In vitro characterization of the immune response of recovered COVID-19 patients and healthy controls to SARS-CoV-2.

Published: 11-08-2020
Last updated: 25-03-2025

- To assess the in vitro memory T cell response to 20 therapeutic SARS-CoV-2 vaccine candidate synthetic long peptides (SLPs);- To assess the in vitro humoral immune response to 20 therapeutic SARS-CoV-2 vaccine candidate SLPs.

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

Summary

ID

NL-OMON50131

Source
ToetsingOnline

Brief title
Recovered Covid-19 patients blood sampling

Condition

- Viral infectious disorders

Synonym
Corona, COVID-19, SARS-CoV-2

Research involving
Human

Sponsors and support

Primary sponsor: ISA Pharmaceuticals B.V.
Source(s) of monetary or material Support: ISA Pharmaceuticals B.V.

Intervention

Keyword: Blood sampling, COVID-19, Immune response, SARS-CoV-2

Outcome measures

Primary outcome

* Memory T cell response as assessed by interferon-* enzyme-linked immune absorbent spot (ELISpot) assay and/ or enzyme-linked immunosorbent assay (ELISA) and intracellular cytokine staining (ICS) after stimulation of peripheral blood mononuclear cells (PBMCs) with each of the 20 therapeutic SARS-CoV-2 vaccine candidate SLPs

Secondary outcome

* Serum IgG antibodies as measured by ELISA against each of the 20 therapeutic SARS-CoV-2 vaccine candidate SLPs

Study description

Background summary

In December 2019, a newly identified coronavirus, called severe acute respiratory syndrome coronavirus-2 (SARS-CoV-2), emerged in China causing coronavirus disease-2019 (COVID-19). The rapid global outbreak of SARS-CoV-2 led the World Health Organization (WHO) to characterize COVID-19 as a pandemic. Millions of people have been affected by the disease and worldwide incidence and mortality are still increasing. At this moment, a tremendous amount of research is being conducted in search of a potential prophylactic COVID-19 vaccine. Such vaccines may be deployed for widespread global immunization programs to protect against COVID-19. Before a highly effective prophylactic vaccine can be developed, licenced and become widespread available there remains an unmet medical need for curative treatment modalities against COVID-19. There is currently no proven curative treatment available against COVID-19. Treatment with the licensed nucleoside analogue remdesivir reduces hospitalization duration, but its effect on disease mortality and progressions remains disputed. Current investigational therapeutics for COVID-19 mainly focus on drugs with antiviral activity, immunomodulatory drugs or convalescent

plasma/antibodies, and prophylactic vaccines. Far less research effort has been put into the development of a therapeutic vaccine for COVID-19. Such a therapeutic vaccine can be administered after SARS-CoV-2 infection has occurred and could in theory prevent subsequent (severe) disease by targeted immunotherapy. Therapeutic vaccines against COVID-19 are therefore an attractive treatment modality that warrants further investigation.

ISA Pharmaceuticals B.V. is developing a therapeutic vaccine against SARS-CoV-2, called ISA106, for patients recently infected with SARS-CoV-2. This vaccine is intended as a therapeutic modality as well as preventive for patients at increased risk of severe illness from COVID-19 and related death, such as older patients and patients with certain underlying diseases (eg, diabetes). Severe patients appear to be characterized by an impaired T cell immune response. This deficient T cell response may represent a relevant therapeutic vaccine target.

The ISA106 vaccine is based on synthetic long peptides (SLPs) in order to boost T cell immunity. SLPs are aimed to be taken up and processed by antigen-presenting dendritic cells (DCs) before they are presented rather than direct binding to major histocompatibility complex (MHC) class I molecules on the cell surface. This should facilitate a stronger and more effective immune response than with a vaccine based on exact MHC-binding peptides. SLPs are degraded by DCs into antigenic protein fragments, called epitopes. These epitopes can stimulate both CD4+ helper T cells and CD8+ T cells responses.

Potential ISA106 vaccine candidate epitope-rich SLPs were selected by integrating different sources of available data. This included T cell epitope predictions generated by predictive algorithms to identify candidate targets for immune responses to SARS-CoV-2. This was combined with the observation that SARS-CoV-2 is closely related to SARS-CoV that caused the severe acute respiratory syndrome (SARS) outbreak in 2002-2004. Epitopes conserved among both coronaviruses are considered promising targets for immune recognition of SARS-CoV-2 and selected accordingly. The pool of potential T cell epitopes was further refined by utilizing proprietary algorithms developed by ISA Pharmaceuticals B.V. that also take into account the feasibility of producing the epitope-rich SLPs under good manufacturing practice (GMP) conditions. Furthermore, the actual T cell responses observed in COVID-19 patients and epitopes predicted to elicit a IgG antibody response were considered. This approach yielded 20 potential ISA106 vaccine candidate epitope-rich SLPs, each of a length of 25-35 amino acids, together covering the anticipated most immunogenic sequences of the spike (S), membrane (M) and nucleocapsid (N) proteins of SARS-CoV-2.

Before ISA106 will be taken into phase 1 clinical testing, the elicited immune response to the SLPs should be characterized in vitro to guide to the final selection of most immunogenic SLPs. The current study is intended to stimulate blood from recovered COVID-19 patients and healthy controls in vitro with the

current 20 candidate SLPs. This study is essential for the determination of the final ISA106 vaccine composition.

Study objective

- To assess the in vitro memory T cell response to 20 therapeutic SARS-CoV-2 vaccine candidate synthetic long peptides (SLPs);
- To assess the in vitro humoral immune response to 20 therapeutic SARS-CoV-2 vaccine candidate SLPs.

Study design

This is an exploratory study that is part of the development trajectory of a therapeutic SARS-CoV-2 vaccine. A total of 14 subjects will be enrolled: 10 recovered COVID-19 patients and 4 healthy controls. The study will consist of a single visit, the total duration of the study for each subject will not be more than half a day. During the visit, subject*s eligibility for this study will be assessed prior to sample collection and blood will collected for the study endpoints.

Study burden and risks

No investigational drug will be administered to the volunteers. The invasive procedures under this protocol will be restricted to blood sample collection (venipuncture). The burden for the volunteer related to the study procedures is limited. Only well-established methods of sample collection will be applied, with a known and limited risk and no or mild discomfort for the volunteer. In addition, all collections will be performed by qualified medical staff.
No clinical benefit can be expected from this study for the participating subjects.

Contacts

Public
ISA Pharmaceuticals B.V.

J.H. Oortweg 19
Leiden 2333 CH
NL
Scientific
ISA Pharmaceuticals B.V.

J.H. Oortweg 19
Leiden 2333 CH

NL

Trial sites

Listed location countries

Netherlands

Eligibility criteria

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

Inclusion criteria

Inclusion criteria for both recovered COVID-19 patients and healthy participants
1. Participant must sign the study informed consent form prior to any study-mandated procedure indicating that he or she understands the purpose, procedures and potential risks, and is willing to participate in the study;
2. Participant is male or female and between 18 and 65 years of age, inclusive, at the time of enrollment;
3. Participant is willing and able to complete the study procedures;
4. Participant has a primary care physician at the time of enrollment;
5. Participant is not taking any immunosuppressive medication or other immunomodulating agents (including investigational drugs) for at least 3 weeks prior to study blood sampling.

Inclusion criteria for recovered COVID-19 patients only
1. Participant reports a previous positive diagnostic test result for SARS-CoV-2 infection (serological testing or viral RNA detection by PCR testing);
2. Participant had clinical symptoms of COVID-19 (including, but not limited to: cough, fever, shortness of breath, sudden onset of anosmia, ageusia or dysgeusia). The diagnosis of COVID-19 must be the most plausible cause of the reported symptoms, as deemed by the study physician;
3. Participant has recovered from COVID-19 for at least three weeks prior to study blood sampling (residual symptoms such as, but not limited to, fatigue and reduced exercise tolerance - that would not jeopardize study endpoints - are allowed at the investigator*s discretion).

Inclusion criteria for healthy participants only

1. Participant is generally healthy in the investigator*s clinical judgment, as determined by medical history evaluation, including no clinically significant disorder, condition, infection or disease that would interfere with the study evaluation, procedures or completion.

Exclusion criteria

Exclusion criteria for both recovered COVID-19 patients and healthy participants
1. Participant with a whole blood donation or loss of >500 ml within 21 days before study blood sampling;
2. Any known factor, condition, or disease that might interfere with compliance, study conduct or interpretation of the results, as deemed by the investigator.

Exclusion criteria for healthy participants only
1. Participant reports a previous positive diagnostic test result for SARS-CoV-2 infection (serological testing or viral RNA detection by PCR testing);
2. Participant developed clinically overt symptoms of COVID-19 following close contact with a proven SARS-CoV-2 positive patient, but was not tested (e.g. due to limited test capacity and regulations at that time);
3. Participant who is currently working, or has worked in an occupation with a high risk of exposure to SARS-CoV-2 (e.g. health care worker).

Study design

Design

Study type: Observational invasive

Masking:	Open (masking not used)
Control:	Uncontrolled
Primary purpose:	Other

Recruitment

NL

Recruitment status:	Completed
Start date (anticipated):	17-08-2020
Enrollment:	14
Type:	Actual

Ethics review

Approved WMO Date:	11-08-2020
Application type:	First submission
Review commission:	METC Leiden-Den Haag-Delft (Leiden) metc-ldd@lumc.nl

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: 20400
Source: NTR
Title:

In other registers

Register	ID
CCMO	NL74814.058.20

Study results

Date completed:	16-09-2020
Results posted:	10-12-2020

First publication
28-10-2020

URL result
URL
Type
int
Naam

M2.2 Samenvatting voor de leek
URL

Internal documents
File