Clinical trial results:
A Multisite Randomized Clinical Trial Evaluating BP1.3656 Versus Placebo For Alcohol Use Disorder Treatment

Summary

EudraCT number	2017-000069-57
Trial protocol	BG NL
Global end of trial date	24 November 2021

Results information

Result version number	v1 (current)
This version publication date	21 August 2024
First version publication date	21 August 2024

Trial information

Trial identification

Sponsor protocol code	P15-01

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT03424824
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	BIOPROJET PHARMA
Sponsor organisation address	9 rue rameau, Paris, France, 75002
Public contact	Bioprojet Clinical Development department, BIOPROJET PHARMA, 33 147036633, contact@bioprojet.com
Scientific contact	Bioprojet Clinical Development department, BIOPROJET PHARMA, 33 147036633, contact@bioprojet.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	10 June 2022
Is this the analysis of the primary completion data?	Yes
Primary completion date	24 November 2021
Global end of trial reached?	Yes
Global end of trial date	24 November 2021
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To assess tolerance and efficacy of 12 weeks BP1.3656 at 30 µg OD vs 60 µg OD vs 90 µg OD versus placebo to reduce alcohol consumption in alcohol dependent patients

Protection of trial subjects:

The study was performed in accordance with the Ethical principles stated in the Declaration of Helsinki, the international recommendation of Good Clinical Practices (ICH-E6) as well as with the local regulation.
Written approval/favourable opinion from the IEC and authorization/non-objection from the regulatory authorities were obtained, as well as until other GCP prerequisites were fulfilled prior to the study being implemented in a clinical site.
The study was monitored by monitors designated by the Sponsor who regularly checked compliance with the protocol and ethical requirements. The monitors compared selected key data collected in the CRF with source data, and verified Drug Accountability and Informed Consent. The study was as well monitored centrally in order to detect any risk. If new safety information became available, this new information was communicated without delay to the patient, the Investigator, the Ethics Committee, and Regulatory Authorities whenever required.
Prior to the initiation of the study at Clinical site level, the study was submitted to the Independent Ethics Committee (IEC) with all the documents required by local regulations and any other documents that were requested. According to local regulations, the appropriate documents were submitted to the relevant competent authority for authorization or non objection.
Voluntary written Informed Consent Form (ICF) was obtained from each patient prior to performing any study related procedures in compliance with the recommendations of the Good Clinical Practices.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	09 January 2018
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	Russian Federation: 64
Country: Number of subjects enrolled	Bulgaria: 138
Country: Number of subjects enrolled	France: 8
Worldwide total number of subjects	210
EEA total number of subjects	146

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)	210
From 65 to 84 years	0
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

From January 2018 to August 2021, a total of 210 patients were randomized (ITT population) at 18 active study centres in 3 countries (France, Bulgaria, Russia).

Pre-assignment

Screening details:

A total of 237 patients were screened. 210 out of the 237 were randomized to receive either the active drug, BP1.3656 (150 patients), or the placebo (60 patients).

Pre-assignment period milestones

Number of subjects started	210
Number of subjects completed	209

Pre-assignment subject non-completion reasons

Reason: Number of subjects	Physician decision: 1

Period 1

Period 1 title	Double-blind 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:

The following controls were employed to maintain the double-blind status:
– The placebo tablets were identical in appearance to the BP1.3656 tablets
– Treatment allocation was done through IWRS
– Patients, Investigator and sponsor (and their representatives) remained blinded to the treatment randomization code.
During each interim analysis the independent third party statistician analyzed the data and decided about continuation or not. He was the only person allowed to receive the rando list

Arms

Are arms mutually exclusive?	Yes
Arm title	BP1.3656 30 µg (treatment arm)

Arm description:

tablets of 30 µg : per os 1 tablet / day during 12 weeks

Arm type	Experimental
Investigational medicinal product name	BP1.3656
Investigational medicinal product code	BP1.3656
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

30 µg 1 tablet per os / day

Arm title	BP1.3656 60 µg (treatment arm)

Arm description:

tablets of 60 µg : per os 1 tablet / day during 12 weeks

Arm type	Experimental

Investigational medicinal product name	BP1.3656
Investigational medicinal product code	BP1.3656
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:
60 µg 1 tablet per os / day

