Immunological effects of an acellular pertussis booster vaccination in children, young adults and elderly with different immunisation background.
An international study in Finland, the Netherlands and the United Kingdom

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Investigate the effects of aP booster vaccination in children, young adults and elderly on the (long-term) immune response to B. pertussis in three European countries with a different epidemiological background and primary vaccination schedule for...

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

Summary

ID

NL-OMON45409

Source
ToetsingOnline

Brief title
Booster against pertussis (Bert)

Condition

- Bacterial infectious disorders

Synonym
Pertussis, Whoping Cough

Research involving

Human

Sponsors and support

Primary sponsor: RIVM
Source(s) of monetary or material Support: GlaxoSmithKline,Innovative Medicines Initiative 2 (IMI2) ,Sanofi-aventis

Intervention

Keyword: Booster vaccination, Pertussis, Whooping cough

Outcome measures

Primary outcome

PT specific IgG antibodies at day 28 (T4).

Secondary outcome

Secondary study parameters/outcome of the study (if applicable):

*PT specific IgG antibodies and their avidity at T0, T4 and T5.

Specific IgG-levels to other pertussis vaccine antigens, as well as to

non-pertussis antigens will be determined at T0, T4 and T5, using a PERISCOPE

serological multiplex immunoassay.

* Functional pertussis-specific antibody levels will be determined in serum

samples at T0, T4 and T5, using PERISCOPE core assays as described in section

8.3.4. Differences in levels of functional antibodies will be measured before

and after vaccination. Functional antibody assays include bacterial adherence

inhibition (BAI), PT neutralisation (PTNA), serum bactericidal activity (SBA),

and bacterial opsonophagocytosis assay (OPA). Other serological parameters such

as avidity, subclass distribution (IgA, IgM) are optional in serum samples.

* Antigen-specific memory B cell responses at time points T0, T2, T4 and T5

will be measured to determine the effects of aP booster vaccination in

children, young adults and elderly, using PERISCOPE B cell core assay.

* Characterisation of the effect of an aP booster on the specific T cell immune response, both early after the boost and later on, in different age groups, vaccinated initially either with a whole cell or an acellular vaccine.

* Collection and biobanking of biological samples to be used for testing in novel exploratory immunoassays and for possible bridging to other pertussis vaccine studies.

Exploratory study parameters/outcome of the study (if applicable):

* Differences in T cell programming will be measured on fresh blood samples or frozen PBMC samples in an exploratory PERISCOPE T cell assay. This assay includes but is not limited to multi-colour flow cytometry and/or mass cytometry (CyTOF), combined with supernatant cytokine analysis.

* To assess differences in epigenetic imprinting of immune cells by primary vaccination on dTap-IPV booster vaccination, material for epigenetic markers will be isolated before and after vaccination. If differences in (functional) immunological memory are observed, epigenetic markers related to immune function will be analysed.

* Gene expression differences in response to dTap-IPV booster vaccination will be measured in immune cells, from before and after vaccination.

* Intra-individual changes in cell subsets in response to vaccination will be measured on fresh blood samples by flow cytometry (EuroFlow) and/or mass cytometry (CyTOF).

* Changes in the B cell receptor repertoire will be examined, as this will

provide information on the impact of vaccination in different priming backgrounds and ages.

* Cytokine production will be evaluated after ex vivo restimulation of PBMCs/whole blood, and potentially also directly in serum, taken before and after vaccination.

* The soluble factors in the eluate from nasosorption (including cytokines/chemokines) will be analysed by Luminex MIA, BAI and SBA.

Study description

Background summary

Pertussis, or whooping cough, is caused by the bacterium Bordetella pertussis (B. pertussis) and is an acute and serious respiratory infection, in particular for young and unvaccinated children. However, despite high vaccination coverage (95%), pertussis is re-emerging in the Netherlands since 1996. This phenomenon is also observed in most other western countries. The most recent epidemic in 2012 in the United Kingdom (UK) and the Netherlands highlighted the vulnerability of infants for a pertussis infection, causing 15 deaths all together. The pertussis infection rate in adolescents and adults has increased as well in the past years. This elevated incidence in adults is a risk factor for young babies, since infants are most often infected with B. pertussis through their mother.

The main purpose of this study is to investigate the dynamics and longitudinal effects of an acellular pertussis (aP) booster vaccination in children, young adults and elderly, on long-term humoral and cellular memory immunity against B. pertussis. The study will be performed in three European countries (UK, Finland and the Netherlands) with a different epidemiological background for pertussis incidence. In addition, different age groups had different primary schedules with whole cell pertussis (wP) or aP vaccines in their first year of life. Long-term memory responses will be analysed following aP booster vaccination to provide a detailed understanding of immunity to B. pertussis and to assess novel biomarkers as potential surrogates of long-lived protective immunity. This will include a detailed assessment of antigen-specific B and T cell responses and serology assays for pertussis antigens. In addition, the effect of booster vaccination on dynamic changes in immune cell subsets and

gene transcription will be investigated.

Study objective

Investigate the effects of aP booster vaccination in children, young adults and elderly on the (long-term) immune response to B. pertussis in three European countries with a different epidemiological background and primary vaccination schedule for pertussis.

Study design

longitudinal intervention study

Intervention

Participants will receive one injection of reduced diphtheria toxoid, tetanus toxoid and reduced acellular pertussis vaccine (dTap)-IPV, (Boostrix® IPV, GlaxoSmithKline (GSK)) combination vaccine intramuscularly in the upper arm. Mucosal samples will be taken before (T0), at 28 days (T4) and 1 year (T5) after vaccination. Venous blood samples will be drawn at T0 and at 1 (T1), 7 (T2), 14 (T3) days post-intervention, T4 and T5. Adults (cohorts C and D) will donate blood samples at T0, T2, T3, T4 and T5. Children will donate only at selected time points. All children in cohorts A and B will donate blood samples at T0, T4 and T5. Additionally, the children will be further divided in subcohorts for additional blood draws at one of the following time points: cohorts A at T2 or T3, cohort B at T1, T2 or T3. Summarising, children will be asked to donate blood 4 times, and young adults and elderly will be asked to donate blood 5 times in total over the entire study duration of 12 months. Mucosal samples will be taken at T0, T4 en T5.

Study burden and risks

Participants will benefit from participating in this study by receiving an additional Boostrix® IPV vaccination. From the worldwide public health perspective, participation in this study will contribute to insight in pertussis immunity. Although vaccination and especially venepunctures may be unpleasant, they are considered low risk invasive procedures. These risks will be mitigated by the performance of all procedures by experienced personnel. The sampling frequency is intensive for the young adults and elderly. To minimise sampling frequency for children, cohorts A and B will be divided into one of the subcohorts (i.e. the three *fixed* time points plus one additional time point). This will also minimise the total blood volume drawn from children in the first two weeks post-intervention.
Boostrix® IPV is a registered vaccine. Adverse reactions (ARs) to the vaccine may occur but they are expected to be mainly local and transient. Severe allergic reactions to one of the vaccine components are unlikely to occur.

Boostrix® IPV booster vaccination in children and adults is a common procedure in a large number of countries already.

Contacts

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Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Adolescents (12-15 years)
Adolescents (16-17 years)
Adults (18-64 years)
Children (2-11 years)
Elderly (65 years and older)

Inclusion criteria

* normal general health;
* within the right age group for the cohort;
* received all regular vaccines for their age group according to the Dutch National immunisation programme (NIP), UK NIP or Finnish NIP; a copy of the vaccination booklet will be included in the participant*s documents. If booklet is not available for cohorts A, B and C,

vaccination status will be checked with regulatory agencies / General practitioner. For cohort D this booklet might not be available due to their age;
* provision of written informed consent (see section 11.2 for details);
* willing to adhere to the protocol and be available during the study period.

Exclusion criteria

* present evidence of serious disease(s) within the last 3 months before inclusion requiring immunosuppressive or immune modulating medical treatment, such as systemic corticosteroids, that might interfere with the results of the study;
* chronic infection;
* known or suspected immune deficiency;
* history of any neurologic disorder, including epilepsy;
* previous administration of serum products (including immunoglobulins) within 6 months before vaccination and blood sampling;
* known or suspected allergy to any of the vaccine components (by medical history);
* occurrence of serious adverse events (SAEs) after primary DTwP-IPV (Diphtheria, Tetanus, whole-cell Pertussis, Polio) vaccination, DTaP-IPV (Diphtheria, Tetanus, acellular Pertussis, Polio) vaccination or any other vaccination (by medical history);
* vaccination with any other pertussis vaccine than those described in the inclusion criteria (i.e. only according to NIP);
* vaccination with any other Diphtheria, Tetanus and polio (DT-IPV) vaccine in the last 5 years, DT-IPV vaccination according to NIP in cohort B is no exclusion;
* children between 8 and 10 years of age eligible for cohort A in the Netherlands who have already received the DT-IPV booster vaccination according to the Dutch NIP around 9 years of age;
* mixed whole-cell pertussis (wP) and acellular pertussis (aP) priming within a participant, cohort B;
* Pregnancy

Study design

Design

Study phase:	4
Study type:	Interventional
Masking:	Open (masking not used)
Control:	Uncontrolled
Primary purpose:	Other

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	02-10-2017
Enrollment:	134
Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	Boostrix-Polio

Ethics review

Approved WMO Date:	07-06-2017
Application type:	First submission
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	01-09-2017
Application type:	First submission
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	12-04-2018
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	25-05-2018
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

No registrations found.

In other registers

Register	ID
EudraCT	EUCTR2016-003678-42-NL
CCMO	NL60807.100.17