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Patients with congenital antithrombin deficiency undergoing a pharmacokinetic assessment, surgery or giving birth are treated with Atenativ, an antithrombin concentrate

Submission date
08/06/2022

Recruitment status
No longer recruiting

Registration date
12/07/2022

Overall study status
Completed

Last Edited
06/08/2024

Condition category
Haematological Disorders

[ ] Prospectively registered
[ ] Protocol
[ ] Statistical analysis plan
[ ] Results
[ ] Individual participant data
[ ] Record updated in last year

Plain English summary of protocol

Background and study aims
Congenital antithrombin deficiency is a disorder of blood clotting. People with this condition are at a higher-than-average risk of developing abnormal blood clots. This includes thrombotic events (TEs), when a blood clot forms inside a blood vessel and blocks the flow of blood, or thromboembolic events (TEEs), when a blood clot forms in a blood vessel, breaks loose into the blood stream and blocks another vessel elsewhere. The study drug that is being tested is an antithrombin concentrate called Atenativ. Atenativ is manufactured by Octapharma and has already been approved in about 30 countries worldwide. Atenativ is recommended for prevention of thrombotic and thromboembolic events in patients with congenital antithrombin deficiency in high-risk situations such as surgery and childbirth.

Who can participate?
Patients aged 18 to 80 years with congenital antithrombin deficiency and a personal or family history of TEs or TEEs. For the Treatment Phase: either non-pregnant patients scheduled for elective surgical procedure(s) known to be associated with a high risk of TEs or TEEs, or pregnant patients of at least 27 weeks gestational age who are scheduled for caesarean section or delivery

What does the study involve?
Patients may participate in the Pharmacokinetic (PK) Phase and/or the Treatment Phase in any order. For any patient wishing to participate in both phases of the study, a separate screening visit is required for each phase, including separate informed consent, after which the patient may be re-enrolled in the study. Results will be collected from patients who perform either the PK Phase, the Treatment Phase, or both phases. Each patient may only participate in the Treatment Phase for one surgery or delivery. Screening will be performed between 28 days and 1 day prior to patients entering the PK Phase or surgical patients entering the Treatment Phase. For pregnant women entering the Treatment Phase, screening will be performed 28 ± 3 days prior to the due date or 14 ± 3 days prior to planned caesarean section. For the PK Phase, measurement of antithrombin activity and antithrombin antigen will be performed at a central

laboratory. All other measurements will be performed at the study sites' local laboratories. Patients are followed up for a maximum of 30 days after the first Atenativ treatment.

What are the possible benefits and risks of participating?
Antithrombin concentrate is recommended for the prevention of abnormal clotting events in patients with congenital antithrombin deficiency in high-risk situations such as surgery and delivery. Patients taking part in this study will be observed and monitored very closely. There is no guarantee that patients will have any direct medical benefits by taking part in this research study, but support providing information about the study drug, Atenativ, which may have a future benefit to others. There are treatment alternatives to Atenativ. These include other antithrombin concentrates and low molecular weight heparin.
Any therapy may have unwanted or adverse effects. In people who have taken medications that are made from human blood, such as Atenativ, the following have been reported occasionally: allergic or hypersensitivity reactions, for example, swelling of eyes, face or tongue, burning and stinging at the injection site, fever, chills, urticaria (hives), nausea, vomiting, dyspnea or breathlessness, headache, dizziness, vertigo, wheezing, changes in blood pressure, pounding heart, lethargy, restlessness, back pain, sweating, flushing, tingling or even shock. However, Atenativ is registered in 30 countries for around 40 years, and experience in patients, including pregnant women, has shown that Atenativ is considered a well-tolerated antithrombin concentrate.

Where is the study run from?
Octapharma AG (Switzerland)

When is the study starting and how long is it expected to run for?
January 2022 to June 2025

Who is funding the study?
Octapharma AG (Switzerland)

Who is the main contact?
Martina Jansen, martina.jansen@octapharma.com

Contact information

Type(s)
Scientific

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Additional identifiers

ClinicalTrials.gov (NCT)
NCT04918173

Clinical Trials Information System (CTIS)
2021-004307-40

Integrated Research Application System (IRAS)
1004451

Central Portfolio Management System (CPMS)
51373

Protocol serial number
ATN-106

Study information

Scientific Title
A multicentre, prospective, open-label, uncontrolled Phase III study to assess the efficacy, safety and pharmacokinetics of Atenativ in patients with congenital antithrombin deficiency undergoing surgery or delivery

Acronym
ATN-106

Study objectives
No hypothesis testing due to rare disease and a small patient number.

This study assesses the incidence of the composite of thrombotic events (TEs) and thromboembolic events (TEEs) in patients with congenital antithrombin deficiency under cover of Atenativ for surgical procedures or parturition.

Ethics approval required
Old ethics approval format

Ethics approval(s)
Approved 25/01/2022, Georgetown University IRB (SW104 Medical Dental Building, 3900 Reservoir Road, NW Washington, DC 20057, USA; +1 (0)202 687 1506; irboard@georgetown.edu), ref: STUDY 00004624

Primary study design
Interventional

Study design
Multicentre prospective open-label uncontrolled Phase III trial

Study type(s)
Treatment

Health condition(s) or problem(s) studied

Congenital antithrombin deficiency

Interventions
The study will consist of two phases:

A Pharmacokinetic (PK) Phase to assess the PK of Atenativ following a single infusion in non-pregnant patients with congenital antithrombin deficiency

A Treatment Phase to determine the efficacy and safety of Atenativ in:
1. Elective surgical procedures known to be associated with a high risk for occurrence of TEs and TEEs in non-pregnant surgical patients
2. Pregnant patients scheduled for caesarean section or delivery

Patients may participate in the PK Phase and/or the Treatment Phase in any order. Results will be collected from patients who perform either the PK Phase, the Treatment Phase, or both phases. Each patient may only participate in the Treatment Phase for one surgery or delivery. The dosing, frequency of IMP administration and duration of treatment varies from subject to subject. Only for the PK Phase is a single dose of 60 IU/kg bw defined.

Intervention Type
Biological/Vaccine

Phase
Phase III

Drug/device/biological/vaccine name(s)
Atenativ

Primary outcome(s)
Incidence of the composite of TEs and TEEs in patients with congenital antithrombin deficiency under cover of Atenativ for surgical procedures or parturition to 30 days post-treatment initiation

Key secondary outcome(s)
1. PK parameters following a single dose of Atenativ in patients with congenital antithrombin deficiency measured at baseline, 20 min, 1 h, 3 h, 8 h, 24 h, 48 h / 2 days, 72 h / 3 days, 96 h / 4 days, 120 h / 5 days, 144 h / 6 days, 168 h / 7 days, 192 h / 8 days, 240 h / 10 days, 288 h / 12 days, 336 h / 14 days:
1.1. Area under the curve (AUCnorm(0–∞))
1.2. Maximum plasma concentration (Cmax)
1.3. Half-life (t1/2)
1.4. Mean residence time (MRT)
1.5. Clearance (CL)
1.6. Incremental in vivo recovery (IVR; peak concentration of antithrombin observed within the first hour after infusion)
1.7. Volume of distribution at steady state (Vss)
1.8. Time to reach Maximum Plasma Concentration (Tmax)
2. Efficacy parameters: AT activity, aPTT PT INR, fibrinogen measured at screening visit, baseline, 20 min, 1 h, 3 h, 8 h, 24 h, 48 h / 2 days, 72 h / 3 days, 96 h / 4 days, 120 h / 5 days, 144 h / 6 days, 168 h / 7 days, 192 h / 8 days, 240 h / 10 days, 288 h / 12 days, 336 h / 14 days, 30 days (follow-up)
3. Safety parameters:

3.1. AEs and SAEs recorded at 0, 20 min, 1 h, 3 h, 8 h, 24 h, 48 h / 2 days, 72 h / 3 days, 96 h / 4 days, 120 h / 5 days, 144 h / 6 days, 168 h / 7 days, 192 h / 8 days, 240 h / 10 days, 288 h / 12 days, 336 h / 14 days, 30 days (follow-up)
3.2. Length of hospital stay, recorded at discharge
3.3. Vital signs (BP, pulse, temperature, respiration rate) measured at screening visit, baseline, 20 min, 1 h, 3 h, 8 h, 24 h, 48 h / 2 days, 72 h / 3 days, 96 h / 4 days, 120 h / 5 days, 144 h / 6 days, 168 h / 7 days, 192 h / 8 days, 240 h / 10 days, 288 h / 12 days, 336 h / 14 days, 30 days (follow-up)
3.4. Standard haematological and clinical laboratory parameters measured at screening visit, baseline, 1 h, 24 h, 48 h / 2 days, 72 h / 3 days, 96 h / 4 days, 120 h / 5 days, 144 h / 6 days, 168 h / 7 days, 192 h / 8 days, 240 h / 10 days, 288 h / 12 days, 336 h / 14 days, 30 days (follow-up)

Completion date
30/06/2025

Eligibility

Key inclusion criteria
1. Adult male or female patients ≥18 and ≤80 years of age
Solely in the US, four male or female patients between ≥12 and <17 years of age will be enrolled into the PK phase, and the treatment phase, if needed
2. Documented congenital antithrombin deficiency, defined by plasma level of antithrombin ≤60%
3. Personal or family history of TEs or TEEs
4. For the Treatment Phase: either
4.1. Non-pregnant surgical patients scheduled for elective surgical procedure(s) known to be associated with a high risk for occurrence of TEs or TEEs, or
4.2. Pregnant patients of at least 27 weeks gestational age who are scheduled for caesarean section or delivery
5. For female patients of childbearing potential entering the PK Phase who are not known to be pregnant, and for female surgical patients of childbearing potential entering the Treatment Phase for any procedure other than caesarean section or delivery, a negative urine pregnancy test at screening and at baseline
6. Patient has provided informed consent

Participant type(s)
Patient

Healthy volunteers allowed
No

Age group
Mixed

Lower age limit
18 Years

Upper age limit
80 Years

Sex

All

Key exclusion criteria
1. Requires emergency surgery or emergency caesarean section
2. Has undergone surgery within the last 6 weeks
3. History or suspicion of another hereditary thrombophilic disorder other than antithrombin deficiency (e.g., activated protein C [APC] resistance/Factor V Leiden, Protein S or C deficiency, prothrombin gene mutation [G20210A], or acquired [lupus anticoagulant] thrombophilic disorder)
4. Malignancies, renal failure, or severe liver disease (aspartate aminotransferase [ASAT] >5 times the upper limit of normal)
5. Body mass index >40 kg/m² (for non-pregnant patients, only)
6. Known hypersensitivity or allergic reaction to antithrombin or any of the excipients in Atenativ
7. History of anaphylactic reaction(s) to blood or blood components
8. Refusal to receive a transfusion of blood-derived products
9. Administration of any antithrombin concentrate or antithrombin-containing blood product other than the study medication within 14 days of either of the two phases of the study
10. Prior diagnosis of heparin-induced thrombocytopenia
11. TE or TEE within the last 6 months
12. Female patients who are nursing at the time of screening
13. Have participated in another investigational study within the last 30 days

Date of first enrolment
30/06/2022

Date of final enrolment
31/08/2024

Locations

Countries of recruitment
United Kingdom

Austria

France

Germany

Hungary

Italy

Spain

United States of America

Study participating centre

Craig Kessler
Washington, DC
United States of America
20057

Sponsor information

Organisation
Octapharma (Switzerland)

ROR
https://ror.org/002k5fe57

Funder(s)

Funder type
Industry

Funder Name
Octapharma

Alternative Name(s)
Octapharma AG

Funding Body Type
Private sector organisation

Funding Body Subtype
For-profit companies (industry)

Location
Switzerland

Results and Publications

Individual participant data (IPD) sharing plan
Individual data will be shared with e.g. the FDA, in order to register Atenativ on the US market, only.

IPD sharing plan summary
Stored in non-publicly available repository