QuantiFERON®-CMV study
PATIENT INFORMATION SHEET

Target of the study:

To assess when Cytomegalovirus (CMV) immune reconstitution occurs post allogeneic Hematopoietic Stem Cell Transplantation (HSCT) by using the Qiagen QuantiFERON®-CMV assay.

Title of the study:

Evaluation of the clinical usefulness of QuantiFERON®-CMV assay in identifying when patients reconstitute their immunity against CMV after undergoing allogeneic HSCT.

IRAS Reference Number 321427

You are being invited to consider taking part in a study. Before you decide whether or not to take part, it is important for you to understand why the study is being done and what it will involve. Please take time to read the following information and ask us if there is anything that is not clear or if you would like more information. Take time to decide whether or not you wish to take part.

Introduction

This study aims to use a laboratory test, called QuantiFERON®-CMV, to measure when your immune system can effectively control CMV infection following allogeneic Hematopoietic Stem Cell Transplant (HSCT).

What is CMV?

CMV a virus that establishes a lifelong dormant infection in a subset of white blood cells. About 40 to 50% of the human adult population is infected with CMV in the UK. CMV can reactivate from dormancy leading to the production of infectious virus that can cause severe disease affecting multiple organs including lungs, bowel and eyes in individuals who are immunocompromised, such as transplant patients. CMV is one of the most important infectious agents in the setting of transplantation and for this reason allogeneic-HSCT recipient and donors are tested with the aim to match the CMV status (CMV infected recipients are matched with CMV infected donors and vice versa) to minimise the risk of CMV disease. The management of CMV infection and disease is a very important aspect of your post-transplant care.

How does the immune system effectively control CMV infection?

The immune system uses a variety of cells to protect the body from infections. For viruses, including CMV, key cells conferring protection are a subset of white blood cells called "*T-cytotoxic cells*". These cells need time to start functioning properly following allogeneic-HSCT, particularly during the first few months post-transplant. The following measures are part of post-transplant standard of care during this critical period, when your immune system is impaired and therefore unable to effectively fight the virus:

- If you are CMV antibody positive you are prescribed an antiviral drug that prevents CMV reactivations.
- Your blood is monitored for CMV viral load at least once per week to detect the virus reactivation early before it causes disease.

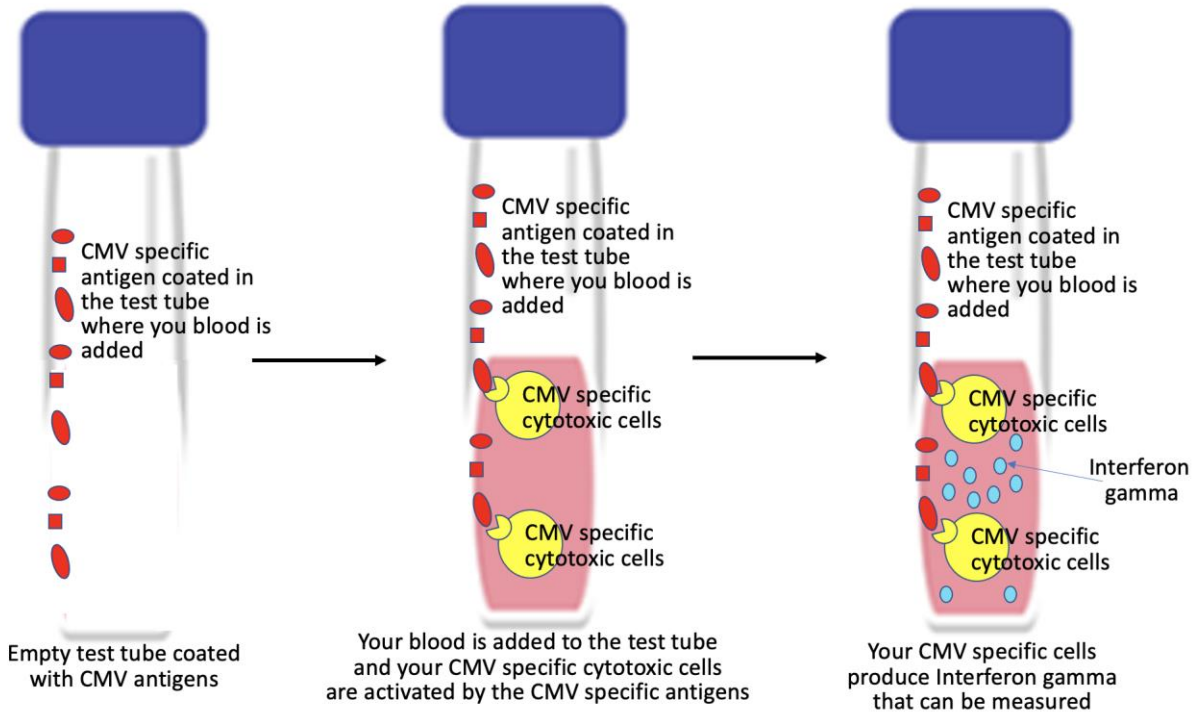
- Should reactivation occur you will be treated with a different anti-CMV drug to suppress viral replication.

At some time, post-HSCT, the immune system gradually starts building up the ability to control CMV infection. This process is called “immune reconstitution”. When immune reconstitution has taken place, antiviral drugs and CMV viral load monitoring are no longer needed. The identification of the timepoint when reconstitution of CMV immunity occurs is important for optimizing your care. In the current clinical practice, there are no specific laboratory tests able to assess if and when CMV immune reconstitution has occurred.

What is QuantiFERON®-CMV?

The QuantiFERON®-CMV is a laboratory test able to determine if your “*T-cytotoxic cells”* work properly by measuring the presence of a protein, called gamma-Interferon, produced by these cells when they are exposed to CMV in the blood tube (see figure below). Previous studies have shown that patients with a positive QuantiFERON®-CMV test are significantly more likely to remain free from CMV disease, compared to patients with a negative QuantiFERON®-CMV test. This suggests that QuantiFERON®-CMV test may help to establish when CMV prophylaxis and CMV viral load monitoring can be safely discontinued and may also predict the risk of developing CMV disease in the transplant patients negative for the test.

The QuantiFERON®-CMV assay is a commercial test produced by a company called Qiagen. Although commercially available for quite some time, it has not been implemented as part of the post-transplant standard of care in the UK. If this study will show the clinical usefulness of QuantiFERON®-CMV, we plan to offer this test for routine clinical use.



Since some previous studies showed that the QuantiFERON®-CMV test may not detect all forms of CMV immunity we are going to additionally use, for this study, another technique called ‘flow cytometry’ to measure the number of your immune cells able to control CMV infection. We will therefore be able

to compare the results obtained with QuantiFERON®-CMV test with those obtained with the Flow cytometry. In this way we will better understand if the QuantiFERON®-CMV test can be used as routine diagnostic test in clinical practice.

What is flow cytometry?

Flow cytometry involves labelling the cells from your blood with markers only expressed on the cell subsets of interest. Lasers are then used to detect the markers. For this study we will be looking at how many *T-cytotoxic cells* are in your blood using flow cytometry and whether these are expressing markers associated with the ability to kill CMV infected cells. We will also use your blood sample to quantify how many '*T-helper cells'* are present; *'T-helper cells'* assist *T-cytotoxic cells* so that T-cytotoxic cells are better able to fight viral infections. This information will help us to better define which immune cell subsets provide protection from CMV disease. Flow cytometry is for research use only.

1. What is the purpose of this study?

- To optimise patient management with regards to CMV infection post allogeneic-stem cell transplantation.
- QuantiFERON®-CMV test results will inform when CMV antiviral prophylaxis and CMV viral load monitoring can be safely discontinued
- QuantiFERON®-CMV test results can identify post allogeneic-HSCT patients at risk of developing late CMV disease.

2. Why have I been asked to take part in this research trial?

You have been asked because:

- You have been diagnosed with a haematological malignancy for which allogeneic-HSCT will be performed with the intent to cure your cancer.
- You are at risk of developing CMV disease since
    - You have antibodies to CMV (this means that you are infected with this virus) or
    - You are CMV antibody negative but your donor has CMV antibodies (this means your donor is infected with CMV and, as a consequence, there is a small risk of acquiring the infection through your donor's stem cells)
- You are above 18 years old

3. Do I have to take part?

No. It is entirely up to you to decide whether or not to take part. If, after reading this information sheet, you decide to take part you will be asked to sign a Consent Form. Signing this means you understand what is involved, any questions you have were answered so you could understand and that you agree to take part. If you decide to take part, you are still free to change your mind at any time and without giving a reason. If you decide to withdraw, or decide not to take part, this will not affect your care.

4. What does taking part involve?

Taking part to the study involves donating 10 ml of blood at the timepoints illustrated in the table below. Until day 180 the blood will be collected at the same time of other routine blood tests. No blood samples will be collected for the study if no blood samples are going to be taken for routine clinical investigations.

Blood sampling for QuantiFERON®-CMV study

Timepoints			Volume collected	Time shift accepted
1	Day 0 – date of initiation of conditioning regimen	You will be an in-patient at this stage	10 ml	+/- 5 days
2	Day 30 post allogeneic-HSCT	You may be an out-patient; the blood test for the study will be collected together with routine blood tests	10 ml	+/- 5 days
3	Day 60 post allogeneic-HSCT	You are likely to be an out-patient; the blood test for the study will be collected during a follow up visit together with routine blood tests	10 ml	+/- 5 days
4	Day 90 post allogeneic-HSCT	You are likely to be an out-patient; the blood test for the study will be collected during a follow up visit together with routine blood tests	10 ml	+/- 5 days
5	Day 120 post allogeneic-HSCT	You are likely to be an out-patient; the blood test for the study will be collected during a follow up visit together with routine blood tests	10 ml	+/- 5 days
6	Day 150 post allogeneic-HSCT	You are likely to be an out-patient; the blood test for the study will be collected during a follow up visit together with routine blood tests	10 ml	+/- 5 days
7	Day 180 post allogeneic-HSCT	You are likely to be an out-patient; the blood test for the study will be collected during a follow up visit together with routine blood tests	10 ml	+/- 5 days

How will your samples be used?

Your blood samples will be used to perform the QuantiFERON®-CMV in the Southampton Specialist Virology Centre, University Hospital Southampton, and to additionally perform complementary studies on the function of your T-immune cells by using a flow cytometer at the University of Southampton (laboratory located within University Hospital Southampton). These additional studies will be key in confirming the clinical usefulness of the QuantiFERON®-CMV assay.

There will not be long term storage of the specimens (individual samples will be stored for fewer than 6 months since collection and then discarded) .

5. What are the risks and side effects of taking part?

Blood collection - If you consent for the study, you will be asked to have up to 7 blood tests over the course of 6 months. We will aim to do these at the same time of your clinical appointments to the hospital. If your clinical team considers that taking an additional blood sample is not appropriate because, for example, you are anaemic (low red blood cell count), this will not be performed.

There will not be any negative impact on your medical care that will continue as normal.

6. Will I benefit from taking part in this research trial?

There may not be direct benefit to you from taking part in this study since it will take time to analyse the data generated by the study. We hope that the results of our study will help us to understand if the QuantiFERON-CMV is useful for establishing when CMV immune reconstitution takes place. If this is

the case, the test will be introduced for routine clinical use, thus helping other allogeneic-HSCT patients in the future.

You will be informed by your transplant team about the outcome of the study.

7. Will my taking part in this study be kept confidential?

Yes. All the information about your participation in this study will be kept strictly confidential. The handling, processing, storage and destruction of study information and data will be conducted in accordance with the General Data Protection Regulation (GDPR) 2018.

How will the research team use information about you?

- Information from your medical records will be used for this research project. This information is held at the hospital site and will include your:
  - Name
  - Hospital number
  - Date of Birth
- We will use the information to do the research or to check your records to make sure that the research is being done properly.
- People who do not need to know who you are will not be able to see your name or contact details. Your data will have a code number instead.
- We will keep all information about you safe and secure.
- Once we have finished the study, we will keep some of the data so we can check and analyse the results of the study. We will write a study report in a way that no-one can work out that you took part in the study.

What are your choices about how your information is used?

- You can stop being part of the study at any time, without giving a reason, but we will keep information about you that we already have.
- We need to manage your records in specific ways for the research to be reliable. This means that we won't be able to let you see or change the data we hold about you.

Where can you find out more about how your information is used?

- You can find out more about how we use your information:
- at www.hra.nhs.uk/information-about-patients/
- or see the HRA leaflet: www.hra.nhs.uk/patientdataandresearch
- by asking us directly (see email at the bottom of this form).

8. What will happen to the results of the research?

We plan to publish the results in a peer reviewed scientific journal. You will not be identified in any report or publication.

9. Will I be informed of the outcome of the research?

It is unlikely that the results from your samples influence your medical care, since the analysis of the data will not be performed in real time, but at the end of the study.

10. Who is organising and funding this study?

The study is being organised by doctors and scientists from the Southampton Specialist Virology Centre (University Hospital Southampton) and the University of Bournemouth in partnership with the UHS Stem Cell Transplant Unit. Funding is through the Southampton Specialist Virology Centre (SSVC) fund, with the aim to support the research and development of new diagnostic tests for the benefit of patients. The doctors conducting the study are not being paid to perform the study.

11. Will there be any payment for taking part?

No payment will be made to you for taking part in this study.

12. Will travel costs be reimbursed?

The procedure for the research will take place alongside routine clinical visits that are scheduled almost weekly during the 6 months following allogenic-HSCT. Therefore, travel costs will not be reimbursed for out-patient visits.

13. Who has ethically reviewed this study?

This study has been reviewed and approved by HRA Seasonal REC and has obtained ethical approval.

14. Contact for further information:

If you require any further information or have any concerns while taking part in this study, please contact one of the following people:
Dr Emanuela Pelosi, Consultant Medical Virologist, Chief Investigator: Emanuela.Pelosi@uhs.nhs.uk
Dr Sarah Buchan, Principal Academic in Immunology, Coinvestigator: sbuchan@bournemouth.ac.uk
Sponsor's data protection officer: dataprotection@uhs.nhs.uk, telephone number 023 8120 4743

15. Contact point for complaints to the PIS who is independent from the study team:

Patient advice and Liaison service (PALS), pals@uhs.nhs.uk, telephone number 023 8120 6325

If you take part in this study, you will be given a copy of this information sheet and a copy of the signed consent.

Thank you for taking the time to read this information sheet

Copies of the participant information sheet are stored in the office of the medical study team at the Southampton Specialist Virology Centre and distributed to the participants through the stem cell transplant nurses. The electronic form of the participant information sheet is securely filed on the hard drive of the Microbiology and Virology Department.