Clinical trial results:
Tolerability and analgesic efficacy of Loxapine in patients with refractory, chemotherapy-induced neuropathic pain

Summary

EudraCT number	2014-005440-17
Trial protocol	DE
Global end of trial date	12 July 2017

Results information

Result version number	v1 (current)
This version publication date	17 July 2022
First version publication date	17 July 2022
Summary attachment (see zip file)	Publication_Loxapin_Front_Pharmacol_10:838 (Schmiedl_Loxapin.pdf)

Trial information

Trial identification

Sponsor protocol code	LOX_2015_PILOT

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT02820519
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Witten/Herdecke University
Sponsor organisation address	Alfred-Herrhausen-Straße 50, Witten, Germany,
Public contact	Philipp Klee-Institut, HELIOS Klinikum Wuppertal, Klinikum der Privaten Universität Witten/Herdecke, 0049 2028961854, zks@uni-wh.de
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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	10 July 2018
Is this the analysis of the primary completion data?	Yes
Primary completion date	04 May 2017
Global end of trial reached?	Yes
Global end of trial date	12 July 2017
Was the trial ended prematurely?	Yes

Notes:

General information about the trial

Main objective of the trial:

Tolerability of Loxapine in patients with chemotherapy-induced neuropathic pain

Protection of trial subjects:

The study was approved by an independent ethics committee (Witten/Herdecke University; F-183/2014). The study was conducted in conformity with the ethical standards according to the Declaration of Helsinki and Good Clinical Practice guidelines. This pilot study was primarily designed as a safety study evaluating the tolerability of loxapine in non-psychiatric patients. In case of an acceptable tolerability and if a clinically relevant analgesic efficacy was not reached, loxapine dosage was increased (second episode: 10 mg t.i.d., third episode: 20 mg b.i.d., fourth episode: 20 mg t.i.d). In case of an acceptable tolerability and if a clinically relevant analgesic efficacy was achieved, the dosage of loxapine was not changed. In case of clinically relevant (serious) adverse events [(S)AEs], loxapine dosage was reduced or the treatment was interrupted or stopped (irrespective of the analgesic efficacy).After the first IMP intake, a daily assessment of neuropathic pain using the 11-point NRS, of adverse events, and of analgesic co-medication were conducted by the patients and documented in a diary.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	07 June 2016
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	Germany: 4
Worldwide total number of subjects	4
EEA total number of subjects	4

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)	1
From 65 to 84 years	3
85 years and over	0

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

6 patients were screened of which 4 were enrolled and 2 were not enrolled. Of the patients not enrolled 1 did not meet the inclusion criteria and 1 met the exclusion criteria.

Period 1

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

Arms

Arm title	Loxapin

Arm description:

Dose escalation of loxapine

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

Dosage and administration details:

10mg loxapine twice daily for the first treatment episode (days 1-14), in case of acceptable tolerability and clinically relevant analgesic efficacy the dosage was not changed, in case of acceptable tolerability and no clinically relevant analgeisc efficacy the dose was increased (second episode 10mg thrice daily, third episode 20mg twice daily, fourth episode 20mg twice daily)

Number of subjects in period 1	Loxapin
Started	4
Completed	2
Not completed	2
Adverse event, non-fatal	2

Baseline characteristics

Reporting groups

Reporting group title	Overall trial

Reporting group description: -

Reporting group values	Overall trial	Total	
Number of subjects	4	4	
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)	1	1	
From 65-84 years	3	3	
85 years and over	0	0	
Gender categorical Units: Subjects			
Female	1	1	
Male	3	3	

Subject analysis sets

Subject analysis set title	Loxapine
Subject analysis set type	Full analysis

Subject analysis set description:

All enrolled patients treated with loxapine

Reporting group values	Loxapine		
Number of subjects	4		
Age categorical Units: Subjects			
In utero	0		
Preterm newborn infants (gestational age < 37 wks)	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)	1		
From 65-84 years	3		
85 years and over	0		

Gender categorical Units: Subjects			
Female	1		
Male	3		

End points

End points reporting groups

Reporting group title	Loxapin
Reporting group description:	
Dose escalation of loxapine	
Subject analysis set title	Loxapine
Subject analysis set type	Full analysis
Subject analysis set description:	
All enrolled patients treated with loxapine	

Primary: First occurence of (serious) adverse event

End point title	First occurence of (serious) adverse event[1]
End point description:	
First occurence of (serious) adverse event leading to dose reduction or withdrawal. However, due to the study ending prematurely and the low number of patients enrolled no statistical analysis was possible.	
End point type	Primary
End point timeframe:	
During treatment with loxapine (8 weeks treatment duration)	

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: This pilot study was primarily designed as a safety study evaluating the tolerability of loxapine in non-psychiatric patients. Hence, the primary endpoint was initially defined as the first occurrence of a (serious) adverse event leading to dose reduction or withdrawal of loxapine ("event"). However, the planned statistical analysis was not feasible due to the premature termination of the study and small number of subjects enrolled. Therefore, purely descriptive analysis was conducted.

End point values	Loxapin	Loxapine		
Subject group type	Reporting group	Subject analysis set		
Number of subjects analysed	4	4		
Units: events	4	4		

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information	
Timeframe for reporting adverse events:	
Whole study period (from screening visit to follow up visit)	
Assessment type	Systematic

Dictionary used	
Dictionary name	MedDRA
Dictionary version	19.0

Reporting groups	
Reporting group title	Loxapin

Reporting group description: -

Serious adverse events	Loxapin		
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 4 (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	Loxapin		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	4 / 4 (100.00%)		
Vascular disorders			
Hypertension			
subjects affected / exposed	1 / 4 (25.00%)		
occurrences (all)	1		
Nervous system disorders			
Burning sensation			
subjects affected / exposed	1 / 4 (25.00%)		
occurrences (all)	1		
Allodynia			
subjects affected / exposed	1 / 4 (25.00%)		
occurrences (all)	1		
Somnolence			

subjects affected / exposed	4 / 4 (100.00%)		
occurrences (all)	5		
Muscle rigidity			
subjects affected / exposed	1 / 4 (25.00%)		
occurrences (all)	3		
Akathisia			
subjects affected / exposed	1 / 4 (25.00%)		
occurrences (all)	2		
Bradykinesia			
subjects affected / exposed	1 / 4 (25.00%)		
occurrences (all)	1		
Parkinsonian gait			
subjects affected / exposed	2 / 4 (50.00%)		
occurrences (all)	2		
Tremor			
subjects affected / exposed	2 / 4 (50.00%)		
occurrences (all)	2		
Oromandibular dystonia			
subjects affected / exposed	1 / 4 (25.00%)		
occurrences (all)	1		
Trismus			
subjects affected / exposed	1 / 4 (25.00%)		
occurrences (all)	1		
Memory impairment			
subjects affected / exposed	1 / 4 (25.00%)		
occurrences (all)	1		
Dizziness			
subjects affected / exposed	1 / 4 (25.00%)		
occurrences (all)	1		
Restlessness			
subjects affected / exposed	1 / 4 (25.00%)		
occurrences (all)	1		
General disorders and administration site conditions			
Fatigue			

subjects affected / exposed occurrences (all)	1 / 4 (25.00%) 1		
Eye disorders Vision blurred subjects affected / exposed occurrences (all)	 1 / 4 (25.00%) 1		
Gastrointestinal disorders Nausea subjects affected / exposed occurrences (all)	 1 / 4 (25.00%) 1		
Respiratory, thoracic and mediastinal disorders Pleural mesothelioma malignant recurrent subjects affected / exposed occurrences (all)	 1 / 4 (25.00%) 1		
Skin and subcutaneous tissue disorders Pruritus subjects affected / exposed occurrences (all)	 1 / 4 (25.00%) 1		
Renal and urinary disorders Urinary retention subjects affected / exposed occurrences (all)	 1 / 4 (25.00%) 1		
Psychiatric disorders Decreased activity subjects affected / exposed occurrences (all) Agitation subjects affected / exposed occurrences (all) Fear subjects affected / exposed occurrences (all) Initial insomnia subjects affected / exposed occurrences (all)	 1 / 4 (25.00%) 1 1 / 4 (25.00%) 1 1 / 4 (25.00%) 1 1 / 4 (25.00%) 1		
Musculoskeletal and connective tissue disorders			

Spinal pain subjects affected / exposed occurrences (all)	1 / 4 (25.00%) 1		
Arthralgia subjects affected / exposed occurrences (all)	1 / 4 (25.00%) 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? Yes

Date	Interruption	Restart date
12 July 2017	After enrolling four subjects, the study was prematurely terminated due to a high number of (non-serious) drug-related adverse events and a negative risk–benefit evaluation.	-

Notes:

Limitations and caveats

None reported