International Trial for Pediatric Hepatic Tumours

Published: 19-03-2019
Last updated: 15-05-2024

Primary Objectives: -To evaluate if the treatment of Low Risk HB can be reduced (Group B1) -To compare different induction treatment regimens for Intermediate risk HB (Group C) -To compare different post induction treatment...

Ethical review	Approved WMO
Status	Other
Health condition type	Hepatobiliary neoplasms malignant and unspecified
Study type	Interventional

Summary

ID

NL-OMON25549

Source
Nationaal Trial Register

Brief title
PHITT

Condition

- Hepatobiliary neoplasms malignant and unspecified

Synonym
Livertumour

Health condition

Hepatoblastoma, Hepatocellular carcinoma

Research involving
Human

Sponsors and support

Primary sponsor: University of Birmingham
Source(s) of monetary or material Support: EU HORIZON 2020

Intervention

Explanation

Outcome measures

Primary outcome

Depends on the subgroup; EFS, FFS, OS, toxicity, chemo-related cardiac-, nephro- and oto-toxicity, response, resectability, hearing loss

Secondary outcome

Depends on the subgroup; EFS, FFS, OS, toxicity, chemo-related cardiac-, nephro- and oto-toxicity, response, resectability, hearing loss

Study description

Background summary
Primary liver tumours (hepatoblastoma (HB) and hepatocellular carcinoma (HCC)) in children account for 1% of paediatric tumours. The incidence, however, has been increasing with improved neonatal care for preterm infants, who have an increased risk of developing HB. HB has an annual incidence of 0.8 per million children. HCC is less common in children.

Currently, the 5 year overall survival (OS) for children with HB is variable and ranges from about 50-

100% depending on the disease characteristics. Among those ‘cured’, current treatment regimens

have a risk of significant toxicities including cisplatin-induced oto-toxicity and nephrotoxicity,

doxorubicin-induced cardiomyopathy and secondary leukaemia. In patients treated for HB with 600

mg/m2 of cumulative cisplatin, hearing loss to the point of requiring augmentation devices occurs in half of all patients, severely impacting childhood development and quality of life.

The lethal impact of anthracycline-induced cardiomyopathy and secondary leukaemia is self-evident.

The Paediatric Hepatic International Tumour Trial (PHITT) trial will investigate whether reductions in therapy reduce the risk of both short- and long-term side effects for patients with good prognosis without compromising their good outcomes and whether intensifying treatments with the introduction of new agents improves outcomes for those with a poor prognosis.

Study objective
Primary Objectives:

-To evaluate if the treatment of Low Risk HB can be reduced (Group B1)

-To compare different induction treatment regimens for Intermediate risk HB (Group C)

-To compare different post induction treatment regimens for High Risk HB (Group D2)

-To determine if the outcome is improved when GEMOX is added to PLADO in the treatment of

unresected hepatocellular carcinoma HCC (Group F)

-To collect samples for biological and toxicity studies. (All groups)

Study design
The PHITT trial is a collaborative trial involving three major clinical groups running paediatric liver

tumour trials the International Society of Paediatric Oncology Epithelial Liver Tumour Group (SIOPEL), the Liver Tumour Committee of the Children's Oncology Group, USA (COG), the Japanese Children's Cancer Group (JCCG). The European arm of the study is led by the SIOPEL group and is sponsored by the University of Birmingham, UK and detailed in this protocol. It is anticipated that the other trial groups will use a similar protocol, with an overall analysis of all patients taking place. PHITT is the clinical trial within the Children's Liver Tumour European Research Network (ChiLTERN) Programme. Biology and pathology research will be done in collaboration with the ChilTERN Programma.

The PHITT is an international, over-arching phase III trial, with four randomised comparisons, for paediatric, adolescent and young adult patients with newly diagnosed HB and HCC. This trial includes a registration phase (trial entry) where patients will give consent for the analysis of their biological samples, tumour pathology and imaging reports to determine the grading and status of the disease, before being allocated in a Treatment Group. Patients with HB are classed into four risk-stratified groups and treated using different regimens.

