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A trial assessing the effectiveness of candidate interventions in preventing COVID-19 disease in adults

Submission date
21/05/2020

Recruitment status
No longer recruiting

Registration date
26/05/2020

Overall study status
Completed

Last Edited
06/05/2022

Condition category
Infections and Infestations

[X] Prospectively registered
[_] Protocol
[_] Statistical analysis plan
[_] Results
[_] Individual participant data
[_] Record updated in last year

Plain English summary of protocol

Current plain English summary as of 06/01/2021:
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.
In 2020, the virus has spread to many countries around the world. As of January 2021, it is advised that people minimize travel and social contact, and regularly wash their hands to reduce the spread of the virus.
Groups who are at a higher risk from infection with the virus, and therefore of developing COVID-19, include people aged over 70 years, people who have long-term health conditions (such as asthma or diabetes), people who have a weakened immune system and people who are pregnant. People in these groups, and people who might come into contact with them, can reduce this risk by following the up-to-date advice to reduce the spread of the virus.
Adults are at risk of contracting this potentially deadly disease. Thus an effective pre-emptive intervention needs to be developed to decrease the occurrence of symptomatic COVID-19, and to mitigate its severity in adults at risk.
Several medications show promise as potential preventative agents for COVID-19 but it is not yet known if any of them will turn out to be effective. The CROWN CORONATION Trial has been designed to investigate various approaches and to answer two questions:
1. Whether adults who receive the candidate prophylactic (preventative) agent are at lower risk of developing COVID-19 infection
2. Whether adults who do get infected experience a milder disease if they have received the candidate prophylactic agent
In order to answer these questions, researchers are conducting a clinical trial. Participants will be adults who are considered a vulnerable population due to their high frequency of exposure to patients infected with COVID-19.
The first approach being studied is boosting the general immune system by giving a single dose

of the measles, mumps and rubella (MMR) vaccine. Several studies have suggested that as well as boosting immunity to measles, mumps and rubella, this vaccine can give a generalised immunity to viral illnesses. If successful, it could reduce the risk of developing the severe complications of COVID-19 and act as a bridge until a COVID-19 specific vaccine is found.

Who can participate?
Adults without clinical evidence of COVID-19 infection aged 18 and older

What does the study involve?
Participants will be randomly allocated to receive the MMR vaccine or placebo. Participants and researchers will not know which group they are in. The researchers will send weekly SMS texts to remind participants to report how they are feeling and if they have any symptoms. Participants will be followed up over a period of 5 months.

What are the possible benefits and risks of participating?
A benefit from this study is that the information will help improve treatment for future adults to prevent them from getting COVID-19. In addition, if participants develop COVID-19 they can be provided with information about ongoing COVID-19 treatment studies. The most important risk of taking part is that the participants may develop a side effect from receiving the vaccine.

Where is the study run from?
Comprehensive Clinical Trial Unit at University College London (UK)

When is the study starting and how long is it expected to run for?
March 2020 to January 2022

Who is funding the study?
The COVID-19 Therapeutics Accelerator

Who is the main contact?
Unfortunately, this study is not recruiting public volunteers at this time. This is because the research isn't ready for volunteers yet or the researchers are directly identifying volunteers in certain areas or hospitals. Please do not contact the research team as they will not be able to respond. For more information about COVID-19 research, visit the Be Part of Research homepage.

Previous plain English summary from 17/08/2020 to 06/01/2021:
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.

In 2020, the virus has spread to many countries around the world and neither a vaccine against the virus or specific treatment for COVID-19 has yet been developed. As of March 2020, it is advised that people minimize travel and social contact, and regularly wash their hands to reduce the spread of the virus.

Groups who are at a higher risk from infection with the virus, and therefore of developing COVID-19, include people aged over 70 years, people who have long-term health conditions

(such as asthma or diabetes), people who have a weakened immune system and people who are pregnant. People in these groups, and people who might come into contact with them, can reduce this risk by following the up-to-date advice to reduce the spread of the virus.

Front line medical staff are at risk of contracting this potentially deadly disease. Thus an effective pre-emptive intervention needs to be developed to decrease the occurrence of symptomatic COVID-19, and to mitigate its severity in front line medical staff, while a vaccine is developed.

Several medications show promise as potential preventative agents for COVID-19 but it is not yet known if any of them will turn out to be effective. The CROWN CORONATION Trial has been designed to investigate various approaches and to answer two questions:
1. Whether healthcare workers who receive the candidate prophylactic (preventative) agent are at lower risk of developing COVID-19 infection
2. Whether healthcare workers who do get infected experience a milder disease if they have received the candidate prophylactic agent

In order to answer these questions, researchers are conducting a clinical trial. Participants will be frontline healthcare workers who are considered a vulnerable population due to their high frequency of exposure to patients infected with COVID-19.

The first approach being studied is boosting the general immune system by giving a single dose of the measles, mumps and rubella (MMR) vaccine. Several studies have suggested that as well as boosting immunity to measles, mumps and rubella, this vaccine can give a generalised immunity to viral illnesses. If successful, it could reduce the risk of developing the severe complications of COVID-19 and act as a bridge until a COVID-19 specific vaccine is found.

Who can participate?
Healthcare workers without clinical evidence of COVID-19 infection aged 18 and older

What does the study involve?
Participants will be randomly allocated to receive the MMR vaccine or placebo. Participants and researchers will not know which group they are in. The researchers will send weekly SMS texts to remind participants to report how they are feeling and if they have any symptoms. Participants will be followed up over a period of 5 months.

What are the possible benefits and risks of participating?
A benefit from this study is that the information will help improve treatment for future healthcare workers to prevent them from getting COVID-19. In addition, if participants develop COVID-19 they can be provided with information about ongoing COVID-19 treatment studies. The most important risk of taking part is that the participants may develop a side effect from receiving the vaccine.

Where is the study run from?
Comprehensive Clinical Trial Unit at University College London (UK)

When is the study starting and how long is it expected to run for?
March 2020 to August 2021

Who is funding the study?
The COVID-19 Therapeutics Accelerator

Who is the main contact?
Unfortunately, this study is not recruiting public volunteers at this time. This is because the research isn't ready for volunteers yet or the researchers are directly identifying volunteers in certain areas or hospitals. Please do not contact the research team as they will not be able to respond. For more information about COVID-19 research, visit the Be Part of Research homepage.

Original plain English summary:
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.
In 2020, the virus has spread to many countries around the world and neither a vaccine against the virus or specific treatment for COVID-19 has yet been developed. As of March 2020, it is advised that people minimize travel and social contact, and regularly wash their hands to reduce the spread of the virus.
Groups who are at a higher risk from infection with the virus, and therefore of developing COVID-19, include people aged over 70 years, people who have long-term health conditions (such as asthma or diabetes), people who have a weakened immune system and people who are pregnant. People in these groups, and people who might come into contact with them, can reduce this risk by following the up-to-date advice to reduce the spread of the virus.
Front line medical staff are at risk of contracting this potentially deadly disease. Thus an effective pre-emptive intervention needs to be developed to decrease the occurrence of symptomatic COVID-19, and to mitigate its severity in front line medical staff, while a vaccine is developed.
There is growing evidence suggesting that Chloroquine, an anti-malarial drug that has been in common use for the last 70 years, that is a broad-spectrum anti-viral medication which, through its mode of action could potentially prevent the development of severe COVID-19 symptoms. However, despite the potential benefit, due to immunosuppressant proprieties of chloroquine, there is the risk that this medication may increase the risk of COVID-19 and other infections, so widespread adoption should be approached with caution. There are no randomised trial or real-world data on whether or not chloroquine is effective at preventing or mitigating COVID-19 in humans thus the need for the study.

CROWN CORONATION is an international trial in healthcare workers at risk of contracting COVID-19, investigating the use of chloroquine to prevent the development of symptomatic COVID-19, reduce the severity of symptoms and to find the minimum effective dosing schedule of chloroquine to prevent symptomatic COVID-19 in at risk healthcare workers.

Who can participate?
Healthcare workers without clinical evidence of COVID-19 infection aged 18 years and older

What does the study involve?
Participants will be randomly allocated to receive one of three different doses of chloroquine, or placebo for a maximum of three months. Participants and researchers will not know which group they are in.

What are the possible benefits and risks of participating?
A benefit from this study is that the information we receive will help is improve treatment for

future healthcare workers to prevent them from getting COVID-19. In addition if participants develop COVID-19 they can be provided with information about ongoing COVID-19 treatment studies.
The most important risk of taking part is that the participants may develop a side effect from taking the medication.

Where is the study run from?
Comprehensive Clinical Trial Unit at University College London

When is the study starting and how long is it expected to run for?
March 2020 to January 2022

Who is funding the study?
Bill and Melinda Gates Foundation (USA)

Who is the main contact?
Unfortunately, this study is not recruiting public volunteers at this time. This is because the research isn't ready for volunteers yet or the researchers are directly identifying volunteers in certain areas or hospitals. Please do not contact the research team as they will not be able to respond. For more information about COVID-19 research, visit the Be Part of Research homepage.

Contact information

Type(s)
Public

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Additional identifiers

ClinicalTrials.gov (NCT)
NCT04333732

Clinical Trials Information System (CTIS)
2020-001402-38

Integrated Research Application System (IRAS)
282280

Central Portfolio Management System (CPMS)
45647

Protocol serial number
CTU/2020/352

Study information

Scientific Title
An international, Bayesian platform adaptive, randomized, placebo-controlled trial assessing the effectiveness of candidate interventions in preventing COVID-19 disease in adults

Acronym
CROWN CORONATION

Study objectives
Current study hypothesis as of 06/01/2021:
To determine the effectiveness of the active arm(s) in preventing symptomatic (i.e. any of the following: cough, shortness of breath or difficulty breathing, fever, chills, muscle pain, sore throat, new loss of taste or smell, nausea, vomiting, or diarrhoea), laboratory test-confirmed COVID-19 in adults with repeated exposures to SARS-CoV-2 by day 60 after receiving trial treatment.

Previous study hypothesis from 17/08/2020 to 06/01/2021:
To determine the effectiveness of the active arm(s) in preventing symptomatic (i.e. any of the following: cough, shortness of breath or difficulty breathing, fever, chills, muscle pain, sore throat, new loss of taste or smell, nausea, vomiting, or diarrhoea), laboratory test-confirmed COVID-19 in healthcare workers with repeated exposures to SARS-CoV-2 by day 60 after receiving trial treatment.

Original study hypothesis:
To determine the effectiveness of chloroquine prophylaxis in preventing symptomatic (i.e. any of the following: cough, shortness of breath or difficulty breathing, fever, chills, muscle pain, sore throat, new loss of taste or smell), laboratory test-confirmed COVID-19 in healthcare workers with repeated exposures to SARS-CoV-2.

Ethics approval required
Old ethics approval format

Ethics approval(s)
Approved 30/04/2020, East Midlands-Nottingham 2 Research Ethics Committee (The Old Chapel, Royal Standard Place, Nottingham, NG1 6FS, UK; +44 (0)0207 104 8103; nottingham2.rec@hra.nhs.uk), ref: 20/EM/0116

Primary study design
Interventional

Study design
Platform adaptive international multi-centre randomized placebo-controlled trial

Study type(s)
Prevention

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

Interventions
Updated 06/01/2021:
Participants will be adults at risk of contracting SARS-CoV-2.

Current interventions as of 17/08/2020:
The CROWN CORONATION trial is an international, Bayesian platform adaptive, randomised, placebo-controlled trial.

Participants will be healthcare workers at risk of contracting SARS-CoV-2. Participants will be randomized to education and surveillance plus Placebo for a period of up to 60 days or to a study arm with active interventions. To begin with, participants will be randomized to receive the Measles, Mumps & Rubella vaccine (MMR vaccine), or a placebo injection. New dosage-based arm(s) or drugs might be added or removed depending on the emerging evidence.

All participants in the active treatment arm will receive a single dose of the MMR vaccine, administered by deep subcutaneous injection into the upper arm. The vaccine should be administered within 7 days from randomization. Those allocated to the control arm will receive a placebo injection, administered in the same manner as the treatment arm.

The trial will evaluate which, of the intervention arms is the most effective at decreasing the incidence of symptomatic COVID-19 disease, without unacceptable side effects or safety events.

Participants will complete weekly data logs via SMS texting. Therefore, all participants will need to have access to a mobile phone in order to do this. In addition, participants will be asked to log into an online self-report form once a month to provide more detailed information on their

health and medication adherence. Self-reported information will be collected up until 5 months after the end of treatment or death. Participants will be provided with a secure log-in to enable them to complete trial questionnaires and daily data logs.

All participants will have a blood test on entry, during and exit of the study. They will also take a self-administered nose swab if they have symptoms and think they may have contracted COVID-19.

Previous interventions (please note these interventions did not receive MHRA approval and were never applied):
The CROWN CORONATION trial is an international multi-centre randomised, placebo-controlled trial.

Participants will be front line healthcare workers at risk of contracting COVID-19 (SARS-CoV-2), randomised to one of 4 groups stratified by trial site and participant age (under 50 & over 50). The four groups will be:
1. 500 mg chloroquine phosphate weekly
2. 500 mg chloroquine phosphate twice weekly
3. 250 mg chloroquine phosphate daily
4. Placebo

All participants in the active treatment arms will receive an induction dose of 2000 mg chloroquine phosphate taken divided between 4 daily doses before starting the weekly, twice weekly or daily dose regimen. Those in the placebo group will be asked to take the equivalent number of placebo tablets.

The trial will evaluate which, of the above intervention arms is the most effective at decreasing the incidence of symptomatic COVID-19 disease, without unacceptable side effects or safety events.

All participants will be asked to complete twice-weekly logs via SMS message. Therefore, all participants will need to have access to a mobile phone in order to do this. In addition, participants will be asked to log into an online self-report form once a month to provide more detailed information on their health and medication adherence. Self-reported information will be collected up until 2 months after the end of treatment or death. Participants will be provided with a secure log-in to enable them to complete trial questionnaires and daily data logs.
To help participants to adhere to the treatment regime they are randomised to a support system using two way SMS messages that has been used in other research (HIV PrEP). As well as completing the daily and monthly logs, participants will be sent reminders of when to collect more medication by SMS.

At the time of randomisation, participants will be given 72 hours to collect their trial medication or placebo. They will be asked to take a form of identification to a dispensing station, where a pharmacist will dispense trial medication/placebo. Only one dispensing event will take place per participant. At the end of their time in the trial, participants will be asked to drop off any unused trial medication or placebo to the collection point. Participants will be asked to take the trial medication for a maximum of 3 months if they do not experience any trial events: the participant is diagnosed with COVID-19 and decides to join a different treatment intervention trial or are prescribed chloroquine by their treating physician; the participant reports a complication, safety concern or side effect necessitating stopping taking the trial medication or placebo; or the participant is no longer at risk from contact with SARS-CoV-2 infected patients.

All participants will have a blood test on entry and exit of the study. They will also take a self-administered nose swab if they have symptoms and think they may have contracted COVID-19.

Intervention Type
Biological/Vaccine

Phase
Phase III

Drug/device/biological/vaccine name(s)
Current as of 17/08/2020: Measles, Mumps & Rubella vaccine (MMR vaccine). New dosage-based arm(s) or drugs might be added or removed depending on the emerging evidence Previous: Chloroquine phosphate

Primary outcome(s)
Current primary outcome measure as of 17/08/2020:
Symptomatic COVID-19: Clinical diagnosis of COVID-19 with laboratory confirmation (i.e. based on viral PCR), and symptoms of COVID-19 (cough, shortness of breath or difficulty breathing, fever, chills, muscle pain, sore throat, new loss of taste or smell, nausea, vomiting, or diarrhea) by day 60 after receiving trial treatment.

