C1 inhibitor study

Short title: C1-inhibitor improves recovery of red blood cell transfusion in patients suffering from autoimmune hemolytic anemia – an open-labeled pilot trial

Principal investigator: Dr. Josephine M.I. Vos

Sponsor: Academic Medical Center (AMC), Department of Hematology

EudraCT nr. (if applicable): 2012-003710-13

Patient population:

Required no. of patients (if applicable): 10

Type of study: prospective open label study

Study objectives:

Primary objectives: The C1-Inh in AIHA study investigates whether co-administration of C1-inh concentrate in patients suffering from AIHA needing RBC transfusion:

- improves recovery of RBC transfusion
- inhibits complement activation and deposition on RBC via the classical pathway of complement
- is safe

Secondary objectives: The C1-Inh in AIHA study investigates whether co-administration of C1-inh concentrate in patients suffering from AIHA needing RBC transfusion:

- Attenuates the pro-inflammatory response in AIHA
- Affects the response to the basic treatment targeting autoantibody production

Status: Open for accrual

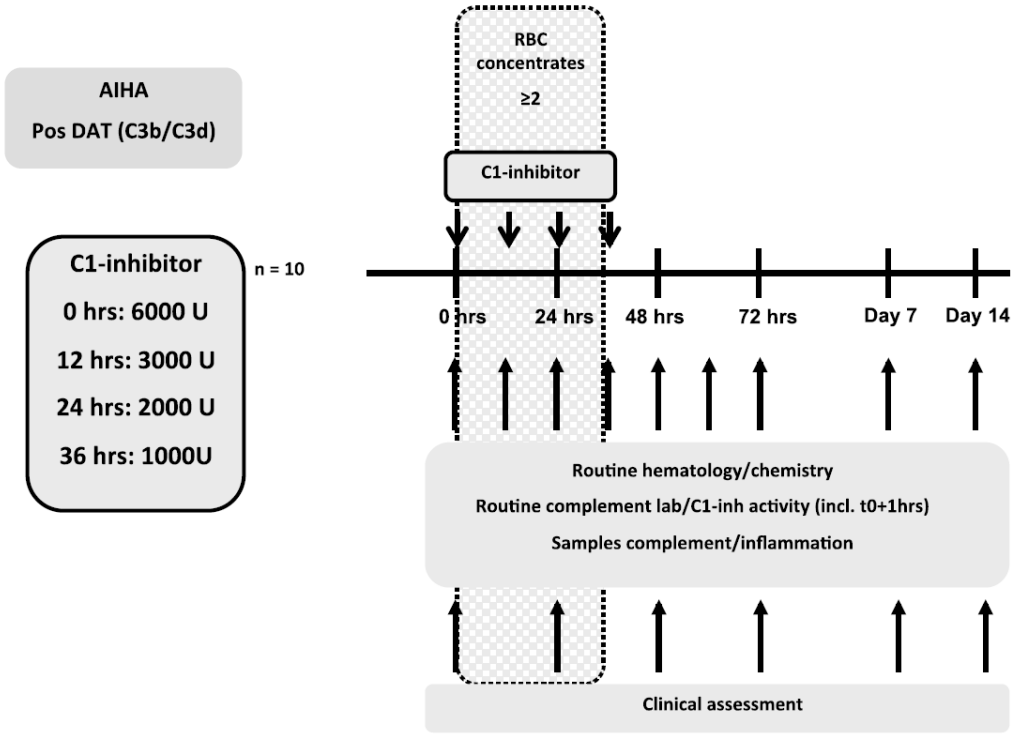
Participating sites: Amsterdam UMC, location AMC

Contact for more information: Dr. J.M.I. Vos, hemat.trial@amsterdamumc.nl

These will mostly be urgent cases so please reach out to our Trialbureau, Dr Vos or the hematologist on call by telephone in case of a potential study candidate

Summary (optional):

Deze "proof of principal" studie is geschikt voor patienten complementgemedieerde AIHA met acute tranfusie behoefte van tenminste 2 erytrocyten concentraten en een Hb van 5.0 mmol/L of lager. Rondom de transfusie wordt de c1-inhibitor Cinryze toegediend. De patient zal tenminste 72 uur in het AMC worden opgenomen.



Subject eligibility criteria:

Inclusion criteria:

4.1 Eligibility for registration

Patients suffering from AIHA are eligible for the study if there is evidence for complement-mediated destruction of RBC by autoantibodies and there is an acute indication for RBC transfusion. The decision on whether there is an indication for RBC transfusion is left to the treating physician and is based on the clinical assessment and not by a hemoglobin threshold.

4.1.1 Inclusion criteria

- Positive (≥1+) monospecific antiglobulin test for C3b and/or C3d with/without positivity for IgM OR
- strongly positive (≥3+) monospecific antiglobulin test for C3b and/or C3d with positivity for IgG
- Indication for a transfusion with at least 2 red packed cell concentrates based on the clinical
- assessment by the hematologist in charge
- Hemoglobin value at least < 5 mmol/L (8 g/dl) with/without clinical symptoms
- Clinical signs of hemolysis: not-detectable haptoglobin (mandatory) and increased lactate
- dehydrogenase (LDH) eventually combined with hyperbilirubinemia (increased direct and/or
- indirect bilirubin), lactate.
- Age ≥ 18 years
- Written informed consent
- Women of child bearing potential must have had a negative serum pregnancy test 7 days prior to
- the start of study drug

Exclusion criteria:

- History of arterial and/or venous thromboembolic events in the absence of an actual treatment
- with Vitamin K-antagonists
- Concomitant use of therapeutic doses of heparin
- Female patients who are pregnant or breast feeding or adults of reproductive potential who are
- not using effective birth control methods. If barrier contraceptives are being used, these must be
- continued throughout the trial by both sexes. Oral contraceptives only are not acceptable.
- Patients with known HIV seropositivity or chronic active hepatitis
- Patients who have any severe and/or uncontrolled medical condition or other conditions that could
- affect their participation in the study such as:
    - cerebrovascular accidents ≤ 6 months before study drug start
    - uncontrolled hypertension