Long-Term Follow-Up of Patients who have received an Autologous Antigen-Specific Chimeric Antigen Receptor T Regulatory Cell Therapy (TX200-TR101) in a prior clinical study.

Published: 29-12-2022
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This study has been transitioned to CTIS with ID 2024-512580-31-00 check the CTIS register for the current data. PrimaryTo evaluate the long-term safety and tolerability of TX200-TR101 up to 15 years post-TX200-TR101 infusion/baseline.SecondaryTo...

Ethical review	Approved WMO
Status	Pending
Health condition type	Immune disorders NEC
Study type	Observational invasive

Summary

ID

NL-OMON56013

Source
ToetsingOnline

Brief title
Long-Term Follow-Up of TX200-TR101 (STEADFAST Long Term)

Condition

- Immune disorders NEC
- Nephropathies

Synonym
Allograft rejection, Renal transplant rejection

Research involving
Human

Sponsors and support

Primary sponsor: Sangamo Therapeutics France SAS
Source(s) of monetary or material Support: Sangamo Therapeutics France SAS

Intervention

Keyword: Immunosuppression, Kidney Transplant, Long-Term Follow-up (LTFU) Study, TX200-TR101

Outcome measures

Primary outcome

From the day of TX200-TR101 infusion through to 15 years post-TX200-TR101

infusion/baseline:

• Overall survival

• Incidence and grade of Serious Adverse Events (SAEs).

Secondary outcome

Secondary

From the day of TX200-TR101 infusion through to 15 years post-TX200-TR101

infusion/baseline:

• Incidence of immune-mediated rejection in terms of BCAR episodes according to

the Banff criteria (including type, severity and timing)

• Incidence of graft loss due to rejection

• Incidence and severity of chronic graft dysfunction, as measured by eGFR

• Incidence and (semi-quantitative) intensity of de novo donor-specific

anti-HLA antibodies (DSA).

Exploratory

From the day of TX200-TR101 infusion through to 15 years post-TX200-TR101

infusion/baseline:

• Number of in-patient days in hospital

• Incidence of any Adverse Events (AE) considered related to TX200-TR101 according to the investigator

• Incidence of Adverse Events of Special Interest (AESI), including (irrespective of grade):

o Any infection requiring medical intervention; any infection that is suspected or confirmed opportunistic in nature; new-onset diabetes mellitus (NODM), new incidence or exacerbation of a pre-existing neurological disorder; new incidence or exacerbation of a prior rheumatological or other autoimmune disorder; new incidence of a haematological disorder; new incidence or exacerbation of hypertension, new malignancy, or new (up-to 8 years post-infusion) dyslipidaemia requiring medical intervention

• Change in immunosuppression regimen to include:

o Target levels in blood for each immunosuppressant.

o Number and name of drugs given to achieve intended level of immunosuppression.

o Any incidence of rescue medication given to avoid potential imminent rejection episode.

• Incidence of anti-drug antibodies against HLA-A2 CAR-Tregs.

• From the day of TX200-TR101 infusion/baseline through to 15 years post-TX200-TR101 infusion/baseline, any of the following:

o Death, or;

o Incidence of immune-mediated rejection in terms of BCAR episodes according to the Banff criteria (including type, severity and timing), or;

o Incidence of graft loss due to rejection, or;

o Incidence and severity of chronic graft dysfunction, as measured by eGFR

Absolute value and change from baseline in SF-36v2 from the day of TX200-TR101

infusion through to 15 years post-TX200-TR101 infusion/baseline.

Levels (absolute values) of HLA-A2 CAR-Tregs from the day of infusion through

to 5 years post-TX200-TR101 infusion/baseline.

Study description

Background summary

TX200-TR101, the study drug that subjects received in the previous study (TX200-KT02) through infusion, is being investigated further in this study for long-term effects and safety when it is administered to subjects with End-Stage Renal Disease (ESRD). The study drug is made from their own cells, which are modified and designed to modulate the immune system after they have received a donated kidney. The safety and effects of the study drug are being compared by utilising a control group of subjects.

Please refer to protocol section 1 (p17-19) for more information.

Study objective

This study has been transitioned to CTIS with ID 2024-512580-31-00 check the CTIS register for the current data.

Primary
To evaluate the long-term safety and tolerability of TX200-TR101 up to 15 years post-TX200-TR101 infusion/baseline.

Secondary
To evaluate the effect of TX200-TR101 on long-term graft-related outcomes up to 15 years post-TX200-TR101 infusion/baseline.

Exploratory
To evaluate the effect of TX200-TR101 on long-term safety outcomes up to 15 years post-TX200-TR101 infusion/baseline.
To evaluate the composite efficacy profile of TX200-TR101 up to 15 years post-TX200-TR101 infusion/baseline.

To evaluate quality of life over time up to 15 years post-TX200-TR101 infusion/baseline.
To evaluate the long-term persistence of CAR-Tregs up to 5 years post-TX200-TR101 infusion/baseline (if available).

Study design

Subjects will be invited to enrol in this LTFU study after they have either completed the week 84 visit or have withdrawn from the Phase I/IIa study (TX200-KT02). Subjects will be invited to read and sign the informed consent. Transplant recipients who were administered TX200 TR101 in the TX200-KT02 study will then proceed to have an additional 13.5 years of follow-up after completion of the end of the TX200-KT02 study with administration of TX200-TR101. Since these subjects will have completed the 1.5 years of follow-up post-dosing with TX200 TR101 in the TX200-KT02 study, this LTFU will thus enable the subjects to have a total of 15 years of observation post-treatment with TX200-TR101.