Previous primary outcome measure:
Clinical diagnosis of COVID-19 with laboratory confirmation (i.e. based on viral PCR or serology), with limitation of activities (WHO Severity Scale 2-8) or symptoms of COVID-19 (cough, shortness of breath or difficulty breathing, fever, chills, muscle pain, sore throat, new loss of taste or smell) over the treatment period of 90 days

Key secondary outcome(s)
Current secondary outcome measures as of 17/08/2020:
1. The severity of COVID-19 over the study period of 150 days:
1.1. Uninfected – no clinical or virologic evidence of infection (Score = 0)
1.2. Ambulatory – no limitation of activities (score=1) or with limitation (Score=2)
1.3. Hospitalized – mild no oxygen (Score=3) or with oxygen (Score=4), hospitalized severe – Score=5-7*, dead (Score=8)
2. Primary endpoint, but instead of the 60-day time-window, over the course of the first 30 days of treatment
3. Symptomatic COVID-19 (with subsequent virological confirmation) during the 5-month study period
4. Incident COVID-19 during the 60-day study period, which includes asymptomatic infections identified by serology samples taken at the time-point of study exit

Previous secondary outcome measures:
1. The severity of COVID-19 over the study period of 150 days
1.1. Uninfected – no clinical or virologic evidence of infection (Score = 0)
1.2. Ambulatory – no limitation of activities (score=1) or with limitation (Score=2)
1.3. Hospitalized – mild no oxygen (Score=3) or with oxygen (Score=4), hospitalized severe – Score=5-7*, dead (Score=8)
2. Primary endpoint, but instead of the 90-day time-window, over the course of the 1st 30 days of treatment
3. Primary endpoint, but instead of the 90-day time-window, over the course of the first 60 days of treatment

4. The incidence of: pneumonia; respiratory failure requiring intubation; acute respiratory distress syndrome; delirium; shock requiring vasopressor medications; sepsis; acute kidney injury; acute liver injury; death. Case definitions will be decided a priori
5. Duration of intensive care unit stay
6. Duration of hospital day
7. Symptomatic COVID-19 (with subsequent virological confirmation) during the 5-month study period
8. Incident COVID-19 during the 5-month study period, which includes asymptomatic infections identified by serology samples taken at the time-point of study exit
9. Safety Outcomes: Determined according to the CTCAE for grading severity of adult adverse events, with specific focus on the events of retinopathy (visual impairment), cardiomyopathy, arrhythmias, myopathies, hypoglycaemia and death, over the 150 days

Completion date
11/01/2022

Eligibility

Key inclusion criteria
Current inclusion criteria as of 06/01/2021:
1. Volunteers without clinical evidence of COVID-19 infection aged 18 years and older
2. Adults with a high risk of developing COVID-19 due to their potential exposure to patients with SARS-CoV-2 infection
3. Must have a mobile phone and access to the internet for data collection purposes
4. Participants who are willing and able to provide informed consent via an electronic consent process

Previous inclusion criteria:
1. Volunteers without clinical evidence of COVID-19 infection aged 18 years and older
2. Healthcare workers based in a primary, secondary or tertiary healthcare setting with a high risk of developing COVID-19 due to their potential exposure to patients with SARS-CoV-2 infection
3. Must have a mobile phone and access to the internet for data collection purposes
4. Participants who are willing and able to provide informed consent via an electronic consent process

Participant type(s)
Healthy volunteer

Healthy volunteers allowed
No

Age group
Adult

Lower age limit
18 Years

Sex
All

Total final enrolment
3412

Key exclusion criteria
Current exclusion criteria as of 14/05/2021:
1. Weight outside range 50 kg – 120 kg (110 lb – 265 lb).
2. Prior enrolment into this or other COVID-19 interventional prevention or treatment trials (observational trials not excluded).
3. Self-reported or laboratory confirmed previous or current diagnosis of SARS-CoV-2 or COVID-19.
4. Self-reported current acute respiratory infection.
5. Concurrent and/or recent use of the investigational product/s, a product considered to be equivalent to the investigational product/s, or any other product that is likely to interfere with the investigational products in this trial or the interpretation of the trial data.
6. Self-reported known allergies to any of the IMPs and excipients of the IMPs and placebo.
7. Self-reported presence or history of the conditions listed in the appendix relevant to that IMP
8. Self-reported current use of medication with known to interact with any of the medications listed in the appendices.
9. Inability or unwillingness to be followed up for the trial period.

Additional to the set of exclusions for participants in the 'MMR vs Placebo' arm:
1. Pregnant women.
2. Individuals receiving high dose corticosteroids, other immuno-suppressive drugs, alkylating agents or anti-metabolites.
3. Individuals undergoing radiotherapy.
4. Any malignant disease either untreated or currently undergoing therapy.
5. History of administration of gammaglobulin or blood transfusions within the previous 3 months.
6. Participants with an allergy to the MMR vaccine or its components, including neomycin.
7. Idiopathic thrombocytopenic purpura (ITP).
8. Untreated tuberculosis.
9. Prior receipt of a specific SARS-CoV-2 vaccine.
10. Planned receipt of a live attenuated vaccine in the 60 days after receiving the study vaccination.
11. Planned receipt of any vaccine other than the study intervention up to 14 days after the study vaccination. NB: Planned receipt of an inactivated influenza vaccine (via injection) is not an exclusion criterion but it must be given at least 72 h before or after the trial MMR vaccine or placebo to permit clearer recognition of any possible SAEs from administration of the study medication.
12. Any confirmed or suspected immunosuppressive or immunodeficient state, including untreated HIV infection with a CD4T count <200/ml.
13. Asplenia

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Previous exclusion criteria as of 06/01/2021:
The following participants cannot participate in this arm of the trial:
1. Pregnant women
2. Individuals receiving high dose corticosteroids, other immunosuppressive drugs, alkylating agents or anti-metabolites
3. Individuals undergoing radiotherapy
4. Any malignant disease either untreated or currently undergoing therapy

5. History of administration of gammaglobulin or blood transfusions within the previous 3 months
6. Participants with an allergy to the MMR vaccine or its components, including neomycin
7. Idiopathic thrombocytopenic purpura (ITP)
8. Untreated tuberculosis
9. Prior receipt of a specific SARS-CoV-2 vaccine
10. Planned receipt of a live attenuated vaccine in the 60 days after receiving the study vaccination
11. Planned receipt of any vaccine other than the study intervention up to 14 days after the study vaccination
NB: Planned receipt of an inactivated influenza vaccine (via injection) is not an exclusion criterion but it must be given at least 72 hours before or after the trial MMR vaccine or placebo to permit clearer recognition of any possible SAEs from administration of the study medication
12. Any confirmed or suspected immunosuppressive or immunodeficient state, including untreated HIV infection with a CD4T count <200 /mL.
13. Asplenia

Previous exclusion criteria from 17/08/2020 to 06/01/2021:
1. Weight outside range 50 kg – 120 kg (110 lbs – 265 lbs)
2. Prior enrolment into this or other COVID-19 interventional prevention or treatment trials (observational trials not excluded)
3. Self-reported or diagnosed current infection with SARS-CoV-2 or previous COVID-19 diagnosis
4. Self-reported current acute respiratory infection
5. Concurrent and/or recent involvement in other research or use of the investigational product /s, a product considered to be equivalent to the investigational product/s, or any other product that is likely to interfere with the investigational products in this trial used within three months of study enrolment
6. Self-reported known allergies to any of the IMPs and excipients of the IMPs and placebo
7. Self-reported presence or history of the conditions listed in the appendix relevant to that IMP
8. Self-reported current use of medication with known to interact with any of the medications listed in the appendices
9. Inability or unwillingness to be followed up for the trial period

Additional to the set of exclusions for participants in the “MMR vs Placebo” arm:
1. Pregnant women
2. Individuals receiving high dose corticosteroids, other immunosuppressive drugs, alkylating agents or anti-metabolites
3. Individuals undergoing radiotherapy
4. Any malignant disease either untreated or currently undergoing therapy
5. History of administration of gammaglobulin or blood transfusions within the previous 3 months
6. Participants with an allergy to the MR (MMR) vaccine or its components, including neomycin
7. Idiopathic thrombocytopenic purpura (ITP)
8. Untreated tuberculosis
9. Prior receipt of any vaccines (licensed or investigational) ≤30 days before enrolment
10. Planned receipt of any vaccine other than the study intervention within 30 days before and after the study vaccination
11. Prior receipt of an investigational or licensed vaccine likely to impact on interpretation of the trial data (e.g. Adenovirus vectored vaccines, any coronavirus vaccines).
12. Any confirmed or suspected immunosuppressive or immunodeficient state, including untreated HIV infection with a CD4T count <200 /ml
13. Asplenia

Original exclusion criteria:
1. Weight outside range 50 kg – 120 kg (110 lbs – 265 lbs)
2. Prior enrolment into this or other COVID-19 interventional prevention or treatment trials (observational trials not excluded)
3. Self-reported or diagnosed current infection with SARS-CoV-2 or previous COVID-19 diagnosis
4. Self-reported current acute respiratory infection
5. Concurrent and/or recent involvement in other research or use of chloroquine /hydroxychloroqine or any other 4-aminoquinolone or another experimental investigational medicinal product that is likely to interfere with the study medication within three months of study enrolment
6. Current use of antimalarial agents (lumefantrine, mefloquine, pyronaridine or amodiaquine), or any other drugs that may cause a dangerous drug interaction
7. Self-reported known allergies to the IMP and excipients of IMP and placebo
8. Self-reported presence or history of the following conditions: Retinopathy or retinal disease; Cardiomyopathy (structural or ischemic heart disease); Cardiac arrhythmia; known personal or family history of prolonged QTc; Psoriasis; Porphyria cutanea tarda; Epilepsy; Myasthenia gravis; Myopathy of any cause; Serious hepatic or renal disease; Electrolyte abnormalities; self-reported severe depression or suicidality; currently undergoing treatment for tuberculosis
9. Self-reported current use of medication with known serious hepatotoxic effects or known interaction with chloroquine, including anti-TB treatment
10. Self-reported use of medications which prolong the QTc interval
11. Inability or unwillingness to be followed up for the trial period
12: Women who verbally state they are pregnant or breastfeeding or who intend to get pregnant within the next 3 months. (UK and IRE)

Date of first enrolment
26/10/2020

Date of final enrolment
19/01/2021

Locations

Countries of recruitment
United Kingdom

England

Ghana

South Africa

United States of America

Zambia

Zimbabwe

Study participating centre

University College London
London
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W1W 7TY

Sponsor information

Organisation
University College London

ROR
https://ror.org/02jx3x895

Funder(s)

Funder type
Research organisation

Funder Name
The COVID-19 Therapeutics Accelerator

Results and Publications

Individual participant data (IPD) sharing plan
The datasets generated during and/or analysed during the current study will be stored in a publically available repository.
IPD (individual patient data) pseudo-anonymised will be shared at https://www.ucl.ac.uk/library/research-support/research-data-management/ucl-research-data-repository, in line with open access policy from the funders https://www.gatesfoundation.org/How-We-Work/General-Information/Open-Access-Policy
Sharing will start when we reach database lock at the end of trial, after the last patient finishes their follow-up and all data for all patients is included in the dataset.

IPD sharing plan summary
Stored in publicly available repository

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
HRA research summary			28/06/2023	No	No
Study website	Study website	11/11/2025	11/11/2025	No	Yes