Pilot Study of BB3 to Improve Renal Function in Patients with Signs and Symptoms of Significant Renal Injury after Kidney Transplantation from Donors after Cardiac Death

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To evaluate the safety and activity of BB3 compared to placebo in improving renal function in the immediate post-transplant period in patientswho have received a DCD kidney transplantation.

Ethical review	Approved WMO
Status	Recruitment stopped
Health condition type	Nephropathies
Study type	Interventional

Summary

ID

NL-OMON39114

Source
ToetsingOnline

Brief title
BB3 in kidney transplantation

Condition

- Nephropathies
- Renal and urinary tract therapeutic procedures

Synonym
Delayed graft function

Research involving
Human

Sponsors and support

Primary sponsor: Angion Biomedica Corp.
Source(s) of monetary or material Support: Angion (sponsor)

Intervention

Keyword: Delayed graft function, kidney-injury, kidneytransplantation, non-heart-beating

Outcome measures

Primary outcome

The primary analysis to assess the activity of BB3 compared to placebo will be

the mean difference in creatinine clearance over time using

selective 24-hour urine collections from the transplanted kidney from the first

infusion of study drug through day 7 post-transplant. If a subject

has more than one creatinine value assessed during the 24-hour urine

collection, the mean of the values will be used for calculation of

creatinine clearance.

Secondary outcome

Safety

Pharmacokinetics

Incidence of delayed graft function

Mean urine output

number of acute rejections

hospitalstay

Study description

Background summary

Kidney transplantation from donors after cardiac death (DCD) is associated with a high risk for delayed graft function (DGF) due to ischemic acute kidney injury (AKI). BB3 is a small-molecule hepatocyte growth factor mimetic that has been shown to improve early graft function after kidney transplantation in rats and dogs.

Study objective

To evaluate the safety and activity of BB3 compared to placebo in improving renal function in the immediate post-transplant period in patients who have received a DCD kidney transplantation.

Study design

The primary intent is a paired-kidney design. This means that both recipients must participate in the study. In some cases, this isn*t possible. For example: if both kidneys are allocated to our centre, it is possible that the first recipient gives consent and is included in the study. This recipient will be randomized to receive either BB3 or placebo, while the second recipient is not yet available for consent. If the second recipient doesn*t want to participate, the first recipient, who already got the first infusion, would be excluded, according to the paired-kidney study design. Inclusion of an unpaired-kidney recipient will allow inclusion of these subjects into the analysis.

Intervention

One group receives 4 intravenous infusions of 2 mg/kg BB3 at 6-9, 24±3, 48±3 and 72±3 hours following kidney transplantation and the other group receives an equal volume of normal saline at the same time points.

Study burden and risks

Participation in this trial requires 40 additional blood samples (2.5 ml), 7 additional spot urine samples (10 ml), 7 additional 24-hour urine collections, no additional site visits, 1 medical history, 2 full physical examinations, 8 abbreviated physical examinations, 2 fundoscopic examinations, 9 electrocardiograms and no questionnaires. If a subject is discharged prior to day 28 after transplantation, the subject will receive a 'urine' diary to record the daily volume of urine up to and including day 14 and on day 28 after transplantation.
Infusion of the study drug was well tolerated in healthy volunteers and dialysis patients. At the dose used in this study, no toxic effects of the drug were observed in rats and dogs. Patients will benefit from participating if BB3 indeed improves early graft function after DCD kidney transplantation.

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

1. Subjects must sign the informed consent document prior to performance of any study related procedure including the Screening procedure.
2. Males and females * 18 years of age.
3. Had renal transplantation due to end stage disease requiring chronic dialysis.
4. Study drug can be administered within 6 to 36 hours after transplantation.
5. Received kidney from donor after cardiac death.
6. DCD kidney fulfills the clinical site*s criteria for transplantation.
7. Creatinine clearance from the transplanted kidney over a 2-hour collection period is <10 mL/min, OR no urine output or < 50 cc/H over a 24 hour period, OR normal urine output following transplantation that diminished to < 50 cc/H over a 24 hour period OR Creatinine reduction ratio 24 hours after transplantation to pre-transplantation is < 30%.;8. Dry weight * 100 kg.

9. Women of child bearing potential have a negative pregnancy test prior to transplantation.
10. Women of child bearing potential (including perimenopausal women who have had a menstrual period within 1 year) must agree to use 2 forms of effective birth control regimen (at least one-barrier method) during the 28-day study period. Men must agree to use condoms during the study period; a condom with spermicide is considered a single barrier.
11. In the opinion of the Investigator, the subject is capable of understanding and complying with the protocol.

Exclusion criteria

1. Mean arterial pressure <40 mmHg or cardiac index <1.8 L/min/m2.
2. Recipient of multiple organ transplantation or scheduled for multiple organ transplantation.
3. Recipient of kidney from a pediatric donor age 10 years or less.
4. Recipient age > 75 years.
5. Patients with ASA 4 or 5
6. Patients with chronic obstructive pulmonary disease (COPD) GOLD IV
7. Has measurable donor-specific antibody or positive cross-match requiring deviation from standard immunosuppressive therapy.
8. Currently participating in or has participated in an investigational drug or medical device study within 30 days or five half-lives, whichever is longer, prior to enrolment into this study.
9. Concurrent sepsis or active bacterial infection.
10. Have an active malignancy or history of solid, metastatic or hematologic malignancy with the exception of basal or squamous cell carcinoma of the skin that has been removed.
11. Women of child bearing potential who is breast feeding.
12. History of positive HIV test.
13. History of rheumatoid arthritis.
14. History of proliferative retinopathy or laser surgery for retinopathy.
15. Subjects who have a penicillin allergy.
16. Subjects who require the cytochrome P450 1A2 (CYP1A2) inhibitors, or are receiving ciprofloxacin and fluvoxamine (Luvox®).;17. Subject is unwilling or unable to comply with the protocol or to cooperate fully with the Investigator or the site personnel.
18. Subject is not deemed medically stable for the study in the opinion of the Investigator or the subject*s primary nephrologist.

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:	Recruitment stopped
Start date (anticipated):	19-11-2011
Enrollment:	18
Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	BB3
Generic name:	BB3

Ethics review

Approved WMO Date:	19-04-2010
Application type:	First submission
Review commission:	METC academisch ziekenhuis Maastricht/Universiteit Maastricht, METC azM/UM (Maastricht)
Approved WMO Date:	23-09-2010
Application type:	First submission
Review commission:	METC academisch ziekenhuis Maastricht/Universiteit Maastricht, METC azM/UM (Maastricht)
Approved WMO Date:	10-07-2012
Application type:	Amendment
Review commission:	METC academisch ziekenhuis Maastricht/Universiteit Maastricht, METC azM/UM (Maastricht)
Approved WMO Date:	31-10-2012

Application type:	Amendment
Review commission:	METC academisch ziekenhuis Maastricht/Universiteit Maastricht, METC azM/UM (Maastricht)
Approved WMO Date:	12-11-2012
Application type:	Amendment
Review commission:	METC academisch ziekenhuis Maastricht/Universiteit Maastricht, METC azM/UM (Maastricht)
Approved WMO Date:	28-03-2013
Application type:	Amendment
Review commission:	METC academisch ziekenhuis Maastricht/Universiteit Maastricht, METC azM/UM (Maastricht)
Approved WMO Date:	29-07-2013
Application type:	Amendment
Review commission:	METC academisch ziekenhuis Maastricht/Universiteit Maastricht, METC azM/UM (Maastricht)
Approved WMO Date:	21-10-2013
Application type:	Amendment
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
EudraCT	EUCTR2010-019243-19-NL
CCMO	NL31820.068.10