Welcome

Welcome to the fourth edition of the PHITT Clinical Trial newsletter.

We would like to thank all of our UK and International colleagues for working hard this year to open sites and recruit patients into the trial. We hope that 2019 will see the trial open in all of the expected countries and sites and that the trial is successful in offering treatment to as many patients as possible.

Wishing you a very Merry Christmas and a Happy New Year! The PHITT Team, CRCTU

15 Months On

The Trial has been open to recruitment now for 15 months. There are now 17 sites open in the UK: Southampton, Leicester and Cardiff are yet to open. There are now 5 Countries open: Republic of Ireland (1 out of 1 site open), Spain (6 out of 20 sites open), Norway (1 out of 4 sites open), Switzerland (8 out of 9 sites open) and France (2 out of 26 sites open) with more NCCs to open soon.

A total of 30 patients has been recruited into the PHITT study so far, 24 from the UK and 6 from Spain, in all Treatment Groups (A to F) and including Trial Entry Only.

The main news is that Version 3.0 of the PHITT Trial Protocol will be issued around Christmas 2018. See Page 3 for further information. Subsequently, this also means that Patient Information Sheets, CRFs and the PHITT Trial Online Database will be updated.

STOP PRESS!!

Version 3.0 of The PHITT Trial Protocol is about to be issued!

Key

Open PHITT NCC
Planned PHITT NCC

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15 Months On -

Trial Recruitment and Data Return

The Table shows the recruitment figures and the percentage CRF return rate up to 4th December 2018. Now that the PHITT Trial Online Database is open, the percentage CRF return has improved considerably. Please continue to complete Case Report Forms and Sample Forms on the PHITT Trial Online Database.

Thank you to all active sites for participating in the PHITT Trial. Please continue to publicise this clinical trial, screen potential patients and recruit them if they prove eligible.

<table>
<thead>
<tr>
<th>Site Name</th>
<th>Country</th>
<th>Site Activation Date</th>
<th>Number of Patients Recruited</th>
<th>Percentage CRF Return Rate</th>
</tr>
</thead>
<tbody>
<tr>
<td>The Great North Children’s Hospital, Newcastle</td>
<td>UK</td>
<td>21-Mar-2018</td>
<td>1</td>
<td>100%</td>
</tr>
<tr>
<td>Alder Hey Children’s Hospital, Liverpool</td>
<td>UK</td>
<td>08-Dec-2017</td>
<td>1</td>
<td>100%</td>
</tr>
<tr>
<td>Royal Manchester Children’s Hospital</td>
<td>UK</td>
<td>20-Sep-2017</td>
<td>3</td>
<td>95%</td>
</tr>
<tr>
<td>Bristol Royal Hospital for Children</td>
<td>UK</td>
<td>29-Nov-2017</td>
<td>3</td>
<td>93%</td>
</tr>
<tr>
<td>Royal Marsden Hospital, Sutton</td>
<td>UK</td>
<td>28-Sep-2017</td>
<td>5</td>
<td>78%</td>
</tr>
<tr>
<td>Hospital Universitario Son Espases, Mallorca</td>
<td>Spain</td>
<td>18-Jul-2018</td>
<td>1</td>
<td>71%</td>
</tr>
<tr>
<td>Addenbrookes Hospital, Cambridge</td>
<td>UK</td>
<td>25-Aug-2017</td>
<td>3</td>
<td>70%</td>
</tr>
<tr>
<td>Birmingham Children’s Hospital</td>
<td>UK</td>
<td>11-May-2018</td>
<td>2</td>
<td>66%</td>
</tr>
<tr>
<td>Nottingham Children’s Hospital</td>
<td>UK</td>
<td>10-Jan-2018</td>
<td>3</td>
<td>65%</td>
</tr>
<tr>
<td>Hospital Universitari Vall D’Hebron, Barcelona</td>
<td>Spain</td>
<td>25-May-2018</td>
<td>2</td>
<td>54%</td>
</tr>
<tr>
<td>Hospital Universitario 12 de Octubre, Madrid</td>
<td>Spain</td>
<td>24-Apr-2018</td>
<td>1</td>
<td>45%</td>
</tr>
<tr>
<td>Leeds General Infirmary</td>
<td>UK</td>
<td>01-Feb-2018</td>
<td>3</td>
<td>43%</td>
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<tr>
<td>Hospital Universitario de Cruces, Bizkaia</td>
<td>Spain</td>
<td>29-May-2018</td>
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<td>31%</td>
</tr>
<tr>
<td>Hospital Universitario Virgen del Rocio, Sevilla</td>
<td>Spain</td>
<td>02-Jul-2018</td>
<td>1</td>
<td>25%</td>
</tr>
</tbody>
</table>

Associated PHITT Trials

The international collaborative partners of the PHITT trial are now open to recruitment.

In the USA, the Children’s Oncology Group (COG) opened the Pediatric Hepatic Malignancy International Therapeutic Trial (PHITT) on 23rd May, 2018.

In Japan, the Japan Children’s Cancer Group (JCCG) opened PHITT on 1st November, 2018.
**Version 3.0 of the PHITT Trial Protocol**

The major changes to the new Version 3.0 of the PHITT Trial Protocol are:-

- **Sodium thiosulfate (STS)** is permitted in Groups A, B and C, but it must not be used for patients in Groups D, E and F.

- **Dexrazoxane** is permitted for patients receiving doxorubicin at the discretion of the treating centre.

- **The Rapid Central Pathology Review** increased to include HB patients who are over 8 years of age and/or AFP values less than 100 and all patients with HCC.

- **Treatment Group Eligibility:**
  - Treatment Group Specific Exclusion Criteria added— see the protocol for further details.

- For Concomitant Medication, the **use of live attenuated vaccines is prohibited**.

- Neutropenia has been removed from the list of events that should be reported on an Expected SAR Form.

- **Group B2** patients (non-randomised arm) will now have 6 cycles of cisplatin therapy.

- **Group C: Group CSVD** patients will receive vincristine and 5-FU on Day 1 to be in line with common practice.

- **Group D induction** treatment schedule now specifies the cisplatin dose as always 70mg and doxorubicin is now given on days 57 and 58 in Block A3.

- **Group D** patients include those resected with macroscopic disease.

- **Group E** patients should have no macroscopic disease.

- **Group F** patients include those resected with macroscopic disease.

- **Database web address** has been updated.

- **Group D: Groups D2 and D3** have been renamed as ‘Group D2 (CD/CE)’ and ‘Group D2 (CD/VI)’ respectively.
Dose Modifications are given for Pulmonary Toxicity

Patient Assessments at Screening and During Treatment:

All patients: Blood pressure, sodium and ammonia tests have been removed and a test for magnesium has now been added

Group B: The tumour assessments time-points for Groups B1 and B2 have now been clarified

Group C – SIOPEL-3HR: Tumour assessment post-surgery time-point removed to match the treatment (Figure 6 in the PHITT Protocol)

There is now a defined allowance for flexibility in treatment and study evaluation timings to be +/- 3 days

Screening and Treatment Assessments: Country specific requirements have been added

Screening: Magnesium tests, Prothrombin time (PT) during coagulation and other serology as per local practice have been added. Also, GFR and Audiology tests have been added in line with assessment tables

Contact the PHITT Trial Team

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