A Phase 1, Single-Center, Double-Blind, Placebo Controlled Study in Healthy Subjects to Assess the Safety, Tolerability, Pharmacokinetics, and Pharmacodynamics of Intravenous ABP-700 after a Single Ascending Bolus Dose

No registrations found.

Ethical review	Positive opinion
Status	Other
Health condition type	-
Study type	Interventional

Summary

ID

NL-OMON27439

Source
Nationaal Trial Register

Health condition

Preliminary safety study, first in human

Sponsors and support

Primary sponsor: Annovation Biopharma
(University Medical Center Groningen)
Source(s) of monetary or material Support: Annovation Biopharma

Intervention

Outcome measures

Primary outcome

1. Safety and Tolerability as assessed through: AEs, physical examination, safety laboratory tests (serum chemistry, hematology, arterial blood gas, urinalysis, and coagulation), vital signs (blood pressure [including mean arterial pressure], heart rate, and body temperature), ECGs (12-lead ECG and 3-lead ECG), infusion site reaction monitoring, and respiratory function (respiratory pattern and occurrence of apnea). Timepoints: Day 1, 2 and 5.
2. Evaluation of cortisol levels before dosing and after synthetic ACTH administration will be evaluated to assess the effect of ABP-700 on adrenal function. Timepoints: Day 1

Secondary outcome

1. PK properties of ABP-700 will be evaluated by assessing PK parameters from plasma concentrations from venous and arterial samples

2. The PD profile of ABP-700 will be evaluated using onset of sedation/anesthesia, level of sedation/anesthesia over time, emergence from sedation/anesthesia, and duration of sedation/anesthesia as markers.

Study description

Background summary

Background: The highly dynamic nature of surgical and procedural intervention, as well as the short duration of these procedures, demands the development of potent yet rapidly reversible anesthetic agents. Ideally, the pharmacokinetics (PK) and pharmacodynamics (PD) of these anesthetic agents should be better matched to both the procedures being performed. ABP-700 is a newly developed, potent, positive allosteric modulator of the GABAA receptor. Its mechanism of action is via potentiation of GABAA receptor activation produces its sedative and anesthetic effects. ABP-700 contains an ester bond that was precisely designed to undergo rapid hydrolysis in the body by nonspecific tissue esterases that produce an inactive carboxylic acid metabolite.

Purpose: To assess the safety and tolerability of single ascending IV bolus doses of ABP-700

Design: This is a Single-Center, Double-Blind, Placebo Controlled Study in Healthy Subjects to Assess the Safety, Tolerability, Pharmacokinetics, and Pharmacodynamics of Intravenous ABP-700 after a Single Ascending Bolus Dose. Safety and tolerability will be assessed through monitoring of AEs, physical examination, safety laboratory tests (serum chemistry, hematology, arterial blood gas, urinalysis, and coagulation), vital signs (blood pressure [including mean arterial pressure], heart rate, and body temperature), ECGs (12-lead ECG and 3-lead ECG), infusion site reaction monitoring, and respiratory function (respiratory

pattern and occurrence of apnea). Evaluation of cortisol levels before dosing and after synthetic ACTH administration will be evaluated to assess the effect of ABP-700 on adrenal function. The PK properties of ABP-700 and it's primary metabolite will also be evaluated.

Study objective

Assess the safety and tolerability of single ascending IV bolus doses of ABP-700

Study design

Day 1, 2 and 5

Intervention

ABP-700 or Placebo

Contacts

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Eligibility criteria

Inclusion criteria

1. Healthy, adult, men and women, 18-45 years of age, inclusive.

2. Continuous non-smoker who has not used nicotine-containing products for at least 6 months prior to the first dose.

3. Body Mass Index (BMI) ≥ 17.5 and ≤ 30.0 kg/m2, inclusive, and a total body weight >50 kg, at screening and check-in.

4. Medically healthy with no clinically significant laboratory findings, vital signs or ECGs, as deemed by the PI.

5. Women must be of non-childbearing potential, i.e., must have undergone one of the following sterilization procedures at least 6 months prior to the first dose:

a. hysteroscopic sterilization;

b. bilateral tubal ligation or bilateral salpingectomy;

c. hysterectomy;

d. bilateral oophorectomy;

or be postmenopausal with amenorrhea for at least 1 year prior to the first dose and FSH serum levels consistent with postmenopausal status.

6. Non-vasectomized men must agree to use a condom with spermicide or abstain from sexual intercourse during the study until 90 days beyond the last dose of study medication. Men who have been vasectomized less than 4 months prior to study start must follow the same restrictions as non-vasectomized men.

7. Men must agree not to donate sperm from the first dose until 90 days after dosing.

8. Obtain a score of I or II using the Modified Mallampati Scoring.

9. Understand the study procedures in the informed consent form(s) (ICF(s)), and be willing and able to comply with the protocol.

10. Agree not to make any public disclosure of personal medical data related to the study or other information related to the study, including posting on any website or social media site (e.g., Facebook, Twitter, etc.).

Exclusion criteria

1. History or presence of significant cardiovascular disease, or cardiovascular disease risk factors, hyperlipidemia, coronary artery disease, or any known genetic pre disposition to cardiac arrhythmia (including long QT syndrome.)

2. History or presence of significant pulmonary, hepatic, renal, hematological, gastrointestinal, endocrine, immunologic, dermatologic, neurological (inclusive of any seizure disorder), or psychiatric disease.

3. History of any illness that, in the opinion of the PI, might confound the results of the study or pose an additional risk to the subject by their participation in the study.

4. Surgery within the past 90 days prior to dosing judged by the PI to be clinically relevant.

5. History of febrile illness within 5 days prior to dosing.

6. History or presence of alcoholism, drug abuse or illicit drug use within the past 2 years.

7. History of regular alcohol consumption exceeding 7 drinks/week for women or 14 drinks/week for men (1 drink = 5 ounces (150 mL) of wine or 12 ounces (360 mL) of beer or 1.5 ounces (45 mL) of hard liquor) within 6 months of screening.

8. Hypersensitivity or idiosyncratic reaction to components of ABP-700 or placebo (meglumine and/or sulfobutylether-beta-cyclodextrin) egg, egg products, soybeans, soy, or to compounds related to the study medications.

9. History or presence of adrenal insufficiency as defined by serum cortisol level <6 mcg/dL at screening (as defined by Debono et al., [7]).

10. Women who are pregnant or lactating.

11. FSH levels less than 30 IU/L.

12. Positive results for the urine drug screen and alcohol breath test at screening or check-in (Day -1).

13. Positive urine cotinine at screening.

14. Positive results at screening for human immunodeficiency virus (HIV), hepatitis B surface antigen (HBsAg), or hepatitis C antibodies (HCV).

15. Single 12-lead ECG demonstrating QTcF interval >450 msec at screening and Day -1.

16. Unable to refrain from or anticipates the use of any drug, including prescription and non-prescription medications, herbal remedies, or vitamin supplements beginning approximately 14 days prior to dosing (with exception of lidocaine which will be used for arterial line placement) and throughout the study. Ibuprofen (1.2 g per 24 hour period) may be permitted during the study at the PI’s discretion.

17. Use of any drugs known to be, hormonal replacement therapy, inducers of cytochrome P450 (CYP) enzymes, including St. John’s Wort, within 28 days prior to the first dose of study medication (with exception of lidocaine which will be used for arterial line placement). Appropriate sources will be consulted by the PI to confirm lack of PK/PD interaction with study medication(s).

18. Have been on a diet incompatible with the on-study diet, in the opinion of the PI, within

the 28 days prior to the first dose of study medication(s), and throughout the study.

19. Blood donation or significant blood loss within 90 days prior to dosing.

20. Plasma donation within 7 days prior to dosing.

21. Participation in another clinical trial within 90 days prior to dosing. The 90-day window will be derived from the date of the last study procedure (such as last blood collection or dosing) in the previous study to Day 1 of the current study.

Study design

Design

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

Recruitment

NL

Recruitment status:	Other
Start date (anticipated):	22-04-2014
Enrollment:	60
Type:	Unknown

Ethics review

Positive opinion

Date:	29-04-2014
Application type:	First submission

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
NTR-new	NL4421
NTR-old	NTR4545
Other	130574 CS0214 : ANVN-01

Study results

Summary results
None