



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 ($\geq 3\%$) non-serious adverse events (AEs)

| | |
|---|---|
| End point title | Number of participants with common ($\geq 3\%$) 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 ($\geq 3\%$ 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 | 6 / 102 (5.88%) | | |
| occurrences (all) | 7 | | |
| Constipation | | | |
| subjects affected / exposed | 5 / 102 (4.90%) | | |
| occurrences (all) | 6 | | |
| Nausea | | | |
| subjects affected / exposed | 5 / 102 (4.90%) | | |
| occurrences (all) | 5 | | |
| Skin and subcutaneous tissue disorders | | | |
| Pruritus | | | |
| subjects affected / exposed | 7 / 102 (6.86%) | | |
| occurrences (all) | 7 | | |
| Musculoskeletal and connective tissue disorders | | | |
| Arthralgia | | | |
| subjects affected / exposed | 5 / 102 (4.90%) | | |
| occurrences (all) | 6 | | |
| Infections and infestations | | | |
| Nasopharyngitis | | | |
| subjects affected / exposed | 5 / 102 (4.90%) | | |
| occurrences (all) | 5 | | |
| Bronchitis | | | |
| subjects affected / exposed | 4 / 102 (3.92%) | | |
| occurrences (all) | 4 | | |
| Sinusitis | | | |
| subjects affected / exposed | 4 / 102 (3.92%) | | |
| occurrences (all) | 4 | | |
| Upper respiratory tract infection | | | |
| subjects affected / exposed | 4 / 102 (3.92%) | | |
| occurrences (all) | 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