Immune responses to influenza and pneumococcal conjugate vaccines in older adults compared to middle-aged adults and adults.

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Ethical review	Approved WMO
Status	Completed
Health condition type	Other condition
Study type	Interventional

Summary

ID

NL-OMON54826

Source
ToetsingOnline

Brief title
VITAL

Condition

- Other condition
- Viral infectious disorders

Synonym
Aging, Prevention

Health condition

immuunsysteem

Research involving
Human

Sponsors and support

Primary sponsor: RIVM
Source(s) of monetary or material Support: Innovative Medicines Initiative (IMI)

Intervention

Keyword: Aeging, Immuun responses, Infectious diseases

Outcome measures

Primary outcome

The primary endpoints are to compare vaccine-induced specific serum antibody levels for both the influenza quadrivalent influenza vaccine (QIV) and the pneumococcal PCV13 vaccine (geometric mean titters (GMTs) for influenza and geometric mean concentrations (GMCs) for pneumococcal vaccine* in older adults with those in middle-aged adults and adults one month post vaccination.

Secondary outcome

The secondary parameters/endpoints are:

1) to compare induction and persistence of vaccine-induced serum antibody and T cell responses by measurement of vaccine-specific antibody titers and specific T-cell immunity pre- and post-vaccination between older adults, middle-aged adults and adults.
2) to determine the impact of (changes in) clinical baseline and (immunological) biomarker status as candidate predictive markers for vaccine responsiveness. Data collected in questionnaires (a.o. general health and quality of life, medical history and life style) and by measurements of local

and systemic immune status and systemic cellular composition will be correlated with vaccine responses and compared across older adults, middle-aged adults and adults.

Exploratory endpoints consist of in-depth analysis of the quality of the vaccine-induced innate, humoral (local and systemic) and cellular immune responses, and compare the impact of the biological and genetic baseline status on the vaccine responses between older adults, middle-aged adults and adults.

Study description

Background summary

Due to the increase in the percentage of adults of 65 years and older, a population that is more vulnerable to infections due to a decline in immune responses with ageing (immunosenescence), the number of people with severe infectious disease-related health problems is increasing. Vaccines are one of the most effective means to protect against different infections. However, the responses to vaccines in elderly may vary considerably. All participants will receive a seasonal influenza vaccine, and a pneumococcal vaccine and optional a COVID-19 vaccine to study different vaccine concepts in the same individuals. The influenza vaccine will induce a booster response since only subjects who have had an influenza vaccination in the previous year will be included, whereas the pneumococcal vaccine will be the first dose inducing a primary response to the vaccine serotypes. The COVID-19 vaccine is a combination of prime-boost vaccination with an mRNA vaccine concept. This approach allows comparison of primary and booster(s) vaccine response from different vaccine concepts in the different age groups. Knowledge on which parameters of the immune system or external factors contribute to decreased immune responsiveness to vaccines can provide leads to improve vaccine responsiveness in general. In addition, this information can be used to predict effective or non-effective immune responses in specific subsets of individuals. Eventually this information may help to design optimal future vaccination strategies.

Study objective

The main objective of this trial will be to get a better insight in the

influence of age and age-related changes by internal and external factors on vaccine-induced immune responses and gain knowledge on the trajectory of immune decline in older adults, pre-elderly (middle-aged) adults in comparison to adults with the ultimate goal to formulate evidence-based strategies to improve immunity to vaccines in the ageing population.

Study design

Longitudinal intervention study

Intervention

All subjects will receive the seasonal quadrivalent inactivated influenza vaccine (QIV) (2019-2020) (autumn 2019) and the 13-valent pneumococcal conjugate vaccine (PCV13) (spring 2020- spring 2021) and optionally an mRNA COVID-19 (booster(s)) vaccine.

Study burden and risks

The burden associated with participation involves collection of blood samples by venipuncture (9 times; 48 to 107 ml per visit with a mean total volume of 634 ml over an 24 month period), blood collection by fingerstick (2 time 300 ul), nasopharyngeal and oropharyngeal swabs (3 times), saliva samples (5 times) and feces (2 times). In case of participation to the SARS-CoV-2 sub study, additional visits involves collection of blood by venipuncture (4 times, 7-43 ml per visit, with a mean total volume of 64ml over 12 month period), blood collection by fingerstick (1 time, 300 µl) and nasopharyngeal and oropharyngeal swabs (4 times). Participants of the SARS-CoV-2 booster dose response study, will have a vaccination/blood collection visit and 3 follow-up finger prick collections over a 12 month period. A subset of the participants will be asked to three times donate a larger blood volume collected by venipuncture during study visits (44 ml per visit) and 1 additional fingerstick blood sample (1 time 300 ul),
3 additional nose (or saliva) fluids samples. All booster dose participants will be asked to complete a total of
4 additional questionnaires. For these participants the 12 months post second COVID vaccine dose follow-up visit (visit Te) will not be performed.
All extra SARS-CoV-2 booster participants will have a vaccination/ blood collection and 3 follow-up finger prick collections (4x 300uL) over a 12 month period. Depending on the timing of the extra booster, one or multiple timepoints of the previous booster study will be skipped.

In the autumn of 2022 all participants older than 60 years of age were invited for the follow up of the autumn 2022 COVID-19 booster vaccination. The follow-up was comparable to the follow-up of the previous boosters, as previously described, which included additional blood collection timepoints 1

month, 6 months and12 months post vaccination (3x, 300uL for for the finger pricks). For the subgroup the timepoint 1 months and 6 months post vaccinations will be a venipuncture (44mL per home visit). The pre-vaccination sample will replace the last timepoint of the previous booster. Analysis of immunological response to additional autumn 2023 COVID-19 booster vaccination will require additional blood collection timepoints 1 month and 12 months post vaccination (3x, 30uL for finger pricks). For the subgroup, the pre and 1 month post vaccination will be venipuncture (44mL per home visit) and mucosal lining fluid will be collected. The timepoint 12 months post vaccination will include a fingerprick and the collection of mucosal lining fluid for all the participants. The pre-vaccination sample will coincide with 12 month post autumn 2022 booster vaccination timepoint.

All participants will receive a pneumococcal vaccination that they otherwise would not have had. In addition, the subject will be asked to fill in questionnaires, perform a grip strength test (3 times) and have the blood pressure measured (3 times). The samples and results of the measurements (such as blood pressure and grip test) will be collected during a total of 11 visits. For the oldest age group, visits will be home visits, whereas for the other two age groups, visits will be at a study location close to their office/work.

The potential risks are considered minimal. The pneumococcal vaccine has been registered in Europe and the US and has been used for several years in children and adults. Adverse events related to pneumococcal vaccination are comparable with events associated with other vaccines such as local injection site reactions, general fatigue, headache, diarrhea and vomiting. The benefit for the individual subjects who participate in this trial is protection against pneumococcal disease (e.g. pneumonia, sepsis and meningitis) by vaccination with a pneumococcal conjugate vaccine (PCV13). The results of the study may contribute to a better control of respiratory diseases in older age groups on a population level in the future. All subjects are eligible for influenza vaccination and therefore influenza vaccination is not considered a benefit for this study population.

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

•Be 25 years or older at the time of inclusion.
•Have received a seasonal influenza vaccination in previous season (2018-2019).
•Be capacitated.
•Have signed Informed Consent

Exclusion criteria

•Having had a previous pneumococcal vaccination (PCV or the 23-valent pneumococcal polysaccharide vaccine (PPV23)).
•Known or suspected allergy to any of the vaccine components or having experienced a previous severe adverse reaction to any vaccine.
•Receipt of any high-dose (>= 20 mg of prednisone daily or equivalent) daily corticosteroids (local incl. inhaled steroids are acceptable) within 2 weeks of study entry
•Repeated use of any high dose of corticosteroids (a dose of > 30 mg of prednisone or equivalent per day for multiple days) in the recent past.
•Receipt of an organ- or bone marrow transplant
•Have a (functional) asplenie.
•Receipt of chemotherapy in the last 3 years.
•Receipt of blood products or immunoglobulin, within three months of study entry.
•Known or suspected coagulation disorder that in the opinion of the investigator would contraindicate against receiving an intramuscular injection

or undergo frequent blood sampling.
•Known anemia, measured as Hb < (8,5 mmol/l for men and 7,5 mmol/l for woman; NHG standard Anemia)
•Known to be positive for human immunodeficiency virus (HIV), and/or hepatitis C virus (HCV) and/or hepatitis B virus (HBV).
•Known or suspected immunodeficiency or use of immunosuppressive therapy that according to the investigator, in consultation with a medical expert, contraindicates a Prevnar-13 vaccination.

Exclusion criteria COVID-19 vaccination study

•Treatment with COVID-19 monoclonal antibodies less that 3 months before COVID-19 vaccination.
•Known pregnancy at the moment of COVID-19 vaccination.

Study design

Design

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

Recruitment

NL

Recruitment status:	Completed
Start date (anticipated):	26-08-2019
Enrollment:	385
Type:	Actual

Medical products/devices used

Registration:	No
Product type:	Medicine
Brand name:	COVID-19 mRNA vaccine
Product type:	Medicine

Brand name:	Prevenar-13
Product type:	Medicine
Brand name:	seasonal Quadrivalent inactivated Influenza Vaccine

Ethics review

Approved WMO Date:	30-04-2019
Application type:	First submission
Review commission:	METC NedMec
Approved WMO Date:	19-06-2019
Application type:	First submission
Review commission:	METC NedMec
Approved WMO Date:	24-06-2020
Application type:	Amendment
Review commission:	METC NedMec
Approved WMO Date:	25-06-2020
Application type:	Amendment
Review commission:	METC NedMec
Approved WMO Date:	06-01-2021
Application type:	Amendment
Review commission:	METC NedMec
Approved WMO Date:	14-01-2021
Application type:	Amendment
Review commission:	METC NedMec
Approved WMO Date:	22-02-2021
Application type:	Amendment
Review commission:	METC NedMec
Approved WMO Date:	06-03-2021

Application type:	Amendment
Review commission:	METC NedMec
Approved WMO Date:	02-11-2021
Application type:	Amendment
Review commission:	METC NedMec
Approved WMO Date:	03-11-2021
Application type:	Amendment
Review commission:	METC NedMec
Approved WMO Date:	09-03-2022
Application type:	Amendment
Review commission:	METC NedMec
Approved WMO Date:	14-08-2023
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Utrecht (Utrecht)
Approved WMO Date:	24-08-2023
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Utrecht (Utrecht)
Approved WMO Date:	29-09-2023
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Utrecht (Utrecht)
Approved WMO Date:	05-10-2023
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Utrecht (Utrecht)
Approved WMO Date:	18-08-2024
Application type:	Amendment
Review commission:	METC NedMec
Approved WMO Date:	21-08-2024

Application type:	Amendment
Review commission:	METC NedMec

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	EUCTR2019-000836-24-NL
CCMO	NL69701.041.19