National Research Ethics Committee

NREC-CT B Meeting

08 February 2023

Attendance

Name	Role
Dr Cliona McGovern	Chairperson, NREC-CT B
Mr Philip Berman	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
Ms Paula Prendeville	Committee Member, NREC-CT B
Prof. Colm O'Donnell	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
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 of Office, National Office for RECs
Ms Rachel McDermott	Programme Administrator, 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. Abhay Pandit, Ms Caoimhe Gleeson, Ms Serena Bennett, Prof. John Faul, Dr Jean Saunders, Ms Mandy Daly, Mr Gavin Lawler

Quorum for decisions: Yes

Agenda

- Welcome & Apologies
- 23-NREC-CT-007
- 23-NREC-CT-009
- 23-NREC-CT-010
- 23-NREC-CT-013
- 22-NREC-CT-179
- AOB

- The Chair welcomed the NREC-CT B.
  - The minutes from the previous NREC-CT B meeting on 11 January 2023 were approved.
  - The NREC Business Report was discussed and noted.

Applications

23-NREC-CT-007

Principal Investigator: Prof Christopher McGuigan

Study title: A randomized, double-blind, double-dummy, parallel-group study, comparing the efficacy and safety of remibrutinib versus teriflunomide in participants with relapsing multiple sclerosis, followed by extended treatment with open-label remibrutinib

EudraCT: 2020-005899-36

Lead institution: St. Vincent's 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 details of the standard of care for relapsing multiple sclerosis (RMS) in Ireland. The NREC-CT requested clarification as to whether standard of care treatment will be withheld from participants as a result of participation in the trial and requested clarification as to what would happen if the trial drug proved inefficacious.
- The NREC-CT noted that participants will be on an arm of the trial for a long period (up to 2.5 years) and requested details of the monitoring and support provided to those not benefitting.
- The NREC-CT requested further information is provided regarding the potential advantages for a participant to enrol in the trial, where they have a 50/50 chance of being given a drug already approved for RMS and a 50/50 chance of being given an unproven drug.
- The NREC-CT requested that alternatives to trial participation are clearly explained to participants in the PISCF.
- The NREC-CT noted that this study goes directly to phase III without an intervening phase II study and requested the following:
- The NREC-CT noted that the Direct to Phase 3 Rationale Document, appears to be missing its appendix section (including detail of The FDA Type C pre-IND Meeting minutes and the EMA ’s Scientific Advice Letter) and requested that the complete document is made available for review.
- The NREC-CT requested detail as to the current status of the trial drug regarding regulatory review, feedback and approval (FDA, EMA & HPRA).
- The NREC-CT requested that details regarding any global interim analysis conducted to date is provided to NREC-CT for review.
- The NREC-CT noted the recruitment arrangements in Ireland are not well described and requested the following:
- The NREC-CT requested that the total number of participants expected to be recruited in Ireland and at each site is added to the Application Form
- The NREC-CT requested further detail on trial recruitment to date, from a global perspective.
- The NREC-CT noted a number of typos /errors in the Application Form and requested that this document is thoroughly reviewed for errors and amended accordingly.

- The NREC-CT noted that the GP letter states that the core part of the study will last 30 weeks while other documents state 30 months and requested that this is corrected and aligned across all documentation.
- The NREC-CT noted the inclusion of a C-SSRS and requested the following:
    - details of provisions in place to support participants, should the questionnaire indicate a mental health issue:
    - Details of the training and qualifications of the person administering the C-SSRS
    - Acknowledgement in the PIL/ICF that completion of this assessment may cause distress, and clarification as to the pathway of care and referral offered to participants displaying a mental health issue.
- The NREC-CT noted that participant participants are advised to talk to their friends and relatives regarding participant in this trial and requested that the participant's GP is also added to this list.
- The NREC-CT noted that the potential benefits of trial participation is listed as having access to expert medical care and requested that this is removed.
- The NREC-CT noted that the optional / genetic consent forms are vague in their description of what these additional tests are being done for, and requested that these forms are amended in line with the HSE National Policy for Consent in Health and Social Care Research https://hseresearch.ie/wp-content/uploads/2023/02/HSE-National-Policy-for-Consent-in-Health-and-Social-Care-Research-compressed.pdf
- The NREC-CT noted that there is inconsistent use of terms for participants/ subjects/ patients across all documents and within documents, and recommended that this is aligned across documentation.
- The NREC-CT requested that CVs are provided for the PIs from TUH (Dr Karen O'Connell) and SJH (Dr Hugh Kearney), detailing previous clinical trial experience and evidence of up-to-date ICH-GCP certification, and their suitability to run this trial.
- The NREC-CT noted that the SSA for TUH has not been submitted and requested that this is submitted for review.
- The PISCF states that 'Some studies may use artificial intelligence (AI) as part of the study. The Sponsor is committed to using AI in an ethical way' and requested further detail on the proposed use of AI in the trial and that this is explained to participants in the PISCF.
- The NREC-CT noted that Pregnant Participant / Partner PISCF suggests retaining data for 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 commended the applicant for the excellent reimbursement arrangements in place.

23-NREC-CT-009

Principal Investigator: Prof Orla Hardiman

Study title: Phase IIIb, Open Label Extension Study Evaluating The Safety And Tolerability of AMX0035 Up To 108 Weeks In Adult Participants with Amyotrophic Lateral Sclerosis (ALS) Previously Enrolled In Study A35-004 (PHOENIX)

EudraCT: 2022-002348-33

Lead institution: 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 NREC-CT noted that if study participants are unable to visit the study site, then a local GP or home nurse will be asked to take blood samples and requested further detail on this process, including data protection arrangements / anonymisation procedures in place.
- The NREC-CT requested a more detailed account of the recruitment arrangements is described in the Application Form.
- The NREC-CT requested that a lay summary PISCF is made available for participants, highlighting the pertinent issues that trial participation will involve. This NREC guide may be useful: https://www.nrecoffice.ie/pil-summary-guidance/
- The NREC-CT noted a number of typos and requested that documents are thoroughly proofread for accuracy and amended accordingly.
- The NREC-CT requested that it is explained to participants in the PISCF the reason why they return all unused, unopened sachets as well as all empty sachets and drug boxes to the study site.
- The NREC-CT suggested that information in the appendix of the PISCF should be moved into the body of the PISCF as it is core information to the study.
- The NREC-CT requested that an explanation of the term ‘long-term living status’ (p10), should be provided to the participant.
- The NREC-CT noted that the confidentiality statement (p10) contradicts what is later stated in the data protection section and requested that this is aligned.

- The NREC-CT requested that details of who the Drug Safety Monitoring Board are, and the role that have they in this study is clearly explained to the participant.
- The NREC-CT noted that there is incomplete information provided on Pg 13/14, and requested a detailed edit is required to ensure it aligns with EU data requirements not US data requirements.
- The NREC-CT noted that future use of data is confined to the disease area and requested the following:
    - That consent for future use of samples is provided on a separate consent form and not bundled.
    - Consent for future use is made optional for study participation.
- The NREC-CT noted that data is being transferred outside of EU and requested that the data protection arrangements in place are clarified.
- The NREC-CT requested a more detailed account of the compensation arrangements including travel reimbursement, in place for participants is provided in the PISCF including information of the process involved in reimbursement of trial related expenses.

23-NREC-CT-010

Principal Investigator: Prof Glen Anthony Doherty

Study title: A Combined Phase 2 (12 Weeks)/Phase 3 (52 Weeks), Randomized, Double-blind, Placebo-controlled Multicenter Study Investigating the Efficacy and Safety of AMT-101 in Subjects with Chronic Pouchitis.

EudraCT: 2020-000048-73

Lead institution: St. Vincent's 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 noted that a GP letter was not included in the submission and requested that a GP letter is provided for review.
- The NREC-CT noted that 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 request confirmation that subsequent research ethics review will be sought for specific future research once clearly defined.

- The NREC-CT requested that reference to NREC having access to study information is removed from the PISCF.
- The NREC-CT queried whether the Ireland (English) versions of the Validated Questionnaires were now available for submission to the ethics committee, as per the cover letter.
- The NREC-CT noted that 3rd party data access has not been addressed and requested that this is amended across all relevant documentation.
- The NREC-CT noted that participants are advised that they 'may' be reimbursed for trial related expenses and requested that this is changed to 'will' be reimbursed.
- the NREC-CT requested that the PISCF is amended to make it clear to participants what trial related expenses can be claimed and the process involved in reimbursement.

23-NREC-CT-013

Principal Investigator: Prof Orla Hardiman

Study title: A Phase 2,Randomized, Double-Blind, Placebo-Controlled, Parallel Study to Assess the Efficacy, Safety, Tolerability, PK, and Biomarker Effects of PTC857 in Adult Subjects With Amyotrophic Lateral Sclerosis (CARDINALS)

EudraCT: 2021-006511-29

Lead institution: 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 NREC-CT requested justification for the number of participants on the PK arm**.**

- The NREC-CT requested justification for the upper age limit in the eligibility criteria.
- The NREC-CT noted that patients with a personal or first-degree family history of breast cancer are excluded from the study and queried why patients with ductal cancer in situ are also not excluded.
- The NREC-CT noted that participants are to undergo regular mammograms and requested that a breast exam is also performed during the physical exam, considering the potential side effects of the trial drug.
    - Furthermore, the NREC-CT requested that the follow-up period is extended beyond 5 years should a tumour develop outside of the study window.
- The NREC-CT noted that the consent process is not well described in the Application Form and requested that a more detailed account of the consenting process is added.
- The NREC-CT noted that participants are required to reuse syringes and requested that participants are provided with single use disposable syringes.
- The NREC-CT noted that the study groups are not described on pg. 4 of the PISCF and requested this is amended.
- The NREC-CT requested that reference to the CSF risks is removed from the PISCF, as this procedure is not part of the trial in Ireland.
- The NREC-CT requested that NREC is removed from the list of study contacts.
- The NREC-CT noted the inclusion of a C-SSRS and requested the following:
    - Details of provisions in place to support participants, should the questionnaire indicate a mental health issue:
    - Details of the training and qualifications of the person administering the C-SSRS.
    - Acknowledgement in the PISCF that completion of this assessment may cause distress, and clarification as to the pathway of care and referral offered to participants displaying a mental health issue.
- The NREC-CT noted that participants are required to complete a lengthy set of questionnaires and requested details of provisions in place should participants have difficulty in completing questionnaires, due to the nature of the condition / issues with motor skills.
- The NREC-CT noted that an impartial witness / carer is included in the consent form and requested that a statement is provided to clarify that the impartial witness / carer is not consenting on the participant's behalf, and that signed participant consent is still required.
- The NREC-CT requested clarity regarding consenting of participants onto the trial, who lack decision-making capacity. The Committee noted that the amendment (S.I. No. 18 of 2021) to the Data Protection Act 2018 (Section 36(2) (Health Research) Regulations) in 2021 provides for participants who lacks decision-making capacity to be enrolled in a study in the absence of consent, if the study is in the vital interest of the person. Note, a legal representative cannot lawfully consent for the processing of personal data for health research, on behalf of a participant who lacks decision-making capacity to consent.

    - The applicants must specify whether they are relying on this amendment. If not, it will be necessary to apply for a consent declaration from the HRCDC to ensure compliance with the Regulations.

- The NREC-CT requested reference to the Health Research Regulations 2018, and if required, to the Health Research Consent Declaration Committee in participant materials and is clearly included in the consenting process.
- The NREC-CT noted that the PISCF (main, LTE) is seeking blanket consent for future / additional use of samples / data, for unspecified purposes, without further consent. This type of consent is 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 in a separate consent form.
    - The NREC request confirmation that subsequent research ethics review will be sought for specific research once clearly defined.
- The NREC-CT noted that Pregnant Partner PISCF suggests retaining health data for 50 years and requested the following:
    - Justification for the retention of data for 50 years
    - Details of the process 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 in the PISCF and the DPIA there is reference to ‘’personal data’, ‘coded personal data’ and ‘’personal coded data’ and that these terms are used interchangeably making it difficult to decipher what personal data is available to whom and requested that this is amended.
- The NREC-CT requested that evidence of up-to date ICH-GCP certification is provided for the PI.
- The NREC-CT requested the following:
    - A detailed description of the trial related expenses participants are permitted to claim (such as travel, parking, refreshments, etc.) is provided in the PISCF and welcome letter, so participants are reassured that trial participation will not leave them out-of-pocket.
    - Details as to how overnight accommodation will be accommodated especially if participants require an overnight stay in Dublin, which may be expensive and could leave participants out of pocket.
    - Details on the process involved in claiming expenses and how and when they will be reimbursed.

- The NREC-CT requests that a participant should be permitted to bring a companion for these visits, and that this companion should also be eligible for reimbursement.

22-NREC-CT-079

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 The Committee was unable to give a favourable ethics opinion on the research

- NREC-CT Decision:

- Unfavourable

- Key reasons for Unfavourable Decision

- The The NREC-CT were not reassured regarding the support and safety provisions in place to protect participants throughout the trial.
- The NREC-CT deemed that insufficient safeguards were in place to protect participants should the trial halt prematurely in Ireland.
- The NREC-CT had concerns regarding participant burden, which were not alleviated following the response to RFI.
- The NREC-CT considered that the compensation proposed reflects undue inducement to participate in the study which was deemed unethical.

- AOB: