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Clinical study to investigate the pharmacokinetics, efficacy, safety and immunogenicity of human-cl rhFVIII in previously treated patients with severe haemophilia A

Submission date 23/01/2009	**Recruitment status** No longer recruiting	[X] Prospectively registered [_] Protocol [_] Statistical analysis plan [_] Results [_] Individual participant data [_] Record updated in last year
Registration date 03/02/2009	**Overall study status** Completed	
Last Edited 03/02/2009	**Condition category** Haematological Disorders	

Plain English summary of protocol
Not provided at time of registration

Contact information

Type(s)
Scientific

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Additional identifiers

Clinical Trials Information System (CTIS)
2008-006172-29

Protocol serial number
GENA-09

Study information

Scientific Title

Study objectives
Comparison of pharmacokinetics of human-cl rhFVIII and Kogenate®/Helexate® in severe haemophilia A patients, followed by a 6-month open prophylactic treatment period to investigate the efficacy.

Ethics approval required
Old ethics approval format

Ethics approval(s)
Ministry of Health and Social Affairs of the Russian Federation, Federal Supervision Service for Public Health and Social Affairs gave approval on the 16th January 2009 (ref: no. 6)

Study design
Prospective randomised cross-over open-label trial

Primary study design
Interventional

Study type(s)
Treatment

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

Interventions
In the cross-over PK phase (part I), the PK properties of human-cl rhFVIII and Kogenate® /Helexate® will be studied: each one single treatment with 50 IU rFVIII/kg body weight (BW) will be given intravenously als a bolus injection. Subjects who completed part I will then be followed up for a period of 6 months and at least 50 EDs (part II). During this phase, prophylactic and on-demand treatments with human-cl rhFVIII are documented. The subjects get 30 IU rFVIII/kg BW every other day as a prophylactic treatment. Bleedings are treated in addition. Dose and duration of these treatments depend on the severity and the site of the bleeding. All treatments are intravenous injections.

Intervention Type
Drug

Phase
Phase II

Drug/device/biological/vaccine name(s)
Human-cl rhFVIII, Kogenate®/Helexate®

Primary outcome(s)

To compare the area under curve (AUC) of human-cl rhFVIII and Kogenate®/Helexate® for FVIII:C using both the chromogenic (CHR) and the one-stage (OS) assays and the actual potency of human-cl rhFVIII and Kogenate®/Helexate®.

Key secondary outcome(s))
1. Pharmacokinetic (PK) parameters:
1.1. In vivo half-life (T1/2), Cmax, Tmax, MRT, Vd, and CL, calculated for FVIII:C using both the CHR and the OS assays and the actual potency of human-cl rhFVIII and Kogenate®/Helexate®
1.2. In-vivo recovery calculated from the FVIII levels before and peak level obtained in the 0.25, 0.5, 0.75, or 1 hour post-infusion samples
2. Efficacy in prophylactic treatment:
2.1. Overall efficacy assessment after a total of 50 EDs and at the end of the study
2.2. The frequency of bleeds under prophylactic treatment
2.3. Study drug consumption data (FVIII IU/kg per month, per year) per subject and in total
2.4. Efficacy assessment of each IMP injection and an overall efficacy assessment at the end of each BE
2.5. Surgical prophylaxis: the overall efficacy assessment after the end of the surgical prophylactic treatment phase by the surgeon and haematologist
2.6. Average and maximum expected estimated blood loss compared to the actual estimated blood loss
3. Safety: clinical tolerability assessed by:
3.1. Monitoring vital signs: blood pressure, heart rate, respiratory rate and body temperature will be assessed at pre-defined time-points
3.2. Laboratory parameters: the following routine safety laboratory parameters will be tested at pre-defined time-points:
3.2.1. Haematological parameters: red blood cell count, white blood cell count, haemoglobin, haematocrit, and platelet count
3.2.2. Clinical chemistry: total bilirubin, alanine aminotransferase, aspartate transaminase, blood urea nitrogen, serum creatinine, lactate dehydrogenase (LDH)
3.2.3. Serum electrolytes: sodium, potassium, bicarbonate, calcium
3.2.4. Urine analysis: urine dipstick chemical analysis (leucocyturia, haematuria, proteinuria, glucose, ketones, bilirubin, nitrites if positive including microscopic examination)
3.3. Monitoring adverse events (AEs): at each study visit, all adverse events are documented by the Investigator.
3.4. Inhibitors against FVIII and anti-rhFVIII antibodies determined at pre-determined time points and in cases where an inhibitor development is suspected
3.5. Immunogenicity: inhibitor activity will be determined by the modified Bethesda assay (Nijmegen modification) at study entry, then immediately before the first human-cl rhFVIII administration, after 1 ED, after 10 to 15 EDs and the 3-months and 6-months visit. At the same time-point the anti-rhFVIII antibodies will be measured.

Completion date
01/12/2009

Eligibility

Key inclusion criteria
1. Must have severe haemophilia A (FVIII:C less than 1%; historical value as documented in subject records)
2. Aged greater than 18 and less than 65 years, male
3. Body weight 45 kg to 110 kg

4. Previously treated with FVIII concentrate, at least 150 exposure days (EDs)
5. Immunocompetent (CD4+ count greater than 200/µL)
6. Negative for human immunodeficiency virus (HIV) and hepatitis C virus (HCV) or respective viral load less than 200 particles/µL
7. Freely given written informed consent

Participant type(s)
Patient

Healthy volunteers allowed
No

Age group
Adult

Lower age limit
18 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. Severe liver or kidney disease (alanine aminotransferase [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. Participation in another clinical study currently or during the past month

Date of first enrolment
01/03/2009

Date of final enrolment
01/12/2009

Locations

Countries of recruitment
Austria

Russian Federation

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