Response to pneumococcal en Hib vaccination in lymphoma patients treated with chemotherapy and rituximab.

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Ethical review	Approved WMO
Status	Will not start
Health condition type	Bacterial infectious disorders
Study type	Interventional

Summary

ID

NL-OMON39920

Source
ToetsingOnline

Brief title
PNEUMOTUXIVAC

Condition

- Bacterial 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: lymphoma, pneumoccocus, rituximab, vaccination

Outcome measures

Primary outcome

Antibody titres against S. Pneumonia and H. influenzae type b (in *g/mL)

vaccine before and after vaccinations. Titres will be interpreted and

classified in responder or non-responder.

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-gamma 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.

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 immune suppressive (chemo) therapy, patients are prone to develop infectious complications with Hemophilus infleunza type B (Hib) or S. pneumoniae. There is no data on the infectionrates of S.pneumoniae and Hib in patients with NHL who were treated with chemotherapy and rituximab. However vaccination seems indicated for this patientgroup. Little is known about the effect of rituximab and chemotherapy on the response to pneumoccocal and Hib vaccination.

Study objective

To compare the number of responders to vaccination with pneumococcal and conjugated Hib vaccine at different time points after last dose of rituximab, to investigate what the ideal moment of vaccination would be.
Secondly to study the immune-response to vaccination with conjugated Hib and pneumococcal vaccine after treatment with rituximab in relation to the reconstitution of immune-function (in terms of number and subsets of B-cells, lymphocyte subsets, immunoglobulin levels and IgG subclasses, CD4+ IFN-gamma production, BAFF, CXCl13 and IL-10).

Study design

The design is a randomised trial. A total of hundred-fifty-two (152) patients with non-Hodgkin*s lymphoma, who were treated with rituximab in the last five months before start of the study and are in remission, will be included. Patients will be randomised for early vaccination (six months after rituximab) or late vaccination (twelve months after rituximab). Two and six months after the first vaccination with synflorix (conjugated pneumococcal vaccine) and act-Hib (conjugated Hib vaccine), the second and third vaccination will be given with synflorix and act-Hib and pneumovax (pneumococcal polysaccharide vaccine) and act-Hib respectatively.

Intervention

- At the first visit when patients are randomized, blood will be drawn and the first vaccination with Prevnar 13 and Act-Hib will be given.
- 3 weeks later, blood will be drawn.
- 2 months later, the second vaccination with Prevnar 13 and Act-Hib will be

given.
- 3 weeks after de second vaccination, blood will be drawn.
- 8 months later, the third vaccination with Pneumovax and Act-Hib will be given.
- 3 weeks after the 3rd vaccination, blood will be drawn.
-14 months later, blood will be drawn.

Study burden and risks

Patients will be vaccinated at three separate moments with pneumococcal and conjugated Hib vaccines that are indicated for this patient group according to existing vaccination protocols. Blood samples will be drawn before the first vaccination and three weeks after each vaccination and six months after last vaccination, so five blood samples will be drawn. The vaccine will be used in the authorised form and for the 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 Hib and S. pneumoniae.

Contacts

Public
Sint Antonius Ziekenhuis

Koekoekslaan 1
Nieuwegein 3435 CM
NL
Scientific
Sint Antonius Ziekenhuis

Koekoekslaan 1
Nieuwegein 3435 CM
NL

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 five months before start of the study.
3. Age * 18 years.
4. Signing of informed consent.

Exclusion criteria

1. Completion of rituximab therapy >5-6 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.
4. Vaccination with Hib or pneumococcal vaccine in the last fifteen months before start of the study

Study design

Design

Study type: Interventional

Masking:	Open (masking not used)
Control:	Uncontrolled
Primary purpose:	Prevention

Recruitment

NL

Recruitment status:	Will not start
Enrollment:	152
Type:	Anticipated

Medical products/devices used

Product type:	Medicine
Brand name:	Act-Hib
Product type:	Medicine
Brand name:	Pneumovax
Product type:	Medicine
Brand name:	Prevnar 13

Ethics review

Approved WMO Date:	18-06-2012
Application type:	First submission
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	14-06-2013
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	10-07-2013
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	22-11-2013
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	17-02-2014
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: 27098
Source: NTR
Title:

In other registers

Register	ID
EudraCT	EUCTR2012-001843-34-NL
CCMO	NL40482.100.12
Other	volgt
OMON	NL-OMON27098