Clinical trial results:
DOUBLE BLIND RANDOMIZED STUDY TO ASSESS THE EFFICACY OF BF2.649
COMPARED TO PLACEBO IN ADD-ON TO SODIUM OXYBATE
IN THE TREATMENT OF NARCOLEPTIC PATIENTS
WITH RESIDUAL EXCESSIVE DAYTIME SLEEPINESS (EDS) DURING 8 WEEKS.

Summary

EudraCT number	2011-000084-27
Trial protocol	DE ES FI
Global end of trial date	12 August 2014

Results information

Result version number	v1 (current)
This version publication date	21 July 2016
First version publication date	21 July 2016

Trial information

Trial identification

Sponsor protocol code	P10-01/BF2.649

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT01789398
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Bioprojet
Sponsor organisation address	9 rue Rameau , Paris, France, 75005
Public contact	Bioprojet clinical department , Bioprojet, +33 01 47 03 66 33,
Scientific contact	Bioprojet clinical department , Bioprojet, +33 01 47 03 66 33,

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	14 September 2015
Is this the analysis of the primary completion data?	Yes
Primary completion date	12 August 2014
Global end of trial reached?	Yes
Global end of trial date	12 August 2014
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To show relevant beneficial effect of BF2.649 on EDS compared to placebo in add on to sodium oxybate in narcoleptic patients with residual EDS.
To characterize the efficacy of BF2.649 compared to placebo in showing an incremental improvement to the situation achieved by the use of sodium oxybate particularly in terms of a reduction of EDS as measured by the ESS scale. In addition the change in the average number of cataplexy attacks per week was assessed.

Protection of trial subjects:

Tolerability as measured by Treatment Emergent Adverse Events (TEAE), changes in physical examination and vital signs.

Background therapy:

The study treatment is compared to placebo in add-on to sodium oxybate.

Evidence for comparator: -

Actual start date of recruitment	20 September 2012
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: 6
Country: Number of subjects enrolled	Finland: 10
Country: Number of subjects enrolled	France: 4
Country: Number of subjects enrolled	Germany: 12
Country: Number of subjects enrolled	Italy: 16
Worldwide total number of subjects	48
EEA total number of subjects	48

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	0

months)	
Children (2-11 years)	0
Adolescents (12-17 years)	0
Adults (18-64 years)	45
From 65 to 84 years	3
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

Main inclusion criteria:
Diagnosis of narcolepsy (ICSD-2)
Patients complaining of residual EDS
Main non-inclusion criteria:
Untreated sleep apnea disorder

Pre-assignment

Screening details:

Study duration for each patient: 12 weeks (1 week of wash-out + 2 weeks for baseline + 8 weeks under double blind study treatment + 1 week for study treatment wash-out).
Selected : 51 patients
Full Analysis Set (FAS): 48 patients
Intent To Treat set (ITT): 46 patients
Per Protocol Set: 45 patients

Pre-assignment period milestones

Number of subjects started	51[1]
Number of subjects completed	48

Pre-assignment subject non-completion reasons

Reason: Number of subjects	Not met entry criteria: 2
Reason: Number of subjects	Not willing to participate in the study: 1

Notes:

[1] - The number of subjects reported to have started the pre-assignment period are not the same as the worldwide number enrolled in the trial. It is expected that these numbers will be the same.
Justification: 51 subjects were screened. 48 subjects were enrolled.
There was 3 screen failures

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, Carer, Assessor

Blinding implementation details:

Active treatments and placebo were manufactured according to random code list. No distinction was performed regarding the final batch number.

Arms

Are arms mutually exclusive?	Yes
Arm title	Placebo

Arm description:

Placebo

Arm type	Placebo
Investigational medicinal product name	Placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Capsule
Routes of administration	Buccal use

Dosage and administration details:

Placebo

Arm title	BF2.649
Arm description: BF2.649	
Arm type	Experimental
Investigational medicinal product name	BF2.649
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Capsule
Routes of administration	Buccal use

Dosage and administration details:

Uptitration: 5 the 10mg
Stable dose: 10; 20 or 40 mg

Number of subjects in period 1	Placebo	BF2.649
Started	22	26
Completed	20	26
Not completed	2	0
Protocol deviation	1	-
Lack of efficacy	1	-

Baseline characteristics

Reporting groups	
Reporting group title	Placebo
Reporting group description:	
Placebo	
Reporting group title	BF2.649
Reporting group description:	
BF2.649	

Reporting group values	Placebo	BF2.649	Total
Number of subjects	22	26	48
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			
FAS and Total safety population (N=48)			
Units: years			
arithmetic mean	42.7	42.57	
standard deviation	± 12.01	± 12.92	-
Gender categorical			
FAS and Safety population (N=48)			
Units: Subjects			
Female	7	7	14
Male	15	19	34

Subject analysis sets	
Subject analysis set title	Full Analysis Set (FAS)
Subject analysis set type	Full analysis
Subject analysis set description:	
Full Analysis Set (FAS)	
Subject analysis set title	Safety Set
Subject analysis set type	Per protocol
Subject analysis set description:	
Safety Set	
Subject analysis set title	Intent To Treat set (ITT)
Subject analysis set type	Intention-to-treat

Subject analysis set description:

Intent To Treat set (ITT)

Subject analysis set title	Per Protocol Set
Subject analysis set type	Per protocol

Subject analysis set description:

Per Protocol Set

Reporting group values	Full Analysis Set (FAS)	Safety Set	Intent To Treat set (ITT)
Number of subjects	48	48	46
Age categorical Units: Subjects			
In utero Preterm newborn infants (gestational age < 37 wks) Newborns (0-27 days) Infants and toddlers (28 days-23 months) Children (2-11 years) Adolescents (12-17 years) Adults (18-64 years) From 65-84 years 85 years and over			
Age continuous			
FAS and Total safety population (N=48)			
Units: years			
arithmetic mean	42.63	42.63	
standard deviation	± 12.38	± 12.38	±
Gender categorical			
FAS and Safety population (N=48)			
Units: Subjects			
Female	14	14	
Male	34	34	

Reporting group values	Per Protocol Set		
Number of subjects	45		
Age categorical Units: Subjects			
In utero Preterm newborn infants (gestational age < 37 wks) Newborns (0-27 days) Infants and toddlers (28 days-23 months) Children (2-11 years) Adolescents (12-17 years) Adults (18-64 years) From 65-84 years 85 years and over			
Age continuous			
FAS and Total safety population (N=48)			
Units: years			

arithmetic mean standard deviation	±		

Gender categorical			
FAS and Safety population (N=48)			
Units: Subjects			
Female Male			

End points

End points reporting groups

Reporting group title	Placebo
Reporting group description: Placebo	
Reporting group title	BF2.649
Reporting group description: BF2.649	
Subject analysis set title	Full Analysis Set (FAS)
Subject analysis set type	Full analysis
Subject analysis set description: Full Analysis Set (FAS)	
Subject analysis set title	Safety Set
Subject analysis set type	Per protocol
Subject analysis set description: Safety Set	
Subject analysis set title	Intent To Treat set (ITT)
Subject analysis set type	Intention-to-treat
Subject analysis set description: Intent To Treat set (ITT)	
Subject analysis set title	Per Protocol Set
Subject analysis set type	Per protocol
Subject analysis set description: Per Protocol Set	

Primary: Epworth Sleepiness Scale

End point title	Epworth Sleepiness Scale[1]
End point description:	
End point type	Primary

End point timeframe:

Change from baseline.
Baseline (Mean of pre-treatment measures at V1 and V2), End of double-blind phase (Mean of post-treatment measures at V5 and V6).

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: Not specified.

End point values	Placebo	BF2.649	Intent To Treat set (ITT)	
Subject group type	Reporting group	Reporting group	Subject analysis set	
Number of subjects analysed	20	26	46	
Units: N-P ANCOVA				
number (not applicable)	-2.08	-2.6	-2.37	

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information	
Timeframe for reporting adverse events: Throughout the study	
Assessment type	Systematic
Dictionary used	
Dictionary name	MedDRA
Dictionary version	17.1
Reporting groups	
Reporting group title	Placebo
Reporting group description: -	
Reporting group title	BF2.649
Reporting group description: -	

Serious adverse events	Placebo	BF2.649	
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 22 (0.00%)	0 / 26 (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	Placebo	BF2.649	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	2 / 22 (9.09%)	6 / 26 (23.08%)	
Nervous system disorders			
Headache			
subjects affected / exposed	2 / 22 (9.09%)	6 / 26 (23.08%)	
occurrences (all)	3	9	
Dizziness			
subjects affected / exposed	0 / 22 (0.00%)	1 / 26 (3.85%)	
occurrences (all)	0	1	
General disorders and administration site conditions			
Gastrointestinal disorder			
subjects affected / exposed	0 / 22 (0.00%)	1 / 26 (3.85%)	
occurrences (all)	0	1	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
15 December 2011	Adding of 3 weeks of follow-up [1 extra week (at baseline period) & 2 weeks at the end of study to assess the occurrence or not of withdrawal symptoms]. Patient diary recorded and collected during all the study duration.
05 April 2012	Adding of 2 visits: a screening visit V0, three weeks prior to the study treatment randomization for patient under psychotropic medication and a control treatment visit at V7 to ensure patient monitoring. Reducing to one week the withdrawal assessment period and providing placebo to all patients during that period. Eliminating SART assessment. Eliminating BF2.649 plasma dosage. Adding an ECG at visit V4.
10 December 2012	Increase of BF2.649 (Pitolisant) dose up to 40 mg per day.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported