Clinical trial results:
Prospective naturalistic clinical trail with loxapine in agitated patients with personality disorder

Summary

EudraCT number	2016-004884-38
Trial protocol	ES
Global end of trial date	18 June 2019

Results information

Result version number	v1 (current)
This version publication date	07 November 2021
First version publication date	07 November 2021

Trial information

Trial identification

Sponsor protocol code	FER-LOX-2016-01

Additional study identifiers

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

Notes:

Sponsors

Sponsor organisation name	VHIR
Sponsor organisation address	Passeig Vall Hebron 119-129, Barcelona, Spain, 08035
Public contact	Joaquin Lopez-Soriano, Vall d'Hebron University Hospital, 34 934894295, joaquin.lopez.soriano@vhir.org
Scientific contact	Psychiatry service, Vall d'Hebron University Hospital, 34 934894295,

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	18 June 2019
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	18 June 2019
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The main objective of the clinical trial is to assess the effectiveness, defined as time respone of loxapine 9.1mg in acute pre/agitated patients with personality disorder. This respones is define as 1 (very much improvement) or 2 (much improvement) score in the Clinical Global Impression – Improvement scale (CGI-I)

Protection of trial subjects:

It was ensured that the recruitment procedures did not imply any modification in the medical treatment that the participants could receive in case they did not wish to participate

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	02 October 2017
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: 30
Worldwide total number of subjects	30
EEA total number of subjects	30

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)	30
From 65 to 84 years	0
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

Thirty adult patients were consecutively recruited for the study from December 2017 to June 2019 when they attended the Psychiatry Emergency Departments for agitation as the highest priority goal treatment

Pre-assignment

Screening details:

Inclusion criteria for this study included being aged between 18 and 65 years, presenting moderate-severe agitation according to Clinical Global Impression-Severity (CGI-S) scoring (GCI-S ≥ 3 and ≤ 5), being diagnosed with PD according to the Diagnostic and Statistical Manual of Mental Disorder 5th edition (DSM-5), and signing informed consent.

Period 1

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

Arms

Arm title	Inhaled Loxapine

Arm description: -

Arm type	Experimental
Investigational medicinal product name	Loxapine
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Pressurised inhalation, solution
Routes of administration	Inhalation use

Dosage and administration details:

A single dose of 9.1 mg inhaled loxapine

Number of subjects in period 1	Inhaled Loxapine
Started	30
Completed	30

Period 2

Period 2 title	10 minutes treatment
Is this the baseline period?	No
Allocation method	Not applicable
Blinding used	Not blinded

Arms	
Arm title	IL 10 minutes
Arm description: -	
Arm type	Experimental
Investigational medicinal product name	Loxapine
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Pressurised inhalation, solution
Routes of administration	Inhalation use

Dosage and administration details:

A single dose of 9.1 mg inhaled loxapine

Number of subjects in period 2	IL 10 minutes
Started	30
Completed	30

Period 3	
Period 3 title	30 minutes treatment
Is this the baseline period?	No
Allocation method	Not applicable
Blinding used	Not blinded

Arms	
Arm title	IL 30 minutes
Arm description: -	
Arm type	Experimental
Investigational medicinal product name	Loxapine
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Pressurised inhalation, solution
Routes of administration	Inhalation use

Dosage and administration details:

A single dose of 9.1 mg inhaled loxapine

Number of subjects in period 3	IL 30 minutes
Started	30
Completed	30

Baseline characteristics

Reporting groups	
Reporting group title	Overall trial

Reporting group description: -

Reporting group values	Overall trial	Total	
Number of subjects	30	30	
Age categorical Units: Subjects			
Adults (18-64 years)	30	30	
Age continuous Units: years			
arithmetic mean	39.0		
standard deviation	± 9.7	-	
Gender categorical Units: Subjects			
Female	20	20	
Male	10	10	

End points

End points reporting groups	
Reporting group title	Inhaled Loxapine
Reporting group description: -	
Reporting group title	IL 10 minutes
Reporting group description: -	
Reporting group title	IL 30 minutes
Reporting group description: -	

Primary: ACES	
End point title	ACES
End point description:	
Agitation-Calmness Evaluation scale. A single item that evaluates general agitation and sedation at the moment of the assessment. It ranges from 1 (severe agitation) to 9 (unarousable)	
End point type	Primary
End point timeframe:	
30 minutes after treatment	

