Clinical trial results:
An exploratory, randomized, double blind, placebo controlled, parallel groups Phase II clinical trial to evaluate the efficacy and safety of E-52862 (400 mg) by oral route, in patients with post-herpetic neuralgia (PHN).

Summary

EudraCT number	2012-000399-41
Trial protocol	ES
Global end of trial date	27 November 2013

Results information

Result version number	v1 (current)
This version publication date	29 July 2016
First version publication date	29 July 2016

Trial information

Trial identification

Sponsor protocol code	ESTEVE-SIGM-203

Additional study identifiers

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

Notes:

Sponsors

Sponsor organisation name	Laboratorios Dr. Esteve. S.A. (ESTEVE)
Sponsor organisation address	Avda. Mare de Déu de Montserrat, 221, Barcelona, Spain, 08041
Public contact	Jesús Cebrecos. Study Medical Monitor, Laboratorios Dr. Esteve. S.A., +34 934466000, jcebrecos@esteve.es
Scientific contact	Jesús Cebrecos. Study Medical Monitor, Laboratorios Dr. Esteve. S.A. , +34 934466000, jcebrecos@esteve.es

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	20 October 2014
Is this the analysis of the primary completion data?	Yes
Primary completion date	27 November 2013
Global end of trial reached?	Yes
Global end of trial date	27 November 2013
Was the trial ended prematurely?	Yes

Notes:

General information about the trial

Main objective of the trial:

The primary objective of this study is to assess the analgesic efficacy of E-52862 in subjects with moderate to severe postherpetic neuralgia

Protection of trial subjects:

The study has been conducted in compliance with the protocol, regulatory requirements, good clinical practice (GCP) and the ethical principles of the latest revision of the Declaration of Helsinki as adopted by the World Medical Association.

Background therapy:

Subjects were treated with stable doses of gabapentin or pregabalin for at least one month prior to the screening visit, and continued taking the same doses for the duration of the study at the investigator's criteria.

Evidence for comparator: -

Actual start date of recruitment	29 November 2012
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	Spain: 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)	2
From 65 to 84 years	11

85 years and over	0

Subject disposition

Recruitment

Recruitment details:

The study was conducted in Spain, during 29-Nov-2012 (FSFV) and 30-Oct-2013 (LSLV)

Pre-assignment

Screening details:

Male and female adults with a diagnosis of moderate to severe pain of PHN for more than 3 months since the resolution of rash but no more than 5 years, treated with stable doses of gabapentin or pregabalin for at least 1 month prior to the screening, who were able to continue taking the same doses for the duration of the study at the IPs criteria

Period 1

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

Arms

Are arms mutually exclusive?	Yes
Arm title	E-52862

Arm description: -

Arm type	Experimental
Investigational medicinal product name	E-52862
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Capsule
Routes of administration	Oral use

Dosage and administration details:

400 mg once a day

Arm title	Control

Arm description: -

Arm type	Placebo
Investigational medicinal product name	Placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Capsule
Routes of administration	Oral use

Dosage and administration details:

1 capsule of placebo once a day

Number of subjects in period 1	E-52862	Control
Started	4	9
Completed	4	9

Baseline characteristics

Reporting groups	
Reporting group title	E-52862
Reporting group description: -	
Reporting group title	Control
Reporting group description: -	

Reporting group values	E-52862	Control	Total
Number of subjects	4	9	13
Age categorical Units: Subjects			
Adults (18-84 years)	4	9	13
Age continuous Units: years arithmetic mean full range (min-max)	 72 66 to 79	 75 34 to 80	 -
Gender categorical Units: Subjects			
Female	2	4	6
Male	2	5	7
Duration of post-herpetic neuralgia Units: months arithmetic mean full range (min-max)	 20.25 14.64 to 27.21	 13.19 2.61 to 57.96	 -

Subject analysis sets	
Subject analysis set title	Safety analysis set
Subject analysis set type	Safety analysis

Subject analysis set description:

All randomised subjects who receive at least 1 dose of the study drug. Safety analysis will be performed on the safety set.

Subject analysis set title	Full analysis set
Subject analysis set type	Full analysis

Subject analysis set description:

The Full Analysis Set (FAS) was defined as all randomized patients who took study medication and provided at least one valid baseline and one on-treatment observation for efficacy variables.

