National Research Ethics Committee

NREC-CT B Meeting

11 January 2023

Attendance

Name	Role
Dr Cliona McGovern	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
Dr Eimear McGlinchey	Committee Member, NREC-CT B
Mr Gavin Lawler,	Committee Member, NREC-CT B
Ms Paula Prendeville	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 David Smith	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
Dr Jane Bryant	Programme Officer, National Office for RECs

Dr Susan Quinn	Programme Manager, National Office for RECs
Dr Emma Heffernan*	Project Officer, National Office for RECs

*Drafted minutes

Apologies: Prof. Colm O'Donnell, Dr Jean Saunders, Mr Philip Berman, Prof Andrew Green, Prof. Abhay Pandit & Prof. John Faul

Quorum for decisions: Yes

Agenda

- Welcome & Apologies
- 2022-500275-31-00
- 2022-501417-31-00
- 2022-501007-28-00
- 22-NREC-CT-186
- 22-NREC-CT-179
- AOB

- The Chair welcomed the NREC-CT B.
  - The minutes from the previous NREC-CT B meeting on 23 November 2022 were approved.
  - The NREC Business Report was discussed and noted.

Applications

2022-500275-31-00

Principal Investigator: Prof. Niamh O'Connell

Study title: A phase 3b open-label, multicenter study evaluating physical activity and joint health in previously treated patients ?12 years of age with severe haemophilia A treated with intravenous recombinant coagulation factor VIII Fc-von Willebrand Factor-XTEN fusion protein (rFVIIIFc-VWF-XTEN; efanesoctocog alfa) for 24 months

EudraCT: 2022-500275-31-00

Lead institution: St James's Hospital

- 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 The NREC-CT requested further information on when and how an Impartial Witness would be used in the informed consent process, as detailed on Page 14 of the Main PIS-ICF. The HSE National Policy for Consent in Health and Social Care Research (https://hseresearch.ie/wp-content/uploads/2022/12/HSE-National-Policy-for-Consent-in-Health-and-Social-Care-Research-web.pdf) contains information on the context for Impartial Witnesses in Ireland.
- The NREC-CT requested clarification on how long participants' personal data will be stored, as durations of both 7 and 15 years are listed in the PIS-ICF documents (Main PIS-ICF Page 17, Pregnant Participant PIS-ICF Page 7).

2022-501417-31-00

Principal Investigator: Prof Fergal Kelleher, Dr Jarushka Naidoo

Study title: A Phase 3, Randomized, Double-blind, Active-Comparator-Controlled Clinical Study of Adjuvant MK-7684A (Vibostolimab with Pembrolizumab) Versus Adjuvant Pembrolizumab in Participants with High-risk Stage II-IV Melanoma (KEYVIBE-010)

EudraCT: 2022-501417-31-00

Lead institution: St James's Hospital, Beaumont Hospital

- 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 The NREC-CT noted that the EMA provided scientific advice on the study design, specifically regarding the choice of participant group for investigation of this IMP in combination with the Standard of Care (SoC), and the comparison to the small sample size of the participant group in the previous study of this IMP. The NREC-CT requested clarification on whether this advice has been acted upon in the current protocol
- The NREC-CT noted the number of scans proposed for participants as part of the trial and follow up may be considered excessive participant burden, and requested that further justification be provided, and information on the cumulative risks of all scans be added to the Main Consent Form.
- The NREC-CT requested that further information on long-term side effects of the IMP should be included in the Main Consent Form.

2022-501007-28-00

Principal Investigators: Dr Deirdre O'Mahony, Prof. Janice Walshe, Dr Jennifer Westrup, Dr Michael Martin, Prof. Patrick Morris, Prof. Seamus O'Reilly

Study title: EMBER-4: A Randomized, Open-Label, Phase 3 Study of Adjuvant Imlunestrant vs Standard Adjuvant Endocrine Therapy in Patients who have Previously Received 2 to 5 years of Adjuvant Endocrine Therapy for ER+, HER2- Early Breast Cancer with an Increased Risk of Recurrence

EudraCT: 2022-501007-28-00

Lead institutions: Bon Secours, St Vincent's University Hospital, The Beacon, Sligo University Hospital, Beaumont Hospital, Cork University Hospital

- NREC-CT comments:

