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A study to see if a drug called gemtuzumab ozogamicin is a useful treatment for patients with immune disorders called haemophagocytic lymphohistiocytosis (HLH) or macrophage activation syndrome (MAS), or for patients with cancer

Submission date
03/12/2020

Recruitment status
No longer recruiting

Registration date
15/12/2020

Overall study status
Completed

Last Edited
30/05/2025

Condition category
Cancer

[X] Prospectively registered
[_] Protocol
[_] Statistical analysis plan
[X] Results
[_] Individual participant data

Plain English summary of protocol

Background and study aims
Immune system disorders cause abnormally low activity or over activity of the immune system. We want to improve the treatment of patients with immune disorders called haemophagocytic lymphohistiocytosis (HLH) and macrophage activation syndrome (MAS) which has come back (relapsed) or has not responded to previous treatment (refractory). We also want to improve treatment for those with cancers that have relapsed or are refractory to treatment.
Specifically, we are studying:
• Whether a drug called gemtuzumab ozogamicin elicits a biological response.
• Whether gemtuzumab ozogamicin works against HLH/MAS and cancer and is safe.

Who can participate?
Patients who have been diagnosed with primary or secondary HLH/MAS that is relapsing /refractory to treatment at time of enrolment or have a solid cancer which is refractory to treatment or they have relapsed.

What does the study involve?
Gemtuzumab ozogamicin will be given every 3 weeks for a total of 3 doses via an infusion into the vein (a needle in the arm or via a central line). Each infusion will be given in this hospital and take two hours. During each treatment the patient will have their blood pressure, heart rate and temperature measured whilst gemtuzumab ozogamicin is being administered. On weeks 2 and week 3 and for two weeks following the third dose, gemtuzumab ozogamicin will not be given but participants will still have a physical examination, blood tests, and an assessment of disease will in previous weeks.
In addition, the following extra research samples will be taken from the patients:

Blood will be collected for research. This sample will be used in laboratory studies to understand if gemtuzumab ozogamicin treatment has reduced the number of CD33 immune cells and for additional research studies.

What are the possible benefits and risks of participating?
We hope that patients treated with gemtuzumab ozogamicin will have a reduction in CD33 immune cells, and this may improve their current symptoms and disease.
However, we cannot promise that the patients will benefit from participating in this trial as this is the first time gemtuzumab ozogamicin has been tested in people with these conditions.
All the information that we get from this trial will be used to help improve the future treatment of people with HLH/MAS and/or refractory or relapsed solid cancers.
Although gemtuzumab ozogamicin has not been given to people with HLH/MAS or solid cancer before, it has been used to treat people with other conditions. Therefore we know what most of the side effects of treatment are.

Where is the study run from?
Cancer Research UK Clinical Trials Unit at the University of Birmingham (UK)

When is the study starting and how long is it expected to run for?
February 2020 to March 2025

Who is funding the study?
Little Princess Trust via the Children's Cancer and Leukaemia Group (UK) and Eveson Charitable Trust (UK)

Who is the main contact?
The main contact is the trial coordinator at the Cancer Research UK Clinical Trials Unit at gotham@trials.bham.ac.uk. They will be able to put you in touch with the chief investigator of the trial if this is required.

Contact information

Type(s)
Principal Investigator

Contact name
Prof Gary Middleton

ORCID ID
https://orcid.org/0000-0001-5695-3474

Contact details
School of Cancer Sciences
University of Birmingham
Edgbaston

Birmingham
United Kingdom
B15 2TT
+44 (0)121 371 2000
G.Middleton@bham.ac.uk

Additional identifiers

EudraCT/CTIS number
2020-002428-36

IRAS number
285470

ClinicalTrials.gov number
Nil known

Secondary identifying numbers
CPMS 47063, Grant Code CCLGA 2019 30, IRAS 285470

Study information

Scientific Title
A phase II trial to assess the activity of Gemtuzumab Ozogamicin Therapy in Haemophagocytic lymphohistiocytosis (HLH) or Macrophage activation syndrome (MAS) or relapsed/refractory solid tumours (GOTHAM)

Acronym
GOTHAM

Study objectives
Current study hypothesis as of 16/03/2023:
Gemtuzumab ozogamicin 3 mg/m2/dose given on Days 1, 22, and 43 has an effect on the levels of CD33+ myeloid cells in the blood in two parallel groups: patients with primary or secondary HLH or MAS disease that is relapsing/refractory to treatment at the time of enrolment and patients with relapsed/refractory solid tumours)

Previous study hypothesis:
Gemtuzumab ozogamicin 3 mg/m2/dose given on Days 1, 8, and 15 has an effect on the levels of CD33+ myeloid cells in the blood in two parallel groups: patients with primary or secondary HLH or MAS disease that is relapsing/refractory to treatment at the time of enrolment and patients with relapsed/refractory solid tumours)

Ethics approval required
Old ethics approval format

Ethics approval(s)
Approved 02/12/2020, South Central - Hampshire A Research Ethics Committee (Level 3, Block B, Whitefriars, Lewins Mead, Bristol, BS1 2NT, UK; +44 (0)207 1048033; hampshirea.rec@hra.nhs.uk), ref: 20/SC/0362

Study design
Interventional non-randomized study

Primary study design

Interventional

Secondary study design
Non randomised study

Study setting(s)
Hospital

Study type(s)
Treatment

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

Health condition(s) or problem(s) studied
Haemophagocytic lymphohistiocytosis, macrophage activation syndrome, relapsed/refractory solid tumours

Interventions
Current interventions as of 16/03/2023:
GOTHAM is a Phase II multicentre clinical trial of gemtuzumab ozogamicin. The trial aims to determine whether gemtuzumab ozogamicin elicits a biological response (a change in the number of CD33-positive cells) and whether it works against HLH/MAS and cancer and is safe. There are also other exploratory biological endpoints.
Potential patients and their parents/guardian/legal representative (if applicable) will be approached by a Consultant or delegate working on this study. If the patient and their parent /guardian/legal representative are satisfied with the age-appropriate information given and have had the chance to discuss the study with both the research team and their family and friends, they will be asked to sign a consent form if they wish to participate.

Before treatment starts:
The patient will undergo the following tests which would typically be part of the patient's standard of care if receiving treatment for their disease:
•Physical examination (including weight)
•Measurement of blood pressure, heart rate, and temperature
•Blood tests
•Pregnancy test (for female patients of child-bearing potential only)
•Assessment of their disease. How this is done is dependent on the type of disease. This may involve Blood tests (if the patient has HLH/MAS) or scans (if the patient has cancer- routine care for these patients).

During treatment:
Gemtuzumab ozogamicin will be given once every 3 weeks for 3 doses via an infusion into their vein (a needle in the arm or via a central line). Each infusion will be given in this hospital and take two hours. Around 1 hour before treatment with gemtuzumab ozogamicin, pre-medication drugs will be given in order to reduce the chance of having a reaction. These drugs will include a steroid, an antihistamine and paracetamol.
During each treatment the participant will have their blood pressure, heart rate and temperature measured whilst gemtuzumab ozogamicin is being administered.

Before each treatment (i.e. once a week) the patient will be assessed by the doctor or nurse to see how they have been. They will be physically examined including measuring weight (and height at the first visit). Blood tests performed to ensure it is safe to deliver the treatment and to monitor disease.

An assessment of disease will be performed during treatment: blood tests for HLH/MAS patients will be performed weekly. Scans will only be performed in cancer patients if part of routine care.

In addition, we would like to take extra blood samples. This involves providing between 3 - 7 teaspoons of blood (depending on if a child or an adult) before treatment. These samples will be used in laboratory studies to understand if gemtuzumab ozogamicin treatment has reduced the number of CD33 immune cells (primary endpoint) and for exploratory endpoint analysis:
• To assess the change in IL-1/IL-6/TNF-α in the plasma
• To assess the change of CD33+ cells in the bone marrow/ tumour tissue (as available)

On weeks 2 and week 3, gemtuzumab ozogamicin will not be given but there will still be a physical examination, blood tests, and an assessment of disease like in previous weeks. In addition, we would again like to take the 3 - 7 teaspoons extra blood for the primary endpoint analysis and exploratory research. These same assessments will also be done in the 2 weeks after the last dose of gemtuzumab ozogamicin.

