A Phase 2, Comparative Randomised Trial to Evaluate the impact of reduced COVID-19 mRNA vaccination regimen on immunological responses and reactogenicity in paediatric subjects with prior SARS-CoV-2 immunity

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Primary ObjectiveTo determine if the humoral immune response of a single compared to a two dose COVID-19 vaccination regimen is non-inferior in paediatric subjects who are immunologically primed by natural infection. Secondary Objective(s) 1.To...

Ethical review	Approved WMO
Status	Completed
Health condition type	Viral infectious disorders
Study type	Interventional

Summary

ID

NL-OMON54453

Source
ToetsingOnline

Brief title
CoVacc

Condition

- Viral infectious disorders

Synonym
Coronavirus, SARS-CoV-2

Research involving

Human

Sponsors and support

Primary sponsor: Universitair Medisch Centrum Utrecht
Source(s) of monetary or material Support: Horizon 2020

Intervention

Keyword: Children, Dose, SARS-CoV-2, Vaccination

Outcome measures

Primary outcome

The geometric mean ratio of neutralizing titers against wild type virus (Virus Neutralization Assay) at day 28 after completion of the control versus the intervention regimen of the vaccine.

Secondary outcome

Safety:

-The percentage of subjects reporting at least one solicited systemic adverse events Grade >= 2 (AEs) in the 7 days after any vaccine dose, as measure of systemic reactogenicity.

-The percentage of subjects reporting solicited local and systemic adverse events (AEs) for 7 days after each vaccine dose.

-The percentage of subjects reporting unsolicited AEs for 14 days after each vaccine dose.

-The percentage of subjects reporting serious adverse events (SAEs) Grade >=3 on the Common Toxicity Criteria or Adverse Events of Special interest (AESI) until 12 months post-vaccination.

Immunogenicity:

-Neutralizing titers against wild type virus (Virus Neutralization Assay) at 6

and 12 months post-vaccination.

-Quantitative enzyme-linked immunosorbent assay (anti-RBD-ELISA) at 28 days, 6

months and 12 months post-vaccination.

-Geometric Mean Fold Ratio in SARS-CoV-2 serum anti-RBD antibody titer from

before vaccination to each subsequent time points at 1, 6 and 12 months

post-vaccination.

-Neutralizing titers against variants of concern (Virus Neutralization Assay)

at day 28 and 6 months post-vaccination.

Study description

Background summary

Since early in the pandemic, it has been evident that the disease severity and transmissibility from SARS-CoV-2 infection in children and adolescents are reduced compared to adults. Yet paediatric hospitalisations and deaths do occur, in particular in subjects without any prior immunity to the virus and when virus circulation in the community is high. SARS-CoV-2 infections in children and adolescents may also serve as a reservoir of the virus, thereby maintaining community transmission and fuelling the emergence of new mutant strains. The role of children in the spread of COVID-19 seems to be affected by different contact patterns and hygienic habits, so that more intense contact and mixing patterns, for example in schools, could offset the effect of reduced susceptibility and infectivity. As children have been *last in line* - if at all included- in vaccination programs across Europe and globally, an increasing fraction of vaccine eligible children will consist of non- naïve individuals.
In combination with the emerge of the rapidly spreading Omicron variant in early 2022, it is estimated that the vast majority of the population has experienced a SARS-CoV-2 infection at some point. This ensures that almost every child who will receive a corona vaccination in the future has already been in contact with the virus.
Evidence from adult clinical studies reveals that in individuals with a previous SARS*CoV*2 infection, a single dose of messenger RNA (mRNA) vaccine is

immunologically equivalent, or even superior, to a full vaccine schedule in naïve individuals. These observations demonstrate that the first vaccine dose serves as a booster in naturally infected adult individuals and therefore it is sufficient to administer just a single dose as the primary vaccine series. As a result, European countries have adopted a single*dose primary series mRNA vaccine strategy for adolescents and adults with evidence of prior SARS*CoV*2 infection. However, although some countries recommend a single dose as vaccination regime for children 5-11 years with prior SARS*CoV*2, a single dose is not indicated in the current SmPC due to lack of data.
From theory however, it is most plausible that a similar approach could be used in children 5*11 years old with prior infection. A single dose primary series would have several advantages over a two*dose approach for several reasons. First, it reduces the burden of injections and side effects in children.
Second, it lowers the risk of rare side effects such as myocarditis due to immune hyperstimulation. Third, it supports and overall dose sparing strategy. Fourth, it may reduce the risk of original antigenic sin due to repeated selective stimulation of the immune response to the vaccine type of SARS*CoV*2. This could be of particular importance in light of the partial immune escape seen with emerging variants of concern (VoCs). Since the Omicron variant became dominant, the risk of developing severe COVID-19 from a SARS-CoV-2 infection is now low for most children aged 5 to 11. The risk is higher for children with serious underlying medical conditions. For this reason, most European countries have now adjusted their vaccination advice for children aged 5-11 years of age, so that vaccination is only offered to children with an increased medical risk.

Study objective

Primary Objective
To determine if the humoral immune response of a single compared to a two dose COVID-19 vaccination regimen is non-inferior in paediatric subjects who are immunologically primed by natural infection.

Secondary Objective(s)
1.To assess the safety and reactogenicity profile of a single dose COVID-19 vaccine regimen against SARS-CoV-2 in paediatric subjects with a history of prior SARS-CoV-2 infection, compared to the two dose regimen.
2.To assess the medium (6 months) and long term (12 month) humoral immune response of the single COVID-19 vaccine dosing regimen against wild-type SARS-CoV-2 in paediatric subjects with a history of prior SARS-CoV-2 infection.
3.To assess the short (28 days), medium and long term humoral immune response of the single dose COVID-19 vaccine regimen against SARS-CoV-2 variants of concern (VoCs) in paediatric subjects with a history of prior SARS-CoV-2 infection.

Study design

The design is a comparative randomised Phase 2 study in healthy children to evaluate immunogenicity and safety profiles of a single dose COVID-19 mRNA vaccination regimen in paediatric subjects with prior SARS-CoV-2 infection. The protocol will have two arms. The population consists of paediatric subjects with documented evidence of prior SARS-CoV-2 infection. Subjects will be randomised to receive either 1) BNT162b2 first dose followed by a second BNT162b2 dose (control arm), or 2) a single dose of BNT162b2 vaccine (intervention arm). The subjects will be fully vaccinated with either the 10 µg Original Comirnay or the 5/5 µg Comirnaty Original/Omicron BA.4-5. Randomisation will be stratified by sex and centre.

Intervention

The protocol will have two arms. Subjects will be randomised to receive either 1) BNT162b2 first dose followed by a second BNT162b2 dose (control arm), or 2) a single dose of BNT162b2 vaccine (intervention arm). The subjects will be fully vaccinated with either the 10 µg Original Comirnay or the 5/5 µg Comirnaty Original/Omicron BA.4-5.
Randomisation will be stratified by sex and centre.

Study burden and risks

Participation in this clinical trial poses a minimal risk of inconvenience through sample collection and attendance of follow-up visits. Furthermore the Investigational Product is already registered for the study population. Therefore, subjects volunteering for this trial are not considered to be at additional risk in relation with the authorized standard of care vaccine administration. There is a very small risk that a single dose regimen is less effective against severe COVID-19. However, even without vaccination the risk of severe COVID-19 is already extremely low in this age group, such that any small effect on efficacy would have minimal or no health consequences. Benefits for the subjects in the intervention group are related to potential achievement of immunogenicity while providing lower reactogenicity in this group receiving a single dose.

Contacts

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Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Children (2-11 years)

Inclusion criteria

1.Aged >=5 years to <=11 years of age on day of signing the informed consent form.
2.In good health or stable clinical condition.
3.Legally Acceptable Representative (LAR) has reviewed the subject information and signed the informed consent form on behalf of the subject and the subject has expressed willingness to participate.

Exclusion criteria

1.Has previously received any investigational or licensed COVID-19 vaccine.
2. Has known congenital or acquired immune disorder or immunodeficiency that may interfere with vaccine response e.g. known infection with human immunodeficiency virus (HIV) with low CD4 count or other immunosuppression at time of signing informed consent form.
3. Has a history of autoimmune disease or an active autoimmune disease requiring therapeutic intervention (including systemic glucocorticoids), or findings that may have a significant effect on the target endpoints and which may therefore mask or inhibit the therapeutic effect under investigation as judged by the investigator.
4. Bleeding diathesis or condition associated with prolonged bleeding that would, in the opinion of the investigator, contraindicate intramuscular injection or venepuncture.
5. History of severe adverse reaction associated with a vaccine and/or severe

allergic reaction (eg, anaphylaxis) to any component of the study intervention(s).
6. Receipt of medications intended to prevent COVID-19.
7. Uses drugs with significant interaction with the investigational product or has any contraindications as per the Summary of Product Characteristics.
8. Other medical or psychiatric condition or laboratory abnormality that may increase the risk of study participation or, in the investigator*s judgment, make the subject inappropriate for the study.
9. Has any kind of dependency on the principal investigator or member of the study team or LAR is employed by the principal investigator or within the same department as the PI or study team at the institution where the study is executed.
10. Is unable to report solicited adverse events.

Study design

Design

Study phase:	2
Study type:	Interventional
Intervention model:	Parallel
Allocation:	Randomized controlled trial
Masking:	Open (masking not used)
Control:	Active
Primary purpose:	Treatment

Recruitment

NL

Recruitment status:	Completed
Start date (anticipated):	24-08-2022
Enrollment:	50
Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	Comirnaty Original/Omicron BA.4-5
Product type:	Medicine

Brand name:	Original Comirnaty

Ethics review

Approved WMO Date:	08-10-2021
Application type:	First submission
Review commission:	CCMO: Centrale Commissie Mensgebonden Onderzoek (Den Haag)
Approved WMO Date:	24-11-2021
Application type:	First submission
Review commission:	CCMO: Centrale Commissie Mensgebonden Onderzoek (Den Haag)
Approved WMO Date:	28-01-2022
Application type:	Amendment
Review commission:	CCMO: Centrale Commissie Mensgebonden Onderzoek (Den Haag)
Approved WMO Date:	06-04-2022
Application type:	Amendment
Review commission:	CCMO: Centrale Commissie Mensgebonden Onderzoek (Den Haag)
Approved WMO Date:	05-04-2023
Application type:	Amendment
Review commission:	CCMO: Centrale Commissie Mensgebonden Onderzoek (Den Haag)
Approved WMO Date:	20-04-2023
Application type:	Amendment
Review commission:	CCMO: Centrale Commissie Mensgebonden Onderzoek (Den Haag)

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	EUCTR2021-005043-71-NL
CCMO	NL79226.000.21

Study results

Date completed: 10-04-2024

Results posted: 01-11-2024

First publication
01-11-2024