A Prospective, Open-label, Multicenter, Randomized Study to Evaluate the Benefits and Risks of Conversion of Existing Adolescent Renal Allograft Recipients Aged 12 to Less Than 18 Years of Age to a Belatacept-based Immunosuppressive Regimen as Compared to Continuation of a Calcineurin Inhibitor-based Regimen, and Their Adherence to Immunosuppressive Medications

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This study has been transitioned to CTIS with ID 2022-501677-39-00 check the CTIS register for the current data. Evaluation of patient and functional graft survival of adolescent renal allograft recipients converted from CNI to belatacept-based...

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

Summary

ID

NL-OMON52226

Source
ToetsingOnline

Brief title
IM103-402

Condition

- Renal disorders (excl nephropathies)

Synonym
Kidney transplant, Renal Allograft

Research involving
Human

Sponsors and support

Primary sponsor: Bristol-Myers Squibb
Source(s) of monetary or material Support: Pharmaceutical Industry

Intervention

Keyword: Adolescent, Belatacept, Renal, Transplant

Outcome measures

Primary outcome

Primary Endpoint

Proportion of participants who survive with a functional graft with an eGFR >

30 mL/min/1.73 m2 (updated Schwartz formula) at 24 months post-randomization.

Secondary outcome

Secondary Endpoints

• Participant and graft survival: Proportion of participants who:

* survive with a functioning graft at 6 and 12 months post-randomization.

* survive at 6, 12 and 24 months post-randomization.

* experience death-censored graft loss by 6, 12 and 24 months post

randomization.

Study description

Background summary

Renal transplantation is the treatment of choice for most patients with end stage renal disease, as it offers the best option for long-term survival with an improved quality of life. In turn, successful kidney transplantation is heavily dependent upon lifelong administration of immunosuppressive medications with diverse safety profiles and off-target effects that, in and of themselves, may have an adverse impact on quality of life, thereby predisposing to non-adherence with the prescribed regimens.
Adolescent renal allograft recipients are at significantly higher risk of renal allograft graft failure than are younger children or adults 31-45 years of age;

Belatacept was developed to address the medical need for a novel immunosuppressive therapy for kidney transplant recipients that can avoid the renal, cardiovascular, and metabolic toxicities of existing, calcineurin inhibitor (CNI)-based regimens, while offering comparable short-term patient and graft survival. The calcineurin inhibitors have also been associated with adverse effects on neurological and cognitive function that may interfere with work and school, as well as with untoward effects on physical appearance that, in turn, may discourage regular adherence to the prescribed oral dosing regimen.

Belatacept is administered by intravenous infusion under medical supervision every 4 weeks, thus providing an opportunity for more frequent monitoring of compliance with prescribed, orally administered concomitant immunosuppressive drugs.

Study objective

This study has been transitioned to CTIS with ID 2022-501677-39-00 check the CTIS register for the current data.

Evaluation of patient and functional graft survival of adolescent renal allograft recipients converted from CNI to belatacept-based immunosuppression at least 6 months post-transplant as compared to those of recipients remaining on CNI at 24 months post-randomization.

Study design

This is a Phase 3b, open-label, randomized, multicenter study that will evaluate the benefits and risks of conversion from CNI- to belatacept-based immunosuppression following a 3-6-month CNI taper when compared to continuation of CNI-based immunosuppression in adolescent renal

transplant recipients.

Intervention

Upon meeting the enrollment criteria, participants will be randomized in a 2:1 ratio to one of two open-label treatment arms:
Arm 1: Conversion from established CNI treatment to belatacept following taper and discontinuation of CNI.
Arm 2: Continue established CNI treatment at doses sufficient to achieve trough whole blood concentrations (C0 levels) of 50 - 250 ng/mL (CsA) or 4 - 11 ng/mL (TAC).

Study burden and risks

• A complete physical examination
• Vital signs
• Performing of a chest X-Ray if results are not available from one previously done during the 6 months before this visit.
• Performing of an ECG (electrocardiogram) to check their heart rate and rhythm.
• Performing of a urine or blood pregnancy for all female participants.
• Blood draws for analyses
• Collection of a urine sample to check for protein, glucose (sugar), red and white blood cells, and the creatinine level.
• Usage of a nasal swab to test for a current infection with SARS-CoV-2, the coronavirus virus. This test must be negative in order for the subject to take part in the study. If this test is positive, they may be retested one more time, after at least 10 days.
• Completion of 3 questionnaires on the following points during the study: Day 1 and Months 6, 12, 18, and 24; and Day 1 and Months 3, 6, 9, 12, 15, 18, 21 and 24 (child + parent).

