Clinical trial results:
An open-label, single arm, repeat dose, multi-center study to evaluate the use of an autoinjector for the subcutaneous administration of mepolizumab in subjects with severe eosinophilic asthma (Study 204959)

Summary

EudraCT number	2016-001832-36
Trial protocol	GB DE SE Outside EU/EEA
Global end of trial date	30 November 2017

Results information

Result version number	v1 (current)
This version publication date	06 June 2018
First version publication date	06 June 2018

Trial information

Trial identification

Sponsor protocol code	204959

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,
Public contact	GSK Response Center, GlaxoSmithKline, 1 866-435-7343,
Scientific contact	GSK Response Center, GlaxoSmithKline, 1 866-435-7343,

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	19 March 2018
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	30 November 2017
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To assess the use of the combination product, mepolizumab liquid drug product in autoinjector for the subcutaneous self-administration of mepolizumab by participants with severe eosinophilic asthma

Protection of trial subjects:

The participants were educated by site staff prior to self-administration and their first scheduled dose was supervised in the clinic by site staff. Additionally, the IFU instructed the participants on the safe use of the device.

A plastic needle guard shields the needle before and after injection to minimise the potential for needle stick injuries. Following injection, the needle guard re-extends and locks in place to cover the needle.

The risk of systemic reactions associated with a mAb therapy was mitigated with AE monitoring, participant monitoring for 1 h following in clinic injections, and participant instructions to call the investigator and/or go to an Emergency Department for any unusual symptoms.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	04 May 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	Australia: 17
Country: Number of subjects enrolled	Canada: 15
Country: Number of subjects enrolled	Germany: 26
Country: Number of subjects enrolled	Russian Federation: 9
Country: Number of subjects enrolled	Sweden: 5
Country: Number of subjects enrolled	United Kingdom: 19
Country: Number of subjects enrolled	United States: 68
Worldwide total number of subjects	159
EEA total number of subjects	50

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)	11
Adults (18-64 years)	122
From 65 to 84 years	26
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

Participants with severe eosinophilic asthma, were enrolled at 16 sites in the United States of America, 6 sites in Germany, 5 sites in the United Kingdom, 4 sites in Canada, 3 sites in Australia, 2 sites in Russia and 2 sites in Sweden. The study duration lasted from 04 May 2017 to 30 November 2017.

Pre-assignment

Screening details:

Of the total 181 participants screened, 22 were screen failures and 159 were enrolled in this open-label, single arm, repeat dose study of mepolizumab and attempted to self-administer at least one dose of study treatment.

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 Liquid Autoinjector

Arm description:

Participants (or their caregivers) self-administered, 100 milligram (mg) mepolizumab liquid drug product subcutaneously every 4 weeks (3 doses) as a single injection using autoinjector, in the thigh, abdomen or upper arm (caregiver only) for 12 weeks.

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

Dosage and administration details:

Participants self-administered mepolizumab liquid drug product using an autoinjector (100 milligrams) in the thigh, abdomen or administered in the upper arm (caregiver only) subcutaneously every 4 weeks for 12 weeks.

Number of subjects in period 1	Mepolizumab Liquid Autoinjector
Started	159
Completed	157
Not completed	2
Physician decision	1
Adverse event, non-fatal	1

Baseline characteristics

Reporting groups	
Reporting group title	Mepolizumab Liquid Autoinjector
Reporting group description:	
Participants (or their caregivers) self-administered, 100 milligram (mg) mepolizumab liquid drug product subcutaneously every 4 weeks (3 doses) as a single injection using autoinjector, in the thigh, abdomen or upper arm (caregiver only) for 12 weeks.	

Reporting group values	Mepolizumab Liquid Autoinjector	Total	
Number of subjects	159	159	
Age categorical Units: Subjects			
Age continuous Units: years			
arithmetic mean	49.3		
standard deviation	± 16.18	-	
Gender categorical Units: Subjects			
Female	98	98	
Male	61	61	
Race/Ethnicity, Customized Units: Subjects			
African American/African Heritage	25	25	
Asian - Central/South Asian Heritage	2	2	
Asian - East Asian Heritage	1	1	
Asian - South East Asian Heritage	3	3	
White - Arabic/North African Heritage	1	1	
White - White/Caucasian/European Heritage	126	126	
Other	1	1	

End points

End points reporting groups

Reporting group title	Mepolizumab Liquid Autoinjector

Reporting group description:

Participants (or their caregivers) self-administered, 100 milligram (mg) mepolizumab liquid drug product subcutaneously every 4 weeks (3 doses) as a single injection using autoinjector, in the thigh, abdomen or upper arm (caregiver only) for 12 weeks.

Primary: Percentage of participants with successful self-administration of their observed third dose at Week 8 – Autoinjector with Standard Label + Pictogram

End point title	Percentage of participants with successful self-administration of their observed third dose at Week 8 – Autoinjector with Standard Label + Pictogram[1]

End point description:

Due to differences in the labelling requirements among regulatory authorities around the world, two different labelling approaches were included in this global study: labelling that includes a pictogram plus standard labelling elements, or a standard labelling without the pictogram. Participants (and/or their caregiver) attended three on treatment visits at Week 0, 4, 8, and End of Study Visit. Training on the study treatment, device handling and administration technique was provided by the investigator or qualified site staff at Week 0 and then first dose was self-administered under observation of investigator/site staff in clinic. Second dose self-administered unobserved, at home (Week 4) and third dose was self-administered under the observation of investigator/site staff in clinic (Week 8). All Subjects (Safety) Population included all enrolled participants attempting at least one self-administration of mepolizumab. Only participants with data available at Week 8 were analyzed.

End point type	Primary

End point timeframe:

Week 8

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: No statistical analysis was performed

End point values	Mepolizumab Liquid Autoinjector			
Subject group type	Reporting group			
Number of subjects analysed	103[2]			
Units: Percentage of participants				
Percentage of participants	99			

Notes:

[2] - All Subjects (Safety) Population

Statistical analyses

No statistical analyses for this end point

Primary: Percentage of participants with successful self-administration of their observed third dose at Week 8 – Autoinjector with Standard Label only

End point title	Percentage of participants with successful self-administration of their observed third dose at Week 8 – Autoinjector with Standard Label only[3]

End point description:

Due to differences in the labeling requirements among regulatory authorities around the world, two different labeling approaches were included in this global study: labeling that includes a pictogram plus standard labeling elements, or a standard labeling without the pictogram. Participants (and/or their caregiver) attended three on treatment visits at Week 0, Week 4, Week 8, and the End of Study Visit. Training on the study treatment, device handling and administration techniques was provided by the investigator or qualified site staff at Week 0 and then first dose was self-administered under observation of investigator/site staff in clinic. Second dose self-administered unobserved, at home (Week 4) and third dose was self-administered under the observation of investigator/site staff in clinic (Week 8). Only participants with data available at Week 8 were analyzed

End point type	Primary

End point timeframe:

Week 8

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: No statistical analysis was performed

End point values	Mepolizumab Liquid Autoinjector			
Subject group type	Reporting group			
Number of subjects analysed	54[4]			
Units: Percentage of participants				
Participants	98			

Notes:

[4] - All Subjects (Safety) Population

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of participants with successful self-administration of their unobserved dose at Week 4 – Autoinjector with Standard Label + Pictogram

End point title	Percentage of participants with successful self-administration of their unobserved dose at Week 4 – Autoinjector with Standard Label + Pictogram

End point description:

Due to differences in the labeling requirements among regulatory authorities around the world, two different labeling approaches were included in this global study: labeling that includes a pictogram plus standard labeling elements, or a standard labeling without the pictogram. Data for participants (and/or their caregiver) self-administering the second dose unobserved, at home (Week 4) using Autoinjector with Standard Label + Pictogram has been presented. Only participants with data available at Week 4 were analyzed.

End point type	Secondary

End point timeframe:

Week 4

End point values	Mepolizumab Liquid Autoinjector			
Subject group type	Reporting group			
Number of subjects analysed	103[5]			
Units: Percentage of participants				
Percentage of participants	98			

Notes:

[5] - All Subjects (Safety) Population

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of participants with successful self-administration of their unobserved dose at Week 4 – Autoinjector with Standard label only

End point title	Percentage of participants with successful self-administration of their unobserved dose at Week 4 – Autoinjector with Standard label only

End point description:

Due to differences in the labeling requirements among regulatory authorities around the world, two different labeling approaches were included in this global study: labeling that includes a pictogram plus standard labeling elements, or a standard labeling without the pictogram. Data for participants (and/or their caregiver) self-administering the second dose unobserved, at home (Week 4) using Autoinjector with Standard Label has been presented. Only participants with data available at Week 4 were analyzed.

End point type	Secondary

End point timeframe:

Week 4

End point values	Mepolizumab Liquid Autoinjector			
Subject group type	Reporting group			
Number of subjects analysed	54[6]			
Units: Percentage of participants				
Percentage of participants	96			

Notes:

[6] - All Subjects (Safety) Population

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

On-treatment serious adverse events (SAEs) and non-serious AEs were collected from start of Study Treatment (Week 0) until the End of Study/Early Withdrawal Visit (Week 12)

Adverse event reporting additional description:

On-treatment SAEs and non-serious AEs are reported for All Subjects (Safety) Population

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	20.1

Reporting groups

Reporting group title	Mepolizumab Liquid Autoinjector

Reporting group description:

Participants (or their caregivers) self-administered, 100 milligram (mg) mepolizumab liquid drug product subcutaneously every 4 weeks (3 doses) as a single injection using autoinjector, in the thigh, abdomen or upper arm (caregiver only) for 12 weeks.

Serious adverse events	Mepolizumab Liquid Autoinjector		
Total subjects affected by serious adverse events			
subjects affected / exposed	4 / 159 (2.52%)		
number of deaths (all causes)	0		
number of deaths resulting from adverse events			
Injury, poisoning and procedural complications			
Cervical vertebral fracture			
subjects affected / exposed	1 / 159 (0.63%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Facial bones fracture			
subjects affected / exposed	1 / 159 (0.63%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Rib fracture			
subjects affected / exposed	1 / 159 (0.63%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Road traffic accident			

subjects affected / exposed	1 / 159 (0.63%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Skull fractured base			
subjects affected / exposed	1 / 159 (0.63%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
General disorders and administration site conditions			
Chest discomfort			
subjects affected / exposed	1 / 159 (0.63%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Respiratory, thoracic and mediastinal disorders			
Alveolitis allergic			
subjects affected / exposed	1 / 159 (0.63%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Asthma			
subjects affected / exposed	1 / 159 (0.63%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Pneumothorax			
subjects affected / exposed	1 / 159 (0.63%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		

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

Non-serious adverse events	Mepolizumab Liquid Autoinjector		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	27 / 159 (16.98%)		
Nervous system disorders			

Headache subjects affected / exposed occurrences (all)	8 / 159 (5.03%) 11		
Infections and infestations Nasopharyngitis subjects affected / exposed occurrences (all) Upper respiratory tract infection subjects affected / exposed occurrences (all) Lower respiratory tract infection subjects affected / exposed occurrences (all) Urinary tract infection subjects affected / exposed occurrences (all)	 9 / 159 (5.66%) 11 6 / 159 (3.77%) 6 5 / 159 (3.14%) 5 5 / 159 (3.14%) 5		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
06 October 2016	Amendment 01: • To refine the criteria for a successful injection following a use-related risk review • To amend Exclusion Criterion 7 to allow either Fridericia's or Bazett's to be used as the correction formula for heart rate when measuring the QT interval • To remove Exclusion Criterion 15 as the exclusion of pregnant or lactating females is covered in Inclusion Criterion 9 • To correct minor typographical errors
15 February 2017	Amendment 02: • To include information regarding a change to the labelling of the autoinjector so that two different labelling formats will be used, depending on geographical region • To increase the participant numbers as a result of the introduction of two different label formats and to indicate that the results will be presented separately according to the label format • To amend inclusion criterion 5 to allow participants to be enrolled who require high dose inhaled corticosteroids to prevent exacerbations but who may not have received continuous high dose inhaled corticosteroids due to financial or tolerance issues • To remove 'incidence of asthma exacerbations' as safety endpoint and reclassify as an other endpoint • To change the wording to indicate that all used autoinjectors should to be returned to GSK rather than just faulty devices • To remove reference to a practice injection into a foam pad prior the first injection at Visit 2 • To add the assessment of asthma exacerbations during the study to the Time and Events table and under Section 7.7.8 • To correct minor typographical errors

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported