



ChiLTERN

Children's Liver Tumour
European Research Network



UNIVERSITY OF
BIRMINGHAM



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Welcome

Welcome to the **eighth** edition of the PHITT Clinical Trial newsletter.

The PHITT Trial remains **Open to Recruitment**, even though the major news is that the coronavirus pandemic is affecting clinical trials, by having meetings, conferences and monitoring visits being postponed or cancelled, site staff being re-deployed to other duties or working from home (including the CRCTU) and also some hospitals are suspending the recruitment of patients until further notice. We appreciate the current situation and burden on the various countries healthcare systems and the priority being patient safety. We understand the challenges running ongoing clinical trials and appreciate all your ongoing efforts. However, The PHITT Trial still remains open if sites are able to recruit safely and the PHITT Trial Team, even though presently working from home, can still be contacted by email for advice. **Stay safe and Keep healthy.** The PHITT Team, CRCTU.

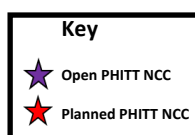
2.5 Years On

A total of **128 patients** has been recruited into the PHITT Trial so far from the NCCS and sites open—with more still to open. This is summarised in **Table 1** below.

Table 1. Summary of the Number of PHITT NCC Sites Open and Patients Recruited

NCC	Sites Open	Patients Recruited
Austria	3 out of 5	1
Belgium	7 out of 8	5
The Czech Republic	2 out of 2	3
France	29 out of 29	27
Germany	11 out of 28	3
The Netherlands	1 out of 1	3
Norway	3 out of 4	3
Poland	2 out of 12	0
The Republic of Ireland	1 out of 1	3
Spain	16 out of 16	23
Switzerland	9 out of 9	7
UK	21 out of 21	50

Figure 1. A Map of Europe Showing PHITT Trial NCCs



Please try and open the remaining sites, so that they can make contributions towards helping the trial to reach its target over the next year.

2.5 Years On - Trial Recruitment and Data Return

To all active sites for participating in the PHITT Trial, if you are able to, with the current situation, please try and continue to offer, screen, consent and recruit potential patients if they prove eligible.

Table 2 below shows the recruitment figures and the percentage CRF return rate up to 18th March 2020. Thank you to all of the sites for generally improving the overall percentage CRF return rate. Please continue to complete Case Report Forms and Sample Forms (with their accompanying CLCN Kit Forms) on the PHITT Trial Online Database.

Table 2. Highest and Lowest Percentage CRF Return Rates by Site

Site Name	Country	Site Activation Date	Number of Patients Recruited	Percentage CRF Return Rate
Hopital Morvan, Brest	France	19-Dec-18	1	95%
St James's University Hospital, Leeds	UK	14-Dec-18	1	95%
Hospital Universitario 12 de Octubre, Madrid	Spain	24-Apr-2018	1	94%
Bristol Royal Hospital for Children	UK	29-Nov-2017	4	93%
Royal Marsden Hospital, Sutton	UK	28-Sep-2017	6	93%
Centre Hospitalier Universitaire (CHU) de Rennes	France	06-Nov-2018	1	93%
Sheffield Children's Hospital	UK	26-Jan-2018	1	93%
Royal Manchester Children's Hospital	UK	20-Sep-2017	6	92%
Hospital Universitario Virgen del Rocío, Sevilla	Spain	02-Jul-18	3	92%
Centre Hospitalier Universitaire Vaudois, Lausanne	Switzerland	02-Oct-2018	1	91%
Universitair Ziekenhuis Gent	Belgium	11-Apr-2019	2	50%
Centre Hospitalier Regional de la Citadelle, Liege	Belgium	11-Apr-2019	1	48%
University Hospital Brno	Czech Republic	05-Nov-2019	2	39%
Hopital Armand-Trousseau, Paris	France	21-Dec-19	1	37%
Hospital General Universitario Gregorio Marañon, Madrid	Spain	05-Apr-2019	1	20%

Forthcoming DMC Meeting

The next Data Monitoring Committee (DMC) meeting for the PHITT trial is due to be held on the 12th May, 2020. Please, if at all possible, complete as many CRFs on the PHITT Trial Online Database, several weeks before this date, so that the trial data can be analysed ready for the meeting. Especially try and complete forms that are still 'Saved' and not yet 'Sent'. If you have any problems completing forms, then please contact the PHITT Trial Team by email (phitt@trials.bham.ac.uk). Thank you.

Registration Onto the PHITT Trial

It is extremely important that the PHITT Trial Protocol registration procedure is followed.

The Protocol is very clear on the trial entry process. **A patient cannot be treated as part of the PHITT trial until they have been allocated a trial number (TNO), assigned to a Treatment Group and Randomised in the case of Groups C and F and the following forms are entered onto the PHITT Trial Online Database:**

- Trial Entry Eligibility & Trial Entry Form - **confirms trial eligibility and allocates a Patient TNO**
- Treatment Group Eligibility Form - **confirms Treatment Group eligibility**
- Treatment Group Registration Form - **assigns patient to a Treatment Group**
- Randomisation Form (Groups C and F only) - **randomises patient to treatment arm**

There is also a mandatory requirement for those patients that meet the Rapid Central Pathology Review criteria for confirmation of diagnosis from an International Pathologist to confirm treatment group eligibility urgently.

ALL staff with either a **PI** (Investigator), or **TR** (Trial administrators) profile have read/write access to the PHITT Trial Online Database and therefore can complete **ALL** the required CRF forms. The PHITT Trial Team can arrange a training teleconference if sites/NCCs think this is necessary and can re-send mislaid or not received database logins.

Finally, if you are in **any doubt** as to whether a patient is eligible for the trial or that trial treatment can/should commence please contact your NCC or the PHITT Trial Team at phitt@trials.bham.ac.uk and we will advise.

Randomisations During the PHITT Trial

It is extremely important that the PHITT Trial Protocol randomisation process is followed during the trial.

These randomisations **must happen in real-time** and sites **must not** do these randomisations retrospectively. As a reminder, the Randomisation Form must be completed for these 2 Treatment Groups at the correct treatment time-point and regardless of the Treatment Arm they eventually follow.

Group B: The Randomisation Form **must** be completed after the patient has received two cycles of chemotherapy and been considered for surgery, whether or not the patient is to be randomised—Group B1 for resected patients or Group B2 for un-resected patients.

Group D: The Randomisation Form **must** be completed after the patient has received three cycles of induction chemotherapy, surgery and response assessment, whether or not the patient is to be randomised—Group D1 for patients in Metastatic Complete Remission or Group D2 for patients **not** in Metastatic Complete Remission.

The above information is documented in the current PHITT Protocol, v3.0 vd17-Oct-2018, at Section 10.2.2 for Treatment Group B and section 10.2.4 for Treatment Group D.

Please let the PHITT Trial Team at phitt@trials.bham.ac.uk know if you have any questions regarding Treatment Groups B and D randomisations or require any further clarification.

Central Radiological Review

A retrospective central radiology review will be performed for all patients entering the PHITT Trial by a panel of international radiologists.

Please send CDs of the imaging data, from the patients Baseline and Pre-surgery tumour evaluations, from using MRI and CT scans, to the PHITT Trial Office. Please only mark the CDs with the patients trial number TNO and the type and date(s) of the assessments and accompany them with a completed PHITT Central Radiology Review Shipment Form.

The imaging data recorded on the CDs **must be anonymised** in terms of the patient details and any identifiers, otherwise they **will not** be accepted by the PHITT Trial Office. The CDs and shipment forms must also anonymised of the patient details and any identifiers.

PHITT Trial Sample Collection



**Figure 2. FFPE Blocks
Containing Cancer Tissue**

Even though the collection of samples is not mandatory, The PHITT Trial Team would like to give a big Thank You to all of the hard work that Sites have put into the collection and storage of patient samples, the completion of sample forms and organising the samples shipment to the various Analysis Laboratories, as part of the PHITT Trial.

However due to the current situation, any samples collected for IGTP, Spain, must be stored in conditions as described in the PHITT Laboratory Manual (v5.0 vd27-Jan-2020), as they cannot be shipped to them at the present. Also, fresh samples cannot be collected and shipped to the PDX Centres, at present. The PHITT Trial Team will advise when it is okay to ship certain PHITT patient samples



**Figure 3. HE Slides
Containing Cancer
Tissue**

Contact the PHITT Trial Team

Due to the Coronavirus Pandemic, the PHITT Trial Team are, along with the rest of the CRCTU, presently working from home and can only be contacted directly by email, preferably by using the PHITT Trial email address

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