A multisite randomized clinical trial evaluating BP1.3656 vs placebo for alcohol use disorder treatment.

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Ethical review	Approved WMO
Status	Will not start
Health condition type	Psychiatric disorders NEC
Study type	Interventional

Summary

ID

NL-OMON45553

Source
ToetsingOnline

Brief title
BP15-01

Condition

- Psychiatric disorders NEC

Synonym
alcohol use disorder, alcoholism

Research involving
Human

Sponsors and support

Primary sponsor: Bioprojet Pharma
Source(s) of monetary or material Support: Bioprojet Pharma

Intervention

Keyword: addiction, alcohol use disorder, BP1.3656, reduce alcohol consumption

Outcome measures

Primary outcome

The primary outcome of the study is the decrease in number of monthly heavy drinking days (HDD: * 60 g/day in men and * 40 g/day) form baseline to end of the double blind randomization phase.

Secondary outcome

The secondary parameters in this study are:

* Total daily alcohol consumption (TAC: total alcohol consumption) from baseline to end of treatment;
* Percent of patients without heavy drinking days during the 12 weeks double-blind, randomized treatment (continuous controlled drinking= CCD);
* Percent of Abstinent Days during the 12 weeks double-blind, randomized treatment (PAD: percent of abstinent days);
* Continuous Abstinence Duration during the 12 weeks double-blind, randomized treatment (CAD: continuous abstinence duration);
* 4-week point prevalence abstinence at end of treatment;
* Improvement in alcohol biomarkers (e.g. ALAT, ASAT, % CDT) during the 12 weeks double-blind, randomized treatment;
* Craving (Obsessive Compulsive Drinking Scale) during the 12 weeks double-blind, randomized treatment;
* Beck Depression Inventory (BDI) during the 12 weeks double-blind, randomized

treatment;

* Treatment retention during the 12 weeks double-blind, randomized treatment;

* Safety will be assessed by evaluation of treatment emergent adverse events (TEAE), physical examinations, clinical laboratory tests (blood chemistry, hematology and urinalysis), subsequent end of treatment potential withdrawal, evaluation scales and physical examination, measurement of heart rat, blood pressure and body weight at each study visit. If at ECG Fridericia's corrected QT-interval *500 ms, or if difference to baseline is * 60ms, it will be required to check ECG by second measurement.

Study description

Background summary

Alcohol use disorder remains a highly stigmatized, under-diagnosed and under-treated disease. The current approved medications show inconsistent success in reducing relapse or drinking. Because alcohol dependence is such a common and devastating disease, there is an ongoing search for new treatments that could be more effective and better tolerated. Therefore, the development and testing of medications that target novel brain systems involved in alcohol dependence is of acute interest to patients, clinicians and researchers.
Studies in rats suggest that the histamine H3 receptor inverse agonist BP1.3656 significantly decreases alcohol self-administration in alcohol dependent rats. Moreover, BP1.3656 decreases reinstatement in alcohol dependent rats.

Study objective

The primary objective of this study is to assess tolerance and efficacy of 12 weeks BP1.3656 (30 µg or 60 µg OD versus placebo) to reduce alcohol consumption in alcohol dependent patients.

Study design

The study starts as a multi-center, randomized, double-blind, placebo-controlled trial with 12 weeks BP1.3656 (30µg of 60µg, OD) treatment versus placebo to reduce alcohol consumption in patients with moderate to

severe DSM-5 alcohol use disorder. This randomized phase ends with a one week single-blind placebo treatment. Total duration of the study is maximal 15 weeks:

* 2 weeks of screening, during which a screening and baseline visit are performed;
* 12 weeks of double blind treatment phase, during which 5 visits are performed;
* 1 week of single blind treatment phase with placebo, during which one phone contact is scheduled, concluded by a site visit.

Intervention

Beside treatment with the study medication (either placebo or active medication BP1.3656 30 µg or 60 µg once daily, per os), patients have to follow cognitive behavioral therapy (CBT) during the first 12 weeks of the study. Furthermore, several neuropsychiatric questionnaires have to be completed both at start of the study and during the study. It concerns the MINI, CIWA-Ar and AASE at the start and the TLFB (as a patient diary), SF-12 Healt Survey, BDI, AUDIT, OCDS and PSQI both at start and during the study.

Blood and urine samples will be collected to assess hematology, clinical chemistry and serology (at screening and during final visit of double blind phase) to assess alcohol biomarkers and liver function (at baseline, V2, 4 and 6).
Urine will be collected to measure ethyl glucuronide (EtG), an alcohol metabolite (at baseline, V2, 4 and 6). Standard urinalysis will be done at baseline, as well as a urine drug screen. At each visit, an alcohol breath test will be done.

Study burden and risks

Both psychosocial support approaches and pharmacological agents are current treatments for alcohol use disorder. Pharmacological treatment of patients with an alcohol use disorder is needed to alleviate withdrawal symptoms, reduce craving and prevent relapses. Several drugs are approved for the treatment of alcohol use disorder, these compounds are all directed at full abstinence and they all have side effects. Patients, while recognizing their alcohol problem, are unable or unwilling to completely stop consuming alcohol, leading to an inevitable deterioration over time of their psycho-physical state and social relationships. Reduction may be an opportunity to prepare the individual for achieving complete abstinence (the ultimate goal). Reduction of alcohol consumption could be achieved by using BP1.3656, taken once daily.

