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A Phase I/II study evaluating the safety and activity of pegylated recombinant human arginase (BCT-100) in relapsed/refractory cancers of children and young adults

Submission date
12/03/2018

Recruitment status
No longer recruiting

Registration date
27/03/2018

Overall study status
Completed

Last Edited
18/11/2025

Condition category
Cancer

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

Plain English summary of protocol

Background and study aims
The aim of this study is to assess the safety and activity of pegylated recombinant human arginase (BCT-100) in children and young people with relapsed/refractory leukaemia, neuroblastoma, sarcoma and high-grade gliomas (brain cancers). Currently the outcomes for these patients are poor and the treatment options are limited with significant side effects. Therefore new treatments which work in different ways to standard chemotherapy are urgently needed. Research has shown that arginine (a nutrient) is important in the survival of cancer cells. BCT-100 is a drug which can reduce arginine levels and starve cancer cells – a completely new approach. BCT-100 has been tested in adults and has been shown to be active with almost no side effects. This study will test whether this dose of BCT-100 is also safe and active in children and young adults with relapsed/refractory leukaemia, neuroblastoma, sarcoma and high-grade glioma. The study will also look at how BCT-100 is broken down in the body and look for new markers of treatment response.

Who can participate?
Children and young adults (aged 1 to 25) with relapsed cancers (leukaemia, neuroblastoma, sarcoma and high-grade gliomas)

What does the study involve?
BCT-100 is given as weekly intravenous infusions (into a vein) over one hour in an outpatient setting. The dose is given at 7-day intervals (+/- 1 day). The dose is increased or decreased based on both safety (side effects) and the successful depletion of arginine in the participants. BCT-100 should at first be given for 8 weeks, i.e. 8 doses, but participants may receive treatment beyond 8 weeks if there is an ongoing clinical benefit.

What are the possible benefits and risks of participating?
This study aims to find the dose which balances high effectiveness with few side effects, and this will then be tested in a larger group. This study will test this drug on four different disease types

for relapsed/refractory patients. The options for these patients can be limited and often are associated with a large burden of side effects. BCT-100 has been found to be very well tolerated with few side effects. However, this is the first study involving children.

Where is the study run from?
Hospitals in the UK, Italy, Germany, Netherlands, Spain, Ireland, Denmark and Australia

When is the study starting and how long is it expected to run for?
January 2017 to October 2021

Who is funding the study?
1. Cancer Research UK
2. Imagine For Margo - Children without Cancer

Who is the main contact?
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Contact information

Type(s)
Scientific

Contact name
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Additional identifiers

Clinical Trials Information System (CTIS)
2017-002762-44

ClinicalTrials.gov (NCT)
NCT03455140

Protocol serial number
37340

Study information

Scientific Title
A Phase I/II study evaluating the safety and activity of Pegylated recombinant human Arginase (BCT-100) in Relapsed/refractory cancers of Children and young adults

Acronym
PARC

Study objectives
PARC is an international phase I/II trial evaluating the safety and activity of pegylated recombinant human arginase (BCT-100) in children and young people with relapsed/refractory leukaemia, neuroblastoma, sarcoma and high grade gliomas (brain cancers). Currently the outcomes for these patients are poor and the therapeutic options are limited with a significant toxicity burden. Therefore new treatments which work in different ways to standard chemotherapy are urgently needed. Research has shown that arginine (a nutrient) is important in the survival of cancer cells. BCT-100 is a drug which can deplete arginine levels and starve cancer cells – a completely new approach. BCT-100 has been tested in adults and shown to be active with almost no side-effects. This trial will test whether this dose of BCT-100 is also safe and active in children and young adults with relapsed/refractory leukaemia, neuroblastoma, sarcoma and high grade glioma. The trial will also study how BCT-100 is broken down in the body and look for new biological markers of treatment response. Up to 64 children and young adults with relapsed cancers will be recruited over 2 years.

Ethics approval required
Old ethics approval format

Ethics approval(s)
Leicester South Research Ethics Committee, 05/03/2018, ref: 18/EM/0024

Study design
Non-randomized; Interventional; Design type: Treatment, Drug

Primary study design
Interventional

Study type(s)
Treatment

Health condition(s) or problem(s) studied
Relapsed/refractory cancers of children and young adults

Interventions
There is no randomisation for this single-arm trial. BCT-100 is administered as weekly intravenous infusions over one hour which may be administered in an outpatient setting. The dose must be administered at 7-day intervals (+/- 1 day).

For phase I the starting dose will be 1600 U/kg and dose escalation/de-escalation is based on both the safety profile (occurrence of DLT) and the successful depletion of arginine in patients. This will establish the phase II recommended dose. BCT-100 should initially be given for 8 weeks, i.e. 8 doses but may receive treatment beyond 8 weeks if there is ongoing clinical benefit. Total trial duration is two years and follow up is minimum one year.

Intervention Type
Drug

Phase
Phase I/II

Drug/device/biological/vaccine name(s)
Pegylated recombinant human arginase (BCT-100)

Primary outcome(s)
Phase I: the safe and optimal (in terms of arginine depletion) RP2D of BCT-100 as determined by:
1. Safety profile as measured by the occurrence/non-occurrence of DLT within 28 days of treatment with BCT-100
2. Optimal dose as measured by the complete depletion of arginine. This is defined as AAD <8μM arginine in the blood after 3 doses of BCT-100

Phase II: disease response (Complete Response (CR) or Partial Response (PR)) after 8 weeks of treatment with BCT-100 as defined by:
Group 1 (Leukaemia): CR, Complete response with incomplete count recovery (CRi), Complete response without platelet recovery (CRp; Acute Lymphoblastic Leukaemia (ALL) only), or PR determined by bone marrow, peripheral blood count/blasts and extramedullary disease (AML criteria based on Cheson et al 2003)
Group 2 (Neuroblastoma): CR/PR determined by cross-sectional imaging by CT or MRI, MIBG scan and bone marrow evaluation using the International Neuroblastoma Response Criteria (INRC)
Group 3 (Sarcoma): CR/PR determined by cross-sectional imaging by CT or MRI using RECIST version 1.1
Group 4 (High grade glioma): CR/PR determined by cross-sectional imaging by MRI using RANO criteria

Key secondary outcome(s))
Current secondary outcome measures as of 02/02/2023:
1. Incidence and severity of Adverse Events (AEs) defined by National Cancer Institute Common Terminology Criteria for Adverse Events (CTCAE) v4 as measured from the date of commencement of protocol-defined treatment until 28 days after the administration of the last dose of trial treatment
2. Disease response (CR / PR) at any time during treatment with BCT-100:
Group 1 (Leukaemia): CR, Complete response with incomplete count recovery (CRi), Complete response without platelet recovery (CRp; Acute Lymphoblastic Leukaemia (ALL) only), or PR determined by bone marrow, peripheral blood count/blasts and extramedullary disease (AML criteria based on Cheson et al 2003)
Group 2 (Neuroblastoma): CR/PR determined by cross-sectional imaging by CT or MRI, MIBG scan and bone marrow evaluation using the International Neuroblastoma Response Criteria (INRC)
Group 3 (Sarcoma): CR/PR determined by cross-sectional imaging by CT or MRI using RECIST version 1.1
Group 4 (High-grade glioma): CR/PR determined by cross-sectional imaging by MRI using RANO criteria
3. Progression-free survival, measured using follow-up data (patients followed up for at least 1 year)
4. Overall survival, measured using follow-up data (patients followed up for at least 1 year)

5. Pharmacokinetic (PK) profile of BCT-100 concentration in blood, bone marrow, and cerebrospinal fluid (CSF) samples prior to doses 1, 5, 9, 17 & 25
6. Arginine concentrations in blood, bone marrow, and CSF samples prior to doses 1, 5, 9, 17 & 25

Previous secondary outcome measures:
1. Incidence and severity of Adverse Events (AEs) defined by National Cancer Institute Common Terminology Criteria for Adverse Events (CTCAE) v4 as measured from the date of commencement of protocol-defined treatment until 28 days after the administration of the last dose of trial treatment
2. Disease response (CR / PR) at any time during treatment with BCT-100:
Group 1 (Leukaemia): CR, Complete response with incomplete count recovery (CRi), Complete response without platelet recovery (CRp; Acute Lymphoblastic Leukaemia (ALL) only), or PR determined by bone marrow, peripheral blood count/blasts and extramedullary disease (AML criteria based on Cheson et al 2003)
Group 2 (Neuroblastoma): CR/PR determined by cross-sectional imaging by CT or MRI, MIBG scan and bone marrow evaluation using the International Neuroblastoma Response Criteria (INRC)
Group 3 (Sarcoma): CR/PR determined by cross-sectional imaging by CT or MRI using RECIST version 1.1
Group 4 (High-grade glioma): CR/PR determined by cross-sectional imaging by MRI using RANO criteria
3. Progression-free survival, measured using follow-up data (patients followed up for at least 1 year)
4. Overall survival, measured using follow-up data (patients followed up for at least 1 year)
5. Pharmacokinetic (PK) profile of BCT-100 concentration in blood, bone marrow, and cerebrospinal fluid (CSF) samples prior to doses 1, 4, 8, 16 and 24
6. Arginine concentrations in blood, bone marrow, and CSF samples prior to doses 1, 4, 8, 16 and 24

