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Efficacy and safety of two dose regimens of Octaplex® in patients with intracranial haemorrhage related to oral anticoagulant therapy

Submission date 04/09/2008	**Recruitment status** No longer recruiting	[_] Prospectively registered [_] Protocol
Registration date 13/10/2008	**Overall study status** Completed	[_] Statistical analysis plan [_] Results
Last Edited 13/10/2008	**Condition category** Circulatory System	[_] Individual participant data [_] Record updated in last year

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
LEX-206

Study information

Scientific Title
Efficacy and safety of two dose regimens of Octaplex® in patients with intracranial haemorrhage related to oral anticoagulant therapy: a multicentre, prospective, randomised, open-label study

Study objectives
To compare the efficacy of two dose regimens of Octaplex® on the international normalised ratio (INR) at 10 ± 5 minutes after the end of injection in patients with intracranial haemorrhage related to oral anticoagulant therapy.

Ethics approval required
Old ethics approval format

Ethics approval(s)
Ethics approval received from the Ouest III Ethics Committee (Poitiers, France) on the 7th February 2008 (ref: 08.01.01)

Study design
Interventional, prospective, multicentre, randomised, open-label, phase III, parallel group trial

Primary study design
Interventional

Study type(s)
Treatment

Health condition(s) or problem(s) studied
Intracranial haemorrhage (intracerebral and acute subdural haematoma)

Interventions
Octaplex® intravenous administration at the inclusion, 25 IU/kg or 40 IU/kg according to the randomisation. In addition, administration of 5 mg vitamin K, intravenous infusion for all the patients.

Possibility of two more administrations upon INR results:
1. A rescue dose at 10 ± 5 minutes after the first administration if INR not corrected (INR greater than 1.5), intravenous administration within 10 minutes, dose administrated = theoretical dose calculated according to the Summary of Product Characteristics (SmPC) - dose administrated at the inclusion (25 or 40 IU/kg)
2. New dose at 6 hours if INR greater than 2, dose calculated according the SMPc, intravenous administration within 10 minutes

Comparison of two doses of Octaplex®, no placebo or other treatment used. Patients will be followed up during 30 days or less if discharged.

Intervention Type
Drug

Phase
Phase III

Drug/device/biological/vaccine name(s)
Octaplex®

Primary outcome(s)
INR at 10 ± 5 minutes after the end of injection in patients with intracranial haemorrhage related to oral anticoagulant therapy, measured by local laboratories (standard method).

Key secondary outcome(s))
Efficacy:
1. Laboratory parameters (coagulation): INR, prothrombin time (PT), thrombin generation assay (TGA), coagulation factors II, VII, IX and X, protein C and protein S at 10 ± 5 minutes, 1, 3, 6 and 24 hours after the end of injection. All these parameters will be analysed by local or central laboratory using standard methods.
2. Medical imaging (CT scan): volume of haematoma at 48 hours after the end of injection (or earlier in case of neurological worsening assessed by National Institutes of Health [NIH] Stroke Scale); the computed tomography images at T0 and T48 hours will be analysed by the central neuroradiology centre with the software OSIRIX
3. Clinical status: Glasgow Coma Scale (score: 3 - 15) and NIH Stroke Scale at 1, 24 and 48 hours, and on days 3 and 30 (or earlier if patient discharged) after the end of injection
4. Global outcome:
4.1. Survival (is the patient dead? Yes or No)
4.2. Extended Glasgow Outcome Scale (GOS) (score: 1 - 8, 1 = dead, 8 = upper good recovery)
4.3. Modified Rankin Scale (MRS) (score: 0 - 6, 0 = no symtoms at all, 6 = dead)
4.4. Barthel Index (score: 0 - 100, 100 = patient is continent, feeds himself, dresses himself, gets up out of bed and chairs, bathes himself, walks at least a block, and can ascend and descend stairs)
All measured on day 30 (or earlier if patient discharged) after the end of injection.
5. Overall clinical response: this assessment will be done by the investigator using a verbal rating scale:
5.1. None: in spite of sufficient treatment uncontrolled intracranial bleeding growth requiring additional measures
5.2. Moderate: in spite of sufficient treatment uncontrolled intracranial bleeding and haematoma growth; no additional measures required
5.3. Excellent: intracranial bleeding and haematoma growth under control, comparable to a normal patient
Measured 48 hours after the end of injection.

Safety:
6. Study drug actually received
7. Adverse events (AEs) during the whole stay in all patients. AEs will be followed closely by a Data Monitoring Committee (DMC) whose assignment will be to identify possible thromboembolic complications. The DMC will be entitled to issue recommendations to the sponsor and the investigators regarding the continuation or the modification of the study if there is a suspicion of increased risk of thromboembolic complications in the high dose group.
8. Vital signs: continuous monitoring of arterial blood pressure, heart rate, respiratory rate and body temperature during the whole stay in the investigator's ward; recording of values and abnormalities at 10 ± 5 minutes, 1, 6, 24 and 48 hours and on days 3 and 30 (or earlier if patient discharged) after the end of injection
9. Electrocardiogram (ECG): continuous surveillance during the whole stay in the investigator's ward; recording of abnormalities at 10 ± 5 minutes, 1, 3, 6, 24 and 48 hours and on days 3 and 30 (or earlier if patient discharged) after the end of injection

10. Laboratory parameters (coagulation markers): D-dimers, prothrombin fragments F1+2 at 10 ± 5 minutes, 1, 3, 6 and 24 hours after the end of injection
11. Other laboratory parameters: troponins, electrolytes, urea, creatinine, liver function and haematology at 24 hours after the end of injection
12. Digital glucose at 24 hours after the end of injection

Quality of life measurements:
13. Pharmaco-economic patient questionnaire at month 3
14. 36-item short form health survey (SF-36) questionnaire at month 3

Completion date
31/03/2009

Eligibility

Key inclusion criteria
1. Patients of 18 years of age or older, either sex
2. Intracranial haemorrhage (intracerebral and acute subdural) confirmed by medical imaging (computed tomography only)
3. Use of oral anticoagulant, only vitamin K antagonist
4. Written informed consent from the patient or a legally acceptable representative if the subject is unable to provide informed consent, or from the investigator and an independent witness from the investigator and the sponsor, if no legally acceptable representative is available at inclusion

Participant type(s)
Patient

Healthy volunteers allowed
No

Age group
Adult

Lower age limit
18 years

Sex
All

Key exclusion criteria
1. Deep coma on admission (score 3 to 5 on the Glasgow Coma Scale) because their probability of survival is close to zero
2. Septic shock or severe sepsis in the past fourteen days prior to inclusion
3. Crush injury in the past seven days prior to inclusion
4. Known or suspected disseminated intravascular coagulation
5. Pulmonary embolism or phlebitis in the last 3 months prior to inclusion
6. Patients receiving vitamin K prior to admission to investigational centre
7. Known allergy to vitamin K or to any of its excipients
8. Hypersensitivity to the active substances of Octaplex® (human coagulation factors II, VII, IX

and X) or to any of its excipients (heparin and sodium citrate)
9. Known allergy to heparin or history of heparin-induced thrombocytopenia
10. Participation in another clinical study, currently or during the past three months
11. Pregnant or lactating women
12. Jehovah's witnesses

Date of first enrolment
10/09/2008

Date of final enrolment
31/03/2009

Locations

Countries of recruitment
France

Study participating centre
Groupe Hospitalier Pitié Salpêtrière
Paris
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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?
Participant information sheet	Participant information sheet	11/11/2025	11/11/2025	No	Yes