The COMplement Prospective Evaluation of Thrombotic microangiopathy on Endothelium (COMPETE) Study

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To evaluate the prevalence of C-TMA in patients presenting with TMA, either with coexisting conditions or not. Furthermore, (i) the diagnostic performance of an in-house developed ex vivo test, (ii) dynamics of complement measures during follow-up,...

Ethical review	Approved WMO
Status	Recruiting
Health condition type	Haemolyses and related conditions
Study type	Observational non invasive

Summary

ID

NL-OMON54987

Source
ToetsingOnline

Brief title
COMPETE

Condition

- Haemolyses and related conditions
- Nephropathies
- Embolism and thrombosis

Synonym
atypical hemolytic uremic syndrome, Thrombotic microangiopathy

Research involving
Human

Sponsors and support

Primary sponsor: Medisch Universitair Ziekenhuis Maastricht

Source(s) of monetary or material Support: Alexion Pharmaceuticals,Alexion Pharmaceuticals Inc.

Intervention

Keyword: Complement, Hemolytic uremic syndrome (HUS), Kidney biopsie, Thrombotic microangiopathy (TMA)

Outcome measures

Primary outcome

The prevalence of C-TMA in patients presenting with TMA, either with coexisting conditions or not.

Secondary outcome

The secondary parameters are based on the clinical course of disease, including hematologic and renal response, refractory TMA, renal recovery, chronic kidney disease, end-stage kidney disease, and death.

Study description

Background summary

Thrombotic microangiopathy (TMA) can occur on the background of complement dysregulation, i.e., complement-mediated TMA (C-TMA). According to HUS International*s nomenclature, complement dysregulation should be considered in patients not presenting with coexisting conditions linked to TMA. Provocative studies, however, demonstrated that complement dysregulation can be the key causative factor of poor kidney outcomes in patients presenting with coexisting conditions, having impact on treatment and prognosis.

Study objective

To evaluate the prevalence of C-TMA in patients presenting with TMA, either with coexisting conditions or not. Furthermore, (i) the diagnostic performance of an in-house developed ex vivo test, (ii) dynamics of complement measures during follow-up, and (iii) clinical, pathologic, and genetic correlates will be assessed.

Study design

Single-center, prospective, observational cohort study.

Study burden and risks

Patients will be treated and monitored according to routine clinical practice and therefore, the burden is considered extremely low. The correct recognition of patients with C-TMA, however, is of utmost importance given the safety and efficacy of therapeutic complement inhibition in patients with C-TMA. Thus, the current study may safe kidneys in patients with TMA and, in particular, those presenting with coexisting conditions.

Contacts

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Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Adults (18-64 years)

Inclusion criteria

In order to be eligible to participate in this study, a subject must meet all of the following criteria:
- Males or females at least 18 years of age;
- Have acute kidney injury, defined as estimated GFR <45 mL/min/1.73m2;
- Have documented TMA either on peripheral blood, defined as Coombs negative microangiopathic hemolytic anemia (hematocrit <30%, hemoglobin <6.5 mmol/L [<10 g/dL], lactate dehydrogenase >500 U/L, and either schistocytes on peripheral blood smear or undetectable haptoglobin), and platelets <150,000 per µL, or kidney biopsy;
- Have primary atypical HUS or a coexisting condition linked to C-TMA:
-- Hypertensive emergency, defined as SBP/DBP of >180/120 mmHg and impending organ damage secondary to hypertension (at least one of the following: neurologic disease, hypertensive retinopathy grade III and/or IV, left ventricular hypertrophy); OR
-- Pregnancy, including 12 weeks postpartum; OR
-- Kidney donor recipient; OR
-- Systemic auto-immune disease associated with TMA, including systemic sclerosis, systemic lupus erythematosus, anti-phospholipid syndrome;
- Have the ability to understand the requirements of the study, provide written informed consent, and comply with the study protocol procedures.

Exclusion criteria

A potential subject who meets any of the following criteria will be excluded from participation in this study:
- Have secondary causes of hypertensive emergency, including renovascular hypertension, Cushing syndrome, aldosteronism, pheochromocytoma, thyroid disease;
- Have a nephropathy not related to thrombosis on kidney biopsy;
- Have ADAMTS13 deficiency, defined as ADAMTS13 activity <10%;
- Have a positive stool culture for Shiga toxin producing bacteria;
- Have positive serologic test for viral infections, including HIV and CMV;
- Have a history of malignant disease, excluding non-melanoma skin cancer;
- Have a history of bone marrow or solid organ transplantation;
- Received at least one of the following agents: chemotherapeutics, calcineurin inhibitors, sirolimus, anti-VEGF agents;
- Have a history of recent past exposure to illicit drug(s).

Study design

Design

Study type: Observational non invasive

Masking:	Open (masking not used)
Control:	Uncontrolled
Primary purpose:	Basic science

Recruitment

NL

Recruitment status:	Recruiting
Start date (anticipated):	18-08-2021
Enrollment:	42
Type:	Actual

Ethics review

Approved WMO

Date:	11-08-2021
Application type:	First submission
Review commission:	METC academisch ziekenhuis Maastricht/Universiteit Maastricht, METC azM/UM (Maastricht)

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
ClinicalTrials.gov	NCT04745195
CCMO	NL74928.068.20