AntiBody response in Risk groups to COrona Vaccination treated in the Adrz hospital:

Published: 26-02-2021
Last updated: 04-04-2024

In the coming months, immunocompromised patients treated in our hospital will be requested to undergo vaccination if they comply with the National Institute for Public Health guidelines. For all subgroups, it is of utmost importance to assess the...

Ethical review	Approved WMO
Status	Pending
Health condition type	Autoimmune disorders
Study type	Observational invasive

Summary

ID

NL-OMON50794

Source
ToetsingOnline

Brief title
AbriCoVa

Condition

- Autoimmune disorders
- Miscellaneous and site unspecified neoplasms benign
- Renal disorders (excl nephropathies)

Synonym
immunocompromised patients, patients with decreased defense against infections

Research involving
Human

Sponsors and support

Primary sponsor: Interne Geneeskunde

Source(s) of monetary or material Support: Stcihting Wonder en Stichting Ter bevordering van Zorgprojecten en Onderzoek Intern Geneeskunde

Intervention

Keyword: BNT162b2, Immunocompromised, Immunogenicity, mRNA1273

Outcome measures

Primary outcome

Vaccine efficacy (SARS CoV incidence within a follow up of at least 2 years)

Quality and quantity of the antbody response to the vaccines in 5 patient

groups compared to healthy volunteers

Secondary outcome

Adverse effects after first and second vaccination

Study description

Background summary

The SARS COV-2 pandemic has prompted the (bio)medical, pharmaceutical, governmental, as well as global organizations such as the WHO, to quickly develop safe and effective vaccines in order to control the outbreak, minimize morbidity and mortality, and limit the societal and economic impact. . In the Netherlands, the government has pre-ordered a number of vaccines from various companies and currently (February 2021) two different vaccines, based on the advice of the National Institute for Public Health and the Environment, are in use and the vaccination process has started.
The two vaccines - BNT162b2 (provided by Pfizer Biontech) and mRNA1273 (provided by Moderna)- are messenger RNA vaccines, encoding the S1 spike protein of SARS-CoV-2. After injection, the vaccine particles bump into cells and fuse to them, releasing mRNA. The cell*s molecules read its sequence and build spike proteins. The mRNA from the vaccine is eventually destroyed by the cell, leaving no permanent trace. Some of the spike proteins form spikes that migrate to the surface of the cell and stick out their tips. The vaccinated cells also break up some of the proteins into fragments, which they present on their surface. These protruding spikes and spike protein fragments can then be

recognized by the immune system. When a vaccinated cell dies, the debris will contain many spike proteins and protein fragments, which can then be taken up by a type of immune cell called an antigen-presenting cell. The cell presents fragments of the spike protein on its surface. When other cells called helper T cells detect these fragments, the helper T cells can raise the alarm and help marshal other immune cells to fight the infection.

Measurements performed to test the immunogenicity of the candidate vaccines:

Functional neutralizing antibodies to SARS COV-2 that are produced following vaccination (against the spike glycoprotein and the receptor-binding domain) are considered as potential biomarkers of protective efficacy (1). This is why drug companies firstly performed Phase 1 studies to find the right vaccine and its right dose based on such biomarker assays (2,3). For instance , the degree of immunogenicity produced by BNT162b2 was measured as follows: SARS-COV-2 serum neutralization assay and receptor-binding domain [RBD]-binding or S1-binding IgG direct Luminex immunoassays were conducted before the administration of vaccine or placebo, at 7 days and 21 days after the first dose, and at 7 days (i.e., day 28) and 14 days (i.e., day 35) after the second dose.

Protective efficacy in terms of infection risk

The efficacy of BNT162b2 and mRNA1273 has been underlined by two prospective placebo-controlled randomized trials with large patients groups in order to acquire a sufficient number of events after short follow up (4,5). The 2 studies however excluded the following patient groups:

mRNA1273
- Immunosuppressive or immunodeficient state, including human immunodeficiency virus (HIV) infection, asplenia, and recurrent severe infections
- Has received systemic immunosuppressants or immune-modifying drugs for >14 days in total within 6 months prior to Screening (for corticosteroids >=20 milligram (mg)/day of prednisone equivalent).

BNT162b2
- Immunocompromised individuals with known or suspected immunodeficiency, as determined by history and/or laboratory/physical examination
- Individuals who receive treatment with immunosuppressive therapy, including cytotoxic agents or systemic corticosteroids, eg, for cancer or an autoimmune disease, or planned receipt throughout the study

Apparently, the investigators either expected the vaccine to be less effective in these patient groups and/or they may have been cautious with regards to vaccination safety.

Currently, there are no data on the efficacy and safety of these vaccines in

patients using high dose steroids or other immunosuppressive agents, patients with a solid or hematological malignancy and patients who have undergone a solid organ or hematopoietic stem cell transplantation.

The Dutch Society of Hematology (NVvH) has issued a vaccination guideline, which states that -irrespective of disease or therapy type- postponement is not necessary if patients are requested to come by for vaccination (https://hematologienederland.nl/covid-19/). Furthermore, The NVvH, as well as the Dutch Society of Medical Oncology, the Dutch Nephrology Federation and the Dutch Society of Gastroenterologists have collaborated with the National Institute for Public Health in the preparation of a general guideline for immunocompromised patients (https://lci.rivm.nl/handleiding-covid-19-vaccinatie-van-immuungecompromitteerde-patienten).

