ISRCTN14503847 https://doi.org/10.1186/ISRCTN14503847

Developing genetic tests to diagnose, monitor and guide treatment decisions for children and young people whose cancer has returned

Submission date 14/02/2025	**Recruitment status** Recruiting	[X] Prospectively registered [_] Protocol [_] Statistical analysis plan [_] Results [_] Individual participant data [X] Record updated in last year
Registration date 28/03/2025	**Overall study status** Ongoing	
Last Edited 28/03/2025	**Condition category** Cancer	

Plain English summary of protocol

Background and study aims
This is a UK research study testing tumour (somatic) and normal (germline) DNA and RNA for genetic changes in children and young people with relapsed/refractory cancer. This will be done by comparing the genetic information in the patient's healthy cells with their cancer cells, and following them over time to detect changes earlier than their scans. This information will be used to see if it can help to guide new treatment strategies and personalise cancer treatment for patients based on their genetic information.

Who can participate?
UK children and young adults whose cancer has either come back (relapsed) or not responded to treatment (refractory) and have undergone or will undergo a routine biopsy/surgery to obtain tumour tissue or bone marrow.

What does the study involve?
Participants with a solid tumour provide a blood sample and a piece (or pieces, if available) of tumour collected from their most recent biopsy or surgery. Participants with leukaemia provide a bone marrow sample. The results of the tests are relayed back to the patient's doctor via an expert panel who make recommendations on any available treatments. Patients and/or their parents are asked in advance to consider what information they want to receive in relation to any abnormal genetic results either in the tumour or their normal (germline) genetic code. In addition, the data collected is used and shared for the purposes of clinical research.

What are the possible benefits and risks of participating?
Benefits: It is unlikely there will be an individual benefit for the patient by taking part in the StratMedPaediatrics2 study. The greatest benefits of the work may not be expected for several years and therefore will predominantly help future patients. However, should something be found in the genetic information of the patient's tumour which may help in the understanding or treatment of the patient's cancer then the patient's clinical team will be able to use this information (for example provide a treatment option i.e. clinical trial or early indication that the treatment is not working). For solid tumour patients, as the tumour sample will already have

been or is due to be taken as part of the care at the hospital, the patient will only have blood tests taken whilst on the study. The discomfort of this blood test is just like any other blood test. For leukaemia patients, the bone marrow sample will already have been or is due to be taken as part of the care at the hospital.

Where is the study run from?
1. Royal Aberdeen's Children Hospital
2. Royal Belfast Hospital for Sick Children
3. Birmingham Children's Hospital
4. Bristol Royal Hospital for Children
5. Addenbrooke's Hospital
6. Noah's Ark Children's Hospital for Wales
7. Royal Hospital for Sick Children Edinburgh
8. Royal Hospital for Children
9. Leeds General Infirmary
10. Leicester Royal Infirmary
11. Alder Hey Children's Hospital
12. Great Ormond Street Hospital for Children
13. Royal Manchester Children's Hospital
14. Royal Victoria Infirmary
15. Queen's Medical Centre, Nottingham
16. John Radcliffe Hospital
17. Sheffield Children's Hospital
18. Southampton General Hospital
19. University College London Hospital
20. Royal Marsden Hospital Sutton

When is the study starting and how long is it expected to run for?
March 2023 to October 2032

Who is funding the study?
Cancer Research UK

Who is the main contact?
Ms Amina Bukhari, stratmedpaeds2@trials.bham.ac.uk

Plain English summary under review with external organisation

Contact information

Type(s)
Public, Scientific

Contact name
Ms Amina Bukhari

Contact details
Trial Coordinator
Children's Cancer Trials Team
Cancer Research UK Clinical Trials Unit
School of Medical Sciences

The University of Birmingham
Edgbaston
Birmingham
United Kingdom
B15 2TT
+44 (0)121 414 7851
StratMedPaeds2@trials.bham.ac.uk

Additional identifiers

EudraCT/CTIS number
Nil known

IRAS number
346034

ClinicalTrials.gov number
Nil known

Secondary identifying numbers
CPMS 64809, Cancer Research UK Grant Code CRCEMA-Jul23/100001

Study information

Scientific Title
Stratified Medicine Paediatrics 2

Acronym
StratMedPaeds2 / SMPaeds2

Study objectives
This is a UK research study testing tumour (somatic) and normal (germline) DNA and RNA for genetic changes in children and young people with relapsed/refractory cancer. This will be done by comparing the genetic information in the patient's healthy cells with their cancer cells. This information will be used to see if it can help to guide new treatment strategies and personalise cancer treatment for patients based on their genetic information.

Ethics approval required
Ethics approval required

Ethics approval(s)
Approved 29/11/2024, Yorkshire & The Humber - Leeds East Research Ethics Committee (2 Redman Place, Stratford, London, E20 1JQ, United Kingdom; +44 207 104 8171, 2071048137, 207 104 8357; leedseast.rec@hra.nhs.uk), ref: 24/YH/0218

Study design
Observational clinical laboratory study

Primary study design
Observational

Secondary study design
Cohort study

Study setting(s)
Hospital

Study type(s)
Diagnostic

Participant information sheet
Not available in web format, please use the contact details below to request a patient information sheet

Health condition(s) or problem(s) studied
Relapsed/refractory solid tumours (including lymphomas) or leukaemia

Interventions
StratMedPaeds2 is a prospective cohort molecular profiling study that will generate highly annotated clinical and molecular data to highlight novel and potentially druggable dependencies enriched at the time of cancer relapse, in support of a cohort of aligned experimental clinical trials that seek to deploy molecularly targeted drugs and immunotherapies, within molecularly enriched and serially monitored trial designs. Descriptive, highly clinically annotated molecular datasets will be developed on the spectrum and frequency of genetic, epigenetic and immune-microenvironmental changes that characterise relapsed childhood solid tumours. This information will be made available within a shared database, to deliver a harmonised and comprehensive information resource that can be readily used for clinical management and research. This will report in detail on the test performance parameters of the methodologies developed, and within the limitations of a relatively small study in rare disease indications, output statistically powered conclusions where possible on the best use of the tests developed, to support future clinical integration of the technologies. Of particular importance for the study is to investigate the clinical utility of liquid biopsies, and their ability to detect novel and potentially actionable events at relapse compared to existing tissue-biopsy testing.

StratMedPaeds2 will open in the UK across 20 paediatric primary treatment centres. The centres have been chosen based on their clinical expertise in the treatment of children with cancer. The recruitment target for the duration of the study is 400 patients.

For patients who meet the eligibility criteria for the study, the investigator will provide them /their families with information to allow a decision regarding their participation. The patient /parent/guardian will be required to provide consent for the collection and analysis of the patient samples, the collection of relevant clinical information, the return of clinical results back to their investigator, the use of and sharing of data for research, teaching, commercial and scientific publications, and the sharing of samples for other and future ethically approved research projects.

If informed consent is given, the investigator will conduct a screening evaluation to ensure that the patient satisfies all eligibility criteria. Following consent, the site investigators will register the patient onto the study, thus obtaining a patient-specific unique study ID number for that patient. Following registration, the site team must send the baseline ('study entry') following samples to the central sample hub at Great Ormond Street Hospital. All samples are taken

outside of the study as part of the patient's standard care, except for one blood sample in solid tumour patients.

The samples are then analysed at the central sample hub at Great Ormond Street Hospital (GOSH), this would also happen as part of the patient's standard care, the Institute of Cancer Research (ICR)/Royal Marsden Hospital, and University of Birmingham (UoB) as part of the StratMedPaeds2 research.

The findings from this analysis will be presented to a Molecular Tumour Board (MTB) based at Great Ormond Street Hospital. At the MTB, selected findings of clinical significance will be presented to (as a minimum) a pathologist, molecular pathologist and an oncologist for a combined review of the molecular findings in context. The MTB will discuss and finalise the presented findings and will report to the referring clinician, site pathologist and CRCTU.

Information about a patient's participation in a clinical trial and survival outcome will be collected for at least 3 years, this may be extended until all patients have a minimum of 3 years of follow-up.

Intervention Type
Other

Phase
Not Specified

Primary outcome measure
Genetic changes in the patient's relapsed/refractory cancer cells will be studied using genetic analysis in both the tumour and blood at the time of relapse and throughout their treatment journey to fulfil the following objectives:
1. The proportion of patients in whom clinically relevant genomic events are detected at the time of relapse
2. The proportion of patients in whom treatment is altered or who have a positive diagnosis as a direct result of either tissue or liquid biopsies.
3. The frequency and spectrum of events detected at the time of relapse

Secondary outcome measures
Genetic changes in the patient's relapsed/refractory cancer cells will be studied using genetic analysis in both the tumour and blood at the time of relapse and throughout their treatment journey to fulfil the following objectives:
1. Proportion of diagnoses that are refined as a result of molecular testing
2. Percentage of cases in which long-read sequencing reports a methylation classifier for diagnosis of CNS tumours and sarcoma
3. The proportion of patients on therapy who develop actionable or novel treatment resistance
4. mutations identified in serial liquid biopsy
5. Association of ctDNA levels by serial liquid biopsy during treatment with clinical and/or radiological Indicators of progression
6. The turnaround time (TAT) from receipt of sample at GOSH to discussion of results at MTB
7. The identification of events which contribute to TAT, beginning from patient consent to final reporting via the MTB

Overall study start date
23/03/2023

Completion date
01/10/2032

Eligibility

Key inclusion criteria
1. Age 0-21 years (patients > 21yo where primary cancer is classified as a “paediatric specific malignancy”)
2. Patients with relapsed/refractory paediatric solid & CNS tumours, Leukaemia and Lymphoma. Note: refractory leukaemia will only be eligible where no standard 2nd line treatment is available. Contact the leukaemia lead prior to registration
3. For solid tumours: Patient has a Formalin fixed paraffin embedded (FFPE) tumour (mandatory) and fresh frozen tumour (if available) from a biopsy, resection or other surgical procedure that was taken within 8 weeks prior to study entry (as part of NHS SoC). Fresh frozen tumour tissue is highly encouraged*1.
4. For leukaemia –Viable fresh or frozen Bone Marrow aspirate sample taken at a prior assessment within 8 weeks prior to study entry*2 (taken as part of NHS SoC) For BM and combined relapses where bone marrow is unavailable, a peripheral blood sample can be provided if circulating blasts are confirmed on morphology or flow cytometry.
5. For isolated CNS/Combined relapses where bone marrow is unavailable or BM is uninvolved with leukaemia, a CSF sample should be provided (taken as part of NHS SoC).
6. Written informed consent of patient/parent/guardian

*1. To allow full multi-omic analysis both fresh frozen and Formalin fixed paraffin embedded (FFPE) tumour plus a blood sample for constitutional (germline) and circulating tumour (ct) DNA will need to be available. Original diagnostic slides should be submitted at the same time as block from current relapse/refractory episode either in the same shipment (see laboratory manual for further details). For CNS tumours only: blood and CSF samples paired with initial SoC tumour tissue samples
*2. Where available, a cerebrospinal fluid (CSF) sample in the event of an isolated or combined CNS relapse should also be provided in addition to the bone marrow aspirate.

Participant type(s)
Patient

Age group
Mixed

Lower age limit
0 Years

Upper age limit
21 Years

Sex
Both

Target number of participants
Planned Sample Size: 400; UK Sample Size: 400

Key exclusion criteria
Not meeting the participant inclusion criteria

Date of first enrolment
14/04/2025

Date of final enrolment
14/09/2029

Locations

Countries of recruitment
England

Northern Ireland

Scotland

United Kingdom

Wales

Study participating centre
NHS Grampian
Summerfield House
2 Eday Road
Aberdeen
United Kingdom
AB15 6RE

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

Study participating centre
Alder Hey Childrens NHS Foundation Trust
Alder Hey Hospital
Eaton Road
West Derby

Liverpool
United Kingdom
L12 2AP

Study participating centre
Belfast City Hospital
51 Lisburn Rd
Belfast
United Kingdom
BT9 7AB

Study participating centre
Birmingham Women's and Children's NHS Foundation Trust
Steelhouse Lane
Birmingham
United Kingdom
B4 6NH

Study participating centre
University Hospitals Bristol and Weston NHS Foundation Trust
Trust Headquarters
Marlborough Street
Bristol
United Kingdom
BS1 3NU

Study participating centre
Cardiff & Vale University Lhb
Woodland House
Maes-y-coed Road
Cardiff
United Kingdom
CF14 4HH

Study participating centre
Lothian
Waverleygate
2-4 Waterloo PLACE
Edinburgh

City of Edinburgh
United Kingdom
EH1 3EG

Study participating centre
Gartnavel Royal Hospital
1055 Great Western Road
Glasgow
United Kingdom
G12 0XH

Study participating centre
Great Ormond Street Hospital for Children NHS Foundation Trust
Great Ormond Street
London
United Kingdom
WC1N 3JH

Study participating centre
St James University Hospital NHS Trust
St James's University Hospital
Beckett Street
Leeds
United Kingdom
LS9 7TF

Study participating centre
Leicester Royal Infirmary
Infirmary Square
Leicester
United Kingdom
LE1 5WW

Study participating centre
Manchester University NHS Foundation Trust
Cobbett House
Oxford Road
Manchester
United Kingdom
M13 9WL

Study participating centre
The Newcastle upon Tyne Hospitals NHS Foundation Trust
Freeman Hospital
Freeman Road
High Heaton
Newcastle upon Tyne
United Kingdom
NE7 7DN

Study participating centre
Nottingham University Hospitals NHS Trust
Trust Headquarters
Queens Medical Centre
Derby Road
Nottingham
United Kingdom
NG7 2UH

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

Study participating centre
The Royal Marsden NHS Foundation Trust
Fulham Road
London
United Kingdom
SW3 6JJ

Study participating centre
Sheffield Childrens Hospital
Western Bank
Sheffield
United Kingdom
S10 2TH

Study participating centre
Southampton General Hospital
Tremona Road
Southampton
United Kingdom
SO16 6YD

Study participating centre
University College London Hospitals NHS Foundation Trust
250 Euston Road
London
United Kingdom
NW1 2PG

Sponsor information

Organisation
Institute of Cancer Research

Sponsor details
Royal Cancer Hospital
123 Old Brompton Road
London
England
United Kingdom
SW7 3RP
-
Emma.Pendleton@icr.ac.uk

Sponsor type
Hospital/treatment centre

Website
https://www.icr.ac.uk/

ROR
https://ror.org/043jzw605

Funder(s)

Funder type
Government

Funder Name
Cancer Research UK

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

Funding Body Type
Private sector organisation

Funding Body Subtype
Other non-profit organizations

Location
United Kingdom

Results and Publications

Publication and dissemination plan
Planned publication in a peer-reviewed journal

Intention to publish date
01/10/2033

Individual participant data (IPD) sharing plan
The datasets generated during and/or analysed during the current study will be stored in a non-publicly available repository, Palantir's Foundry SaaS platform, hosted within the United Kingdom (UK).

- The type of data that will be shared: Pseudonymised Health data, genetic data
- When the data will become available and for how long: The data will be available throughout the study and into the follow-up period (a total of 7.5 years) Analysed full and partial data will be undertaken again throughout the study with the first potential availability being 1 year after the study opening
- By what access criteria the data will be shared including with whom: Trial Data Management Group decide access on a case-by-case basis, based on their legal need for access. Other researchers and groups.
- For what types of analyses, and by what mechanism: Sequencing, genome, spatial
- Whether consent from participants was obtained: Consent will be obtained for all study participants
- Comments on data anonymisation: Data is pseudonymised at the point of study enrolment (study ID is allocated upon registration and used throughout the study)
- Any ethical or legal restrictions, any other comments: Bound by clinical REC approval conditions and sponsor conditions

IPD sharing plan summary
Data sharing statement to be made available at a later date