



Clinical trial results:

A Phase 2a, Multi-Centre, Randomised, Double-Blind, Parallel Group, Placebo-Controlled Study to Evaluate Efficacy, Safety and Tolerability of Inhaled GRC 17536, Administered for 4 Weeks, in Patients with Refractory Chronic Cough

Summary

EudraCT number	2013-002728-17
Trial protocol	GB
Global end of trial date	30 July 2014

Results information

Result version number	v2 (current)
This version publication date	10 March 2016
First version publication date	24 July 2015
Version creation reason	New data added to full data set Public contact name changed to Amol Pendse (Amol.Pendse@glenmarkpharma.com)

Trial information

Trial identification

Sponsor protocol code	GRC17536-204
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Additional study identifiers

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

Notes:

Sponsors

Sponsor organisation name	Glenmark Pharmaceuticals S.A
Sponsor organisation address	Chemin de la Combeta, 5, Ch-2300 , La Chaux-de-fonds, Switzerland,
Public contact	Amol Pendse, Glenmark Pharmaceuticals S.A, +91 2267720000, Amol.Pendse@glenmarkpharma.com
Scientific contact	Dr. Monika Tandon, Glenmark Pharmaceuticals S.A, +91 2267720000, Monika.Tandon@glenmarkpharma.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	19 May 2015
Is this the analysis of the primary completion data?	Yes
Primary completion date	30 July 2014
Global end of trial reached?	Yes
Global end of trial date	30 July 2014
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To evaluate the effect of GRC 17536 on 24 hour cough frequency using the Leicester cough monitor (LCM) in patients with refractory chronic cough.

Protection of trial subjects:

In the interests of subject safety and acceptable standards of medical care the Investigator was permitted to prescribe treatment(s) at his/her discretion. All treatments taken by the subjects during the study were recorded in the subjects' CRF (medication, dose, treatment duration and indication).

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	22 November 2013
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	United Kingdom: 52
Worldwide total number of subjects	52
EEA total number of subjects	52

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)	0
Adults (18-64 years)	28
From 65 to 84 years	24
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

Date of first patient enrollment: 22 Nov 2013

Date of last patient completed: 30 Jul 2014

Country: United Kingdom

Pre-assignment

Screening details:

Screening period: 2 weeks, Patients with refractory chronic cough

Period 1

Period 1 title	GRC 17536 Vs Placebo (overall period)
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Double blind
Roles blinded	Subject, Investigator, Monitor, Data analyst, Assessor

Arms

Are arms mutually exclusive?	Yes
Arm title	GRC 17536

Arm description:

Dose: GRC 17536 10 mg BID (approximately 12 hr apart) for 28 days (Days 1 to 28 inclusive).

Administration: GRC 17536 will be orally-inhaled using a MIAT monodose inhaler.

Arm type	Experimental
Investigational medicinal product name	GRC 17536 10 mg
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Inhalation powder, hard capsule
Routes of administration	Inhalation use

Dosage and administration details:

GRC 17536 10 mg BID (approximately 12 hr apart) for 28 days (Days 1 to 28).

Arm title	Placebo
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Arm description:

Dose: Placebo BID (approximately 12 hr apart) for 28 days (Days 1 to 28 inclusive).

Administration: Placebo will be orally-inhaled using a MIAT monodose inhaler.

Arm type	Placebo
Investigational medicinal product name	Placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Inhalation powder, hard capsule
Routes of administration	Inhalation use

Dosage and administration details:

Placebo BID (approximately 12 hr. apart) for 28 days (Days 1 to 28).

Number of subjects in period 1	GRC 17536	Placebo
Started	26	26
Completed	23	25
Not completed	3	1
Adverse event, non-fatal	2	1
Protocol deviation	1	-

Baseline characteristics

Reporting groups

Reporting group title	GRC 17536
Reporting group description: Dose: GRC 17536 10 mg BID (approximately 12 hr apart) for 28 days (Days 1 to 28 inclusive). Administration: GRC 17536 will be orally-inhaled using a MIAT monodose inhaler.	
Reporting group title	Placebo
Reporting group description: Dose: Placebo BID (approximately 12 hr apart) for 28 days (Days 1 to 28 inclusive). Administration: Placebo will be orally-inhaled using a MIAT monodose inhaler.	

Reporting group values	GRC 17536	Placebo	Total
Number of subjects	26	26	52
Age categorical Units: Subjects			
In utero	0	0	0
Preterm newborn infants (gestational age < 37 wks)	0	0	0
Newborns (0-27 days)	0	0	0
Infants and toddlers (28 days-23 months)	0	0	0
Children (2-11 years)	0	0	0
Adolescents (12-17 years)	0	0	0
Adults (18-64 years)	0	0	0
From 65-84 years	0	0	0
Adults (18-75 years)	26	26	52
85 years and over	0	0	0
Age continuous Units: years			
arithmetic mean	62.46	63.08	
standard deviation	± 9.07	± 6.566	-
Gender categorical Units: Subjects			
Female	15	16	31
Male	11	10	21

Subject analysis sets

Subject analysis set title	GRC 17536
Subject analysis set type	Full analysis
Subject analysis set description: The Full Analysis Set (FAS) comprised of all randomized patients with at least one post-baseline assessment of the primary endpoint.	
Subject analysis set title	Placebo
Subject analysis set type	Full analysis
Subject analysis set description: The Full Analysis Set (FAS) comprised of all randomized patients with at least one post-baseline assessment of the primary endpoint.	

Reporting group values	GRC 17536	Placebo	
Number of subjects	23	22	
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)	0	0	
Adults (18-64 years)	0	0	
From 65-84 years	0	0	
Adults (18-75 years)	23	22	
85 years and over	0	0	
Age continuous			
Units: years			
arithmetic mean	62.51	62.94	
standard deviation	± 7.84	± 7.78	
Gender categorical			
Units: Subjects			
Female	13	13	
Male	10	9	

End points

End points reporting groups

Reporting group title	GRC 17536
Reporting group description: Dose: GRC 17536 10 mg BID (approximately 12 hr apart) for 28 days (Days 1 to 28 inclusive). Administration: GRC 17536 will be orally-inhaled using a MIAT monodose inhaler.	
Reporting group title	Placebo
Reporting group description: Dose: Placebo BID (approximately 12 hr apart) for 28 days (Days 1 to 28 inclusive). Administration: Placebo will be orally-inhaled using a MIAT monodose inhaler.	
Subject analysis set title	GRC 17536
Subject analysis set type	Full analysis
Subject analysis set description: The Full Analysis Set (FAS) comprised of all randomized patients with at least one post-baseline assessment of the primary endpoint.	
Subject analysis set title	Placebo
Subject analysis set type	Full analysis
Subject analysis set description: The Full Analysis Set (FAS) comprised of all randomized patients with at least one post-baseline assessment of the primary endpoint.	

Primary: Change in log 24 hour cough frequency from baseline to end of treatment between GRC 17536 and placebo

End point title	Change in log 24 hour cough frequency from baseline to end of treatment between GRC 17536 and placebo
End point description:	
End point type	Primary
End point timeframe: 4 weeks	

End point values	GRC 17536	Placebo		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	23	22		
Units: Number				
log mean (standard deviation)	-0.2 (± 0.397)	-0.21 (± 0.479)		

Statistical analyses

Statistical analysis title	Statistical Analysis of Primary Efficacy Endpoint
Comparison groups	GRC 17536 v Placebo

Number of subjects included in analysis	45
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.9804
Method	ANCOVA

Adverse events

Adverse events information

Timeframe for reporting adverse events:

8 weeks

Assessment type	Systematic
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Dictionary used

Dictionary name	MedDRA
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Dictionary version	14.1
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Reporting groups

Reporting group title	Placebo
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Reporting group description:

Dose: Placebo BID (approximately 12 hr apart) for 28 days (Days 1 to 28 inclusive).

Administration: Placebo will be orally-inhaled using a MIAT monodose inhaler.

Reporting group title	GRC 17536
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Reporting group description:

Dose: GRC 17536 10 mg BID (approximately 12 hr apart) for 28 days (Days 1 to 28 inclusive).

Administration: GRC 17536 will be orally-inhaled using a MIAT monodose inhaler.