Arm title	Placebo arm

Arm description:
tablets of placebo : per os 1 tablet / day during 12 weeks

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:
1 tablet per os / day

Arm title	BP1.3656 90 µg (treatment arm)

Arm description:
tablets of 90 µg : per os 1 tablet / day during 12 weeks

Arm type	Experimental
Investigational medicinal product name	BP1.3656
Investigational medicinal product code	BP1.3656
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:
90 µg 1 tablet per os / day

Number of subjects in period 1[1]	BP1.3656 30 µg (treatment arm)	BP1.3656 60 µg (treatment arm)	Placebo arm
Started	40	45	60
Completed	32	39	57
Not completed	8	6	3
Physician decision	2	1	1
Consent withdrawn by subject	3	3	2
Adverse event, non-fatal	1	-	-
Lost to follow-up	1	-	-
Protocol deviation	1	2	-

Number of subjects in period 1[1]	BP1.3656 90 µg (treatment arm)
Started	64
Completed	62
Not completed	2

Physician decision	-
Consent withdrawn by subject	2
Adverse event, non-fatal	-
Lost to follow-up	-
Protocol deviation	-

Notes:

[1] - The number of subjects reported to be in the baseline period are not the same as the worldwide number enrolled in the trial. It is expected that these numbers will be the same.
Justification: 209 patients out of the 210 randomized patients received at least one dose of study drug and have been reported with a baseline value and at least one post-baseline value to compute the primary endpoint (FAS population).

Period 2

Period 2 title	Single-blind period
Is this the baseline period?	No
Allocation method	Randomised - controlled
Blinding used	Single blind
Roles blinded	Subject

Arms

Arm title	Placebo arm

Arm description:

tablets of placebo : per os 1 tablet / day during 1 week

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:

1 tablet per os / day

Number of subjects in period 2	Placebo arm
Started	190
Completed	189
Not completed	1
Consent withdrawn by subject	1

Baseline characteristics

Reporting groups	
Reporting group title	BP1.3656 30 µg (treatment arm)
Reporting group description: tablets of 30 µg : per os 1 tablet / day during 12 weeks	
Reporting group title	BP1.3656 60 µg (treatment arm)
Reporting group description: tablets of 60 µg : per os 1 tablet / day during 12 weeks	
Reporting group title	Placebo arm
Reporting group description: tablets of placebo : per os 1 tablet / day during 12 weeks	
Reporting group title	BP1.3656 90 µg (treatment arm)
Reporting group description: tablets of 90 µg : per os 1 tablet / day during 12 weeks	

Reporting group values	BP1.3656 30 µg (treatment arm)	BP1.3656 60 µg (treatment arm)	Placebo arm
Number of subjects	40	45	60
Age categorical Units: Subjects			
Adults (18-34 years)	5	6	10
Adults (35-49 years)	26	25	26
Adults (50-64 years)	9	14	24
Adults >= 65 years	0	0	0
Age continuous Units: years			
arithmetic mean	42.9	44.7	45.7
standard deviation	± 8.5	± 9.2	± 9.8
Gender categorical Units: Subjects			
Female	12	15	21
Male	28	30	39
BMI in classes Units: Subjects			
<25 kg/m2	22	22	33
25 to <30 kg/m2	13	16	24
>=30 kg/m2	5	7	3

Reporting group values	BP1.3656 90 µg (treatment arm)	Total	
Number of subjects	64	209	
Age categorical Units: Subjects			
Adults (18-34 years)	12	33	
Adults (35-49 years)	34	111	
Adults (50-64 years)	18	65	
Adults >= 65 years	0	0	

Age continuous Units: years			
arithmetic mean	44.6		
standard deviation	± 10.5	-	
Gender categorical Units: Subjects			
Female	11	59	
Male	53	150	
BMI in classes Units: Subjects			
<25 kg/m2	33	110	
25 to <30 kg/m2	23	76	
>=30 kg/m2	8	23	

Subject analysis sets

Subject analysis set title	Full Analysis Set
Subject analysis set type	Full analysis

Subject analysis set description:

Subset of the ITT population having taken at least one dose of drug and having been reported with a baseline value and at least one post-baseline value to compute the primary endpoint.

Reporting group values	Full Analysis Set		
Number of subjects	209		
Age categorical Units: Subjects			
Adults (18-34 years)	33		
Adults (35-49 years)	111		
Adults (50-64 years)	65		
Adults >= 65 years	0		
Age continuous Units: years			
arithmetic mean	44.6		
standard deviation	± 9.6		
Gender categorical Units: Subjects			
Female	59		
Male	150		
BMI in classes Units: Subjects			
<25 kg/m2	110		
25 to <30 kg/m2	76		
>=30 kg/m2	23		

End points

End points reporting groups

Reporting group title	BP1.3656 30 µg (treatment arm)
Reporting group description: tablets of 30 µg : per os 1 tablet / day during 12 weeks	
Reporting group title	BP1.3656 60 µg (treatment arm)
Reporting group description: tablets of 60 µg : per os 1 tablet / day during 12 weeks	
Reporting group title	Placebo arm
Reporting group description: tablets of placebo : per os 1 tablet / day during 12 weeks	
Reporting group title	BP1.3656 90 µg (treatment arm)
Reporting group description: tablets of 90 µg : per os 1 tablet / day during 12 weeks	
Reporting group title	Placebo arm
Reporting group description: tablets of placebo : per os 1 tablet / day during 1 week	
Subject analysis set title	Full Analysis Set
Subject analysis set type	Full analysis
Subject analysis set description: Subset of the ITT population having taken at least one dose of drug and having been reported with a baseline value and at least one post-baseline value to compute the primary endpoint.	

Primary: Decrease in nHDD (number of monthly heavy drinking days)

End point title	Decrease in nHDD (number of monthly heavy drinking days)
End point description: The study primary endpoint aimed to assess the decrease in nHDDs (≥ 60 g/day in men and ≥ 40 g/day in women) from baseline to end of the double-blind randomised study treatment period (12-week).	
End point type	Primary
End point timeframe: nHDD from baseline to final time (end of Double-Blind period)	

End point values	BP1.3656 30 µg (treatment arm)	BP1.3656 60 µg (treatment arm)	Placebo arm	BP1.3656 90 µg (treatment arm)
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	40	45	60	64
Units: nHDD at final time				
arithmetic mean (standard deviation)	10.96 (± 10.10)	8.57 (± 8.08)	10.23 (± 9.49)	12.27 (± 10.22)

Statistical analyses

Statistical analysis title	Adjusted mean difference
Statistical analysis description: a stepdown strategy is used to assess the significance of doses: The highest dose is tested first, and the	

significance of the lower dosages is only considered conditionally to the significant effect of the previous dose

Comparison groups	BP1.3656 90 µg (treatment arm) v Placebo arm
Number of subjects included in analysis	124
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001
Method	ANCOVA
Parameter estimate	adjusted mean difference
Point estimate	0.37
Confidence interval	
level	90 %
sides	2-sided
lower limit	-2.01
upper limit	2.74
Variability estimate	Standard error of the mean
Dispersion value	1.44

Adverse events

Adverse events information

Timeframe for reporting adverse events:

AE assessment will be performed throughout the trial once the patient has signed informed consent. During 30 days after patient study discontinuation any relevant AE should be reported by the investigator.

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	24.1

Reporting groups

Reporting group title	BP1.3656 30 µg (treatment arm)
Reporting group description:	
tablets of 30 µg per os 1 tablet / day	
Reporting group title	BP1.3656 60 µg (treatment arm)
Reporting group description:	
tablets of 60 µg per os 1 tablet / day	
Reporting group title	Placebo arm
Reporting group description:	
tablets of placebo per os 1 tablet / day	
Reporting group title	BP1.3656 90 µg (treatment arm)
Reporting group description:	
Tablets of 90 µg per os 1 tablet / day	

