ISRCTN64894508 https://doi.org/10.1186/ISRCTN64894508

Radiotherapy (miBG) in neuroblastoma combined with chemotherapy (talazoparib)

Submission date
02/07/2025

Recruitment status
Recruiting

Registration date
30/10/2025

Overall study status
Ongoing

Last Edited
30/10/2025

Condition category
Cancer

[ ] Prospectively registered
[ ] Protocol
[ ] Statistical analysis plan
[ ] Results
[ ] Individual participant data
[X] Record updated in last year

Plain English summary of protocol

Background and study aims
The MINT study is a clinical trial for children/young adults with neuroblastoma which has not responded to initial treatment (relapsed/refractory). Neuroblastoma is the most common solid tumour occurring outside the brain in childhood. Neuroblastoma remains a significant cause of cancer-related death in children. More than 2250 cases per year are diagnosed in North America, Canada and Europe. Overall survival is below 50% and there is a need to develop new treatment strategies.
131I-MIBG therapy, a form of targeted radiotherapy, is a well-established and effective treatment for neuroblastoma. However, response rates vary and it is unclear which patients are most likely to benefit. A class of targeted drugs (called PARP inhibitors) have been shown to act as a radio-sensitiser (make the cancer cells more sensitive to radiation) in laboratory studies. Adding a PARP inhibitor to 131I-MIBG therapy may be an effective treatment for relapsed or refractory neuroblastoma. It may also be effective in treating neuroblastoma with specific mutations in certain genes. These gene mutations make it harder for neuroblastoma cells to repair DNA after being damaged.

Who can participate?
Patients aged over 1 year with neuroblastoma

What does the study involve?
Participants will be treated with a drug called talazoparib (a PARP inhibitor) in combination with 131I-MIBG therapy. The participants will be split into two groups, depending on whether they have specific gene mutations. The study will look at whether these mutations could indicate how well the talazoparib increases the effect of the 131I-MIBG therapy. The study will also determine the recommended dose of talazoparib by monitoring side effects. All participants will receive one course of talazoparib with 131I-MIBG and a stem cell rescue infusion. Participants will be followed up for at least 2 years after the treatment to understand disease response and side effects.

What are the possible benefits and risks of participating?
The treatment you receive in this trial may help treat the neuroblastoma. We cannot promise to what extent the trial will help you but the information we get from this trial will help improve

the treatment of people with neuroblastoma in the future.
As the effectiveness of the treatment regimens have not been established in a paediatric population, the patient group includes patients for whom no treatment of greater curative potential is available and the alternative management, including best supportive care/palliation will be explained to the patient and/or family, to enable an informed decision regarding trial participation.
There is a risk that if a patient (or their partner) becomes pregnant while receiving trial treatment or immediately after, the unborn baby could be affected. For this reason, sites will ensure that all females of childbearing potential undergo a urine pregnancy test before receiving trial medications and at the end of treatment. We will also educate all patients of childbearing potential regarding the need for adequate contraception whilst they are receiving trial drugs and for 6 months afterwards. Should a patient or their partner become pregnant between the time of commencing study treatment and up to 30 days after completion, trial participation will be terminated for safety reasons and the pregnancy outcome will be monitored. If a patient's partner becomes pregnant during this period, we would also like to collect details of the outcome of the pregnancy with their permission.
During the trial, patients will have blood samples taken for trial-related purposes. The risks of having blood taken from a vein include pain, bruising or infection at the site where the blood was taken, and fainting. Where possible blood will be taken from a patient's Hickman line or Portacath rather than directly from a vein; there is still a small risk of infection associated with doing this. Where possible, blood samples taken for research purposes will be taken at the same time as routine blood sampling to minimise distress to patients. Guidance from the Health Research Ethics Committee will be adhered to regarding the maximum volumes of blood collected for research purposes.
By participating in this trial, patients may have more imaging investigations than if they were not enrolled on the study. Radiation may cause cell damage which can, after many years or decades, become cancerous.
In order for some scans to be performed, contrast agents are given through the patient’s central line or cannula. Whilst these contrast agents allow doctors to gain a clear picture of what is happening inside the body, they also carry a small risk themselves. A small number of people have an allergic reaction to them which, while usually mild and easily treatable, can be life-threatening. For this reason, we ask that all patients/parents tell their doctor if they have experienced a previous reaction to contrast agents.
During the informed consent process, participants or their parents (if aged under 16 years) will be given the option of the patient contributing a blood sample for genetic DNA analysis. It is possible in rare cases that the analysis of this sample could uncover findings that may have direct implications on the patient’s clinical care (e.g. a rare genetic abnormality). Participants /parents are fully informed that should they agree to having this sample taken and this situation arises, their study doctor will be informed and will take the necessary steps to refer the patient for the relevant clinical care.
As with all clinical trial studies, the drug treatments may involve risks that are already known, as well as risks that are currently unknown. Patients will be closely monitored for side effects throughout the course of the treatment and during follow-up.

Where is the study run from?
University of Birmingham (UK)

When is the study starting and how long is it expected to run for?
June 2025 to June 2028

Who is funding the study?
Solving Kids' Cancer (USA)

Who is the main contact?
mint@trials.bham.ac.uk

Plain English summary under review with external organisation

Contact information

Type(s)
Scientific

Contact name
Dr Catherine Cochrane

Contact details
Research Strategy and Services Division
Ash House
The University of Birmingham
Edgbaston
Birmingham
United Kingdom
B15 2TT
+44 (0)7814 650003
mint@trials.bham.ac.uk

Type(s)
Principal investigator

Contact name
Dr Sally George

Contact details
123 Old Brompton Road
London
United Kingdom
SW7 3RP
+44 (0)20 34376114
Sally.George@icr.ac.uk

Additional identifiers

Clinical Trials Information System (CTIS)
Nil known

Integrated Research Application System (IRAS)
1010040

ClinicalTrials.gov (NCT)
Nil known

Protocol serial number
RG_24-039

Study information

Scientific Title
A biomarker-enriched Phase I/II clinical trial of 131I-MIBG therapy with talazoparib for the treatment of relapsed and/or refractory neuroblastoma

Acronym
MINT

Study objectives
Primary objectives:
1. To determine the recommended phase II dose (RP2D) of talazoparib when given in combination with 131I-mIBG
2. To determine the safety and tolerability of talazoparib and 131I-mIBG combination therapy

Secondary objectives:
1. To determine the anti-tumour activity of talazoparib and 131I-mIBG in relapsed/refractory neuroblastoma
2. To determine the anti-tumour activity of talazoparib and 131I-mIBG in relapsed/refractory neuroblastoma with genetic alterations predicted to result in PARP inhibitor sensitivity (Group A patients)
3. To determine progression-free and overall survival in patients treated with talazoparib and 131I-mIBG

Ethics approval required
Ethics approval required

Ethics approval(s)
notYetSubmitted, ref: 25/EE/0158

Study design
Open controlled trial

Primary study design
Interventional

Study type(s)
Safety

Health condition(s) or problem(s) studied
Relapsed and refractory high-risk neuroblastoma

Interventions
Participants will be treated with a drug called talazoparib (a PARP inhibitor) in combination with 131I-MIBG therapy. The participants will be split into two groups, depending on whether they have specific gene mutations: Group A molecularly enriched and Group B non-enriched. The treatment is the same for all patients and is detailed below.

Day 1: Talazoparib (capsule) administration with starting dose of 600 mcg/m2, Day 1-6 with BD loading dose on Day 1.
Day 3: 131I-mIBG (IV infusion) administration at a fixed dose of 666 MBq/kg (18 mCi/kg)
Day 17: PBSC rescue

As this is a talazoparib dose-finding trial, there may be an escalation to 600 mcg/m2 D1-14, or a de-escalation to either 450 mcg/m2 D1-6 or 300 mcg/m2 D1-6, depending on any dose-limiting toxicities found. Some patients may be eligible for a second cycle of this treatment based on clinical decision and if they meet the eligibility criteria for a second course.

Participants will be followed up every 3 months for at least 2 years. Follow-up assessments include the following: review of adverse events and concomitant medication, physical examination, haematology and biochemistry blood tests and thyroid function. 131I-MIBG scan every 3 months for the first year and 6 monthly after.

Participant registration will occur online via our eRDC system.

Intervention Type
Drug

Phase
Phase II

Drug/device/biological/vaccine name(s)
Talazoparib, 131I-mIBG (Iobenguane I 131)

Primary outcome(s)
1. Incidence of dose-limiting toxicities (DLTs), where a DLT is defined as any of the following occurring from day 1 of treatment for 8 weeks (until Day 56), which is not attributable to the disease or disease-related processes under investigation and is considered at least possibly related to talazoparib or 131I-mIBG treatment:
Dose-limiting non-haematological toxicity:
Any Grade 3 or 4 non-haematological excluding:
1.1. Grade 3 nausea, vomiting and dehydration
1.2. Grade 3 anorexia or weight loss resulting from anorexia
1.3. Grade 3 fatigue
1.4. Grade 3 liver enzyme elevation that returns to ≤grade 1 or baseline by day 56
1.5. Grade 3 electrolyte abnormality requiring less than 24 hours of inpatient management
1.6. Grade 3 or 4 serum amylase elevation that resolves to ≤grade 2 within 14 days and is not accompanied by lipase elevation or grade ≥3 salivary gland toxicity
1.7. Grade 3 infection
1.8. Grade 3 fever
1.9. Grade 3 febrile neutropenia
Dose-limiting haematological toxicity (in the absence of progressive bone marrow disease):
2.1. Neutrophil (ANC) <0.5 x 10e9/L at or after 28 days following PBSC reinfusion (Day 45)
2.2. Platelet count <20 x 10e9/L at or after 56 days following PBSC reinfusion (Day 73)
2.3. Infusion of additional PBSC for any medical reason after the initial stem cell reinfusion has been given AND prior to engraftment of neutrophils or platelets after that initial PBSC reinfusion.
Measured using a one-stage Bayesian Continual Reassessment Method (CRM) at 8 weeks following one course of treatment.

2. Incidence of adverse events (AEs) and serious adverse events (SAEs) measured from day 1 of trial treatment through to day 84 will be summarised through tabulation and reviewed at 8 weeks, 1 year and 2 years following one course of treatment by the Safety Review and Dose Decision Committee (SRDD).

Key secondary outcome(s))
1. Disease response to treatment, assessed by the NANT Criteria at 8 weeks following the initiation of 1 course of treatment
2. Overall survival, defined as the time from enrolment to death from any cause, will be measured as point estimate of the response rate along with an associated confidence interval for the overall patient population after at least 2 years following 1 course of treatment.
3. Progression-free survival, defined as the time from enrolment to disease progression or relapse

Completion date
30/06/2028

Eligibility

Key inclusion criteria
1. Patients must be >1 year of age at time of registration on study.
2. Patients must have a diagnosis of neuroblastoma either by histological verification of neuroblastoma and/or demonstration of tumour cells in the bone marrow with increased urinary catecholamines.
3. Patients must have high-risk neuroblastoma according to COG risk classification 2021 at the time of study registration.
4. Patients must have at least ONE of the following: recurrent/progressive disease; refractory disease; persistent disease
5. Patients must have evidence of abnormal mIBG uptake at one site (primary tumour, bone or soft tissue) within the 28 days prior to entry on study and following any intervening therapy.
6. Patients must have an available archival tissue sample OR an available genetic sequencing report from an approved laboratory detailing cancer-specific alterations in somatic and germline DNA
7. Patients require a minimum available stem cell dose of 1.5 x 10e6/kg CD34+ cells/kg. If patients receive a second cycle of treatment, they must have a further 1.5 x 10e6/kg CD34+ cells /kg available for use.
8. Patients must have a Lansky (<16 years) or Karnofsky (>16 years) score of 60.
9. Patients must have adequately recovered from clinically significant acute toxic effects of all prior therapy prior to study registration. Patients must not have received the therapies indicated below within the specific time period prior to study registration on this study:
9.1. Last dose of any myelosuppressive chemotherapy was given at least 2 weeks before study enrolment
9.2. Biologic (anti-neoplastic agent; includes retinoids): must have received last dose at least 7 days prior to study enrolment.
9.3. Monoclonal antibodies: must have received last dose at least 7 days or 3 half-lives, whichever is longer, prior to study enrolment.
9.4. Radiation: Patients must not have received radiation for a minimum of 2 weeks prior to study enrolment.
9.5. Prior 131I-mIBG: Patients previously treated with 131I-mIBG are eligible if:
9.5.1. at least 6 months from the date of last 131I-mIBG
9.5.2. Response other than progressive disease on first restaging after 131I-mIBG

9.5.3. Cumulative lifetime dose of 131I-mIBG at enrolment <18 mCi/kg
9.6. Patients are eligible 6 weeks after myeloablative therapy with autologous stem cell transplant
10. Organ function requirements:
10.1. ANC ≥0.75 x 10e9/L
10.2. Platelet count: ≥50 x 10e9/L
10.3. Serum creatinine </=1.5 x ULN
10.4. Ejection fraction (>/=55%) or Fractional shortening (>/=28%)
10.5. Total bilirubin <=1.5x ULN
10.6. SGPT (ALT) and SGOT (AST) </=3x ULN
11. Written informed consent for trial participation must be obtained from patient or parent /guardian

Participant type(s)
Patient

Healthy volunteers allowed
No

Age group
Mixed

Lower age limit
1 years

Sex
All

Key exclusion criteria
1. Patients who are pregnant, breastfeeding or unwilling to use effective contraception during the study.
2. Patients who in the opinion of the investigator may not be able to comply with the safety monitoring requirements of the study.
3. Patients with disease of any major organ system that in the opinion of the investigator would compromise their ability to withstand therapy.
4. Previous allogeneic or solid organ transplant.
5. Patients who are on haemodialysis.
6. Patients with active or uncontrolled infection. Patients on prolonged antifungal therapy are still eligible if they are culture negative, afebrile, and meet other organ function criteria.
7. Known active infection with HIV, hepatitis B or hepatitis C (routine testing of patients is not required)
8. The maximum total allowance dose of 131I-mIBG that can be given per institutional guidelines must be at least 90% of the calculated 131I-mIBG dose or the patient is not eligible.
9. Patients and/or families who are physically and psychologically unable to cooperate with the radiation safety isolation.

Date of first enrolment
01/12/2024

Date of final enrolment
30/06/2028

Locations

Countries of recruitment
United Kingdom

England

Scotland

Canada

Germany

Netherlands

Spain

Study participating centre
The Royal Marsden Hospital
Fulham Road
London
United Kingdom
SW3 6JJ

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

Study participating centre
Uclh
250 Euston Road
London
United Kingdom
NW1 2PQ

Study participating centre
Hospital for Sick Children
555 University Avenue

Toronto
Canada
M5G 1X8

Study participating centre
Princess Máxima Center for Pediatric Oncology
Heidelberglaan 25
Utrecht
Netherlands
3584 CS

Study participating centre
Charité Universitätsmedizin Berlin
Campus Virchow-Klinikum
Augustenburger Platz 1
Berlin
Germany
13353

Sponsor information

Organisation
University of Birmingham

ROR
https://ror.org/03angcq70

Funder(s)

Funder type
Charity

Funder Name
Solving Kids' Cancer

Alternative Name(s)
Solving Kids' Cancer, Inc., Solving Kids' Cancer Inc, SKC

Funding Body Type
Government organisation

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

Location
United States of America

Results and Publications

Individual participant data (IPD) sharing plan
The data-sharing plans for the current study are unknown and will be made 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?
Participant information sheet	Participant information sheet	11/11/2025	11/11/2025	No	Yes