



## Clinical trial results:

**A multi-centre, open label, single arm, 32-week treatment study in subjects with severe eosinophilic asthma not optimally controlled with current omalizumab treatment who are who are switched from omalizumab to mepolizumab 100mg subcutaneous (study number 204471-the OSMO study)**

### Summary

EudraCT number	2015-003697-32
Trial protocol	NL ES DE SE FR BE Outside EU/EEA
Global end of trial date	31 May 2017

### Results information

Result version number	v1
This version publication date	14 December 2017
First version publication date	14 December 2017

### Trial information

#### Trial identification

Sponsor protocol code	204471
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#### 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?	Yes

Notes:

## Results analysis stage

Analysis stage	Final
Date of interim/final analysis	14 September 2017
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	31 May 2017
Was the trial ended prematurely?	No

Notes:

## General information about the trial

Main objective of the trial:

To describe in a pragmatic setting whether there is an improvement in asthma control, from the beginning to the end of the study, when directly switched to mepolizumab in subjects with a severe eosinophilic asthma phenotype not optimally controlled on omalizumab.

Protection of trial subjects:

Numbing cream or spray was permitted at the site of injection and rescue medications (salbutamol/albuterol) are available to the participant throughout the study.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	17 March 2016
Long term follow-up planned	Yes
Long term follow-up rationale	Ethical reason
Long term follow-up duration	2 Years
Independent data monitoring committee (IDMC) involvement?	No

Notes:

## Population of trial subjects

### Subjects enrolled per country

Country: Number of subjects enrolled	Belgium: 1
Country: Number of subjects enrolled	France: 31
Country: Number of subjects enrolled	Germany: 13
Country: Number of subjects enrolled	Netherlands: 9
Country: Number of subjects enrolled	Spain: 12
Country: Number of subjects enrolled	Sweden: 3
Country: Number of subjects enrolled	Argentina: 37
Country: Number of subjects enrolled	Canada: 22
Country: Number of subjects enrolled	United States: 17
Worldwide total number of subjects	145
EEA total number of subjects	69

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)	2
Adults (18-64 years)	112
From 65 to 84 years	31
85 years and over	0

## Subject disposition

### Recruitment

Recruitment details:

Participants with severe eosinophilic asthma who were receiving omalizumab, but were not optimally controlled were enrolled in this open-label study and received mepolizumab 100 milligrams (mg) subcutaneously (SC) every 4 weeks for 32 weeks with last dose on Week 28. The study was conducted at 46 centers from 17 March 2016 to 31 May 2017.

### Pre-assignment

Screening details:

Screening was performed at Visit 1 (Week -1). A total of 206 participants were screened of which 54 participants were screen failures. Seven additional participants were reported as pre-screen failures. The remaining 145 participants received at least one dose of mepolizumab.

### 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 100 mg SC
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Arm description:

Eligible participants received mepolizumab 100 mg SC doses into the upper arm or thigh every 4 weeks over a period of 32 weeks, with the last dose administered at Week 28, along with their current maintenance therapy except omalizumab.

Arm type	Experimental
Investigational medicinal product name	Albuterol/ Salbutamol metered dose inhaler (MDI)
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Inhalation powder
Routes of administration	Inhalation use

Dosage and administration details:

Albuterol/ Salbutamol MDIs were provided as a rescue inhaler to be used to primarily treat asthma symptoms on an as needed basis.

Investigational medicinal product name	Mepolizumab
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Powder for solution for injection
Routes of administration	Subcutaneous use

Dosage and administration details:

Eligible participants received Mepolizumab 100 milligrams (mg) injection via subcutaneous (SC) route into the upper arm or thigh every 4 weeks over a period of 28 weeks.

<b>Number of subjects in period 1</b>	Mepolizumab 100 mg SC
Started	145
Completed	138
Not completed	7
Consent withdrawn by subject	5

Lack of efficacy	1
Protocol deviation	1

## Baseline characteristics

### Reporting groups

Reporting group title	Mepolizumab 100 mg SC
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Reporting group description:

Eligible participants received mepolizumab 100 mg SC doses into the upper arm or thigh every 4 weeks over a period of 32 weeks, with the last dose administered at Week 28, along with their current maintenance therapy except omalizumab.

