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A study of 177 lutetium dotatate in children with primary refractory or relapsed high-risk neuroblastoma

Submission date	Recruitment status	[_] Prospectively registered
20/12/2013	No longer recruiting	[_] Protocol
Registration date	**Overall study status**	[_] Statistical analysis plan
20/12/2013	Completed	[X] Results
Last Edited	**Condition category**	[_] Individual participant data
12/03/2020	Cancer	

Plain English summary of protocol
http://www.cancerresearchuk.org/cancer-help/trials/a-trial-looking-177-lutetium-dotatate-neuroblastoma-children-young-people-ludo?

Contact information

Type(s)
Scientific

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Additional identifiers

Clinical Trials Information System (CTIS)
2012-000510-10

Protocol serial number
13254

Study information

Scientific Title
A Phase IIa trial of 177 177 lutetium dotatate in children with primary refractory or relapsed high-risk neuroblastoma

Acronym
LuDo

Study objectives
High-risk neuroblastoma is a common childhood cancer. Initial standard chemotherapy treatment produces responses in about two thirds of patients, many of whom will later relapse. The others have primary refractory disease. Overall cure rates are low, and so effective new treatments are needed.

Many neuroblastoma cells express somatostatin receptors. Radiolabelled octreotide analogues can be used for nuclear medicine imaging and therapy of somatostatin receptor positive tumours. 68Ga DOTATATE and 177Lu DOTATATE have been shown to be effective octreotide analogues for imaging and treatment respectively of neuroendocrine cancers in adults.

The primary aims of this study are to evaluate the toxicity and the efficacy of 177Lu DOTATATE in children with relapsed or refractory high-risk neuroblastoma. Secondary, translational, aims are to investigate 68Ga DOTATATE PET/CT for imaging of neuroblastoma, in comparison with the standard of 123I-mIBG, to assess the relationship between the expression of somatostatin receptors measured by immunohistochemistry in archived neuroblastoma tissue from each patient with their imaging, and to correlate tumour radiation dosimetry with response.

This will be a Phase II clinical trial using a Simon Two Stage Minimax design. This requires 14 patients in Stage 1. If three or more responses are seen, another 10 patients will be recruited in Stage 2. If eight or more responses are seen in these 24 patients, then the treatment will be deemed worthy of further investigation in this patient group.

Ethics approval required
Old ethics approval format

Ethics approval(s)
London-Hampstead Ethics Board, First MREC approval date 10/10/2012, ref: 12/LO/1422

Study design
Non-randomised interventional treatment trial

Primary study design
Interventional

Study type(s)
Treatment

Health condition(s) or problem(s) studied
Topic: National Cancer Research Network; Subtopic: Paediatric Oncology; Disease: Brain and Nervous System

Interventions
177Lutetium DOTATATE: The investigational medicinal product (IMP) for the study. Patients will receive up to a maximum of 4 administrations 8 weeks apart.
68Ga DOTATATE PET/CT: Potential patients for this study will require a 68Ga DOTATATE PET/CT to assess eligibility. Uptake in the tumour at least as high as the uptake in the liver must be demonstrated for a patient to be eligible.
Amino acid solution infusion: An amino acid solution is infused over 4 hours concurrently with the radionuclide administration to reduce renal tubular uptake and minimise nephrotoxicity.
SPECT/CT dosimetry: In radionuclide therapy there is an uncertain relationship between the administered activity (in GBq) of the drug and the absorbed dose (in Gray).
Therefore following administration whole body and SPECT/CT dosimetry will be performed to accurately determine the dose received by the whole body, bone marrow, kidneys and the tumour.
Whole blood profile: Weekly bloods will be taken to perform assessment of haematological toxicity

Study Entry : Registration only

Intervention Type
Drug

Phase
Not Applicable

Drug/device/biological/vaccine name(s)
Lutetium dotatate

Primary outcome(s)
Response rate; Timepoint(s): 1 month

Key secondary outcome(s))
1. Overall survival; Timepoint(s): Follow up for 5 years
2. Progression-free survival; Timepoint(s): Follow up for 5 years
3. Toxic effects

Completion date
01/04/2015

Eligibility

Key inclusion criteria
1. Histologically confirmed diagnosis of neuroblastoma
2. Relapsed or primary refractory high-risk neuroblastoma (International Neuroblastoma Staging System stage 4 or International Neuroblastoma Risk Group staging System M)
3. Age >18 months and <18 years of age at the time of enrolment into the study
4. Life expectancy of greater than 3 months
5. Performance Status:
5.1. Karnofsky 50% or more (for patients >12 years of age)
5.2. Lansky 50% or more (for patients <12 years of age)
5.3. Adequate recovery from major surgery prior to receiving study treatment

5.4. Uptake in primary tumour or metastatic tumour deposits on 68Gallium DOTATATE PET/CT at least as high as the liver uptake and performed within a month prior to trial
5.5. IMIBG and FDG PET/CT within a month prior to trial entry
5.6. Two-week washout from any prior treatment
5.7. Patients must have recovery of hematological toxicity following previous therapy
6. Laboratory requirements within 7 days of commencement of therapy
6.1. Absolute neutrophil count > 1.0 x 10^9/L
6.2. Absolute platelets > 100 x 10^9/L
7. Biochemistry:
7.1. Bilirubin within normal range
7.2. ALT within 2.5 x ULN
7.3. ALP within 5 x ULN
7.4. Glomerular filtration rate >50 mL/min/1.73m2
8. Before patient registration, written informed consent
9. Parents or other appropriate adult to sign the local Comforters and Carers consent before patient registration
10. Agreed to a follow-up of 5 years.

Participant type(s)
Patient

Healthy volunteers allowed
No

Age group
Child

Lower age limit
18 months

Upper age limit
18 years

Sex
All

Total final enrolment
21

Key exclusion criteria
1. Not fit enough to undergo proposed study treatment
2. Concurrent treatment with any antitumour agents
3. Prior treatment with other radiolabelled somatostatin analogues
4. Any psychological, familial, sociological or geographical condition potentially hampering compliance with the study protocol and follow-up schedule; those conditions should be discussed with the patient or legal guardian before registration in the trial

Date of first enrolment
19/03/2013

Date of final enrolment

01/04/2015

Locations

Countries of recruitment
United Kingdom

England

Study participating centre
Cancer Research UK Clinical Trials Unit
Birmingham
United Kingdom
B15 2TT

Sponsor information

Organisation
University of Birmingham (UK)

ROR
https://ror.org/03angcq70

Funder(s)

Funder type
Charity

Funder Name
Cancer Research UK (UK) Grant Codes: C17807/A14091

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

Results and Publications

Individual participant data (IPD) sharing plan

IPD sharing plan summary

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Results article	results	01/09/2020	12/03/2020	Yes	No
Basic results			21/06/2019	No	No
HRA research summary			28/06/2023	No	No
Participant information sheet	Participant information sheet	11/11/2025	11/11/2025	No	Yes