ISRCTN13695430 https://doi.org/10.1186/ISRCTN13695430

A feasibility trial to assess recruitment rates and ctDNA reporting times for patients with resected stage IIB/IIC/IIIA melanoma

Submission date 06/09/2024	**Recruitment status** No longer recruiting	[X] Prospectively registered [_] Protocol [_] Statistical analysis plan [_] Results [_] Individual participant data [X] Record updated in last year
Registration date 25/09/2024	**Overall study status** Ongoing	
Last Edited 01/10/2026	**Condition category** Cancer	

Plain English summary of protocol

Background and study aims

We are looking for new and better ways to manage melanoma, an aggressive type of skin cancer. Surgery to remove the melanoma will cure the majority of patients with early-stage disease. However, a small percentage of these patients will go on to develop further disease, which may spread to other places in their bodies. At present, following surgery, patients with early-stage melanoma can either choose to have close monitoring with regular scans and skin checks or they can have a year of drug treatment. This study is testing whether we can follow patients with regular blood tests looking for DNA that comes from the cancer (ctDNA) and only treat those patients that become ctDNA positive, indicating cancer is still present. Critically, this test can identify early melanoma relapse when it is not visible on imaging. Thus, we can reduce the amount of unnecessary drug treatment and potential side effects for patients by using ctDNA testing. Patients will remain in the study for at least 5 years and will be seen in hospital clinics. This is a feasibility study, which means that the researchers are looking at whether a large-scale study could be possible by first of all working with a smaller number of participants. They want to know if they can recruit enough patients in 12 months and analyse blood tests promptly. If it is feasible, they will then be looking to expand DETECTION-2 into a much larger Phase III study which will involve a larger number of participants to compare treatments.

Who can participate?

Patients over 16 years of age with resected stage IIB/IIC/IIIA, BRAF/NRAS/TERT promoter mutated cutaneous melanoma

What does the study involve?

Patients will be required to consent to the trial and have the correct mutation. They will then be randomly put into either a group to receive drug treatment as they would usually do in standard of care or to not receive drug treatment but instead have regular blood tests to monitor their ctDNA. The visit schedule for those receiving drug treatment will depend on the drug given. Those on ctDNA blood testing would be seen every 3 months in the first 3 years and every 6 months in years 4 and 5 to have a check-up and their blood taken for ctDNA. All patients will continue with routine standard-of-care scans (CT but maybe MRI or PET depending on local

hospital policy). These would occur every 3 months in year 1, every 6 months in years 2 and 3, and then annually in years 4 and 5. If patients relapse during the trial or have a positive ctDNA test result they would be offered additional treatment according to local standard of care policies.

What are the possible benefits and risks of participating?
It is hoped that the treatment strategy will help patients but this cannot be guaranteed. Patients receiving standard-of-care drug treatment may benefit from this. They may also have potentially harmful side effects. Patients receiving ctDNA monitoring may benefit from not receiving drug treatment at that point and the potential harmful side effects as they will only receive drug treatment when the ctDNA test suggests they have a higher risk of relapse. There is a small chance that the cancer might not be picked up early by the blood test but the treatments we give in melanoma work very well even at this time. Patients receiving drug treatment will have more visits at the start of the study than those on ctDNA monitoring. The information from this study may help improve the future treatments for patients with stage IIB/IIC/IIIA melanoma.

Where is the study run from?
The study is being run by the Southampton Clinical Trials Unit at the University of Southampton, in collaboration with The Christie NHS Foundation Trust (sponsor) and the University of Manchester (UK)

When is the study starting and how long is it expected to run for?
March 2024 to February 2031

Who is funding the study?
Cancer Research UK

Who is the main contact?
Prof. Paul Lorigan, Detection2@soton.ac.uk

https://www.cancerresearchuk.org/about-cancer/find-a-clinical-trial/a-study-looking-at-a-blood-test-to-see-whether-further-treatment-is-needed-after-having-surgery-to#undefined

Contact information

Type(s)
Scientific

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Additional identifiers

Integrated Research Application System (IRAS)
341779

Central Portfolio Management System (CPMS)
58643

Protocol serial number
CRCCTA-Nov23/100005

Study information

Scientific Title
DETECTION-2 feasibility: A feasibility trial to assess recruitment rates and ctDNA reporting times for patients with resected stage IIB/IIC/IIIA melanoma

Acronym
DETECTION-2

Study objectives
Surgery to remove the melanoma will cure the majority of patients with early-stage disease. However, a small percentage of these patients will go on to develop further disease, which may spread to other places in their bodies. At present, following surgery, patients with early-stage melanoma can either choose to have close monitoring with regular scans and skin checks or they can have a year of drug treatment. This study is testing whether we can follow patients with regular ctDNA (circulating tumour DNA found in the blood) tests and only treat those patients that become ctDNA positive indicating disease activation. Thus reduce the amount of unnecessary drug treatment and potential side effects for patients by using ctDNA testing. This test can identify early melanoma relapse when it is not visible on imaging.

Ethics approval required
Old ethics approval format

Ethics approval(s)
Approved 29/07/2024, Yorkshire & The Humber - Sheffield Research Ethics Committee (NHS Blood and Transplant Blood Donor Centre, Holland Drive, Newcastle upon Tyne, Tyne and Wear, NE2 4NQ, UK; +44 (0)2071048139, +44 (0)2071048135, +44 (0)207 104 8210; sheffield.rec@hra.nhs.uk), ref: 24/YH/0142

Primary study design
Interventional

Study design
Randomized controlled trial

Study type(s)
Treatment

Health condition(s) or problem(s) studied
Skin cancer

Interventions
Pre-screening:
Potentially eligible patients will provide consent for their tumour sample (already obtained for diagnosis) to be sent to the Manchester Centre for Genomic Medicine to undergo mutational analysis. Patients whose tumour has a confirmed mutation (called BRAF, NRAS or TERT) will be eligible to proceed. Depending on the sites local patient pathways, patients can consent to the pre-screening first and the main study at a later date, or consent to the main study immediately.

Screening:
If not already done, patients will provide consent for the main study and undergo screening assessments including a physical examination, review of medical history, and a CT scan (which may have already been done). If all eligibility criteria are met, the patient may be randomised.

Randomisation:
Participants will be randomised at a ratio of 1:1 to either Arm A (standard of care adjuvant treatment) or Arm B (treatment based on regular monitoring of circulating tumour DNA [ctDNA]).

Arm A:
Participants will discuss their standard of care adjuvant treatment options with their doctor and proceed with 1 year of treatment, followed by 4 more years of follow-up. Visit frequency during the treatment phase will depend upon the treatment given. After treatment, patients will continue to be followed up as per the protocol schedule (designed to match standard of care). CT scans will be completed as per the protocol, designed to match standard of care. Any standard of care assessments before, during and after treatment will continue (e.g. blood tests, pregnancy tests, ECGs) and symptom-led physical exams and disease assessments will be completed at each visit. If the cancer returns, patients will proceed with standard-of-care treatment.

Arm B:
Participants will have a baseline blood sample collected for ctDNA analysis at the National Biomarker Centre in Manchester, and again at each visit, as per the protocol schedule (which matches Arm A) for a total of 5 years. Sites are expected to send ctDNA samples on the day of collection and ctDNA test results will be returned to the site within 10 working days of sample collection. CT scans will be completed as per the protocol, designed to match standard of care. Any standard-of-care assessments will continue (e.g. blood tests, pregnancy tests, ECGs) and symptom-led physical exams and disease assessments will be completed at each visit.

ctDNA test outcomes:
1. Negative ctDNA result (ctDNA not detected) - participant continues with ctDNA monitoring
2. Positive ctDNA result (ctDNA detected) - participant will discuss standard of care treatment options and proceed with treatment
3. Uninformative ctDNA result - occasionally a test may need to be re-done due to strict quality assurance processes at the NBC laboratory.
If there is a local relapse of the cancer (with negative ctDNA result), the participant will undergo

surgery to remove the cancer and may continue with ctDNA monitoring. If there is distant relapse, the participant will cease ctDNA monitoring and proceed with standard of care treatment as per their discussions with their doctor.
- Visit schedule for both Arm A & B

The visit schedule has been designed to best match standard of care follow-up for this patient group.
Year 1: 3-monthly visits (months 3, 6, 9 and 12) - (Arm A patients will also have treatment visits as per standard care. The number of visits will depend on the treatment)
Year 2: 3-monthly visits (months 15, 18, 21 and 24)
Year 3: 3-monthly visits (months 27, 30, 33 and 36)
Year 4: 6-monthly visits (months 42 and 48)
Year 5: 6-monthly visits (months 54 and 60)

CT scans:
CT scan frequency is designed to match standard of care as best as possible. Scans will be 3-monthly until 12 months, then 6-monthly until 36 months, then annually until 60 months. Brain scans (CT or MRI) will be completed 6-monthly until 36 months, then annually until 60 months.

Data collection:
To minimise the burden on sites, data collection will occur via an annual minimal eCRF that will collect details of cancer treatments, adverse events, relapse event data, CT scan details, concomitant medications and ECOG score (the worst score recorded over the previous 12 months). In addition, for Arm B participants, the research team will need to enter the date of collection, date of receipt of result, and test result for each ctDNA blood test.

Intervention Type
Other

Primary outcome(s)
1. Recruitment rate assessed by a randomised patient count following a recruitment period of 12 months (aim is for ≥50 patients randomised)
2. The proportion of ctDNA results returned to site ≤10 working days from the sample being taken (aim is for this proportion to be 95% or above)

Key secondary outcome(s)
1. Relapse-free survival (RFS) defined as time from randomisation to radiological or clinical (confirmed histologically) relapse or death from any cause
2. Distant metastatic-free survival (DMFS) defined as time from randomisation to radiological distant metastatic relapse or death from any cause
3. Overall survival (OS) defined as the time from randomisation to death from any cause
4. Time from randomisation in Arm B to detection of ctDNA for those patients who had a ctDNA positive result
5. The number of patients in Arm B with undetectable ctDNA (according to the DETECTION-2 assay) but with clinical/radiological relapse and site of relapse (local or distant in addition to organ site) over the course of the trial
6. Sites of local and distant metastatic relapse determined using clinical judgement or CT/PET /MRI scans over the course of the trial
7. Adverse events measured according to Common Terminology Criteria for Adverse Events (CTCAE) v5.0 (coded using MedDRA) over the course of the trial

Completion date
28/02/2031

Eligibility

Key inclusion criteria
1. Histological confirmation of cutaneous melanoma
2. >=16 years
3. Stage IIB or IIC or IIIA melanoma. SLNB is highly encouraged to ensure accurate staging but is not mandatory. If no SLNB is to be performed then the primary must be at least TIIIA
4. Complete resection (adequate margins as determined by multi-disciplinary team or local /national guidelines, including SLNB if performed) must have been performed within 12 weeks prior to randomisation. If a patient is randomised to Arm A, treatment should be commenced no later than 14 weeks following surgery and with complete wound healing from surgery.
5. Disease-free status documented both clinically and radiologically within 4 weeks prior to randomisation
6. Mutation confirmed in BRAF (p.V600E, p.V600K and p.V600R) /NRAS (p.Q61R, p.Q61K, p.Q61L and p.G12D) /TERT promoter (c.146 C> T and c.124 C> T), which can be tracked in ctDNA with exact point mutation known
7. No prior immunotherapy, chemotherapy, vaccine therapy or BRAF/MEK targeted therapy
8. ECOG performance status 0/1
9. Adequate organ function:
9.1. WBC >=2.0 x 10e9/L
9.2. Absolute neutrophil count (ANC) >=1.5 x 10e9/L
9.3. Platelets >=100 x 10e9/L
9.4. Haemoglobin >=90 g/L
9.5. Creatinine clearance >30 ml/minute using Cockcroft-Gault
9.6. AST <=1.5 x ULN
9.7. ALT <=1.5 x ULN
9.8. Bilirubin <= 1.5 x ULN unless the patient has familial hyperbilirubinaemia)
10. Written informed consent

Participant type(s)
Patient

Healthy volunteers allowed
No

Age group
Mixed

Lower age limit
16 Years

Upper age limit
100 Years

Sex
All

Total final enrolment
65

Key exclusion criteria
1. Known severe medical or physiological or psychological co-morbidities conditions that would compromise or impede participation or contraindications to therapeutics
2. Pregnant or breastfeeding females
3. Current other malignancy or history of another malignancy within the last 3 years. Patients who have been disease-free for 3 years, (i.e., patients with second malignancies that have been definitively treated at least 3 years ago) or patients with a history of completely resected non-melanoma skin cancer or melanoma in situ are eligible.
4. In patients planned to have immune therapy only (including BRAF wild type), patients with active, known or suspected autoimmune disease are excluded from enrolment apart from those patients with the following conditions
4.1. Type 1 diabetes mellitus
4.2. Rheumatoid arthritis not requiring disease-modifying drugs
4.3. Hypothyroidism only requiring hormone replacement
4.4. Skin disorders (such as vitiligo, psoriasis or alopecia) not requiring systemic treatment
4.5. Autoimmune conditions not expected to recur in the absence of an external trigger. Many patients with these conditions have now been treated with immune therapy. A discussion about the potential risk of worsening of these conditions should be had with the patient prior to consent.
5. In patients planned to have immune therapy only (including BRAF wild type), patients with a condition requiring ongoing/long-term (> 3 months) systemic treatment with either corticosteroids (> 10 mg daily prednisone equivalent) or other immunosuppressive medications. Inhaled or topical steroids and adrenal replacement steroid doses < = 10 mg daily prednisolone equivalent are permitted in the absence of active autoimmune disease.
6. Patients with interstitial lung disease that is symptomatic or may interfere with the detection or management of suspected drug-related pulmonary toxicity.
7. History of allergies or adverse drug reaction to any of the of the intended standard of care therapies or to any monoclonal antibody.
8. Known Human Immunodeficiency Virus (HIV), Hepatitis B Virus (HBV), or Hepatitis C Virus (HCV) infection.

Date of first enrolment
27/11/2024

Date of final enrolment
29/11/2025

Locations

Countries of recruitment
United Kingdom

England

Study participating centre

The Christie
550 Wilmslow Road
Withington
Manchester
England
M20 4BX

Study participating centre
Addenbrookes
Addenbrookes Hospital
Hills Road
Cambridge
England
CB2 0QQ

Study participating centre
Poole General Hospital
St Mary's Carpark
Longfleet Road
Poole
England
BH15 2JB

Study participating centre
Royal Preston Hospital
Sharoe Green Lane
Fulwood
Preston
England
PR2 9HT

Study participating centre
Southampton General Hospital
Tremona Road
Southampton
England
SO16 6YD

Study participating centre
Weston Park Cancer Centre
Weston Park Hospital

Whitham Road
Sheffield
England
S10 2SJ

Study participating centre
Beatson West of Scotland Cancer Centre
1053 Great Western Road
Glasgow
Scotland
G12 0YN

Study participating centre
Royal United Hospital Bath
Combe Park
Bath
England
BA1 3NG

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

Study participating centre
Royal Marsden Hospital
Royal Marsden Hospital
Downs Road
Sutton
England
SM2 5PT

Study participating centre
The Royal Marsden Hospital
Fulham Road

London
England
SW3 6JJ

Study participating centre
St James University Hospital
Gledow Wing
Beckett Street
Leeds
England
LS9 7TF

Study participating centre
Nottingham City Hospital
Hucknall Road
Nottingham
England
NG5 1PB

Sponsor information

Organisation
The Christie NHS Foundation Trust

ROR
https://ror.org/03v9efr22

Funder(s)

Funder type
Government

Funder Name
Cancer Research UK

Alternative Name(s)
CR_UK, Cancer Research UK - London, Cancer Research UK (CRUK), CRUK

Funding Body Type
Private sector organisation

Funding Body Subtype
Other non-profit organizations

Location
United Kingdom

Results and Publications

Individual participant data (IPD) sharing plan
In order to meet its ethical obligation to responsibly share data generated by interventional clinical trials, SCTU operates a transparent data-sharing request process. As a minimum, anonymous data will be available for request from 3 months after the publication of an article, to researchers who provide a completed Data Sharing request form that describes a methodologically sound proposal, for the purpose of the approved proposal and if appropriate a signed Data Sharing Agreement. Data will be shared once all parties have signed relevant data-sharing documentation.

Researchers interested in the data are asked to complete the Request for Data Sharing form (CTU/FORM/5219) (template located on the SCTU website https://www.southampton.ac.uk/ctu) to provide a brief research proposal on how they wish to use the data. It will include; the objectives, what data are requested, timelines for use, intellectual property and publication rights, data release definition in the contract and participant informed consent etc. If considered necessary, a Data Sharing Agreement from Sponsor may be required.

IPD sharing plan summary
Available on request