Clinical trial results:
An open-label, single arm, repeat dose, multi-center study to evaluate the use of a safety syringe for the subcutaneous administration of mepolizumab in subjects with severe eosinophilic asthma (Study 205667)

Summary

EudraCT number	2016-001831-10
Trial protocol	SE NL Outside EU/EEA
Global end of trial date	08 August 2017

Results information

Result version number	v1 (current)
This version publication date	26 January 2018
First version publication date	26 January 2018

Trial information

Trial identification

Sponsor protocol code	205667

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, 866 4357343,
Scientific contact	GSK Response Center, GlaxoSmithKline, 866 4357343,

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 November 2017
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	08 August 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 safety syringe for the subcutaneous self-administration of mepolizumab by participants with severe eosinophilic asthma

Protection of trial subjects:

The participants were educated by the staff prior to self-administration and their first scheduled dose was supervised in the clinic by the staff. Additionally, the IFU instructed the participants on the safe use of the device. A plastic/rubber needle shield protects the needle before injection to minimize the potential for needle stick injuries. The needle automatically retracted into the syringe body after the injection."
The risk of systemic reactions associated with a mAb therapy was mitigated with AE monitoring, subject monitoring for 1 h following in clinic injections, and subject 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	01 February 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	Canada: 10
Country: Number of subjects enrolled	Netherlands: 13
Country: Number of subjects enrolled	Russian Federation: 10
Country: Number of subjects enrolled	Sweden: 9
Country: Number of subjects enrolled	United States: 16
Worldwide total number of subjects	58
EEA total number of subjects	22

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	0

months)	
Children (2-11 years)	0
Adolescents (12-17 years)	2
Adults (18-64 years)	48
From 65 to 84 years	8
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

Participants with severe eosinophilic asthma, were enrolled at 4 sites in the United States of America, 3 sites in the Netherlands, 3 sites in the Russian Federation, 3 sites in Sweden, and 2 sites in Canada. The study duration lasted from 01 February 2017 to 08 August 2017.

Pre-assignment

Screening details:

Of the total 58 participants screened, 2 were screen failures and 56 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 Safety Syringe

Arm description:

The participants (or their caregivers) self-administered, 100 milligram (mg) mepolizumab liquid drug product subcutaneously every 4-weeks (3-doses) as a single injection using safety syringe, 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 syringe
Routes of administration	Subcutaneous use

Dosage and administration details:

Dose of 100 mg per milliliter (mL); 1.0 mL (deliverable) as subcutaneous injection every 4 weeks

Number of subjects in period 1[1]	Mepolizumab Liquid Safety Syringe
Started	56
Completed	55
Not completed	1
Lack of efficacy	1

Notes:

[1] - The number of subjects reported to be in the baseline period are not the same as the worldwide number enrolled in the trial. It is expected that these numbers will be the same.
Justification: Of the total 58 participants screened, 2 were screen failures and 56 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.

Baseline characteristics

Reporting groups	
Reporting group title	Mepolizumab Liquid Safety Syringe

Reporting group description:

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

Reporting group values	Mepolizumab Liquid Safety Syringe	Total	
Number of subjects	56	56	
Age categorical Units: Subjects			
Age continuous Units: years arithmetic mean standard deviation	 50.8 ± 12.98	 -	
Gender categorical Units: Subjects			
Female	33	33	
Male	23	23	
Race/Ethnicity, Customized Units: Subjects			
Asian- Central/South Asian Heritage	1	1	
Black Or African American Heritage	8	8	
White Heritage	47	47	

End points

End points reporting groups

Reporting group title	Mepolizumab Liquid Safety Syringe

Reporting group description:

The participants (or their caregivers) self-administered, 100 milligram (mg) mepolizumab liquid drug product subcutaneously every 4-weeks (3-doses) as a single injection using safety syringe, 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

End point title	Percentage of participants with successful self-administration of their observed third dose at Week 8[1]

End point description:

During the clinic visits the Investigator or designee evaluated if the participants were able to self-administer the third dose at Week 8 by visual inspection immediately following injection and by using an 'Observer checklist' based on the safety syringe Instructions for Use (IFU). The 'self-administration' was defined as administration of mepolizumab liquid drug product in safety syringe either by the participants themselves or by their caregiver. Failure to perform one of the critical steps was deemed to be failure to successfully administer the injection. Participants with data available at Week 8 have been presented. Analysis was performed on All Subjects (Safety) Population which comprised of all enrolled participants attempting at least one self administration of mepolizumab liquid drug product in a safety syringe.

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: There are no statistical data to report.

End point values	Mepolizumab Liquid Safety Syringe			
Subject group type	Reporting group			
Number of subjects analysed	55[2]			
Units: Percentage of participants				
Percentage of participants	100			

Notes:

[2] - All Subjects (Safety) Population

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of participants with successful self-administration of their unobserved second dose outside the clinic setting at Week 4

End point title	Percentage of participants with successful self-administration of their unobserved second dose outside the clinic setting at Week 4

End point description:

The participant (or caregiver), self-administered the dose of study treatment outside the clinic and without observation during Week 4, up to 24 hours after attending clinic Visit 3. The 'self-administration' was defined as either administration of mepolizumab liquid drug product in safety syringe by the

participants themselves or by their caregiver. The participant/caregiver completed an 'At home Checklist' outlining the various steps in the IFU to use the safety syringe. On returning to clinic the investigator inspected whether the returned safety syringe showed any signs that the full dose had not been administered.

End point type	Secondary

End point timeframe:

Week 4

End point values	Mepolizumab Liquid Safety Syringe			
Subject group type	Reporting group			
Number of subjects analysed	56[3]			
Units: Percentage of participants				
Percentage of participants	100			

Notes:

[3] - 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 adverse events (AEs) and serious AEs (SAEs) were collected from time of study treatment administration (Week 0) to up to Week 12

Adverse event reporting additional description:

AEs and SAEs were collected in All subject Population which comprised of all enrolled participants attempting at least one self administration of mepolizumab liquid drug product in a safety syringe.

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	20.0

Reporting groups

Reporting group title	Mepolizumab Liquid Safety Syringe

Reporting group description:

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

Serious adverse events	Mepolizumab Liquid Safety Syringe		
Total subjects affected by serious adverse events			
subjects affected / exposed	3 / 56 (5.36%)		
number of deaths (all causes)	0		
number of deaths resulting from adverse events			
Respiratory, thoracic and mediastinal disorders			
Asthma			
subjects affected / exposed	2 / 56 (3.57%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
Infections and infestations			
Diverticulitis			
subjects affected / exposed	1 / 56 (1.79%)		
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 Safety Syringe		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	4 / 56 (7.14%)		
Infections and infestations			
Viral upper respiratory tract infection			
subjects affected / exposed	4 / 56 (7.14%)		
occurrences (all)	4		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
06 October 2016	1. To refine the criteria for a successful injection following a use-related risk review 2. 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 3. To remove Exclusion Criterion 15 as the exclusion of pregnant or lactating females is covered in Inclusion Criterion 9 4. To correct the EudraCT No. 5. To correct minor typographical errors

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported