Alkaline Phosphatase to prevent ischemia reperfusion injury in living kidney transplantation

Published: 28-08-2018
Last updated: 12-04-2024

To study the potential of alkaline phosphatase to protect against ischemia-reperfusion injury in living donor kidney transplantation.

Ethical review	Approved WMO
Status	Recruitment stopped
Health condition type	Renal disorders (excl nephropathies)
Study type	Interventional

Summary

ID

NL-OMON50363

Source
ToetsingOnline

Brief title
APhIRI

Condition

- Renal disorders (excl nephropathies)
- Renal and urinary tract therapeutic procedures

Synonym
Ischemia reperfusion injury in kidney transplantation

Research involving
Human

Sponsors and support

Primary sponsor: Vrije Universiteit Medisch Centrum
Source(s) of monetary or material Support: Alloksys Life Sciences B.V.

Intervention

Keyword: Alkaline phosphatase, Ischemia-reperfusion injury, Kidney transplantation

Outcome measures

Primary outcome

- Graft function 12 months after kidney transplantation (eGFR and iohexol

clearance)

- Safety outcome:% infusion related reactions/ side effects

Secondary outcome

- eGFR and creatinine clearance at 3 months

- *Rate of fall in creatinin* in the first 48 hours after transplantation

- Cytokine profiles in peripheral blood samples

- Urinary *kidney damage markers*: retinolbinding protein; KIM1; NGAL ; (assay

NephroCheck)

- Incidence of biopsy proven rejection

Study description

Background summary

- Ischemia Reperfusion Injury (IRI) after kidney transplantation is a distinct medical problem with no effective treatment options. IRI will compromise long-term renal outcome due to ischemic mediated inflammation. Alkaline phosphatase has the potential to attenuate the harmful immune response due to IRI.

Study objective

To study the potential of alkaline phosphatase to protect against ischemia-reperfusion injury in living donor kidney transplantation.

Study design

A double blind randomized, placebo controlled trial

Intervention

The intervention group will be treated with either alkaline phosphatase or placebo at the induction of transplantation, followed by continuous infusion for 24 hours. This treatment will be on top of *standard of care*.

Study burden and risks

- All participant will receive an iv access on their fore-arm for bolus and continuous infusion of the study agent/placebo. Standard of care medication will be administered via a different access (central venous catheter; standard of care).
- There is a small risk that this protein based drug will cause an allergic reaction. However, since the study drug is a bovine protein, all patients are already desensitized due to consumption of dietary bovine proteins.
- In terms of the immune response, the proposed effect of alkaline phosphatase is to dampen the immune response following ischemic injury.
- Veganists and strict vegetarians will be excluded from this trial
- No Alkaline Phosphatase related specific adverse effects were observed in the placebo controlled sepsis trial. In this study renal function improved in patients treated with alkaline phosphatase. The number and severity of adverse effects were similar between the two groups. In cardiothoracic trials the morbidity and immortality were increased in the placebo arm.

In the first 6 days after kidney transplantation, blood and urine samples are collected on different time points. A total amount of 60ml (6x10ml) of blood will be stored until analysis via a cental venous catheter (standard of care). At 12 months a iohexol clearance will be measured at the reseach facility. After injection of iohexol, blood will be drawn 8 times in 3 hours to measure iohexol levels and calculate the clearance.

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

- Age >18
- Recipients of a living donor kidney

Exclusion criteria

- Strict vegetarians or veganists. These individuals have higher potential risk to an allergic reaction to the infused bovine protein.
- History of allergy to bovine proteins
- Not standard immunosuppression at time of transplantation (see protocol)

Study design

Design

Study phase:	3
Study type:	Interventional

Intervention model:	Parallel
Allocation:	Randomized controlled trial
Masking:	Double blinded (masking used)
Control:	Placebo
Primary purpose:	Prevention

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	27-05-2019
Enrollment:	40
Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	bRESCAP
Generic name:	Alkalische fosfatase

Ethics review

Approved WMO Date:	28-08-2018
Application type:	First submission
Review commission:	METC Amsterdam UMC
Approved WMO Date:	20-12-2018
Application type:	First submission
Review commission:	METC Amsterdam UMC
Approved WMO Date:	11-12-2019
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	23-03-2020
Application type:	Amendment

Review commission:	METC Amsterdam UMC
Approved WMO Date:	28-07-2020
Application type:	Amendment
Review commission:	METC Amsterdam UMC

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	EUCTR2017-004737-85-NL
CCMO	NL64080.029.17