Clinical trial results:
Open-label, Interventional, Cohort Study to Evaluate Long-term Safety of Dupilumab in Patients with Moderate to Severe Asthma who Completed the TRAVERSE-LTS12551 Clinical Trial

Summary

EudraCT number	2017-002134-23
Trial protocol	FR BE DE NL Outside EU/EEA
Global end of trial date	18 February 2022

Results information

Result version number	v1 (current)
This version publication date	02 September 2022
First version publication date	02 September 2022

Trial information

Trial identification

Sponsor protocol code	LPS15023

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT03620747
WHO universal trial number (UTN)	U1111-1196-5369
Other trial identifiers	Study name: TRAVERSE-LPS15023

Notes:

Sponsors

Sponsor organisation name	Sanofi aventis recherche & développement
Sponsor organisation address	1 avenue Pierre Brossolette, Chilly-Mazarin, France, 91380
Public contact	Trial Transparency Team, Sanofi aventis recherche & développement, Contact-US@sanofi.com
Scientific contact	Trial Transparency Team, Sanofi aventis recherche & développement, Contact-US@sanofi.com

Notes:

Paediatric regulatory details

Is trial part of an agreed paediatric investigation plan (PIP)	No
Does article 45 of REGULATION (EC) No 1901/2006 apply to this trial?	No
Does article 46 of REGULATION (EC) No 1901/2006 apply to this trial?	Yes

Notes:

Results analysis stage

Analysis stage	Final
Date of interim/final analysis	28 March 2022
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	18 February 2022
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To describe the long-term safety of dupilumab in treatment of subjects with moderate to severe asthma who completed the previous asthma clinical trial (TRAVERSE-LTS12551 [EudraCT number: 2013-003856-19]).

Protection of trial subjects:

The study was conducted by investigators experienced in the treatment of adult and adolescent subjects. The parent(s) or guardian(s) 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 minimised. The number of blood samples as well as the amount of blood drawn were adjusted according to age and weight. A topical anesthesia may have been used to minimise distress and discomfort. Adult subjects were fully informed of all pertinent aspects of the clinical trial as well as the possibility to discontinue at any time in language and terms appropriate for the subject and considering the local culture. During the course of the trial, subjects were provided with individual subject cards indicating the nature of the trial the subject is participating, contact details and any information needed in the event of a medical emergency. Collected personal data and human biological samples were processed in compliance with the Sanofi-Aventis Group Personal Data Protection Charter ensuring that the Group abides by the laws governing personal data protection in force in all countries in which it operates.

Background therapy:

Subjects continued background therapy of moderate or high-dose inhaled corticosteroid (ICS) as maintained in TRAVERSE-LTS12551. Background therapy was modified during the study based on Investigator's judgment. Subjects used additional asthma controller therapies initiated during TRAVERSE-LTS12551. Subjects received salbutamol/albuterol hydrofluoroalkane pressurised metered dose inhalers (MDI) or levosalbutamol/levalbuterol hydrofluoroalkane pressurised MDI as reliever medication during the LPS15023 study.

Evidence for comparator: -

Actual start date of recruitment	30 August 2018
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	Netherlands: 1
Country: Number of subjects enrolled	Belgium: 1
Country: Number of subjects enrolled	France: 23
Country: Number of subjects enrolled	Germany: 19
Country: Number of subjects enrolled	South Africa: 33
Country: Number of subjects enrolled	Israel: 7
Country: Number of subjects enrolled	Canada: 26

Country: Number of subjects enrolled	Argentina: 113
Country: Number of subjects enrolled	Japan: 103
Country: Number of subjects enrolled	United States: 67
Worldwide total number of subjects	393
EEA total number of subjects	44

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)	8
Adults (18-64 years)	306
From 65 to 84 years	79
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

The study was conducted at 138 sites in 10 countries. A total of 393 subjects were enrolled in the study between 30 August 2018 and 27 August 2020.