Serious adverse events	Placebo	GRC 17536	
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 26 (0.00%)	2 / 26 (7.69%)	
number of deaths (all causes)	0	0	
number of deaths resulting from adverse events	0	0	
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Breast cancer			
subjects affected / exposed	0 / 26 (0.00%)	1 / 26 (3.85%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac disorders			
Atrioventricular block first degree			
subjects affected / exposed	0 / 26 (0.00%)	1 / 26 (3.85%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

Frequency threshold for reporting non-serious adverse events: 5 %

Non-serious adverse events	Placebo	GRC 17536	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	16 / 26 (61.54%)	16 / 26 (61.54%)	
Investigations			
BLOOD GLUCOSE DECREASED			
subjects affected / exposed	0 / 26 (0.00%)	1 / 26 (3.85%)	
occurrences (all)	0	1	
RED BLOOD CELL SEDIMENTATION RATE INCREASED			
subjects affected / exposed	2 / 26 (7.69%)	1 / 26 (3.85%)	
occurrences (all)	2	1	
HAEMOGLOBIN DECREASED			
subjects affected / exposed	1 / 26 (3.85%)	0 / 26 (0.00%)	
occurrences (all)	1	0	
HAEMATOCRIT DECREASED			
subjects affected / exposed	1 / 26 (3.85%)	0 / 26 (0.00%)	
occurrences (all)	1	0	
PLATELET COUNT INCREASED			
subjects affected / exposed	1 / 26 (3.85%)	0 / 26 (0.00%)	
occurrences (all)	1	0	
BLOOD UREA DECREASED			
subjects affected / exposed	1 / 26 (3.85%)	0 / 26 (0.00%)	
occurrences (all)	1	0	
ASPARTATE AMINOTRANSFERASE INCREASED			
subjects affected / exposed	1 / 26 (3.85%)	0 / 26 (0.00%)	
occurrences (all)	1	0	
BLOOD ALKALINE PHOSPHATASE INCREASED			
subjects affected / exposed	1 / 26 (3.85%)	0 / 26 (0.00%)	
occurrences (all)	1	0	
URINE BILIRUBIN INCREASED			
subjects affected / exposed	1 / 26 (3.85%)	0 / 26 (0.00%)	
occurrences (all)	1	0	
URINE KETONE BODY PRESENT			
subjects affected / exposed	1 / 26 (3.85%)	0 / 26 (0.00%)	
occurrences (all)	1	0	
PROTEIN URINE PRESENT			

subjects affected / exposed	1 / 26 (3.85%)	0 / 26 (0.00%)	
occurrences (all)	1	0	
ALANINE AMINOTRANSFERASE INCREASED			
subjects affected / exposed	1 / 26 (3.85%)	0 / 26 (0.00%)	
occurrences (all)	1	0	
GAMMA-GLUTAMYLTRANSFERASE INCREASED			
subjects affected / exposed	1 / 26 (3.85%)	0 / 26 (0.00%)	
occurrences (all)	1	0	
BILIRUBIN CONJUGATED INCREASED			
subjects affected / exposed	1 / 26 (3.85%)	0 / 26 (0.00%)	
occurrences (all)	1	0	
UROBILINOGEN URINE INCREASED			
subjects affected / exposed	1 / 26 (3.85%)	0 / 26 (0.00%)	
occurrences (all)	1	0	
HAEMOPHILUS TEST POSITIVE			
subjects affected / exposed	1 / 26 (3.85%)	0 / 26 (0.00%)	
occurrences (all)	1	0	
BLOOD CHOLESTEROL INCREASED			
subjects affected / exposed	1 / 26 (3.85%)	0 / 26 (0.00%)	
occurrences (all)	1	0	
BLOOD TRIGLYCERIDES INCREASED			
subjects affected / exposed	1 / 26 (3.85%)	0 / 26 (0.00%)	
occurrences (all)	1	0	
Nervous system disorders			
DIZZINESS			
subjects affected / exposed	0 / 26 (0.00%)	1 / 26 (3.85%)	
occurrences (all)	0	2	
HEADACHE			
subjects affected / exposed	4 / 26 (15.38%)	5 / 26 (19.23%)	
occurrences (all)	5	7	
MIGRAINE			
subjects affected / exposed	0 / 26 (0.00%)	1 / 26 (3.85%)	
occurrences (all)	0	2	
TENSION HEADACHE			

