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

Published: 20-10-2015
Last updated: 19-04-2024

Primary objectives:• To assess the safety and tolerability of induction doses of ABP-700 • To optimize induction dosing of ABP-700 in combination with pre-medicationsSecondary objectives:• To characterize the pharmacokinetics (PK) of ABP-700 and its...

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| **Ethical review** | Approved WMO |
| **Status** | Recruitment stopped |
| **Health condition type** | Other condition |
| **Study type** | Interventional |

## Summary

### ID

NL-OMON43769

**Source**
ToetsingOnline

**Brief title**
ANVN-01-05 (CS0249)

### Condition

- Other condition

**Synonym**
Not applicable

**Health condition**

anesthesia

**Research involving**
Human

## Sponsors and support

**Primary sponsor:** The Medicines Company
**Source(s) of monetary or material Support:** The Medicines Company

## Intervention

**Keyword:** Open label, PD, PK, Safety

## Outcome measures

### Primary outcome

Safety and Tolerability

### Secondary outcome

PK and PD

# Study description

### Background summary

ABP-700 is an intravenous (IV) sedative-hypnotic agent currently in Phase I clinical development and is being developed the induction of general anesthesia and procedural sedation in patients undergoing diagnostic or therapeutic procedures.

### Study objective

Primary objectives:
• To assess the safety and tolerability of induction doses of ABP-700
• To optimize induction dosing of ABP-700 in combination with pre-medications

Secondary objectives:
• To characterize the pharmacokinetics (PK) of ABP-700 and its primary metabolite (CPM-acid)
• To assess the pharmacodynamics (PD) of ABP-700
• To investigate dose response and PK/PD relationships

### Study design

Phase 1, Single-Center, Open Label, Induction Dose of ABP-700 in Healthy, Adult

Subjects

**Intervention**

The study will start with a screening. At the screening a physical examination will take place and a few other standard medical assessments will be performed (ECG,vital signs). Furthermore a blood and urine sample will be taken for laboratory tests and an alcohol breathtest and drug screen will be done.

During the stay in the clinic the subject will receive either a pre-treatment medication or no pre-treatment medication, followed by the research medication once on Day 1. Safety will be monitored and sedation/anesthesia will be assessed throughout the study. Arterial and venous serial blood samples will be collected. The subjects will be asked for possible side effects on regular basis.

Finally, a follow-up visit will take place.

**Study burden and risks**

The study drug has been previously tested in 233 humans and was generally well tolerated. A number of side-effects, possibly linked to use of the study drug, were reported. The most common side effect (occurring in more than 5% of ABP-700 treated subjects) were involuntary muscle movements (twitching and uncontrollable movements), hyperventilation (breathing very heavily), tachycardia (fast heart beat), restlessness, increased blood pressure, hiccups, abnormal respiration, decreased oxygen saturation (lower levels of oxygen in the blood than normal), generalized myoclonus (involuntary twitching or jerks of muscles or groups of muscles), headache, injection site reaction (pain, redness, swelling and/or warmth at the site of the administration of the drugs), nausea, snoring, tachypnea (breathing very fast), tiredness, vomiting, yawning, emergence delirium(a condition in which coming out of anesthesia is accompanied by mental and physical agitation), lightheadedness, cannula site reaction (pain, redness, swelling, irritation and/or warmth at the site of the cannula), apnea (no breathing), and sighing. These side-effects are all consistent with the mechanism of action observed with this type of medication.

The most frequently reported side-effects of fentanyl are: respiratory depression (too shallow or slow breathing, shortness of breath, short periods of not breathing), skeletal and chest muscle rigidity and slow heart rate. If respiratory distress occurs it may sometimes be necessary to give naloxone, a so-called antidote, to counteract the effects of fentanyl (an antidote is a substance to counteract injurious effects).

The most frequently reported side-effects of midazolam are: headache, nausea, drowsiness, vomiting, hiccups, coughing and pain, redness and hardening of the

skin after injection.

Side effects of remifentanil include: loss of consciousness, a high incidence of apnea, muscle rigidity, and tachycardia.

All drugs have a potential risk of causing an allergic reaction, which if not treated promptly, could become life threatening. The subjects will be closely monitored for any allergic reactions and emergency treatment will be provided as needed.

The blood collection procedure is not dangerous, but may cause discomfort or bruising. Occasionally, fainting or an infection at the blood sampling site can occur.

## Contacts

**Public**
The Medicines Company

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US
**Scientific**
The Medicines Company

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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. Healthy, adult, men and women, 18-55 years of age, inclusive, at screening.
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 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, midazolam, 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 µg/dL at screening.
10. Women who are pregnant or lactating.
11. Positive results for the urine drug screen and alcohol breath test at screening or check-in (Day -1).
12. Positive urine cotinine at screening.
13. Positive results at screening for human immunodeficiency virus (HIV), hepatitis B surface antigen (HBsAg), or hepatitis C antibodies (HCV).
14. Single 12-lead ECG demonstrating QTcF interval >450 msec at screening.
15. 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.
16. 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).
17. 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.
18. Blood donation or significant blood loss within 90 days prior to dosing.
19. Plasma donation within 7 days prior to dosing.
20. 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.
21. Subjects who previously received ABP-700.

# Study design

## Design

**Study type:** Interventional

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| Masking: | Open (masking not used) |
| Control: | Uncontrolled |

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| Primary purpose: | Treatment |

## Recruitment

NL

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|---|---|
| Recruitment status: | Recruitment stopped |
| Start date (anticipated): | 09-11-2015 |
| Enrollment: | 120 |
| Type: | Actual |

## Medical products/devices used

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|---|---|
| Product type: | Medicine |
| Brand name: | ABP-700 |
| Generic name: | ABP-700 |
| Product type: | Medicine |
| Brand name: | Fentanyl citrate |
| Generic name: | Fentanyl |
| Registration: | Yes - NL intended use |
| Product type: | Medicine |
| Brand name: | Midazolam hydrochloride |
| Generic name: | Midazolam |
| Registration: | Yes - NL intended use |
| Product type: | Medicine |
| Brand name: | Remifantanil |
| Generic name: | Remifentanil |
| Registration: | Yes - NL intended use |

# Ethics review

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|---|---|
| Approved WMO Date: | 20-10-2015 |
| Application type: | First submission |
| Review commission: | BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen) |
| Approved WMO Date: | 26-10-2015 |

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| Application type: | First submission |
| Review commission: | BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen) |
| Approved WMO Date: | 16-02-2016 |
| Application type: | Amendment |
| Review commission: | BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen) |
| Approved WMO Date: | 24-02-2016 |
| Application type: | Amendment |
| Review commission: | BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen) |

# 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 | EUCTR2015-004358-16-NL |
| CCMO | NL55224.056.15 |