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Immunomonitoring by virus-specific T-cells and evaluation as a prognostic marker for virus-induced diseases after solid organ transplantation

Submission date 29/04/2009	**Recruitment status** No longer recruiting	[X] Prospectively registered [X] Protocol [_] Statistical analysis plan [X] Results [_] Individual participant data
Registration date 17/06/2009	**Overall study status** Completed	
Last Edited 18/02/2021	**Condition category** Surgery	

Plain English summary of protocol
Not provided at time of registration

Contact information

Type(s)
Scientific

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Additional identifiers

Protocol serial number
IVIST01

Study information

Scientific Title

A monocentre, randomised, open-labeled study to steer immunosuppressive and antiviral therapy by measurement of virus (cytomegalovirus [CMV], adenovirus [ADV], herpes simplex virus [HSV]) specific T-cells in addition to determination of trough levels of immunosuppressants in paediatric kidney and liver allograft recipients: an explorative study

Acronym
IVIST

Study objectives
Monitoring of virus-specific T-cells followed by therapeutic intervention can prolong kidney function and reduce viral infections after solid organ transplantation.

Ethics approval required
Old ethics approval format

Ethics approval(s)
Ethics Committee of the Medical School of Hannover, 21/11/2008, ref: 5067

Study design
Monocentre randomised open-label study

Primary study design
Interventional

Study type(s)
Treatment

Health condition(s) or problem(s) studied
Paediatric kidney transplantation

Interventions
Antiviral prophylaxis and management should be based on the individual risk assessed by the amount of virus-specific T-cells. Immunosuppressive therapy should be adopted due to the levels of virus-specific T-cells as a direct measure of the intensity of immunosuppression in comparison to classical trough-level monitoring. Patients should be randomised prospectively in a group with monitoring of virus-specific T-cells and in a group that is treated conservatively.

The immunosuppressive therapy will be steered in all patients by classical serum-drug levels. In the intervention group, the relative percentage of virus-specific T-cells will be detected. In case of high levels (50% above the average detected in step 1) the dose of immunosuppression will be increased 20%, in case of low levels (50% below the average detected in step 1), the dose of immunosuppression will be decreased 20%.

In the non-intervention group, valganciclovir will be administered for 3 months, starting at time of transplantation in CMV-IgG negative children who receive an organ from a CMV IgG positive donor. Valganciclovir will also be given in case of CMV infection or reactivation for 3 months. In the intervention group, valganciclovir will only be administered prophylactically in CMV-IgG negative children who receive an organ from a CMV IgG positive donor and who do not have any CMV-specific T-cells before transplantation. In case of CMV-infection or reactiviation, valganciclovir therapy will only be carried out until there is a sufficient number of CMV specific T-cells. In the intervention group, valganciclovir will also be administered, when the levels of CMV-

specific T-cells falls below the threshold (that is actually determined in our ongoing study) that makes a CMV-reactivation likely.

Thereby the number of viral infections (especially CMV) should be reduced. By more specific use of antiviral therapy and immunosuppression, nephrotoxic effects of calcineurin inhibitors and antiviral agents should be decreased.

Intervention Type
Drug

Phase
Not Applicable

Drug/device/biological/vaccine name(s)
Valganciclovir

Primary outcome(s)
To determine whether the glomerular filtration rate (GFR) (Cystatin C, Filler) 2 years after transplantation is higher, if antiviral therapy and immunosuppressive therapy are additionally steered, based on the number of virus-specific T-cells.

Key secondary outcome(s))
1. Reduction of viral infections after solid organ transplantation
2. Optimisation of the individual timing of antiviral therapy
3. Optimisation of the immunosuppressive therapy
4. Reduction of nephrotoxic effects of cyclosporin A (CsA) and antiviral agents by optimised dosing
5. Premature study discontinuations due to adverse events (AEs)

All secondary outcome measures will be assessed continuously until the end of the study.

Completion date
30/06/2010

Eligibility

Key inclusion criteria
1. Patients who are males or non-pregnant females between the ages of 0 and 16 years
2. Patients after kidney or liver transplantation
3. Patients who receive their first or second transplantation
4. Patients who are single-organ recipients
5. If patients are women of childbearing potential, they must have a negative serum pregnancy test with a sensitivity equal to at least 50 mIU/ml before transplantation
6. If patients are women of childbearing potential, they must use two reliable forms of contraception simultaneously unless abstinence is the chosen method. Effective contraception must be used before transplantation, during therapy, and for 6 weeks following discontinuation of immunosuppressive therapy.
7. Patients' guardians must be capable of understanding the purpose and risks of the study
8. Patients whose guardians are willing to give written informed consent and willing to participate in and comply with the study protocol. Patients above 7 years have to agree with the study in addition to the informed consent of the legally authorised representative.

Participant type(s)
Patient

Healthy volunteers allowed
No

Age group
Child

Upper age limit
16 years

Sex
All

Total final enrolment
64

Key exclusion criteria
1. Patients participating in other studies or participated within the last four weeks
2. Patients who are highly sensitised
3. Patients who have previously undergone two organ transplantations
4. Hypersensitivity to any of the components of the medication used
5. Patients from other centres, who are not followed in the outpatient unit of the Hannover Medical School
6. Patients with a peak or current panel-reactive antibodies (PRA) of greater than 50%
7. Pregnant and/or lactating women and women of childbearing potential who are unwilling or unable to use contraception methods as specified
8. Patients whose guardians do not understand the requirements of the study
9. Patients with known positive human immunodeficiency virus-1 (HIV-1) or hepatitis C virus (HCV) test or the presence of hepatitis B surface antigen (HBsAg)
10. Patients with malignancies or history of malignancy, despite post-transplant lymphoproliferative disease
11. Patients who are not eligible in the opinion of the physician
12. Significant medical history and/or treatments for cardiac, renal, neurological, hepatic, endocrine diseases, or any laboratory abnormality indicative of a significant underlying condition, that may interfere with patients safety, compliance, or study evaluations, according to the investigator's opinion

Date of first enrolment
01/10/2009

Date of final enrolment
30/06/2010

Locations

Countries of recruitment
Germany

Study participating centre
Hannover Medical School (MHH)
Hannover
Germany
D-30655

Sponsor information

Organisation
Medical School of Hannover (MHH) (Germany)

ROR
https://ror.org/00f2yqf98

Funder(s)

Funder type
Hospital/treatment centre

Funder Name
Novartis

Alternative Name(s)
Novartis AG, Novartis International AG

Funding Body Type
Government organisation

Funding Body Subtype
For-profit companies (industry)

Location
Switzerland

Funder Name
Medical School of Hannover (MHH) (Germany) - IFB Transplantation

Results and Publications

Individual participant data (IPD) sharing plan

IPD sharing plan summary

Not provided at time of registration

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Results article	results	01/02/2021	18/02/2021	Yes	No
Protocol article	protocol	15/08/2014		Yes	No