C1-inhibitor improves efficacy of red blood cell transfusion in patients suffering from autoimmune hemolytic anemia * an open-labeled pilot trial

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Ethical review	Approved WMO
Status	Recruitment stopped
Health condition type	Immune system disorders congenital
Study type	Interventional

Summary

ID

NL-OMON55361

Source
ToetsingOnline

Brief title
C1-Inh in AIHA

Condition

- Immune system disorders congenital

Synonym
Anemia, Autoimmune Hemolytic Anemia

Research involving
Human

Sponsors and support

Primary sponsor: Academisch Medisch Centrum

Source(s) of monetary or material Support: Ministerie van OC&W,Takeda

Intervention

Keyword: AIHA, C1-inhibitor, red cell Transfusion

Outcome measures

Primary outcome

* improvement of the recovery of RBC transfusion- as defined as a decrease of

hemoglobin <1 g/dl (0.6 mmol/L) /24 hrs

* inhibition of complement activation and deposition on RBC via the classical

pathway of complement

* safety

Secondary outcome

* Inhibition of the pro-inflammatory response

Study description

Background summary

Autoimmune hemolytic anemia (AIHA) is characterized by premature destruction of red blood cell (RBC) due autoantibodies directed to RBC antigens with or without activation of the classical pathway of complement. Activation of the classical pathway of complement by autoantibodies of the IgM isotype can lead to life-threatening intravascular hemolysis with an acute consumption of oxygen carriers, resulting in acute tissue hypoxia. However, the efficacy of life-saving transfusion is severely compromised since the RBC autoantibodies react with both recipient and donor RBCs, leading to a rapid destruction of donor RBCs as well. C1-esterase inhibitor (C1-inh) is an efficient inhibitor of the classical pathway of complement. C1-inh is being used for 30 years to treat patients with hereditary angioedema. In addition, C1-inh is successfully used in diseases caused by ischemia-reperfusion injury and sepsis. In all these applications C1-inh turned out to have an excellent safety profile.
Because C1-inh is an efficient inhibitor of the classical pathway of complement with an excellent safety profile we hypothized that C1-inh might inhibit autoantibody mediated destruction of donor RBS in order to improve efficacy of

RBC transfusion.

Study objective

The aim of the present *proof-of-principle* study is to test in patients suffering from AIHA whether co-administration of C1-inh improves the recovery of RBC transfusion by the inhibition of the activation of the classical pathway of complement. In addition, the effects of C1-inh on the pro-inflammatory response in AIHA patients will be investigated.

Study design

This is a prospective, multicenter, national open label study to test the efficacy of C1-inh to improve the efficacy of RBC transfusion in patients with AIHA

Intervention

Patients will receive C1-inh: 6000 Units before the transfusion and thereafter 3000U, 2000U and 1000U every 12 hours

Study burden and risks

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Contacts

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Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Adults (18-64 years)
Elderly (65 years and older)

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 < 3 mmol/L (5 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

Study design

Design

Study phase:	2
Study type:	Interventional
Masking:	Open (masking not used)
Control:	Uncontrolled
Primary purpose:	Treatment

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	04-06-2014
Enrollment:	10
Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	C1 esterase inhibitor
Generic name:	cinryze
Registration:	Yes - NL outside intended use

Ethics review

Approved WMO

Date:	27-11-2012
Application type:	First submission
Review commission:	METC Amsterdam UMC

Approved WMO

Date:	08-01-2013
Application type:	Amendment
Review commission:	METC Amsterdam UMC

Approved WMO

Date:	21-03-2013
Application type:	First submission
Review commission:	METC Amsterdam UMC

Approved WMO

Date:	26-03-2013
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	24-01-2014
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	28-01-2014
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	08-04-2020
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	23-04-2020
Application type:	Amendment
Review commission:	METC Amsterdam UMC

Study registrations

Followed up by the following (possibly more current) registration

No registrations found.

Other (possibly less up-to-date) registrations in this register

No registrations found.

In other registers

Register	ID
EudraCT	EUCTR2012-003710-13-NL
CCMO	NL41820.018.12

Register	ID
Other	NL8164