PLEASE NOTE: This trial has been registered retrospectively.

Trial Description

Title
Torque Teno virus quantification for the prediction of graft rejection after kidney transplantation

Trial Acronym
TTV-POET

URL of the trial
[---]*

Brief Summary in Lay Language
Common diseases such as hypertension or diabetes may lead to kidney damage and sometimes even irreversible loss of kidney function. Transplantation of a donor kidney can replace renal function. After transplantation the foreign kidney is under constant attack by the body’s own immune system. Most of the time acute damage can be prevented by drugs that inhibit the immune response, but chronic rejection processes may still going on and lead to functional loss of the transplanted kidney. There is no sufficient diagnostic test to predict these rejection processes precisely. Scientific data indicate that the amount of Torque Teno virus (TTV) associates with the activity of the immune system and thus indirectly indicate the risk of rejection. The virus causes no disease, is detectable in about 90% of the patients and can be quantified by a small blood sample from the vein. Therefore sera derived from 800 patients after kidney transplantation will be tested. The submitted project should clarify whether screening of TTV level in the blood of patients after kidney transplantation can predict organ rejection. The results of this study might lead to the establishment of TTV as a novel diagnostic tool for organ rejection after kidney transplantation and thus provide a valuable basis for early rejection therapy or adaptation of immunosuppressive drugs to prevent organ loss.

Brief Summary in Scientific Language
Large registry analyses have failed to demonstrate major improvements in the long-term survival of standard kidney transplants (KTX) over the last decades. In this context, organ rejection has been established as a major risk factor for decreased long-term graft function and allograft loss and there is a great need for markers that could be used as screening tools for under-immunosuppression or clinically silent rejection processes. A promising candidate for such immunologic monitoring might be the apathogenic Torque Teno virus (TTV), which elicits humoral and innate immune response. TTV has prevalence up to 90% and recent studies suggest that the viral load may be dependent on the immunological status of the host. In preparation for the present project we analysed TTV load in the peripheral blood of 715 KTX recipients at a single snap-shot and found an inverse association between late antibody-mediated rejection (ABMR) and TTV load. TTV
was also associated with the type and amount of immunosuppression. We hypothesize that the TTV level is directly influenced by the level of immunosuppression and thus indirectly associates with ABMR. Our preliminary results provide a valuable basis to test the potential of TTV quantification for risk prediction of organ rejection after KTX. Within the present project TTV load will be quantified by means of real time PCR in two cohorts (cohort A, part A; cohort B, part B) at the Medical University of Vienna. Within part A, a retrospective observational case-control study, longitudinally collected sera (pre-transplant, post-transplant month 1, 3, 6, 9, 12 and yearly thereafter) and within part B, a prospective observational cohort study, pre transplant and post transplant monthly collected sera of 300 KTX patients will be analyzed. The primary end point consists of organ rejection defined by the current BANFF scheme including acute and chronic humoral and cellular rejection (indication biopsies in part A and indication and protocol biopsies in part B) with a statistical power of >0.8 (two-sided type I error of 5%). Secondary end points include clinical and immunological baseline characteristics, type and amount of immunosuppression, medical adherence, graft function, donor-specific antibody kinetic, infectious complications, graft loss, cancer and death. For statistical evaluation general linear modeling and C statistics will be performed. The project will span over 36 month and will be conducted by Prof. Bond (transplant nephrology; primary investigator, project management), Prof. Puchhammer-Stöckl (virology; virologic analysis) and Prof. Herkner (epidemiology; statistical evaluation). The study has the potential to establish TTV as a novel in vitro marker for risk prediction of organ rejection after KTX. Timely identification of sub-clinical rejection might provide a useful basis for the implementation of therapeutic interventions preventing the occurrence of refractory rejection.

Do you plan to share individual participant data with other researchers?

[---]*

Description IPD sharing plan

[---]*

Organizational Data

- **DRKS-ID:** DRKS00012335
- **Date of Registration in DRKS:** 2017/04/26
- **Date of Registration in Partner Registry or other Primary Registry:** [---]*
- **Investigator Sponsored/Initiated Trial (IST/IIT):** yes
- **Ethics Approval/Approval of the Ethics Committee:** Approved
- **(leading) Ethics Committee Nr.:** 1785/2016, Ethikkommission der Medizinischen Universität Wien

Secondary IDs
Health condition or Problem studied

- ICD10: **T86.1** - Kidney transplant failure and rejection
- ICD10: **Z94.0** - Kidney transplant status

Interventions/Observational Groups

- **Arm 1:** Cohorte A: 500 NTX patients, retrospective analysis of serum at pre-NTX and post NTX months 1, 3, 6, 9, 12 and annually thereafter, other clinical data such as immunosuppression, graft function, infections and malignomas

  *Cohorte B: 300 NTX patients, prospective analysis of serum at pre-NTX and at every outpatient visit (not more than once a month) until month 24 post NTX, other clinical data such as immunosuppression, graft function, infections and malignomas*

Characteristics

- Study Type: **Non-interventional**
- Study Type Non-Interventional: **Observational study**
- Allocation: **Other**
- Blinding: [---]*
- Who is blinded: [---]*
- Control: **Other**
- Purpose: **Prognosis**
- Assignment: **Other**
- Phase: **0**
- Off-label use (Zulassungsüberschreitende Anwendung eines Arzneimittels): **N/A**

Primary Outcome

association of TTV level and organ rejection

Secondary Outcome

association of TTV level and clinical and immunological baseline characteristics, type and amount of immunosuppression, medical adherence, graft function [estimated glomerular filtration load (eGFR) and proteinuria], donor-specific antibodies (DSA) kinetic, infectious complications and cancer, death

Countries of recruitment
Locations of Recruitment

- University Medical Center Medizinische Universität Wien, Wien

Recruitment

- Planned/Actual: Actual
- (Anticipated or Actual) Date of First Enrollment: 2016/12/01
- Target Sample Size: 300
- Monocenter/Multicenter trial: Monocenter trial
- National/International: National

Inclusion Criteria

- Gender: Both, male and female
- Minimum Age: 18 Years
- Maximum Age: 99 Years

Additional Inclusion Criteria

kidney transplantation

Exclusion criteria

none

Addresses

- Primary Sponsor

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  Währinger Gürtel 18-20
  1090 Wien
  Austria

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- Contact for Scientific Queries
Contact for Scientific Queries

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Sources of Monetary or Material Support

- Public funding institutions financed by tax money/Government funding body (German Research Foundation (DFG), Federal Ministry of Education and Research (BMBF), etc.)

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Telephone: [---]*
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E-mail: [---]*
URL: [---]*

Status

- Recruitment Status: Recruiting complete, follow-up continuing

- Reason, if "Recruitment stopped after recruiting started" or "Recruiting withdrawn before recruiting started": [---]*

- Reason, if Reason for Recruiting Stop "Other": [---]*
DRKS-ID: **DRKS00012335**
Date of Registration in DRKS: **2017/04/26**
Date of Registration in Partner Registry or other Primary Registry: [---]*

- Study Closing (LPLV): [---]*
- Number of Participants in Germany after Recruiting complete: **0**
- Total Number of Participants (all Sites worldwide) after Recruiting complete: **307**

**Trial Publications, Results and other documents**

* This entry means the parameter is not applicable or has not been set.
*** This entry means that data is not displayed due to insufficient data privacy clearing.