Clinical trial results:
Evaluation of orvepitant in an exploratory open-label clinical study in chronic treatment-refractory cough (The "VOLCANO-1" Study)

Summary

EudraCT number	2014-003947-36
Trial protocol	GB
Global end of trial date	26 October 2015

Results information

Result version number	v1 (current)
This version publication date	18 May 2017
First version publication date	18 May 2017

Trial information

Trial identification

Sponsor protocol code	NT2014/Orv/Prot001

Additional study identifiers

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

Notes:

Sponsors

Sponsor organisation name	NeRRe Therapeutics Ltd
Sponsor organisation address	SBC, Incubator Building, Gunnels Wood Rd, Stevenage, United Kingdom, SG1 2FX
Public contact	Elizabeth Ballantyne, NeRRe Therapeutics Ltd, 44 07826 846960, Elizabeth.Ballantyne@nerretherapeutics.com
Scientific contact	Elizabeth Ballantyne, NeRRe Therapeutics Ltd, 44 07826 846960, Elizabeth.Ballantyne@nerretherapeutics.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	22 June 2016
Is this the analysis of the primary completion data?	Yes
Primary completion date	26 October 2015
Global end of trial reached?	Yes
Global end of trial date	26 October 2015
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To evaluate the change in objectively recorded daytime cough frequency in chronic treatment-refractory cough patients at Week 4 after treatment with orvepitant (30 mg given once daily [od], orally).

Protection of trial subjects:

The study was conducted in adherence to ICH principles of Good Clinical Practice (GCP), as required by European Directive 2001/20/EC and 2005/28/EC and local rules relevant to the use of new therapeutic agents within the United Kingdom, and adherence to the general principles that have their origins in the Declaration of Helsinki. Subjects were provided with the Participant Information Sheet and Informed Consent Form for their prior review and approval before any study related procedures and subsequent participation in the study.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	02 March 2015
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: 13
Worldwide total number of subjects	13
EEA total number of subjects	13

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)	9
From 65 to 84 years	4

85 years and over	0

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

Male and female subjects from 18 to 75 years with a diagnosis of chronic treatment-refractory cough based on a minimum of > 3 months of symptoms were enrolled on this study.

Period 1

Period 1 title	Overall trial (overall period)
Is this the baseline period?	Yes
Allocation method	Not applicable
Blinding used	Not blinded

Blinding implementation details:

Single-arm open-label study.

Arms

Arm title	Orvepitant 30 mg

Arm description: -

Arm type	Experimental
Investigational medicinal product name	Orvepitant 30 mg
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

30 mg orvepitant was administered once daily for 4 weeks. Orvepitant was administered as oral tablets taken with or without food each day in the evening before bedtime.

Number of subjects in period 1	Orvepitant 30 mg
Started	13
Completed	13

Baseline characteristics

Reporting groups	
Reporting group title	Overall trial

Reporting group description: -

Reporting group values	Overall trial	Total	
Number of subjects	13	13	
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)	9	9	
From 65-84 years	4	4	
85 years and over	0	0	
Age continuous Units: years			
arithmetic mean	60.1		
full range (min-max)	51 to 75	-	
Gender categorical Units: Subjects			
Female	11	11	
Male	2	2	

End points

End points reporting groups

Reporting group title	Orvepitant 30 mg

Reporting group description: -

Primary: Daytime cough frequency

End point title	Daytime cough frequency[1]

End point description:

Change in objective cough frequency at Week 4 compared to Baseline.

End point type	Primary

End point timeframe:

Change at Week 4 compared to Baseline

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 EudraCT system only allows a statistical analysis result to be entered with at least 2 comparison groups. This was a single arm study. Comparison of objective daytime cough frequency at Week 4 compared to Baseline gave a Wald p-value of P<0.001.

End point values	Orvepitant 30 mg			
Subject group type	Reporting group			
Number of subjects analysed	13			
Units: N/A				
arithmetic mean (confidence interval 95%)	-18.9 (-28.3 to -9.6)			

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information	
Timeframe for reporting adverse events: AEs were recorded from the time that the ICF was signed until the Follow-up visit.	
Assessment type	Systematic
Dictionary used	
Dictionary name	MedDRA
Dictionary version	19.0
Reporting groups	
Reporting group title	Orvepitant 30 mg

Reporting group description: -

Serious adverse events	Orvepitant 30 mg		
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 13 (0.00%)		
number of deaths (all causes)	0		
number of deaths resulting from adverse events	0		

Frequency threshold for reporting non-serious adverse events: 0 %

Non-serious adverse events	Orvepitant 30 mg		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	9 / 13 (69.23%)		
Injury, poisoning and procedural complications			
Muscle strain			
subjects affected / exposed	1 / 13 (7.69%)		
occurrences (all)	1		
Vascular disorders			
Hot flush			
subjects affected / exposed	1 / 13 (7.69%)		
occurrences (all)	1		
Nervous system disorders			
Sciatica			
subjects affected / exposed	1 / 13 (7.69%)		
occurrences (all)	1		
Lethargy			

subjects affected / exposed occurrences (all) Somnolence subjects affected / exposed occurrences (all) Dizziness subjects affected / exposed occurrences (all)	1 / 13 (7.69%) 1 2 / 13 (15.38%) 2 1 / 13 (7.69%) 1		
General disorders and administration site conditions Fatigue subjects affected / exposed occurrences (all)	 2 / 13 (15.38%) 2		
Gastrointestinal disorders Dry mouth subjects affected / exposed occurrences (all) Toothache subjects affected / exposed occurrences (all) Nausea subjects affected / exposed occurrences (all) Diarrhoea subjects affected / exposed occurrences (all)	 1 / 13 (7.69%) 1 1 / 13 (7.69%) 1 1 / 13 (7.69%) 1 1 / 13 (7.69%) 1		
Respiratory, thoracic and mediastinal disorders Cough subjects affected / exposed occurrences (all) Oropharyngeal pain subjects affected / exposed occurrences (all)	 2 / 13 (15.38%) 2 1 / 13 (7.69%) 1		
Skin and subcutaneous tissue disorders Night sweats subjects affected / exposed occurrences (all)	 1 / 13 (7.69%) 1		

Hyperhidrosis subjects affected / exposed occurrences (all)	1 / 13 (7.69%) 1		
Psychiatric disorders Depression subjects affected / exposed occurrences (all)	1 / 13 (7.69%) 1		
Musculoskeletal and connective tissue disorders Periarthritis subjects affected / exposed occurrences (all) Neck pain subjects affected / exposed occurrences (all) Back pain subjects affected / exposed occurrences (all) Pain in extremity subjects affected / exposed occurrences (all)	1 / 13 (7.69%) 1 1 / 13 (7.69%) 1 1 / 13 (7.69%) 1 1 / 13 (7.69%) 2		
Infections and infestations Nasopharyngitis subjects affected / exposed occurrences (all) Urinary tract infection subjects affected / exposed occurrences (all)	1 / 13 (7.69%) 1 1 / 13 (7.69%) 1		

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