Serious adverse events	BP1.3656 30 µg (treatment arm)	BP1.3656 60 µg (treatment arm)	Placebo arm
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 43 (0.00%)	0 / 43 (0.00%)	2 / 60 (3.33%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events	0	0	0
Injury, poisoning and procedural complications			
Facial bones fracture			
subjects affected / exposed	0 / 43 (0.00%)	0 / 43 (0.00%)	0 / 60 (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
Foot fracture			
subjects affected / exposed	0 / 43 (0.00%)	0 / 43 (0.00%)	1 / 60 (1.67%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hand fracture			

subjects affected / exposed	0 / 43 (0.00%)	0 / 43 (0.00%)	0 / 60 (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
Gastrointestinal disorders			
Gastric ulcer			
subjects affected / exposed	0 / 43 (0.00%)	0 / 43 (0.00%)	1 / 60 (1.67%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Serious adverse events	BP1.3656 90 µg (treatment arm)		
Total subjects affected by serious adverse events			
subjects affected / exposed	1 / 64 (1.56%)		
number of deaths (all causes)	0		
number of deaths resulting from adverse events	0		
Injury, poisoning and procedural complications			
Facial bones fracture			
subjects affected / exposed	1 / 64 (1.56%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Foot fracture			
subjects affected / exposed	0 / 64 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Hand fracture			
subjects affected / exposed	1 / 64 (1.56%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Gastrointestinal disorders			
Gastric ulcer			
subjects affected / exposed	0 / 64 (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	BP1.3656 30 µg (treatment arm)	BP1.3656 60 µg (treatment arm)	Placebo arm
Total subjects affected by non-serious adverse events			
subjects affected / exposed	0 / 43 (0.00%)	9 / 43 (20.93%)	8 / 60 (13.33%)
Nervous system disorders			
Headache			
subjects affected / exposed	0 / 43 (0.00%)	3 / 43 (6.98%)	2 / 60 (3.33%)
occurrences (all)	0	3	2
Gastrointestinal disorders			
Nausea			
subjects affected / exposed	0 / 43 (0.00%)	2 / 43 (4.65%)	3 / 60 (5.00%)
occurrences (all)	0	2	3
Psychiatric disorders			
Insomnia			
subjects affected / exposed	0 / 43 (0.00%)	4 / 43 (9.30%)	3 / 60 (5.00%)
occurrences (all)	0	4	3
Abnormal dreams			
subjects affected / exposed	0 / 43 (0.00%)	0 / 43 (0.00%)	0 / 60 (0.00%)
occurrences (all)	0	0	0
Dysphoria			
subjects affected / exposed	0 / 43 (0.00%)	0 / 43 (0.00%)	0 / 60 (0.00%)
occurrences (all)	0	0	0

Non-serious adverse events	BP1.3656 90 µg (treatment arm)		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	19 / 64 (29.69%)		
Nervous system disorders			
Headache			
subjects affected / exposed	1 / 64 (1.56%)		
occurrences (all)	1		
Gastrointestinal disorders			
Nausea			
subjects affected / exposed	5 / 64 (7.81%)		
occurrences (all)	5		
Psychiatric disorders			
Insomnia			
subjects affected / exposed	5 / 64 (7.81%)		
occurrences (all)	6		

Abnormal dreams subjects affected / exposed occurrences (all)	4 / 64 (6.25%) 4		
Dysphoria subjects affected / exposed occurrences (all)	4 / 64 (6.25%) 4		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
28 September 2017	This amendment changed the protocol initially approved on the following topics: - Suppression of the Netherlands clinical investigation centre - Change of Coordinator Investigator - Correction of the randomization ratio - Inclusion of additional exams at screening visit - Modification of exams time-points from visit 0 (baseline) to the screening visit - Inclusion of additional liver function tests at each visit from screening visit to visit 6 (end of double-blind period) - Addition of BP1.3656 pharmacokinetic (PK) assessment - Modification of Time Line Follow Back presentation - Modification of M.I.N .I utilization in the study - Modification of AUDIT frequency utilization - Modification of PSQI frequency utilization - Modification of SF-12 frequency utilization - Addition of information related to preclinical and clinical data of BP1.3656 compound - Correction of typo errors
11 June 2018	Following the participation of a new country in the study and the possibility for patients to not be involved in the pharmacokinetics dosing, we revised the protocol version 2.0 dated September 28th 2017. The version 3.0 was created on this occasion. The modifications introduced in the version 3.0 allowed us to update protocol according new versions of Investigator's Brochure (version 7.0, May 30th 2018) and Investigational Medicinal Product Dossier (version 5.0, May 23rd 2018) and to add clarifications of some processes.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported