Alkaline Phosphatase as treatment of Ischemia Reperfusion Injury to prevent delayed graft function in deceased donor kidney transplantation

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This study has been transitioned to CTIS with ID 2024-515480-66-01 check the CTIS register for the current data. To attenuate the impact and duration of delayed graft funtion by dampening schemia reperfusion injury

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

Summary

ID

NL-OMON51462

Source
ToetsingOnline

Brief title
APhIRI II

Condition

- Renal disorders (excl nephropathies)

Synonym
acute kidney damage, acute kidney injury

Research involving
Human

Sponsors and support

Primary sponsor: Nefrologie

Source(s) of monetary or material Support: Alloksys Life Sciences,Health Holland BV,Health Holland BV en Allokys Life sciences BV

Intervention

Keyword: Alkaline phosphatase, DCD, Ischemia reperfusion damage, kidney transplantation

Outcome measures

Primary outcome

- Difference between treatment and placebo group in duration of delayed graft failure (DGF). DGF is defined as need for dialysis, excluding short sessions for hyperkalemia. DGF is defined as need for dialysis, excluding single sessions for hyperkalemia.

Secondary outcome

- Mean duration of hospitalization after kidney transplantation
- Incidence of persistent dialysis DGF (> 14 days)
- Incidence of DGF using functional and dialysis definition and a combination of the two
- Duration of DGF using functional and dialysis definition and a combination of the two
- Dall of serum creatinine in the first week after transplantation
- Kidney perfusion contrast renography at day 6
- Creatinine clearance at 3 months and 1 year after transplantation
- Proteinuria at 3 months and 1 year after transplantation
- Estimated renal glomerular filtration rate (eGFR) calculated with MDRD and the CKD-epi formula at 3 months and 1 year after transplantation

- Primary non-function (defined as dialysis dependency or creatinine

clearance <20ml/min at 3 months)

- Incidence of biopsy proven rejection within one year follow-up period

- All-cause mortality at day 28 and 90 and 1 year

Study description

Background summary

Delayed graft function (DGF) is a growing problem as more kidneys from deceased donors are used in transplantation procedures. DGF is caused in part by ischemia reperfusion injury (IRI). Alkaline phosphatase can dephosphorylate toxic adenosine triphosphate which is a big contributer to the extent of IRI. This could lead to less kidney damage and better graft function.

Study objective

This study has been transitioned to CTIS with ID 2024-515480-66-01 check the CTIS register for the current data.

To attenuate the impact and duration of delayed graft funtion by dampening schemia reperfusion injury

Study design

randomized double blind placebo-controlled trial

Intervention

30,000IU of bRESCAP or placebo

Study burden and risks

- Alkaline phosphatase has the potential to dampen the damage caused by impaired perfusion of the kidney. Supplementation could thereby possibly reduce the impact of ischemia reperfusion injury (IRI) in transplantation surgery.
- There are many pathophysiologic similarities between acute kidney injury (AKI) and kidney damage in transplantation surgery. IRI and harmful immune response play a large role in AKI of any cause, studying the effects of alkaline phosphatase in transplantation surgery could lead to the improvement

of therapeutic options for all AKI patients.
- Previous trials in sepsis AKI patients have shown a beneficial effect of exogenous alkaline phosphatase on kidney function and mortality. It is possible that this effect will be observed in transplant patients as well.
- Kidney transplant patients receive double intravenous access as standard of care, study medication can be administered over one of these access sites. Also, daily venipunctures are part of standard of care. Thus, there is no need for extra invasive procedures.
- There is a small risk that this protein-based drug will cause an allergic reaction. However, since the study drug made form bovine protein, all patients will be desensitized due to consumption of dietary bovine proteins. Vegans and strict vegetarians will be excluded from this trial.
- No specific adverse effects of exogenous AP were observed in previous trials and the number and severity of adverse effects were similar when compared to placebo.
- Addition to total fluid load will not be a problem since total extra infusion during the 3 day treatment period will be 150ml.

Contacts

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Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Adults (18-64 years)

Inclusion criteria

- Age > 18
- Recipients of a donor awaiting cardiac death on the intensive care (definition of a donor cardiac death type III according to the *Maastricht classification*)
- Written informed consent

Exclusion criteria

- Strict vegetarians or vegans
- History of allergy to bovine proteins

Study design

Design

Study phase:	2
Study type:	Interventional
Intervention model:	Parallel
Allocation:	Randomized controlled trial
Masking:	Double blinded (masking used)
Control:	Placebo
Primary purpose:	Treatment

Recruitment

NL

Recruitment status:	Recruiting
Start date (anticipated):	22-05-2023
Enrollment:	70
Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	bovine rescue alkaline phosphatase (bRESCAP)
Generic name:	bovine intestinal alkaline phosphatase

Ethics review

Approved WMO Date:	16-08-2022
Application type:	First submission
Review commission:	METC Amsterdam UMC
Approved WMO Date:	24-08-2022
Application type:	First submission
Review commission:	METC Amsterdam UMC
Approved WMO Date:	11-12-2023
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
EU-CTR	CTIS2024-515480-66-01

Register	ID
EudraCT	EUCTR2021-006767-14-NL
CCMO	NL79196.018.22