End point values	Inhaled Loxapine	IL 10 minutes	IL 30 minutes	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	30	30	30	
Units: units				
number (confidence interval 95%)	2 (2 to 2)	4 (4 to 4.25)	4 (4 to 6)	

Statistical analyses

Statistical analysis title	ACES score
Comparison groups	Inhaled Loxapine v IL 10 minutes
Number of subjects included in analysis	60
Analysis specification	Pre-specified
Analysis type	non-inferiority
P-value	< 0.001
Method	Wilcoxon (Mann-Whitney)

Statistical analysis title	ACES score 30 min
Comparison groups	Inhaled Loxapine v IL 30 minutes

Number of subjects included in analysis	60
Analysis specification	Pre-specified
Analysis type	non-inferiority
P-value	< 0.001
Method	Wilcoxon (Mann-Whitney)

Primary: PANSS-EC

End point title	PANSS-EC

End point description:

Excited Component of the Positive and Negative Syndrome scale (PANSS-EC) [29]: a 5-item scale (low impulse control, tension, hostility, lack of cooperation and excitement), with a rating from 1 to 7 per item. Scores higher than 20 indicate severe agitation.

End point type	Primary

End point timeframe:

30 minutes after treatment

End point values	Inhaled Loxapine	IL 10 minutes	IL 30 minutes	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	30	30	30	
Units: units				
number (confidence interval 95%)	21.5 (19.5 to 24.25)	8 (6 to 14.25)	5 (5 to 7)	

Statistical analyses

Statistical analysis title	PANSS-EC 10 minutes
Comparison groups	Inhaled Loxapine v IL 10 minutes
Number of subjects included in analysis	60
Analysis specification	Pre-specified
Analysis type	non-inferiority
P-value	< 0.001
Method	Wilcoxon (Mann-Whitney)

Statistical analysis title	PANSS-EC 30 minutes
Comparison groups	Inhaled Loxapine v IL 30 minutes

Number of subjects included in analysis	60
Analysis specification	Pre-specified
Analysis type	non-inferiority
P-value	< 0.001
Method	Wilcoxon (Mann-Whitney)

Secondary: PANSS-EC T	
End point title	PANSS-EC T
End point description: PANSS-EC Tension item	
End point type	Secondary
End point timeframe: 30 minutes after treatment	

End point values	Inhaled Loxapine	IL 10 minutes	IL 30 minutes	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	30	30	30	
Units: units				
number (confidence interval 95%)	4 (4 to 6)	2 (1 to 3)	1 (1 to 1.25)	

Statistical analyses

Statistical analysis title	PANSS-EC T 10 minutes
Comparison groups	Inhaled Loxapine v IL 10 minutes
Number of subjects included in analysis	60
Analysis specification	Pre-specified
Analysis type	non-inferiority
P-value	< 0.001
Method	Wilcoxon (Mann-Whitney)

Statistical analysis title	PANSS-EC T 30 minutes
Comparison groups	Inhaled Loxapine v IL 30 minutes
Number of subjects included in analysis	60
Analysis specification	Pre-specified
Analysis type	non-inferiority
P-value	< 0.001
Method	Wilcoxon (Mann-Whitney)

Adverse events

Adverse events information[1]	
Timeframe for reporting adverse events: 30 minutes after tretament	
Assessment type	Systematic

Dictionary used	
Dictionary name	MedDRA
Dictionary version	22.1

Reporting groups	
Reporting group title	Total adverse events
Reporting group description: -	

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

Frequency threshold for reporting non-serious adverse events: 5 %

Non-serious adverse events	Total adverse events		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	0 / 30 (0.00%)		

Notes:

[1] - There are no non-serious adverse events recorded for these results. It is expected that there will be at least one non-serious adverse event reported.
Justification: No significant adverse effects were registered. Given the low time considered and safety of the treatment, no adverse effects were expected in such a short time (30 minutes).

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.

Loxapine efficacy could not be directly compared with other treatments. Results of the mixed effect logistic regression models must be interpreted with caution, not allowing to obtain robust estimates. A small sample size was used.

Notes: