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PRETZCEL: CD8 minibody repeatability study

Submission date
07/06/2022

Recruitment status
No longer recruiting

Registration date
03/10/2022

Overall study status
Completed

Last Edited
20/06/2024

Condition category
Cancer

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

Plain English summary of protocol

Background and study aims
A type of white blood cell, called CD8 T cells, is an essential part of the body's immune defense against cancer and other diseases. However, it is difficult to track these cells in the body. A new agent, crefmirlimab berdoxam, a modified antibody that attaches itself to T cells can be used to track CD8 T cells in the body after it is attached to a small amount of radioactivity (called a radiotracer as the radioactivity traces a particular molecule in the body) and imaged with positron emission tomography (PET) scans. For the new agent to be used with confidence in the development of new drugs or for clinical assessment, we need to check if the scanning method is reliable. In this study, we aim to investigate this by doing PET scans twice under similar circumstances in the same patient.

Who can participate?
Twelve patients, all aged over 18 years old who are either being actively monitored for their kidney cancers or on treatment with immune system modifying therapy (immunotherapy) for their melanoma (a type of skin cancer) will be studied.

What does the study involve?
Scans will be done on each occasion about 24 hours after the injection of the radiotracer. The radiotracer has been well tolerated by more than 100 research participants who have received it but is yet to be approved for use as a licensed imaging agent. The radiotracer will be manufactured in mainland Europe and transported to the UK for study use and given after it is approved for clinical use by the manufacturing site. Each participant will be in the study for up to 12 weeks. Participants will be recruited and scanned at the Hull University Teaching Hospitals NHS Trust and the study is expected to be open to recruitment for approximately 12 months.

What are the possible benefits and risks of participating?
The PIS will detail participant risks and will form an essential part of the discussion at the time of consent. The study is voluntary and patients approached will consider the risks without any influence from the study team.
The IMP, ^{89}Zr crefmirlimab berdoxam has been administered to more than 100 participants so far and has been well tolerated. There have been no reports of allergic reactions, so far. Participants will be monitored for at least an hour after IMP administration. We will also collect any self-reported adverse event until 33 days (equivalent to 10 half-lives of the radioisotope Zr-89) after the last infusion of the IMP. Any emerging safety concerns will be identified quickly and the

study will be paused or halted, if required and the appropriate regulatory authorities notified.
All study participants will be cancer patients and will have had routine whole-body CT imaging as part of disease management. By taking part in this study, the study interventions will expose patients to additional radiation equivalent to 26 years of UK background radiation. The risk of developing a radiation-induced second cancer by taking part in the study is 1 in 338 (0.3%) for people aged 18-50 years. This compares to a lifetime risk of 1 in 2 (50%) for a person born after 1960 in the UK developing cancer. We will seek UK ARSAC approval for the administration of radiation.
Men and women will be advised to use reliable contraception that will be detailed in the PIS during the study and for 30 days afterward to mitigate the risk of radiation exposure to the unborn foetus. Urine pregnancy tests for women of childbearing potential will be performed at screening and before each study IMP administration. Should a participant become pregnant (or the female partner of a male participant), the participants will undergo counseling and the pregnancy will be followed up to its conclusion.
Patients will be advised to follow radiation protection procedures and will consent to take part only if they can comply with the radiation protection measures. Study participants will need to avoid close contact (<1 m) with family members, friends or carers for 7 days after IMP administration, from pregnant women and children under 5 years, for 14 days, and avoid sleeping in the same bed as anyone else for 14 days. They will also be requested to take special care after voiding their bladder and bowels and requested to flush the toilet twice after use. We have been conservative in our radiation protection measures as published scientific data is limited on the radiation protection measures Zr-89. We will perform body count measurements after IMP administration obtains real-life data and will adopt an individualised risk approach based on this. We will provide a worksheet based on the body rate count performed an hour after the IMP administration indicating how long the radiation protection measures detailed above need to be followed. We estimate that the measures would be less stringent; however, it is also possible that in some participants that this may be more stringent.
Participants will need to make extra hospital visits for this study. The IMP administration visits will last up to 2 hours once and up to 3 hours once. Similarly, the participants will need to spend about 90 minutes during each of their PET-CT scan visits. Blood sampling and insertion of a venous cannula may be associated with local pain and rarely bruising at the site. Rarely, tissue extravasation of the IMP may occur. However, the study procedures require that the viability of the venous line needs to be checked before IMP administration. In case, tissue extravasation does occur, local procedures will be followed and the adverse event will be followed until it is resolved. PET-CT scan requires the participants to lie on their back for 60 minutes and staff will ensure that the participants are comfortable prior to scan start. The scan will be stopped at any time if the participant cannot continue with the scan.
In recognition of participants taking part in this research for altruistic reasons with no direct clinical benefit to the participants and for the discomfort and inconvenience caused to the participants, a nominal honorarium of £100 per completed scan will be offered to the participants either as a shopping voucher or in cash.
The risk profile of the study has been categorised as a Type C study due to the IMP status being non-marketed. All Serious Adverse Events will be reported during the study with no exemptions. Although the participants have cancer and may be undergoing routine treatment, comorbidities and mortality is expected to be low. As the study sample size is small and we expect no more than 2 participants to be in the study at any one time, the study will not employ a Data and Ethics Monitoring Committee or Trial Steering Group. However, regular sponsor oversight reporting and monitoring of safety data will take place throughout the study.

Where is the study run from?
Hull University Teaching Hospitals NHS Trust (UK). Sponsored by ImaginAb, Inc (USA).

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

Who is funding the study?
ImaginAb, Inc (USA)

Who is the main contact?
Ms Bronwen Williams, bronwen.williams@hyms.ac.uk

Study website
https://www.hull.ac.uk/work-with-us/research/institutes/health-trials

Contact information

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Scientific

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Additional identifiers

EudraCT/CTIS number
2022-000944-31

IRAS number
1005934

ClinicalTrials.gov number
NCT05744128

Secondary identifying numbers
IAB-CD8-204, IRAS 1005934, CPMS 54400

Study information

Scientific Title
Positron emission tomography Repeatability Evaluation of Tissue Zirconium 89ZR CrEfmirLimab berdoxam uptake (PRETZCEL)

Acronym
PRETZCEL

Study objectives
1. To evaluate test/re-test reliability of ^{89}Zr crefmirlimab berdoxam PET imaging in tumours and normal tissues
2. To assess tolerability of ^{89}Zr crefmirlimab berdoxam PET scans in patients with cancer

Ethics approval required
Old ethics approval format

Ethics approval(s)
Approved 02/09/2022, East Midlands – Nottingham 2 REC (Equinox House, City Link, Nottingham, NG2 4LA, UK; +44 207 104 8169; nottingham2.rec@hra.nhs.uk), ref: 22/EM/0137

Study design
Phase IIb repeatability study

Primary study design
Interventional

Secondary study design
Non randomised study

Study setting(s)
Hospital

Study type(s)
Treatment

Participant information sheet
Participant information sheet not available externally.

Health condition(s) or problem(s) studied
Melanoma, renal cell carcinoma

Interventions
Each participant will undergo two PET scans over a 4 to 8 week period depending on patient cohort. The scans will be done on each occasion about 24 h after the injection of the radiotracer, ^{89}Zr crefmirlimab berdoxam. Imaging results will be available after the second PET-CT scan.

Intervention Type
Drug

Phase
Phase III

Drug/device/biological/vaccine name(s)
^{89}Zr crefmirlimab berdoxam

Primary outcome measure
1. Differences in normal tissue, and tumor uptake, measured standardized uptake values (SUV mean, SUVmax, and SUVpeak) between the two PET-CT scans at baseline and 4-8 weeks
2. Differences in normal tissue, and tumor uptake normalized to a reference region measured as standardized uptake value ratio between the two PET-CT scans at baseline and 4-8 weeks

Secondary outcome measures
Safety measured using the incidence of adverse events collected between the start of the trial and 33 days after the participants' last PET-CT scan

Overall study start date
01/06/2022

Completion date
29/05/2024

Eligibility

Key inclusion criteria
All participants:
1. Aged ≥18 years
2. ≥1 imageable primary or metastatic lesion ≥1 cm in the lymph nodes or soft tissue excluding bone on the most recent standard of care imaging done within the last 3 months
3. Agree to follow contraceptive advice while on study until 33 days after ending participation

Cohort 1:
1. Melanoma on single or multiple agent Immune Checkpoint Blockade (ICB) therapy with stable response status following initiation of therapy
2. Stable disease observed over ≥2 consecutive standard of care CT scans (usually done 8-12 weeks apart) after initiation of therapy

Cohort 2:
1. Untreated renal cell carcinoma on active surveillance

Participant type(s)
Patient

Age group
Adult

Lower age limit
18 Years

Sex
Both

Target number of participants
12

Key exclusion criteria
1. Uncontrolled infection or other concurrent malignancies or conditions that may confound interpretation of the scans in the opinion of the study doctor
2. Urinary catheters or stoma bags
3. Patients who have received a COVID vaccine can be included in the study but can only be scanned after a washout period of 2 weeks after the vaccine. If patients have a COVID vaccine after the first PET-CT scan, the second PET-CT scan will be delayed for ≥2 weeks after the COVID vaccine.
4. Taking steroids, except those on replacement dose of steroids for adrenal or pituitary insufficiency. Patients requiring steroids as therapy for an unresolved immune therapy related adverse event will be excluded.
5. Taking immunosuppressive medication e.g. cyclosporine, azathioprine, or janus kinase inhibitors
6. Enrolled in another therapeutic intervention study
7. Any other contraindication that makes the patient unsuitable to take part in the study in the opinion of the investigator
8. Women of child bearing potential who are pregnant or breastfeeding on study entry
9. Unable to provide informed consent

Date of first enrolment
15/12/2022

Date of final enrolment
29/05/2024

Locations

Countries of recruitment
England

United Kingdom

Study participating centre
Castle Hill Hospital
Hull University Teaching Hospitals NHS Trust
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Sponsor information

Organisation
ImaginAb (United States)

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Sponsor type
Industry

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Funder(s)

Funder type
Industry

Funder Name
ImaginAb, Inc

Results and Publications

Publication and dissemination plan

1. Internal report
2. Conference presentation
3. Publication on website
4. Other publication
5. Submission to regulatory authorities

This is a commercially sponsored study and the raw data will not be shared. However, the study results may be presented at conferences and published in peer-reviewed scientific journals

Intention to publish date

01/08/2025

Individual participant data (IPD) sharing plan

Data sharing statement to 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