Completion date
16/10/2022

Eligibility

Key inclusion criteria
1. Aged 1- <25 years old at the time of study registration
2. Histologically confirmed disease in one of the following four groups:
2.1. Group 1 - Acute lymphoblastic leukaemia (ALL) and acute myeloid leukaemia (AML)
2.2. Group 2 - Neuroblastoma
2.3. Group 3 - Sarcoma
2.4. Group 4 - High grade glioma (as defined by 2016 WHO CNS classification)
3. Radiological or laboratory evidence of disease progression (during or after completion of first line treatment) or any subsequent recurrence (biopsy at relapse is not mandated)
4. Measurable bone marrow disease (group 1) or at least one evaluable radiological site of disease (group 2, 3 and 4)
5. Adequate liver function defined as a total bilirubin ≤1.5x the upper limit of normal for age and ALT ≤ 3x the upper limit of normal for age
6. Documented negative pregnancy test for female patients of childbearing potential within 7 days of trial entry
7. Sexually active patients must agree to use adequate and appropriate contraception while on study drug and for 12 months following treatment discontinuation
8. Written informed consent given by patient and/or parents/legal representative

Participant type(s)
Patient

Healthy volunteers allowed
No

Age group
Mixed

Lower age limit
1 years

Upper age limit
24 years

Sex
All

Total final enrolment
49

Key exclusion criteria
1. Previous treatment with another therapeutic arginine-depleting drug (bacterial or human) or arginase inhibitor
2. Presence of any >= CTCAE grade 3 clinically significant treatment-related toxicity from prior therapies
3. Pregnant or lactating female
4. Evidence of uncontrolled infection

Date of first enrolment
16/04/2018

Date of final enrolment
01/12/2021

Locations

Countries of recruitment
United Kingdom

England

Scotland

Australia

Denmark

Germany

Ireland

Italy

Netherlands

Spain

Study participating centre
Birmingham Children’s Hospital
Steelhouse Lane
Birmingham
England
B4 6NH

Study participating centre
Addenbrooke’s Hospital
Hills Road
Cambridge
England
CB2 0QQ

Study participating centre
Royal Manchester Children's Hospital
Oxford Road
Manchester
England
M13 9WL

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

Study participating centre
Bristol Royal Hospital for Children
24 Upper Maudlin St

Bristol
England
BS2 8BJ

Study participating centre
Leeds General Infirmary
Great George St
Leeds
England
LS1 3EX

Study participating centre
Royal Hospital for Sick Children (Glasgow)
1345 Govan Road
Glasgow
Scotland
G51 4TF

Study participating centre
Our Lady’s Children’s Hospital
Cooley Road
Crumlin
Drimnagh
Dublin
Ireland
D12 V004

Study participating centre
Royal Children's Hospital, Melbourne
50 Flemington Road
Parkville
Victoria
Australia
3052

Study participating centre
Sydney Children's Hospital
High St
Randwick

Sydney
Australia
NSW 2031

Study participating centre
The Children's Hospital at Westmead
Cnr Hawkesbury Road and Hainsworth Street
Westmead
Sydney
Australia
NSW 2145

Study participating centre
Women's and Children's Hospital
72 King William Rd
North Adelaide
Australia
SA 5006

Study participating centre
Princess Margaret Hospital
Roberts Rd
Subiaco
Perth
Australia
WA 6008

Study participating centre
Princess Maxima Center for pediatric oncology
Heidelberglaan 25
Utrecht
Netherlands
3584 CS

Sponsor information

Organisation
University of Birmingham

ROR
https://ror.org/03angcq70

Funder(s)

Funder type
Charity

Funder Name
Cancer Research UK; Grant Codes: C47669/A24836

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
Imagine For Margo - Children without Cancer; Grant Codes: ITCC-062

Results and Publications

Individual participant data (IPD) sharing plan
The datasets generated during and/or analysed during the current study are/will be available upon request from the Cancer Research UK Clinical Trials Unit (CRCTU) at the University of Birmingham. The (CRCTU) is committed to responsible and controlled sharing of anonymised clinical trial data with the wider research community to maximise potential patient benefit while protecting the privacy and confidentiality of study participants. Participant data and the associated supporting documentation (metadata) will typically be available for all CRCTU clinical trials within 6 months after the publication of the outcome measures unless the trial results are to be used as part of a regulatory submission where release of the data may be delayed or be subject to the approval of a third party. Requests for historical clinical trial data will be dealt with on a case-by-case basis. For trials with long term follow-up, primary outcome data (e.g. response) may be available before secondary outcome data (e.g. survival). Each request will be reviewed independently by the CRCTU Directors in discussion with the Chief Investigator and relevant Trial Management Group and/or independent Trial Steering Committee (as applicable to the trial). In making their decision the Director’s Committee will consider the scientific validity

of the request, the qualifications of the research group, the views of the Chief Investigator and trial management and/or steering committees, consent arrangements, the practicality of anonymising the requested data and contractual obligations. Where the CRCTU Directors and appropriate Trial Committees are supportive of the request, and where not already obtained, consent for data transfer will be sought from the Sponsor of the trial before notifying the applicant of the outcome of their request. It is anticipated that applicants will be notified of a decision within 3 months.

IPD sharing plan summary

Available on request

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Results article		31/01/2024	15/02/2024	Yes	No
Basic results	version 1.0b	23/02/2023	27/02/2023	No	No
HRA research summary			26/07/2023	No	No
Participant information sheet	Participant information sheet	11/11/2025	11/11/2025	No	Yes