Clinical trial results:
A Phase IIa study of the efficacy and safety of oral LAT8881 in neuropathic pain

Summary

EudraCT number	2018-004534-15
Trial protocol	GB
Global end of trial date	04 May 2020

Results information

Result version number	v1 (current)
This version publication date	20 June 2021
First version publication date	20 June 2021

Trial information

Trial identification

Sponsor protocol code	LAT-NP-001

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT03865953
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Lateral Pharma Pty Ltd
Sponsor organisation address	Level 14, 114 William Street, MELBOURNE, Australia, 3000
Public contact	Research & Clinical Trials, Lateral Pharma Pty Ltd, info@lateral-pharma.com
Scientific contact	Research & Clinical Trials, Lateral Pharma Pty Ltd, info@lateral-pharma.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	06 July 2020
Is this the analysis of the primary completion data?	Yes
Primary completion date	03 May 2020
Global end of trial reached?	Yes
Global end of trial date	04 May 2020
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To evaluate the efficacy (whether the drug works) of oral LAT8881 in neuropathic pain compared with placebo, when assessed by change in mean pain intensity scores from baseline to the end of four weeks treatment, based on an 11 point numeric pain rating scale (NPRS).

Protection of trial subjects:

This study was conducted in compliance with the study protocol, the requirements and obligations of the International Conference on Harmonisation (ICH) and Good Clinical Practice (GCP) guidelines, Integrated Addendum to ICH E6(R1): Guideline for Good Clinical Practice E6(R2), the World Medical Association Declaration of Helsinki and its amendments and all applicable local guidelines, laws and regulations.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	20 March 2019
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: 12
Country: Number of subjects enrolled	Australia: 41
Worldwide total number of subjects	53
EEA total number of subjects	0

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)	31
From 65 to 84 years	22

85 years and over	0

Subject disposition

Recruitment

Recruitment details:

The study was conducted at 8 sites in total, including Australia (6 sites) and the United Kingdom (2 sites). Enrolment commenced in March 2019 and concluded in February 2020.

Pre-assignment

Screening details:

One hundred and eight (108) subjects signed consent and underwent screening procedures, Fifty-three (53) subjects were eligible and randomized, 25 to LAT8881 then placebo (Group 1) and 28 to placebo then LAT8881 (Group 2) treatment groups.

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, Assessor

Blinding implementation details:

Only the staff involved in the generation of the randomisation schedule and labelling of clinical trial supplies had access to the randomisation code during study conduct

Arms

Are arms mutually exclusive?	Yes
Arm title	LAT8881 then Placebo

Arm description:

Following a first baseline assessment of 7 days, 1 x 30 mg capsule of LAT8881 taken by mouth, twice daily (morning and evening) during the four-week treatment period. After washout of 14 days, followed by a second baseline of 7 days, matching placebo 1 x 30 mg capsule taken by mouth, twice daily (morning and evening) during the second four-week treatment period.

Arm type	Experimental
Investigational medicinal product name	LAT8881
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Capsule
Routes of administration	Oral use

Dosage and administration details:

one LAT8881 capsule taken in the morning and one LAT8881 capsule taken in the evening

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

Dosage and administration details:

one placebo capsule taken in the morning and one placebo capsule taken in the evening

Arm title	Placebo then LAT8881

Arm description:

Following a seven day initial baseline, matching placebo (containing excipients only) 1 x 30 mg capsule, taken by mouth, twice daily (morning and evening) during the four-week treatment period. After washout of 14 days, followed by a second baseline of seven days, 1 x 30 mg capsule of LAT8881 taken by mouth, twice daily (morning and evening) during the second four-week treatment period.

Arm type	Experimental

Investigational medicinal product name	LAT8881
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Capsule
Routes of administration	Oral use

Dosage and administration details:

one LAT8881 capsule taken in the morning and one LAT8881 capsule taken in the evening

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

Dosage and administration details:

one placebo capsule taken in the morning and one placebo capsule taken in the evening

Number of subjects in period 1	LAT8881 then Placebo	Placebo then LAT8881
Started	25	28
Treatment Period 1	25	28
Treatment Period 2	23	27
Completed	23	25
Not completed	2	3
Lost to follow-up	2	2
Protocol deviation	-	1

Baseline characteristics

Reporting groups	
Reporting group title	Overall trial

Reporting group description: -

Reporting group values	Overall trial	Total	
Number of subjects	53	53	
Age categorical Units: Subjects			
Age continuous Units: years			
arithmetic mean	59.8		
standard deviation	± 10.13	-	
Gender categorical Units: Subjects			
Female	22	22	
Male	31	31	
Neuropathic Pain History Units: Subjects			
Postherpetic Neuralgia	10	10	
Diabetic Peripheral Neuropathy	43	43	

End points

End points reporting groups

Reporting group title	LAT8881 then Placebo

Reporting group description:

Following a first baseline assessment of 7 days, 1 x 30 mg capsule of LAT8881 taken by mouth, twice daily (morning and evening) during the four-week treatment period. After washout of 14 days, followed by a second baseline of 7 days, matching placebo 1 x 30 mg capsule taken by mouth, twice daily (morning and evening) during the second four-week treatment period.

Reporting group title	Placebo then LAT8881

Reporting group description:

Following a seven day initial baseline, matching placebo (containing excipients only) 1 x 30 mg capsule, taken by mouth, twice daily (morning and evening) during the four-week treatment period. After washout of 14 days, followed by a second baseline of seven days, 1 x 30 mg capsule of LAT8881 taken by mouth, twice daily (morning and evening) during the second four-week treatment period.

Subject analysis set title	LAT8881
Subject analysis set type	Per protocol

Subject analysis set description:

A per-protocol (PP) population was based on duration of investigational medical product (IMP) treatment and protocol deviations. This population excluded subjects with inadequate exposure to IMP or who had other major protocol deviations. Rules for this population were included in the SAP. The PP population was the primary population to analyse efficacy endpoints. Demographic and baseline characteristics of the PP population were also be presented.

Subject analysis set title	Placebo
Subject analysis set type	Per protocol

Subject analysis set description:

A per-protocol (PP) population was based on duration of investigational medical product (IMP) treatment and protocol deviations. This population excluded subjects with inadequate exposure to IMP or who had other major protocol deviations. Rules for this population were included in the SAP. The PP population was the primary population to analyse efficacy endpoints. Demographic and baseline characteristics of the PP population were also be presented.

Primary: Absolute change in mean pain score

End point title	Absolute change in mean pain score

End point description:

The 11-point numeric pain rating scale (NPRS) ranges from 0 (“no pain”) to 10 (“worst pain imaginable”). A larger negative number represents a greater reduction in pain. The efficacy of oral LAT8881 in neuropathic pain was compared with placebo, when assessed by change in mean pain intensity scores, using this 11 point numeric pain rating scale.

End point type	Primary

End point timeframe:

from baseline to the last week of each treatment period (Week 4)

End point values	LAT8881	Placebo		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	23[1]	25[2]		
Units: 0-11				
arithmetic mean (standard deviation)	-0.87 (± 1.533)	-0.74 (± 2.090)		

Notes:

[1] - 23 subjects completed the LAT-8881 to Placebo arm of the study.

[2] - 25 subjects completed the Placebo-LAT8881 arm of the study

Statistical analyses

Statistical analysis title	Absolute Change in Mean Pain Score

Statistical analysis description:

Subject numbers gave a 90% power to demonstrate a statistically significant difference in the mean change from baseline NPRS for the active treatment compared with placebo of at least 1 unit, with a two sided test at a 5% level of significance

Comparison groups	LAT8881 v Placebo
Number of subjects included in analysis	48
Analysis specification	Pre-specified
Analysis type	superiority[3]
P-value	= 0.67
Method	Mixed models analysis
Parameter estimate	Mean difference (net)
Point estimate	-0.14
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.76
upper limit	0.49

Notes:

[3] - Analysis used a two-period two-treatment crossover design, with 23 subjects completing the LAT8881-Placebo arm and 25 subjects the Placebo-LAT8881 arm, therefore 48 subjects in total were analysed.

Secondary: Change in NPRS Score After the First and Last Dose of LAT8881 and Placebo

End point title	Change in NPRS Score After the First and Last Dose of LAT8881 and Placebo

End point description:

To investigate the effect of oral LAT8881 in neuropathic pain compared with placebo, as measured by the numeric pain rating score (NPRS). The 11-point numeric pain rating scale ranges from 0 (“no pain”) to 10 (“worst pain imaginable”). A larger negative number represents a greater reduction in pain.

End point type	Secondary

End point timeframe:

Pre-dose, 0.5,1,2,4 and 6 hours after the first and last dose of LAT8881 and placebo

End point values	LAT8881	Placebo		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	14	14		
Units: 0-11				
arithmetic mean (standard deviation)				
0.5 hours after first dose	-0.1 (± 0.77)	-0.2 (± 1.53)		
1 hour after first dose	-0.4 (± 0.63)	-0.6 (± 1.95)		
2 hours after first dose	-0.1 (± 0.95)	-0.8 (± 2.26)		

4 hours after first dose	0.1 (± 1.07)	-0.6 (± 2.17)		
6 hours after first dose	0.0 (± 0.68)	-0.7 (± 1.77)		
0.5 hours after last dose	-0.6 (± 2.43)	-0.4 (± 0.84)		
1 hour after last dose	-0.5 (± 2.58)	-0.4 (± 1.02)		
2 hours after last dose	-0.8 (± 2.19)	-0.1 (± 0.77)		
4 hours after last dose	-0.5 (± 2.26)	-0.4 (± 0.93)		
6 hours after last dose	-0.7 (± 1.93)	-0.4 (± 0.84)		

Statistical analyses

No statistical analyses for this end point

Secondary: Change in Mean Pain Scores After 1, 2 and 3 Weeks of Treatment, Using NPRS

End point title	Change in Mean Pain Scores After 1, 2 and 3 Weeks of Treatment, Using NPRS

End point description:

To investigate the effect of oral LAT8881 on mean pain scores in neuropathic pain compared with placebo, as measured by the numeric pain rating scale (NPRS). The 11-point numeric pain rating scale ranges from 0 (“no pain”) to 10 (“worst pain imaginable”). A larger negative number represents a greater reduction in pain.

End point type	Secondary

End point timeframe:

1,2 and 3 weeks

End point values	LAT8881	Placebo		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	49	50		
Units: 0-11				
arithmetic mean (standard deviation)				
Week 1	-0.50 (± 1.374)	-0.55 (± 1.268)		
Week 2	-0.73 (± 1.487)	-0.91 (± 1.623)		
Week 3	-0.84 (± 1.610)	-0.84 (± 1.884)		

Statistical analyses

No statistical analyses for this end point

Secondary: 30% Responder Rate in Oral LAT8881 Compared With Placebo, as Assessed by the Numeric Pain Rating Scale.

End point title	30% Responder Rate in Oral LAT8881 Compared With Placebo, as Assessed by the Numeric Pain Rating Scale.

End point description:

To determine the proportion of subjects with at least a 30% reduction in mean NPRS after 4 weeks treatment. The 11-point numeric pain rating scale (NPRS) ranges from 0 (“no pain”) to 10 (“worst pain imaginable”). A larger negative number represents a greater reduction in pain.

End point type	Secondary

End point timeframe:

4 weeks

End point values	LAT8881	Placebo		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	50	50		
Units: Count of Participants	20	19		

Statistical analyses

No statistical analyses for this end point

Secondary: 50% Responder Rate in Oral LAT8881 Compared With Placebo

End point title	50% Responder Rate in Oral LAT8881 Compared With Placebo

End point description:

To determine the proportion of subjects with at least a 50% reduction in mean the numeric pain rating scale (NPRS) after 4 weeks treatment. The 11-point numeric pain rating scale ranges from 0 (“no pain”) to 10 (“worst pain imaginable”). A larger negative number represents a greater reduction in pain.

End point type	Secondary

End point timeframe:

4 weeks

End point values	LAT8881	Placebo		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	50	50		
Units: Count of Participants	6	9		

Statistical analyses

No statistical analyses for this end point

Secondary: Maximum Change in Mean NPRS

End point title	Maximum Change in Mean NPRS

End point description:

To determine the maximum effects of oral LAT8881 in neuropathic pain, compared with placebo, as measured by the numeric pain rating scale (NPRS). The 11-point numeric pain rating scale ranges from 0 (“no pain”) to 10 (“worst pain imaginable”). A larger negative number represents a greater reduction

in pain.

End point type	Secondary

End point timeframe:

During the 4 week treatment period

End point values	LAT8881	Placebo		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	50	50		
Units: 0-11				
arithmetic mean (standard deviation)	-1.53 (± 1.372)	-1.55 (± 1.414)		

Statistical analyses

No statistical analyses for this end point

Secondary: Change in Functioning as Assessed by the Brief Pain Inventory Interference Scale (BPI)

End point title	Change in Functioning as Assessed by the Brief Pain Inventory Interference Scale (BPI)

End point description:

To evaluate the effects of oral LAT8881, compared with placebo, on functioning when measured by the Brief Pain Inventory Interference Scale (BPI). The BPI assesses the severity of pain and its impact on functioning. Patients are asked to assess the level of interference experienced across seven items; general activity, mood, walking ability, normal work, relations with other people, sleep and enjoyment of life, with a "0" meaning "no interference, and a "10", at the top end of the scale, meaning "complete interference". A reduction in mean score indicates a decrease in interference

End point type	Secondary

End point timeframe:

4 weeks

End point values	LAT8881	Placebo		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	50	50		
Units: 0-10				
arithmetic mean (standard deviation)	-0.57 (± 1.833)	-1.12 (± 1.967)		

Statistical analyses

No statistical analyses for this end point

Secondary: Change in Pain Characteristics and Intensity, as Assessed by the Short

Form McGill Pain Questionnaire (SF-MPQ-2)

End point title	Change in Pain Characteristics and Intensity, as Assessed by the Short Form McGill Pain Questionnaire (SF-MPQ-2)

End point description:

To evaluate the effect of oral LAT8881, compared with placebo, on pain symptoms in subjects with neuropathic pain,
when measured by the Short Form McGill Pain Questionnaire (SF-MPQ-2). The SF-MPQ-2 contains 22 descriptors of
pain and related symptoms, each scored from "0" (none) to "10" (worst possible). A larger negative number represents
a greater reduction in pain.

End point type	Secondary

End point timeframe:

4 weeks

End point values	LAT8881	Placebo		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	50	50		
Units: 0-11				
arithmetic mean (standard deviation)	-0.66 (± 1.343)	-0.63 (± 1.701)		

Statistical analyses

No statistical analyses for this end point

Secondary: Change in Neuropathic Pain Symptoms, as Assessed by Neuropathic Pain Symptom Inventory (NPSI)

End point title	Change in Neuropathic Pain Symptoms, as Assessed by Neuropathic Pain Symptom Inventory (NPSI)

End point description:

The Neuropathic Pain Symptom Inventory (NPSI) contains ten items related to different pain descriptors (e.g. burning,
squeezing, electric-shock, stabbing, tingling), allowing the assessment of the different dimensions of neuropathic pain,
and two items related to the frequency and duration of pain. Each pain descriptor is rated on an 11-point numeric
rating scale from 0 (no pain) to 10 (worst imaginable pain). Total pain intensity score is calculated by the sum of the 10
descriptors. A higher score indicates a higher pain intensity.

End point type	Secondary

End point timeframe:

4 weeks

End point values	LAT8881	Placebo		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	50	50		
Units: 0-11				
arithmetic mean (standard deviation)	-6.0 (± 14.52)	-7.4 (± 16.94)		

Statistical analyses

No statistical analyses for this end point

Secondary: Change in Emotional Functioning, as Assessed by the Beck Depression Inventory-II

End point title	Change in Emotional Functioning, as Assessed by the Beck Depression Inventory-II

End point description:

To evaluate the effect of oral LAT8881, compared with placebo, on emotional functioning when measured by the Beck Depression Inventory-II (BDI-II). The BDI-II consists of 21 items; each item is a list of four statements arranged in order of increasing severity about a particular symptom of depression. Each statement is scored from 0 to 3. Each of the 21 items is summed to give a single score for the BDI-II. Scores can range from 0 (no depression) to 63 (severe depression). An increase from baseline to the end of treatment indicates a deterioration.

End point type	Secondary

End point timeframe:

4 weeks

End point values	LAT8881	Placebo		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	50	50		
Units: 0-63				
arithmetic mean (standard deviation)	-1.1 (± 4.14)	-1.2 (± 7.98)		

Statistical analyses

No statistical analyses for this end point

Secondary: Patient Global Impression of Change Score

End point title	Patient Global Impression of Change Score

End point description:

The Patient Global Impression of Change (PGIC) is a a single-item rating by subjects of their improvement with treatment during a clinical trial. It asks the subject to rate their improvement with therapy on a 7-point scale, ranging from substantially worse ("0") to substantially improved ("7"), with no change ("4") as the mid-point. A score above 4 indicates an improvement.

End point type	Secondary

End point timeframe:

4 weeks

End point values	LAT8881	Placebo		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	50	50		
Units: 0-7				
arithmetic mean (standard deviation)	4.5 (± 1.23)	4.8 (± 1.33)		

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Adverse events were collected from the first dose of study treatment until the End of Study visit, maximum 93
days

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	22.0

Reporting groups

Reporting group title	LAT8881

Reporting group description:

1 x 30 mg capsule of LAT8881 taken by mouth, twice daily (morning and evening) during the four-week treatment period

Reporting group title	Placebo

Reporting group description:

1 x 30 mg capsule of placebo, taken by mouth, twice daily (morning and evening) during the four-week treatment period

Serious adverse events	LAT8881	Placebo	
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 51 (0.00%)	0 / 51 (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: 5 %

Non-serious adverse events	LAT8881	Placebo	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	5 / 51 (9.80%)	6 / 51 (11.76%)	
Nervous system disorders			
Headache			
subjects affected / exposed	2 / 51 (3.92%)	4 / 51 (7.84%)	
occurrences (all)	3	4	
Infections and infestations			
Upper respiratory tract infection			
subjects affected / exposed	3 / 51 (5.88%)	3 / 51 (5.88%)	
occurrences (all)	4	3	

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