National Research Ethics Committee

NREC-CT B Meeting

21 September 2022

Attendance

Name	Role
Dr Jean Saunders	Chairperson, NREC-CT B
Prof. John Faul	Deputy Chairperson, NREC-CT B
Ms Serena Bennett	Committee Member, NREC-CT B
Dr Enda Dooley	Committee Member, NREC-CT B
Dr Lorna Fanning	Committee Member, NREC-CT B
Dr John Hayden	Committee Member, NREC-CT B
Dr Mary McDonnell Naughton	Committee Member, NREC-CT B
Mr Gavin Lawler,	Committee Member, NREC-CT B
Prof. Colm O'Donnell	Committee Member, NREC-CT B
Ms Mandy Daly	Committee Member, NREC-CT B
Ms Caoimhe Gleeson	Committee Member, NREC-CT B
Dr Mark Robinson	Committee Member, NREC-CT B
Ms Mandy Daly	Committee Member, NREC-CT B
Prof Andrew Green	Committee Member, NREC-CT B
Ms Susan Kelly	Committee Member, NREC-CT B
Ms Deirdre MacLoughlin	Committee Member, NREC-CT B
Prof Seamus O'Reilly	Committee Member, NREC-CT B
Dr Christina Skourou	Committee Member, NREC-CT B
Dr Emily Vereker	Head, National Office for RECs
Ms Patricia Kenny	Project Officer, National Office for RECs

Dr Jane Bryant*	Project Officer, National Office for RECs
Ayesha Carrim	Programme Officer, National Office for RECs
Dr Emma Heffernan*	Project Officer, National Office for RECs

*Drafted minutes

Apologies: Dr Cliona McGovern, Prof David Smith, Mr Philip Berman, Ms Paula Prendeville, Dr Eimear McGlinchey, Prof. Abhay Pandit

Quorum for decisions: Yes

Agenda

- Welcome & Apologies
- 22-NREC-CT-149
- 22-NREC-CT-148
- 22-NREC-CT-150
- 22-NREC-CT-151
- AOB

- The Chair welcomed the NREC-CT B.
  - The minutes from the previous NREC-CT B meeting on 17 August 2022 were approved.
  - The NREC Business Report was discussed and noted.

Applications

22-NREC-CT-149

Principal Investigator: Dr Mark Doherty

Study title: Study title: Brightline-1: A Phase II/III, randomized, open-label, multicenter study of BI 907828 compared to doxorubicin as first line treatment of patients with advanced dedifferentiated liposarcoma

EudraCT: 2021-002392-20

- NREC-CT comments:

- The NREC-CT B agreed that additional information was required to inform its deliberations before a final ethics position could be returned. RFI

- NREC-CT Decision:

- Request for more information

- Additional Information Required

- The NREC-CT B noted in the Protocol that “tumour biopsy results will provide valuable information and will assist clinical decisions for future patients. Hence, the benefit is assumed to outweigh the risks associated with the biopsy”. The Committee request clarification on whether this biopsy is necessary, given that no benefits to the participant are noted. Further detail on the risks associated with the procedure should also be added to the PIL.
- The NREC-CT B requested clarification on whether p53 status will be determined before enrolment.
- The NREC-CT B noted that participants with terminal illness were not selected on the NREC application form for inclusion and requested clarification on whether this is the case.
- The NREC-CT B noted that recruitment material is being prepared. The Committee request that these materials be submitted for review once completed.
- The NREC-CT B requested clarification that withdrawal of consent to participate should halt processing of personal data, negating the requirement for a separate process.
- The NREC-CT B requested that explicit consent be sought for sharing of a participant’s samples.
- The NREC-CT B requested that the section of the PIL containing potential side effects should be consistently denoted in percentages, rather than the number of participants that may experience same.
- The NREC-CT B requested further detail on the stated risk of developing cardiomyopathy.
- The NREC-CT B requested that the section of the PIL on data transfer should indicate that personal data transferred to third parties is pseudonymised, as per the DPIA.
- The NREC-CT B noted the number of appendices in the PIL, which makes the information more difficult to access. The Committee suggest that the PIL would benefit from addition of a summary document.
- The NREC-CT B requested rephrasing of the explanation of the Bone Scan procedure to include further detail.
- The NREC-CT B requested that the phone number of the Irish DPC be added to the PIL, should participants wish to contact the office of the DPC.

