Evaluation of the Benefits and Risks in Maintenance Renal Transplant Recipients Following Conversion to Nulojix® (belatacept)-based Immunosuppression

Published: 28-06-2013
Last updated: 24-04-2024

Primary1. To evaluate patient and functional graft survival in stable renal transplant recipients (6-60 months post transplantation) converted from CNI to belatacept-based immunosupression as compared to those continuation of CNI based...

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

Summary

ID

NL-OMON47903

Source
ToetsingOnline

Brief title
kidney transplant
IM103116

Condition

- Other condition

Synonym
kidney, kidney transplant

Health condition

kidney transplant

Research involving
Human

Sponsors and support

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

Intervention

Keyword: IM103116, kidney transplant

Outcome measures

Primary outcome

Proportion of subjects who survive with a functional graft at 24 months post randomization.

Secondary outcome

* Patient and Graft Survival

* Proportion of subjects who survive with a functional graft at 12 months post-randomization

* Acute Rejection

* The incidence and severity of clinically suspected, biopsy-proven acute rejection at 12 and 24 months post- randomization

* Renal Function

* Mean change in cGFR (per 4-variable MDRD equation) from baseline to 12 and 24 months post-randomization (% and absolute)

* Slopes of cGFR and 1/serum creatinine respectively from baseline as well as Month 3 to 12 and 24 months post-randomization

* Proportion of subjects with > 5% and > 10% improvement over baseline in cGFR at 12 and 24 months post randomization

* Urine protein/ creatinine ratio (UPCR) at baseline, 3, 6, 12, and 24 months post randomization

* Hypertension

* Mean change in systolic and diastolic blood pressure from baseline to 12 and 24 months post randomization, and intensity of anti-hypertensive treatment regimens at 12 and 24 months.

* Donor Specific Antibodies

* Incidence of de novo donor specific antibodies at Day 1, 12 and 24 months post-randomization

* Safety and tolerability of a belatacept-based immunosuppressive regimen

* All adverse events

* Adverse events of special interest

* Clinically significant changes in vital signs

* Laboratory test abnormalities

* Clinical tolerability of the drug

Study description

Background summary

There is no formal research hypothesis for this study. The purpose of this study is to assess
the safety and efficacy of conversion from CNI to belatacept in stable EBV+ adult recipients of a renal allograft
from a living donor or a deceased donor between 6 - 36 months prior to enrollment.

Study objective

Primary

1. To evaluate patient and functional graft survival in stable renal transplant recipients (6-60 months post transplantation) converted from CNI to belatacept-based immunosupression as compared to those continuation of CNI based immunosuppression at 24 months post-randomization.

Secondary
To evaluate the effect of conversion from CNI to belatacept on the following:
1. Composite of patient and functional graft survival at 12 months post-randomization
2. The incidence and severity of clinically suspected biopsy-proven acute rejection at 12 and 24 months post- randomization
3. Renal function as assessed by:
- Mean change in cGFR (MDRD) from baseline to D1-12/24 months post-randomization (% and absolute)
- Slopes of cGFR and 1/serum creatinine respectively from baseline as well as Month 3 to 12 and 24 months post-randomization
- Proportion of subjects with > 5% and > 10% improvement over baseline in cGFR at 12 and 24 months post-randomization
- Urine protein/ creatinine ratio (UPCR) at baseline, 3, 6, 12, and 24 months post-randomization
4. Mean change in systolic and diastolic blood pressure and intensity of treatment regimen from baseline to 12 and 24 months post-randomization
5. Incidence of donor specific antibodies (DSA) at Baseline/Day 1, Months 12 and 24 post-randomization
6. Occurrence of symptom occurrence and symptom distress measured with the MTSOSDS-R 59 at baseline, week 6, and Months 3, 6, and 12 post- randomization
7. Safety and tolerability of a belatacept-based immunosuppressive regimen

Study design

This is a randomized, open-label, active-controlled, parallel-group study. Approximately 440 subjects on CNI-based regimens will be randomized in a 1:1 ratio to treatment with either belatacept or continued treatment with their established CNI. All subjects will also receive a background maintenance immunosuppressive regimen of mycophenolate mofetil (MMF) or mycophenolic acid (MPA), with adjunctive daily corticosteroids, according to their immunosuppressive regimen at the time of enrollment. Enrollment will be monitored, and if necessary restricted, to ensure no more than 25% of patients are maintained on CsA at enrollment. In addition, participation by patients receiving the maintenance immunosuppressive combination of tacrolimus with mycophenolate sodium will be limited to no more than approximately 1/3 of all subjects.

A 1 month lead-in will be employed to confirm a stable CNI (TAC or CsA) trough concentration. A serum creatinine (SCr) value within 3 months of enrollment and within ±10% of the screening SCr value is required to confirm stable renal function. Subjects will be stratified by site and baseline cGFR (* 30 to < 45

mL/min/1.73 m2 or * 45 to 75 mL/min/1.73 m2). Subjects will also be randomized with a 1:2 ratio for baseline cGFR * 30 to < 45 mL/min/1.73 m2 or * 45 to 75 mL/min/1.73 m2. Subjects with a baseline cGFR > 60 mL/min/1.73 m2 must have documentation of CNI toxicity to be included in the study.

Intervention

Group 1: Convert to Belatacept in doses of 5 mg/kg intravenous
Group 2: Continue established CNI treatment twice daily doses by mouth as directed

Study burden and risks

NA

Contacts

Public
Bristol-Myers Squibb

Chaussée de la Hulpe 185
Brussels 1170
BE
Scientific
Bristol-Myers Squibb

Chaussée de la Hulpe 185
Brussels 1170
BE

Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Adults (18-64 years)

Elderly (65 years and older)

Inclusion criteria

1) Men and women, ages 18 -75 inclusive
2) Adult recipients of a renal allograft from a living donor or a deceased donor between 6-36 months prior to enrollment
3) Receiving a stable regimen of CNI (CsA or TAC) on a background regimen of MMF or MPA, with concomitant daily corticosteroids for * 1 calender month prior to randomization.
4) cGFR * 30 and * 75 mL/min/1.73 m2 (Modification of Diet in Renal Disease study [MDRD] 7-point formula). Subjects with cGFR > 60 ml/min/1.73m2 must have evidence of CNI toxicity (eg, renal, neurologic, hematologic or cardiovascular/metabolic causes).
5) Stable renal function within 3 months prior to enrollment (as defined by one local laboratory
serum creatinine value ± 10% of the local laboratory screening value)

Exclusion criteria

1) Recipients with EBV serostatus negative or unknown
2) History of acute rejection (AR) within 3 months prior to enrollment
3) History of positive donor specific antibodies (DSA)
4) History of antibody mediated rejection
5) Positive T-cell lymphocytotoxic cross match
6) Proteinuria >1 g/day or > 0.5 g/day if diabetic

Study design

Design

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

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	12-05-2014
Enrollment:	32
Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	Belatacept
Generic name:	Belatacept
Registration:	Yes - NL intended use

Ethics review

Approved WMO

Date:	28-06-2013
Application type:	First submission
Review commission:	METC Leiden-Den Haag-Delft (Leiden) metc-ldd@lumc.nl

Approved WMO

Date:	04-09-2013
Application type:	First submission
Review commission:	METC Leiden-Den Haag-Delft (Leiden) metc-ldd@lumc.nl

Approved WMO

Date:	06-11-2013
Application type:	Amendment
Review commission:	METC Leiden-Den Haag-Delft (Leiden) metc-ldd@lumc.nl

Approved WMO

Date:	08-11-2013

Application type:	Amendment
Review commission:	METC Leiden-Den Haag-Delft (Leiden)
	metc-ldd@lumc.nl

Approved WMO

Date:	03-12-2013
Application type:	Amendment
Review commission:	METC Leiden-Den Haag-Delft (Leiden)
	metc-ldd@lumc.nl

Approved WMO

Date:	27-02-2014
Application type:	Amendment
Review commission:	METC Leiden-Den Haag-Delft (Leiden)
	metc-ldd@lumc.nl

Not approved

Date:	04-03-2014
Application type:	Amendment
Review commission:	METC Leiden-Den Haag-Delft (Leiden)
	metc-ldd@lumc.nl

Approved WMO

Date:	15-04-2014
Application type:	Amendment
Review commission:	METC Leiden-Den Haag-Delft (Leiden)
	metc-ldd@lumc.nl

Approved WMO

Date:	24-04-2014
Application type:	Amendment
Review commission:	METC Leiden-Den Haag-Delft (Leiden)
	metc-ldd@lumc.nl

Approved WMO

Date:	27-11-2014

Application type: Amendment

Review commission: METC Leiden-Den Haag-Delft (Leiden)

metc-ldd@lumc.nl

Approved WMO
Date: 05-12-2014

Application type: Amendment

Review commission: METC Leiden-Den Haag-Delft (Leiden)

metc-ldd@lumc.nl

Approved WMO
Date: 10-12-2014

Application type: Amendment

Review commission: METC Leiden-Den Haag-Delft (Leiden)

metc-ldd@lumc.nl

Approved WMO
Date: 29-01-2015

Application type: Amendment

Review commission: METC Leiden-Den Haag-Delft (Leiden)

metc-ldd@lumc.nl

Approved WMO
Date: 04-02-2015

Application type: Amendment

Review commission: METC Leiden-Den Haag-Delft (Leiden)

metc-ldd@lumc.nl

Approved WMO
Date: 06-08-2015

Application type: Amendment

Review commission: METC Leiden-Den Haag-Delft (Leiden)

metc-ldd@lumc.nl

Approved WMO
Date: 16-09-2015

Application type:	Amendment
Review commission:	METC Leiden-Den Haag-Delft (Leiden)
	metc-ldd@lumc.nl

Approved WMO Date:	30-09-2015
Application type:	Amendment
Review commission:	METC Leiden-Den Haag-Delft (Leiden)
	metc-ldd@lumc.nl

Approved WMO Date:	16-08-2016
Application type:	Amendment
Review commission:	METC Leiden-Den Haag-Delft (Leiden)
	metc-ldd@lumc.nl

Approved WMO Date:	21-10-2016
Application type:	Amendment
Review commission:	METC Leiden-Den Haag-Delft (Leiden)
	metc-ldd@lumc.nl

Approved WMO Date:	16-11-2016
Application type:	Amendment
Review commission:	METC Leiden-Den Haag-Delft (Leiden)
	metc-ldd@lumc.nl

Approved WMO Date:	11-08-2017
Application type:	Amendment
Review commission:	METC Leiden-Den Haag-Delft (Leiden)
	metc-ldd@lumc.nl

Approved WMO Date:	04-09-2017

Application type:	Amendment
Review commission:	METC Leiden-Den Haag-Delft (Leiden)
	metc-ldd@lumc.nl

Approved WMO Date:	10-01-2018
Application type:	Amendment
Review commission:	METC Leiden-Den Haag-Delft (Leiden)
	metc-ldd@lumc.nl

Approved WMO Date:	24-09-2018
Application type:	Amendment
Review commission:	METC Leiden-Den Haag-Delft (Leiden)
	metc-ldd@lumc.nl

Approved WMO Date:	03-12-2018
Application type:	Amendment
Review commission:	METC Leiden-Den Haag-Delft (Leiden)
	metc-ldd@lumc.nl

Approved WMO Date:	03-04-2019
Application type:	Amendment
Review commission:	METC Leiden-Den Haag-Delft (Leiden)
	metc-ldd@lumc.nl

Approved WMO Date:	22-05-2019
Application type:	Amendment
Review commission:	METC Leiden-Den Haag-Delft (Leiden)
	metc-ldd@lumc.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
EudraCT	EUCTR2012-001314-42-NL
ClinicalTrials.gov	NCT01820572
CCMO	NL44706.058.13

Study results

Results posted: 02-06-2021

Actual enrolment: 38

First publication
08-11-2020