Clinical trial results:
A randomized, double-blind, placebo controlled, parallel group, multicentric, phase IIa clinical trial to evaluate the safety, tolerability and therapeutic efficacy of daily oral treatment with NFX88 on neuropathic pain in patients with spinal cord injury.

Summary

EudraCT number	2018-004792-13
Trial protocol	ES
Global end of trial date	12 April 2022

Results information

Result version number	v1 (current)
This version publication date	20 May 2023
First version publication date	20 May 2023
Summary attachment (see zip file)	Protocol Synopsis (NFX-88 Protocol Synopsis V1.0 28Dec2018 English FINAL.pdf)

Trial information

Trial identification

Sponsor protocol code	NFX88-2A-2018

Additional study identifiers

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

Notes:

Sponsors

Sponsor organisation name	Neurofixpharma
Sponsor organisation address	Calle del Adaja, 3 Parque Científico de la Universidad de Salamanca Edificio M3 PB05 Sala 1, Salamanca, Spain, 37185
Public contact	Miguel Angel Ávila Santiago, Neurofixpharma S.A., 0034 674052566, miguelangel.avila@neurofixpharma.com
Scientific contact	Miguel Angel Ávila Santiago, Neurofixpharma S.A., 0034 674052566, miguelangel.avila@neurofixpharma.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	29 November 2022
Is this the analysis of the primary completion data?	Yes
Primary completion date	12 April 2022
Global end of trial reached?	Yes
Global end of trial date	12 April 2022
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The primary objective is to assess the safety and tolerability of NFX88 in spinal cord injury patients with neuropathic pain over ninety-day treatment period.

Protection of trial subjects:

Treated in routine care

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	01 June 2019
Long term follow-up planned	Yes
Long term follow-up rationale	Safety, Efficacy
Long term follow-up duration	1 Months
Independent data monitoring committee (IDMC) involvement?	No

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Spain: 61
Worldwide total number of subjects	61
EEA total number of subjects	61

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)	56
From 65 to 84 years	5
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

Recruitment phase: ~18 months
60 patients to be recruited in 4 arms

Pre-assignment

Screening details:

Patients should undergo a baseline visit within 7 days prior to their study randomisation. The Principal Investigator or his/her designee will obtain written informed consent before any study related procedures are performed.

Pre-assignment period milestones

Number of subjects started	61
Number of subjects completed	61

Period 1

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

Blinding implementation details:

Due to the objectives of the study, the identity of placebo and NFX88 treatment will both be blinded. Patients will be randomised to receive any of them in a double-blind model such that neither the investigator nor the patient will know which combination is being administered.

Arms

Are arms mutually exclusive?	Yes
Arm title	ARM 1: 1.05 g/day

Arm description:

1.05 g/day NFX88

Arm type	Experimental
Investigational medicinal product name	NFX88
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

1.05 g/day oral use

Arm title	ARM 2. 2.1g/day NFX88

Arm description:

2.10 g/day NFX88

Arm type	Active comparator
Investigational medicinal product name	NFX88
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details: 2.10 g/day ORAL USE	

Arm title	ARM 3: 4.2 g/day
Arm description: 4.20 g/day NFX8	
Arm type	Active comparator
Investigational medicinal product name	NFX88
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use
Dosage and administration details: 4.20 g/day ORAL USE	
Arm title	ARM 4: 0.0 g/day
Arm description: PLACEBO	
Arm type	Placebo
Investigational medicinal product name	PLACEBO
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use
Dosage and administration details: ORAL USE	

Number of subjects in period 1	ARM 1: 1.05 g/day	ARM 2. 2.1g/day NFX88	ARM 3: 4.2 g/day
Started	15	15	16
Completed	12	11	12
Not completed	3	4	4
Consent withdrawn by subject	1	-	1
Physician decision	-	2	-
Adverse event, non-fatal	1	1	2
Lost to follow-up	1	-	-
Protocol deviation	-	1	1

Number of subjects in period 1	ARM 4: 0.0 g/day
Started	15
Completed	9
Not completed	6
Consent withdrawn by subject	1
Physician decision	-

Adverse event, non-fatal	1
Lost to follow-up	-
Protocol deviation	4

Baseline characteristics

Reporting groups	
Reporting group title	Randomization

Reporting group description: -

Reporting group values	Randomization	Total	
Number of subjects	61	61	
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)		0	
From 65-84 years		0	
85 years and over		0	
Age continuous			
Male or Female 18 to 65 years of age			
Units: years			
arithmetic mean	47.2		
full range (min-max)	22 to 67	-	
Gender categorical			
Male or Female 18 to 65 years of age			
Units: Subjects			
Female	12	12	
Male	49	49	

End points

End points reporting groups	
Reporting group title	ARM 1: 1.05 g/day
Reporting group description: 1.05 g/day NFX88	
Reporting group title	ARM 2. 2.1g/day NFX88
Reporting group description: 2.10 g/day NFX88	
Reporting group title	ARM 3: 4.2 g/day
Reporting group description: 4.20 g/day NFX8	
Reporting group title	ARM 4: 0.0 g/day
Reporting group description: PLACEBO	

Primary: Safety and tolerability of NFX88 administered by 90 days

End point title	Safety and tolerability of NFX88 administered by 90 days

End point description:

Safety and tolerability of NFX88 administered for ninety days will be evaluated by assessing the number, severity, and type of Adverse Event, including changes in vital signs, safety laboratory values (haematology, clinical chemistry and urinalysis), ECGs, and MAS (Modified Ashworth Scale) (e.g. to monitor spasticity worsening) and ASIA (e.g. to monitor neurological worsening) scores.

Non-worsening of spasticity and motor score will be obtaining as the non-increase of the scales values MAS and ASIA, respectively, from the beginning to the end of the treatment.

End point type	Primary

End point timeframe:

Safety and tolerability of NFX88 administered for 3 months will be assessed by the number, severity, and type of Adverse Events from screening visit (-7 days) to the Follow up visit (120 days after the start of the treatment)

End point values	ARM 1: 1.05 g/day	ARM 2. 2.1g/day	ARM 3: 4.2 g/day	ARM 4: 0.0 g/day
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	15	15	16	15
Units: Adverse Events				
Severe	1	2	3	1
Mild	14	4	18	14
Moderate	1	0	3	1

Statistical analyses

Statistical analysis title	Safety analysis

Statistical analysis description:

CODING: For the analysis, each adverse event (AE) was coded as a binary variable (Present/Absent) in

each study subject. AEs defined as “unsafe levels” of some lab parameter or clinical outcome (vital signs, ECGs, ASIA
and MAS scales) were also coded as binary. If the same AE occur at different degrees of severity several binary variables were calculated

Comparison groups	ARM 1: 1.05 g/day v ARM 2. 2.1g/day NFX88 v ARM 3: 4.2 g/day v ARM 4: 0.0 g/day
Number of subjects included in analysis	61
Analysis specification	Pre-specified
Analysis type	other[1]
P-value	≤ 0.05
Method	Fisher exact

Notes:

[1] - Tables with counts and proportions of each AE in each arm were compiled. For the intervention arms, exact confidence intervals for the proportion of each AE were estimated. Comparison of the risk of each
EA between arms was done with Fisher’s exact tests. To increase power, the patients from the three intervention doses were analyzed together in one intervention arm. If some AE turned out to be relatively
common, a logistic regression model was built to examine if there is a dose-response ef

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Safety and tolerability of NFX88 administered for 90 days was assessed in the different visits: Since SV (- 7days) to Follow-up visit (120 days after the beginning of the treatment)

Adverse event reporting additional description:

Safety and tolerability of NFX88 administered for 3 months will be assessed by the number, severity, and type of Adverse Events, including changes in:
- Vital signs.
- ECG.
- Clinical laboratory parameters
- Spasticity score as determined by MAS
-Sensory and motor function by ASIA scale

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	22.1

Reporting groups

Reporting group title	ARM 1: 1.05 g/day
Reporting group description:	
1.05 g/day NFX88	
Reporting group title	ARM 2. 2.1g/day NFX88
Reporting group description:	
2.10 g/day NFX88	
Reporting group title	ARM 3: 4.2 g/day
Reporting group description:	
4.20 g/day NFX8	
Reporting group title	ARM 4: 0.0 g/day
Reporting group description:	
PLACEBO	

Serious adverse events	ARM 1: 1.05 g/day	ARM 2. 2.1g/day NFX88	ARM 3: 4.2 g/day
Total subjects affected by serious adverse events			
subjects affected / exposed	1 / 15 (6.67%)	2 / 15 (13.33%)	1 / 16 (6.25%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events	0	0	0
Vascular disorders			
Vascular insufficiency			
subjects affected / exposed	0 / 15 (0.00%)	1 / 15 (6.67%)	0 / 16 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory, thoracic and mediastinal disorders			

Respiratory disorder			
subjects affected / exposed	0 / 15 (0.00%)	0 / 15 (0.00%)	1 / 16 (6.25%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 3
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Renal and urinary disorders			
Sepsis			
subjects affected / exposed	0 / 15 (0.00%)	0 / 15 (0.00%)	0 / 16 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Urinary tract infection			
subjects affected / exposed	1 / 15 (6.67%)	1 / 15 (6.67%)	0 / 16 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Serious adverse events	ARM 4: 0.0 g/day		
Total subjects affected by serious adverse events			
subjects affected / exposed	1 / 15 (6.67%)		
number of deaths (all causes)	0		
number of deaths resulting from adverse events	0		
Vascular disorders			
Vascular insufficiency			
subjects affected / exposed	0 / 15 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Respiratory, thoracic and mediastinal disorders			
Respiratory disorder			
subjects affected / exposed	0 / 15 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Renal and urinary disorders			
Sepsis			
subjects affected / exposed	1 / 15 (6.67%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Urinary tract infection			

subjects affected / exposed	0 / 15 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		

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

Non-serious adverse events	ARM 1: 1.05 g/day	ARM 2. 2.1g/day NFX88	ARM 3: 4.2 g/day
Total subjects affected by non-serious adverse events			
subjects affected / exposed	2 / 15 (13.33%)	1 / 15 (6.67%)	4 / 16 (25.00%)
Gastrointestinal disorders			
Gastrointestinal disorder			
subjects affected / exposed	1 / 15 (6.67%)	0 / 15 (0.00%)	1 / 16 (6.25%)
occurrences (all)	1	0	1
Renal and urinary disorders			
Infection			
subjects affected / exposed	1 / 15 (6.67%)	1 / 15 (6.67%)	3 / 16 (18.75%)
occurrences (all)	1	1	3

Non-serious adverse events	ARM 4: 0.0 g/day		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	4 / 15 (26.67%)		
Gastrointestinal disorders			
Gastrointestinal disorder			
subjects affected / exposed	1 / 15 (6.67%)		
occurrences (all)	3		
Renal and urinary disorders			
Infection			
subjects affected / exposed	3 / 15 (20.00%)		
occurrences (all)	5		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
23 May 2019	Initial protocol v1.0 dated 28dec2018 – Conditional approval obtained on 23May2019. New version of IMPD had to be submitted and approved before study start.
29 April 2020	Protocol v2.0 dated 13Mar2020 relevant amendment to increase the recruitment period, increase age inclusion criteria, clarify traumatic spinal cord injury meaning and specify more clearly the washout period for opioids and cannabinoids. Approved on 29Apr2020
18 November 2020	Protocol v3.0 dated 25Sep2020 relevant amendment to include the option for home visit due to COVID pandemic. Approved on 18Nov2020
20 March 2021	Protocol v4.0 dated 22Feb2021 relevant amendment to decrease the total number of patients to be included in the trial to 48. Approved on 20Mar2021
27 October 2021	Protocol v5.0 dated 09Sep2021 relevant amendment to decrease the total number of patients to be included in the trial to 44. Approved on 27Oct2021

Notes:

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.

The recruitment and following up o the patients was slower and more complicated than usual due to the COVID pandemic situation during the years this study was carried on.

Notes: