ISRCTN53507177 https://doi.org/10.1186/ISRCTN53507177

Clinical trial studying antibody treatment combined with COVID-19 vaccination in immunocompromised individuals

Submission date
09/06/2022

Recruitment status
No longer recruiting

Registration date
12/10/2022

Overall study status
Completed

Last Edited
29/05/2025

Condition category
Infections and Infestations

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

Plain English summary of protocol

Background and study aims
The RAPID-PROTECTION study is trying to find a new way to protect patients who may be more vulnerable to developing severe COVID-19 due to current health conditions. Despite repeated vaccinations against COVID-19, some people with impaired immune systems caused by cancer and its treatment, inflammatory conditions, and those with organ transplants and other serious health conditions remain at very high risk of catching COVID-19 and becoming unwell.
AZD7442 (Evusheld) is a long-acting antibody treatment which has been shown in clinical trials to prevent COVID-19 infection for a year after a single dose of two injections. AZD7442 has been approved for use in the United States for the prevention of COVID-19 and in the UK to prevent COVID-19.
Vaccines require a healthy immune system to generate protective immunity. AZD7442 may prevent COVID-19 in people with impaired immune systems that may not have responded to repeated vaccinations against COVID-19. Unlike vaccinations, which take several doses given weeks apart to reach maximum effectiveness, AZD7442 reaches effective levels within the body a few hours after an injection. Additionally, unlike vaccines, AZD7442 does not depend on a healthy immune system to generate protective immunity.
The RAPID-PROTECTION trial will determine the levels of immune protection that AZD7442 offers patients at the very highest risk of COVID-19 infection using laboratory-based tests and whether or not this protection can be further enhanced by repeated vaccination against COVID-19.

Who can participate?
Patients aged 18 years and over with haematological malignancies (blood cancer), solid tumours, kidney and liver disorders, and inflammatory disorders.

What does the study involve?
All the participants in the study will receive AZD7442 and then 28 days later a COVID-19 vaccination with either the Moderna vaccine or Pfizer/BioNTech vaccine that have been approved for use in the UK. All participants will be followed up for one year following AZD7442 administration. The follow-up assessments will include clinical reviews, vital signs, concomitant

medications reviews, toxicity assessments, blood sample collections, safety blood samples, routine nasal PCR swabs for SARS-CoV-2 (for a subset of participants), and participant behavioural questionnaires. Participants will be asked to attend clinic for follow-up visits scheduled at 42, 56, 112, 180, 273 and 364 days after the AZD7442 injection.
If a participant develops COVID-19 symptoms during the study they must take a lateral flow test and self-report the result to the study team. In this eventuality, the participant will be asked questions about their symptom severity and will be required to take a nasal swab at home, and return this in the freepost packaging to the laboratory for PCR testing.

What are the possible benefits and risks of participating?
Other studies have shown that AZD7442 protects people from getting severe COVID-19 infections for 6 to 12 months. However, it is not know how long this protection lasts in people who are immunocompromised. This is one of the questions this study aims to answer. The participant may also benefit from having an additional COVID-19 vaccine booster.
Taking part will contribute to research that may benefit many people who are immunocompromised during the COVID-19 pandemic. The study may also find out more about how monoclonal antibodies and the immune system works which may improve research in the future.
As with similar medicines, there are potential risks of side effects such as allergic reactions to AZD7442 (at the injection site and around the body); however, there are no reports of serious reactions in the information collected in previous studies. Participants will be closely monitored for adverse reactions at each visit. They will be provided with the contact details of the local site team to report symptoms/adverse reactions whilst in the study, which the Principal Investigator will monitor. Blood tests performed during the study will monitor participant safety and symptoms.
The number of visits and their purpose is explained in the patient information sheet. It is anticipated that the burden of additional visits will be outweighed by patients' interest in participating in the trial. Possible adverse events of blood collection are tenderness, pain, bleeding, bruising and/or infection at the needle puncture site. Trained medical staff will perform the blood collection procedures and will make every effort to lessen any discomfort. Although the clinical care team will do their best to limit exposure to potential infections during hospital visits, there may be an increased risk of contracting COVID-19.

Where is the study run from?
Centre for Trials Research in Cardiff University (UK)

When is the study starting and how long is it expected to run for?
June 2022 to August 2024

Who is funding the study?
AstraZeneca (UK)

Who is the main contact?
RAPID-PROTECTION@cardiff.ac.uk

Study website
https://www.cardiff.ac.uk/centre-for-trials-research/research/studies-and-trials/view/rapid-protection

Contact information

Type(s)
Scientific

Contact name
Dr CTR RAPID-PROTECTION trial team

Contact details
Centre for Trials Research
College of Biomedical & Life Sciences
Cardiff University
6th Floor
Neuadd Meirionnydd
Heath Park
Cardiff
United Kingdom
CF14 4YS
-
RAPID-PROTECTION@cardiff.ac.uk

Additional identifiers

EudraCT/CTIS number
2021-006703-15

IRAS number
1004764

ClinicalTrials.gov number
Nil known

Secondary identifying numbers
SPON1884-21, IRAS 1004764, CPMS 51571

Study information

Scientific Title
RAPID-PROTECTION: an adaptive clinical trial of AZD7442 and SARS-CoV-2 vaccination in immunosuppressed patients highly vulnerable to infection with SARS-CoV-2 virus

Acronym
RAPID-PROTECTION

Study objectives
Primary objectives:
1. To assess the pharmacokinetics of AZD7442 administered as a single dose of 600 mg IM in immunosuppressed patients
2. To assess the safety and tolerability of a single IM dose of AZD7442, followed by a SARS-CoV2 vaccine booster 28 days later with reference to serious adverse events (SAEs) in highly vulnerable patients
3. To assess the SARS-CoV-2 specific humoral and cellular immune response against SARS-CoV-2

variants, when a SARS-CoV-2 vaccine is administered 28 days after AZD7442 in patients who are immune-suppressed
4. To assess the effect of a SARS-CoV-2 vaccine on AZD7442 monoclonal antibody titres
5. To assess neutralizing antibodies to SARS-CoV-2 using validated wild-type neutralization assay or pseudo-neutralization assays over time

Secondary objectives:
1. The incidence of participants who have a post-treatment response (negative/low at baseline to positive at any time post-baseline) for SARS-CoV-2 nucleocapsid antibodies
2. The incidence of SARS-CoV-2 infection in trial participants
3. Sequencing of confirmed SARS-CoV2 infections to identify SARS-CoV2 variants and potential AZD7442 escape variants
4. To assess the behaviour of the trial participants before and after the trial treatment
5. To assess if different SARS-CoV-2 vaccines will preferentially enhance humoral and/or T cell responses in immune-suppressed patients receiving AZD7442
6. To assess the severity of SARS-CoV-2 infection in participants contracting COVID-19 within the duration of the trial

Ethics approval required
Old ethics approval format

Ethics approval(s)
Approved 25/07/2022, London - Fulham Research Ethics Committee (Barlow House, 3rd Floor, 4 Minshull Street, Manchester, M1 3DZ, UK; +44 (0)207 104 8084, +44 (0)207 104 8035, +44 (0)207 104 8109; fulham.rec@hra.nhs.uk), ref: 22/HRA/0359

Study design
Non-randomized study

Primary study design
Interventional

Secondary study design
Non randomised study

Study setting(s)
Other

Study type(s)
Prevention

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

Health condition(s) or problem(s) studied
Patients with immunosuppressive conditions who are highly vulnerable to COVID-19 (SARS-CoV-2 infection) and have one of the following diseases: haematological malignancies, solid tumours, renal and hepatic disorders, inflammatory disease

Interventions

All the participants in the study will receive a 600 mg single dose of AZD7442 administered intramuscularly into the upper arm at the time of registration. Participants will then be randomised using a web-based system to receive a single dose of one of three UK-approved SARS-CoV2 vaccine boosters (currently vaccines by Moderna and Pfizer/BioNTech) 28 days later. Up to 350 participants will be recruited across five UK sites from groups known to be highly vulnerable to SARS-CoV-2 and that have one of the following diseases: haematological malignancies, solid tumours, renal and hepatic disorders, and inflammatory disease.

All participants will be followed up for 1 year following AZD7442 administration. The follow-up assessments will include clinical reviews, vital signs, concomitant medications reviews, toxicity assessments, blood sample collections, safety blood samples, routine nasal PCR swabs for SARS-CoV-2 (for a subset of participants), and participant behavioural questionnaires.

Intervention Type
Biological/Vaccine

Phase
Phase II

Drug/device/biological/vaccine name(s)
AZD7442

Primary outcome measure
1. The pharmacokinetics of AZD7442 will be assessed using serum samples taken on Day 0 (Predose AZD7442), and days 28, 112, 180, 273 and 364 post AZD7442 treatment
2. Safety and tolerability of a single IM dose of AZD7442 followed by a SARS-CoV2 vaccine booster 28 days later, assessed by monitoring the SAE reporting using CTCAE v5.0 throughout the trial
3. Levels of serum spike (S) and the nucleocapsid (N) antigens and specific antibody and T cell responses will be measured from serum samples taken on Day 0 (Predose AZD7442), and days 28, 42, 56, 112, 180, 273 and 364 post AZD7442 treatment to assess humoral and cellular immune response against SARS-CoV-2 variants
4. Levels of SARS-CoV-2 neutralizing antibodies will be measured using serum samples taken on Day 0 (Predose AZD7442) and post AZD7442 treatment to assess the effect of a SARS-CoV-2 vaccine on AZD7442 monoclonal antibody titres

Secondary outcome measures
1. Incidence of a subset of participants who have a post-treatment response (negative/low at baseline to positive at any time post-baseline) for SARS-CoV-2 nucleocapsid antibodies will be assessed using serum samples taken on Day 0 (Predose AZD7442), and days 28, 112, 180, 273 and 364 post AZD7442 treatment
2. The incidence of SARS-CoV-2 infection in trial participants will be measured by ad-hoc PCR testing in symptomatic patients throughout the trial and by routine (asymptomatic) nasal PCR swabs taken from a subset of participants on Day 0 (Predose AZD7442), and days 28, 112, 180, 273 and 364 post AZD7442 treatment
3. PCR testing of all nasal swabs taken by participants will undergo sequencing to identify SARS-CoV2 variants and potential AZD7442 escape variants at baseline and if they are positive for COVID following dosing with AZD7442
4. Behaviour of trial participants assessed using validated behavioural questionnaires (risk behaviour changes, PROMIS 10, EQ-5D-5L) completed by participants at baseline and on days 112, 180 and 364

5. The humoral and/or T cell responses in participants randomised to receive different SARS-CoV-2 vaccines will be compared using serum samples taken on Day 0 (Predose AZD7442), and days 28, 42, 56, 112, 180, 273 and 364 post AZD7442 treatment
6. Disease severity in participants contracting SARS-CoV-2 within the duration of the trial assessed using the WHO Clinical Progression Scale as and when patients get infections

Overall study start date
07/06/2022

Completion date
29/08/2024

Eligibility

Key inclusion criteria
1. Provide written informed consent
2. Previous completed SARS-CoV-2 vaccinations given as part of standard care at the time of enrolment
3. Able and willing (in the Investigator's opinion) to comply with all trial requirements
4. Willingness to practice continuous effective contraception during the first 3 months of the trial and if appropriate, a negative pregnancy test on the day of screening
5. Provide access to all medical records with respect to current and past medical treatments
6. Have one or more of the eligible conditions specified in the protocol (haematological malignancies, solid tumours, renal and hepatic disorders, inflammatory disease)
7. Adults ≥18 years

Participant type(s)
Patient

Age group
Adult

Lower age limit
18 Years

Sex
Both

Target number of participants
350

Total final enrolment
148

Key exclusion criteria
Current exclusion criteria as of 18/11/2022:

1. Significant infection or other acute illness, including fever >100°F (>37.8°C) on the day prior to or day of screening
2. Prognosis of fewer than 6 months

3. Eastern Cooperative Oncology Group (ECOG) Performance status of >2
4. Planned receipt of any vaccine other than the trial intervention within 30 days before and after each trial intervention (day 0 and day 28) with the exception of the seasonal influenza vaccination, and non-COVID vaccinations in the case of patients receiving a haemopoietic stem cell transplant
5. History of reactions likely to be exacerbated by any component of AZD7442 and SARS-CoV2 vaccine
6. Anaphylactic reaction following administration of a vaccine
7. Known history of allergy or reaction to any component of the trial drug formulation
8. Patients who are pregnant or lactating at trial entry or planning to become pregnant within 3 months after AZD7442 administration
9. Previous hypersensitivity, clinically significant infusion-related reaction, or severe adverse reaction following administration of a mAb
10. Any prior receipt of other mAb indicated for the prevention or treatment of SARS-CoV-2 or COVID-19
11. Clinically significant bleeding disorder (in the opinion of the investigator e.g., factor deficiency, coagulopathy, or platelet disorder), or prior history of significant bleeding or bruising following IM injections or venepuncture
12. Any other significant disease, disorder, or finding that may significantly increase the risk to the participant because of participation in the trial, affect the ability of the participant to participate in the trial, or impair interpretation of the trial data
13. Receipt of any IMP in the preceding 90 days or expected receipt of IMP during the period of trial follow-up, or concurrent participation in another interventional trial unless IMP is essential to clinical care
14. Blood drawn in excess of a total of 450 mL (1 unit) for any reason within 30 days prior to randomization
15. A history of hypersensitivity reactions including anaphylaxis and angioedema following administration of a COVID-19 vaccine
16. A history of thrombocytopenia, including immune thrombocytopenia (ITP) following administration of a COVID-19 vaccine
17. A history of Guillain-Barré Syndrome
18. Patients with acute promyelocytic leukaemia
19. Individuals with a known history of capillary leak syndrome (CLS)

———

Previous exclusion criteria:

