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Investigating infection risk and the microbiome in blood cancer patients treated with CD19 CAR-T therapy

Submission date 07/05/2026	**Recruitment status** Recruiting	[X] Prospectively registered [X] Protocol [_] Statistical analysis plan [_] Results [_] Individual participant data [X] Record updated in last year
Registration date 08/05/2026	**Overall study status** Ongoing	
Last Edited 03/06/2026	**Condition category** Cancer	

Plain English summary of protocol

Background and study aims
Blood cancer patients are vulnerable to infections due to having a weakened immune system. The overall aim of this study is to improve our understanding of infections that may occur following a new type of advanced cancer treatment called CAR-T therapy. In CAR-T therapy, the patient's own immune cells are reprogrammed to fight cancer cells. CAR-T therapy can be very successful in treating a type of blood cancer called B-cell lymphoma. However, these patients can remain vulnerable to infections long-term after receiving CAR-T treatment, including bacteria and viruses such as flu and Covid-19.

This study will investigate how common infections are after CAR-T therapy in adult patients with B-cell lymphoma, which patients are at highest risk of getting infections, which bugs tend to cause these infections and how they can be prevented and treated, and how a patient’s microbiome affects their infection risk and cancer outcomes. The microbiome refers to all the tiny bugs (microbes) that live in or on a person. The microbiome plays an important role in health and disease, although its role in CAR-T patients is not fully understood. This study will focus particularly on the microbes living in the gut and inside the nose.

Who can participate?
Adult patients aged 18 years and over with high grade B-cell lymphoma who are being treated with CD19 CAR-T therapy.

What does the study involve?
The study will follow up a group participants for one year after they start CAR-T therapy. Data and samples will be collected from these patients to study the infections they get, their outcomes after CAR-T treatment, and their microbiome.

Clinical data will be collected by asking the patients directly and by review of their medical records. Nose swabs (similar to Covid-19 tests), stool (poo) samples, and a blood sample, will be collected at three scheduled time points: prior to starting CAR-T therapy, 7-14 days after receiving the CAR T-cells, and approximately 3-4 months later. If the patients are admitted to

hospital during follow-up then additional samples may be collected, along with any leftover samples that are collected as part of their routine NHS care, once NHS diagnostic testing is completed.

Participants will also be asked to collect their own nose swabs from home over the course of the study whenever they have symptoms of a cold or flu, which can be posted to the study team for analysis using provided envelopes. A questionnaire asking about their symptoms (eg. whether they have a cough, sore throat, headache etc) will accompany the self-collected nose swabs. Participants will be invited to submit a repeat nose swab and questionnaire one week after the first one for each episode of the common cold or flu.

The microbes present in the samples will be analysed in detail, for example by genetic testing, to better understand which microbes cause infections in these patients, how they spread, and what the best treatments are. Information on the patient's demographics (eg. their age, sex etc), medical background, cancer treatments, medical test results, microbiome, and immune system, will be analysed to determine risk factors for developing infections after CAR-T therapy.

Data will also be included from adult patients that previously received CAR-T therapy for treatment of high grade B-cell lymphoma at participating centres, collected by the patient's direct care team.

What are the possible benefits and risks of participating?
Participants will receive a £25 Amazon gift voucher when they sign up. Otherwise, there are no direct benefits to the patient for participating in the study. Individual results will not be fed back to participants as they do not conform to required clinical diagnostic standards and are intended for research purposes only. It is hoped that the study will ultimately benefit other patients in future by improving the prevention and treatment of infections in patients undergoing CAR-T therapy.

The study is observational, meaning there is no change to the patient's treatment. The risks to the patient for participating are therefore very low. There may be some inconvenience associated with donation of poo samples, nose swabs, and blood samples, but it should not be dangerous. The nose swabs used in this study are of the front part of the nose, so the swab only goes in about half an inch into each nostril. If done gently and safely, this kind of nose swab is very safe; serious injury is extremely unlikely. Rare risks may include causing local injury to the nose, nosebleeds, retained swab, infection, or – extremely rarely – skull base damage and spinal fluid leak. However, the risk of serious harm is extremely low, as the swabs are not going far back into the nose. Instructions on how to collect the nose swabs safely will be provided. The risks from collecting blood samples are also very low, and may include bleeding or infection, but this is very unlikely to be severe. Poo samples, nose swabs and blood tests are collected very routinely and safely in the NHS.

If the burden of providing any of the samples, including the self-collected nose swabs during follow-up, becomes too much or cannot be tolerated by a participant for any reason, they can stop providing any particular sample at any time, whilst still remaining in the study, if they would like.

Another category of risk is inappropriate data release; however, this study will ensure that patient data is handled as securely as is reasonably possible. Personal data will be stored on NHS servers with restricted access to appropriate and trained personnel including clinical and trained research staff. Only anonymised samples and data will be provided to researchers based outside of the NHS. Scientific publications and presentations will not include personal identifiable data.

Where is the study run from?
The study is co-sponsored by Cambridge University Hospitals NHS Foundation Trust (CUH) and Cambridge University Department of Medicine. Other UK haematology centres performing CAR-T therapy will collaborate for patient recruitment. Wellcome Sanger Institute and University of Oxford Big Data Institute are collaborating research centres.

When is the study starting and how long is it expected to run for?
June 2026 to May 2031.

Who is funding the study?
The main funder is Blood Cancer UK. Additional funding comes from the National Institutes of Health and Care Research (NIHR), the NIHR Cambridge Biomedical Research Centre (BRC), and the Wellcome Sanger Institute.

Who is the main contact?
Dr William Hamilton, Chief Investigator, micro-cart@medschl.cam.ac.uk.

Contact information

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Additional identifiers

Integrated Research Application System (IRAS)
348968

Central Portfolio Management System (CPMS)
64590

Study information

Scientific Title
Investigating molecular microbiology and infectious disease in blood cancer patients following CD19 CAR-T therapy

Acronym
Micro-CART

Study objectives
This study aims to investigate infectious disease risk, pathogen molecular microbiology and the microbiome in adult patients with high grade B-cell lymphoma undergoing CD19 CAR-T therapy. A secondary aim is to investigate microbial diversity, virulence mechanisms and antimicrobial resistance (AMR) in immunocompromised patients more widely.

Specific study objectives are:
1) To determine the burden of infectious complications in adult patients with high grade B-cell lymphoma following CD19 CAR-T therapy.

2) To investigate risk factors for developing infections in these patients (including identifying correlates of protection against infections).

3) To describe pathogen molecular microbiology post- CD19 CAR-T therapy (including microbial AMR, virulence mechanisms, and genetic diversity).

4) To investigate how the gut and respiratory tract microbiomes change over time post CD19 CAR-T therapy, and their associations with infection risk and patient outcomes.

Ethics approval required
Ethics approval required

Ethics approval(s)
Approved 05/05/2026, London – Bloomsbury (Health Research Authority 2 Redman Place Stratford, London, E20 1JQ, United Kingdom; +44 0207 104 8171; bloomsbury.rec@hra.nhs.uk), ref: 26/LO/0278

Primary study design
Observational

Secondary study design
Longitudinal study

Study type(s)

Health condition(s) or problem(s) studied
Adult patients with high-grade B-cell lymphoma undergoing treatment with CD19 chimeric antigen receptor (CAR) T-cells.

Interventions
This multi-centre observational study has two components: (1) prospective recruitment of a cohort of patients with high grade B-cell lymphoma undergoing CD19 CAR-T therapy for sampling and longitudinal follow-up; (2) retrospective data collection on patients who have previously undergone CD19 CAR-T therapy for treatment of high grade B-cell lymphoma from participating centres.

(1) Prospective cohort
A prospective longitudinal cohort design will be used. 120 adult patients with high grade B-cell lymphoma undergoing CD19 CAR-T therapy will be followed up with longitudinal data and sample collection for 12 months post- CAR T-cell infusion. The study is observational and not interventional; all patients will receive standard of care in the UK National Health Service (NHS).

Participants will be recruited from haematology clinics when they agree to undertake CAR-T therapy and will provide written informed consent. Participants will receive a £25 Amazon gift voucher for signing up to the study. Clinical and demographic data will be collected for all participants by asking them directly and by accessing their medical records. Patients will be followed up over the study period via review of their medical records to determine CAR-T complications and their treatments, episodes of infection/ illness, hospitalisations, cancer outcome, and, if relevant, cause of death. Patients may be contacted by telephone by the study team up to a maximum of four times over the 12 months of follow-up if clarification is required.

The participant's microbiome and immune system will be analysed using three types of samples – a stool (poo) sample, a nose swab, and a blood sample – collected at three scheduled time points:
(1) Baseline sample: Can be taken any time after recruitment into the study, before lymphodepleting chemotherapy is started for their CAR-T therapy.
(2) Infusion sample: Collected within 7-14 days post- CAR-T infusion (can be earlier if the patient is planned for discharge before day 7).
(3) Convalescent sample: Approximately 3-4 months post-infusion (allowing flexibility for clinic timing, up to a range of 3-9 months post-infusion).

The nose swabs used in this study are of the anterior (front part) of the nose. The swabs should be inserted no further than 0.5 inch/ 1.3cm into the nostril; they are not deep nasopharyngeal

swabs - this reduces associated risks for collection. Samples and data from the prospective cohort will be collected by members of the clinical team and study team researchers who have received appropriate training for handling clinical and research data securely.

Any samples and/or pathogen isolates collected from the participants as part of their routine NHS care at the participating sites may be accessed for the study, once NHS diagnostic testing is completed. Patient identifiers (e.g. sticky labels including the patient's name and hospital number) will be removed from these samples and replaced with anonymised study codes before they are transported outside of clinical laboratories to research centres.

During follow-up (most likely outside of hospital), participants will also be invited to submit a 'symptom survey' detailing their symptoms and to post in self-collected nose swabs whenever they experience episodes of the 'common cold', flu-like illness, or respiratory tract infections. The swabs will be posted to the study team for analysis using pre-addressed/ stamped envelopes. An instruction sheet on how to collect the anterior nose swabs will be provided to all participants along with the swabs, survey sheets and postage bags. After symptom onset, participants will be invited to repeat the survey and another nose swab one week later.

Samples will undergo microbiological analyses including microbial whole genome sequencing, metagenomic sequencing, molecular testing, and microbial culture and phenotypic characterisation (such as response to treatments, vaccines and immune mediators). Samples will also be used to study the immune system, for example, by measurement of antibody levels, anti-pathogen immunity, neutralisation assays, and soluble immune mediators such as cytokine levels.

Follow-up will end at death, confirmed progression of haematological malignancy, palliation, or 12 months post- CAR-T infusion. Additional samples may be requested if the participant is admitted to hospital during the 12 months of follow-up. Patients may be contacted by the study team outside of hospitalisation episodes to request additional samples and information within the 12 months of follow-up or for up to 12 months beyond this (24 months total post- CAR T-cell infusion). Patients will be contacted a maximum of four times in the first 12 months and twice in the second 12 months. Maximum samples that will be requested, in addition to the set protocol, are: 2x nose swabs, 1x stool sample, and 1x blood sample.

(2) Retrospective data
Where available, data will be collected retrospectively on adult patients with high grade B-cell lymphoma who received CD19 CAR-T therapy at participating centres previously. The retrospective data will supplement the data collected from the prospective cohort to increase sample size for analysis. The retrospective data will be collected by members of the direct care team at each site, via review of patient medical records and datasets already collected/ available at the sites.

The retrospective data to be collected will include details on any infections that occurred in the 12 months post- CD19 CAR T-cell infusion, microbiology results, and potential risk factors for infection such as cytopaenias and immunosuppressive treatments received to manage complications such as cytokine release syndrome (CRS) or immune effector cell associated neurotoxicity syndrome (ICANS).

For both the prospective and retrospective cohorts, patient identifiable data will be stored and analysed only on NHS systems. Only anonymised data will be collated and analysed by academic/ research/ commercial organisations based outside of the NHS, such as at Cambridge University, Wellcome Sanger Institute, and Oxford University.

In summary, through both the prospective and retrospective study arms, the study will produce rich data and samples from adult patients with high grade B-cell lymphoma treated with CD19 CAR-T therapy. This will inform strategies to prevent and manage infections in these vulnerable patients, a key priority to maximise the potential of CAR-T therapy to benefit people with blood cancer.

Intervention Type
Not Specified

Primary outcome(s)
1. Infectious disease epidemiology measured using routine diagnostics, metagenomics, whole genome sequencing, molecular testing, microbial culture, serology, and clinical diagnosis retrieved from medical records at up to 1 year after CAR T-cell infusion

2. Risk factors for predicting infection risk measured using a review of medical records including previous blood test results, past medical history, information on participant's blood cancer and treatments received, medical imaging results, microbiology results, and information on participant's immune system at throughout 1 year of follow-up after CAR T-cell infusion

3. Characterisation of pathogen molecular microbiology measured using metagenomics, whole genome sequencing, molecular testing, microbial culture and phenotyping at throughout 1 year of follow-up after CAR T-cell infusion

4. Microbiome measured using metagenomics, whole genome sequencing, molecular testing, microbial culture and phenotyping at prior to commencing CAR-T therapy, within days 7-14 post CAR T-cell infusion (earlier if patient will be discharged before day 7), and 3-4 months post CAR T-cell infusion (allowed range of 3-9 months). Additional nose swab samples provided by participants through self-collection for up to 1 year post CAR T-cell infusion.

Key secondary outcome(s)

Completion date
31/05/2031

Eligibility

Key inclusion criteria
1. Male or female sex
2. Age 18 years or older to no upper limit
3. Has mental capacity to give informed consent
4. Has a confirmed diagnosis of high-grade B-cell lymphoma
5. Planned to undertake therapy with CAR-T cells targeting CD19 as a treatment for their lymphoma (any CD19 targeting CAR T-cell product can be included)

Healthy volunteers allowed
No

Age group
Mixed

Lower age limit

18 Years

Upper age limit
120 Years

Sex
All

Total final enrolment
0

Key exclusion criteria
1. Age below 18 years
2. Not able to provide informed consent eg lacks capacity
3. Patient is a prisoner
4. Patient is pregnant
5. Previous receipt of an allogeneic bone marrow transplant (allo-HSCT)
6. A history of recurrent or serious nosebleeds, or nasal polyps, or any other abnormalities or on-going medical conditions affecting the nose that would contra-indicate taking nasal swabs
7. Having undergone nasal surgery in the last year
8. Having had a broken nose in the last year
9. Any defects of the skull base or hard palate

Date of first enrolment
01/06/2026

Date of final enrolment
31/05/2028

Locations

Countries of recruitment
United Kingdom

England

Study participating centre
Cambridge University Hospitals NHS Foundation Trust
Cambridge Biomedical Campus
Hills Road
Cambridge
England
CB2 0QQ

Study participating centre
Oxford University Hospitals NHS Foundation Trust
John Radcliffe Hospital

Headley Way
Headington
Oxford
England
OX3 9DU

Study participating centre
University Hospitals Birmingham NHS Foundation Trust
Queen Elizabeth Hospital
Mindelsohn Way
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B15 2GW

Sponsor information

Organisation
University of Cambridge

ROR
https://ror.org/013meh722

Organisation
Cambridge University Hospitals NHS Foundation Trust

ROR
https://ror.org/04v54gj93

Funder(s)

Funder type

Funder Name
Blood Cancer UK

Alternative Name(s)
Blood Cancer UK Research

Funding Body Type

Private sector organisation

Funding Body Subtype
Trusts, charities, foundations (both public and private)

Location
United Kingdom

Funder Name
Wellcome

Alternative Name(s)

Funding Body Type
Private sector organisation

Funding Body Subtype
International organizations

Location
United Kingdom

Funder Name
National Institute for Health and Care Research

Alternative Name(s)
National Institute for Health Research, NIHR Research, NIHRresearch, NIHR - National Institute for Health Research, NIHR (The National Institute for Health and Care Research), NIHR

Funding Body Type
Government organisation

Funding Body Subtype
National government

Location
United Kingdom

Results and Publications

Individual participant data (IPD) sharing plan

IPD sharing plan summary

Not expected to be made available

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Protocol file	version 2		08/05/2026	No	No