If the patient has solid cancer, scans may be performed to monitor the disease. These scans will only be performed if requested as part of standard treatment.

After treatment has completed, assessments will be performed according to the hospital's usual routine practice and no extra samples are required for the trial unless the participant progresses or relapses.

All patients will be followed-up for a minimum of one year after the end of treatment.

Further samples for research: Patients will be asked if they wish to consent to donate excess bone marrow and tumour tissue samples available from procedures done as routine practice either before or during the trial for research purposes. No additional interventions are required.

Previous interventions:
GOTHAM is a Phase II multicentre clinical trial of gemtuzumab ozogamicin. The trial aims to determine whether gemtuzumab ozogamicin elicits a biological response (a change in the number of CD33-positive cells) and whether it works against HLH/MAS and cancer and is safe. There are also other exploratory biological endpoints.
Potential patients and their parents/guardian/legal representative (if applicable) will be approached by a Consultant or delegate working on this study. If the patient and their parent /guardian/legal representative are satisfied with the age-appropriate information given and have had the chance to discuss the study with both the research team and their family and friends, they will be asked to sign a consent form if they wish to participate.

Before treatment starts:
The patient will undergo the following tests which would typically be part of the patient's standard of care if receiving treatment for their disease:
•Physical examination (including weight)
•Measurement of blood pressure, heart rate, and temperature
•Blood tests
•Pregnancy test (for female patients of child-bearing potential only)

•Assessment of their disease. How this is done is dependent on the type of disease. This may involve Blood tests (if the patient has HLH/MAS) or scans (if the patient has cancer- routine care for these patients).

During treatment:
Gemtuzumab ozogamicin will be given once a week for 3 weeks via an infusion into their vein (a needle in the arm or via a central line). Each infusion will be given in this hospital and take two hours. Around 1 hour before treatment with gemtuzumab ozogamicin, pre-medication drugs will be given in order to reduce the chance of having a reaction. These drugs will include a steroid, an antihistamine and paracetamol.
During each treatment the participant will have their blood pressure, heart rate and temperature measured whilst gemtuzumab ozogamicin is being administered.

Before each treatment (i.e. once a week) the patient will be assessed by the doctor or nurse to see how they have been. They will be physically examined including measuring weight (and height at the first visit). Blood tests performed to ensure it is safe to deliver the treatment and to monitor disease.

An assessment of disease will be performed during treatment: blood tests for HLH/MAS patients will be performed weekly. Scans will only be performed in cancer patients if part of routine care.

In addition, we would like to take extra blood samples. This involves providing between 3 - 7 teaspoons of blood (depending on if a child or an adult) before treatment. These samples will be used in laboratory studies to understand if gemtuzumab ozogamicin treatment has reduced the number of CD33 immune cells (primary endpoint) and for exploratory endpoint analysis:
• To assess the change in IL-1/IL-6/ TNF-α in the plasma
• To assess the change of CD33+ cells in the bone marrow/ tumour tissue (as available)

On weeks 4 and week 5, gemtuzumab ozogamicin will not be given but there will still be a physical examination, blood tests, and an assessment of disease like in previous weeks. In addition, we would again like to take the 3 - 7 teaspoons extra blood for the primary endpoint analysis and exploratory research.

If the patient has solid cancer, scans may be performed to monitor the disease. These scans will only be performed if requested as part of standard treatment.

After 5 weeks assessments will be performed according to the hospital's usual routine practice and no extra samples are required for the trial unless the participant progresses or relapses.

All patients will be followed-up for a minimum of one year after the end of treatment.

Further samples for research: Patients will be asked if they wish to consent to donate excess bone marrow and tumour tissue samples available from procedures done as routine practice either before or during the trial for research purposes. No additional interventions are required.

Intervention Type
Drug

Phase
Phase II

Drug/device/biological/vaccine name(s)

Gemtuzumab ozogamicin

Primary outcome measure
Current primary outcome measure as of 16/03/2023:
CD33+ cell count in the blood samples of patients collected on day 1, day 8, day 15, day 22, 43, 50 and 57

Previous primary outcome measure:
CD33+ cell count in the blood samples of patients collected on day 1, day 8, day 15, day 22 and day 29

Secondary outcome measures
Measured using patient records up to 1 year after the end of treatment:
1. Overall Survival time - defined as the time from the date of entry into the trial to the date of death
2. Progression-free survival (PFS) time (Group 2 only) - defined as the time from the date of entry into the trial to the date of disease progression
3. Grade 3 and 4 adverse events

Overall study start date
01/02/2020

Completion date
01/03/2025

Eligibility

Key inclusion criteria
1. Aged >1 year old at the time of trial entry
2. Diagnosis of primary or secondary HLH or MAS disease that is relapsing/refractory to treatment at time of enrolment (Group 1)
OR
3. Histologically confirmed diagnosis of solid cancer with radiological or clinical evidence of disease progression (during or after completion of at least one previous treatment) or any subsequent recurrence (biopsy at relapse is not mandated) (Group 2)
Note: patients who meet the inclusion criteria for both groups 1 and 2 should be entered into group 1
3.1.Group 2 only – must have adequate liver function:
3.1.1. Total bilirubin ≤x2 upper limit of normal (ULN)
3.1.2. Aspartate aminotransferase (AST) and/or alanine aminotransferase (ALT) ≤2.5 x ULN
4. Documented negative pregnancy test for female patients of childbearing potential within 7 days prior to trial entry
5. Sexually active patients must agree to use 2 methods of adequate and appropriate contraception while on trial drug and for 4 months (male) and 7 months (female) following treatment discontinuation
6. Written informed consent given by patient and/or parents/legal guardian

Participant type(s)
Patient

Age group

Mixed

Lower age limit
1 Years

Sex
Both

Target number of participants
Planned Sample Size: 20; UK Sample Size: 20

Total final enrolment
7

Key exclusion criteria
1. Evidence of sinusoidal obstruction syndrome (SOS)/veno-occlusive disease (VOD)
2. Previous treatment with another CD33 targeting antibody or immunotoxin
3. Hypersensitivity to gemtuzumab ozogamicin or to any of the excipients
4. Pregnant or lactating female

Date of first enrolment
30/06/2021

Date of final enrolment
31/12/2023

Locations

Countries of recruitment
England

United Kingdom

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

Study participating centre
Queen Elizabeth Hospital
University Hospitals Birmingham NHS Foundation Trust
Mindelsohn Way
Edgbaston

Birmingham
United Kingdom
B15 2GW

Sponsor information

Organisation
University of Birmingham

Sponsor details
Room 117
Aston Webb Building
Edgbaston
Birmingham
England
United Kingdom
B15 2TT
+44 (0)121 415 8011
researchgovernance@contacts.bham.ac.uk

Sponsor type
University/education

Website
http://www.birmingham.ac.uk/index.aspx

ROR
https://ror.org/03angcq70

Funder(s)

Funder type
Charity

Funder Name
Children's Cancer and Leukaemia Group

Alternative Name(s)
Children's Cancer & Leukaemia Group, UK Children's Cancer and Leukaemia Group, THE CHILDREN'S CANCER AND LEUKAEMIA GROUP, CCLG

Funding Body Type
Government organisation

Funding Body Subtype
Trusts, charities, foundations (both public and private)

Location
United Kingdom

Funder Name
Eveson Charitable Trust

Results and Publications

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

Intention to publish date
01/03/2026

Individual participant data (IPD) sharing plan
The current data sharing plans for this study are unknown and will be 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
Basic results	version 1.0	30/05/2025	30/05/2025	No	No