rVA576 (Coversin) Long Term Safety and Efficacy Surveillance Study

Published: 16-11-2017
Last updated: 04-01-2025

* The purpose of this study is to to determine the safety profile of long-termCoversin treatment.* To observe the long term safety and efficacy of Coversin over periods in excess of 6 months* To assess the long term patient acceptability of Coversin...

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

Summary

ID

NL-OMON48556

Source
ToetsingOnline

Brief title
Conserve study

Condition

- Haemolyses and related conditions

Synonym
PNH (acquired heolitic anemia) and aHUS (disruptionof the complement system)

Research involving
Human

Sponsors and support

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

Intervention

Keyword: aHUS, Coversin, Long-term safety/efficacy, PNH

Outcome measures

Primary outcome

Primary Safety and Efficacy Endpoints:

Long term safety of rVA576 (Coversin) as assessed by SAEs, AEs, vital signs, immunogenicity assessments, results of appropriate standard laboratory tests (clinical chemistry, haematology, coagulation, urinalysis, and ADA) and results of electrocardiograms (ECGs).

Secondary outcome

PNH Secondary:

1.Proportion of subjects with thrombotic and haemolytic event-free status during each 3 month time period since the start of the study.

2.Time to thrombotic or haemolytic event since the start of the study.

3.Proportion of subjects who require PRBC transfusion during each 3-month period since the start of the study and over the entire period of the study, with analysis of i) subjects who were transfusion-dependent when they started receiving rVA576 (Coversin), ii) subjects who weretransfusion-independent when they started receiving rVA576 (Coversin), and iii) all subjects, and further stratification of these proportions by a) patients who were complement inhibitor-naïve prior to treatment with rVA576 (Coversin), and b) patients who received treatment with another complement inhibitor before switching to rVA576 (Coversin).

4.Time to first transfusion since joining the study.

5.Proportion of subjects with no adverse change in overall scores of Quality of Life using the EORTC QLQ-C30, the EQ-5D-5L and FACIT-F instruments at each 3-month time period since the start of the study.

6.Proportion of subjects with serum Lactate Dehydrogenase (LDH) <1.8, >1.8 to 2.4, >2.4 to 3, and >3 times the upper limit of normal (ULN) at each 3-month time period since the start of the study.

7.Proportion of subjects with median serum Lactate Dehydrogenase (LDH) <1.8, >1.8 to 2.4, >2.4 to 3, and >3 times the upper limit of normal (ULN) over the entire duration of the study.

8.Proportion of transfusion-independent subjects at each 3-month time point, with haemoglobin (g/L) above the baseline haemoglobin value they had at the start of the trial from which they entered CONSERVE. With baseline for CAPSTONE (AK580) defined as the haemoglobin value at which they received their qualifying transfusion (the set point) or for COBALT (AK579) and CONSENT (AK578) the haemoglobin value at which patients entered those trials. With separate analysis of subjects who were i) transfusion-independent prior to receiving rVA576 (Coversin) and remain transfusion-independent and ii) transfusion-dependent prior to receiving rVA576 (Coversin).

9.Proportion of transfusion-independent subjects over the entire duration of the study with mean haemoglobin (g/L) above the baseline haemoglobin value they had at the start of the trial from which they entered CONSERVE. With baseline haemoglobin defined as for the previous secondary endpoint (#8). With separate analysis of subjects who were

i) transfusion-independent prior to receiving rVA576

(Coversin) and remain transfusion-independent and ii) transfusion-dependent

prior to receiving rVA576 (Coversin).

10.Proportion of patients experiencing Major Adverse Vascular Events (MAVE)

over the entire period of the study.

11.Time to first Major Adverse Vascular Event (MAVE) for each subject since

joining the study.

12.Number of Major Adverse Vascular Events (MAVE) over the entire period of the

study.

aHUS Secondary:

aHUS Secondary:

1.Proportion of subjects with Normal Platelet count [defined as Platelet count

* 150 x109/L] at each 3-month time point since the start of the

study and over the entire period of the study.

2.Proportion of subjects entering study with complete TMA response who continue

to exhibit complete TMA response with preserved renal

function, defined as hematologic normalization (platelet count *150 X 109/L and

LDH * ULN) and preservation of kidney function (<25%

increase in SCr from baseline of previous study), during each 3-month time

period since the start of this study.

3.Proportion of subjects with complete TMA response with improved renal

function defined as normalization of haematological parameters

(normalisation of platelet count and LDH*ULN) and * 25% decrease in SCr from

baseline of previous study during each 3-month time period

since the start of the study.

4.Proportion of subjects who exhibit haematological normalisation (platelet

count *150 X 109/L and LDH * ULN) during each 3-month time

period since the start of this study.

5.Proportion of subjects with improvement in renal function defined as a

decrease in SCr over three consecutive measurements from baseline of

previous study without the need for dialysis even if not within the normal

range.

6.Proportion of subjects who are TMA event-free during each 3-month time period

since the start of the study.

7.Platelet mean count change at each 3-month time period since the start of the

study.

8.Quality of Life measures from baseline at 3 monthly intervals up to the end

of study in FACIT-F instrument and the EQ-5D-5L instrument.

Additional Endpoints:

*PK and PD parameters during treatment.

Study description

Background summary

PNH and aHUS are serious acquired blood diseases in which a person's own blood cells are not protected against a part of our body*s immune system called the complement system.
Coversin is a small protein that inhibits one of the complement factors in the complement system that is responsible for damaging your own cells without affecting other parts of the complement system. It may help to reduce the

damage to your blood cells that occurs in PNH and aHUS and may reduce the symptoms of the diseases.

Study objective

* The purpose of this study is to to determine the safety profile of long-termCoversin treatment.

* To observe the long term safety and efficacy of Coversin over periods in excess of 6 months

* To assess the long term patient acceptability of Coversin using the EORTC QLQ-C30 and the EQ-5D-5L instruments and the Sponsor non validated questionnaire

* To observe the changes, if any, in the production of anti-drug antibodies (ADA) and whether such antibodies are, or become, neutralising

* To assess the effects, if any, on any changes in formulation or drug delivery that may be introduced during the study period

Study design

Open-label, non-comparative, observational.

Intervention

Daily subcutanous administration of Coversin.

Study burden and risks

While using complement inhibitor, patients should be constantly alert for meningitis symptoms.

Quality of life questionnaries have to be completed at start, after 3, 6, 9,12,18, 24, 30, 36 months and at the end of study.

Patients have to use adequeate contraceptive precautions.

Pregnancy test for women of childbearing potential must be done monthly and till 90 days after the last dose.

During all visits blood samples will be collected.

Daily self-injections subcutaneously. It treatment is successful, the daily subcutaneous adminstration 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

1) Patients 18 years and above successfully treated with rVA576 (Coversin) under other Akari clinical trial protocols and wish to remain on rVA576 (Coversin) at the conclusion of that trial
2) In the opinion of the treating responsible clinician patient is receiving clinical benefit from continued treatment with study drug.
3) Evidence of sustained total complement inhibition by CH50 assay
4) Women of childbearing potential (WOCBP) must agree to use effective contraception consistently throughout the study and have a negative pregnancy test at screening. Women are considered post-menopausal and not of child-bearing potential if they have had 12 months of amenorrhea and considered sterile if they have had surgical bilateral oophorectomy (with or without hysterectomy) or tubal ligation at least six weeks previously.
5) Males with a childbearing potential partner must agree to use effective contraception consistently OR have had a vasectomy.

6) Weight >50kg.
7) Received appropriate prophylaxis against Neisseria meningitidis infection, by both immunisation and continuous or intermittent antibiotics.
8) Patient is willing to give voluntary written informed consent.
9) The patient is willing in the process of preparation and self administration of the study drug.

Exclusion criteria

1) Patient experienced any safety event in the previous study protocol, which puts the patient at unacceptable risk in the current protocol in the clinical judgement of the investigator and sponsor.
2) Patient is unwilling to complete the Quaity of Life instruments and diary card
3) Evidence of active meningococcal infection (swab testing not required)
4) On concurrent treatment with another complement inhibitor
5) If female, the subject is pregnant or lactating or intending to become pregnant before, during, or within 90 days after last dose; or intending to donate ova during such period.
6) If male, the subject intends to donate sperm during this study or for 90 days after last dose.
7) Failure to satisfy the Investigator of fitness to participate for any reason or condition which, in the opinion of the investigator, cold increase the subject's risk from participating in the study or confound
the outcome of the study.
8) Use of prohibited medication (e.g. eculizumab (Soliris®)
9) The subject has a history of drug abuse (defined as any illicit drug use) or a history of alcohol abuse within one year prior to screening.
10) Participation in other clinical trials with investigational product.

Study design

Design

Study phase:	3
Study type:	Interventional
Masking:	Open (masking not used)
Control:	Uncontrolled
Primary purpose:	Treatment

Recruitment

NL

Recruitment status:	Completed
Start date (anticipated):	20-03-2018
Enrollment:	1
Type:	Actual

Medical products/devices used

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

Ethics review

Approved WMO Date:	16-11-2017
Application type:	First submission
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)
Approved WMO Date:	23-01-2018
Application type:	Amendment
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)
Approved WMO Date:	14-02-2018
Application type:	First submission
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)
Approved WMO Date:	14-06-2018
Application type:	Amendment
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)
Approved WMO Date:	09-08-2018
Application type:	Amendment
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)
Approved WMO	

Date:	10-09-2018
Application type:	Amendment
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)
Approved WMO Date:	13-03-2019
Application type:	Amendment
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)
Approved WMO Date:	19-03-2019
Application type:	Amendment
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)
Approved WMO Date:	06-05-2019
Application type:	Amendment
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)
Approved WMO Date:	16-05-2019
Application type:	Amendment
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)
Approved WMO Date:	22-08-2019
Application type:	Amendment
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)
Approved WMO Date:	28-08-2019
Application type:	Amendment
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)
Approved WMO Date:	03-12-2019
Application type:	Amendment
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)
Approved WMO Date:	06-01-2020
Application type:	Amendment
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)
Approved WMO	

Date:	17-03-2020
Application type:	Amendment
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)
Approved WMO Date:	18-03-2020
Application type:	Amendment
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)
Approved WMO Date:	26-05-2020
Application type:	Amendment
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)
Approved WMO Date:	16-06-2020
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	EUCTR2016-004129-18-NL
CCMO	NL61226.091.17

Study results

Date completed:	09-06-2020

Results posted:	02-07-2021
Actual enrolment:	1

Summary results
Trial ended prematurely

First publication
02-07-2021