- The NREC-CT B requested that the consent section should be layered, in line with best practice.
- The NREC-CT B suggested that Phase II and Phase III studies be detailed in separate consent forms.
- The NREC-CT requested that detail on the ionising radiation dose to participants and risk stratification be added to the PIL, and to be specific to the Irish setting.
- The NREC-CT B requested clarification on whether the study will cover companion costs in addition to participant costs.

22-NREC-CT-148

Principal Investigator: Prof Orla Hardiman

Study Title: A PHASE 3, OPEN-LABEL EXTENSION OF COURAGE-ALS (CY 5031)

EudraCT: 2021-004727-33

- **NREC-CT comments:**

- Based on the above, the NREC-CT B agreed that this application be designated as favourable with conditions

- **NREC-CT Decision:**

- Favourable with conditions

- **Conditions of Approval**

- The NREC-CT B noted the proposed start date of 1st of July on the NREC application form and requested clarification that the study has not yet started.
- The NREC-CT B requested more specific detail on the recruitment strategy of participants from the preceding double-blind trial.
- The NREC CT-B requested a definition of who would be considered an impartial witness, as per Addendum B in the PISCF.
- The NREC-CT B request that references to other jurisdictions be removed from the PISCF and to ensure all such references pertain to the Irish setting.
- The NREC-CT B requested that the following sentence in the Pregnant Partner PISCF be rephrased to include more lay terminology; ‘To protect your privacy, you will be included in the assigned code for your partner, and your research records will be labelled with that code’
- The NREC-CT B noted in the Pregnant Partner PISCF, a significant amount of detail is asked about the pregnancy, including the name and contact details of the woman’s obstetrician. The Committee requested that consent be sought from the pregnant partner

for the study team to contact her obstetrician. If consent is not granted, the obstetrician's contact details should not be requested.

- The NREC-CT B noted that participants will be provided with the most recently approved version of the PISCF during clinic visits, or via mail or email. The Committee requested clarification that the informed consent process will be carried out in the clinic.
- The NREC-CT B requested clarification on whether parking expenses will be reimbursed to participants during clinic visits.
- The NREC- B noted that the consent material layout is not in line with best practice and requested that the applicant provides participants with a layered approach to consent.

22-NREC-CT-150

Principal Investigator: Prof. Michael O'Reilly

Study title: A Randomised, Double-Blind, Placebo-Controlled, Dose Ranging Study to Evaluate the Efficacy and Safety of SPR001 (Tildacerfont) in Adult Subjects with Classic Congenital Adrenal Hyperplasia

EudraCT: 2019-004764-22

- NREC-CT comments:

- The NREC-CT B agreed that additional information was required to inform its deliberations before a final ethics position could be returned.

- NREC-CT Decision:

- Request for more information

- Additional Information Required

- The NREC-CT B requested clarification on participant progression through the trial, in particular, details on whether the results be evaluated at the end of each part, before progressing to the next and how participants receiving the placebo will be progressed through the 3 parts of the trial.
- The NREC-CT B requested further information on recruitment, specifically:
    - How participants are recruited to the trial;
    - The justification for limiting participants to those attending the study team's own clinics;
    - Further details on the availability of translators to support participants who do not speak English as their first language, including a more detailed description of how this will work in practice, and what arrangements are in place for participants who may not adequately understand verbal or written information.

    - Similarly, rather than using an independent witness, can provisions be made for those with visual impairment to consent for themselves if required, e.g., braille or Browse Aloud software?

- The NREC-CT B noted insufficient detail on withdrawal and requested further information on any withdrawal phenomena upon discontinuation of the trial drug.
- The NREC-CT B queried whether the sponsor will be carrying out genetic testing to clarify the subtype of classical CAH in participants. If they will be, how will they plan to feedback those clinically relevant results to participants?
- The NREC-CT B noted that the 'Cahmelia 204' is written on the Tote bag. A Google search of the term clearly indicates the nature of the trial, and this could potentially breach participant privacy and confidentiality. The NREC-CT B requested that participants are provided with a Tote bag that does not display trial branding / identifiers or a justification provided.
- The NREC-CT B noted that home health visits will be carried out during the trial by a 'home health care provider' and requested further detail on the nature of these visits conducted by the home health care provider, specifically:
    - Details as to the contractual relationship and indemnity arrangements between the home care provider company and the trial sponsor
    - Details as to the training provided to home care providers
    - Details as to the monitoring in place for participants as they complete the e-diary– will there be live monitoring?
    - Details as to the reporting relationship between the home care provider and the PI and details of arrangements in place should a participant display a psychological issue / suicidal ideation.
- The NREC-CT B noted the inclusion of an e-diary and noted that completion of this e-diary may be triggering to participants and requested the following details:
    - Acknowledgement in the PISCF that completion of this ediary may cause distress;
    - Clarification as to the pathway of care and referral offered to participants displaying suicidal ideation.
- The NREC-CT B noted that participants are offered a stipend for regular use of the e-diary, which may be seen as an inducement to participate and requested that participants are not provided with a stipend for completing the e-diary or a strong justification to be provided.
- The NREC-CT requested the following is amended in the PISCF documents –
    - The terms 'metabolic parameters' and 'biomarker testing,' are clearly explained to participants;
    - Procedures such as ECG and U/S are described as 'non-invasive';
    - The term 'TARTS' is clearly explained, and details are provided in the Protocol as to how this will be discussed with participants, considering the sensitive nature of the condition.

- The NREC-CT B requested that clarity is provided in the PIS/ICF regarding genetic testing for optional research, and to note the following;
    - The genetic testing requested must be restricted, defined and clearly explained to participants in the PISCF;
    - Explicit consent obtained for genetic testing needs to be in a separate ICF document;
    - Further ethical approval will need to be obtained before any unrelated research can take place using these samples.
- The NREC-CT B noted that participants are required to follow a restricted diet while participating in the trial and that the Food Guidance Document does not sufficiently describe the dietary requirements. The NREC-CT-B requested the following:
    - That the dietary requirements participants are requested to follow are clearly explained in Food Guidance Document, using lay terminology, and a more detailed account of the specific dietary requirements required are also elucidated in the PISCF
    - Details on the supports available to participants when following these dietary requirements, which should be elucidated in the PISCF;
    - The ICF document should highlight the need for participants to adhere to a specific diet while participating in the trial.
    - That a more detailed account of the requirement to complete an e-diary is elucidated in the PISCF.
- The NREC-CT noted that section F5 of the NREC Application Form states that results from the Trial will be available to participants upon request to the Study Investigator, however this is not mentioned in the PISCF. The NREC-CT requested that this is added to the PISCF.
- The NREC- noted that the consent material layout in the Optional Pre-screening document is not in line with best practice and requested that the applicant provides participants with a layered approach to consent.
- The NREC-CT B noted that the SSA for Beaumont Hospital is lacking in sufficient detail and requested that a more comprehensive SSA is provided.

22-NREC-CT-151

Principal Investigator: Prof. Michael O'Reilly

Study title: A Randomized, Double-Blind, Placebo-Controlled Study to Evaluate the Efficacy and Safety of SPR001 (Tildacerfont) in Reducing Supraphysiologic Glucocorticoid Use in Adult Subjects with Classic Congenital Adrenal Hyperplasia

EudraCT: 2019-004765-40

- NREC-CT comments:

- The NREC-CT B agreed that additional information was required to inform its deliberations before a final ethics position could be returned.

- NREC-CT Decision:

- Request for more information

- Additional Information Required RFI

- The NREC-CT B noted that race and ethnicity data is being collected from participants and requested details on the scientific value of collecting such data.
- The NREC-CT B requested further information on recruitment, specifically:
    - How participants are recruited to the trial;
    - The justification for limiting participants to those attending the study team's own clinics;
    - Further details on the availability of translators to support participants who do not speak English as their first language, including a more detailed description of how this will work in practice, and what arrangements are in place for participants who may not adequately understand verbal or written information.
    - Similarly, rather than using an independent witness, can provisions be made for those with visual impairment to consent for themselves if required, e.g., braille or Browse Aloud software?
- The NREC-CT B notes that participants will be provided with a Tote bag, and request clarification on the following:
- The Tote bag appears to have a foil lining. Details on whether there are temperature control requirements for the trial drug should be clarified, and if necessary, added to the Protocol and PISCF.
- The NREC-CT B noted that the 'Cahmelia 204' is written on the Tote bag. A Google search of the term clearly indicates the nature of the trial, and this could potentially breach participant privacy and confidentiality. The NREC-CT B requested that participants are provided with a Tote bag that does not display trial branding / identifiers.
- The NREC-CT B noted the inclusion of an e-diary and noted that completion of this e-diary may be triggering to participants and requested the following details:
    - Acknowledgement in the PISCF that completion of this ediary may cause distress;
    - Clarification as to the pathway of care and referral offered to participants displaying suicidal ideation.
- The NREC-CT B noted that participants are offered a stipend for regular use of the e-diary, which may be seen as an inducement to participate, and requested that

participants are not provided with a stipend for completing the e-diary or a strong justification to be provided

- The NREC-CT noted that it is the responsibility of the Study Investigator to inform participants about incidental findings and requested further detail on this process.
- The NREC-CT B also requested that participants are given the option of opting out of being informed about incidental findings
- The NREC-CT noted that section F5 of the NREC Application Form states that results from the Trial will be available to participants upon request to the Study Investigator, however this is not mentioned in the PISCF. The NREC-CT requested that this is added to the PISCF.
- The NREC-CT B noted that participants are required to follow a restricted diet while participating in the trial and that the Food Guidance Document does not sufficiently describe the dietary requirements. The NREC-CT-B requested the following:
    - That the dietary requirements participants are requested to follow are clearly explained in Food Guidance Document, using lay terminology, and a more detailed account of the specific dietary requirements required are also elucidated in the PISCF
    - Details on the supports available to participants when following these dietary requirements, which should be elucidated in the PISCF;
    - The ICF document should highlight the need for participants to adhere to a specific diet while participating in the trial.
    - That a more detailed account of the requirement to complete an e-diary is elucidated in the PISCF
- The NREC-CT B requested that clarity is provided in the PIS/ICF regarding genetic testing and noted that genetic testing requested must be restricted and defined and clearly explained to participants in the PISCF.
    - Furthermore, explicit consent obtained for genetic testing need to be in a separate ICF document.
- The NREC-CT B also noted that further ethical approval will need to be obtained before any unrelated research can take place using these samples
- The NREC- noted that the consent material layout in the Optional Pre-screening document is not in line with best practice and requested that the applicant provides participants with a layered approach to consent.
- The NREC-CT B noted that the SSA for Beaumont Hospital is lacking in sufficient detail and requested that a more comprehensive SSA is provided.
- The NREC-CT B noted that section of the Application Form G4, Conflict of Interest, has not been completed and requested that this is completed.
- The NREC-CT B requested that the CVs of both the PI, Prof O'Reilly, and Dr Dennedy are revised to include previous clinical trial experience and evidence of current ICH-GCP certification

- The NREC-CT B noted that the submitted DPIA was not sufficiently trial-specific and requested that the DPIA is amended to include details regarding the data processing and confidentiality measures in place for third party vendors, including the TrialPACE App, the Scout and Home Care Providers.
- The NREC-CT B noted use of apps for sensitive information and would like confirmation appropriate security updates will be pushed to users as needed.
- The NREC- B noted that the study insurance certificate provided does not cover the whole trial duration and requests assurance that the trial will be adequately insured for the whole duration and will cover all sites.
- Furthermore, the NREC-CT noted that OLE is not included on the Insurance Certificate and requested that this is amended.

- AOB:

The Chair closed the meeting