Reporting group values	Mepolizumab 100 mg SC	Total	
Number of subjects	145	145	
Age categorical			
Units: Subjects			

Age continuous			
Units: years			
arithmetic mean	53.6		
standard deviation	± 13.83	-	
Gender categorical			
Units: Subjects			
Female	86	86	
Male	59	59	
Race/Ethnicity, Customized			
Units: Subjects			
Asian- Central/South Asian Heritage	2	2	
Asian- East Asian Heritage	1	1	
Asian- South East Asian Heritage	2	2	
Black or African American heritage	11	11	
White- Arabic/ North African Heritage	4	4	
White- White/Caucasian/European Heritage	124	124	
Multiple-Black/African American and White Heritage	1	1	

## End points

### End points reporting groups

Reporting group title	Mepolizumab 100 mg SC
Reporting group description:	
Eligible participants received mepolizumab 100 mg SC doses into the upper arm or thigh every 4 weeks over a period of 32 weeks, with the last dose administered at Week 28, along with their current maintenance therapy except omalizumab.	

### Primary: Mean Change from Baseline in Asthma Control Questionnaire-5 (ACQ-5) score at Week 32

End point title	Mean Change from Baseline in Asthma Control Questionnaire-5 (ACQ-5) score at Week 32 <sup>[1]</sup>
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#### End point description:

The ACQ-5 is a five-item, self-completed questionnaire, which is used as a measure of asthma control of a participant. The five questions enquire about the frequency and/or severity of symptoms over the previous week. The response options for all these questions range from zero (no impairment) to six (total impairment) scale. ACQ-5 score range from 0 to 6. Higher scores indicate worsening of condition. Baseline was defined as the latest available assessment prior to first dose of mepolizumab. Change from Baseline at Week 32 was calculated as Week 32 value of ACQ-5 score minus Baseline value and was analyzed using Mixed Model Repeated Measures allowing for covariates of region, baseline maintenance OCS therapy, exacerbations in the year prior to the study (as ordinal variable) and visit.

End point type	Primary
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#### End point timeframe:

Baseline and at Week 32

#### 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: The system does not permit reporting of statistical analyses for studies with only 1 reporting group.

End point values	Mepolizumab 100 mg SC			
Subject group type	Reporting group			
Number of subjects analysed	145 <sup>[2]</sup>			
Units: Score on ACQ-5 scale				
least squares mean (standard error)				
Score on ACQ-5 scale	-1.45 (± 0.107)			

#### Notes:

[2] - Intent-to-treat - all participants who received at least one dose of mepolizumab

### Statistical analyses

No statistical analyses for this end point

### Secondary: Mean change from Baseline in St. George's Respiratory Questionnaire (SGRQ) score at Week 32

End point title	Mean change from Baseline in St. George's Respiratory Questionnaire (SGRQ) score at Week 32
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#### End point description:

The SGRQ Questionnaire is a well-established, self-completed tool, comprising of 50 questions with 76 weighted responses designed to measure Quality of Life in participants with diseases of airway

obstruction. It consists of two parts; Part 1 produces the symptom score and Part 2 produces the activity and impact score. A Total score is also calculated which summarizes the impact of the disease on overall health status. Scores are expressed as a percentage of overall impairment where 100 represents worst possible health status and zero indicates best possible health status. Baseline was defined as the latest available assessment prior to first dose of mepolizumab. Change from Baseline at Week 32 was calculated as Week 32 value of SGRQ score minus Baseline value and was analyzed using Mixed Model Repeated Measures allowing for covariates of region, baseline maintenance OCS therapy, exacerbations in the year prior to the study (as an ordinal variable) and visit.

End point type	Secondary
End point timeframe:	
Baseline and at Week 32	

<b>End point values</b>	Mepolizumab 100 mg SC			
Subject group type	Reporting group			
Number of subjects analysed	145 <sup>[3]</sup>			
Units: Total score on SGRQ scale				
least squares mean (standard error)				
Total score on SGRQ scale	-19.0 (± 1.64)			

Notes:

[3] - Intent-to-treat - all participants who received at least one dose of mepolizumab

## Statistical analyses

No statistical analyses for this end point

## Secondary: The rate of clinically significant asthma exacerbations over 32 weeks' treatment

End point title	The rate of clinically significant asthma exacerbations over 32 weeks' treatment
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End point description:

Clinically significant exacerbations of asthma were defined as worsening of asthma which requires use of systemic corticosteroids and/or hospitalization and/or Emergency Department (ED) visits. The frequency of clinically significant asthma exacerbations over 32 weeks' treatment was analyzed using Negative Binomial Regression via generalized estimating equations with a covariate of time period (pre-treatment versus on- and off treatment) and logarithm of time as an offset variable. The estimated rate ratio (Pre-Treatment vs. On + Off-Treatment) was 0.36 with 95% CI as 0.28, 0.47. Note: Pre-treatment includes exacerbations during 12 months prior to the Screening; On + Off-Treatment includes exacerbations between first dose and study conclusion (regardless of treatment discontinuation).

