Coversin in paroxysmal nocturnal haemoglobinuria (PNH) in patients with resistance to eculizumab due to complement C5 polymorphisms (VIP study 578)

Published: 10-12-2015
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To determine the safety and efficacy of coversin in the treatment of patients with PNH resistant to eculizumab.

Ethical review	Approved WMO
Status	Recruitment stopped
Health condition type	Haemolyses and related conditions
Study type	Interventional

Summary

ID

NL-OMON42383

Source
ToetsingOnline

Brief title
Coversin in PNH patients with resistance to eculizumab

Condition

- Haemolyses and related conditions

Synonym
acquired hemolytic anemia, PNH

Research involving
Human

Sponsors and support

Primary sponsor: Akari Therapeutics Plc
Source(s) of monetary or material Support: Akari Therapeutics Plc

Intervention

Keyword: Coversin, Eculizumab-resistance, PNH

Outcome measures

Primary outcome

Significant reduction in mean serum LDH from Day 0 to Day 28

Secondary outcome

Change in LDH from Day 0 (pre-dose) at monthly intervals after Day 28

Change in proportion of PNH clone Day 0 * Day 90

Change in mean Hb Day 0 * Day 90

Change in mean Hp Day 0 * Day 90

Change in FACIT score Day 0 * Day 28 - Day 90 - Day 180

Change in EORTC QLQ C30 score Day 0 * Day 28 - Day 90 * Day 180

Study description

Background summary

PNH is a serious acquired blood disorder in which the own blood cells are not

protected against complement. Under the influence of activated complement, the blood cells are lysed with severe disease symptoms as a result.

The only registered agent for the treatment of PNH is eculizumab (Soliris). Eculizumab acts by binding complement factor C5 that is circulating in the blood and thus prevents activation of the complement. The blood cells survive and the disease symptoms are reduced.

A small number of PNH patients have a polymorphism in C5 which prevents eculizumab from binding to C5. Eculizumab does not work in these patients.

Coversin is a new agent that also binds complement factor C5, but at a different part of the C5 protein compared to eculizumab. In the laboratory it has been shown that coversin binding is not influenced by the C5 polymorphism. Coversin inhibits complement activation in a similar way as eculizumab does.

Coversin has been tested in healthy volunteers and administration of coversin was shown to be safe. The new product is now being developed for the treatment of PNH and in particular of PNH patients who are resistant to eculizumab as a result of a C5 polymorphism.

Study objective

To determine the safety and efficacy of coversin in the treatment of patients with PNH resistant to eculizumab.

Study design

Open label, non-comparative

Intervention

Daily subcutanous administration of coversin.

Study burden and risks

While using complement inhibitors, patients should be constantly alert for meningitis symptoms (also applies to standard treatment with eculizumab).

Quality of life questionnaires have to be completed at start, after 28 days, after three months and after six months.

Patients have to use adequate contraceptive precautions.

During the first 6 months, control visits will take place more often than usual. Appr. 10-12 extra visits. During all visits blood samples will be

collected

At the start of the treatment, patients are hospitalized for at least two nights (pharmacokinetics).

Daily self-injections subcutaneously. Upon initiation of treatment, patients will be instructed how to inject thelselves subcutaneously. If treatment is successful, the daily subcutaneous administration continues indefinately.

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

Patients with known paroxysmal nocturnal haemoglobinuria (PNH);LDH *1.5 ULN;Resistance to eculizumab proven by both a recognised C5 polymorphism on genetic screening and

complement inhibition on CH50 ELISA of <100% at concentrations of eculizumab in excess of 50µg/mL;Willing to self-inject Coversin daily or to receive daily subcutaneous injections by a home nurse or in a doctor*s office or hospital clinic;Willing to receive appropriate prophylaxis against Neisseria infection by either or both immunisation or continuous or intermittent antibiotics;Males or females taking adequate contraceptive precautions if of childbearing potential, 18 * 80 years of age;Body weight * 50kg and * 100kg ;The patient has provided written informed consent.;Willing to avoid prohibited medications for duration of study (see Exclusion Criteria);Must be counselled regarding the possible reproductive risks of using Coversin and be advised to use an adequate method of contraception pending further data on reproductive toxicology.

Exclusion criteria

Body weight <50kg or > 100kg ;Pregnancy (females);Use of tizanidine (if on ciprofloxacin);Use of eculizumab (Soliris®) should be discontinued before coversin therapy is commenced. Ideally this should be 2 or more weeks before. ;Known allergy to ticks or severe reaction to arthropod venom (e.g. bee or wasp venom);Failure to satisfy the PI off fitness to participate for any other reason

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):	28-01-2016
Enrollment:	1
Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	Coversin (rVA576)
Generic name:	Coversin (rVA576)

Ethics review

Approved WMO Date:	10-12-2015
Application type:	First submission
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)
Approved WMO Date:	13-01-2016
Application type:	First submission
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)
Approved WMO Date:	25-02-2016
Application type:	Amendment
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)
Approved WMO Date:	06-04-2016
Application type:	Amendment
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)
Approved WMO Date:	15-11-2016
Application type:	Amendment
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)
Approved WMO Date:	19-01-2017
Application type:	Amendment
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)
Approved WMO Date:	02-05-2017
Application type:	Amendment
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)

Approved WMO Date:	06-06-2017
Application type:	Amendment
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)
Approved WMO Date:	07-08-2017
Application type:	Amendment
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)
Approved WMO Date:	15-08-2017
Application type:	Amendment
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)
Approved WMO Date:	23-08-2017
Application type:	Amendment
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)
Approved WMO Date:	20-09-2017
Application type:	Amendment
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)
Approved WMO Date:	08-11-2017
Application type:	Amendment
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)
Approved WMO Date:	16-01-2018
Application type:	Amendment
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)
Approved WMO Date:	26-02-2018
Application type:	Amendment
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)
Approved WMO Date:	26-09-2018
Application type:	Amendment
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)

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	EUCTR2015-003778-34-NL
ClinicalTrials.gov	NCT02591862
CCMO	NL54988.091.15