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Prospective clinical study in children with severe haemophilia A to investigate clinical efficacy, immunogenicity, pharmacokinetics, and safety of Human-cl rhFVIII

Submission date
24/01/2011

Recruitment status
No longer recruiting

Registration date
23/02/2011

Overall study status
Completed

Last Edited
13/12/2017

Condition category
Haematological Disorders

[ ] Prospectively registered
[ ] Protocol
[ ] Statistical analysis plan
[X] Results
[ ] Individual participant data

Plain English summary of protocol
Not provided at time of registration

Contact information

Type(s)
Scientific

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Additional identifiers

Protocol serial number
GENA-03

Study information

Scientific Title

Prospective clinical study in children with severe haemophilia A to investigate clinical efficacy, immunogenicity, pharmacokinetics, and safety of Human-cl rhFVIII

Study objectives
Investigation of efficacy and safety (and pharmacokinetics in 50% of the patients included) of Human-cl rhFVIII in severe haemophilia A children (2 - 12 years old), followed for a 6-month open prophylactic treatment period.

On 03/01/2012 the overall trial end date was changed from 01/12/2011 to 01/10/2012. The countries of recruitment were changed to include Romania and Serbia.

Ethics approval required
Old ethics approval format

Ethics approval(s)
Ethics Committee of Brno, Czech Republic, 23/06/2010, ref: 049/10MEK

Study design
Prospective cross-over (part I) open-label trial

Primary study design
Interventional

Study type(s)
Treatment

Health condition(s) or problem(s) studied
Severe haemophilia A

Interventions
This study schedules two patient groups and two study phases. One patient group passes through both study phases, whereas the other patient group undergoes the second study phase only.

Study phase I ('pharmacokinetic phase') is intended to give information about the pharmacokinetics of Human-cl rhFVIII and is applicable for half of the patients included into this study. Within this phase, patients will visit their study doctor twice for the purpose of a drug administration and subsequent blood collections. The first time, the blood samples will be taken after the injection of the actually used FVIII concentrate, while the other time, the same procedure will be done after Human-cl rhFVIII administration. All patients having completed study phase I are intended to continue with study phase II.

The remaining half having not been included into study phase I, will only partake in the second study phase ('open treatment phase') which is intended to prove the efficacy of a prophylactic six-month treatment with Human-cl rhFVIII. As the need arises, also on demand treatment with Human-cl rhFVIII will be possible. Further aims of this study phase would be to investigate the immunogenic and the safety potential of Human-cl rhFVIII.

Within study phase II, five consultations with the study physician will take place. Three of them will comprehend a blood collection by which an exclusion of inhibitors will be ensured. The remaining two visits are for incremental recovery purposes, meaning that after having taken a

reference blood sample, Human-cl rhFVIII will be administered, followed by two further blood sample withdrawals.

In either case the study starts with a Screening Visit, comprehending identical general basic investigations for all patients.

Intervention Type
Other

Phase
Not Applicable

Primary outcome(s)
1. Efficacy of prophylactic treatment: the frequency of breakthrough bleeds under prophylactic treatment will be calculated. Study drug consumption data (FVIII IU/kg, extrapolated to monthly and yearly usage) both per subject and in total will be evaluated
2. Efficacy of on-demand treatment of breakthrough bleeding episodes

Key secondary outcome(s))
1. Pharmacokinetic parameters: in 50% of the included patients the following pharmacokinetic parameters of Human-cl rhFVIII are determined and compared with the previously used FVIII concentrate: in vivo half-life (T1/2), AUC, Cmax, Tmax, MRT, Vd, and CL. These PK parameters will be calculated for FVIII:C using both the CHR and the OS assays and the actual potency of Human-cl rhFVIII
2. In-vivo recovery: will be calculated - also over time - from the FVIII levels before and peak level obtained in the 0.5 or 2 hours post-infusion samples
3. The immunogenic potential of Human-cl rhFVIII is investigated by controlling the inhibitor titre
4. The efficacy of Human-cl rhFVIII in surgeries is assessed
5. The safety of Human-cl rhFVIII in terms of adverse event monitoring is assessed

Completion date
01/10/2012

Eligibility

Key inclusion criteria
1. Must have severe haemophilia A (FVIII:C less than 1%; historical value as documented in subject records)
2. Previously treated with FVIII concentrate, at least 50 EDs
3. Immunocompetent (CD4+ count above greater than 200/µL)
4. Human immunodeficiency virus (HIV) negative or respective viral load less than 200 particles /µL or less than 400,000 copies/ml
5. Freely given written informed consent by parents or legal guardian
6. Aged between 2 and 12 years, males only

Participant type(s)
Patient

Healthy volunteers allowed
No

Age group
Child

Lower age limit
2 years

Upper age limit
12 years

Sex
Male

Key exclusion criteria
1. Other coagulation disorder than haemophilia A
2. Present or past FVIII inhibitor activity (greater than 0.6 BU)
3. Target joints
4. Severe liver or kidney disease (alanine aminotranferase [ALAT] and aspartate aminotransferase [ASAT] levels greater than 5 times of upper limit of normal, creatinine greater than 120 µmol/L)
4. Receiving or scheduled to receive immuno-modulating drugs (other than anti-retroviral chemotherapy) such as alpha-interferon, prednisone (equivalent to greater than 10 mg/day), or similar drugs
5. Current participation in another clinical study
6. Participation in another interventional clinical study with administration of investigational medical product (IMP) in the course of the past 3 months, except studies investigating already registered FVIII products

Date of first enrolment
01/01/2011

Date of final enrolment
01/10/2012

Locations

Countries of recruitment
United Kingdom

Austria

Czech Republic

France

Germany

Poland

Romania

Russian Federation

Serbia

Türkiye

Study participating centre
Oberlaaerstrasse 235
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Sponsor information

Organisation
Octapharma AG (Switzerland)

ROR
https://ror.org/002k5fe57

Funder(s)

Funder type
Industry

Funder Name
Octapharma AG (Switzerland)

Results and Publications

Individual participant data (IPD) sharing plan

IPD sharing plan summary
Not provided at time of registration

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Results article	results	01/03/2016		Yes	No