End point type	Secondary
End point timeframe:	
Up to Week 32	

<b>End point values</b>	Mepolizumab 100 mg SC			
Subject group type	Reporting group			
Number of subjects analysed	145 <sup>[4]</sup>			
Units: Exacerbation rate per year				
number (not applicable)				
Exacerbation rate per year	1.18			



Notes:

[4] - Intent-to-treat - all participants who received at least one dose of mepolizumab (n=145)

## Statistical analyses

No statistical analyses for this end point

### Secondary: Ratio to Baseline in blood eosinophil count at Week 32

End point title	Ratio to Baseline in blood eosinophil count at Week 32
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End point description:

Blood samples were collected at specific time points to measure blood eosinophils level for evaluation of pharmacodynamic effects in participants with a severe eosinophilic asthma phenotype when they were directly switched to mepolizumab. Baseline was defined as the latest available assessment prior to first dose of mepolizumab and ratio to Baseline at Week 32 was defined as Week 32 value divided by Baseline value and was analyzed using Mixed Model Repeated Measures allowing for covariates of region, Baseline maintenance oral corticosteroid (OCS) therapy, exacerbations in the year prior to the study (as an ordinal variable) and visit. The log transformation was applied to blood eosinophil counts prior to analysis. If a blood eosinophil count of zero was reported, it was imputed with half of the lowest possible blood eosinophil count, where applicable, prior to log transforming the data. The dispersion measure used was log standard error.

End point type	Secondary
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End point timeframe:

Baseline and at Week 32

End point values	Mepolizumab 100 mg SC			
Subject group type	Reporting group			
Number of subjects analysed	145 <sup>[5]</sup>			
Units: Ratio of blood eosionphils				
least squares mean (standard error)				
Ratio of blood eosionphils	0.22 (± 0.106)			

Notes:

[5] - Intent-to-treat - all participants who received at least one dose of mepolizumab

## Statistical analyses

No statistical analyses for this end point

## Adverse events

### Adverse events information

Timeframe for reporting adverse events:

The on-treatment adverse events (AEs) and on-treatment serious AEs (SAEs) are the AE which happened on/after the first dose of mepolizumab date and before/on last dose of mepolizumab date + 28 days.

Adverse event reporting additional description:

AEs and SAEs were collected in intent-To-Treat Population which comprised of all participants who received at least one dose of Mepolizumab.

Assessment type	Systematic
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### Dictionary used

Dictionary name	MedDRA
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Dictionary version	20.0
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### Reporting groups

Reporting group title	Mepolizumab 100 mg SC
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Reporting group description:

Eligible participants received mepolizumab 100 mg SC doses into the upper arm or thigh every 4 weeks over a period of 32 weeks, with the last dose administered at Week 28, along with their current maintenance therapy except omalizumab.

Serious adverse events	Mepolizumab 100 mg SC		
Total subjects affected by serious adverse events			
subjects affected / exposed	16 / 145 (11.03%)		
number of deaths (all causes)	0		
number of deaths resulting from adverse events			
Cardiac disorders			
Coronary artery disease			
subjects affected / exposed	1 / 145 (0.69%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Nervous system disorders			
Cerebrovascular accident			
subjects affected / exposed	1 / 145 (0.69%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Syncope			
subjects affected / exposed	1 / 145 (0.69%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Transient ischaemic attack			

subjects affected / exposed	1 / 145 (0.69%)		
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 / 145 (0.69%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Gastrointestinal disorders			
Abdominal pain upper			
subjects affected / exposed	1 / 145 (0.69%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Dental cyst			
subjects affected / exposed	1 / 145 (0.69%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Respiratory, thoracic and mediastinal disorders			
Asthma			
subjects affected / exposed	7 / 145 (4.83%)		
occurrences causally related to treatment / all	0 / 9		
deaths causally related to treatment / all	0 / 0		
Hypoxia			
subjects affected / exposed	1 / 145 (0.69%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Lung disorder			
subjects affected / exposed	1 / 145 (0.69%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Hepatobiliary disorders			
Cholecystitis			

subjects affected / exposed	1 / 145 (0.69%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
<b>Infections and infestations</b>			
Cellulitis			
subjects affected / exposed	2 / 145 (1.38%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
Pneumonia			
subjects affected / exposed	2 / 145 (1.38%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
Influenza			
subjects affected / exposed	1 / 145 (0.69%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Sepsis			
subjects affected / exposed	1 / 145 (0.69%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Tooth infection			
subjects affected / exposed	1 / 145 (0.69%)		
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 %

<b>Non-serious adverse events</b>	Mepolizumab 100 mg SC		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	107 / 145 (73.79%)		
<b>Nervous system disorders</b>			
Headache			
subjects affected / exposed	41 / 145 (28.28%)		
occurrences (all)	89		

Dizziness subjects affected / exposed occurrences (all)	5 / 145 (3.45%) 6		
General disorders and administration site conditions Fatigue subjects affected / exposed occurrences (all)  Asthenia subjects affected / exposed occurrences (all)  Chest pain subjects affected / exposed occurrences (all)  Injection site reaction subjects affected / exposed occurrences (all)	14 / 145 (9.66%) 20  6 / 145 (4.14%) 8  6 / 145 (4.14%) 10  5 / 145 (3.45%) 23		
Gastrointestinal disorders Nausea subjects affected / exposed occurrences (all)  Diarrhoea subjects affected / exposed occurrences (all)  Abdominal pain upper subjects affected / exposed occurrences (all)	11 / 145 (7.59%) 12  9 / 145 (6.21%) 11  6 / 145 (4.14%) 8		
Respiratory, thoracic and mediastinal disorders Cough subjects affected / exposed occurrences (all)  Rhinitis allergic subjects affected / exposed occurrences (all)  Dyspnoea subjects affected / exposed occurrences (all)	11 / 145 (7.59%) 13  10 / 145 (6.90%) 12  7 / 145 (4.83%) 15		

Dysphonia subjects affected / exposed occurrences (all)	5 / 145 (3.45%) 5		
Oropharyngeal pain subjects affected / exposed occurrences (all)	5 / 145 (3.45%) 5		
Musculoskeletal and connective tissue disorders			
Arthralgia subjects affected / exposed occurrences (all)	14 / 145 (9.66%) 20		
Back pain subjects affected / exposed occurrences (all)	13 / 145 (8.97%) 15		
Myalgia subjects affected / exposed occurrences (all)	7 / 145 (4.83%) 8		
Musculoskeletal pain subjects affected / exposed occurrences (all)	6 / 145 (4.14%) 7		
Neck pain subjects affected / exposed occurrences (all)	6 / 145 (4.14%) 8		
Infections and infestations			
Viral upper respiratory tract infection subjects affected / exposed occurrences (all)	24 / 145 (16.55%) 33		
Bronchitis subjects affected / exposed occurrences (all)	19 / 145 (13.10%) 23		
Influenza subjects affected / exposed occurrences (all)	11 / 145 (7.59%) 14		
Rhinitis subjects affected / exposed occurrences (all)	11 / 145 (7.59%) 11		
Sinusitis			

subjects affected / exposed	8 / 145 (5.52%)		
occurrences (all)	10		
Gastroenteritis viral			
subjects affected / exposed	5 / 145 (3.45%)		
occurrences (all)	5		
Urinary tract infection			
subjects affected / exposed	5 / 145 (3.45%)		
occurrences (all)	7		

## More information

### Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
23 March 2016	Secondary Medical Monitor details updated to reflect changes in personnel; investigational new drug (IND) Number added; The wording of the primary objective was revised to reflect the pragmatic approach of the study; In risk assessment section "Subjects are to be monitored post-injection for one hour" was changed to "Subjects are to be monitored post-injection for one hour for the first 3 injections, then per institutional guidelines"; Inclusion criterion 6, was updated to include long-acting anticholinergic (tiotropium bromide); Required Criteria to Start Treatment. No. 2, "run-in" was added for consistency; Liver Chemistry Stopping Criteria "Appendix 2" was corrected to "Appendix 5" as this was a typographical error; Corrected QT interval (QTc) Stopping Criteria "change from Baseline (Visit 2)", was replaced with "change from screening (Visit 1)". In addition, "Baseline (Visit 2)" was changed to "Screening (Visit 1)" as this was a typographical error; Ventolin Diskus for Sweden was added to reflect its use as a rescue medication in Sweden. "MDI", was replaced by "rescue inhaler"; Time and Event Table was updated. The "x", in Dispense paper diary/worksheet row for The Exit Visit/Early withdrawal Visit column, was removed to correct a typographical error. In addition, in the table footnote the assay for Hepatitis C was updated; Pre and post bronchodilator forced expiratory volume in one second (FEV1), "long-acting anticholinergic (LAMA)" was added; Clinical Safety Laboratory Assessments Table 5 footnote, "Appendix 2", was changed to "Appendix 5" as this was typographical error; Biomarker(s)/Pharmacodynamic Markers, a sentence referring to the blinding of eosinophil counts was removed; Appendix 7 Sub-section 12.7.2 last bullet point, Appendix 2 was replaced by Appendix 5 to correct a typographical error; Typographical errors were corrected throughout the document.

Notes:

### Interruptions (globally)

Were there any global interruptions to the trial? No

### Limitations and caveats

None reported