Immunity to varicella-zoster virus in immunocompromised renal disease patients

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

Summary

ID

NL-OMON45220

Source
ToetsingOnline

Brief title
Immunity to VZV in renal disease

Condition

- Immune disorders NEC
- Viral infectious disorders
- Renal disorders (excl nephropathies)

Synonym
immunosuppression by chronic renal failure/renal replacement therapy amd renal transplantation transplantation

Research involving
Human

Sponsors and support

Primary sponsor: Universitair Medisch Centrum Groningen
Source(s) of monetary or material Support: Ministerie van OC&W

Intervention

Keyword: immune compromised state, renal disease, varicella-zoster virus

Outcome measures

Primary outcome

Main study endpoint will be cell-mediated immunity, as assessed by two different methods. The first method is to determine production of interferon-* by T cells in response to VZV stimulation using the enzyme linked immunosorbent spot (ELISpot) assay, expressed as number of spot-forming cells per 2x10^5 peripheral blood mononuclear cells. The second method is determining proliferating capacity of CD4+ and CD8+ T cells in response to VZV stimulation using carboxyfluorescein succinimidyl ester (CFSE) dye dilution proliferation assays. Proliferating capacity will be expressed using proliferation indices.

Secondary outcome

Inter alia, antibody levels to VZV will be determined. For all secundary study parameters, please see 2.2 of the research protocol (C1).

Study description

Background summary

Varicella-zoster virus (VZV) causes varicella (chickenpox) as a primary infection and herpes zoster (shingles) when reactivating. Patients with chronic kidney disease, especially patients receiving renal replacement therapy, and renal transplantation patients are immunocompromised because of their uraemic state and immunosuppressive therapies, respectively. As a result of the

immunocompromisation in these patients, risk of infections among which infection with VZV, is increased. The risk of herpes zoster in these patient groups is estimated to be 3-15 times higher than in the general population. A primary varicella infection or reactivation causes serious threats in these immunocompromised patients as even a lethal outcome is possible.

Study objective

More knowledge on immunity to VZV in these patient groups is necessary to be able to design preventive strategies to VZV infections in the future. To reach these goals, the proposed study is divided into two parts. The first part aims to determine both VZV specific cellular and humoral immunity in patients receiving renal function replacing therapy, patients before and after renal transplantation and to compare these results to those in healthy controls. In the second part, the standard procedure of twice vaccinating VZV seronegative patients awaiting renal transplantation will be utilized to study the effect of introduction of VZV in this patient group.

Study design

The first part of the study, determining basic VZV specific immunity in patients receiving renal function replacing therapy and renal transplantation patients compared to healthy controls, will be an observational study.
The second part of the study, evaluating the effect of VZV vaccination in VZV seronegative patients awaiting renal transplantation, before and after transplantation, will be an observational pilot study.

Study burden and risks

The burden and risks associated with participation in this study will be minimal as blood drawing will be combined with purposes other than this study, as explained in the ABR-form and research protocol. For the first part of the study, 40 mL of blood is required from patients receiving renal function replacing therapy and healthy controls. Peripheral blood mononuclear cells (PBMC) from before transplantation of recipients of renal allografts partly are already present in a Biobank. Additional blood post-transplantation will be requested from these patients at visit of the out-patient clinic.
For the second part of the study, drawing of extra blood (40 mL) will be required on at least 5 occasions, but up to 10 occasions when a patient is to receive a renal allograft.
As only a limited amount of extra blood will be drawn at the different time points, only in exceptional cases an additional puncture will be necessary and even then the risks of venapuncture are small when executed by experienced persons, in our opinion the importance of the study outweighs burden associated with participation

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

In order to be eligible to participate in this study, a patient must meet all of the following criteria:
* Provision of written informed consent
* *18 years of age
* For the first part of the study, dependent on which group the participant is included in:
o Receiving renal replacement therapy *1 time per week, or
o Presence of stored blood samples before and after kidney transplantation in existing Biobank
* For the second part of the study: VZV seronegativity
o Subject is a VZV seronegative pre-renal transplantation patient and
o Intended administration of VZV vaccine Provarivax;For healthy controls, the following criteria must be met:

* Provision of written informed consent
* *18 years of age

Exclusion criteria

A potential subject who meets any of the following criteria will be excluded from participation in this study:
* Pregnancy
* Malignancy (at present or <2 years ago), except for skin malignancies;For patients receiving renal function replacement therapy:
* Underlying auto-immune disorder as cause for need renal function replacement therapy
* Use of immunosuppressive medication other than *7.5 mg prednisolone/day, or immunostimulatory medication
* Less than 3 months duration of renal replacement therapy;For participants receiving VZV vaccination, the second part of the study:
* No administration of VZV vaccine Varivax due to any reason

Study design

Design

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

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	25-11-2014
Enrollment:	210
Type:	Actual

Ethics review

Approved WMO Date:	03-10-2014
Application type:	First submission
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)
Approved WMO Date:	21-04-2015
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)
Approved WMO Date:	28-06-2017
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)

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
CCMO	NL49283.042.14