National Research Ethics Committee

NREC-CT Meeting

01 May 2024

Attendance

Name	Role
Prof Mary Donnelly	Chairperson, NREC-CT C
Prof John Faul	Deputy Chairperson, NREC-CT C
Dr Jean Saunders	Deputy Chairperson, NREC-CT C
Prof Austin Duffy	Committee Member, NREC-CT C
Prof Fionnuala Breathnach	Committee Member, NREC-CT C
Dr Susan Finnerty	Committee Member, NREC-CT C
Prof Andrew Smyth	Committee Member, NREC-CT C
Dr Steve Meaney	Committee Member, NREC-CT C
Dr Dervla Kelly	Committee Member, NREC-CT C
Ms Susan Kelly	Committee Member, NREC-CT C
Dr Deborah Wallace	Committee Member, NREC-CT C
Mr Gerry Eastwood	Committee Member, NREC-CT C
Mr Philip Berman	Committee Member, NREC-CT C
Prof Anne Mathews	Committee Member, NREC-CT C
Ms Aileen Sheehy	Programme Manager, National Office for RECs
Dr Laura Mackey	Programme Officer, National Office for RECs
Dr Susan Quinn	Programme Manager, National Office for RECs
Dr Emma Heffernan*	Project Officer, National Office for RECs
Ms Rachel McDermott	Project Administrator, National Office for RECs

Apologies: Ms Paula Prendeville

Quorum for decisions: Yes

Agenda

- Welcome & Apologies
- 22-NREC-CT-050_Mod-4
- 23-NREC-CT-025_Mod-2
- 2022-502442-27-00 SM1
- 2022-502684-37-00 SM3
- 2023-505874-14-00 SM2
- 22-NREC-CT-101_Mod-2
- 21-NREC-CT-122_Mod-4
- 2022-502937-24-00 SM1
- AOB

- The Chair welcomed the NREC-CT C.
  - The minutes from the previous NREC-CT C meeting on 03/04/2024 were approved.
  - The NREC Business Report was discussed and noted.

Applications

22-NREC-CT-050_Mod-4

Study title: A randomized, double-blind, parallel-group, multicentre, phase II study to compare the efficacy and tolerability of fulvestrant (FaslodexTM) 500mg with placebo and fulvestrant (FaslodexTM) 500mg in combination with PD0332991 (Palbociclib) as first line treatment for postmenopausal women with hormone receptor-positive metastatic breast cancer, who have completed at least 5 years of adjuvant endocrine therapy and remained disease free for more than 12 months following its completion or have “de novo” metastatic disease “The FLIPPER Study”

- **NREC-CT Decision:**

- Favourable

23-NREC-CT-025_Mod-2

Study title: A Phase 1-3 Study to Evaluate the Efficacy, Safety, Pharmacokinetics and Pharmacodynamics of Intrathecally Administered ION363 in Amyotrophic Lateral Sclerosis Patients with Fused in Sarcoma Mutations (FUS-ALS)

- **NREC-CT Decision:**

- Favourable

2022-502442-27-00 SM1

Institutions: University Hospital Galway, St Vincent's University Hospital, Connolly Hospital

Study title: A Phase 3, randomised, double-blind, parallel-group, event-driven, cardiovascular safety study with BI 456906 administered subcutaneously compared with placebo in participants with overweight or obesity with established cardiovascular disease (CVD) or chronic kidney disease, and/or at least two weight-related complications or risk factors for CVD

- **NREC-CT Decision:**

- Request for more information

- **Additional Information Required**

Part II Considerations

- **Subject information and informed consent form**
- The NREC-CT noted that pg. 7 of the PISCF states ‘If you do not have enough space in your fridge, you can discuss with your trial doctor for the options available’ and requested that the options available are described in the PISCF, so participants are fully informed.
- The NREC-CT noted that the description of ‘Anti-Drug antibodies/ Neutralising antibody (ADA/Nab)’ on pg. 9 of the PISCF is not presented using a participant friendly approach and requested that Anti-Drug antibodies/ Neutralising antibody (ADA/Nab) is explained to participants in the PISCF using plain English suitable for

a lay audience (a similar description to the one used in the L2_ Other subject information-e-glossary-script-IE document may be helpful)
    - This explanation should include an explanation of why the test needs to be undertaken and what the testing process involves for participants.
- The NREC-CT noted that a number of documents related to econsent have been submitted for review and requested clarification as to whether the sponsor is considering undertaking econsent in the future. The NREC-CT noted that any change to the current consenting process would require ethics approval and in the case of econsent, a strong justification should be provided.

2022-502684-37-00 SM3

Institutions: St Vincent's University Hospital

Study title: A Phase 1/2 First-in-Human Study of the Safety and Efficacy of IMC-F106C as a Single Agent and in Combination with Checkpoint Inhibitors in HLA-A*02:01-Positive Participants with Advanced PRAME-Positive Cancers

- **NREC-CT Decision:**

- Request for more information

- **Additional Information Required**

Part I Considerations

- Page 5 of the protocol describes a Study Procedures Manual, and this document should be submitted for review.

Part II Considerations

- **Subject information and informed consent form**
- The NREC-CT noted a reference to the NHS in the L1_SIS_and_ICF_Ireland_Combination_Therapy_Arm_D, L1_SIS_and_ICF_Ireland_Combination_Therapy_Arm_F, and L1_SIS_and_ICF_Ireland_IMC-F106C-101_Combination_Therapy_Arm_B_C_E_G documents and requested that these is updated to reference Irish entities.
- The NREC-CT requested that all comments referring to previous RFIs are removed from tracked change documents before re-submission.
- The NREC-CT requested that all previously approved changes to the PISCF documents are integrated and are not presented as tracked changes in documents, as this makes any new changes difficult to differentiate.
- The NREC-CT noted that the PISCF documents state that participant's personal data may be published and sent to regulatory authorities or health insurers in Ireland or other countries and requested clarification as to why a participant's personal data may be shared with their health insurers.
- Although not part of the substantial amendment, the NREC-CT noted that the L1_SIS and ICF_IRE_Main Monotherapy_Arm A PISCF (pg. 10) is seeking blanket consent for future 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 requested that future research is restricted to 'specified health research, either in relation to a particular area or more generally in that area or a related area of health research, or part thereof' (i.e. Lung Cancer) and this is clearly stated in the main body and informed consent sections of all relevant PISCFs.The NREC-CT requested the following:

- i) that consent for future use of samples is provided on a separate consent form (details regarding future described on pg. 10 the Main PISCF should be moved to a separate document that includes both a patient information section and an informed consent section, placeholders for the signatures of the person taking consent and the participant) and not bundled (a tick box for participant initials should be provided along each consent item)
- ii) is made optional
- 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 research that is outside the scope of the current research area, and this is captured in the PISCFs.

2023-505874-14-00 SM2

Institutions: Tallaght University Hospital, La Nua Day Hospital, Galway

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

- **NREC-CT Decision:**

- Request for more information

- **Additional Information Required**

Part I Considerations

- Please provide details as to what changes have been made to the questionnaires, as it is not clear from the submission.

Part II Considerations

- **Proof of insurance**
- The NREC-CT noted that the insurance certificate states that 20 participants will be enrolled in the study, whereas both the protocol and PISCF documents state that up to 79 participants will be enrolled (approximately 15 in Part A and up to 64 in Part 2). The NREC-CT requested that the insurance certificate is updated to reflect the correct number of potential participants.
- **Recruitment arrangements**

- The NREC-CT noted that the K2 Recruitment Material Pre-screening questionnaire and K2_ Recruitment Material_Online PreScreen contain sensitive questions and requested detail of any supports in place for participants who are deemed not eligible to participate in the study are explained in both documents.
- The NREC-CT noted that the K2_Recruitment Material_Pre-screening Questionnaire is seeking consent to use data as part of a prescreening process and requested further detail of who will be able to access this data, how will the data be used and how long will it be retained for, is clearly described in this document. It should include a clear description of what will happen to the data of participants who are later deemed ineligible to take part in the trial.
- The NREC-CT noted that K2 Recruitment Material Pre-screening questionnaire states that no travel expenses will be paid in Ireland, whereas elsewhere it states that travel expenses will be paid. The NREC-CT requested that it is clarified in the K2 Recruitment Material Pre-screening questionnaire that particpants will be reimbursed for travel expenses in Ireland. The NREC-CT always recommends that basic out-of-pocket expenses should be covered for all trial participants.
- **Subject information and informed consent form**
- The NREC-CT noted that pg. 10 of the PISCF states that participants may be able to enter an extension study and requested that a short description of the extension study is included for participants.
- The NREC-CT noted that pg. 4 of the PISCF states 'For your safety, we are asking you to not drink more than 3 litres of water or clear fluids' and requested that it is stated in the PISCF over what period of time this relates to i.e. over 24 hours.
- The NREC-CT noted that pg. 18 of the PISCF states that 'Representatives of government authorities… may inspect the study files' and requested that this is changed to is changed to 'relevant government competent authority…may inspect the study files'.

22-NREC-CT-101_Mod-2

Study title: A multi-center, randomized, double-blind, placebo-controlled, parallel-group Phase IIIb study evaluating the effect of inclisiranInclisiran on atherosclerotic plaque progression assessed by coronary computed tomography angiography (CCTA) in participants with a diagnosis of non-obstructive coronary artery disease without previous cardiovascular events (VICTORION-PLAQUE)

- **NREC-CT Decision:**

- Request for more information

- **Additional Information Required**

- The NREC-CT noted that an application has been made for 'addition of an option to obtain consent remotely' (pg. 1 Cover Letter) and requested the following:
    - Clarification as to whether the application for remote consent relates only to remote consent in context of public health emergencies. If so, this should be clearly stated in the cover letter and the protocol.

- Strong justification is provided for the addition of remote consent to the current consenting process. This should include detail as to whether this approach is suitable for trial population, the characteristics of the investigational medicinal product(s) (IMP), or the complexity of the trial, including potential risks, burdens, and benefits to the participant.
- A clear description of the remote consenting process should be provided in the protocol (The entire procedure for obtaining informed consent, i.e. the selection, the evaluation of the eligibility, and the actual informed consent process, should be described step-by-step). It would be expected that remote meetings and interviews, where relevant, should take place via a videocall.
- Clarifiation as to how it will be determined that the trial participants have understood the information and that their questions have been answered.
- Clarification as to how the identity of the trial participant and the investigator will be verified.
- Clarification as to how the discussion between the trial participant and the investigator will be captured.
- Clarification as to how the consent documents will be signed by both the participant and investigator.
- Clarification as to how the signatures of both the trial participant and investigator will be verified.
- Clarification as to how any physical exam would be undertaken in the absence of a face-to-face meeting.
- Clarification if participants will be given the option to have the informed consent process on site if this is the preference of either the participant or the investigator.
- Details as to the support available to participants to undertake remote consenting, i.e. IT support.
- Detail as to how the remote consent process complies with the S.I. No. 190/2004, GDPR and ICH-GCP.

21-NREC-CT-122_Mod-4

Study title: A Prospective Phase III Multi-center, 2-Year Placebo Controlled, Double Blind Study to Evaluate the Efficacy and Safety of “Kamada-AAT for Inhalation” 80 mg per Day in Adult Patients with Congenital Alpha-1 Antitrypsin Deficiency with Moderate and Severe Airflow Limitation (40% ≤ FEV1 ≤ 80% of predicted; FEV1/SVC ≤ 70%), Followed by a 2-Year Open-Label Extension

- **NREC-CT Decision:**

- Request for more information

- **Additional Information Required**

- The NREC-CT requested that participants are clearly informed on pg. 4 of the Main PISCF that participation in the open label extension is optional.

- The NREC-CT requested that participants are informed on pg. 4 of the Main PISCF that if they do not wish to continue into the Open Label Extension their participation in the current trial will not be impacted.
- The NREC-CT requested that explicit consent is sought for participation in the Open Label Extension in the Participant informed Consent Form.
- The NREC-CT noted that the letter 'A' is missing from the word 'Authorization' in the title of 5.5. Almac Patient Consent for Direct to Patient_Kamada-008 ver 1.0_14Mar2024 and requested that this is corrected.
- Although not part of the substantial amendment, the NREC-CT noted that future research as described in the Main PISCF refers to 'coded information' and requested clarification as to whether this refers to anonymised or pseudonymised data.
    - If the term 'coded information' relates to both anonymised and pseudonymised data, then participants should be informed which aspects of their information will be anonymised and which will be pseudonymised. Both terms should be explained to participants.
    - If future research involves anonymised data only then it should be explained to participants in the Main PISCF that this is optional.
- If the term coded information refers to pseudonymised data then this needs to be carried out in line with best practice, the Declaration of Taipei 2016 and 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 requested that future research is restricted to 'specified health research, either in relation to a particular area or more generally in that area or a related area of health research, or part and this is clearly stated in the main body and informed consent sections of the PISCF. The NREC-CT requested the following:
    - i) that consent for future use of samples is provided on a separate consent form (details regarding future use described on pg. 27). The Main PISCF should be moved to a separate document that includes both a patient information section and an informed consent section, placeholders for the signatures of the person taking consent and the participant) and not bundled (a tick box for participant initials should be provided along each consent item).
    - ii) consent for future research is made optional
    - 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, and this option is provided in a separate consent form.
    - The NREC requests confirmation that subsequent research ethics review will be sought for specific research that is outside the scope of the current research area, and this is captured in the PISCF.

2022-502937-24-00 SM1

Institutions: South Infirmary Victoria University Hospital, University Hospital Galway, St James's Hospital, University Hospital Waterford

Study title: A Phase 3 Randomized, Placebo-Controlled, Double-Blind Study to Evaluate Upadacitinib in Combination with Topical Corticosteroids in Adolescent and Adult Subjects with Moderate to Severe Atopic Dermatitis

- **NREC-CT Decision:**

- Request for more information

- **Additional Information Required**

Part I Considerations

- Please provide additional information on the studies M16-045 and M18-891 in the study protocol that would be included in the Long-Term Extension Period.
- Please provide justification for the 10-year extension to the trial.
- Please provide detail as to the trial end points in the protocol

Part II Considerations

- **Subject information and informed consent form**
- The NREC-CT noted that the requirement for WOCBP not to become pregnant over the course of the 10-year extension may have a significant impact on family planning for participants and requested that greater emphasis is placed on this in the M16-047 IE - ICF LTE English PISCF.
- The NREC-CT requested that participants are informed on page 20 of the M16-047 IE ICF Country Sample - Redline Informed Consent Main English PISCF that participating in the long-term extension is optional.
- **Suitability of the clinical trial sites facilities**
- The Site Suitability Assessments must be signed by a person independent from the trial team. In line with the requirements of the Clinical Trial Regulations. the SSA for Galway University Hospital must be signed by the CEO, Head of Clinic / Institution, Director of Research, Clinical Director, or delegate at the site.
- The NREC-CT requested that additional information is added to the SSA on whether the site is involved in the M18-891 study that will also be included in the long-term extension period.
- The National Office requests that all documentation provided in response to RFI is presented in an accessible and searchable format (Word or original PDF). We are unable to accept scanned documents (including documents modified using Optical Character Recognition) as these documents cannot be optimised for use with assistive software.
- **Suitability of the investigator**
- The NREC-CT requested that further detail is added to the relevant clinical trial experience section in the CV for [redacted].
- The NREC-CT requests further information is captured in the CV on whether the PI has involvement in the M18-891 study that will also be included in the long-term extension period.

- AOB: N/A