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Reducing repeat pleural biopsies in suspected cancer

Submission date
07/02/2024

Recruitment status
Recruiting

Registration date
16/02/2024

Overall study status
Ongoing

Last Edited
08/07/2025

Condition category
Cancer

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

Plain English summary of protocol

Background and study aims
Pleural mesothelioma is a cancer that affects the lung lining, caused by asbestos. Despite recent treatment advances, the prognosis is often poor. Prompt diagnosis is vital. A biopsy can diagnose mesothelioma, guide treatment and support compensation claims. However, some people need multiple biopsies, increasing the risk of biopsy-related complications and prolonging the time to diagnosis. Doing additional tests on initial biopsies may increase the chance of diagnosing mesothelioma and avoid repeat biopsies. This would allow anti-cancer treatment to be started sooner and improve survival. The extra tests are not genetic but look for genetic changes in the cancer that allow it to grow and spread. The genetic markers in mesothelioma are called BAP1, p16 and MTAP. If they have disappeared on biopsy mesothelioma is diagnosed. Another study was previously conducted on people with suspected mesothelioma who required further biopsies as their first biopsy did not give a diagnosis (TARGET: https://www.isrctn.com/ISRCTN14024829). It took place in eight UK centres and recruited 59 patients. This study aims to perform these additional tests on their biopsy samples to see whether this would have made the diagnosis sooner and removed the need for further biopsies. It will investigate how many biopsies could have been avoided, how much time would have been saved, how this may have impacted survival and what cost-savings this would have offered the NHS.

Who can participate?
This study includes the 59 participants in the original TARGET study who were recruited between September 2015 and September 2018. No additional participants will be recruited. Should any participants of the original TARGET trial wish to opt-out, they can contact the main contact below.

What does the study involve?
Biopsy samples taken as part of the participants' routine clinical care will be tested for the markers of genetic change in mesothelioma (BAP1, MTAP and p16). The ability to make a diagnosis using these tests will be compared with the original diagnostic pathway, which was before the use of these tests.

What are the possible benefits and risks of participating?
The benefits of enrolling are to future patients, whose diagnostic process could be improved, with no additional requirements of TARGET participants. As there are no additional interventions required of participants and this will not impact management, there are no risks identified.

Where is the study run from?
North Bristol NHS Trust (UK)

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

Who is funding the study?
Southmead Hospital Charity

Who is the main contact?
Geraldine Lynch, Geraldine.lynch@nbt.nhs.uk

Study website
https://www.nbt.nhs.uk/research-development/our-research/current-research/respiratory-research-hub/respiratory-current-research

Contact information

Type(s)
Principal Investigator

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Type(s)
Public, Scientific

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Additional identifiers

EudraCT/CTIS number
Nil known

IRAS number
329574

ClinicalTrials.gov number
Nil known

Secondary identifying numbers
V1.0, IRAS 329574

Study information

Scientific Title
Reducing repeat pleural biopsies in suspected cancer – a study of the TARGET trial cohort comparing the diagnostic yield of standard histology vs additional tests in suspected pleural malignancy

Acronym
REPLICA

Study objectives

Testing for BAP1, P16 FISH and MTAP IHC could remove the need for further invasive procedures in patients with suspected pleural malignancy and an initial non-diagnostic biopsy

Ethics approval required
Ethics approval required

Ethics approval(s)
Approved 28/03/2024, East Midlands - Leicester South Research Ethics Committee (3 Piccadilly Place, London Road, Manchester, M1 3BN, United Kingdom; +44 (0)207 104 8079; Leicestersouth.rec@hra.nhs.uk), ref: 24/EM/0042

Study design
Observational study using historical data and stored samples

Primary study design
Observational

Secondary study design
Cohort study

Study setting(s)
Laboratory, Medical and other records

Study type(s)
Diagnostic

Participant information sheet
No participant information sheet available

Health condition(s) or problem(s) studied
Improving diagnosis in pleural mesothelioma

Interventions
Current interventions as of 06/06/2025:
This is an observational study using historical data and stored samples from a multi-centre randomised controlled trial (TARGET; https://www.isrctn.com/ISRCTN14024829), where each participant will act as a case (additional tests applied to stored samples) and internal control (initial outcomes using standard testing only).

Pleural biopsies of patients with a final diagnosis of mesothelioma will be tested for BAP1 and MTAP using immunohistochemistry (IHC) and in some samples for P16 using fluorescent in-situ hybridisation (FISH).

Previous interventions:
This is an observational study using historical data and stored samples from a multi-centre randomised controlled trial (TARGET; https://www.isrctn.com/ISRCTN14024829), where each participant will act as a case (additional tests applied to stored samples) and internal control (initial outcomes using standard testing only).

Pleural biopsies will be tested for BAP1 and MTAP using immunohistochemistry (IHC) and in some samples for P16 using fluorescent in-situ hybridisation (FISH).

Intervention Type
Other

Primary outcome measure
Identification of malignancy on biopsy measured using immunohistochemistry (IHC) and fluorescent in-situ hybridisation (FISH) in the laboratory at one timepoint

Secondary outcome measures
The total number of biopsies required, time to diagnosis, stage at diagnosis, number of multi-disciplinary team (MDT) discussions, biopsy-associated costs, biopsy-related adverse events and survival measured using data recorded in medical records at one timepoint

Overall study start date
08/10/2022

Completion date
30/09/2025

Eligibility

Key inclusion criteria
All patients who were included in the TARGET trial (ISRCTN14024829).
TARGET eligibility required all of the following to apply:
1. Pleural thickening on CT suspicious for pleural malignancy
2. Have had any form of pleural biopsy in the last 12 months (either by thoracoscopy or under radiological guidance) which was non-diagnostic for cancer
3. Lung cancer/mesothelioma MDT decision to perform further CT-guided biopsy to pursue a diagnosis

Participant type(s)
Patient

Age group
Adult

Lower age limit
18 Years

Sex
Both

Target number of participants
59

Total final enrolment
59

Key exclusion criteria
Not eligible if not recruited to the TARGET trial

Date of first enrolment
29/04/2024

Date of final enrolment
30/09/2025

Locations

Countries of recruitment
England

Scotland

United Kingdom

Wales

Study participating centre
North Bristol NHS Trust
Southmead Hospital
Southmead Road
Westbury-on-trym
Bristol
United Kingdom
BS10 5NB

Study participating centre
Gloucestershire Royal Hospital
Great Western Road
Gloucester
United Kingdom
GL1 3NN

Study participating centre
Norfolk & Norwich University Hospital
Colney Lane
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Norwich
United Kingdom
NR4 7UY

Study participating centre

Northern General Hospital
Northern General Hospital NHS Trust
C Floor, Huntsmnan Building
Herries Road
Sheffield
United Kingdom
S5 7AU

Study participating centre
Royal Stoke University Hospital
Newcastle Road
Stoke-on-trent
United Kingdom
ST4 6QG

Study participating centre
Oxford University Hospitals
John Radcliffe Hospital
Headley Way
Headington
Oxford
United Kingdom
OX3 9DU

Study participating centre
Royal Gwent Hospital
Cardiff Road
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United Kingdom
NP20 2UB

Study participating centre
Queen Elizabeth University Hospital
1345 Govan Road
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United Kingdom
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Sponsor information

Organisation
North Bristol NHS Trust

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Learning & Research (Level 3), Southmead Hospital
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researchsponsor@nbt.nhs.uk

Sponsor type
Hospital/treatment centre

Website
https://www.nbt.nhs.uk/

ROR
https://ror.org/036x6gt55

Funder(s)

Funder type
Charity

Funder Name
Southmead Hospital Charity

Results and Publications

Publication and dissemination plan
The results of this research will be disseminated to patients and carers, fellow mesothelioma researchers and clinicians. Patients will be informed via the local mesothelioma patient group and the annual mesothelioma patient and carer conference. Results will be disseminated to the public via the Bristol Academic Respiratory and UK Pleural Society Twitter feeds. Results will be presented to fellow academics at scientific conferences e.g. the British Thoracic Oncology Group or International Mesothelioma Interest Group meetings. Clinicians will be informed via the UK Pleural Society state-of-the-art meetings and annual update day. The final report will be written up for publication in a peer-reviewed scientific journal, published open-access.

Intention to publish date
04/07/2026

Individual participant data (IPD) sharing plan

Deidentified data from this study will be made available by secure transfer from the corresponding author upon reasonable request from a qualified academic investigator for the sole purpose of replicating results presented in the article, under conditions of appropriate ethical oversight, upon investigator approval and execution of a data use agreement.

IPD sharing plan summary

Available on request

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Protocol file	version 1.0	16/01/2024	07/02/2024	No	No