Strengthening memory immunity in the aged population by vaccinating pre-elderly

Published: 12-05-2014
Last updated: 15-05-2024

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Ethical review	Approved WMO
Status	Recruitment stopped
Health condition type	Other condition
Study type	Interventional

Summary

ID

NL-OMON47511

Source
ToetsingOnline

Brief title
StimulAge study

Condition

- Other condition
- Bacterial infectious disorders

Synonym
Determine differences in vaccine response in the pre-elderly age group (50-65 years of age) to the MenACWY-TT and VZV vaccine.

Health condition

virale infectziekten (niet meer in te vullen boven)

Research involving

Human

Sponsors and support

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

Intervention

Keyword: biomarkers, immunesenescence, immunization, pre-elderly

Outcome measures

Primary outcome

The primary study outcome is to determine differences in vaccine response in the pre-elderly age group (50-65) to the MenACWY-TT and VZV vaccine. Primary parameters to determine these differences will be:

o MenACWY-TT: Meningococcal specific Serum bactericidal antibody (SBA) levels after vaccination

o VZV: memory T cell reponses against VZV after vaccination

Secondary outcome

* Determine biomarkers associated with the immunesenescence process and correlate these to the vaccine response.

o Cytokine levels in serum (for instance: IL-6, TNF*, IL-1*, IL-10, IL-1ra, IL-17 and IFN*)

o Biochemical parameters (for instance: DHEAs, CRP, RF, Vitamin D, cortisol)

o CMV IgG levels in serum

o Total IgG, IgM, and IgA levels

* To determine MenACWY specific IgG, IgM, IgA, IgG-subclasses and avidity in serum;

* To determine VZV specific IgG responses in serum

* To determine general health status of the participant using a short

questionnaire

* Explorative: To determine Meningococcal specific B cell responses

* Explorative: To determine Tetanus specific B and T cell responses

* Explorative: determine additional interesting biomarkers

o miRNA

o mRNA AID

* Explorative: Phenotyping of the total immuun cell subsets using PBMCs and

counting of different lymphocyte subsets

* Explorative: Varicella Zoster specific B cell responses

Study description

Background summary

The world population is ageing. In 2060 about 30% of the population is predicted to be above 65 years, compared to 17.4% in 2010. Population ageing has implications for the medical conditions, as with age the vulnerability for chronic diseases and severe infections increases. Prevention of infectious diseases by immunization of the elderly population is a prerequisite to establish healthy ageing.
Due to the demographic changes in the future population, vaccination programmes need to shift to a life-course scheme. Childhood vaccinations remain extremely important to induce immunity, but it is also necessary to maintain immunity afterwards, before reaching old age. Immunization of elderly is challenging, due to changes in the immune system with age, which cause difficulties to respond to vaccination (immunesenescence). It is suggested that immunization against antigens has to be established before the onset of immunesenescence, most probably in the 5th or 6th decade of life. Using this strategy, the protection of elderly against infectious diseases might be improved. Biomarkers that predict low vaccination responses earlier in life might also help to protect the aged population, since precautions can be taken before the onset of immunesenescence.

The vaccin against Meningococcal A,C,W and Y will be adminstered to part of the participants. This vaccin is used, because the immunity in the adults and elderly population against Meningococcal is very low at this moment. Differences in response will be measured in this pre-elderly study groep at the serological and cellular aspects. Moreover, cellular immunity against the Varicella Zoster vaccin will be studied in a different study group of pre-elderly persons. Implementation of the Varicella Zoster vaccin into the Dutch National Program at this moment is toppic of fierce debate, since the vaccin is not causing optimal protection in elderly persons. The results of this study will contribute to the knowledge connected to immunsenescence and possibly help to set up and effective vaccinescheme for the future.

Study objective

The main objective of this study is to determine differences in vaccine responses in the pre-elderly age group (50-65 years of age) to a primary immunization with vaccine antigens to which no or (very) low pre-vaccination antibody levels and memory cells exist. The MenACWY-TT (against Meningococcal ACWY) and VZV (against Varicella Zoster) vaccines will be used to study these differences. Moreover, biomarkers that predict the responsiveness of pre-elderly persons will be explored.

Study design

Longitudinal intervention study, explorative biomarker study

Intervention

200 (+/- 10) participants receive one vaccination againt MenACWY-TT (Nimenrix - GSK). The vaccination is performed intramuscularly in the upper arm at the start of the study. Blood samples are drawn pre-vaccination and 7 days, 28 days, and 1 year after vaccination. Optional: participants will be asked to participate in a folllow-up study with blood samples drawn 5 and/or 8 years after vaccination.
50 (+/- 10) participants receive one vaccin against Varicella Zoster (Zostavax - Sonifi Pasteur). The vaccination is performed subcutaneously in the upper arm at the start of the study. Blood samples are drawn pre-vaccination and 14 days, 28 days, and 1 year after vaccination. Optional: participants will be asked to participate in a follow-up study with a blood sample drawn 8 years after vaccination.

Study burden and risks

Participants will benefit from participating in this study by receiving an additional vaccination against Meningococcal A,C, W and Y or Varicella Zoster. From the public health perspective, participation in this study will contribute

to improvement of the National Vaccination Prgramm, by improving knowledge of vaccination response at pre-elderly age. Vaccination and venapunctures are unpleasant at the moment of injection, however, they are low risk invasive procedures. Nimenrix and Zostavax are registered vaccines in the Netherlands. Adverse reactions to the vaccines 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. As a compensation for the vaccination and the venapunctures, all participants will receive a total of ¤25,- in vouchers. If participants are participating in the follow-up study, they will receive a voucher of ¤15 for every extra timepoint.

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, participants must meet all of the following criteria:
* General good health
* 50-65 years of age
* Provision of written informed consent;
* Adherent to protocol and available during the study period.

Exclusion criteria

Any of the following criteria will exclude a participant from this study:, * Antibiotic use within 14 days of enrollment;
* Present evidence of serious disease(s) demanding immunosuppressive medical treatment, like corticosteroids, that might interfere with the results of the study within the last 3 months;
* Known or suspected allergy to any of the vaccine components (by medical history);
* Occurrence of serious adverse event after other vaccination (by medical history);
* Known or suspected immune deficiency;
* History of any neurologic disorder, including epilepsy;* Known or suspected coagulation disorder;
* Previous administration of serum products (including immunoglobulins) within 6 months before vaccination and blood sampling;
* Hormone use, such as post-menopausal hormone or contraceptive pills, within the last 3 months;
* Serious surgery within the last 3 months;
* Previous vaccination with the MenC, MenC-TT, or MenACWY-TT vaccine. (for the MenACWY-TT study group)
* Previous meningococcal episode (MenACWY-TT study group)
* Previous vaccination with VZV vaccine (for the VZV study group)
* Previous Varicella Zoster episode (VZV study group)
* Vaccination with DT, DT-IPV, TdaP or T within the past 5 years (for the MenACWY-TT study group)
* Any vaccination within a month before enrollment;
* Pregnant at the start of the study;

Study design

Design

Study phase:	4
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:	Recruitment stopped
Start date (anticipated):	15-09-2014
Enrollment:	207
Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	Nimenrix
Product type:	Medicine
Brand name:	Zostavax

Ethics review

Approved WMO

Date:	12-05-2014
Application type:	First submission
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)

Approved WMO

Date:	20-05-2014
Application type:	First submission
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)

Approved WMO

Date:	18-06-2019
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	19-06-2019
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: 25211
Source: NTR
Title:

In other registers

Register	ID
EudraCT	EUCTR2014-000967-42-NL
Other	NL4518
CCMO	NL48510.100.14
OMON	NL-OMON25211

Study results

Results posted: 04-03-2020

First publication
04-03-2020