Clinical trial results:
A multi-centre, open-label extension, safety study to describe the long-term clinical experience of mepolizumab in participants with hypereosinophilic syndrome (HES) from Study 200622

Summary

EudraCT number	2017-000184-32
Trial protocol	DE GB BE ES FR PL Outside EU/EEA IT RO
Global end of trial date	30 December 2019

Results information

Result version number	v1 (current)
This version publication date	20 June 2020
First version publication date	20 June 2020

Trial information

Trial identification

Sponsor protocol code	205203

Additional study identifiers

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

Notes:

Sponsors

Sponsor organisation name	GlaxoSmithKline
Sponsor organisation address	980 Great West Road, Brentford, Middlesex, United Kingdom, TW8 9GS
Public contact	GSK Response Center, GlaxoSmithKline, 1 8664357343, GSKClinicalSupportHD@gsk.com
Scientific contact	GSK Response Center, GlaxoSmithKline, 1 8664357343, GSKClinicalSupportHD@gsk.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?	No

Notes:

Results analysis stage

Analysis stage	Final
Date of interim/final analysis	13 March 2020
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	30 December 2019
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To describe the long-term safety profile of mepolizumab in participants with HES who took part in Study 200622.

Protection of trial subjects:

Not Applicable

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	13 November 2017
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	Belgium: 10
Country: Number of subjects enrolled	Brazil: 3
Country: Number of subjects enrolled	France: 17
Country: Number of subjects enrolled	Germany: 13
Country: Number of subjects enrolled	Italy: 5
Country: Number of subjects enrolled	Argentina: 6
Country: Number of subjects enrolled	Mexico: 5
Country: Number of subjects enrolled	Poland: 10
Country: Number of subjects enrolled	Romania: 2
Country: Number of subjects enrolled	Russian Federation: 7
Country: Number of subjects enrolled	Spain: 3
Country: Number of subjects enrolled	United Kingdom: 6
Country: Number of subjects enrolled	United States: 15
Worldwide total number of subjects	102
EEA total number of subjects	66

Notes:

Subjects enrolled per age group

In utero	0
Preterm newborn - gestational age < 37	0

wk	
Newborns (0-27 days)	0
Infants and toddlers (28 days-23 months)	0
Children (2-11 years)	0
Adolescents (12-17 years)	4
Adults (18-64 years)	85
From 65 to 84 years	13
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

This was a multi-center, open-label extension study to evaluate the long-term safety profile of mepolizumab in participants with Hypereosinophilic Syndrome (HES). In this study, participants received open-label mepolizumab 300 milligram (mg) subcutaneously (SC).

Pre-assignment

Screening details:

A total of 102 participants who completed the parent study (200622 [NCT02836496]) and met the eligibility criteria were enrolled in this open-label extension study.

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	Mepolizumab 300 mg SC

Arm description:

Participants were administered 300 mg SC mepolizumab every 4 weeks (starting approximately 32 weeks after the first dose of study treatment in Study 200622). The final dose of mepolizumab was administered at Visit 5 (Week 16).

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

Dosage and administration details:

Mepolizumab was administered as three 100 mg SC injections every 4 weeks. It was provided in a 100 mg vial for injection.

Number of subjects in period 1	Mepolizumab 300 mg SC
Started	102
Completed	98
Not completed	4
Consent withdrawn by subject	2
Adverse event, non-fatal	1
Lost to follow-up	1

Baseline characteristics

Reporting groups	
Reporting group title	Mepolizumab 300 mg SC
Reporting group description:	
Participants were administered 300 mg SC mepolizumab every 4 weeks (starting approximately 32 weeks after the first dose of study treatment in Study 200622). The final dose of mepolizumab was administered at Visit 5 (Week 16).	

Reporting group values	Mepolizumab 300 mg SC	Total	
Number of subjects	102	102	
Age categorical Units: Subjects			
In utero	0	0	
Preterm newborn infants (gestational age < 37 wks)	0	0	
Newborns (0-27 days)	0	0	
Infants and toddlers (28 days-23 months)	0	0	
Children (2-11 years)	0	0	
Adolescents (12-17 years)	4	4	
Adults (18-64 years)	85	85	
From 65-84 years	13	13	
85 years and over	0	0	
Age Continuous Units: Years			
arithmetic mean	46.0		
standard deviation	± 15.54	-	
Sex: Female, Male Units: Participants			
Female	55	55	
Male	47	47	
Race/Ethnicity, Customized Units: Subjects			
Asian-East Asian Heritage	1	1	
Black or African American	2	2	
White-White/Caucasian/European Heritage	79	79	
American Indian or Alaskan Native	3	3	
Unknown	17	17	

End points

End points reporting groups

Reporting group title	Mepolizumab 300 mg SC

Reporting group description:

Participants were administered 300 mg SC mepolizumab every 4 weeks (starting approximately 32 weeks after the first dose of study treatment in Study 200622). The final dose of mepolizumab was administered at Visit 5 (Week 16).

Primary: Number of participants with common (>=3%) non-serious adverse events (AEs)

End point title	Number of participants with common (>=3%) non-serious adverse events (AEs)[1]

End point description:

An AE was any untoward medical occurrence in a clinical study participant, temporally associated with the use of a study treatment, whether or not considered related to the study treatment. Serious AE was defined as any untoward medical occurrence that, at any dose results in death, is life-threatening, requires hospitalization or prolongation of existing hospitalization, results in persistent disability/incapacity, congenital anomaly/birth defect or any other situation according to medical or scientific judgment. Non-serious AEs from start of study treatment until 28 days after last dose (up to Week 20) are reported. Number of participants with common (>=3% incidence) non-serious AEs are presented. Safety Population comprised of all participants who received at least one dose of open-label mepolizumab.

End point type	Primary

End point timeframe:

Up to Week 20

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: There are no statistical data to report.

End point values	Mepolizumab 300 mg SC			
Subject group type	Reporting group			
Number of subjects analysed	102[2]			
Units: Participants	34			

Notes:

[2] - Safety Population

Statistical analyses

No statistical analyses for this end point

Primary: Number of participants with serious AEs

End point title	Number of participants with serious AEs[3]

End point description:

An AE was any untoward medical occurrence in a clinical study participant, temporally associated with the use of a study treatment, whether or not considered related to the study treatment. Serious AE was defined as any untoward medical occurrence that, at any dose results in death, is life-threatening, requires hospitalization or prolongation of existing hospitalization, results in persistent disability/incapacity, congenital anomaly/birth defect or any other situation according to medical or scientific judgment. Number of participants with serious AEs are presented.

End point type	Primary

End point timeframe:

Up to Week 28

Notes:

[3] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: There are no statistical data to report.

End point values	Mepolizumab 300 mg SC			
Subject group type	Reporting group			
Number of subjects analysed	102[4]			
Units: Participants	9			

Notes:

[4] - Safety Population

Statistical analyses

No statistical analyses for this end point

Primary: Number of participants with the presence of anti-drug antibody

End point title	Number of participants with the presence of anti-drug

End point description:

Blood samples were analyzed for the presence of anti-mepolizumab antibodies by binding anti-drug antibody (ADA) assay. The binding ADA assay results at each visit were summarized as negative or positive. The binding ADA assay was performed in three steps; screening, confirmation and titration. The screening assay produced a result of positive or negative relative to a screening cut point. Positive samples continued with the confirmation assay, which also produced a result of positive or negative relative to a confirmation cut point. For positive confirmation samples, a titre value was obtained to quantify the degree of binding in a titration assay. Participants were considered 'Positive' if they had a positive confirmation ADA assay result. Only those participants with data available at specified data points were analyzed (represented by n= X in the category titles).

End point type	Primary

End point timeframe:

Baseline (Day 1), Week 20 and Week 28

Notes:

[5] - 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: There are no statistical data to report.

