

# 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

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Primary:\* Phase I: to establish the recommended phase II dose (RP2D) of BCT-100 in children and young adults as assessed by dose limiting toxicity (DLT) and complete arginine depletion.\* Phase II: to determine the activity of single agent BCT-100...

<b>Ethical review</b>	Approved WMO
<b>Status</b>	Recruitment stopped
<b>Health condition type</b>	Other condition
<b>Study type</b>	Interventional

## Summary

### ID

NL-OMON49172

### Source

ToetsingOnline

### Brief title

PARC

### Condition

- Other condition
- Miscellaneous and site unspecified neoplasms malignant and unspecified

### Synonym

relapsed or refractory cancer

### Health condition

onbehandelbare en/of terugkerende vorm van kanker: leukemie, hooggradig glioom,

neuroblastoma, sarcoma

## **Research involving**

Human

## **Sponsors and support**

**Primary sponsor:** Cancer Research UK Clinical Trials Unit

**Source(s) of monetary or material Support:** Cancer Research UK Clinical Trials Unit

## **Intervention**

**Keyword:** BCT-100, Cancer, Children, Phase I/II

## **Outcome measures**

### **Primary outcome**

Phase I: the safe and optimal (in terms of arginine depletion) RP2D of BCT-100

as determined by:

- o Safety profile as measured by the occurrence/non-occurrence of DLT within 28 days of treatment with BCT-100. DLTs are defined in section 3.1.2.

- o Optimal dose as measured by the complete depletion of arginine. This is defined as AAD  $<8\mu\text{M}$  arginine in the blood after 4 doses of BCT-100.

### **Secondary outcome**

Phase II: disease response (Complete Response (CR) or Partial Response (PR))

after 8 weeks of treatment with BCT-100 as defined by:

- o Group 1 (Leukaemia): CR, Complete response with incomplete count recovery

(CRi), Complete response without platelet recovery (CRp; ALL only), or PR

determined by bone marrow, peripheral blood count/blasts and extramedullary disease. (see Appendix 4 for details; AML criteria based on Cheson et al 2003)

- o 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) (Appendix 7).

o Group 3 (Sarcoma): CR/PR determined by cross-sectional imaging by CT or MRI using RECIST version 1.1 (Appendix 5).

o Group 4 (High grade glioma): CR/PR determined by cross-sectional imaging by MRI using RANO criteria (Appendix 6).

## Study description

### Background summary

Arginine is a semi-essential amino acid required for protein synthesis, cell division and a number of intracellular pathways that maintain cell survival. Both solid and haematological cancer cells are dependent on extracellular arginine for survival (arginine auxotrophism) due to the loss of ASS or OTC recycling enzyme expression; making them vulnerable to therapeutic arginine depletion. The most clinically relevant approach to targeting tumour arginine metabolism is through therapeutic arginine depletion with a recombinant enzyme. BCT-100 (BioCancer Treatment International) is a pegylated recombinant human arginase in which a 5000 MW polyethylene glycol moiety has been covalently attached to native human arginase to significantly increase the plasma half-life and sustain arginine depletion.

### Study objective

Primary:

- \* Phase I: to establish the recommended phase II dose (RP2D) of BCT-100 in children and young adults as assessed by dose limiting toxicity (DLT) and complete arginine depletion.
- \* Phase II: to determine the activity of single agent BCT-100 against relapsed/refractory leukaemia, neuroblastoma, sarcoma and high grade glioma in children and young adults as measured by disease response after 8 weeks.

Secondary:

- \* To assess the safety of BCT-100.
- \* To assess disease response at any time during treatment with BCT-100
- \* To assess progression free survival (PFS) and overall survival (OS).
- \* To determine the pharmacokinetics of BCT-100 in the paediatric population.
- \* To assess the duration and magnitude of arginine depletion.

## **Study design**

Phase I aims to determine a safe and optimal (in terms of arginine depletion) dose of BCT-100 using a modified 3+3 design in all patients who meet the eligibility criteria irrespective of disease group.

Phase II will be an expansion study to further evaluate the clinical activity of BCT-100 in 4 diseasespecific paediatric populations. Approximately 6 to 18 subjects are estimated for Part 1, and 52

subjects are planned for Part 2 (13 evaluable subjects in each of 4 groups; evaluable for the purpose of clinical activity analysis is defined as a subject with a pre-dose and at least 1 post-dose disease assessment).

## **Intervention**

BCT-100 should initially be given for 8 weeks, i.e. 8 doses. If approved by the Chief Investigator, patients may receive treatment beyond 8 weeks until disease progression or unacceptable toxicity

BCT-100 should be given on a weekly basis: 100 mL intravenously for 1 hour Dose is dependant on phase of the stage as well as weight of child.

## **Study burden and risks**

As this is the first time BCT-100 will be used in children and young people the side-effects and severity of treatment are unknown. However, when used to treat adults with liver cancer no significant toxicities were identified. The following side effects were observed:

- Diarrhoea
- Abnormalities in liver function
- Shortness of breath
- Abdominal pain

Treating physician will keep a close eye on patient during treatment and all side effects will be recorded and managed accordingly.

Radiation risk

patient may require a CT or MIBG scan as part of the disease assessment. These

scans use ionising radiation. This is thought to be associated with a very small increased risk of developing a second cancer in the future.

#### Contraception and pregnancy

We don't know whether BCT-100 will cause significant harm to an unborn child. Therefore pregnancy must not occur during treatment or within 1 year of completing treatment.

MIBG scan is repeated at week 8 , 16 24 and at the end of the study for neuroblastoma patients, in case screening scan was found positive, This is also the case for bonemarrow sample. In case positive at screening for cancer cells, bone marrow samples will be repeated and considered additional / extra research.

Additional blood and bonemarrowsamples are combined as much as possible with standard samplings.

- At screening a second nbobemarrow sample is collected. This second sample is considered extra/additional research.
- Additional /extra bloodsamples are collected for disease analyses and pharmacodynamics/kinetics : at screening , week 1, 5 9 17 and 25, and at end of study.

Additional:

Preganancy tests for females of childbearing potential.

## Contacts

### Public

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### Scientific

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## Trial sites

## Listed location countries

Netherlands

## Eligibility criteria

### Age

Adolescents (12-15 years)

Adolescents (16-17 years)

Adults (18-64 years)

Children (2-11 years)

Elderly (65 years and older)

## Inclusion criteria

### Inclusion Criteria

- \* Aged 1- <25 years old at the time of study registration
- \* Histologically confirmed disease in one of the following four groups:
  - o Group 1 - Acute lymphoblastic leukaemia (ALL) and acute myeloid leukaemia (AML)
  - o Group 2 - Neuroblastoma
  - o Group 3 - Sarcoma
  - o Group 4 - High grade glioma (as defined by 2016 WHO CNS classification)
- \* 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).
- \* Measurable bone marrow disease (group 1) or at least one evaluable radiological site of disease (group 2, 3 and 4).
- \* Adequate liver function defined as a total bilirubin  $\leq 1.5 \times$  the upper limit of normal for age and ALT  $\leq 3 \times$  the upper limit of normal for age
- \* Documented negative pregnancy test for female patients of childbearing potential within 7 days of trial entry
- \* Sexually active patients must agree to use adequate and appropriate contraception while on study drug and for 12 months following treatment discontinuation (see section 5.3 for details)
- \* Written informed consent given by patient and/or parents/legal representative\*

## Exclusion criteria

Previous treatment with another therapeutic arginine depleting drug (bacterial or human) or arginase inhibitor

- \* Presence of any  $\geq$  CTCAE grade 3 clinically significant treatment-related

toxicity from prior therapies  
\* Pregnant or lactating female  
\* Evidence of uncontrolled infection

## Study design

### Design

Study phase:	2
Study type:	Interventional
Masking:	Open (masking not used)
Control:	Uncontrolled
Primary purpose:	Treatment

### Recruitment

NL	
Recruitment status:	Recruitment stopped
Start date (anticipated):	12-06-2020
Enrollment:	4
Type:	Actual

### Medical products/devices used

Product type:	Medicine
Brand name:	BCT-100
Generic name:	BCT-100

## Ethics review

Approved WMO	
Date:	04-02-2020
Application type:	First submission
Review commission:	METC NedMec
Approved WMO	
Date:	19-03-2020

Application type:	First submission
Review commission:	METC NedMec
Approved WMO Date:	13-05-2020
Application type:	Amendment
Review commission:	METC NedMec
Approved WMO Date:	02-07-2020
Application type:	Amendment
Review commission:	METC NedMec
Approved WMO Date:	22-10-2020
Application type:	Amendment
Review commission:	METC NedMec
Approved WMO Date:	26-10-2020
Application type:	Amendment
Review commission:	METC NedMec
Approved WMO Date:	25-06-2021
Application type:	Amendment
Review commission:	METC NedMec
Approved WMO Date:	07-07-2021
Application type:	Amendment
Review commission:	METC NedMec

## Study registrations

### Followed up by the following (possibly more current) registration

No registrations found.



## Other (possibly less up-to-date) registrations in this register

No registrations found.

## In other registers

Register	ID
EudraCT	EUCTR2017-002762-44-NL
ClinicalTrials.gov	NCT03455140
CCMO	NL71544.041.19

## Study results

Date completed: 18-01-2022

Actual enrolment: 4

### Summary results

Trial is ongoing in other countries