subjects affected / exposed occurrences (all) APHASIA subjects affected / exposed occurrences (all)	1 / 26 (3.85%) 1 1 / 26 (3.85%) 1	0 / 26 (0.00%) 0 0 / 26 (0.00%) 0	
General disorders and administration site conditions OEDEMA PERIPHERAL subjects affected / exposed occurrences (all) FATIGUE subjects affected / exposed occurrences (all)	0 / 26 (0.00%) 0 0 / 26 (0.00%) 0	1 / 26 (3.85%) 1 1 / 26 (3.85%) 1	
Eye disorders Eye pain subjects affected / exposed occurrences (all) CONJUNCTIVITIS ALLERGIC subjects affected / exposed occurrences (all)	0 / 26 (0.00%) 0 0 / 26 (0.00%) 0	1 / 26 (3.85%) 1 1 / 26 (3.85%) 1	
Gastrointestinal disorders NAUSEA subjects affected / exposed occurrences (all) VOMITING subjects affected / exposed occurrences (all) ABDOMINAL DISCOMFORT subjects affected / exposed occurrences (all) DIARRHOEA subjects affected / exposed occurrences (all)	1 / 26 (3.85%) 1 0 / 26 (0.00%) 0 1 / 26 (3.85%) 1 1 / 26 (3.85%) 1	3 / 26 (11.54%) 3 1 / 26 (3.85%) 1 1 / 26 (3.85%) 1 0 / 26 (0.00%) 0	
Respiratory, thoracic and mediastinal disorders OROPHARYNGEAL PAIN subjects affected / exposed occurrences (all)	1 / 26 (3.85%) 1	1 / 26 (3.85%) 1	

DYSпноEA subjects affected / exposed occurrences (all)	0 / 26 (0.00%) 0	1 / 26 (3.85%) 1	
COUGH subjects affected / exposed occurrences (all)	1 / 26 (3.85%) 1	0 / 26 (0.00%) 0	
WHEEZING subjects affected / exposed occurrences (all)	2 / 26 (7.69%) 2	0 / 26 (0.00%) 0	
BRONCHOSPASM subjects affected / exposed occurrences (all)	1 / 26 (3.85%) 1	0 / 26 (0.00%) 0	
Skin and subcutaneous tissue disorders PRURITUS subjects affected / exposed occurrences (all)	1 / 26 (3.85%) 1	1 / 26 (3.85%) 1	
DRUG ERUPTION subjects affected / exposed occurrences (all)	1 / 26 (3.85%) 1	0 / 26 (0.00%) 0	
Psychiatric disorders INSOMNIA subjects affected / exposed occurrences (all)	0 / 26 (0.00%) 0	1 / 26 (3.85%) 1	
ANXIETY subjects affected / exposed occurrences (all)	0 / 26 (0.00%) 0	1 / 26 (3.85%) 1	
Renal and urinary disorders URINARY RETENTION subjects affected / exposed occurrences (all)	0 / 26 (0.00%) 0	1 / 26 (3.85%) 1	
Musculoskeletal and connective tissue disorders BACK PAIN subjects affected / exposed occurrences (all)	0 / 26 (0.00%) 0	2 / 26 (7.69%) 2	
ARTHRALGIA			

subjects affected / exposed	1 / 26 (3.85%)	1 / 26 (3.85%)	
occurrences (all)	1	1	
PAIN IN EXTREMITY			
subjects affected / exposed	0 / 26 (0.00%)	1 / 26 (3.85%)	
occurrences (all)	0	1	
MYALGIA			
subjects affected / exposed	1 / 26 (3.85%)	0 / 26 (0.00%)	
occurrences (all)	1	0	
Infections and infestations			
NASOPHARYNGITIS			
subjects affected / exposed	1 / 26 (3.85%)	1 / 26 (3.85%)	
occurrences (all)	1	1	
URINARY TRACT INFECTION			
subjects affected / exposed	0 / 26 (0.00%)	1 / 26 (3.85%)	
occurrences (all)	0	1	
RHINITIS			
subjects affected / exposed	1 / 26 (3.85%)	0 / 26 (0.00%)	
occurrences (all)	1	0	
VIRAL INFECTION			
subjects affected / exposed	1 / 26 (3.85%)	0 / 26 (0.00%)	
occurrences (all)	1	0	
UPPER RESPIRATORY TRACT INFECTION			
subjects affected / exposed	1 / 26 (3.85%)	0 / 26 (0.00%)	
occurrences (all)	1	0	
LOWER RESPIRATORY TRACT INFECTION			
subjects affected / exposed	1 / 26 (3.85%)	0 / 26 (0.00%)	
occurrences (all)	1	0	
Metabolism and nutrition disorders			
DECREASED APPETITE			
subjects affected / exposed	0 / 26 (0.00%)	1 / 26 (3.85%)	
occurrences (all)	0	1	
HYPERCHOLESTEROLAEMIA			
subjects affected / exposed	1 / 26 (3.85%)	0 / 26 (0.00%)	
occurrences (all)	1	0	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? No

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported