Clinical trial results:
A MULTI-CENTRE, SINGLE DOSE TRIAL TO EVALUATE PHARMACOKINETICS OF PITOLISANT (BF2.649) IN CHILDREN FROM 6 TO LESS THAN 18 YEARS WITH NARCOLEPSY

Summary

EudraCT number	2013-001505-93
Trial protocol	IT FR
Global end of trial date	16 September 2014

Results information

Result version number	v1 (current)
This version publication date	26 June 2022
First version publication date	26 June 2022

Trial information

Trial identification

Sponsor protocol code	P11-11

Additional study identifiers

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

Notes:

Sponsors

Sponsor organisation name	Bioprojet Pharma
Sponsor organisation address	9, rue Rameau, 75002 - Paris, France,
Public contact	Clinical Development Director, Bioprojet Pharma, 33 147036633, contact@bioprojet.com
Scientific contact	Clinical Development Director, Bioprojet Pharma, 33 147036633, contact@bioprojet.com

Notes:

Paediatric regulatory details

Is trial part of an agreed paediatric investigation plan (PIP)	Yes
EMA paediatric investigation plan number(s)	EMEA-001176-PIP01-11
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?	Yes

Notes:

Results analysis stage

Analysis stage	Final
Date of interim/final analysis	09 July 2015
Is this the analysis of the primary completion data?	Yes
Primary completion date	16 September 2014
Global end of trial reached?	Yes
Global end of trial date	16 September 2014
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To determine the pharmacokinetic parameters of pitolisant in narcoleptic children aged from 6 to less than 18 years including at least maximum concentration (Cmax), time of occurrence of maximum concentration (tmax), t1/2, AUC0-t and AUC0-∞ using 6 samples per participant.

Protection of trial subjects:

Physical examination, vital sign, ECG evaluation and haematology/blood chemistry were performed on trial subjects to ensure safety. Adverse events were continuously monitored.

Topical anaesthesia was offered for phlebotomy/ venipuncture. Blood samples were taken using a catheter.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	16 January 2014
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	France: 15
Country: Number of subjects enrolled	Italy: 10
Worldwide total number of subjects	25
EEA total number of subjects	25

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)	12
Adolescents (12-17 years)	13
Adults (18-64 years)	0
From 65 to 84 years	0

85 years and over	0

Subject disposition

Recruitment

Recruitment details:

The study was carried out in 25 narcoleptic children with or without cataplexy (12 males and 13 females), who met all the inclusion criteria and none of the non-inclusion criteria. One patient withdrew from the study. Therefore, 24 patients duly completed the study.

Pre-assignment

Screening details:

Occurred within 2 weeks before starting study medication.
Each patient underwent a medical history and physical examination. Oral and written information about the study was given followed by a questionnaire corresponding to the study inclusion/non-inclusion criteria. Parents or the patient (if old enough), signed the Informed Consent Form.

Pre-assignment period milestones

Number of subjects started	25
Number of subjects completed	25

Period 1

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

Arms

Are arms mutually exclusive?	Yes
Arm title	Sub-group I

Arm description:

from 6 to less than 12 years of age

Arm type	Experimental
Investigational medicinal product name	Pitolisant
Investigational medicinal product code	PF2.649
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Single dose of 20 mg

Arm title	Sub-group II

Arm description:

from 12 to less than 18 years of age

Arm type	Experimental
Investigational medicinal product name	Pitolisant
Investigational medicinal product code	PF2.649
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Single dose of 20 mg

Number of subjects in period 1	Sub-group I	Sub-group II
Started	12	13
Completed	12	12
Not completed	0	1
Protocol deviation	-	1

Baseline characteristics

Reporting groups	
Reporting group title	Sub-group I
Reporting group description: from 6 to less than 12 years of age	
Reporting group title	Sub-group II
Reporting group description: from 12 to less than 18 years of age	

Reporting group values	Sub-group I	Sub-group II	Total
Number of subjects	12	13	25
Age categorical Units: Subjects			
from 6 to less than 12 years of age	12	0	12
from 12 to less than 18 years of age	0	13	13
Gender categorical Units: Subjects			
Female	7	6	13
Male	5	7	12

End points

End points reporting groups

Reporting group title	Sub-group I
Reporting group description: from 6 to less than 12 years of age	
Reporting group title	Sub-group II
Reporting group description: from 12 to less than 18 years of age	

Primary: tmax

End point title	tmax[1]
End point description: Determination of the PK parameters of pitolisant in narcoleptic children from 6 to less than 18 years of age	
End point type	Primary
End point timeframe: PK sampling at Pre-dose, 1, 2, 3, 6, and 10 h post-dose	

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: Categorical data were presented using frequency and percentages of patients, while continuous variables were presented using the arithmetic mean, standard deviation (SD), median, minimum (Min), maximum (Max), and number observations.

End point values	Sub-group I	Sub-group II		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	12	12		
Units: hours				
arithmetic mean (full range (min-max))	2.50 (1.00 to 6.00)	2.00 (1.00 to 3.00)		

Statistical analyses

No statistical analyses for this end point

Primary: Cmax

End point title	Cmax[2]
End point description: Determination of the PK parameters of pitolisant in narcoleptic children from 6 to less than 18 years of age	
End point type	Primary
End point timeframe: PK sampling at Pre-dose, 1, 2, 3, 6, and 10 h post-dose	

Notes:

[2] - 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: Categorical data were presented using frequency and percentages of patients, while

continuous variables were presented using the arithmetic mean, standard deviation (SD), median, minimum (Min), maximum (Max), and number observations.

End point values	Sub-group I	Sub-group II		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	12	12		
Units: ng/mL				
arithmetic mean (standard deviation)	55.50 (± 26.47)	36.47 (± 19.61)		

Statistical analyses

No statistical analyses for this end point

Primary: AUC0-t

End point title	AUC0-t[3]

End point description:

Determination of the PK parameters of pitolisant in narcoleptic children from 6 to less than 18 years of age

End point type	Primary

End point timeframe:

PK sampling at Pre-dose, 1, 2, 3, 6, and 10 h post-dose

Notes:

[3] - 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: Categorical data were presented using frequency and percentages of patients, while continuous variables were presented using the arithmetic mean, standard deviation (SD), median, minimum (Min), maximum (Max), and number observations.

End point values	Sub-group I	Sub-group II		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	12	12		
Units: ng.h/mL				
arithmetic mean (standard deviation)	316.06 (± 151.82)	182.19 (± 92.48)		

Statistical analyses

No statistical analyses for this end point

Primary: AUC0-∞

End point title	AUC0-∞[4]

End point description:

Determination of the PK parameters of pitolisant in narcoleptic children from 6 to less than 18 years of age

End point type	Primary

End point timeframe:

PK sampling at Pre-dose, 1, 2, 3, 6, and 10 h post-dose

Notes:

[4] - 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: Categorical data were presented using frequency and percentages of patients, while continuous variables were presented using the arithmetic mean, standard deviation (SD), median, minimum (Min), maximum (Max), and number observations.

End point values	Sub-group I	Sub-group II		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	2	2		
Units: ng.h/mL				
arithmetic mean (standard deviation)	276.50 (± 23.33)	155.50 (± 28.99)		

Statistical analyses

No statistical analyses for this end point

Primary: t1/2

End point title	t1/2[5]

End point description:

Determination of the PK parameters of pitolisant in narcoleptic children from 6 to less than 18 years of age

End point type	Primary

End point timeframe:

PK sampling at Pre-dose, 1, 2, 3, 6, and 10 h post-dose

Notes:

[5] - 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: Categorical data were presented using frequency and percentages of patients, while continuous variables were presented using the arithmetic mean, standard deviation (SD), median, minimum (Min), maximum (Max), and number observations.

End point values	Sub-group I	Sub-group II		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	2	2		
Units: hours				
arithmetic mean (standard deviation)	3.55 (± 0.21)	3.75 (± 0.07)		

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information	
Timeframe for reporting adverse events: Continuous reporting	
Assessment type	Systematic
Dictionary used	
Dictionary name	MedDRA
Dictionary version	16.1
Reporting groups	
Reporting group title	Sub-group I
Reporting group description: from 6 to less than 12 years of age	
Reporting group title	Sub-group II
Reporting group description: from 12 to less than 18 years of age	

Serious adverse events	Sub-group I	Sub-group II	
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 12 (0.00%)	0 / 13 (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: 0 %

Non-serious adverse events	Sub-group I	Sub-group II	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	2 / 12 (16.67%)	2 / 13 (15.38%)	
Nervous system disorders			
Dizziness			
alternative assessment type: Non-systematic			
subjects affected / exposed	1 / 12 (8.33%)	0 / 13 (0.00%)	
occurrences (all)	1	0	
Headache			
alternative assessment type: Non-systematic			
subjects affected / exposed	1 / 12 (8.33%)	2 / 13 (15.38%)	
occurrences (all)	1	2	
Gastrointestinal disorders			

Diarrhoea			
alternative assessment type: Non-systematic			
subjects affected / exposed	1 / 12 (8.33%)	0 / 13 (0.00%)	
occurrences (all)	1	0	
Vomiting			
alternative assessment type: Non-systematic			
subjects affected / exposed	1 / 12 (8.33%)	0 / 13 (0.00%)	
occurrences (all)	0	0	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
27 November 2013	This amendment presented adaptation of inclusion criteria No. 4 (enlargement of the BMI range in favor of low values with lower limit brought from 22 to 18 kg/m² and for Italian site clarification of laboratory tests results) and No. 8 (change of necessary hormonal contraception at screening to a birth control deemed appropriate by the Investigator) as well as minor changes to maintain consistency across sections of the protocol.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported