A RANDOMIZED, OPEN-LABEL, MULTICENTER TRIAL TO DETERMINE SAFETY AND EFFICACY OF ECULIZUMAB IN THE PREVENTION OF ANTIBODY MEDIATED REJECTION (AMR) IN LIVING DONOR KIDNEY TRANSPLANT RECIPIENTS REQUIRING DESENSITIZATION THERAPY

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The objective of the study is to evaluate the safety and efficacy of eculizumab to prevent AMR in sensitized recipients of living donor kidney transplants requiring desensitization therapy.

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

Summary

ID

NL-OMON39259

Source
ToetsingOnline

Brief title
C10-001, Prevention AMR with eculizimab for kidney transplant recipients

Condition

- Immune disorders NEC
- Nephropathies

Synonym

antibody mediated rejection after kidney transplant, Kidney transplant rejection

Research involving
Human

Sponsors and support

Primary sponsor: Alexion Pharmaceuticals
Source(s) of monetary or material Support: Alexion Pharmaceuticals;Inc

Intervention

Keyword: Antibody Mediated Rejection (AMR), Eculizumab, Kidney transplant, Living donor

Outcome measures

Primary outcome

To evaluate the safety and potential efficacy of eculizumab to prevent AMR in

sensitized recipients of living donor kidney transplants requiring

desensitization therapy

Secondary outcome

Cumulative incidence of AMR that occurs between Week 9 and Month 12

post-transplantation

Study description

Background summary

Over 25% of kidney transplant candidates have antibodies (are sensitized) to potential organ donors. As a result, antibody mediated rejection (AMR) has emerged as a significant clinical problem. Currently, the options to prevent AMR are limited and marginally successful. No products are approved for the treatment of AMR. Eculizumab, an inhibitor of C5, has been shown in hypothesis generating studies to successfully reduce the incidence of AMR following kidney transplantation of sensitized recipients.

Study objective

The objective of the study is to evaluate the safety and efficacy of eculizumab

to prevent AMR in sensitized recipients of living donor kidney transplants requiring desensitization therapy.

Study design

It is a randomized, multicenter, open-label, Phase II, two-arm parallel study.

Intervention

Patients will receive one dose of eculizumab approximately one hour prior to reperfusion of the allograft and will be treated with eculizumab for 9 weeks post-transplantation OR will be treated post-transplantation with the transplant center*s SOC for prophylaxis for AMR (control arm).

Study burden and risks

In total over 3 years the patients will undergo the following procedures other than the Standard Of Care:
Vaccination for Meningitides: 2x (in case the subject received a vaccination before the enrolment only a booster dose is required)
Kidney biopsy: 5x
Blood drawels: 8x (only Eculizumab-arm)
For the Eculizumab treatment arm: 9x infusion with IP
All other procedures are also performed according to the Standard Of Care. 29 blood drawels will also be performed according the Standard Of Care, however the blood amount withdrawn for the study can be slightly more (PK samples). The same amount of hospital visits will be conducted as the Standard of Care, however the spread of the visits is different.
Possible adverse effects of Eculizumab and performed procedures are:
Adverse effects Eculizumab: headache, higher risk of severe meningococcal infections; thrombocytopenia, stomach-ache, constipation, vomiting, diarrhoea, dyspepsia, nausea, chest pain, shivering, infusion related reaction, oedema, pyrexia, fatigue, herpes simplex, nasopharyngitis, viral infection, gastroenteritis, bronchitis, sepsis, septic shock, meningococcal sepsis, muscle pain, back and neck pain, pain in the limbs or joints (arms and legs), muscle spasm, dizziness, dysgeusia, paresthesia, depression, dysuria, spontaneous erection of the penis, infection of the upper airways, urinary tract infection, coughing, pharyngolaryngeal pain, nasal congestion, pruritus, rash, alopecia, dry skin and hot flashes;
Possible adverse effects of the IV katheter and blood-sampling: bleedings, bruises, swelling, clots in the vein, leakage of medication or solution in the surrounding tissue and possibly infection at the insertion site;
Possible adverse effects for the vaccination: temporary local pain or infection at the administration site;
Possible adverse effects for PP: dizziness, nausea, numb feeling, tingling or a light-headedness, mild allergic reaction resulting in fever, shivering and

rash, bacterial infection (especially when a central catheter is used), cramps, numb feeling, bleeding after removal of the clotting drug;
Possible adverse effects for IVIg: functional disorder of or damage to the kidneys or liver, hypotension, headaches, fatigue, shivering, back pain, leg cramps, light-headedness, fever, urticaria, hot flashes, nausea or vomiting, haemolysis, transfusion related lung injury, thrombotic incidents, aseptic meningitis syndrome and acute or severe kidney failure;
Possible adverse effects of the kidney biopsie: allergic reaction to the anaesthetic, pain discomfort bleeding or infections at or near the biopsy site, bleeding from the kidney, hematuria, damage to and loss of the kidney transplant, death, perforation of internal organs (gallbladder, lung, intestines or kidney);

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

- Male or female patients * 18 years old;
- Patients with Stage IV or Stage V chronic kidney disease who will receive a kidney transplant from a living donor to whom they are sensitized and require desensitization prior to transplantation;
- Patients must be willing and able to give written informed consent.

Exclusion criteria

- Has received treatment with eculizumab at any time prior to enrolling in this study;
- ABO incompatible with living donor.

Study design

Design

Study phase:	2
Study type:	Interventional
Intervention model:	Parallel
Allocation:	Randomized controlled trial
Masking:	Open (masking not used)
Control:	Active
Primary purpose:	Prevention

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	10-07-2012
Enrollment:	6
Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	Soliris

Generic name:	Eculizumab
Registration:	Yes - NL outside intended use

Ethics review

Approved WMO Date:	22-11-2011
Application type:	First submission
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	21-06-2012
Application type:	First submission
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	17-09-2012
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	20-09-2012
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	13-11-2012
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	20-12-2012
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	21-02-2013

Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	09-04-2013
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	05-06-2013
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	02-10-2013
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	11-10-2013
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	31-07-2014
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	16-10-2014
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	16-09-2015
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)

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	EUCTR2010-019630-28-NL
ClinicalTrials.gov	NCT01399593
CCMO	NL37145.078.11