• Group 1. subjects in this group will receive belatacept on Days 1, 15, 29, 43, and 57, and then every 28 days after that. In addition, the dose of the CNI will be reduced, and then stopped completely, during the first 12 to 24 weeks after the start of receiving belatacept.
• Group 2. subjects in this group will continue on the same CNI treatment they were receiving when they entered the study.

Monitoring Safety of the subjects
The study subject will receive a dose of belatacept at all study visits, and will be contacted by the study staff within 48 hours after each one, to see if they have experienced any adverse effects during the 24-hour period after each infusion.

If the study doctor suspects that the study subject may be experiencing acute rejection, up to an additional 14 ml of blood (about 3-1/2 teaspoons) will be

collected for related testing. In addition, a kidney biopsy will be needed to determine whether rejection is present.

Safety Follow-up Period:
When the patient stops or completes the study treatment period, they will begin the last part of the study, known as the safety follow-up period. During this period, the study doctor will continue to assess their health. It is important to know, for example, if they have recovered, developed an illness, or suffered an important adverse event.
The follow up period includes a visit for all subjects at week 8 after their last dose of study medication. Subjects in Group 2 (CNI continuation) may have a phone call instead of the clinic visit. If the subject is assigned to Group 1 (conversion to belatacept), and does not continue to receive belatacept after the Month 24 (Week 104) study visit is completed, or earlier if they prematurely discontinue belatacept before or at the time of the week 104 study visit, they will be required to have clinic visits at 8, 12, and 24 weeks after the last dose. Each follow-up visit should last about 1 hour.

Data Monitoring Committee: will be convened to provide oversight of benefit-risk considerations for participants in the study and, if necessary, to make recommendations to BMS to better ensure the ongoing safety of study participants.

Contacts

Public
Bristol-Myers Squibb

Orteliuslaan 1000 Orteliuslaan 1000
Utrecht 3528 BD
NL
Scientific
Bristol-Myers Squibb

Orteliuslaan 1000 Orteliuslaan 1000
Utrecht 3528 BD
NL

Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Adolescents (12-15 years)
Adolescents (16-17 years)

Inclusion criteria

- Male and females between 12 to less than 18 years of age
- Documented EBV seropositivity prior to transplant and randomization
- Receiving a stable regimen of a CNI with a mycophenolate with or without concomitant corticosteroids for > 1 calendar month prior to randomization
- Stable renal function 12 weeks prior to screening based upon investigator assessment and protocol-defined criteria for eGFR and proteinuria

Exclusion criteria

- No treatment for biopsy-proven acute rejection (BPAR) of any degree of severity within 6 calendar months prior to enrollment.
- No history of biopsy confirmed antibody mediated rejection or Banff Grade IIA or higher acute cellular rejection with the current transplant

Study design

Design

Study phase:	3
Study type:	Interventional
Intervention model:	Other
Allocation:	Randomized controlled trial
Masking:	Open (masking not used)
Control:	Active

Primary purpose:	Treatment

Recruitment

NL

Recruitment status:	Recruiting
Start date (anticipated):	23-09-2022
Enrollment:	3
Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	Calcineurin inhibitor
Generic name:	Cyclosporine A
Registration:	Yes - NL intended use
Product type:	Medicine
Brand name:	Calcineurin inhibitor
Generic name:	Tacrolimus
Registration:	Yes - NL intended use
Product type:	Medicine
Brand name:	Nulojix
Generic name:	Belatacept
Registration:	Yes - NL outside intended use

Ethics review

Approved WMO Date:	23-02-2021
Application type:	First submission
Review commission:	METC Amsterdam UMC
Approved WMO Date:	26-07-2021
Application type:	First submission
Review commission:	METC Amsterdam UMC
Approved WMO Date:	10-11-2021

Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	15-11-2021
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	03-02-2022
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	04-03-2022
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	08-06-2022
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	18-07-2022
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	23-11-2022
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	02-12-2022
Application type:	Amendment
Review commission:	MEC Academisch Medisch Centrum (Amsterdam) Kamer G4-214 Postbus 22660 1100 DD Amsterdam 020 566 7389

mecamc@amsterdamumc.nl

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	CTIS2022-501677-39-00
EudraCT	EUCTR2018-000237-12-NL
CCMO	NL75805.018.21