Reporting group values	Safety analysis set	Full analysis set	
Number of subjects	13	13	
Age categorical Units: Subjects			
Adults (18-84 years)	13	13	
Age continuous Units: years arithmetic mean full range (min-max)	 73 34 to 80	 73 34 to 80	

Gender categorical Units: Subjects			
Female	6	6	
Male	7	7	
Duration of post-herpetic neuralgia Units: months			
arithmetic mean	14.64	14.64	
full range (min-max)	2.61 to 57.96	2.61 to 57.96	

End points

End points reporting groups

Reporting group title	E-52862
Reporting group description: -	
Reporting group title	Control
Reporting group description: -	
Subject analysis set title	Safety analysis set
Subject analysis set type	Safety analysis
Subject analysis set description:	
All randomised subjects who receive at least 1 dose of the study drug. Safety analysis will be performed on the safety set.	
Subject analysis set title	Full analysis set
Subject analysis set type	Full analysis
Subject analysis set description:	
The Full Analysis Set (FAS) was defined as all randomized patients who took study medication and provided at least one valid baseline and one on-treatment observation for efficacy variables.	

Primary: NPRS – Average pain – change from baseline to day 28

End point title	NPRS – Average pain – change from baseline to day 28[1]
End point description:	
End point type	Primary
End point timeframe:	
Time specific change from baseline to day 28 in mean pain intensity in the previous 7 days interval measured by a Numerical Pain Rating Scale (NPRS), included in a patient diary (average 24 hour pain)	
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: Considering the final number of patients randomized, the content of the Statistical Analysis Plan (SAP) was updated taking into account this important issue and no statistical comparisons were performed.	

End point values	E-52862	Control		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	4	9		
Units: numeric (pain rating scale)				
arithmetic mean (standard deviation)	-1.53 (± 1.73)	-0.85 (± 1.79)		

Statistical analyses

No statistical analyses for this end point

Secondary: NPRS – Worst pain – change from baseline to day 28

End point title	NPRS – Worst pain – change from baseline to day 28
End point description:	
End point type	Secondary

End point timeframe:

Time specific change from baseline to day 28 in mean pain intensity in the previous 7 days interval measured by a Numerical Pain Rating Scale (NPRS), included in a patient diary (worst 24 hour pain)

End point values	E-52862	Control		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	4	9		
Units: Numerical (Pain rating scale)				
arithmetic mean (standard deviation)	-1.04 (± 1.95)	-0.85 (± 1.88)		

Statistical analyses

No statistical analyses for this end point

Secondary: NPRS – Average pain – change from baseline to day 7, 14 and 21

End point title	NPRS – Average pain – change from baseline to day 7, 14 and 21

End point description:

End point type	Secondary

End point timeframe:

Time specific change from baseline to day 7, 14, and 21, in mean pain intensity in the previous 7 days interval measured by a Numerical Pain Rating Scale (NPRS), included in a patient diary (average 24 hour pain)

End point values	E-52862	Control		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	4	9		
Units: Numerical (Pain rating scale)				
arithmetic mean (standard deviation)				
Day 7 visit	-1.55 (± 1.56)	-0.48 (± 0.98)		
Day 14 visit	-1.01 (± 0.97)	-0.48 (± 1.26)		
Day 21 visit	-0.85 (± 0.84)	-0.85 (± 1.81)		

Statistical analyses

No statistical analyses for this end point

Secondary: NPRS – Worst pain – change from baseline to day 7, 14 and 21

End point title	NPRS – Worst pain – change from baseline to day 7, 14 and 21

End point description:

End point type	Secondary

End point timeframe:

Time specific change from baseline to day 7, 14, and 21, in mean pain intensity in the previous 7 days interval measured by a Numerical Pain Rating Scale (NPRS), included in a patient diary (worst 24 hour pain)

End point values	E-52862	Control		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	4	9		
Units: Numerical (Pain rating scale)				
arithmetic mean (standard deviation)				
Day 7 visit	-0.83 (± 0.29)	-0.39 (± 1.15)		
Day 14 visit	-0.68 (± 1.06)	-0.66 (± 1.23)		
Day 21 visit	-0.37 (± 1.12)	-0.92 (± 1.75)		

Statistical analyses

No statistical analyses for this end point

Secondary: Consumption of pain rescue medication

End point title	Consumption of pain rescue medication

End point description:

Number of patients that required pain rescue medication during the 28 days treatment period.

End point type	Secondary

End point timeframe:

28 days treatment period

End point values	E-52862	Control		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	4	9		
Units: Patients				
Rescue Medication	2	5		
No Rescue Medication	2	4		

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information	
Timeframe for reporting adverse events:	
From the first IMP intake up to two weeks after the last IMP administration	
Adverse event reporting additional description:	
Treatment Emergent Adverse Event are displayed. The AEs that occurred after the first IMP intake are going to be considered as treatment emergent AEs (TEAEs) either serious or not.	
Assessment type	Systematic

Dictionary used	
Dictionary name	MedDRA
Dictionary version	16.1

Reporting groups	
Reporting group title	E-52862
Reporting group description: -	
Reporting group title	Placebo
Reporting group description: -	

Serious adverse events	E-52862	Placebo	
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 4 (0.00%)	0 / 9 (0.00%)	
number of deaths (all causes)	0	0	
number of deaths resulting from adverse events	0	0	

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

Non-serious adverse events	E-52862	Placebo	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	4 / 4 (100.00%)	7 / 9 (77.78%)	
Investigations			
ACTIVATED PARTIAL THROMBOPLASTIN TIME PROLONGED			
subjects affected / exposed	0 / 4 (0.00%)	1 / 9 (11.11%)	
occurrences (all)	0	1	
INTERNATIONAL NORMALISED RATIO INCREASED			
subjects affected / exposed	0 / 4 (0.00%)	1 / 9 (11.11%)	
occurrences (all)	0	1	
Vascular disorders			

HYPERTENSION			
subjects affected / exposed	1 / 4 (25.00%)	1 / 9 (11.11%)	
occurrences (all)	1	1	
Cardiac disorders			
ATRIAL FIBRILLATION			
subjects affected / exposed	0 / 4 (0.00%)	1 / 9 (11.11%)	
occurrences (all)	0	1	
Nervous system disorders			
DIZZINESS			
subjects affected / exposed	2 / 4 (50.00%)	2 / 9 (22.22%)	
occurrences (all)	4	2	
HEADACHE			
subjects affected / exposed	0 / 4 (0.00%)	2 / 9 (22.22%)	
occurrences (all)	0	2	
Blood and lymphatic system disorders			
NEUTROPENIA			
subjects affected / exposed	0 / 4 (0.00%)	1 / 9 (11.11%)	
occurrences (all)	0	1	
General disorders and administration site conditions			
FATIGUE			
subjects affected / exposed	1 / 4 (25.00%)	1 / 9 (11.11%)	
occurrences (all)	1	2	
NON-CARDIAC CHEST PAIN			
subjects affected / exposed	0 / 4 (0.00%)	1 / 9 (11.11%)	
occurrences (all)	0	2	
Gastrointestinal disorders			
CONSTIPATION			
subjects affected / exposed	1 / 4 (25.00%)	0 / 9 (0.00%)	
occurrences (all)	1	0	
DYSPEPSIA			
subjects affected / exposed	1 / 4 (25.00%)	0 / 9 (0.00%)	
occurrences (all)	2	0	
Musculoskeletal and connective tissue disorders			
ARTHRALGIA			
subjects affected / exposed	0 / 4 (0.00%)	1 / 9 (11.11%)	
occurrences (all)	0	2	
PAIN IN EXTREMITY			

subjects affected / exposed occurrences (all)	0 / 4 (0.00%) 0	1 / 9 (11.11%) 1	
Infections and infestations NASOPHARYNGITIS subjects affected / exposed occurrences (all)	1 / 4 (25.00%) 1	0 / 9 (0.00%) 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

Limitations of the trial such as small numbers of subjects analysed or technical problems leading to unreliable data.

Provided study patients could not be recruited at a reasonable rate, the sponsor prematurely terminated the study after a period of 12 months recruitment, with 13 patients randomized.

Notes: