Clinical trial results:
Prospective, Long-Term, Interventional, Active Extension Study to Evaluate the Safety and Tolerability of NBI-921352 as Adjunctive Therapy in Subjects with Focal Onset Seizures (FOS)

Summary

EudraCT number	2021-004265-12
Trial protocol	CZ FR HU ES IT BE
Global end of trial date	11 March 2024

Results information

Result version number	v1 (current)
This version publication date	27 March 2025
First version publication date	27 March 2025

Trial information

Trial identification

Sponsor protocol code	NBI-921352-FOS2022

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT05493293
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Neurocrine Biosciences
Sponsor organisation address	12780 El Camino Real, San Diego, United States, 92130
Public contact	Neurocrine Medical Information, Neurocrine Biosciences Inc., +1 877-641-3461, medinfo@neurocrine.com
Scientific contact	Neurocrine Medical Information, Neurocrine Biosciences Inc., +1 877-641-3461, medinfo@neurocrine.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	11 March 2024
Is this the analysis of the primary completion data?	Yes
Primary completion date	11 March 2024
Global end of trial reached?	Yes
Global end of trial date	11 March 2024
Was the trial ended prematurely?	Yes

Notes:

General information about the trial

Main objective of the trial:

The primary objective for this study is evaluate the long-term safety and tolerability of NBI-921352 in participants with FOS.

Protection of trial subjects:

This study was performed in full compliance with applicable Good Clinical Practice (GCP) and regulations.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	08 November 2022
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	Yes

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Australia: 8
Country: Number of subjects enrolled	Spain: 22
Country: Number of subjects enrolled	Belgium: 6
Country: Number of subjects enrolled	Czechia: 28
Country: Number of subjects enrolled	France: 7
Country: Number of subjects enrolled	Hungary: 6
Country: Number of subjects enrolled	Italy: 5
Worldwide total number of subjects	82
EEA total number of subjects	74

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)	82
From 65 to 84 years	0
85 years and over	0

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

Participants who enrolled directly from Study NBI-921352-FOS2021 did not have a screening period. Participants who did not enroll directly had a screening period of at least 4 weeks.

Period 1

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

Arms

Arm title	NBI-921352

Arm description:

Participants received NBI-921352 3 times per day (TID) for up to 104 weeks.

Arm type	Experimental
Investigational medicinal product name	NBI-921352
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

NBI-921352 was administered per schedule specified in the arm description.

Number of subjects in period 1	NBI-921352
Started	82
Received at Least 1 Dose of Study Drug	82
Completed	0
Not completed	82
Adverse event, serious fatal	1
Consent withdrawn by subject	5
Other Than Specified	21
Adverse event, non-fatal	7
Study Terminated by Sponsor	48

Baseline characteristics

Reporting groups	
Reporting group title	NBI-921352
Reporting group description:	
Participants received NBI-921352 3 times per day (TID) for up to 104 weeks.	

Reporting group values	NBI-921352	Total	
Number of subjects	82	82	
Age categorical Units: Subjects			
Age continuous Units: years			
arithmetic mean	42.8		
standard deviation	± 10.2	-	
Gender categorical Units: Subjects			
Female	42	42	
Male	40	40	
Ethnicity Units: Subjects			
Hispanic or Latino	7	7	
Not Hispanic or Latino	75	75	
Race Units: Subjects			
Asian	1	1	
White	78	78	
Other	2	2	
Not reported	1	1	

End points

End points reporting groups

Reporting group title	NBI-921352

Reporting group description:

Participants received NBI-921352 3 times per day (TID) for up to 104 weeks.

Primary: Number of Participants With Serious Treatment-emergent Adverse Events (TEAEs)

End point title	Number of Participants With Serious Treatment-emergent Adverse Events (TEAEs)[1]

End point description:

A TEAE was an adverse event (AE) with an onset date on or after first dose of study drug and within 14 days after the last dose of study drug. An AE was any untoward medical occurrence in a participant administered the study drug that did not necessarily have a causal relationship with the treatment. A serious adverse event (SAE) was any untoward medical occurrence that at any dose: resulted in death, was life-threatening, required in-patient hospitalization/prolongation of existing hospitalization, was a congenital anomaly, was infection that required treatment parenteral antibiotics, other important medical events which might jeopardize participants, or might require medical/surgical intervention to prevent any of the above. A summary of all Serious Adverse Events and Other Adverse Events (nonserious) regardless of causality is located in the 'Reported Adverse Events' Section. Safety analysis set included all enrolled participants who received at least 1 dose of NBI-921352.

End point type	Primary

End point timeframe:

From first dose of study drug up to Week 111

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: The endpoint was descriptive in nature.

End point values	NBI-921352			
Subject group type	Reporting group			
Number of subjects analysed	82			
Units: participants	7			

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information	
Timeframe for reporting adverse events:	
From first dose of study drug up to Week 111	
Adverse event reporting additional description:	
Safety analysis set included all enrolled participants who received at least 1 dose of NBI-921352.	
Assessment type	Systematic

Dictionary used	
Dictionary name	MedDRA
Dictionary version	26.0

Reporting groups	
Reporting group title	NBI-921352
Reporting group description:	
Participants received NBI-921352 3 times per day (TID) for up to 104 weeks.	

Serious adverse events	NBI-921352		
Total subjects affected by serious adverse events			
subjects affected / exposed	7 / 82 (8.54%)		
number of deaths (all causes)	1		
number of deaths resulting from adverse events			
Nervous system disorders			
Epilepsy			
subjects affected / exposed	1 / 82 (1.22%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Generalised tonic-clonic seizure			
subjects affected / exposed	1 / 82 (1.22%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Seizure			
subjects affected / exposed	1 / 82 (1.22%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Seizure cluster			

subjects affected / exposed	1 / 82 (1.22%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
General disorders and administration site conditions			
Death			
subjects affected / exposed	1 / 82 (1.22%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 1		
Hepatobiliary disorders			
Hepatitis acute			
subjects affected / exposed	1 / 82 (1.22%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Infections and infestations			
COVID-19			
subjects affected / exposed	1 / 82 (1.22%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Metabolism and nutrition disorders			
Hyponatraemia			
subjects affected / exposed	1 / 82 (1.22%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		

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

Non-serious adverse events	NBI-921352		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	41 / 82 (50.00%)		
Nervous system disorders			
Dizziness			
subjects affected / exposed	15 / 82 (18.29%)		
occurrences (all)	27		
Headache			

subjects affected / exposed occurrences (all) Somnolence subjects affected / exposed occurrences (all)	12 / 82 (14.63%) 12 5 / 82 (6.10%) 6		
General disorders and administration site conditions Fatigue subjects affected / exposed occurrences (all)	 10 / 82 (12.20%) 11		
Psychiatric disorders Insomnia subjects affected / exposed occurrences (all)	 6 / 82 (7.32%) 8		
Infections and infestations Upper respiratory tract infection subjects affected / exposed occurrences (all)	 5 / 82 (6.10%) 5		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
22 October 2021	• Inclusion criterion was revised to indicate that hormonal contraception is considered an acceptable method of contraception when used with effective nonhormonal contraception and to clarify that male participants with bilateral orchiectomy are required to use a condom with spermicide. • Specified that known potent inhibitors or inducers of cytochrome P3A4 (CYP3A4) enzymes (other than antiseizure medications [ASMs]) are not permitted during the study. • A statement was added that participants should avoid exposure to excessive sunlight or artificial ultraviolet light during the study and be advised to use sunscreen/sunblock and/or wear protective clothing when exposure could not be avoided. • Added that study treatment discontinuation was required for corrected QT interval using Fridericia's formula (QTcF) change from baseline >60 millisecond (msec) (cardiologist verified) and confirmed with repeated electrocardiogram (ECG) measure. • Added that study treatment discontinuation was required for QTcF of >500 msec (cardiologist verified) on any ECG tracing. • Added a statement that the electronic data capture (EDC) and study-specific electronic case report forms (eCRFs) will comply with European Union General Data Protection Regulation.
18 May 2022	The protocol was revised to allow enrollment of participants who did not enroll directly from FOS2021. A Screening Period of up to 8 weeks and a 1-week open label (OL) Dose Titration Period was added. • Removed statement that participants should avoid excessive sunlight and ultraviolet light exposure during the study. • Added a statement that the Sponsor will store biosamples in a manner compliant with applicable national and local regulations and the requirements of the European Union General Data Protection Regulation. • Added that entries into the daily seizure diary will be reviewed with the participant by qualified study staff personnel who have completed the study-specific training. • Revised methods for measuring body temperature. • Added a statement that study visits may be conducted remotely if in-person visits were not possible for COVID-19-related reasons. • Updated to state that SAEs must be reported immediately and no later than 24 hours of knowledge of the event under any circumstances. • Added that pregnancies in partners of male participants must be reported to Neurocrine Biosciences, Inc (NBI) and that NBI will ask to follow the partner's pregnancy. • Updated Sponsor contact information for reporting SAEs and pregnancies. • Removed the requirement for postbaseline safety data from the definition of the safety analysis set.

04 May 2023	• The secondary objective was recategorized as an 'other' objective. • Changes were made to the study endpoints, and the safety and efficacy analyses were updated to reflect the changes to the endpoints. • Clarified that a Taper Visit is not applicable for participants who withdraw from the study if they have dose de-escalation before the Early Termination Visit. • Increased the frequency of pregnancy testing for female participants of childbearing potential during the OL treatment period and removed the requirement for a confirmatory serum pregnancy test to be conducted at the study center. • Added that the local regulatory authority will be notified if urgent safety measures are required. • Updated statements about the security of information technology systems and Sponsor compliance with applicable laws and regulations for disclosure of study results. • Updated the Schedule of Assessments to clarify timing of seizure diary collection and dispensation.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported