# 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 |
| Scientific contact | Philipp Klee-Institut, HELIOS Klinikum Wuppertal, Klinikum der Privaten Universität Witten/Herdecke, 0049 2028961854, wup-aerzte-pharmakologie@helios-kliniken.de |

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

| | | | |
|---|---|---|---|
| Spinal pain<br>subjects affected / exposed<br>occurrences (all) | 1 / 4 (25.00%)<br>1 | | |
| Arthralgia<br>subjects affected / exposed<br>occurrences (all) | 1 / 4 (25.00%)<br>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