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A new treatment for advanced retinoblastoma in Africa

Submission date
09/10/2025

Recruitment status
Recruiting

Registration date
30/10/2025

Overall study status
Ongoing

Last Edited
10/10/2025

Condition category
Cancer

[X] 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
Retinoblastoma (Rb) affects children and is the commonest cause of death from eye cancer worldwide. Almost all these deaths occur in low /middle income countries (LMICs) where children are diagnosed late with advanced disease (spread beyond the eye) and where no/few trials have been conducted to decide how best to treat them.
Our aim is to significantly improve outcomes for children with advanced Rb by comparing a new chemotherapy treatment combination (topotecan and cyclophosphamide) with the standard three-drug combination (vincristine, etoposide and carboplatin) in Tanzania.

Who can participate?
Children presenting in Tanzania with Rb which has already spread beyond the eye and is therefore life threatening.

What does the study involve?
Participating children will be allocated by chance to a new chemotherapy treatment combination (topotecan and cyclophosphamide) OR the standard three-drug combination (vincristine, etoposide and carboplatin) in Tanzania.

What are the possible benefits and risks of participating?
Tumour spreading into the brain is the usual cause of death from Rb. Topotecan is one of the rare chemotherapy drugs that not only has activity against Rb but can reach into the brain (from the spine where it can be safely injected). There is a real and exciting possibility that this new combination will be a significant improvement in the treatment of this neglected group of children, and ultimately save lives.
All chemotherapy drugs carry risks of serious side effects and these will be closely monitored throughout the study.

Where is the study run from?
Muhimbili University of Health and Allied Sciences, Dar es Salaam, Tanzania

When is the study starting and how long is it expected to run for.?
August 2023 to December 2028

Who is funding the study?
Velux Stiftung

Who is the main contact?
Dr Richard Bowman, richard.bowman@lshtm.ac.uk, richardbowman493@gmail.com

Contact information

Type(s)
Public, Scientific, Principal investigator

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Additional identifiers

Clinical Trials Information System (CTIS)
Nil known

Integrated Research Application System (IRAS)
LSHTM - 28454, NIMR/HQ/R.8a/Vol.IX/4804

ClinicalTrials.gov (NCT)
Nil known

Protocol serial number
Velux Stiftung 1824

Study information

Scientific Title
The TopCAT trial – a randomised controlled trial investigating the survival benefit of adding topotecan/cyclophosphamide to standard therapy for advanced retinoblastoma in Tanzania

Acronym
TopCAT

Study objectives
Primary Objective(s):
To evaluate the effects of adding Topotecan to standard regimens on duration (from time of randomization) of survival of children with advanced retinoblastoma (Rb).

Secondary Objective(s):
1. To determine the incidence of expected severe adverse events as the results of adding topotecan to standard regimens.
2. To determine the relapse of the disease after the patient has been treated with either Topotecan or standard treatment.
3. To determine the resistance of disease to the treatment.

Ethics approval required
Ethics approval required

Ethics approval(s)
approved 01/08/2023, London School Hygiene and Tropical Medicine, National Medical Research Institute of Tanzania (Keppel Street, London, WC1E 7HT, United Kingdom; +44 (0)7847921223; richardbowman493@gmail.com), ref: 28454

Study design
Parallel-arm open-label individually randomized controlled trial

Primary study design
Interventional

Study type(s)
Treatment, Safety, Efficacy

Health condition(s) or problem(s) studied
Retinoblastoma

Interventions
Participating children will be allocated by chance to a new chemotherapy treatment combination (topotecan and cyclophosphamide) OR the standard three-drug combination (vincristine, etoposide and carboplatin) in Tanzania.

Arm A: Standard Care
Arm A patients receive a three-drug regimen administered on Day 1 of each cycle:
Vincristine is given intravenously at a dose of 1.5 mg/m² body surface area (BSA), with a maximum dose of 2 mg. It is administered as a slow bolus over 2-3 minutes, diluted in not less than 10 ml of 0.9% sodium chloride (NaCl). There is a risk of extravasation with this medication.

Etoposide is administered intravenously at 300 mg/m² BSA as a 4-hour infusion. It should be diluted to a concentration of 0.4 mg/ml in 0.9% NaCl. Rapid infusion must be avoided as it will lead to hypotensive crisis.

Carboplatin is given intravenously at 600 mg/m² BSA as a 1-hour infusion, diluted to 0.5 mg/ml in either 5% dextrose (D5%) or dextrose in normal saline (DNS).

Before each cycle, patients must meet specific hematological requirements: absolute neutrophil count (ANC) greater than 1, platelets greater than 100, and adequate levels of hemoglobin, renal function (renal profile), liver function tests (LFTs), and magnesium.

Age-based dose modifications apply: patients less than 6 months old receive 50% of the dose for each drug, those 6 to 12 months old receive 75% of the dose, and patients over 12 months receive the full dose with no modification.

Arm B: Experimental Arm
Arm B patients receive an alternating regimen. They alternate between the standard VEC regimen (as described for Arm A) and an experimental regimen consisting of intravenous topotecan, intravenous cyclophosphamide, and intrathecal topotecan administered as follows:

Topotecan is given intravenously at 1.5 mg/m² BSA daily on Days 1-5 of the cycle. It is administered as a 30-minute infusion, compatible with either 5% dextrose or 0.9% NaCl, with a final concentration of 25-50 mcg topotecan per ml.
Cyclophosphamide is administered intravenously at 200 mg/m² BSA daily on Days 1-5 of the cycle as a 1-hour infusion, diluted to 0.4 mg/ml in 0.9% NaCl.

Intrathecal topotecan is given on Day 1 of each cycle as a bolus injection. The dose is age-dependent: children over 3 years receive 0.4 mg, those between 2 and 3 years receive 0.32 mg, and children under 2 years receive 0.25 mg. The drug is diluted with preservative-free NaCl to a final volume of 3 ml.

Intervention Type
Drug

Phase
Phase II

Drug/device/biological/vaccine name(s)
Topotecan, cyclophosphamide, vincristine, etoposide, carboplatin

Primary outcome(s)
Time to survival from randomization (months)

Key secondary outcome(s))
1. Overall survival measured over 2-year follow up
2. Event-free survival. Events will be defined as:
2.1. Death (disease, treatment related or other)
2.2. Resistant disease (defined as unresectable tumors following neo-adjuvant chemotherapy)
2.3. Local, CNS or other distant relapses (defined as disease considered related to this presentation which returns after an initial response to treatment assessment confirmed a complete response)
2.4. Recurrent disease (defined as a new tumor deemed unrelated to the first disease, including disease beginning in the fellow eye or a tumor appearing at a new retinal site)
3. Treatment toxicity:
3.1. Bone marrow suppression: anaemia, (febrile) neutropenia, thrombocytopenia
3.2. Gastro-intestinal effects include vomiting, anorexia and resulting malnutrition, constipation
3.3. Etoposide infusion related hypotension
3.4. Hearing loss

All harms that will be observed during the study will be reported including resistant disease, local CNS or distant relapse, as well as recurrent disease. Standard CTCAE grading will be used to assess and collect adverse events. All adverse events will be reported to NIMR per protocol. Patients with adverse events will be monitored with weekly lab until return to baseline. Standard prophylactic and supportive care protocols will be implemented, including use of antibiotics for fever and neutropenia during the care for patients with adverse events.

Events and harms will be recorded at all points of the treatment programme and during and standardized follow-up procedure for 2 years post randomization.

Completion date
01/12/2028

Eligibility

Key inclusion criteria
Children presenting with stage 2 or stage 3 retinoblastoma in Tanzania

Participant type(s)
Patient

Healthy volunteers allowed
No

Age group
Child

Lower age limit
0 years

Upper age limit
17 years

Sex
All

Key exclusion criteria
1. Patients with pre-existing chronic illnesses which require treatment may impact on the ability to tolerate chemotherapy or radiotherapy
2. Patients with a history of prior treatment
3. Patients with suspected or documented life-threatening infections (should be established before enrolment)
4. Patients with stage 3 disease who are enucleated up front

Date of first enrolment
01/12/2025

Date of final enrolment
01/12/2027

Locations

Countries of recruitment
Tanzania

Study participating centre
Muhimbili University Health and Allied Sciences
United Nations Road
Dar es Salaam
Tanzania
PO Box 65001

Study participating centre
Bugando Medical Centre
Mwanza
Mwanza
Tanzania
PO Box 1370

Study participating centre
Kilimanjaro Chrsitian Medical Centre
Moshi
Moshi
Tanzania
PO Box 2240

Sponsor information

Organisation
London School of Hygiene & Tropical Medicine

ROR
https://ror.org/00a0jsq62

Funder(s)

Funder type
Charity

Funder Name
Velux Stiftung

Alternative Name(s)
Velux Foundation

Funding Body Type
Private sector organisation

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

Location
Switzerland

Results and Publications

Individual participant data (IPD) sharing plan
The datasets generated during the study will be available on request from Richard Bowman (richardbowman493@gmail.com)

IPD sharing plan summary
Available on request