ISRCTN99606748 https://doi.org/10.1186/ISRCTN99606748

Clinical study in which the long term effect of Human-cl rhFVIII is investigated in children with severe haemophilia A, who were previously treated in the GENA-03 study

Submission date
30/12/2011

Recruitment status
No longer recruiting

Registration date
03/01/2012

Overall study status
Completed

Last Edited
13/03/2020

Condition category
Haematological Disorders

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

Plain English summary of protocol

Background and study aims
When you cut yourself substances in the blood called clotting factors help the blood to clot. Haemophilia A is an inherited condition in which affected males do not produce enough of the clotting factor FVIII, so they have an increased tendency to bleed. Most bleeding occurs in joints and muscles. Without treatment this bleeding leads to long-term illness with severe disability. The aim of this study is to investigate the long-term effectiveness of giving clotting factor FVIII to previously treated children with severe haemophilia A.

Who can participate?
2 – 13 year old boys and girls with severe haemophilia A who completed the previous GENA-03 study.

What does the study involve?
All patients are injected with FVIII three times a week or every other day depending on their clinical needs. In case of bleeding or surgery further injections may be needed. The effectiveness of the treatment is evaluated every 6 months.

What are the possible benefits and risks of participating?
Based on previous clinical use, FVIII is expected to be safe and effective in the prevention and treatment of bleeding and during surgery. The following side effects may also occur: hypersensitivity or allergic reactions, swelling, burning and stinging at the injection site, chills, flushing, rash, headache, low blood pressure, tiredness, feeling sick, restlessness, rapid heart rate, chest tightness, tingling, vomiting, and wheezing. Rarely, such reactions may progress to the point of severe allergic reaction including shock and fever. However, all patients included into this study had been treated with FVIII for at least 6 months already, and none of these side effects were expected.

Where is the study run from?
The study will be conducted in around 10 sites all over Europe, lead by Great Ormond Street Hospital (UK).

When is the study starting and how long is it expected to run for?
October 2011 to March 2014.

Who is funding the study?
Octapharma AG (Switzerland).

Who is the main contact?
Martina Jansen
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Contact information

Type(s)
Scientific

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Additional identifiers

Protocol serial number
GENA-13

Study information

Scientific Title
Clinical study in which the immunogenicity, tolerability and efficacy of Human-cl rhFVIII is investigated in children with severe haemophilia A, who were previously treated in the GENA-03 study

Study objectives
Investigation of long-term efficacy and safety of Human-cl rhFVIII in children with severe haemophilia A (2 - 13 years old), followed up for an open prophylactic treatment until product registration.

Follow up to http://www.isrctn.com/ISRCTN71212110

Ethics approval required
Old ethics approval format

Ethics approval(s)
1. National Research Ethics Service, Riverside, Brighton (UK), 27/09/2011, ref 11/LO/1159
2. University Hospital Brno Ethics Committee, (Czech Republic), 24/08/2011 ref: GENA-13
3. Bioethics Committee, Medical University of Warsaw (Poland), 20/09/2011, ref KB/157/2011
4. People Protection Committee, Paris [Ile de France II] (France), 05/10/2011, ref 2011-08-02

Study design
Prospective open-label trial

Primary study design
Observational

Study type(s)
Treatment

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

Interventions
There is just one treatment arm: prophylactic treatment with rFVIII.
The investigational medicinal product (IMP) name is Human-cl rhFVIII, which is a recombinant factor 8 concentrate from a human cell-line. The product is injected every other day or three times a week (depending on the clinical needs of the patient), at a prophylactic dose of 30 - 40 IU /kg bodyweight. The study will continue until the patients can switch to the registered and launched product. The expected duration of the individual treatment is at least 2 years.

Intervention Type
Biological/Vaccine

Primary outcome(s)
Long-term immunogenicity:
Inhibitor activity will be determined by the modified Bethesda assay (Nijmegen modification) using congenital FVIII-deficient human plasma spiked with Human-cl rhFVIII as a test base, at tri-monthly intervals until study completion. At the same time-points, anti-rhFVIII antibodies will be measured. These parameters will also be determined in case inhibitor development is suspected. Sampling for inhibitor and antibody measurements should be performed not less than 48 hours after the previous administration of any FVIII product, if possible. In case of positive inhibitor results, an inhibitor retesting using a second separately drawn sample should be performed.
Long-term clinical tolerability: Will be assessed by monitoring Adverse Events (AEs) throughout the study duration.

Key secondary outcome(s))
1. Efficacy of prophylactic treatment: Efficacy is to be assessed by evaluating the number of spontaneous breakthrough BEs, as well as by collecting data regarding frequency of IMP injections and regarding the prophylactic IMP doses needed. Overall study drug consumption data (FVIII (IU/kg), per month and per year), per subject and in total, will be analysed.

All efficacy ratings having been assessed as 'excellent' and 'good' will be reported as 'successfully treated'. The proportion of BEs successfully treated with Human-cl rhFVIII will be evaluated both for all BEs, as well as broken down to BEs of different severity.

2. Efficacy of surgical prophylaxis: Efficacy will be assessed by the surgeon at the end of surgery (i.e. after last suture), and postoperatively (i.e. at date of discharge or on postoperative day 6, whichever occurs later), by both the surgeon and the haematologist using predefined study criteria, namely 'excellent', 'good', 'moderate' or 'none'. All efficacy ratings of surgical procedures having been assessed 'excellent' and 'good' will be reported as 'successfully treated'.

Completion date
31/03/2014

Eligibility

Key inclusion criteria
1. Evaluable completion of the preceeding study GENA-03 by having a study participation period of 6 months, provided that prophylaxis with Human-cl rhFVIII is continued without intermediate interruption
2. Voluntarily given, fully informed written and signed consent obtained from the parents (or legal guardians) before any study-related procedures are conducted. The need for obtaining assent will depend on the subjects' developmental stage and intellectual capacity
3. Capability to understand and comply with the relevant aspects of the study

Participant type(s)
Patient

Healthy volunteers allowed
No

Age group
Child

Sex
All

Key exclusion criteria
1. Development of FVIII inhibitors (³0.6 Bethesda Units [BU]) in the course of the GENA-03 study
2. Any severe liver or kidney disease (ALT and AST levels >5 times of upper limit of normal, creatinine >120 µmol/L)

Date of first enrolment
31/10/2011

Date of final enrolment
31/03/2014

Locations

Countries of recruitment

United Kingdom

England

Czech Republic

France

Poland

Russian Federation

Türkiye

Study participating centre
Great Ormond Street Hospital
London
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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
HRA research summary			28/06/2023	No	No