1. Significant infection or other acute illness, including fever >100°F (>37.8°C) on the day prior to or day of screening
2. Prognosis of fewer than 6 months
3. Eastern Cooperative Oncology Group (ECOG) Performance status of >2
4. Planned receipt of any vaccine other than the trial intervention within 30 days before and after each trial intervention (day 0 and day 28) with the exception of the seasonal influenza vaccination, and non-COVID vaccinations in the case of patients receiving a haemopoietic stem cell transplant
5. History of reactions likely to be exacerbated by any component of AZD7442 and SARS-CoV2 vaccine
6. History of laboratory-confirmed SARS-COV-2 within the last 3 months
7. Anaphylactic reaction following administration of a vaccine
8. Known history of allergy or reaction to any component of the trial drug formulation
9. Patients who are pregnant or lactating at trial entry or planning to become pregnant within 3

months after AZD7442 administration
10. Previous hypersensitivity, clinically significant infusion-related reaction, or severe adverse reaction following administration of a mAb
11. Any prior receipt of other mAb indicated for the prevention or treatment of SARS-CoV-2 or COVID-19
12. Clinically significant bleeding disorder (in the opinion of the investigator e.g., factor deficiency, coagulopathy, or platelet disorder), or prior history of significant bleeding or bruising following IM injections or venepuncture
13. Any other significant disease, disorder, or finding that may significantly increase the risk to the participant because of participation in the trial, affect the ability of the participant to participate in the trial, or impair interpretation of the trial data
14. Receipt of any IMP in the preceding 90 days or expected receipt of IMP during the period of trial follow-up, or concurrent participation in another interventional trial unless IMP is essential to clinical care
15. Blood drawn in excess of a total of 450 mL (1 unit) for any reason within 30 days prior to randomization
16. A history of hypersensitivity reactions including anaphylaxis and angioedema following administration of a COVID-19 vaccine
17. A history of heparin-induced thrombocytopenia and thrombosis (HITT or HIT type 2) or cerebral venous sinus thrombosis
18. A history of thrombocytopenia, including immune thrombocytopenia (ITP) following administration of a COVID-19 vaccine
19. A history of Guillain-Barré Syndrome
20. Patients with acute promyelocytic leukaemia
21. Individuals with a known history of capillary leak syndrome (CLS)

Date of first enrolment
15/11/2022

Date of final enrolment
30/04/2023

Locations

Countries of recruitment
England

United Kingdom

Wales

Study participating centre
Churchill Hospital
Churchill Hospital
Old Road
Headington
Oxford
United Kingdom
OX3 7LE

Study participating centre
University Hospital of Wales
Heath Park
Cardiff
United Kingdom
CF14 4XW

Study participating centre
The Royal Marsden Hospital (surrey)
Downs Road
Sutton
United Kingdom
SM2 5PT

Study participating centre
Northampton General Hospital NHS Trust
Cliftonville
Northampton
United Kingdom
NN1 5BD

Study participating centre
The Clatterbridge Cancer Centre NHS Foundation Trust
Clatterbridge Hospital
Clatterbridge Road
Bebington
Wirral
United Kingdom
CH63 4JY

Sponsor information

Organisation
Cardiff University

Sponsor details
Research Governance Coordinator
Research and Innovation Services
Cardiff University

7th Floor
McKenzie House
30-36 Newport Rd
Cardiff
Wales
United Kingdom
CF24 0DE
+44 (0)29208 79130
resgov@cardiff.ac.uk

Sponsor type
University/education

Website
http://www.cardiff.ac.uk/

ROR
https://ror.org/03kk7td41

Funder(s)

Funder type
Industry

Funder Name
AstraZeneca

Alternative Name(s)
AstraZeneca PLC, Pearl Therapeutics

Funding Body Type
Government organisation

Funding Body Subtype
For-profit companies (industry)

Location
United Kingdom

Results and Publications

Publication and dissemination plan

1. Peer-reviewed scientific journals
2. Conference presentation
3. Publication on website
4. Submission to regulatory authorities

Intention to publish date
26/01/2025

Individual participant data (IPD) sharing plan
Data release will require approval by the Trial Management Group (TMG) and the Trial Steering Committee (TSC) and will involve pseudo-anonymised data only. The data-sharing plans for the current study are unknown and will be made available at a later date.

IPD sharing plan summary
Data sharing statement to be made available at a later date

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
HRA research summary			28/06/2023	No	No
Protocol file	version 5.0	09/05/2023	29/08/2024	No	No
Protocol article		20/01/2025	27/01/2025	Yes	No
Statistical Analysis Plan	version 2	22/01/2024	13/03/2025	No	No
Basic results		29/05/2025	29/05/2025	No	No