End point values	Mepolizumab 300 mg SC			
Subject group type	Reporting group			
Number of subjects analysed	102[6]			
Units: Participants				
Baseline, Negative, n=102	101			
Baseline, Positive, n=102	1			
Week 20, Negative, n=101	101			
Week 20, Positive, n=101	0			
Week 28, Negative, n=14	14			
Week 28, Positive, n=14	0			

Notes:

[6] - Safety Population

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Serious AEs were reported from start of study (Week 0) up to end of study (up to Week 28) and non-serious AEs were reported from start of study treatment until 28 days after last dose (up to Week 20)

Adverse event reporting additional description:

Non-serious AEs and serious AEs were reported for Safety Population.

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	22.1

Reporting groups

Reporting group title	Mepolizumab 300 mg SC

Reporting group description:

Participants were administered 300 mg SC mepolizumab every 4 weeks (starting approximately 32 weeks after the first dose of study treatment in Study 200622). The final dose of mepolizumab was administered at Visit 5 (Week 16).

Serious adverse events	Mepolizumab 300 mg SC		
Total subjects affected by serious adverse events			
subjects affected / exposed	9 / 102 (8.82%)		
number of deaths (all causes)	0		
number of deaths resulting from adverse events			
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Peripheral T-cell lymphoma unspecified			
subjects affected / exposed	1 / 102 (0.98%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Injury, poisoning and procedural complications			
Joint dislocation			
subjects affected / exposed	1 / 102 (0.98%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Blood and lymphatic system disorders			
Hypereosinophilic syndrome			

subjects affected / exposed	1 / 102 (0.98%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Gastrointestinal disorders			
Gastroenteritis eosinophilic			
subjects affected / exposed	1 / 102 (0.98%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Infections and infestations			
Bacteraemia			
subjects affected / exposed	1 / 102 (0.98%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Clostridium difficile colitis			
subjects affected / exposed	1 / 102 (0.98%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Diverticulitis			
subjects affected / exposed	1 / 102 (0.98%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Gastrointestinal infection			
subjects affected / exposed	1 / 102 (0.98%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Infective exacerbation of bronchiectasis			
subjects affected / exposed	1 / 102 (0.98%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Mycobacterium abscessus infection			
subjects affected / exposed	1 / 102 (0.98%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		

Perihepatic abscess			
subjects affected / exposed	1 / 102 (0.98%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Pneumonia			
subjects affected / exposed	1 / 102 (0.98%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Sinusitis			
subjects affected / exposed	1 / 102 (0.98%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		

Frequency threshold for reporting non-serious adverse events: 3 %

Non-serious adverse events	Mepolizumab 300 mg SC		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	34 / 102 (33.33%)		
Nervous system disorders			
Headache			
subjects affected / exposed	6 / 102 (5.88%)		
occurrences (all)	7		
General disorders and administration site conditions			
Fatigue			
subjects affected / exposed	4 / 102 (3.92%)		
occurrences (all)	4		
Injection site reaction			
subjects affected / exposed	4 / 102 (3.92%)		
occurrences (all)	11		
Gastrointestinal disorders			
Diarrhoea			
subjects affected / exposed	12 / 102 (11.76%)		
occurrences (all)	13		
Vomiting			

subjects affected / exposed occurrences (all) Constipation subjects affected / exposed occurrences (all) Nausea subjects affected / exposed occurrences (all)	6 / 102 (5.88%) 7 5 / 102 (4.90%) 6 5 / 102 (4.90%) 5		
Skin and subcutaneous tissue disorders Pruritus subjects affected / exposed occurrences (all)	 7 / 102 (6.86%) 7		
Musculoskeletal and connective tissue disorders Arthralgia subjects affected / exposed occurrences (all)	 5 / 102 (4.90%) 6		
Infections and infestations Nasopharyngitis subjects affected / exposed occurrences (all) Bronchitis subjects affected / exposed occurrences (all) Sinusitis subjects affected / exposed occurrences (all) Upper respiratory tract infection subjects affected / exposed occurrences (all)	 5 / 102 (4.90%) 5 4 / 102 (3.92%) 4 4 / 102 (3.92%) 4 4 / 102 (3.92%) 4		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
13 January 2017	Amendment 01: Correct EudraCT number was provided in the protocol.
16 November 2017	Amendment 02: Added the optional biomarker sub-study and updated the text around the HES therapy adjustment after HES flare considering therapy reduction during the study.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported