (± 23000)
Week 24 (n=1,3,2,8)	116000 (± 99999)	141000 (± 30100)	51100 (± 20100)	78500 (± 31600)

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Participants With Treatment-emergent Adverse Events (TEAEs) and Treatment-emergent Serious Adverse Events (TESAEs)

End point title	Number of Participants With Treatment-emergent Adverse Events (TEAEs) and Treatment-emergent Serious Adverse Events (TESAEs)

End point description:

An adverse event (AE) was defined as any untoward medical occurrence in a participant or clinical trial participant, temporally associated with the use of study intervention, whether or not considered related to study intervention. Serious adverse event (SAE) was any untoward medical occurrence that at any dose:
resulted in death, was life-threatening, required inpatient hospitalization or prolongation of existing hospitalization, resulted in persistent or significant
disability/incapacity, was a congenital anomaly/birth defect or was an important medical event. TEAEs were defined as AEs that developed, worsened or became serious during the TE period. The safety population included all enrolled participants who took at least 1 dose of the study intervention, regardless of the amount of intervention administered.

End point type	Secondary

End point timeframe:

From the first dose of study intervention (Day 1) up to end of follow-up, maximum up to 36 weeks

End point values	Dupilumab 200 mg Q4W	Dupilumab 300 mg Q4W	Dupilumab 300 mg Q4W, 600 mg Loading Dose	Dupilumab 200 mg Q2W, 400 mg Loading Dose
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	1	4	2	8
Units: participants				
TEAEs	1	2	2	7
TESAEs	0	0	0	0

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Participants With Anti-drug Antibodies (ADAs) to Dupilumab

End point title	Number of Participants With Anti-drug Antibodies (ADAs) to Dupilumab

End point description:

Blood samples were collected at specified timepoints and ADA samples were assayed using validated methods. Treatment-emergent ADA response was defined as a positive response in the ADA assay post first dose when baseline results were negative or missing. Number of participants with treatment-emergent ADA response is presented. The ADA population included all enrolled participants treated with dupilumab with at least 1 post-baseline ADA result (positive, negative or inconclusive).

End point type	Secondary

End point timeframe:

From the first dose of study intervention (Day 1) up to end of follow-up, maximum up to 36 weeks

End point values	Dupilumab 200 mg Q4W	Dupilumab 300 mg Q4W	Dupilumab 300 mg Q4W, 600 mg Loading Dose	Dupilumab 200 mg Q2W, 400 mg Loading Dose
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	1	3	2	8
Units: participants	0	0	0	0

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in Children’s Dermatology Life Quality Index (C-DLQI) in Participants Aged 4 Years to <12 Years at Week 24

End point title	Change From Baseline in Children’s Dermatology Life Quality Index (C-DLQI) in Participants Aged 4 Years to <12 Years at Week 24

End point description:

The C-DLQI assesses impact of skin disease on children’s health-related quality of life (HRQoL) over the previous week, contains 10 questions related to symptoms feelings associated with disease, impact of disease on leisure, school or holidays, personal relationships, sleep, and side effects of treatment for the skin disease. All questions were scored on 4-point Likert scale:0 (not at all),1 (a little),2 (a lot),3 (very much). Total C-DLQI was calculated by summing the score of each question and ranged from 0 (no impact) to 30 (severe impact). Higher scores indicated poor HRQoL. Mean is presented. Baseline was defined as closest assessment to first study intervention administration on or prior to Day 1 but no later than Day 4. Analysis was performed on intent-to-treat (ITT) population. Only those participants with data collected at Baseline and Week 24 are reported.99999=SD cannot be calculated for 1 participant.

End point type	Secondary

End point timeframe:

Baseline (Day 1) and Week 24

End point values	Dupilumab 200 mg Q4W	Dupilumab 300 mg Q4W	Dupilumab 300 mg Q4W, 600 mg Loading Dose	Dupilumab 200 mg Q2W, 400 mg Loading Dose
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	1	1	2	7
Units: score on a scale				
arithmetic mean (standard deviation)	-3.0 (± 99999)	-6.0 (± 99999)	-10.5 (± 3.5)	-7.3 (± 4.3)

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in Infant’s Dermatitis Quality of Life Index

(IDQOL) in Participants Aged 2 Years to <4 Years at Week 24

End point title	Change From Baseline in Infant's Dermatitis Quality of Life Index (IDQOL) in Participants Aged 2 Years to <4 Years at Week 24

End point description:

The IDQOL questionnaire is completed by child's caregiver/guardian with recall period of 7 days;consists of 10 questions focusing on life quality index (LQI) scored on 4-point Likert scale. Additional question on dermatitis severity scored on a 5-point Likert scale (0 [none] to 4 [extremely severe]) is not considered for calculating total IDQOL.For LQI, score ranges are: Questions 1, 5 to 10: 0 (none) to 3 (all the time/very much). Question 2: 0 (happy), 1 (slightly fretful), 2 (very fretful),3 (always crying). Question 3: 0 (0-15 minutes), 1 (15 minutes-1 hour), 2 (1-2 hours),3 (>2 hours).Question 4: 0 (<1 hour), 1 (1-2 hours), 2 (3-4 hours),3 (>=5 hours). IDQOL total score is sum of score of each question of LQI, ranges from 0 (no impact) to 30 (maximum impact). Higher scores indicated poor HRQoL. Mean is presented. Analysis performed on ITT population. Only those participants with data collected at Baseline and Week 24 are reported. 99999=SD cannot be calculated for 1 participant.

End point type	Secondary

End point timeframe:

Baseline (Day 1) and Week 24

End point values	Dupilumab 200 mg Q4W	Dupilumab 300 mg Q4W	Dupilumab 300 mg Q4W, 600 mg Loading Dose	Dupilumab 200 mg Q2W, 400 mg Loading Dose
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	0[2]	1	0[3]	0[4]
Units: score on a scale				
arithmetic mean (standard deviation)	()	-3.0 (± 99999)	()	()

Notes:

[2] - No participants were analyzed.

[3] - No participants were analyzed.

[4] - No participants were analyzed.

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in Modified Urticaria Activity Score Over 7 Days (mUAS7) at Week 24

End point title	Change From Baseline in Modified Urticaria Activity Score Over 7 Days (mUAS7) at Week 24

End point description:

Modified version of UAS (mUAS) was used for smaller body surface area of child and adolescent participants. The mUAS was derived from sum of daily hives severity score (HSS) (ranging from 0 to 3 [0 = absent; 1 = mild {1 to <10 wheals/24 hours}; 2 = moderate: {10 to 30 wheals/24 hours}; and 3 = intense: {>30 wheals/24 hours or large confluent areas of wheals}]) and daily itch severity score (ISS) (ranging from 0 = none to 3 = intense).Daily mUAS total scores:0 to 6 (0 to 3 for ISS and 0 to 3 for HSS). Daily mUAS scores were summed over 7-day period to create total score ranging from 0 (no urticaria) to 42 (severe urticaria). Completion of mUAS7 was done by child or parent(s)/caregiver(s)/legal guardian(s) for participants aged >=4 years and by parent(s)/caregiver(s) for participants aged <4 years.Mean is presented. Analysis performed on ITT population.Only those participants with data collected at Baseline and Week 24 are reported. 99999=SD cannot be calculated

End point type	Secondary

End point timeframe:

Baseline (Day -7 to Day 1) and Week 24

End point values	Dupilumab 200 mg Q4W	Dupilumab 300 mg Q4W	Dupilumab 300 mg Q4W, 600 mg Loading Dose	Dupilumab 200 mg Q2W, 400 mg Loading Dose
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	1	2	2	5
Units: score on a scale				
arithmetic mean (standard deviation)	-8.0 (± 99999)	-21.4 (± 1.9)	-2.8 (± 1.8)	-7.8 (± 6.6)

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in Itch Severity Score (ISS7) Over 7 Days at Week 24

End point title	Change From Baseline in Itch Severity Score (ISS7) Over 7 Days at Week 24

End point description:

The ISS represents severity of itch on a scale ranging from 0 (none) to 3 (intense). The ISS7 score was the sum of daily ISS scores recorded by a participant at the same time each day over 7 days with an overall scale of 0 (no impact) to 21 (severe impact). Higher scores indicated greater intensity of itch. Mean is presented. Baseline was defined as sum of the 7 daily measurements obtained within the 7 days prior to first study intervention administration. The ITT population included all enrolled participants. Only those participants with data collected at Baseline and Week 24 are reported. 99999=SD cannot be calculated for 1 participant.

End point type	Secondary

End point timeframe:

Baseline (Day -7 to Day 1) and Week 24

End point values	Dupilumab 200 mg Q4W	Dupilumab 300 mg Q4W	Dupilumab 300 mg Q4W, 600 mg Loading Dose	Dupilumab 200 mg Q2W, 400 mg Loading Dose
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	1	2	2	5
Units: score on a scale				
arithmetic mean (standard deviation)	-5.0 (± 99999)	-9.6 (± 3.7)	-1.6 (± 0.6)	-3.4 (± 3.2)

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in Hive Severity Score Over 7 Days (HSS7) at Week 24

End point title	Change From Baseline in Hive Severity Score Over 7 Days (HSS7) at Week 24

End point description:

The HSS7 score is the sum of daily HSS ranging from ranging from 0 to 3 (0 = absent; 1 = mild [1 to <10 wheals/24 hours]; 2 = moderate [10 to 30 wheals/24 hours]; and 3 = intense: [>30 wheals/24 hours or large confluent areas of wheals]) recorded by a participant at the same time of each day over 7 days with an overall scale of 0 (no hives) to 21 (severe hives). Higher scores indicate greater intensity of hives. Mean is presented. Baseline was defined as sum of the 7 daily measurements obtained within the 7 days prior to first study intervention administration. The ITT population included all enrolled participants. Only those participants with data collected at Baseline and Week 24 are reported. 99999=SD cannot be calculated for 1 participant.

End point type	Secondary

End point timeframe:

Baseline (Day -7 to Day 1) and Week 24

End point values	Dupilumab 200 mg Q4W	Dupilumab 300 mg Q4W	Dupilumab 300 mg Q4W, 600 mg Loading Dose	Dupilumab 200 mg Q2W, 400 mg Loading Dose
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	1	2	2	5
Units: score on a scale				
arithmetic mean (standard deviation)	-3.0 (± 99999)	-11.8 (± 1.8)	-1.2 (± 1.2)	-4.4 (± 3.6)

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information	
Timeframe for reporting adverse events:	
From the first dose of study intervention (Day 1) up to end of follow-up, maximum up to 36 weeks.	
Adverse event reporting additional description:	
Analysis was performed on the safety population.	
Assessment type	Systematic

Dictionary used	
Dictionary name	MedDRA
Dictionary version	27.1

Reporting groups	
Reporting group title	Dupilumab 200 mg Q4W
Reporting group description:	
Participants received dupilumab 200 mg SC injection Q4W with no loading dose in children aged >=2 years to <12 years with body weight >=5 kg and <15 kg from Day 1 up to 24 weeks.	
Reporting group title	Dupilumab 300 mg Q4W
Reporting group description:	
Participants received dupilumab 300 mg SC injection Q4W with no loading dose in children aged >=2 years to <6 years with body weight >=15 kg and <30 kg from Day 1 up to 24 weeks.	
Reporting group title	Dupilumab 300 mg Q4W, 600 mg Loading Dose
Reporting group description:	
Participants received dupilumab 300 mg SC injection Q4W with an initial 600 mg loading dose in children aged >=6 years to <12 years with body weight >=15 kg and <30 kg from Day 1 up to 24 weeks.	
Reporting group title	Dupilumab 200 mg Q2W, 400 mg Loading Dose
Reporting group description:	
Participants received dupilumab 200 mg SC injection Q2W with an initial 400 mg loading dose in children aged >=2 years to <12 years with body weight >=30 kg and <60 kg from Day 1 up to 24 weeks.	

Serious adverse events	Dupilumab 200 mg Q4W	Dupilumab 300 mg Q4W	Dupilumab 300 mg Q4W, 600 mg Loading Dose
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 1 (0.00%)	0 / 4 (0.00%)	0 / 2 (0.00%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events	0	0	0

Serious adverse events	Dupilumab 200 mg Q2W, 400 mg Loading Dose		
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 8 (0.00%)		
number of deaths (all causes)	0		
number of deaths resulting from adverse events	0		

Frequency threshold for reporting non-serious adverse events: 0 %

Non-serious adverse events	Dupilumab 200 mg Q4W	Dupilumab 300 mg Q4W	Dupilumab 300 mg Q4W, 600 mg Loading Dose
Total subjects affected by non-serious adverse events			
subjects affected / exposed	1 / 1 (100.00%)	2 / 4 (50.00%)	2 / 2 (100.00%)
Injury, poisoning and procedural complications			
Accidental Overdose			
subjects affected / exposed	0 / 1 (0.00%)	0 / 4 (0.00%)	0 / 2 (0.00%)
occurrences (all)	0	0	0
Vascular disorders			
Internal Haemorrhage			
subjects affected / exposed	0 / 1 (0.00%)	0 / 4 (0.00%)	0 / 2 (0.00%)
occurrences (all)	0	0	0
Nervous system disorders			
Headache			
subjects affected / exposed	0 / 1 (0.00%)	0 / 4 (0.00%)	0 / 2 (0.00%)
occurrences (all)	0	0	0
Migraine			
subjects affected / exposed	0 / 1 (0.00%)	0 / 4 (0.00%)	0 / 2 (0.00%)
occurrences (all)	0	0	0
General disorders and administration site conditions			
Injection Site Reaction			
subjects affected / exposed	0 / 1 (0.00%)	0 / 4 (0.00%)	0 / 2 (0.00%)
occurrences (all)	0	0	0
Fatigue			
subjects affected / exposed	0 / 1 (0.00%)	0 / 4 (0.00%)	0 / 2 (0.00%)
occurrences (all)	0	0	0
Swelling Face			
subjects affected / exposed	0 / 1 (0.00%)	0 / 4 (0.00%)	0 / 2 (0.00%)
occurrences (all)	0	0	0
Pyrexia			

subjects affected / exposed	0 / 1 (0.00%)	0 / 4 (0.00%)	0 / 2 (0.00%)
occurrences (all)	0	0	0
Immune system disorders			
Seasonal Allergy			
subjects affected / exposed	0 / 1 (0.00%)	0 / 4 (0.00%)	0 / 2 (0.00%)
occurrences (all)	0	0	0
Gastrointestinal disorders			
Vomiting			
subjects affected / exposed	0 / 1 (0.00%)	1 / 4 (25.00%)	0 / 2 (0.00%)
occurrences (all)	0	1	0
Lip Swelling			
subjects affected / exposed	0 / 1 (0.00%)	0 / 4 (0.00%)	0 / 2 (0.00%)
occurrences (all)	0	0	0
Diarrhoea			
subjects affected / exposed	0 / 1 (0.00%)	0 / 4 (0.00%)	0 / 2 (0.00%)
occurrences (all)	0	0	0
Abdominal Pain Upper			
subjects affected / exposed	0 / 1 (0.00%)	0 / 4 (0.00%)	0 / 2 (0.00%)
occurrences (all)	0	0	0
Abdominal Discomfort			
subjects affected / exposed	0 / 1 (0.00%)	0 / 4 (0.00%)	0 / 2 (0.00%)
occurrences (all)	0	0	0
Respiratory, thoracic and mediastinal disorders			
Asthma			
subjects affected / exposed	0 / 1 (0.00%)	0 / 4 (0.00%)	0 / 2 (0.00%)
occurrences (all)	0	0	0
Rhinorrhoea			
subjects affected / exposed	1 / 1 (100.00%)	0 / 4 (0.00%)	0 / 2 (0.00%)
occurrences (all)	1	0	0
Skin and subcutaneous tissue disorders			
Skin Discolouration			
subjects affected / exposed	0 / 1 (0.00%)	0 / 4 (0.00%)	0 / 2 (0.00%)
occurrences (all)	0	0	0
Psoriasis			
subjects affected / exposed	0 / 1 (0.00%)	1 / 4 (25.00%)	0 / 2 (0.00%)
occurrences (all)	0	1	0

Psychiatric disorders			
Insomnia			
subjects affected / exposed	0 / 1 (0.00%)	1 / 4 (25.00%)	0 / 2 (0.00%)
occurrences (all)	0	2	0
Infections and infestations			
Gastroenteritis Viral			
subjects affected / exposed	0 / 1 (0.00%)	0 / 4 (0.00%)	0 / 2 (0.00%)
occurrences (all)	0	0	0
Folliculitis			
subjects affected / exposed	0 / 1 (0.00%)	0 / 4 (0.00%)	0 / 2 (0.00%)
occurrences (all)	0	0	0
Conjunctivitis Bacterial			
subjects affected / exposed	0 / 1 (0.00%)	0 / 4 (0.00%)	0 / 2 (0.00%)
occurrences (all)	0	0	0
Covid-19			
subjects affected / exposed	0 / 1 (0.00%)	0 / 4 (0.00%)	0 / 2 (0.00%)
occurrences (all)	0	0	0
Hand-Foot-And-Mouth Disease			
subjects affected / exposed	0 / 1 (0.00%)	0 / 4 (0.00%)	1 / 2 (50.00%)
occurrences (all)	0	0	1
Hordeolum			
subjects affected / exposed	0 / 1 (0.00%)	0 / 4 (0.00%)	1 / 2 (50.00%)
occurrences (all)	0	0	1
Influenza			
subjects affected / exposed	0 / 1 (0.00%)	0 / 4 (0.00%)	1 / 2 (50.00%)
occurrences (all)	0	0	1
Viral Upper Respiratory Tract Infection			
subjects affected / exposed	1 / 1 (100.00%)	1 / 4 (25.00%)	0 / 2 (0.00%)
occurrences (all)	1	1	0
Viral Rash			
subjects affected / exposed	0 / 1 (0.00%)	0 / 4 (0.00%)	0 / 2 (0.00%)
occurrences (all)	0	0	0
Upper Respiratory Tract Infection			
subjects affected / exposed	0 / 1 (0.00%)	0 / 4 (0.00%)	0 / 2 (0.00%)
occurrences (all)	0	0	0
Subcutaneous Abscess			

subjects affected / exposed	0 / 1 (0.00%)	1 / 4 (25.00%)	0 / 2 (0.00%)
occurrences (all)	0	1	0
Nasopharyngitis			
subjects affected / exposed	0 / 1 (0.00%)	0 / 4 (0.00%)	2 / 2 (100.00%)
occurrences (all)	0	0	3
Otitis Media			
subjects affected / exposed	0 / 1 (0.00%)	0 / 4 (0.00%)	1 / 2 (50.00%)
occurrences (all)	0	0	1
Pharyngitis			
subjects affected / exposed	0 / 1 (0.00%)	0 / 4 (0.00%)	0 / 2 (0.00%)
occurrences (all)	0	0	0
Rhinovirus Infection			
subjects affected / exposed	0 / 1 (0.00%)	1 / 4 (25.00%)	0 / 2 (0.00%)
occurrences (all)	0	1	0

Non-serious adverse events	Dupilumab 200 mg Q2W, 400 mg Loading Dose		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	7 / 8 (87.50%)		
Injury, poisoning and procedural complications			
Accidental Overdose			
subjects affected / exposed	1 / 8 (12.50%)		
occurrences (all)	1		
Vascular disorders			
Internal Haemorrhage			
subjects affected / exposed	1 / 8 (12.50%)		
occurrences (all)	1		
Nervous system disorders			
Headache			
subjects affected / exposed	2 / 8 (25.00%)		
occurrences (all)	2		
Migraine			
subjects affected / exposed	1 / 8 (12.50%)		
occurrences (all)	1		
General disorders and administration site conditions			

Injection Site Reaction subjects affected / exposed occurrences (all) Fatigue subjects affected / exposed occurrences (all) Swelling Face subjects affected / exposed occurrences (all) Pyrexia subjects affected / exposed occurrences (all)	1 / 8 (12.50%) 2 1 / 8 (12.50%) 1 1 / 8 (12.50%) 1 1 / 8 (12.50%) 1		
Immune system disorders Seasonal Allergy subjects affected / exposed occurrences (all)	1 / 8 (12.50%) 1		
Gastrointestinal disorders Vomiting subjects affected / exposed occurrences (all) Lip Swelling subjects affected / exposed occurrences (all) Diarrhoea subjects affected / exposed occurrences (all) Abdominal Pain Upper subjects affected / exposed occurrences (all) Abdominal Discomfort subjects affected / exposed occurrences (all)	1 / 8 (12.50%) 1 1 / 8 (12.50%) 1 1 / 8 (12.50%) 1 1 / 8 (12.50%) 1 1 / 8 (12.50%) 1		
Respiratory, thoracic and mediastinal disorders Asthma subjects affected / exposed occurrences (all)	1 / 8 (12.50%) 1		

Rhinorrhoea subjects affected / exposed occurrences (all)	0 / 8 (0.00%) 0		
Skin and subcutaneous tissue disorders Skin Discolouration subjects affected / exposed occurrences (all) Psoriasis subjects affected / exposed occurrences (all)	 1 / 8 (12.50%) 1 0 / 8 (0.00%) 0		
Psychiatric disorders Insomnia subjects affected / exposed occurrences (all)	 0 / 8 (0.00%) 0		
Infections and infestations Gastroenteritis Viral subjects affected / exposed occurrences (all) Folliculitis subjects affected / exposed occurrences (all) Conjunctivitis Bacterial subjects affected / exposed occurrences (all) Covid-19 subjects affected / exposed occurrences (all) Hand-Foot-And-Mouth Disease subjects affected / exposed occurrences (all) Hordeolum subjects affected / exposed occurrences (all) Influenza subjects affected / exposed occurrences (all) Viral Upper Respiratory Tract	 1 / 8 (12.50%) 2 1 / 8 (12.50%) 1 1 / 8 (12.50%) 1 1 / 8 (12.50%) 1 0 / 8 (0.00%) 0 0 / 8 (0.00%) 0 1 / 8 (12.50%) 1		

Infection			
subjects affected / exposed	2 / 8 (25.00%)		
occurrences (all)	3		
Viral Rash			
subjects affected / exposed	1 / 8 (12.50%)		
occurrences (all)	2		
Upper Respiratory Tract Infection			
subjects affected / exposed	1 / 8 (12.50%)		
occurrences (all)	1		
Subcutaneous Abscess			
subjects affected / exposed	0 / 8 (0.00%)		
occurrences (all)	0		
Nasopharyngitis			
subjects affected / exposed	0 / 8 (0.00%)		
occurrences (all)	0		
Otitis Media			
subjects affected / exposed	0 / 8 (0.00%)		
occurrences (all)	0		
Pharyngitis			
subjects affected / exposed	1 / 8 (12.50%)		
occurrences (all)	1		
Rhinovirus Infection			
subjects affected / exposed	0 / 8 (0.00%)		
occurrences (all)	0		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
31 May 2023	The purpose of this amendment was to remove the inclusion of participants with chronic inducible cold urticaria (CICU) following the results of the phase 3 study EFC16720, which evaluated the efficacy and safety of dupilumab in adult participants with CICU who remained symptomatic despite the use of H1-antihistamine treatment. This study did not meet the required efficacy endpoints to continue this program, including the development in the pediatric CICU population. In addition, this amendment modified the inclusion criteria and the PK sampling schedule to increase flexibility and to reduce participant burden related to study visits and procedures.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported