An open-label, single-arm, multicenter study to evaluate the efficacy and safety of caplacizumab and immunosuppressive therapy without first-line therapeutic plasma exchange in adults with immune-mediated thrombotic thrombocytopenic purpura

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This study has been transitioned to CTIS with ID 2024-513262-19-00 check the CTIS register for the current data. Primary objective:- To evaluate the efficacy of caplacizumab in combination with immunosuppressive therapy (IST) without therapeutic...

Ethical review	Approved WMO
Status	Recruiting
Health condition type	Platelet disorders
Study type	Interventional

Summary

ID

NL-OMON53928

Source
ToetsingOnline

Brief title
EFC16521 MAYARI

Condition

- Platelet disorders

Synonym
acquired TTP, immune-mediated TTP

Research involving
Human

Sponsors and support

Primary sponsor: Sanofi BV
Source(s) of monetary or material Support: Sanofi

Intervention

Keyword: Caplacizumab, Efficacy, Safety, Thrombotic thrombocytopenic purpura

Outcome measures

Primary outcome

- Proportion of participants achieving Remission without requiring TPE.

Secondary outcome

- Proportion of participants achieving Remission

- Proportion of participants who require TPE

- The occurrence of adverse events (AEs), serious adverse events (SAEs), and

adverse events of special interest (AESIs)

- Proportion of participants achieving Clinical Response

- Time to platelet count response

- Proportion of participants refractory to therapy

- Proportion of participants with TTP-related death

- Proportion of participants with a clinical exacerbation of iTTP

- Proportion of participants with a clinical relapse of iTTP

Study description

Background summary

Caplacizumab is currently indicated for the treatment of patients with aTTP (also known as iTTP), in combination with TPE and IST. Although TPE has been considered a mainstay of iTTP treatment for several decades, it is a burdensome and invasive procedure for patients, and is associated with significant complications, and a substantial number of patients remains at risk for morbidity and mortality when treated with TPE and immunosuppression alone. Based on pathophysiology of iTTP and mechanism of action of caplacizumab, it is hypothesized that caplacizumab and immunosuppression without initial TPE may be safe and effective as first-line therapy for iTTP. This concept is supported by pre-clinical data (1) as well as emerging real-world clinical evidence (2). Hence, the Sponsor is proposing an open-label, single-arm study to support the hypothesis that caplacizumab and IST can be effectively and safely administered to treat either first or recurrent iTTP episode in adults without first-line TPE, which would be added only if clinically indicated. A successful study will establish a new treatment paradigm and a new standard of care for treatment of iTTP for the use of caplacizumab and immunosuppression without first-line TPE.

Study objective

This study has been transitioned to CTIS with ID 2024-513262-19-00 check the CTIS register for the current data.

Primary objective:
- To evaluate the efficacy of caplacizumab in combination with immunosuppressive therapy (IST) without therapeutic plasma exchange (TPE) in adults with immune mediated thrombotic thrombocytopenic purpura (iTTP)

Secondary objectives:
To evaluate:
- the need for therapeutic plasma exchange in adult participants with an episode of iTTP treated with caplacizumab and IST
- the safety of caplacizumab in combination with IST without 1st line TPE in adults with iTTP
- the effect of treatment with caplacizumab and IST without 1st line TPE on clinical response
- the effect of treatment with caplacizumab and IST without 1st line TPE on restoring platelet counts
- the effect of treatment with caplacizumab and IST without 1st line TPE on refractory disease
- the effect of treatment with caplacizumab and IST without 1st line TPE on clinically relevant iTTP-related events consisting of iTTP-related mortality
- the effect of treatment with caplacizumab and IST without 1st line TPE on clinically relevant iTTP-related events consisting of exacerbation of iTTP
- the effect of treatment with caplacizumab and IST without 1st-line TPE on

clinically relevant iTTP-related events consisting of relapse of iTTP

Study design

Adult participants with clinical diagnosis of initial or recurrent iTTP and a French TMA score of 1 or 2 will be enrolled from sites that are able to obtain baseline of a disintegrin and metalloproteinase with a thrombospondin type 1 motif13 (ADAMTS13) activity test results within 48 hours. Please see Section 4 and Section 5 for study enrollment criteria and eligibility assessments. After confirmation of eligibility to study participation, participants will receive initial treatment consisting of caplacizumab and IST (corticosteroids ± anti-CD20 antibody [rituximab or biosimilar]) without first-line TPE. However, participants may start TPE later, if it is determined that there is lack of adequate response to treatment after the first 24 hours or if there is any clinical deterioration at any time during the study (please see Section 4.1 for additional details). It is expected that the participant is hospitalized when the treatment is started, and the duration of initial hospitalization may vary based on clinical condition of the individual participant. The maximum duration allowed for caplacizumab treatment will be 12 weeks for the presenting episode. The post-treatment follow-up period will be 12 weeks. In case of clinical exacerbation and clinical relapse, please see Section 4 for additional details. This study incorporates the revised consensus outcome definitions for iTTP published by the International Working Group for thrombotic thrombocytopenic purpura (TTP) that reflect current iTTP management (3). A Data Monitoring Committee (DMC) will be appointed to monitor the safety and scientific integrity of this study.

Intervention

Administration of caplacizumab combined with IST, without TPE (standard of care is inclusive of TPE)

Study burden and risks

The patients follow a lot of the normal procedures when treated for TTP: they are hospitalized for their condition and will not stay in the hospital longer than they normally would. The participating PI indicated that day 3 and 4 ECGs are not normally done and the blood sampling done for central lab evaluation and PK/PD/ADA/ADAMTS13 antibodies are extra. Most of these punctions are done together with local lab sampling, which is as per normal follow-up, according to the PI. This means that no extra needle stick is required to do these samples.

Risks related to the caplacizumab treatment are as per normal standard of care treatment, which also includes treatment with caplacizumab.

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

- Participants with a clinical diagnosis of iTTP (initial or recurrent), which includes thrombocytopenia, microangiopathic hemolytic anemia (eg, presence of schistocytes in peripheral blood smear) and relatively preserved renal function. The iTTP diagnosis should be confirmed by ADAMTS13 testing within 48 hours (2 days)

- Participants with a clinical diagnosis of iTTP and a French TMA score of 1 or 2

- A female participant is eligible to participate if she is not pregnant or breastfeeding, and one of the following conditions applies:
Is a woman of nonchildbearing potential (WONCBP)

OR
- Is a woman of childbearing potential (WOCBP) and agrees to use an acceptable contraceptive method during the overall treatment period and for at least 2 months after the last study drug administration

- Male participants with female partners of childbearing potential must agree to follow the contraceptive guidance as per protocol during the overall treatment period and for at least 2 months after last study drug administration

Exclusion criteria

- Platelet count >=100 × 109/L.
- Serum creatinine level >2.26 mg/dL (200 µmol/L) in case platelet count is >30 × 109/L (to exclude possible cases of atypical HUS)

Known other causes of thrombocytopenia including but not limited to:
• Clinical evidence of enteric infection with E. coli 0157 or related organism
• Atypical HUS
• Hematopoietic stem cell, bone marrow or solid organ transplantation-associated thrombotic microangiopathy
• Known or suspected sepsis
• Diagnosis of disseminated intravascular coagulation

- Congenital TTP (known at the time of study entry)
- Clinically significant active bleeding or known co-morbidities associated with high risk of bleeding (excluding thrombocytopenia)
- Inherited or acquired coagulation disorders
- Malignant arterial hypertension
- Participants requiring or expected to require invasive procedures immediately (eg, stroke requiring thrombolytic therapy, those who need mechanical ventilation, etc.)
- Those presenting with severe neurological or severe cardiac disease
- Clinical condition other than that associated with TTP, with life expectancy <6 months, such as end-stage malignancy.

- Known chronic treatment with anticoagulants and anti-platelet drugs that cannot be stopped (interrupted) safely, including but not limited to:
• vitamin K antagonists.
• direct-acting oral anticoagulants.
• heparin or low molecular weight heparin (LMWH).
• non-steroidal anti-inflammatory molecules other than acetyl salicylic acid.

- Participants who were previously enrolled in this clinical study (study EFC16521)
- Participants who received an investigational drug, or device, other than

caplacizumab, within 30 days of anticipated IMP administration or 5 half-lives of the previous investigational drug, whichever is longer.
- Positive result on COVID test.

Study design

Design

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

Recruitment

NL

Recruitment status:	Recruiting
Start date (anticipated):	04-12-2023
Enrollment:	2
Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	Cablivi
Generic name:	caplacizumab
Registration:	Yes - NL intended use

Ethics review

Approved WMO

Date:	03-08-2022
Application type:	First submission
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)

Approved WMO

Date:	18-10-2022
Application type:	First submission
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	28-12-2022
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	04-01-2023
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	10-02-2023
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	04-03-2023
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	12-07-2023
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	19-07-2023
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)

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
Other	2022-001177-31
EU-CTR	CTIS2024-513262-19-00
EudraCT	EUCTR2022-001177-31-NL
CCMO	NL81233.100.22