Single ascending dose study of AP30663

Gepubliceerd: 05-02-2018 Laatst bijgewerkt: 18-08-2022

Evaluation of the safety and tolerability of AP3066 in healthy males

Ethische beoordeling	Positief advies
Status	Werving gestart
Type aandoening	-
Onderzoekstype	Interventie onderzoek

Samenvatting

ID

NL-OMON29359

Bron
NTR

Verkorte titel
Single ascending dose study of AP30663

Aandoening

Atrial fibrillation

Ondersteuning

Primaire sponsor: Acesion Pharma ApS
Ole Maaløes Vej 3
DK-2200 Copenhagen N
Denmark
Overige ondersteuning: Acesion Pharma ApS
Ole Maaløes Vej 3
DK-2200 Copenhagen N
Denmark

Onderzoeksproduct en/of interventie

Uitkomstmaten

Primaire uitkomstmaten

Tolerability / safety endpoints
• Occurrence of all treatment-related AEs;
• Changes in vital signs, temperature, laboratory safety data and ECGs between pre-first infusion and each post-infusion time point;
• Changes in tremorography data;
• Changes in physical examination findings.

Pharmacokinetic endpoints
• Maximum observed plasma concentration (Cmax) for each cohort.
• Time to maximum observed plasma concentration (tmax) for each cohort.
• Area under the plasma concentration-time curve (AUC) for each dosing group (area under the plasma concentration-time curve from time zero to infinity [AUCinf],area under the plasma concentration-time curve from time zero to time of last measurable concentration [AUCtlast], area under the plasma concentration-time curve extrapolated from time t to infinity as a percentage of total AUC [AUC%extrapolated]) for each cohort.
• Apparent clearance (CL), apparent volume of distribution during terminal phase (Vz) and apparent volume of distribution at steady state (Vss) and half-life (t½) for each cohort.
Pharmacodynamic endpoints
• Based on ECG data, the following pharmacodynamic endpoints are deployed:
- RR interval
- PQ, QRS, QT/QTcF interval duration
- P, P', QRS, QRS', T, T' wave duration, amplitude and area
- R axis
- Atrial and ventricular ectopic beats on Holter recording

Toelichting onderzoek

Achtergrond van het onderzoek

The study will be conducted in the Netherlands .

Atrial fibrillation (AF) can be an invalidating arrhythmia, with frequent recurrences requiring pharmacological or electrical cardioversion. Current medical maintenance or ablative procedures are hampered by not infrequent therapy failures. Additionally, pharmacological cardioversion with currently available treatment options is unsuccessful in many patients, predominantly patients with persistent AF.
AP30663 is a first in class compound targeted at cardioversion of both paroxysmal and persistent AF. The compound inhibits the small conductance Ca2+ activated K+ channels (SK channels). These channels are associated with a prolongation of the effective refractory period (ERP) of atrial myocardial cells both in vitro and in vivo.
The current study is a first-in-man study in healthy volunteers, in which AP30663 is administered to assess the safety and tolerability.

Doel van het onderzoek

Evaluation of the safety and tolerability of AP3066 in healthy males

Onderzoeksopzet

Day -1 until Day 8

Onderzoeksproduct en/of interventie

AP30663 and placebo

Contactpersonen

Publiek

-

J. Burggraaf
Zernikedreef 8

Leiden 2235 CL
The Netherlands
+31 71 5246 400

Wetenschappelijk

-

J. Burggraaf
Zernikedreef 8

Leiden 2235 CL
The Netherlands
+31 71 5246 400

Deelname eisen

Belangrijkste voorwaarden om deel te mogen nemen (Inclusiecriteria)

1. Signed informed consent prior to any study-mandated procedure

2. Healthy male subjects, 18 to 45 years of age, inclusive.

3. Body mass index (BMI) between 18 and 30 kg/m2, inclusive at screening, and with a minimum weight of 50 kg.

4. All male volunteers must practice effective contraception during the study and be willing and
able to continue contraception for at least 90 days after their last dose of study treatment.

5. Has the ability to communicate well with the Investigator in the Dutch language and willing to
comply with the study restrictions.

Belangrijkste redenen om niet deel te kunnen nemen (Exclusiecriteria)

1. Evidence of any active or chronic disease or condition that could interfere with, or for which
the treatment might interfere with, the conduct of the study, or that would pose an unacceptable risk to the subject in the opinion of the investigator (following a detailed medical history, physical examination, vital signs (systolic and diastolic blood pressure, pulse rate, body temperature), 12-lead electrocardiogram (ECG), and clinical laboratory parameters (haematology, blood chemistry, and urinalysis)). Minor deviations of laboratory values from the normal range may be accepted, if judged by the Investigator or medically qualified designee as not clinically significant.

2. Clinically significant abnormalities, as judged by the investigator, in laboratory test results (including hepatic and renal panels, complete blood count, chemistry panel and urinalysis). In the case of uncertain or questionable results, tests performed during screening may be repeated before randomization to confirm eligibility or judged to be clinically irrelevant for healthy subjects.

3. Positive Hepatitis B surface antigen (HBsAg), Hepatitis B antibodies, Hepatitis C antibody (HCV Ab), or human immunodeficiency virus antibody (HIV Ab) at screening.

4. Systolic blood pressure (SBP) greater than 140 or less than 90 mm Hg, and diastolic blood pressure (DBP) greater than 90 or less than 50 mm Hg at screening.

5. Abnormal findings in the resting ECG at screening defined as:

- QTcF> 450 or < 300 msec

- Notable resting bradycardia (HR < 45 bpm)

- Notable resting tachycardia (HR > 100 bpm)

- Personal or family history of congenital long QT syndrome or sudden death;

- ECG with QRS and/or T wave judged to be unfavorable for a consistently accurate QT measurement (e.g., neuromuscular artefact that cannot be readily eliminated, arrhythmias, indistinct QRS onset, low amplitude T wave, merged T- and U-waves, prominent U waves);

- Evidence of a sustained atrial or ventricular arrhythmia, either by anamnesis or by Holter or telemetric observation.

- Pre-excitation (Wolff-Parkinson-White syndrome)

- PR interval >220 ms

6. Use of any medications (prescription or over-the-counter [OTC]), within 14 days of investigational product administration, or less than 5 half-lives (whichever is longer). Exceptions are paracetamol (up to 4 g/day) and ibuprofen (up to 1g/day). Other exceptions will only be made if the rationale is clearly documented by the investigator.

7. Use of any vitamin, mineral, herbal, and dietary supplements within 7 days of investigational
product administration, or less than 5 half-lives (whichever is longer). Exceptions will only be made if the rationale is clearly documented by the investigator.

8. Participation in an investigational product or device study within 3 months prior to first dosing, or >4 studies in the year prior to study participation.

9. History of abuse of addictive substances (alcohol, illegal substances) or current use of more
than 21 units alcohol per week, drug abuse, or regular user of sedatives, hypnotics, tranquillizers, or any other addictive agent

10. Positive test for drugs of abuse at screening or pre-dose.

11. Alcohol will not be allowed from at least 24 hours before screening or pre-dose.

12. Current smoker or history of nicotine abuse (average of >5 cigarettes per day for >3 months)

13. Excess in xanthine consumption (more than eight cups of coffee or equivalent per day) or unwilling or unable to abstain from xanthine consumption during the stay at CHDR.

14. Any confirmed significant allergic reactions (urticaria or anaphylaxis) against any drug, or multiple drug allergies (non-active hay fever is acceptable).

15. Loss or donation of blood over 500 mL within three months (males) prior to screening or intention to donate blood or blood products during the study.

16. Any known factor, condition, or disease that might interfere with treatment compliance, study
conduct or interpretation of the results such as drug or alcohol dependence or psychiatric disease.

Onderzoeksopzet

Opzet

Type:	Interventie onderzoek
Onderzoeksmodel:	Parallel
Toewijzing:	Gerandomiseerd
Blindering:	Dubbelblind
Controle:	Placebo

Deelname

Nederland

Status:	Werving gestart
(Verwachte) startdatum:	02-02-2018
Aantal proefpersonen:	48
Type:	Verwachte startdatum

Ethische beoordeling

Positief advies

Datum:	05-02-2018
Soort:	Eerste indiening

Registraties

Opgevolgd door onderstaande (mogelijk meer actuele) registratie

Geen registraties gevonden.

Andere (mogelijk minder actuele) registraties in dit register

Geen registraties gevonden.

In overige registers

Register	ID
NTR-new	NL6825
NTR-old	NTR7012
Ander register	: CHDR1706

Resultaten

Samenvatting resultaten
To be published