Control transplant recipients will undergo the same amount of follow up, which will equate to approximately 13.75 years of follow-up post-end-of-study (control transplant recipients were not administered TX200-TR101 in the TX200-KT02 study).

Subjects will undergo a combination of study visits and phone calls/Home Health visits to gather information on their overall health, including information on any SAEs, any new or change in existing concomitant medications (excluding over-the-counter medications and any vaccinations), any hospitalisations (including for rejection episodes, new or worsening comorbidities, or for any other reason), and information on any new diagnoses or any other events of relevance (e.g., pregnancy). Information on AESI (including infections requiring medical intervention, where severity is Grade 2 or greater; any infection that is suspected or confirmed opportunistic in nature, NODM, new or aggravation of hypertension, new malignancies or new (up-to 8 years) dyslipidemia requiring medical intervention) as well as any AEs considered related to the TX200-TR101 according to the investigator will also be collected.

Subjects will be asked during informed consent whether they give permission for the study doctor to approach the subject*s treating physician (if different) for more information on any health events, where applicable. Subjects will also be asked during informed consent whether, in case any type of biopsy has been obtained (e.g. for suspected malignancy and/or other reason, regardless of relationship to renal disease), they give permission for a copy of the histopathological assessment report to be shared with the study doctor, where applicable.

Study visits are to be combined with standard of care visits where possible, to

minimise the burden on the subjects of additional in-clinic visits.

A subject is considered to have completed the study if he/she has completed the end of study visit at Year 15 post-dosing with TX200-TR101/baseline. A premature discontinuation will occur if a subject who signs the Informed Consent Form (ICF) and is enrolled in the study ceases participation in the study, regardless of circumstances, before the completion of the Year 15 protocol-defined study procedures. Subjects who discontinue from the study prematurely, or are withdrawn from the study for any reason, will be asked to return to the study site for an early termination visit.

In case of death of any TX200-TR101 subject, attempts should be made by the investigator to collect renal allograft biopsy material for histopathological analysis to understand the health of the kidney at the time of the subject*s death. In addition, the investigator should attempt to obtain a report of findings from any autopsy performed.

Study burden and risks

Since there will be no study-related treatment in this long-term follow-up study, there are no new potential risks introduced by participating in this study. There is a general minimal risk associated with conducting blood sample collection/blood draws.

The burden for subjects is minimal during their participation in this LTFU study. Their study visits and procedures are combined with SoC visits and procedures as much as possible. What we learn during the LTFU can help developing treatments for post-transplant care and/or (ESRD related) renal transplants.

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 who enrolled in the Phase I/IIa study TX200-KT02, received a transplanted kidney and have either completed or withdrawn from that study.
2. Willing and able to provide written informed consent (IC) in accordance with local regulations and governing Independent Ethics Committee (IEC)/Institutional Review Board (IRB) requirements prior to any procedure or evaluation performed specifically for the sole purpose of the study.

Exclusion criteria

1. Subjects/persons committed to an institution following an administrative or judicial order.

Study design

Design

Study type:	Observational invasive
Intervention model:	Other
Allocation:	Non-randomized controlled trial
Masking:	Open (masking not used)
Control:	Active
Primary purpose:	Treatment

Recruitment

NL

Recruitment status:	Pending
Start date (anticipated):	01-06-2023
Enrollment:	8
Type:	Anticipated

Medical products/devices used

Registration:	No

Ethics review

Approved WMO Date:	29-12-2022
Application type:	First submission
Review commission:	CCMO: Centrale Commissie Mensgebonden Onderzoek (Den Haag)
Approved WMO Date:	10-03-2023
Application type:	First submission
Review commission:	CCMO: Centrale Commissie Mensgebonden Onderzoek (Den Haag)
Approved WMO Date:	08-05-2023
Application type:	Amendment
Review commission:	CCMO: Centrale Commissie Mensgebonden Onderzoek (Den Haag)
Approved WMO Date:	27-07-2023
Application type:	Amendment
Review commission:	CCMO: Centrale Commissie Mensgebonden Onderzoek (Den Haag)
Approved WMO Date:	15-08-2023
Application type:	Amendment
Review commission:	CCMO: Centrale Commissie Mensgebonden Onderzoek (Den

	Haag)
Approved WMO Date:	21-11-2023
Application type:	Amendment
Review commission:	CCMO: Centrale Commissie Mensgebonden Onderzoek (Den Haag)
Approved WMO Date:	29-11-2023
Application type:	Amendment
Review commission:	CCMO: Centrale Commissie Mensgebonden Onderzoek (Den Haag)
Approved WMO Date:	09-03-2024
Application type:	Amendment
Review commission:	CCMO: Centrale Commissie Mensgebonden Onderzoek (Den Haag)
Approved WMO Date:	26-03-2024
Application type:	Amendment
Review commission:	CCMO: Centrale Commissie Mensgebonden Onderzoek (Den Haag)

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	CTIS2024-512580-31-00

Register	ID
EudraCT	EUCTR2022-002440-40-NL
CCMO	NL82794.000.22