Reported side effects for BP1.3656 are insomnia, local reaction, rhinitis, headache, pollakiuria (abnormally frequent urination), asthenia/somnolence, respiratory disorders, disturbance in attention, gastroenteritis (inflammation of bowel), hot flush, musculoskeletal stiffness, nasopharyngitis, nausea,

tonsillitis, pain in extremity and sweats. These effects were all transient and all resolved spontaneously when treatment was stopped.

The following study procedures will be performed:
* Physical examination at baseline and visit 6

* Vital signs at each site visit

* Recording of ECG at baseline, visit 2, 4 and 6.
Risks related to recording of ECGs can be redness of skin caused by sticky pads.

* Completion of neuropsychiatric questionnaires. It concerns the MINI, CIWA-AR and AASE at start of the study and the TLFB (as a patient diary), SF-12 Health Survey (QoL), BDI, AUDIT, OCDS and PSQI at start and during the study. The completion of questionnaires can result in psychological discomfort.

* Collection of blood to assess clinical chemistry, hematology and serology at baseline and visit 6 (liver functions will be more frequently assessed). Risks related to blood collection can be: fainting, redness, bruising, bleeding or infection at puncture site.

Contacts

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Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Adults (18-64 years)
Elderly (65 years and older)

Inclusion criteria

1. Male of female with moderate or severe DSM-5 alcohol use disorder (based on the alcohol use disorders section of the MINI plus);
2. Ages 18-65;
3. Low to moderate alcohol withdrawal symptoms: CIWA-Ar scale < 10 at baseline assessment;
4. Normal weight: 18 kg/m2 * 35 kg/m2;
5. Excessive alcohol use: number of heavy drinking days (* 60g/day in men and * 40 g/day in women) * 15 during 30 days prior to screening and * 7 during the 2 weeks between screening and baseline;
6. Treatment-seeking, treatment goal: reduced drinking or abstinence;
7. If fertile, both males and females must agree to use effective birth control, agree to continue this method for the duration of the study up until 21 days after study completion and be negative to serum pregnancy test performs at the screening visit. Females should not be breastfeeding.;
8. Adequate social support according to the investigator to comply with the study requirements described in the protocol (e.g. transportation to and from the trial site, self-rating scales, drug compliance, scheduled visits, etc.);
9. Voluntarily expressed willingness to participate in the study, understanding protocol procedues and having signed and dated an informed consent prior to the start of the protocol required procedures while not intoxicated (BAC < 0.05);
10. Willingness to receive psychosocial support.

Exclusion criteria

1. History of delirium tremens, epilepsy, or withdrawal seizures;
2. Clinical depression or suicidality; Beck Depression Inventory (BDI) * 16 and suicidality (item G * 0);
3. Recent illicit drug use, i.e. cannabis, cocaine, amphetamine or opiods;
4. Clinically significant cardiovascular, hematologic, severe hepatic impairment or (FLTs > 3 ULN), renal (stage 2 and 3 according to international classification of renal kidney disease), neurological, endocrinological abnormalities or abnormal clinical laboratory results (in most cases > 3 ULN)
5. History of serious head trauma or injury causing loss of consciousness that lasted more than 3 minutes;
6. HIV positive; HCV postive; HBsAg postive;

7. History of psychosis, or current severe psychiatric disorder, e.g. schizophrenia, bipolar disorder, severe depression or organic brain syndrome unrelated to alcohol abuse;
8. Physical dependence on sedatives or hypnotics that requires pharmacologically supported detox;
9. Receiving ongoing alcohol use disorder medication (e.g. Baclofen);
10. Other active clinically significant illness, which could interfere with the study conduct or counter-indicate the study treatments or place the patient at risk during the trial or compromise the study participation, such as Parkinson*s disease;
11. Known history of syncope, arrhytmia, myocardial infarction or any known significant ECG abnormality;
12. Known hypersensitivity to the tested treatment including active substance and excipients;
13. Participation in clinical trials and receipt of investigational drug(s) during previous 60 days, except as explicitly approve by the principal investigator;
14. Insufficient medical insurance according to local regulations;
15. Pregnant woman or a pregnancy detected with a positive serum pregnancy test performed at the screening visit or lactating women;
16. Male subject who want to conceive a child during the duration of the study up until 21 days after study completion.

Study design

Design

Study phase:	2
Study type:	Interventional
Intervention model:	Parallel
Allocation:	Randomized controlled trial
Masking:	Double blinded (masking used)
Control:	Placebo
Primary purpose:	Treatment

Recruitment

NL

Recruitment status:	Will not start
Enrollment:	15
Type:	Anticipated

Medical products/devices used

Product type:	Medicine
Brand name:	BP1.3656
Generic name:	histamine H3 receptor antagonist / inverse agonist

Ethics review

Approved WMO Date:	13-06-2017
Application type:	First submission
Review commission:	METC Amsterdam UMC
Approved WMO Date:	12-07-2017
Application type:	First submission
Review commission:	METC Amsterdam UMC

Study registrations

Followed up by the following (possibly more current) registration

No registrations found.

Other (possibly less up-to-date) registrations in this register

No registrations found.

In other registers

Register	ID
EudraCT	EUCTR2017-000069-57-NL
CCMO	NL61245.018.17