Intervention
Cisplatin, carboplatin, doxorubicin, 5-fluorouracil, vincristin, irinotecan, etoposide, sorafenib, gemcitabine, oxaliplatin.

Study burden and risks
Patients with a liver tumor should be treated to cure. Also in the current standard treatment, patients would be hospitalized for several days. The toxicity and safety will be closely monitored during this study. The treatment is therefore justified.

In groups A and B, we try to reduce the number of courses and reduce the burden in this protocol. The advantage may be that patients have fewer side effects due to this reduction. A disadvantage may be that patients receive not enough treatment. This is still unknown and subject of this study.

Patients will visit the hospital as many days or less.

Three world-wide commonly used standard treatments are compared in group C. It is still unknown which one is the best and this is the subject of this study. The participant has no direct benefit or disadvantage here.

Two new regimes are added to standard therapy in group D. It may be that this improves the outcome, but that is not proven and subject of this study. The additional medication can cause other or new toxicity. It is possible that the additional medication does not give any improvement.

In group E, patients receive the current standard treatment. In group F, patients receive additional medication. The advantage may be that this results in a better result in this group with a bad

prognosis. However, this is not proven and subject of this study. The disadvantage may be that the additional agents do not give a better result and the medication causes other toxicity. This is justified in patients with this poor prognosis.

In addition to the treatment, blood, tissue and urine will be collected for different studies. In the future this can provide valuable information, the participant has no benefit here now. The disadvantage may be that the patient suffers from pain or stress. The decreases are combined as much as possible with regular decreases, interventions and hospitalization.

Patients have an access

device, that is used for standard care, which keeps the number of injections limited. This part of the study will be terminated if patient oppose or withdraw consent.

Contacts

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Eligibility criteria

Age
Newborns
Newborns
Babies and toddlers (28 days-23 months)
Babies and toddlers (28 days-23 months)
Children (2-11 years)
Children (2-11 years)
Adolescents (12-15 years)
Adolescents (12-15 years)
Adolescents (16-17 years)
Adolescents (16-17 years)

Adults (18-64 years)
Adults (18-64 years)

Inclusion criteria

 Clinical diagnosis of HB* and histologically defined diagnosis of HB or HCC. *Histological confirmation of HB is required except in emergency situations where: a) the patient meets all other eligibility criteria, but is too ill to undergo a biopsy safely, the patient may be enrolled without a biopsy; b) there is anatomic or mechanical compromise of critical organ function by tumour (e.g., respiratory distress/failure, abdominal compartment syndrome, urinary obstruction, etc.); c) uncorrectable coagulopathy. Age ≤30 years. Written informed consent for trial entry.

Exclusion criteria

 Any previous chemotherapy or currently receiving anti-cancer agents; Recurrent disease; Previously received a solid organ transplant; other than orthotopic liver transplantation (OLT); Uncontrolled infection; Unable to follow or comply with the protocol for any reason; Second malignancy; Pregnant or breastfeeding women.

Study design

Design

Study phase:	3
Study type:	Interventional
Intervention model:	Parallel
Allocation:	Randomized controlled trial
Masking:	Open (masking not used)
Control:	Active
Primary purpose:	Treatment

Recruitment

NL

Recruitment status:	Other
Start date (anticipated):	30-07-2019
Enrollment:	450

Type:	Actual

IPD sharing statement

Plan to share IPD: Undecided

Ethics review

Approved WMO Date:	06-03-2019
Application type:	First submission
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)

Study registrations

Followed up by the following (possibly more current) registration

ID: 50638
Bron: ToetsingOnline
Titel:

Other (possibly less up-to-date) registrations in this register

No registrations found.

In other registers

Register	ID
NTR-new	NL7616
CCMO	NL62546.078.18
EudraCT	2016-002828-85
OMON	NL-OMON50638

Study results