Pre-assignment

Screening details:

Subjects with moderate to severe asthma who had completed the parent study TRAVERSE-LTS12551 were enrolled in this current study (LPS15023).

Period 1

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

Arms

Arm title	Dupilumab

Arm description:

Subjects received subcutaneous (SC) dose of dupilumab 300 milligrams (mg) every 2 weeks (q2w) from Week 0 up to Week 132. Subjects who discontinued treatment for greater than or equal to [>=] 6 weeks after study LTS12551, received a 600 mg loading dose of dupilumab on Week 0. Subjects were also on background dose of medium or high dose ICS as maintained in study LTS12551 in combination with controllers (and/or oral corticosteroid [OCS] for those subjects from the original parent study EFC13691 [EudraCT number: 2015-001573-40]). Salbutamol/albuterol hydrofluoroalkane pressurised MDI or levosalbutamol/levalbuterol hydrofluoroalkane pressurised MDI were given as reliever medication as needed during the study.

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

Dosage and administration details:

Subjects received dupilumab 300 mg SC injection q2w for up to 132 weeks.

Number of subjects in period 1	Dupilumab
Started	393
Completed	374
Not completed	19
Subject decision	7
Other	3
Adverse event	6
Poor compliance to protocol	2
Lack of efficacy	1

Baseline characteristics

Reporting groups	
Reporting group title	Dupilumab

Reporting group description:

Subjects received subcutaneous (SC) dose of dupilumab 300 milligrams (mg) every 2 weeks (q2w) from Week 0 up to Week 132. Subjects who discontinued treatment for greater than or equal to [>=] 6 weeks after study LTS12551, received a 600 mg loading dose of dupilumab on Week 0. Subjects were also on background dose of medium or high dose ICS as maintained in study LTS12551 in combination with controllers (and/or oral corticosteroid [OCS] for those subjects from the original parent study EFC13691 [EudraCT number: 2015-001573-40]). Salbutamol/albuterol hydrofluoroalkane pressurised MDI or levosalbutamol/levalbuterol hydrofluoroalkane pressurised MDI were given as reliever medication as needed during the study.

Reporting group values	Dupilumab	Total	
Number of subjects	393	393	
Age categorical			
Units: Subjects			

Age continuous			
Units: years			
arithmetic mean	52.1		
standard deviation	± 14.19	-	
Gender categorical			
Units: Subjects			
Female	231	231	
Male	162	162	

End points

End points reporting groups

Reporting group title	Dupilumab

Reporting group description:

Subjects received subcutaneous (SC) dose of dupilumab 300 milligrams (mg) every 2 weeks (q2w) from Week 0 up to Week 132. Subjects who discontinued treatment for greater than or equal to [>=] 6 weeks after study LTS12551, received a 600 mg loading dose of dupilumab on Week 0. Subjects were also on background dose of medium or high dose ICS as maintained in study LTS12551 in combination with controllers (and/or oral corticosteroid [OCS] for those subjects from the original parent study EFC13691 [EudraCT number: 2015-001573-40]). Salbutamol/albuterol hydrofluoroalkane pressurised MDI or levosalbutamol/levalbuterol hydrofluoroalkane pressurised MDI were given as reliever medication as needed during the study.

Primary: Percentage of Subjects With Treatment-emergent Adverse Events (TEAEs)

End point title	Percentage of Subjects With Treatment-emergent Adverse Events (TEAEs)[1]

End point description:

An Adverse Event (AE) was defined as any untoward medical occurrence in a subject who received study drug and did not necessarily had to have a causal relationship with the treatment. TEAEs were the AEs that developed or worsened or became serious during the TEAE period (defined as the time from the first dose of the investigational medicinal product [IMP] up to 12 weeks after the last dose of the IMP [maximum duration: up to 144 weeks]). Analysis was performed on safety population that included all subjects who had received at least one dose or part of a dose of IMP during the current study.