In general, succesful seroconversion and seroprotection depend on vaccine immunogenicity and host cellular immunity, which could be poorer due to underlying disease and/or immunosuppressive medication. There is no theoretical basis for an increased risk of anaphylaxis.

Study objective

In the coming months, immunocompromised patients treated in our hospital will be requested to undergo vaccination if they comply with the National Institute for Public Health guidelines.

For all subgroups, it is of utmost importance to assess the degree of immunogenicity according to methods (similar to the ones) used in the original Phase 1 and 2 studies.

We plan to prospectively monitor immunogenicity of BNT162b2 and mRNA1273 (according to the measures used in the registration studies), efficacy and toxicity in 5 different groups of immunocompromised patients:
Furthermore , we plan to prospectively monitor adverse effects and vaccine efficacy (i.e. prevention of SARS CoV- 2 infection within a follow up period of at least two years).

Control Group:
A control group comprising 10 healthy volunteers aged 18 years or older will undergo the same study procedures, except for the monitoring of adverse vaccine effects..

Study design

This a prospective observational study, which strives to provide insight in the immunogenicity, toxicity and efficacy of two approved SARS CoV-2 vaccines in 5

subgroups of immunocompromised patients, treated in the Adrz Hospital.

Patient inclusion takes place prior to the first vaccination and the same counts for the volunteers.

The following baseline data will be collected in the CRF:

Patient age
Patient sex
For which disease have the immunosuppressants been prescribed?
Outpatient medication used
Specification of systemic treatment and last date of administration

The study requires 4 hospital visits (before vaccination and 3 weeks, 6 months and 12 months after the second vaccination) for the collection of blood samples (either to to be stored at -70 degrees or used directly, in case of the cellular studies). Whenever possible, the research nurse will make sure that regular blood withdrawals and blood withdrawals for the study take place at the same time.

For registration of adverse events, patients will be requested to fill in a toxicity questionnaire in the weeks following the first vaccination and in the first 2 weeks following the second vaccination. Vaccination date and vaccin name wlll be noted.

For the measurement of vaccine efficacy patients will remain in follow up for at least 2 years, unless they either develop a SARS CoV-2 infection or pass away beforehand..The patients will be asked at the 6 months` and 12 months` visit whether they have developed a SARS CoV-2 infection. At 18 months` and 24 months` patients will be phoned with the same question. In case of a positive answer the SARS CoV-2 test data will be retrieved from the laboratory. Written informed consent for this has been given prior to study inclusion.

Study burden and risks

Burden:
Completion of 2 one page- questionnaires
4 hospital visits for blood withdrawal (whenever possible, the research nurse will make sure that regular blood withdrawals and blood withdrawals for the study take place at the same time)
2 phone calls with the research nurse

Risks:
There are none

Benefit:
No personal benefit

But the study provides insight in the benefit of vaccination in these patient groups

Contacts

Public
Selecteer

s-Gravenpolderseweg 114
Goes 4382 EE
NL
Scientific
Selecteer

s-Gravenpolderseweg 114
Goes 4382 EE
NL

Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Adults (18-64 years)
Elderly (65 years and older)

Inclusion criteria

•Study participant belongs to either of the 6 defined groups and is planned for vaccination with the BNT162b2 or the mRNA1273 vaccine according to the National Institute for Public Health guideline, i.e.:
• Inflammatory bowel disease and on treatment for at least 6 weeks with anti-TNF agents (infliximab, adalimumab and biosimilars)
• post kidney transplantation and on immunosuppressants
• Treated with B-cell depleting, antiCD20 (Obinituzumab or Rituximab) monotherapy for a hematological malignancy in the past 6 months

• Chronic lymphocytic leukemia (CLL), irrespective of stage, not treated for CLL in the past 6 months prior to the first vaccination and no treatment expected within 4 weeks of the second vaccination
• Advanced solid malignancy and on treatment for at least 6 weeks with one or more of the following agents: doxorubicin, cyclophosphamide, docetaxel, cisplatinum, etoposide, irinotecan
• healthy volunteers

• Study participant is older than 17 years and willing to undergo vaccination
• Study participant is able to give written informed consent
• Study participant is able to visit the ADRZ for the scheduled laboratory visits

Exclusion criteria

History of a documented SARS COV-2 infection
Considered as high risk for a hypersensitivity reaction

Study design

Design

Study type:	Observational invasive
Intervention model:	Other
Allocation:	Non-randomized controlled trial
Masking:	Open (masking not used)
Control:	Active
Primary purpose:	Treatment

Recruitment

NL

Recruitment status:	Pending
Start date (anticipated):	22-03-2021
Enrollment:	120
Type:	Anticipated

Medical products/devices used

Product type:	Medicine
Brand name:	BNT162b2
Product type:	Medicine
Brand name:	COVID-19 vaccine Moderna

Ethics review

Approved WMO Date:	26-02-2021
Application type:	First submission
Review commission:	METC Brabant (Tilburg)
Approved WMO Date:	26-04-2021
Application type:	First submission
Review commission:	METC Brabant (Tilburg)

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	EUCTR2021-001032-26-NL
CCMO	NL76816.028.21