

Paediatric hepatic international tumour trial

Submission date 19/04/2017	Recruitment status No longer recruiting	<input checked="" type="checkbox"/> Prospectively registered <input type="checkbox"/> Protocol
Registration date 24/04/2017	Overall study status Ongoing	<input type="checkbox"/> Statistical analysis plan <input type="checkbox"/> Results
Last Edited 26/03/2024	Condition category Cancer	<input type="checkbox"/> Individual participant data <input type="checkbox"/> Record updated in last year

Plain English summary of protocol

<https://www.cancerresearchuk.org/about-cancer/find-a-clinical-trial/a-trial-looking-at-improving-treatment-and-outcome-for-children-with-liver-cancer-phitt>

Study website

www.birmingham.ac.uk/research/activity/mds/trials/crctu/trials/phitt

Contact information

Type(s)

Public

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Additional identifiers

EudraCT/CTIS number

2016-002828-85

IRAS number

212527

ClinicalTrials.gov number

NCT03017326

Secondary identifying numbers

CPMS 33836

Study information

Scientific Title

Paediatric Hepatic International Tumour Trial (PHITT)

Acronym

PHITT

Study objectives

This study aims to:

1. Reduce treatment for very low and low risk group patients, while maintaining the excellent event-free survival (EFS) in these groups to reduce side effects of treatment.
2. Intensify therapy in the high risk group to improve the surgery options available and the event free survival, while testing the use of new drugs in a clinical trial setting.
3. Compare different regimens to improve surgical options in intermediate risk HB
4. Evaluate the biology and genetics of HB and HCC to identify prognostic and toxicity biomarkers.

Ethics approval required

Old ethics approval format

Ethics approval(s)

West Midlands REC – Edgbaston, 10/04/2017, ref: 17/WM/0110

Study design

Randomised; Both; Design type: Treatment, Drug, Cross-sectional

Primary study design

Interventional

Secondary study design

Randomised controlled trial

Study setting(s)

Hospital

Study type(s)

Treatment

Participant information sheet

Not available in web format, please use the contact details below to request a patient information sheet

Health condition(s) or problem(s) studied

Hepatoblastoma or hepatocellular carcinoma

Interventions

The patient will be approached with the option of joining the trial early in the diagnosis. The patient will be asked to confirm their consent to participate in the trial and for a sample of their tumour to be sent for research purposes. An assessment will be made to categorise the level of disease (called PRETEXT staging) using the age, AFP level, presence of metastases and tumour location. The level of disease will be categorised according to analysis by Children's Hepatic tumour International Collaboration (CHIC) - Hepatoblastoma Stratification. If appropriate, the patient will be asked to consent to receive treatment.

The patient will be allocated to one of six different treatment groups, depending on their disease:

Group A: Very Low Risk Hepatoblastoma (HB)

The results from the Central Pathology review of the patient's tumour tissue will be used to determine if the patient should receive cisplatin treatment or no treatment. If the tumour shows "WDF" histology, the patient receives no treatment and is seen at routine visits for follow up assessment only. If the tumour shows "non-WDF" histology, the patient receives a dose of cisplatin on Day 1 of two 21 day cycles.

Group B: Low Risk Hepatoblastoma

These patients will receive a dose of Cisplatin on Day 1 of two 14 day cycles.

The patient is then assessed for surgery to remove the tumour by the Consultant working on the study. If surgery is carried out, the patient is randomised to one of the following two arms:

1. Patient receives cycle 3 and cycle 4 of Cisplatin treatment or
2. Patient receives cycles 4-6 of Cisplatin treatment.

If surgery is not feasible after cycle 1 and cycle 2, the patient receives cycles 3 and 4 of Cisplatin treatment and is re-assessed for surgery. If surgery is still not feasible, the patient receives cycles 5 and 6 of Cisplatin treatment.

Group C: Intermediate Risk Hepatoblastoma

These patients will be randomised to receive one of the following three treatments.

1. SIOPEL3HR: A cardiology assessment to check the patient's heart function will be done prior to receiving treatment. Patients will receive Cisplatin on Day 1, Carboplatin on Day 15 and Doxorubicin on Days 15 & 16 in five 28 day cycles.
2. C5VD: A cardiology assessment will be done prior to receiving treatment. Patients will receive Cisplatin and Doxorubicin on Days 1 & 2; Doxorubicin, 5-Fluorouracil and Vincristine on Day 2; and Vincristine on Days 9 & 16. Each cycle of treatment is repeated after 21 days, and six cycles in total are given.
3. CDDP monotherapy: Patients will receive Cisplatin on Day 1 in six 14 day cycles. Patients will have a CT/MRI scan after the 2nd and 4th cycles of treatment to assess their disease, and have their tumour removed by surgery at an appropriate point in the treatment, depending on the scan results and the decision by their doctor. Following surgery, patients will have further cycles of treatment, until all cycles have been given.

Group D: High Risk Hepatoblastoma

These patients will first undergo induction therapy before undergoing surgery and further treatment.

During induction treatment, patients will receive Cisplatin on Day 1, Cisplatin and Doxorubicin

on Day 8, Doxorubicin on Day 9 and Cisplatin again on Day 15 in three 15 day cycles.

If disease metastases are present after receiving the induction treatment, the patient will be randomised to receive one of the two following treatments:

1. CD/CE: Patients will receive Carboplatin and Doxorubicin (CD) on Day 1, followed by another dose of Doxorubicin on Day 2. Each cycle is 21 days. The patient will receive Carboplatin and Etoposide (CE) on Days 1-4 of Cycle 2. Cycle 1 (CD) and Cycle 2 (CE) will alternate until a total of 6 cycles are given.

2. CD/VI: Patients will receive Carboplatin and Doxorubicin (CD) on Day 1, followed by another dose of Doxorubicin on Day 2. Each cycle is 21 days. The patient will receive Vincristine and Irinotecan (VI) on Day 1 of Cycle 2, followed by more doses of Irinotecan on Days 2-5 of Cycle 2. Cycle 1 (CD) and Cycle 2 (VI) will alternate until a total of 6 cycles are given.

If disease metastases are not present following the induction treatment and surgery, the patient receives Carboplatin and Doxorubicin (CD) as described above.

Group E: Resectable Hepatocellular Carcinoma (HCC)

The type of HCC tumour removed during surgery will determine if the patient should receive PLADO (Cisplatin & Doxorubicin) treatment or no treatment. If the tumour is deemed Fibrolamellar, the patient receives no treatment and is seen at routine visits for follow up assessment only. If the tumour is deemed de novo HCC, the patient should receive a dose of Cisplatin and Doxorubicin on Day 1, and Doxorubicin on Day 2 of four 21 day cycles.

Group F: Unresectable/metastatic Hepatocellular Carcinoma

These patients will be randomised to receive one of the following two treatments:

1. PLADO + Sorafenib: Patients will receive Cisplatin and Doxorubicin on Day 1, Doxorubicin on Day 2 (PLADO) and Sorafenib on Days 3-21 of three 21 day cycles.

2. PLADO + Sorafenib/GEMOX + Sorafenib: Patients will receive Cisplatin and Doxorubicin on Day 1, Doxorubicin on Day 2 (PLADO) and Sorafenib on Days 3-14. Each cycle is 14 days. The patient will receive Gemcitabine, Oxaliplatin and Sorafenib on Day 1, and Sorafenib on Days 2-14 of Cycle 2. Cycle 1 (PLADO+Sorafenib) and Cycle 2 (PLADO+Sorafenib/GEMOX) will alternate until a total of 4 cycles are given.

At the end of the treatment patients will be seen at routine visits once every 3 months for the next 2 years for follow up assessment, including a physical examination, a CT/MRI scan and a blood test for disease indicator Alphafetoprotein levels.

Intervention Type

Other

Phase

Phase III

Primary outcome measure

1. Event-free survival (EFS) is measured as the time from randomisation (or registration into the trial for non-randomised patients) to first failure event or last follow-up date

2. Response in HCC is measured using RECIST version 1.1 criteria, after 3 cycles of PLADO, or 4 cycles of PLADO+S/GEMOX+S in Group F

3. Best Response is measured using RECIST version 1.1 criteria and AFP decline at end of treatment for Groups A, B, C, D and E

Secondary outcome measures

1. Overall survival (OS) is measured as the time from randomisation (or registration for non-randomised patients) to death from any cause
2. Toxicity is measured using Common Terminology Criteria for Adverse Events (CTCAE), at the end of each cycle of treatment
3. Hearing loss is measured using SIOPEL Boston Scale for oto-toxicity at end of treatment and follow up
4. Surgical resectability is measured using surgical outcome during treatment after surgery
5. Adherence to surgical guidelines is measured using the current SIOPEL surgical guidelines and the local clinician's surgical decision to resect after surgical assessment

Overall study start date

01/01/2016

Completion date

30/06/2026

Eligibility

Key inclusion criteria

1. Clinical diagnosis of HB and histologically defined diagnosis of HB or HCC
2. Aged 0-30 years
3. Written informed consent for trial entry

Participant type(s)

Patient

Age group

Mixed

Lower age limit

0 Years

Upper age limit

30 Years

Sex

Both

Target number of participants

Planned Sample Size: 450; UK Sample Size: 100

Key exclusion criteria

1. Any previous chemotherapy or currently receiving anti-cancer agents
2. Recurrent disease
3. Previously received a solid organ transplant
4. Uncontrolled infection
5. Unable to follow the protocol for any reason
6. Second malignancy
7. Pregnant or breastfeeding women

Date of first enrolment

25/08/2017

Date of final enrolment

31/12/2023

Locations

Countries of recruitment

Austria

Belgium

Czech Republic

England

Finland

France

Germany

Ireland

Israel

Netherlands

Northern Ireland

Norway

Scotland

Spain

Switzerland

United Kingdom

Wales

Study participating centre

Aberdeen Royal Infirmary

Foresterhill

Aberdeen

United Kingdom

AB25 2ZN

Study participating centre
Royal Belfast Hospital for Sick Children
180 Falls Road
Belfast
United Kingdom
BT12 6BE

Study participating centre
Birmingham Children's Hospital
Steelhouse Lane
Birmingham
United Kingdom
B4 6NH

Study participating centre
Bristol Royal Hospital for Children
Urbis Education Centre
Bristol
United Kingdom
BS2 8AE

Study participating centre
Addenbrooke's Hospital
Hills Road
Cambridge
United Kingdom
CB2 0QQ

Study participating centre
Our Lady's Children's Hospital
Crumlin
Dublin
Ireland
Dublin 12

Study participating centre
Royal Hospital for Sick Children Edinburgh
9 Sciennes Road
Edinburgh

United Kingdom
EH9 1LF

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

Study participating centre
Leeds General Infirmary
Great George Street
Leeds
United Kingdom
LS1 3EX

Study participating centre
Leicester Royal Infirmary
Infirmary Square
Leicester
United Kingdom
LE1 5WW

Study participating centre
Alder Hey Children's Hospital
Eaton Road
Liverpool
United Kingdom
L12 2AP

Study participating centre
Great Ormond Street Hospital for Children
Great Ormond Street
London
United Kingdom
WC1N 3JH

Study participating centre

Royal Manchester Childrens Hospital
Oxford Road
Manchester
United Kingdom
M13 9WL

Study participating centre
Royal Victoria Infirmary
Queen Victoria Road
Newcastle upon Tyne
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NE1 4LP

Study participating centre
Nottingham City Hospital
City Hospital Campus
Nottingham
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NG5 1PB

Study participating centre
John Radcliffe Hospital
Headley Way
Oxford
United Kingdom
OX3 9DU

Study participating centre
Sheffield Children's Hospital
Western Bank
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S10 2TH

Study participating centre
Southampton General Hospital
Tremona Road
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SO16 6YD

Study participating centre
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Sponsor information

Organisation
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Sponsor type
University/education

ROR
<https://ror.org/03angcq70>

Funder(s)

Funder type
Government

Funder Name
European Commission

Results and Publications

Publication and dissemination plan
Results of this trial will be submitted for publication in peer reviewed journals.

Intention to publish date

01/06/2027

Individual participant data (IPD) sharing plan

The current 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?
HRA research summary			26/07/2023	No	No