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

Published: 04-02-2020
Last updated: 10-04-2024

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

Ethical review	Approved WMO
Status	Recruitment stopped
Health condition type	Other condition
Study type	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, hoogradig glioom,

neuroblastoom, sarcoom

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:

oSafety profile as measured by the occurrence/non-occurrence of DLT within 28

daysof treatment with BCT-100. DLTs are defined in section 3.1.2.

oOptimal dose as measured by the complete depletion of arginine. This is

defined asAAD <8µM 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 oftreatment with BCT-100 as defined by:

oGroup 1 (Leukaemia): CR, Complete response with incomplete count recovery

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

determined bybone marrow, peripheral blood count/blasts and extramedullary

disease.(seeAppendix 4 for details; AML criteria based on Cheson et al 2003)

oGroup 2 (Neuroblastoma): CR/PR determined by cross-sectional imaging by CT

orMRI, MIBG scan and bone marrow evaluation using the International

NeuroblastomaResponse Criteria (INRC) (Appendix 7).

oGroup 3 (Sarcoma): CR/PR determined by cross-sectional imaging by CT or

MRIusing RECIST version 1.1 (Appendix 5).

oGroup 4 (High grade glioma): CR/PR determined by cross-sectional imaging by

MRIusing 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. B oth 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 significant 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 depndant 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 bonemarowsamples are combined as much as possible with standard samplings.
- At screening a second nbobemarow 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

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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 <=1.5x the upper limit of normal for age and ALT <= 3x 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 >= 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 onging in other countries