A Phase 1, Single-Center, Open-Label, Dose Optimization Study of ABP-700 in Healthy, Adult Subjects

No registrations found.

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

Summary

ID

NL-OMON25663

Source
Nationaal Trial Register

Health condition

Preliminary safety study

Sponsors and support

Primary sponsor: Annovation Biopharma, a wholly owned subsidiary of The Medicines Company
Source(s) of monetary or material Support: The Medicines Company

Intervention

Outcome measures

Primary outcome

Safety and Tolerability as assessed through: AEs, physical examination, safety laboratory tests (serum chemistry, hematology, urinalysis, and coagulation), vital signs (blood 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).

Pharmacodynamic driven dose optimization as assessed by MOAA/S and BIS.

Secondary outcome

To characterize the pharmacokinetics (PK) of ABP-700.

To assess the pharmacodynamics (PD) of ABP-700.

To investigate dose response and PK/PD relationships

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 bolus doses of ABP-700 in the presence of pre-medications commonly used in the monitored anesthesia care (MAC) setting. To optimize bolus dosing of ABP-700 in combination with pre-medications

Design: This study is an open-label, parallel, bolus dose study designed to assess the Safety, Tolerability, Pharmacokinetics, and Pharmacodynamics of ABP-700 in combination with pre-medications commonly used in the anesthesia setting. 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, 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). The PK properties of ABP-700 will also be evaluated.

Study objective

This is a normal healthy volunteer study designed to assess the safety and tolerability of bolus doses of ABP-700 in the presence of pre-medications commonly used in the monitored anesthesia care (MAC) setting.

Study design

Screening (-28 days), Check-in (-1 day), Study Days (1-2), Follow-up (day 4-6)

Intervention

ABP-700

Contacts

Public
Hazneplein 1
M.M.R.F. Struys
Groningen 9713 EZ
The Netherlands
Scientific
Hazneplein 1
M.M.R.F. Struys
Groningen 9713 EZ
The Netherlands

Eligibility criteria

Inclusion criteria

1. Healthy, adult, men and women, 18-55 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 out of range laboratory findings, vital signs or ECGs, as deemed by the PI.

5. Women 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 (greater than 30 IU/L).

6. Women of child bearing potential must agree to use one or more of the following forms of contraception from the time of signing the informed consent form through 90 days following the last administration of study medication: hormonal (i.e., oral, transdermal, implant, or injection); double barrier (i.e., condom, diaphragm with spermicide); intrauterine device (IUD); vasectomized partner (six months minimum); or abstinence.

7. 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.

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

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

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

11. 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 (meglumine and/or sulfobutylether-beta-cyclodextrin), fentanyl, sufentanil, remifentanil, midazolam, egg, egg products, soybeans, soy, or to compounds related to the study medications.

9. Women who are pregnant or lactating.

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

11. Positive urine cotinine at screening.

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

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

14. 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 and throughout the study, with the exception of oral contraceptives. Ibuprofen (1.2 g per 24 hour period) may be permitted during the study at the PI’s discretion.

15. 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. Appropriate sources will be consulted by the PI to confirm lack of PK/PD interaction with study medication(s).

16. Have a diet incompatible with the clinic diet, in the opinion of the PI, within the 28 days prior to the first dose of study medication(s), and throughout the study.

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

18. Plasma donation within 7 days prior to dosing.

19. 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.

20. Subjects who previously received ABP-700.

Study design

Design

Study type:	Interventional
Intervention model:	Parallel
Allocation:	Non-randomized controlled trial
Masking:	Open (masking not used)
Control:	N/A , unknown

Recruitment

NL

Recruitment status:	Recruiting
Start date (anticipated):	19-05-2015
Enrollment:	80
Type:	Anticipated

Ethics review

Positive opinion

Date:	30-04-2015
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	NL5027
NTR-old	NTR5173
Other	: 150098-CS0240

Study results