ISRCTN34160010 https://doi.org/10.1186/ISRCTN34160010

A low-intervention study of pre-exposure prophylaxis (PrEP) in healthy volunteers at high risk of coronavirus (SARS-CoV-2) infection.

Submission date
09/09/2020

Recruitment status
No longer recruiting

Registration date
14/09/2020

Overall study status
Completed

Last Edited
06/10/2022

Condition category
Infections and Infestations

[_] Prospectively registered
[X] Protocol
[_] Statistical analysis plan
[X] Results
[_] Individual participant data

Plain English summary of protocol

Background and study aims
COVID-19 is a condition caused by the coronavirus (called SARS-CoV-2) that was first identified in late 2019. This virus can infect the respiratory (breathing) system. Some people do not have symptoms but can carry the virus and pass it on to others. People who have developed the condition may develop a fever and/or a continuous cough among other symptoms. This can develop into pneumonia. Pneumonia is a chest infection where the small air pockets of the lungs, called alveoli, fill with liquid and make it more difficult to breathe.

As of 7th September 2020, more than 27 million confirmed cases and 900 thousand deaths have been reported to the WHO. Healthcare workers (HCWs) are at particularly high risk of acquiring SARS-CoV-2, from repeated exposure to infected patients. To date, no treatments are known to be effective in preventing SARS-CoV-2 infection.

It is thought that SARSCoV2 may use angiotensin-converting enzyme 2 (ACE2) as an entry point to human airways and might reduce ACE2 activity, resulting in pulmonary disorders. There are currently available and well-tolerated medications that have been previously reported to maintain ventilation-perfusion functions of the lung.

This study aims to evaluate whether pre-exposure prophylaxis (PrEP) using a low-dose aerosolized combination of glutathione, inosine, and potassium can prevent SARS-CoV-2 infection in healthy adults who are at high risk for exposure to this infection due to delivering care and services to patients with confirmed COVID-19.

Who can participate?
Healthy volunteers over the age of 18 who deliver care and services to patients with confirmed COVID-19.

What does the study involve?
All participants complete a pre-enrollment evaluation, which included data from SARS-CoV-2 tests performed prior to joining the study. Eligible participants receive low-dose aerosoled

combination medication (glutathione, inosine, and potassium) for 14 days; four inhalation sessions per day, with 4 h between each 5-minute inhalation session. The medication is self-administered for 5-min inhalation session as an aerosol using a personal handheld nebulizer. Data on treatment adherence and adverse events collected 7 and 14 days after the study begins. An additional follow-up will take place 28 days after the study begins.

What are the possible benefits and risks of participating?
The expected benefit of the investigated PrEP is the reduction of SARS-CoV-2 incidence in healthy individuals at high risk of this infection. Taking into account the low doses of the medications, no serious or moderate adverse events (AEs) are expected.

Where is the study run from?
North-Western State Medical University named after I.I. Mechnikov (Russian Federation)

When is the study starting and how long is it expected to run for?
From April 2020 to September 2020

Who is funding the study?
North-Western State Medical University named after I.I. Mechnikov (Russian Federation)

Who is the main contact?
1. Prof. Michael Dubina
michael.dubina@gmail.com
2. Nataliya Shvetc
Nataliya.Shvetc@szgmu.ru
3.Veronika Gomonova
Veronika.Gomonova@szgmu.ru

Contact information

Type(s)
Scientific

Contact name
Prof Michael Dubina

ORCID ID
http://orcid.org/0000-0002-6606-3309

Contact details
19 Zamshina street 55
St. Petersburg
Russian Federation
195221
+7 9219052074
michael.dubina@gmail.com

Type(s)
Public

Contact name

Dr Nataliya Shvetc

Contact details
North-Western State Medical University named after I.I. Mechnikov (NWSMU)
41 Kirochnaya street
St. Petersburg
Russian Federation
191015
+7 8123035000
rectorat@szgmu.ru

Type(s)
Public

Contact name
Dr Veronika Gomonova

Contact details
North-Western State Medical University named after I.I. Mechnikov (NWSMU)
41 Kirochnaya street
St. Petersburg
Russian Federation
191015
+7 8123035000
rectorat@szgmu.ru

Additional identifiers

EudraCT/CTIS number
Nil known

IRAS number

ClinicalTrials.gov number
Nil known

Secondary identifying numbers
MIBVD-19

Study information

Scientific Title
A low-intervention study to determine whether pre-exposure prophylaxis with low dose aerosol combination medication (ACM) can reduce SARS-CoV-2 incidence in healthcare workers exposed to routing COVID-19 positive contacts (LOWACM)

Acronym
LOWACM

Study objectives

The pre-exposure prophylaxis with aerosoled combination medication reduces frequency of SARS-CoV infection in high risk individuals exposed to routine COVID-19 positive contacts

Ethics approval required
Old ethics approval format

Ethics approval(s)
Approved 27/05/2020, Local Ethics Committee at North-Western State Medical University named after I.I. Mechnikov (NWSMU) (41 Kirochnaya street, Russian Federation, 191015; +7 8123035000; rectorat@szgmu.ru), ref: 4.

Study design
Low-intervention prospective open-label single-centre investigator-initiated study

Primary study design
Interventional

Secondary study design
Non randomised study

Study setting(s)
Hospital

Study type(s)
Prevention

Participant information sheet
Not available in web format, please use the contact details below to request a participant information sheet.

Health condition(s) or problem(s) studied
COVID-19 (SARS-CoV-2 infection)

Interventions
Among the full staff of HCWs at a designated COVID-19 hospital, 100 HCWs will be randomly invited to participate in the study by members of a study team in accordance with the protocol. The data from the control group will be collected retrospectively as aggregate data in accordance with local routine Covid-19 surveillance reports.

The aerosolized combination of medications is 3% inosine-glutamyl-cysteinyl-glycine disodium (inosine-glutathione) and 4% potassium chloride. The medication for each 5 min inhalation session is prepared ex tempore by mixing solutions of 1.0 ml inosine-glutathione and 0.25 ml potassium chloride. The medication is self-administered as an aerosol using a personal handheld nebulizer driven by compressed air at 0.25 ml min-1. Eligible participants receive the treatment for 14 days; four inhalation sessions per day with 4 h in between sessions.

Data on treatment adherence and adverse events are collected on day 7 and day 14, with additional follow-up information collected at day 28.

Intervention Type
Drug

Phase
Not Applicable

Drug/device/biological/vaccine name(s)
Inosine-glutamyl-cysteinyl-glycine disodium, potassium chloride

Primary outcome measure
1. New cases of SARS-CoV 2 infection in the treated group and untreated equal population of HCWs measured by study visits, weekly questionnaires, routine genetic tests and IgM/IgG seroconversion at 7,14, and 28 days. Statistical analyses include the assumption that up 11% of HCWs at risk will become infected if no prophylactic treatment is provided. Therefore it is expected that the investigated pre-exposure prophylaxis eliminates SARS-CoV-2 positive cases detected by genetic or immunological tests to 3% or less within 28 days study period; with alpha error rate of 0.05, beta error 0.85, and a sample size of ~100 participants in the study group.
2. Occurrence of adverse events collected at 7 and 14 days

Secondary outcome measures
1. Rate of SARS-CoV 2 infections in the treated group and untreated equal population as determined by study visits, weekly questionnaires, routine genetic tests and IgM/IgG seroconversion at 7,14, and 28 days
2. Rate of SARS-CoV 2 infections in study participants receiving ACM as measured by IgM/IgG seroconversion at 7,14, and 28 days

Overall study start date
22/04/2020

Completion date
02/09/2020

Eligibility

Key inclusion criteria
1. Willing and able to provide informed consent
2. Aged 18-80 years
3. Healthy volunteer
4. Healthcare workers (HCWs) exposed to routine COVID-19 positive contacts
5. Agrees to cooperate adequately to all aspects of the study, can understand the information provided about the study, and is willing to comply with the requirements of the study protocol

Participant type(s)
Health professional

Age group
Adult

Lower age limit
18 Years

Upper age limit

80 Years

Sex
Both

Target number of participants
100

Total final enrolment
99

Key exclusion criteria
1. Detection of SARS-CoV-2 virus RNA by polymerase chain reaction (PCR) in biomaterial samples and/or positive enzyme-linked immunosorbent assay ELISA IgM and ELISA IgG to the virus
2. Hypersensitivity or individual intolerance to the components of the combination therapy according to medical history
4. Criteria related to the concomitant pathology
5. Obviously or likely unable to understand and evaluate the information regarding this study within the process of signing the informed consent form, in particular regarding the expected risks and possible discomfort
6. The inability or unwillingness to follow the rules for carrying out the study and participating in the study

Date of first enrolment
01/06/2020

Date of final enrolment
10/07/2020

Locations

Countries of recruitment
Russian Federation

Study participating centre
North-Western State Medical University named after I.I. Mechnikov
Piskarevskij prospect, 47
St. Petersburg
Russian Federation
195067

Sponsor information

Organisation
North-Western State Medical University named after I.I. Mechnikov

Sponsor details
41 Kirochnaya street
St. Petersburg
Russian Federation
191015
+7 8123035000
rectorat@szgmu.ru

Sponsor type
University/education

Website
https://szgmu.ru/

ROR
https://ror.org/04kayk232

Funder(s)

Funder type
University/education

Funder Name
North-Western State Medical University named after I.I. Mechnikov

Results and Publications

Publication and dissemination plan
Study protocol with statistical analysis plan (SAP) and informed consent form (ICF) will be included as supplementary materials in the subsequent results publication in a peer-reviewed journal.

Intention to publish date
30/10/2020

Individual participant data (IPD) sharing plan
Informed consent will be obtained from all participants of the study. Request for individual de-indentified participant data must be sent to Prof. Michael Dubina at michael.dubina@gmail.com. The data will be available with the subsequent result publication. The data will be made available to researchers whose proposed use of the data has been approved (for a specified purpose).

IPD sharing plan summary
Available on request

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Results article		07/06/2021	09/06/2021	Yes	No
Protocol (other)			06/10/2022	No	No