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Evaluation of a laboratory test called QuantiFERON Cytomegalovirus in allogeneic stem cells transplant patients to assess its ability to detect the timing when the patients' immune system can control cytomegalovirus infection, thus allowing the clinical team the discontinuation of antiviral prophylaxis

Submission date
09/05/2025

Recruitment status
No longer recruiting

Registration date
14/07/2025

Overall study status
Completed

Last Edited
14/07/2025

Condition category
Infections and Infestations

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

Plain English summary of protocol

Background and study aims
This study is looking at a virus called CMV, which can cause serious illness in people who have had a stem cell transplant to treat blood cancers. These patients have weakened immune systems, making them more vulnerable to infections like CMV. The researchers want to find out if a special blood test (called QuantiFERON-CMV) can help doctors understand when a patient's immune system is strong enough to stop CMV from causing illness. This could help doctors decide how long to give antiviral medication after a transplant.

Who can participate?
Adults (18 years or older) who are having a stem cell transplant to treat a blood cancer can take part. They must either already have CMV or be receiving stem cells from a donor who has CMV.

What does the study involve?
Participants will have a small amount of blood taken seven times over six months. The first sample is taken before the transplant begins, and the others are taken at regular intervals after the transplant (days 30, 60, 90, 120, 150, and 180). These samples will be used to test how well the immune system is recovering and responding to CMV.

What are the possible benefits and risks of participating?
There is no direct benefit to participants, but the results may help improve care for future patients. The main risk is the discomfort of having blood taken. The study team will try to take the blood samples during regular hospital visits to avoid extra appointments. If a patient's

doctor thinks it's not safe to take blood (for example, if they are anaemic), the sample won't be taken.

Where is the study run from?
The study is being run at University Hospital Southampton NHS Foundation Trust (UK).

When is the study starting and how long is it expected to run for?
August 2022 to August 2025.

Who is funding the study?
The study is funded by the Southampton Specialist Virology Centre, the Translational Immunology Group at the University of Southampton, and the University of Bournemouth (UK).

Who is the main contact?
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Contact information

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Additional identifiers

Clinical Trials Information System (CTIS)
Nil known

Integrated Research Application System (IRAS)
321427

Protocol serial number
RHM MED1935

Study information

Scientific Title
Evaluation of the clinical usefulness of QuantiFERON®-CMV assay in identifying when patients reconstitute their immunity against cytomegalovirus (CMV) after undergoing allogeneic HSCT: a prospective, non-randomised, open-label study

Acronym
QF CMV

Study objectives
The risk of cytomegalovirus (CMV) reactivation and CMV disease in allogeneic-HSCT patients is correlated with the level of immunosuppression, which is highest during the first 3-4 months post-allogeneic HSCT. However, profound immunosuppression can be prolonged in patients suffering from graft versus host disease.

The current standard of care for CMV infection, post allogeneic-HSCT, includes antiviral prophylaxis with Letermovir (to reduce to a minimum the risk of viral reactivation) and CMV DNA monitoring (to enable the administration of pre-emptive treatment, should viral reactivation occur). These two interventions are effective in managing CMV infection in the first few months post-HSCT. However, there is a caveat associated with Letermovir prophylaxis: the reduction of CMV reactivation rates during prophylaxis is followed by an increased incidence of late CMV disease and CMV-related mortality after day 100, when the drug is discontinued. This is likely due to a delay of CMV T-cell immune reconstitution due to the reduced viral reactivation and antigen stimulation of CMV-specific cytotoxic T-cells during prophylaxis (if the virus does not reactivate, there are no CMV antigens to stimulate CMV-specific cytotoxic T-cells). A delayed immune reconstitution is more remarkable in those patients on prolonged pharmacological immunosuppression due to the persistence of graft versus host disease.

The inability to determine the timing of CMV immune reconstitution represents a diagnostic gap in the management of CMV infection post-allogeneic HSCT. The QuantiFERON®-CMV assay has the potential to address and close this gap by measuring CD8 T-cell IFN-g production in sequential samples post-HSCT. A reliable marker of immune reconstitution would be helpful for clinical decision making, such as the safe discontinuation of CMV DNA monitoring and antiviral prophylaxis. In addition, a negative QuantiFERON®-CMV assay result would provide important information regarding the patients' risk of developing late CMV disease.

We plan to perform QuantiFERON®-CMV assays in parallel with flow cytometry to confirm that QuantiFERON®-CMV assay results are correlated with the reconstitution of CMV-specific T-cell immunity.

Several studies have been published so far documenting the clinical utility of the QuantiFERON®-CMV assay in allogeneic-HSCT recipients. These studies have been performed in several countries, including the USA, Australia, Germany, Italy, Greece and Korea. As far as we are aware, there are no published studies conducted in the United Kingdom.

Ethics approval required
Ethics approval required

Ethics approval(s)
approved 22/06/2023, Stratford Health Research Authority (2 Redman Place, Stratford, E20 1JQ, United Kingdom; +44 (0)20 7104 8049; approvals@hra.nhs.uk), ref: 23/LO/0366

Study design
Single-centre prospective non-randomized open-label study

Primary study design
Interventional

Study type(s)
Diagnostic

Health condition(s) or problem(s) studied
Cytomegalovirus immune reconstitution in recipients of allogeneic haematopoietic stem cell transplant

Interventions
The study aims to measure CMV-specific CD8+ lymphocyte function post-allogeneic-HSCT by using the QuantiFERON®-CMV assay on the DiaSorin Liaison XL Chemiluminescent diagnostic platform located in the Southampton Specialist Virology Centre. Flow cytometry studies, aimed to confirm the QuantiFERON®-CMV assay results, will be performed in the laboratory facilities of the University of Southampton.

Patients will be recruited to the study during routine clinical visits by means of a short verbal explanation and the provision of an information sheet. Participants will sign a consent form. Signed consent forms will be scanned and stored in a secure, dedicated data file on the Virology hard drive.

HSCT recipients will donate seven lithium heparin blood specimens that will be collected together with other blood samples that are part of the routine patient care post-HSCT. Blood

samples will be collected every month for 6 months, with the first sample collected pre-HSCT, on the day patients commence the conditioning regimen. The seventh and last specimen will be collected 6 months post-allogeneic-HSCT.

Intervention Type
Other

Primary outcome(s)
1. Risk of CMV disease is measured using the QuantiFERON-CMV assay on the DiaSorin Liaison XL platform at baseline (hospital admission before conditioning), and monthly until day 180 post-allogeneic-HSCT
2. IFN-gamma production in IU/mL is measured using the QuantiFERON-CMV assay at baseline and monthly until day 180 post-allogeneic-HSCT
3. Presence of CMV-specific CD8+ cells is measured using flow cytometry for CD3, CD4, CD8, CX3CR1, CCR7, and CD45RA at baseline and monthly until day 180 post-allogeneic-HSCT

Key secondary outcome(s))
1. CMV immune reactivity is measured using the QuantiFERON-CMV assay at baseline and monthly until day 180 post-allogeneic-HSCT
2. CMV viral load is measured using weekly CMV DNA PCR testing from blood samples as part of standard of care from baseline until day 180 post-allogeneic-HSCT
3. CMV-specific CD8+ cell immunity is measured using the QuantiFERON-CMV assay at baseline and monthly until day 180 post-allogeneic-HSCT
4. Change in CMV viral load following reactivation is measured using CMV DNA PCR testing at the time of reactivation and in a follow-up blood sample collected 48–72 hours later

Completion date
28/08/2025

Eligibility

Key inclusion criteria
1. Age 18 years and over
2. Male or female
3. CMV IgG positive HSCT recipients, irrespective of the donor’s CMV IgG status
4. CMV IgG negative HSCT recipients with a CMV IgG positive donor

Participant type(s)
Patient

Healthy volunteers allowed
No

Age group
Adult

Lower age limit
18 years

Sex

All

Total final enrolment
30

Key exclusion criteria
1. CMV IgG negative HSCT recipient with a CMV IgG negative donor
2. Absence/withdrawal of consent

Date of first enrolment
25/02/2024

Date of final enrolment
11/02/2025

Locations

Countries of recruitment
United Kingdom

England

Study participating centre
University Hospital Southampton NHS Foundation Trust
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Sponsor information

Organisation
University Hospital Southampton NHS Foundation Trust

ROR
https://ror.org/0485axj58

Funder(s)

Funder type
Hospital/treatment centre

Funder Name
University Hospital Southampton NHS Foundation Trust

Alternative Name(s)

Funding Body Type
Government organisation

Funding Body Subtype
Local government

Location
United Kingdom

Funder Name
University of Southampton

Alternative Name(s)
University of Southampton UK

Funding Body Type
Government organisation

Funding Body Subtype
Universities (academic only)

Location
United Kingdom

Results and Publications

Individual participant data (IPD) sharing plan
Individual participant data from this study will be stored electronically on password protected data files on workstations within the Southampton Specialist Virology Centre by the investigators in a secure, access-controlled environment following the standard operating procedure of the UoS and a HTA licensed tissue bank until the final report of the project has been submitted and accepted for publication. The Chief Investigator will be the custodian of the data. Data will be collected and retained in accordance with the Data Protection Act 2018.
The Chief Investigator and Co-Investigators will have access to the study data for analysis. Unidentifiable patients' data will be analysed in the University Hospital Southampton and the University of Bournemouth (Dr Sarah Buchan, Co-Investigator, is a Principal Academic at the University of Bournemouth).

IPD sharing plan summary
Stored in non-publicly available repository

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Participant information sheet	version 6	20/06/2023	09/05/2025	No	Yes