HR-NBL2 Newsletter

SIOPEN R NET

RANDOMIZED, INTERNATIONAL AND MULTICENTRIC PHASE 3 STUDY THAT EVALUATES AND COMPARES 2 TREATMENT STRATEGIES IN 3 THERAPEUTIC PHASES (INDUCTION, HIGH DOSE CHEMOTHERAPY AND RADIOTHERAPY) FOR PATIENTS WITH HIGH-RISK NEUROBLASTOMA.

Solving Kids' Cancer UK

NEUROBLASTOMA UK
FIGHTING CHILDHOOD CANCER

December 2023

Issue 3

Seasons Greetings!

New Protocol Coming PTO.

Inside this issue

Message from the HR-NBL2 UK Coordinating Investigator and UK Trials Office.

We would like to thank all the staff across all our hospitals for their incredible hard work on HR-NBL2 this year.

The trial has had a very successful year! It feels that at last we are making up ground after a rocky start!

At the trials office we get very excited every time you randomise a new patient or enrol a patient on the next phase of treatment. Please keep the trial on your radar so we sustain this momentum into 2024.

We hope you find this update on the trial interesting and that the 'Key Notices' and info on the upcoming protocol amendment will be helpful to you.

We wish you all a peaceful Christmas and look forward to continuing to work with you in 2024.

Best wishes Dr Elliott, Jen, Hannah & Faiza.

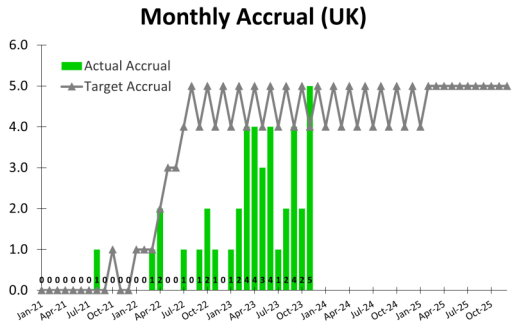
Important! Despite International shortages in vindesine HR-NBL2 is STILL recruiting (PTO).

Recruitment update:

Monthly recruitment has averaged 4 patients over the past 3 months.

UK Recruitment on 1st Dec 2023 was 41. This is great but we are still a very long way from the UK target of 206 patients by Dec 2025! So don't stop keep recruiting!

All eligible patients across the UK should be given the chance to benefit from this trial. If your site is not open please consider if there is a site you could connect potential patients to (see over page for list of open sites).



Reminder: HR-NBL includes:

- **Stage M disease > 12 months, any *MYCN* status**
- **Ms neuroblastoma 12-18 months, any *MYCN* status**
- **L2, M or Ms neuroblastoma with MYCN amplification.**

Site update:

Special mention to **UCLH** and **GOSH.** Both opened for HR-NBL2 since our last newsletter in August 2023.

Our funders are very clear that we must open this trial in all devolved countries of the UK. We hope to open sites in Cardiff, Belfast, Edinburgh and Aberdeen early in 2024. We also want to increase representation across England and are working with Nottingham, Leicester and Southampton to also open soon.

If your site is in set-up please keep us updated on your progress and challenges - If we don't know your problems we can't look for solutions.

GUSTAVE ROUSSY
CANCER CAMPUS
GRAND PARIS

International Sponsor
Gustave Roussy
International Coordinating Investigator
Dr Dominique Valteau-Couant

The Trials office will be closed 21st Dec to 1st Jan inclusive. The mailbox will be checked a couple of times during this period and we will help where we can but for any urgent clinical concerns please contact Dr Martin Elliott directly on 0113 392 8779.

Best wishes for 2024

CANCER RESEARCH UK | Birmingham Cancer Research UK Clinical Trials Unit | UNIVERSITY OF BIRMINGHAM

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CLINICAL QUERIES

Clinical queries during office hours should be directed to the UK Trials Office

SAE REPORTING

Report SAEs to Gustave Roussy online via My eClinical web portal
https://www.evereport.eu/myeclinical/form/IGR/login.php
If portal access is unavailable FAX forms to: +33 (0) 1 42 11 61 50

International phase-3 study to improve treatment for patients with high-risk neuroblastoma

HR-NBL2 News

Notices

Registration & Randomisation

- Patients are not eligible for HR-NBL2 if they have had chemotherapy other than one course of etoposide + carboplatin (no vincristine) before registration.
- Even if a patient registered on HR-NBL2 does not participate in a randomisation you must still enrol them. We will contact you if we don't receive notification your patient has entered the next phase.
- When you enrol a patient please tell us 1.if the patient randomised, 2. the treatment arm assigned and 3. the date the patient will start treatment. Please also send a copy of any consent forms to us to arrive within 1 week of consent.

IMPs

- Vindesine stocks are low internationally and many UK sites are already affected by this shortage. If you do not have enough vindesine to support a patient through all 3 N5 courses of the GPOH induction regimen please do not randomise them for R-I. Instead they must receive Rapid COJEC as non-randomised.
- The UK protocol specific appendix to protocol v1.1 no longer applies. Patients are not to be given vincristine in place of vindesine.
- Some sites have experienced shortages of licensed platinum based drugs (cisplatin and carboplatin). We need to know which patients on HR-NBL2 have received unlicensed drugs. We will be following up for this info in the new year from any sites that have not confirmed details.

Databases

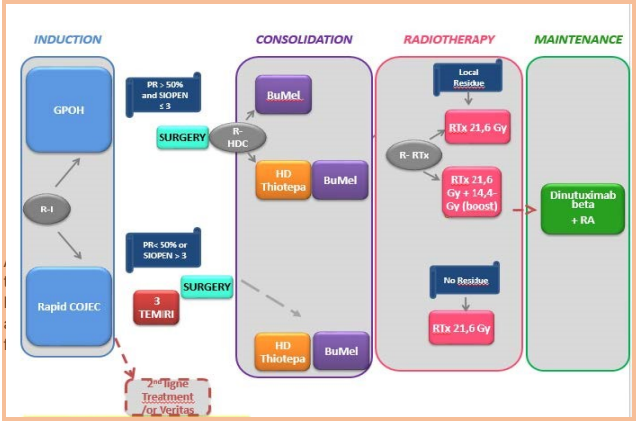
- MyeClinical: Several of you have reported losing access to the MyeClinical database. Please note that if you input wrong passwords to MyeClinical 3 times in succession the system will delete your account! If unsure of your password please choose "Forgot Password" you will then be able to give a new one.
- SAEs are to be reported direct to the international sponsor via the My eClinical Web interface. If portal access is unavailable or your investigators cannot validate online please wet sign your forms and FAX to: +33 (0) 1 42 11 61 50.
- Trial Master: The sponsor has provided a new guide to help you complete the eCRF. We emailed this to sites on 27-Nov-2023 and a copy is located in the 'Documents' section of the eCRF 'Trial Master database. Any queries please bring them to us and we will find out if we don't know.

Patient Videos

Back in March 2023 we informed you of a series of **animated patient information videos** designed to be used alongside existing approved patient documents to help explain to parents and patients about the treatments for High-Risk Neuroblastoma. These are available on our website for investigators (https://www.birmingham.ac.uk/research/crctu/trials/hr-nbl2/investigators.aspx). Please show to your patients and their families.

Protocol update to v3.0 (Substantial Amendment SA08)

- Protocol v3.0 is coming soon. This will be introduced in substantial amendment 08 (SA08). We will send all info to sites once all approvals have been received but just as a brief heads up this is an exciting update that will enable patients who do not make sufficient response at the end of induction therapy to remain on the trial.
- Patients who have an inadequate response to induction chemotherapy will receive 3 courses of TEMIRI (Temozolomide + Irinotecan (both IMPs)) followed by tandem High Dose Chemotherapy with Thiotepa and Bu-Mel and will be potentially eligible for the subsequent radiotherapy randomisation (see figure below).



Consent

- Any patients still undergoing induction treatment when protocol v3.0 is introduced will need to sign an addendum to the old main study Patient Information Sheet.

Extra Tests

- ALK genetic alteration in a diagnostic tumour sample must be determined in a SIOPEN reference laboratory within 21 days of diagnosis.
- All patients must now have an extra mIBG or FDG scan plus an MRI or CT scan of the primary tumour at 6 months and 1 year after end of treatment and in the event of relapse. They must also have a cerebral MRI or CT scan before maintenance, at the end of treatment and in the event of relapse.
- The protocol mentions neuropsychology assessments but in the UK these will not mandated.
- We know that extra scans = extra cost. We have updated the SoECAT to include these additional scans. The SoECAT has been validated and all extra costs will be covered.

UK Hospitals open for HR-NBL2

Recruitment

Addenbrooke's
Alder Hey
Birmingham
Bristol
Glasgow,
GOSH
Leeds
Manchester
Newcastle
John Radcliffe
Royal Marsden
Sheffield
UCLH

Radiotherapy

The Christie
Birmingham QE

International Update

19 Countries now open for HR-NBL2 internationally

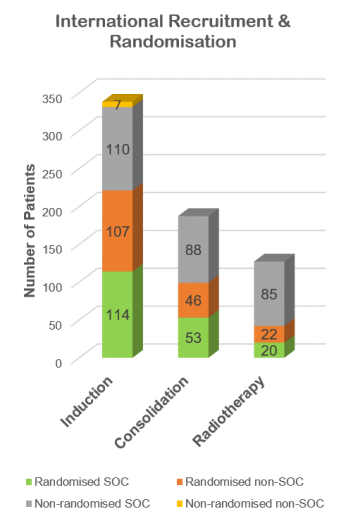
France, UK, The Netherlands, Italy, Greece, Switzerland, Czech Republic, Belgium, Norway, Australia, Slovenia, Germany, Slovenia, Denmark, Norway, Israel, Spain, Austria, Slovakia.

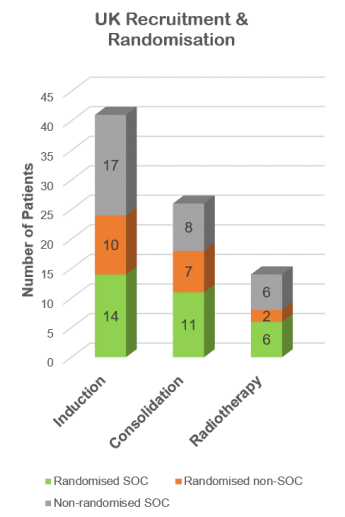
Recruitment Figures

Dec 2023

Total international recruitment: 103 (42% of target)

UK recruitment: 41 (20% of target)





Graphs for International and UK recruitment and randomisation showing the numbers of patients registered on the study at each of the 3 treatment phases and the treatment received. Grey = Non-randomised standard of care (SOC), Green = Randomised SOC, [Rapid COJEC/Bu-Mel/21.6Gy], Orange = Randomised non-SOC [GPOH/Thiotepa + Bu-Mel/21.6Gy+boost]. Yellow = Non-Randomised non-SOC at induction [GPOH].