End point type	Primary

End point timeframe:

From first dose of (IMP) up to 12 weeks after last dose of IMP (maximum duration: up to 144 Weeks)

Notes:

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

End point values	Dupilumab			
Subject group type	Reporting group			
Number of subjects analysed	393			
Units: percentage of subjects				
number (confidence interval 95%)	54.5 (47.40 to 62.26)			

Statistical analyses

No statistical analyses for this end point

Primary: Treatment-emergent Adverse Event Rate (Events/100 Person-years)

End point title	Treatment-emergent Adverse Event Rate (Events/100 Person-years)[2]

End point description:

An AE was defined as any untoward medical occurrence in a subject who received study drug and did not necessarily had to have a causal relationship with the treatment. TEAEs were the AEs that developed or worsened or became serious during the TEAE period (defined as the time from the first dose of the IMP up to 12 weeks after last dose of the IMP [maximum duration: up to 144 weeks]). TEAE event rate

was defined as the number of TEAE events per 100 person-years. Analysis was performed on safety population.

End point type	Primary

End point timeframe:

From first dose of IMP up to 12 weeks after last dose of IMP (maximum duration: up to 144 Weeks)

Notes:

[2] - 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 was descriptive in nature, no statistical analysis was reported.

End point values	Dupilumab			
Subject group type	Reporting group			
Number of subjects analysed	393			
Units: events per 100 person-years				
number (confidence interval 95%)	171.4 (162.71 to 180.43)			

Statistical analyses

No statistical analyses for this end point

Secondary: Adverse Events of Special Interest (AESIs) Event Rate (Events/100 Person-years)

End point title	Adverse Events of Special Interest (AESIs) Event Rate (Events/100 Person-years)

End point description:

An AE was defined as any untoward medical occurrence in a subject who received study drug and did not necessarily had to have a causal relationship with the treatment. AESI were AEs (serious or non-serious) of scientific and medical concern specific to the Sponsor’s product or program, for which ongoing monitoring and immediate notification by the Investigator to the Sponsor was required. AESI event rate was defined as the number of AESI events per 100 person-years. Analysis was performed on safety population.

End point type	Secondary

End point timeframe:

From first dose of IMP up to 12 weeks after last dose of IMP (maximum duration: up to 144 Weeks)

End point values	Dupilumab			
Subject group type	Reporting group			
Number of subjects analysed	393			
Units: events per 100 person-years				
number (confidence interval 95%)	6.0 (4.40 to 7.99)			

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Subjects With Treatment-emergent Serious Adverse Events (TESAEs), Adverse Events of Special Interest (AESIs) and AEs Leading to Study Discontinuation

End point title	Percentage of Subjects With Treatment-emergent Serious Adverse Events (TESAEs), Adverse Events of Special Interest (AESIs) and AEs Leading to Study Discontinuation

End point description:

AE: any untoward medical occurrence in subjects that received IMP and did not necessarily had to have causal relationship with treatment. TEAEs: AEs developed/worsened in grade/become serious during TEAE period (from first dose of IMP up to 12 weeks after last dose of IMP [maximum duration: up to 144 Weeks]). SAE: any untoward medical occurrence at any dose resulted in death, was life-threatening, required inpatient hospitalisation, prolongation of existing hospitalisation, resulted in persistent or significant disability/incapacity, was congenital anomaly/birth defect or was medically important event. AESI:AE (serious/non-serious) of scientific and medical concern specific to Sponsor's product/program, for which ongoing monitoring and immediate notification by Investigator to Sponsor required. Analysis was performed on safety population.

End point type	Secondary

End point timeframe:

From first dose of IMP up to 12 weeks after last dose of IMP (maximum duration: up to 144 Weeks)

End point values	Dupilumab			
Subject group type	Reporting group			
Number of subjects analysed	393			
Units: percentage of subjects				
number (not applicable)				
TESAEs	5.6			
AESIs	6.1			
AEs leading to study discontinuation	1.5			

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

From first dose of IMP up to 12 weeks after last dose of IMP (maximum duration: up to 144 Weeks)

Adverse event reporting additional description:

Reported AEs and deaths were TEAEs that developed or worsened or became serious during the TEAE period (defined as the time from the first dose of the IMP up to 12 weeks after last dose of the IMP). Analysis was performed on safety population.

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	24.1

Reporting groups

Reporting group title	Dupilumab

Reporting group description:

Subjects received SC dose of dupilumab 300 mg q2w from Week 0 up to Week 132. Subjects who discontinued treatment for >= 6 weeks after study LTS12551, received a 600 mg loading dose of dupilumab on Week 0. Subjects were also on background dose of medium or high dose ICS as maintained in study LTS12551 in combination with controllers (and/or OCS for those subjects from the original parent study EFC13691). Salbutamol/albuterol hydrofluoroalkane pressurised MDI or levosalbutamol/levalbuterol hydrofluoroalkane pressurised MDI were given as reliever medication as needed during the study.

Serious adverse events	Dupilumab		
Total subjects affected by serious adverse events			
subjects affected / exposed	22 / 393 (5.60%)		
number of deaths (all causes)	5		
number of deaths resulting from adverse events			
Cardiac disorders			
Cardiac failure congestive			
subjects affected / exposed	1 / 393 (0.25%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Myocardial infarction			
subjects affected / exposed	1 / 393 (0.25%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Nervous system disorders			
Epilepsy			

subjects affected / exposed	1 / 393 (0.25%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Pudendal canal syndrome			
subjects affected / exposed	1 / 393 (0.25%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Pregnancy, puerperium and perinatal conditions			
Abortion spontaneous			
subjects affected / exposed	1 / 393 (0.25%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
General disorders and administration site conditions			
Non-cardiac chest pain			
subjects affected / exposed	1 / 393 (0.25%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Immune system disorders			
Anaphylactic reaction			
subjects affected / exposed	1 / 393 (0.25%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Eye disorders			
Cataract			
subjects affected / exposed	1 / 393 (0.25%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Gastrointestinal disorders			
Abdominal pain			
subjects affected / exposed	1 / 393 (0.25%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Enterovesical fistula			

subjects affected / exposed	1 / 393 (0.25%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Hiatus hernia				
subjects affected / exposed	1 / 393 (0.25%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Pancreatitis				
subjects affected / exposed	1 / 393 (0.25%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 1			
Respiratory, thoracic and mediastinal disorders				
Asthma				
subjects affected / exposed	4 / 393 (1.02%)			
occurrences causally related to treatment / all	0 / 5			
deaths causally related to treatment / all	0 / 0			
Pulmonary embolism				
subjects affected / exposed	1 / 393 (0.25%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 1			
Respiratory failure				
subjects affected / exposed	1 / 393 (0.25%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Tracheal stenosis				
subjects affected / exposed	1 / 393 (0.25%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Hepatobiliary disorders				
Cholecystitis				
subjects affected / exposed	1 / 393 (0.25%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			

Infections and infestations			
Bronchitis			
subjects affected / exposed	1 / 393 (0.25%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
COVID-19			
subjects affected / exposed	3 / 393 (0.76%)		
occurrences causally related to treatment / all	0 / 3		
deaths causally related to treatment / all	0 / 0		
COVID-19 pneumonia			
subjects affected / exposed	3 / 393 (0.76%)		
occurrences causally related to treatment / all	0 / 3		
deaths causally related to treatment / all	0 / 3		
Pneumonia			
subjects affected / exposed	1 / 393 (0.25%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Urinary tract infection			
subjects affected / exposed	1 / 393 (0.25%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		

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

Non-serious adverse events	Dupilumab		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	93 / 393 (23.66%)		
Respiratory, thoracic and mediastinal disorders			
Asthma			
subjects affected / exposed	52 / 393 (13.23%)		
occurrences (all)	77		
Infections and infestations			
COVID-19			
subjects affected / exposed	22 / 393 (5.60%)		
occurrences (all)	24		

Nasopharyngitis subjects affected / exposed occurrences (all)	33 / 393 (8.40%) 36		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? No

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported