Development of humoral and cellular immune response in infants after pneumococcal conjugate vaccinations with Synflorix® or Prevenar-13®

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Primary: To compare immunogenicity (humoral and cellular) induced by PCV10 and PCV13 after the booster dose of a complete vaccination series (3+1, the current NIP schedule)
Secondary: To compare immunogenicity (humoral) induced by PCV10 and PCV13 at...

Ethical review	Approved WMO
Status	Recruitment stopped
Health condition type	Bacterial infectious disorders
Study type	Observational invasive

Summary

ID

NL-OMON37981

Source
ToetsingOnline

Brief title
Pneumococcal immune response to Synflorix® or Prevenar-13® in infants

Condition

- Bacterial infectious disorders

Synonym
pneumococcal infection, Streptococcus pneumonia

Research involving
Human

Sponsors and support

Primary sponsor: RIVM

Source(s) of monetary or material Support: Ministry of VWS

Intervention

Keyword: Cellular and humoral immunity, Pneumococcal conjugate vaccine, Prevenar-13®, Synflorix®

Outcome measures

Primary outcome

Primary

Pneumococcal serotypes

• Cellular immune response (Plasma B cells and memory B cells) immediately

before and 7-9 days after the booster at 11-months of age

• Humoral immune response (antibody concentrations and geometric mean

concentrations (GMT)) at 12 months of age

Secondary outcome

Secondary

Pneumococcal serotypes

• Opsonophagocytoses immediately before and 7-9 days after the booster at

11-months of age

• Avidity at 5, 8, immediately before and 7-9 days after the booster at

11-months and at 12 months of age

• Antibody concentrations and geometric mean concentrations (GMT) at 5, 8,

immediately before and 7-9 days after the booster at 11-months and at 12 months

of age

• Kinetics of antibody concentrations and geometric mean concentrations (GMT)

over time (at 5, 8, 11 and 12 months of age)

DTaP-HIb

• Antibody concentrations and geometric mean concentrations (GMT) at 5, 8, 11

and 12 months of age

Study description

Background summary

Streptococcus pneumonia (SP) is an important cause of morbidity and mortality worldwide, with the highest incidence of disease among children < 2 years of age. Streptococcus pneumonia consisting of > 90 known different serotypes, of which a limited number of about 20 serotypes are known to cause invasive pneumococcal disease (IPD).

Prevenar®, a seven-valent pneumococcal conjugate vaccine (PCV7) was first introduced in the Netherlands immunization program (NIP) for children born after April 2006. It confers protection against serotypes 4, 6B, 9V, 14, 18C, 19F and 23F (see figure 1). It has been introduced in the NIP for vaccination at 2, 3, 4 and 11 months of age. Recently in 2009, two new vaccines were registered, which can in due time replace PCV7 in the NIP. All children born after March 2011 will receive Synflorix®, a ten-valent pneumococcal conjugate vaccine (PCV10) which confers protection against three additional serotypes. Prevenar-13®, a thirteen-valent pneumococcal conjugate vaccine (PCV13) confers protection against another three extra serotypes, but is not implemented in the NIP.

The current study in combination with our previous KOKKI (cellular immunogenicity after PCV7 vaccination) and PIM (comparison of 4 different PCV13 vaccination schedules based on humoral immunogenicity) study can give input to the Health Council (HC) on the best vaccination strategy for pneumococcal vaccination. The outcomes of this trial will provide data on the humoral and cellular immune response of PCV10 and PCV13.

Study objective

Primary: To compare immunogenicity (humoral and cellular) induced by PCV10 and PCV13 after the booster dose of a complete vaccination series (3+1, the current NIP schedule)

Secondary:
To compare immunogenicity (humoral) induced by PCV10 and PCV13 at 5, 8, 11 and 12 months of a complete vaccination series (3+1, the current NIP schedule)

To investigate the possible influence of the pneumococcal vaccination on the serological responses of other vaccine components of the NIP which are administered simultaneously in the other limb (DTaP-Hib)

Study design

A controlled randomized parallel group trial with 2 groups (see figure 2 and table 1).

• Group 1 PCV13
o Divided in group 1a and 1b; 33 infants per group

• Group 2 PCV10
o Divided in group 2a and 2b; 33 infants per group

Group 1 and 2 are split in sub groups in order to reduce the burden of the 8 ml blood samples. Randomization will be done within group 1 and within group 2.

Study burden and risks

One blood collection of 8 ml (2x 4 ml tubes). The burden and risk is considered low.
The children might find the needle scary and it might be painful but only for a few seconds. A local anaesthetic (Emla® crème, Astra Zeneca) may be used to minimize pain. Blood collection could result in a small bruise at the location of injection, which will disappear within a few days.
Group 1; one heel/finger stick sampling, group 2: 3-4 heel/finger sticks sampling. The burden and risk is considered low.

For group 2 (PCV10 group), the children themselves have no direct benefit in participating in this trial. The trial is aimed to study the immune response after 3+1 PCV10 or PCV13 vaccinations. These children, who have followed the Dutch NIP, are the only possible children that can participate in the trial.
Visits will take 10-30 minutes each (depending on the type of blood collection and whether a questionnaire is taken).

Children in group 1 will receive PCV13 vaccinations. The side effects of these vaccinations are expected to be equal to the side effects of PCV10 (which the children would have received as part of the NIP). They will however receive these vaccinations at home to reduce the burden. These children will benefit from the added protection of the three extra serotypes which are not present in the PCV10 vaccination. These children are the only possible study group, since they are eligible for the Dutch NIP. Visits will take maximum 30 minutes each.

Contacts

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Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Children (2-11 years)

Inclusion criteria

• The children have to be of normal health (same health criteria apply as used in well-baby clinics when a child receives a vaccination, e.g. also children with small increases in temperature (<=38.5 °C) or cold are seen as children with normal health)
• The parents/legally representatives have to be willing and able to allow their child to participate in the trial according to the described procedures
• Presence of a signed informed consent (the parents/legally representatives have given written informed consent after receiving oral and written information)
• Group 1: The children are 2 months old (± 2 weeks), have not received any vaccinations and will receive all vaccinations (DTaP-IPV-Hib-HepB and PCV13) by the study team
• Group 2: The children are 4-6 months old and have received three DTaP-IPV-Hib-HepB and PCV10 vaccinations according to the 3+1 schedule of the Dutch NIP*.;*The Dutch NIP 3+1 schedule: All children born as of August 1st 2011 will receive Synflorix (PCV10) and DTaP-IPV-Hib-HepB vaccinations, at the age of 2, 3 4 and 11 months of age.

Exclusion criteria

•Group 1: Previous vaccinations with Prevenar-7 or Synflorix
•Group 2: Previous vaccinations with Prevenar-13 of Prevenar-7
•Vaccinations using a schedule that differs from the Dutch 3+1 schedule
•Presence of a serious disease that requires medical care that can interfere with the results of the study
•Known or expected allergy/hypersensitivity against one of the vaccine ingredients
•Known or suspected immunological disorder
•Previously administration of plasma products (including immunoglobulin), within three months of study enrolment
•Presence of bleeding disorders
•Communication problems that interfere with the trial
•Prematurity (<37 weeks after gestation)

Study design

Design

Study phase:	4
Study type:	Observational invasive
Intervention model:	Parallel
Allocation:	Randomized controlled trial
Masking:	Open (masking not used)
Control:	Active
Primary purpose:	Other

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	25-10-2011
Enrollment:	132
Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	Prevenar-13®

Product type:	Medicine
Brand name:	Synflorix®

Ethics review

Approved WMO Date:	01-08-2011
Application type:	First submission
Review commission:	METC Noord-Holland (Alkmaar)
Approved WMO Date:	07-09-2011
Application type:	First submission
Review commission:	METC Noord-Holland (Alkmaar)
Approved WMO Date:	16-04-2012
Application type:	Amendment
Review commission:	METC Noord-Holland (Alkmaar)
Approved WMO Date:	11-05-2012
Application type:	Amendment
Review commission:	METC Noord-Holland (Alkmaar)

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
EudraCT	EUCTR2011-002103-15-NL
CCMO	NL37173.094.11