ISRCTN10096625 https://doi.org/10.1186/ISRCTN10096625

Immune system changes after thymectomy (removal of the thymus gland) and childhood cardiac (heart) transplant

Submission date
14/10/2022

Recruitment status
No longer recruiting

Registration date
17/10/2022

Overall study status
Ongoing

Last Edited
16/12/2025

Condition category
Infections and Infestations

[_] 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
Post-transplant lymphoproliferative disease (PTLD) is a potentially fatal cancer seen in children who have received an organ transplant. In most children, PTLD is caused by Epstein-Barr Virus (EBV), which infects B-lymphocytes and is also known to cause glandular fever. These infected cells are normally kept under control by the immune system. However, the lifelong medication taken by transplant recipients to prevent organ rejection (immunosuppressants) also diminishes the control of this virus, leading to an abnormal accumulation of infected B-lymphocytes and their transformation into cancerous cells. PTLD affects approximately 1 in every 10 children within the first 5 years following heart transplant, representing a substantially higher risk than following other types of organ transplant. However, the reason for this increased risk is still poorly understood. We have previously identified that children with congenital heart disease are more likely to develop PTLD than children who develop an "acquired" heart disease. We believe this could be linked to their younger age at routine surgical removal of the thymus, a gland in the neck that is important for developing a healthy immune response to EBV.

The aim of this study is to collect clinical information and blood samples from children having a heart transplant to study their immune response to EBV.

Who can participate?
The study would like to recruit any child (0-18 years) who has a heart transplant in the UK. It will also recruit a small number of children having a kidney transplant as a comparison group.

What does the study involve?
Participating in the study involves reading an information sheet, asking questions and then agreeing to take part (consenting). Once part of the study, small additional blood samples will be taken prior to transplant, and during routine follow-up clinic appointments at 3, 6, 12 and 24 months after transplant. No extra appointments for blood tests are needed. The trial team will also collect information from the clinical records.

What are the possible benefits and risks of participating?
The study is intended to further our understanding of the causes of post-transplant lymphoproliferative disorders. Participants will not directly benefit but neither are there any identified risks.

Where is the study run from?
The study is run from the Newcastle upon Tyne Hospitals NHS Foundation Trust and Newcastle University (UK). It is being carried out in collaboration with Great Ormond Street Hospital as these two hospitals undertake all children's heart transplants in the UK.

When is the study starting and how long is it expected to run for?
January 2020 to December 2026

Who is funding the study?
The study is jointly funded by Cancer Research UK and The Lymphoma Research Trust (UK)

Who is the main contact?
Dr Simon Bomken, s.n.bomken@ncl.ac.uk

Contact information

Type(s)
Principal investigator

Contact name
Dr Simon Bomken

ORCID ID
https://orcid.org/0000-0001-9163-5738

Contact details
Level 6, Herschel Building
Brewery Lane
Newcastle upon Tyne
United Kingdom
NE1 7RU
+44 1912082231
s.n.bomken@ncl.ac.uk

Additional identifiers

Integrated Research Application System (IRAS)
298986

Central Portfolio Management System (CPMS)
51000

Study information

Scientific Title

Immunology of thymectomy and childhood cardiac transplant cohort study

Acronym
ITHACA

Study objectives
In children undergoing heart transplant, prior early thymectomy is associated with a dysregulated immune response to Epstein Barr virus infection.

Ethics approval required
Old ethics approval format

Ethics approval(s)
Approved 11/112021, North of Scotland Research Ethics Service (Summerfield House, 2 Eday Road, Aberdeen, AB15 6RE, UK; +44 (0)1224558458; gram.nosres@nhs.scot), ref: 21/NS/0142.

Primary study design
Observational

Study design
Multicentre observational cohort study

Study type(s)
Other

Health condition(s) or problem(s) studied
Response to Epstein Barr virus (EBV) infection in children undergoing heart transplant

Interventions
Blood samples assessing EBV status and to investigate systemic immune parameters will be obtained pre-transplant and during two years following transplant.

Intervention Type
Other

Primary outcome(s)
1. Innate and adaptive immune cell populations will be assessed in peripheral blood samples taken pre-transplant and at 3, 6, 12 and 24 months post-transplant.
2. Peri-transplant EBV-specific immune responses will be assessed in peripheral blood samples taken pre-transplant and at 3, 6, 12 and 24 months post-transplant.

Key secondary outcome(s)
There are no secondary outcome measures

Completion date
31/12/2026

Eligibility

Key inclusion criteria

1. Resident in the UK.
2. Aged 0 – 18 years.
3. Actively listed on the NHS Blood and Transplant (NHSBT) waiting list for a primary organ transplant OR awaiting transplant with a living related donor kidney OR recently transplanted with pre-transplant blood samples available.
4. Written informed consent.

Participant type(s)
Patient

Healthy volunteers allowed
No

Age group
Mixed

Lower age limit
0 Years

Upper age limit
18 Years

Sex
All

Total final enrolment
54

Key exclusion criteria
1. Has a pre-existing diagnosis of an inherited or acquired immunodeficiency
2. Has an underlying thymic disorder
3. Has previously received a bone marrow or organ transplant
4. Has had a previous cancer diagnosis
5. Withheld consent
6. Weight under 2.5 kg

Date of first enrolment
31/03/2022

Date of final enrolment
30/06/2024

Locations

Countries of recruitment
United Kingdom

England

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

Study participating centre
The Royal Victoria Infirmary and Associated Hospitals NHS Trust
Queen Victoria Road
Newcastle upon Tyne
England
NE1 4LP

Study participating centre
Great Ormond Street Hospital
Great Ormond Street
London
England
WC1N 3JH

Sponsor information

Organisation
Newcastle upon Tyne Hospitals NHS Foundation Trust

ROR
https://ror.org/05p40t847

Funder(s)

Funder type
Charity

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

Funder Name
The Lymphoma Research Trust

Results and Publications

Individual participant data (IPD) sharing plan
The datasets generated and/or analysed during the current study will be published as a supplement to the subsequent results publication

IPD sharing plan summary
Published as a supplement to the results publication

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Protocol article		21/10/2023	23/10/2023	Yes	No
HRA research summary			28/06/2023	No	No
Participant information sheet	11-15 years version 2.5.2	07/07/2022	17/10/2022	No	Yes
Participant information sheet	16 years and above version 2.6.2	07/07/2022	17/10/2022	No	Yes
Participant information sheet	6-10 years version 2.6.1	02/12/2021	17/10/2022	No	Yes
Participant information sheet	Parents version 2.5.2	07/07/2022	17/10/2022	No	Yes
Protocol file	version 2.4	07/07/2022	17/10/2022	No	No