Response to vaccination in lymphoma patients treated with CHOP and rituximab.

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Ethical review	Approved WMO
Status	Pending
Health condition type	Viral infectious disorders
Study type	Interventional

Summary

ID

NL-OMON38294

Source
ToetsingOnline

Brief title
RITUXIVAC

Condition

- Viral infectious disorders
- Lymphomas non-Hodgkin's B-cell

Synonym
cancer of the lymph nodes, Lymphoma

Research involving
Human

Sponsors and support

Primary sponsor: Sint Antonius Ziekenhuis
Source(s) of monetary or material Support: Ministerie van OC&W

Intervention

Keyword: chemotherapie, lymphoma, rituximab, vaccination

Outcome measures

Primary outcome

Immune response to vaccination in patients who were treated with rituximab, in association with the reconstitution of immune function. Parameters are:

• Antibody titres the influenza virus vaccine before and after vaccination.

Secondary outcome

• Immunoglobulin levels and subclass.

• Lymphocyte subsets (number of B cells and memory-B cells, CD3, CD4, CD8 and NK cells).

• Production of IFN-* by CD4+ cells. This will be measured in order to investigate if cellular mediated immune responses are intact after rituximab treatment.

• Cytokines and genetic factors (for example BAFF, CXCL13, APRIL) influencing B cell development and survival will be measured in order to determine if there is a correlation between specific cytokines/genetic factors and the observed B-cell depletion/reconstitution.

• Serum rituximab levels.

• The relationship between time after last dose, number of doses of rituximab and chemotherapy and increase in antibody titres. At what time point after rituximab adequate antibody titres can be generated.

Study description

Background summary

Rituximab is a chimeric anti-CD20 monoclonal antibody used in combination with chemotherapy for the treatment of non-Hodgkin*s lymphoma (NHL). Following infusion with rituximab, B-cell depletion in the peripheral blood occurs within days. Levels of normal peripheral B-cells remain low for 2-6 months. Because of the immunosuppressive (chemo) therapy, patients might be prone to develop infections with the influenza virus. Vaccination against this virus is, therefore, indicated for these immunocompromised patients. However little is known about the effect of rituximab with chemotherapy in patients with non-Hodgkin lymphoma on the response to vaccination.

Study objective

To investigate what the ideal moment to vaccinate would be, early (after 2-6 months) or late (after 9-12 months) after cessation of rituximab. Secondly to study the immune-response to vaccination with influenza virus vaccine after treatment with rituximab in relation to the reconstitution of immune-function (in terms of number of B-cells, lymphocyte subsets, immunoglobulin levels and IgG subclasses, CD4+ IFN-* production, BAFF, CXCl13 and IL-10).

Study design

The design is a cohort study with a control group. A total of hundred-twenty (120) patients with non-Hodgkin*s lymphoma, who were treated with rituximab in the last twelve months before start of the study and are in remission, will be included. Patients will be divided in 2 groups: the first group will consist of patients who received the last dose of rituximab 3-6 months ago (= early group), the second group consists of patients who received rituximab 9-12 months ago (= late group). The control group will not be included in the analysis in order to define which moment is the best to vaccinate patients. The control group is initiated in order to serve as a reference of immune components who are measured to be able to investigate the secondary objective. The control group will consist of 40 age, sex and morbidity matched controls who are recruted atthe general practioner.

Intervention

All patients and controls will receive the influenza virus vaccine Influvac®. The vaccine will be used in the authorised form according to existing vaccination protocols for immunocompromised patients. At three different timepoints sera will be taken and investigated. From healthy controls sera will

be taken twice.

Study burden and risks

Patients will be vaccinated with the influenza vaccine at the dutch annual vaccination campaign according to existing vaccination protocols in immune compromised patients. Blood samples will be drawn before vaccination and three weeks after and six months after vaccination, so three blood samples will be drawn. If possible, vaccination will be integrated in normal out-patient clinical visits. The vaccine will be used in the authorised form and for their authorised purpose, therefore no additional risks are to be expected. Patient discomfort might consist of a painful arm/leg after vaccination. Adverse events which are common (0.1-1%) include headache, fever, myalgia, artralgia, nausea, vomiting, and pain and redness at the vaccination spot. Rare events are allergic reactions (very rare leading to shock), angio edema, neurologic disorders and urticaria. Benefit is protection against infection with the influenza virus.

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. Patients with non-Hodgkin*s lymphoma, treated with rituximab (with a range of 6-12 cycles) and who are in remission.
2. Completion of rituximab therapy in the last twelve months before start of the study.
3. Age >= 18 years.
4. Signing of informed consent.;Controls:
1. Age, sex and co-morbidity matched controls

Exclusion criteria

1. Completion of rituximab therapy 7-8 months before start of the study.
2. Fever at time of vaccination.
3. Previous/known allergic reaction to any of the components of the vaccines given.;Controls:
1. Immunocompromised persons will be excluded (for example immunosuppressive medication).

Study design

Design

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

Recruitment

NL
Recruitment status: Pending

Start date (anticipated):	01-09-2012
Enrollment:	160
Type:	Anticipated

Medical products/devices used

Product type:	Medicine
Brand name:	Influvac or Vaxigrip
Product type:	Medicine
Brand name:	Pneumovax
Product type:	Medicine
Brand name:	Synflorix

Ethics review

Approved WMO Date:	17-02-2012
Application type:	First submission
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	11-10-2012
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	16-10-2012
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	19-11-2012
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)

Study registrations

Followed up by the following (possibly more current) registration

No registrations found.

Other (possibly less up-to-date) registrations in this register

ID: 23415
Source: Nationaal Trial Register
Title:

In other registers

Register	ID
EudraCT	EUCTR2011-002932-24-NL
CCMO	NL37320.100.11
Other	NTR3155, NCT01707628
OMON	NL-OMON23415