- The NREC-CT 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 The NREC-CT noted that the EMA provided scientific advice on the study design, specifically regarding the limited efficacy and safety data from previous investigation of this IMP. The NREC-CT requested clarification on whether this advice has been acted upon in the current protocol.
- The NREC-CT noted that the submitted insurance certificate is expired, and requested submission of an up-to-date document

- The NREC-CT noted that reference is made to contacting the participants' GP, and requested that the GP Letter be submitted for review.
- The NREC-CT requested further information on how long a participant will have to consider their participation during the informed consent process, and suggested a minimum of 24 hours.
- The NREC-CT requested greater emphasis on the right of the participant to withdraw at any time, as detailed in the Dr to Patient Letter
- The NREC-CT noted that there are a number of formatting and typographical issues in the Main ICF, including reference to ulcerative colitis; and recommended a full review to enhance readability and comprehension, and correct formatting issues. A short summary of the PIL at the start of the document may also be beneficial.
- The NREC-CT requested clarification on whether the samples for genetic research, tissue samples and biomarker analysis are individually optional or mandatory. There is inconsistent information in the PIL and ICF. If optional, it is recommended to have a separate ICF or section in the Main ICF to consent participants for same.
- The NREC-CT requested clarification on the antibody study included in the ICF that is not described in the PIL.
- The NREC-CT noted that participants should contact the Data Protection Commission with concerns around personal data use and requested that a contact email for the site DPO be added to this section of the Main ICF to handle initial queries.
- The NREC-CT requested the PIL section on expenses be reviewed to make it clear to participants what is and isn't covered if they participate in the study.
- The NREC-CT requested clarification on how long participants' personal data will be stored for, as durations of both 7 and 15 years are detailed in the Main ICF.
- The NREC-CT requested that the dietary advice regarding consumption of grapefruit and the risk of photosensitivity be added to the Participant Information Card. It is also recommended that this information be emphasized more prominently in the Main ICF.
- The NREC-CT noted that technical jargon is used in description of side effects in pages 7-10 of the Main ICF, and requests that lay language is added to these descriptions.
- The NREC-CT noted the PIL includes reference to 'information on your newborn' being gathered if unanticipated births happen and would encourage a more specific statement is included for participants on the type of information that would be gathered.
- The NREC-CT noted the number of scans proposed for participants as part of the trial and follow up may be considered excessive participant burden, and requested that further justification be provided on effect on risk/benefit of partaking, and information on the cumulative risks of all scans be added to the Main Consent Form.

22-NREC-CT-186

Principal Investigator: Dr Maria Byrne

Study title: The cardiovascular safety of cagrilintide 2.4 mg s.c. in combination with semaglutide 2.4 mg s.c. (CagriSema 2.4 mg/2.4 mg s.c.) once weekly in participants with obesity and established cardiovascular disease

EudraCT: 2021-005855-35

Lead institution: The Mater Misericordiae University Hospital

- 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 requested clarification as to whether either of the trial drugs are considered the Standard of Care for obesity in Ireland and requested further information on trial participants eligibility for Semaglutide, which is approved for treatment of obesity. The NREC-CT queried if either of the trial drugs become standard of care during the lifetime of trial, how this will be managed in participants receiving the placebo. The NREC-CT recommended that participants be screened regularly throughout the 3-year study to deem whether they would be eligible for standard of care.
- The NREC-CT noted that the trial will not include a data monitoring committee and requested justification for this.
- The NREC-CT noted that the submission did not include a GP letter and requested that a GP letter is provided for committee review.
- The NREC-CT requested that reference to the use a ‘legal representative’ in section E13 of the NREC Application Form is revised in line with regulations.
- The NREC-CT requested the reference to ‘impartial witness’ in section E10 of the NREC Application Form is removed as it is not in line with regulations.
- The NREC-CT noted that participants will be required to undergo an eye exam and requested that participants are advised to bring a companion with them for this examination, due to the potential side effects of the eye drops.
- The NREC-CT noted that the PI will decide if potential participants have sufficient English language skills to participate in the study. The NREC-CT requested that participants who do not speak English are not excluded from the trial and detail is provided as to how these participants will be accommodated to participate in the trial.
- The NREC-CT requested that the radio advertisement advises participants that expected length of participation in the trial is 3 years.

- The NREC-CT noted that participant's health status will be ascertained from publicly available resources and requested clarification is provided as to what this entails.
- The NREC CT noted the use of the term 'dummy medicine' is used throughout the PIL and requested that this term is replaced with the term 'placebo' and that this term is explained in the PIL.
- The NREC-CT requested that further information is provided to participants in the PIL on the reason for the requirement to remove clothes during study visits.
- The NREC-CT requested further details are provided in the PIL as to the rationale for breast checks for female participants.
- The NREC-CT noted that one of the potential side effects of the IMP includes dizziness and advises participants to be careful driving or using machines. The NREC-CT requested that if participants experience dizziness, they should be advised to report it to their study doctor who will assess their safety and ability to drive or use machinery.
- The NREC-CT noted that on pg. 12 of the PIL care and access to expertise is described as a potential benefit of study participation and requested that this is removed and that participants are advised that they may or may not get a benefit from participating in the trial.
- The NREC-CT noted that participants are advised to contact NREC should they wish to talk to for more information and requested that this is changed to the local hospital site.
- The NREC-CT noted that the consent material layout is not in line with best practice and requests that the applicant provides participants with a layered approach to consent.
- The NREC-CT requested that blank pages are removed from the PIL/Consent
- The NREC-CT noted that the participant signature on the consent form is on a separate page and requested that the signature section is integrated into the main consent form and not on a separate page.
- The NREC-CT noted that participants are provided with certificates of achievement at various points throughout the trial and considered these to be not appropriate and may unduly influence the participant to continue in the study. NREC-CT recommended removal of these certificates.
- The NREC-CT noted that NREC is listed as having access to personal medical files in the PIL and requested that this is removed.
- The NREC-CT noted that participants are provided with a kit including a cool bag requested confirmation that all components of the kit / cool bag are unbranded.
- The NREC-CT noted that pg. 11 of the PIL states 'Information about you, your pregnancy and your baby will be collected' and requested that the consent form is updated to include a section seeking this approval from women in the event they become pregnant.
- The NREC-CT requested that pg.3 of the PIL also includes reference to participant's GP, as a person they may like to talk to.
- The NREC-CT noted that the NREC Application Form states that participant's GPs may be contacted for information and requested that this is explained in the PIL and is added to the consent form.

- The NREC-CT noted that section C.6 of the NREC Application Form refers to 6 participating sites in Ireland and noted that only 5 SSAs have been submitted. The NREC-CT requested clarification as to the number of participating sites in Ireland, noting that an SSA must be submitted for each participating site.
- The NREC-CT noted that one of the PIs on the trial, Prof Carel Le Roux is a member of Novo Nordisk's International Advisory Board and requested clarification on his role within the Advisory Board and if there is a conflict of interest which may impact his suitability as a PI on this trial.
- The NREC-CT requested evidence of up-to-date ICH-GCP certification is provided for all site Principal Investigators.
- The NREC-CT noted that the funding amount is not provided in section G3 of the NREC Application Form and requested that this is amended.
- The NREC-CT deemed that the maximum stated compensation for each trial visit is €20 which seems very low in an Irish context and may leave participants out of pocket. The NREC-CT requested confirmation that participants will be reimbursed for all reasonable out of pocket expenses. The NREC-CT requested that it is made clear to participants in the PIL and includes details on the process involved for claiming expenses.

22-NREC-CT-179

Principal Investigator: Dr John Kelly

Study title: A Pilot Study to Assess the Use of Methylone in the Treatment of Post-PTSD IMPACT-1 (Investigation of Methylone for Post-Traumatic Stress Disorder [PTSD])

EudraCT: 2022-000484-42

Lead institution: Sheaf House, Trinity College Dublin and Tallaght University Hospital

- 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 requested further information is provided on the evidence base for this study.
- The NREC-CT requested further detail on the recruitment process.

- The NREC-CT noted that participants will be tested for drugs of abuse and requested justification for the focus on testing for drugs of abuse among the participant population.
- The NREC-CT noted that reference is made to a 'qualified trained mentor' and requested clarification is provided as to the training and competence of this support person.
    - Furthermore, the NREC-CT requested further clarification as to the purpose and role of the mentor in the trial.
- The NREC-CT noted that participation in the trial is quite onerous on participants and is not well described in the PIL. The NREC-CT requested that a clearer description of the trial requirements is provided in the PIL.
- The NREC-CT noted that participants are required to provide passport / ID and photographs and requested justification for this.
- The NREC-CT requested that all references to UK based entities such as NI number are moved and replaced with appropriate Irish references.
- The NREC-CT noted that section E7 states that participants must be able to speak and understand English and the NREC-CT requested that this is amended in line with Irish legislation.
- The NREC-CT requested justification for the exclusion of potential participations who are not English speakers.
- The NREC-CT requested that a summary PIL is provide for each arm of the study.
- The NREC-CT noted that the NREC Application Form makes reference to biological materials, yet these are not categorised as data in PIS ICF (p.14). The NREC-CT requested that biological samples are categorised as data on pg. 14 of the PISCF and listed in the consent section on pg18.
    - Furthermore, it needs to be clearly stated how long this data will be retained.
- The NREC-CT noted that reference is made to supports being available to participants and requested the following information:
    - Details as to the type of supports available to participants, such as psychological support / emergency support in the case of drug reaction.
    - Details to the support arrangements for participants should they require support when at home.
- The NREC-CT noted that pg. 4 of the PIL states that participants must not drink more than 3 litres of water over the course of each dose session and requested that the rationale for this is elucidated in the PIL.
- The NREC-CT noted that participants are not allowed to discuss their participation in the trial in the media or on the internet and requested the following:
    - Justification for this stipulation
    - Details as to how this will be monitored during the trial.
    - Details as to the potential implications for participants should they discuss the trial in the media or Internet.

- The NREC-CT noted the print is too small in the ICF schedule and may prove difficult for participants to read and requested that this is enlarged.
- The NREC-CT requested clarification is provided for participants in the PIL for ascertaining menopausal status in trial participants.
- The NREC-CT noted that Pregnant Participant / Partner PISCF (p.4) suggests retaining data on a pregnancy or child for at least 25 years and requested that the processes in place for obtaining the consent of the child, on reaching the age of 18, for the retention of their personal data is described in line with Irish data protection law (Data Protection Act 2018 (Section 36(2)) (Health Research) Regulations 2018
- The NREC-CT noted that consent for future research described on pg. 13 and pg14.of the PISCF is seeking blanket consent for future use of samples / data, for unspecified purposes, without further consent. This type of consent not in line with best practice, the Declaration of Taipei 2016 and not in compliance with the Data Protection Act 2018 (Section 36(2) (Health Research) Regulations 2018), where informed participant consent is a mandatory safeguard. The NREC-CT requests i) that consent for future use of samples is provided on a separate consent form and not bundled ii) is made optional, and iii) consent can only be obtained where future use of samples and data is defined such that participants are fully informed, and/or iv) that an option is provided to enable participants to consent to be contacted is provided in a separate consent form.
- The NREC-CT requested confirmation that subsequent research ethics review will be sought for specific research once clearly defined.
- The NREC-CT noted a number of typos across the PISCF and requested that all documents are thoroughly proof-read for accuracy,
- The NREC-CT requested that further details are provided as to the clinical expertise of both PIs in managing PTSD.

  The NREC-CT noted that consent for data retention is undefined and requested that this is amended and aligned across all relevant documentation.
- The PIA states that data ‘may be destroyed’ and requested that it is changed to ‘data will be destroyed’.
- The NREC-CT noted that all sessions will be video recorded and requested the following:
    - Justification for the recording of these sessions.
    - Further detail as to how participants identities will be protected.
    - Clarification as to whether participants will have the option to opt out of video recording.
    - A detailed description of the data protection arrangements in place for the use of video recording, in line with current regulations.
    - The use of videorecording is listed in the consent form.
    - It is specified that participants may have a significant reaction to the medication, and this would be recorded. This is a concern as it places the participant in a vulnerable position and perhaps could elevate their anxiety.

Addressing the safety of the patient and the potential that being videoed could compound their reaction needs further clarity.

  - Further details on what happens to these video recordings in terms of storage, security, retention and who will be able to access them.

- The NREC-CT requested clarification as to how participants will be adequately compensated for their time and effort, considering participating in the trial may impact their ability to undertake paid employment.
- The NREC-CT noted that participants are only being compensated for food and travel and requested that a more detailed account of the compensation available to participants is provided in the PISCF, as well as a description of the process involved in claiming expenses.

- AOB: