National Research Ethics Committee

NREC-CT Meeting

6th November 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
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 Jane Byrant	Programme Officer, National Office for RECs
Dr Susan Quinn	Programme Manager, National Office for RECs
Dr Emma Heffernan*	Project Officer, National Office for RECs
Mr Ciaran Horan	Administrative Assistant, National Office for RECs
Dr Peadar Rooney	Project Officer, National Office for RECs

*Drafted minutes

Apologies: Fionnuala Breathnach, Paula Prendeville

Quorum for decisions: Yes

Agenda

- Welcome & Apologies
- 2024-512998-27-00
- 2024-515451-38-00
- 2024-513958-29-00
- 2024-512477-27-00 SM-1
- 2024-513168-24-00 SM-3
- 2023-507698-16-00 SM-1
- 2024-515198-91-00 SM-1
- AOB

- The Chair welcomed the NREC-CT C.
  - The minutes from the previous NREC-CT C meeting on 2nd October were approved.
  - The NREC Business Report was discussed and noted.

Applications

2024-512998-27-00

Institutions: Beaumont Hospital, University Hospital Limerick, University Hospital Waterford, St Vincent's University Hospital, St James's Hospital

Study title: A Prospective, Open-Label, Randomized, Phase 3 Trial of Acasunlimab (GEN1046) in Combination With Pembrolizumab Versus Docetaxel in Subjects With PD-L1 Positive Metastatic Non-Small Cell Lung Cancer After Treatment With a PD-1/PD-L1 Inhibitor and Platinum-Containing Chemotherapy (ABBIL1TY NSCLC-06)

Dossiers Submitted: Part I & II

- **NREC-CT Decision:**

  Request for Further Information

- **Additional Information Required**

Part II Considerations

1. Proof of insurance

- The NREC-CT noted that the period of insurance is stated as expiring on the 31 March 2025 and requested confirmation that insurance is in place for the duration of the trial.

2. Recruitment arrangements

- The NREC-CT noted that it is not clear from the submission whether participants are being consented at site via an e-consent platform or remotely using e-consent. Please clarify if participants are consenting to participate in the trial at each site using econsent, or remotely at home using e-consent. The recruitment template should also be updated to clearly outline how the e-consent tool will be implemented for this study.
- If participants are undergoing remote consent (i.e. the consenting process is not taking place at site), then please provide the following:
  - A strong rationale for using this approach. 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 Recruitment and informed consent procedure template (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.
  - Clarification 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.
    - Detail as to the supports 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.
- Please clearly explain the consenting process (i.e. clearly state whether participants are undergoing remote consent or not) in sections 1.3 to 1.5 in the K1_NREC_CT_Recruitment_and_informed_consent_procedure_template.

3. Subject information and informed consent form

- The NREC-CT noted that pg. 1 of the Pregnant Partner PISCF states 'The data will protect the integrity of the trial' which may be confusing for participants. The NREC-CT requested that this sentence is rephrased for clarity.
- The NREC-CT noted that pg. 2 of the Pregnant Partner PISCF references Danish law and requested that this is replaced with references to Irish law.
- The NREC-CT noted that the GP letter references the UK regulatory authority (MHRA) and requested that this is replaced with the relevant Irish regulatory authority (HPRA).
- The NREC-CT noted that the GP letter references UK law and requested that this is replaced with relevant Irish / EU legislation.
- The NREC-CT noted that the contraceptive precautions for sexually active male participants is different relative to which arm of the study they are enrolled in and requested that that the rationale for this is explained to participants in the PISCF.
- The NREC-CT requested that participants are informed on pg. 24 of the PISCF that they (and their carer) will be reimbursed for the cost of meals associated with trial visits, as detailed in the P1_Compensation trial participants document.
- The Sponsor is requested to submit any Part 2 documentation that require updates as a result of the Part 1 Assessment. Please include detail of the Part 1 consideration that triggered the update to the Part 2 documentation.
- 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.

2024-515451-38-00

Institutions: Mater Misericordiae University Hospital, St James's Hospital

Study title: A Phase 3, Multicenter, Randomized, Double-Blinded, Placebo-Controlled, Parallel-Arm Study Followed by an Open-Label Arm to Evaluate the Efficacy and Safety of Efgartigimod IV in Adult Participants With Primary Immune Thrombocytopenia

Dossiers Submitted: Part I & II

- **NREC-CT Decision:**

- Request for Further Information

- **Additional Information Required**

Part II Considerations

1. Recruitment arrangements

- The NREC-CT requested confirmation that it will be made clear to participants that their participation in this clinical trial is distinct from their routine clinical care. This should be detailed in section 1.1 of the Recruitment and Informed consent procedure template
- The NREC-CT noted that participants will be given 'ample time' to consider their decision to participate in the trial and requested that participants are advised that they can take the necessary time they need to make a fully informed decision to participate in the research. This should be documented in section 1.6 of the Recruitment and Informed consent procedure template
- The NREC-CT noted that the Patient Letter is not written using a patient friendly approach and requested that the letter is revised to be clear and concise using plain English suitable for a lay audience.
- The NREC-CT requested that the Patient Brochure is revised to explain the following to participants using plain English suitable for a lay audience:
    - The purpose of a 'placebo' and what the term 'blinding' means. This should include an explanation of the potential implications of being randomized to the placebo for participants i.e., that they may not receive any drug.
    - That they may have to cease their current medication to participate in the trial.
    - That the study drug may not be available to them after the study finishes.

2. Subject information and informed consent form

- The NREC-CT noted that section 'What is the Study Drug' on pg. 2 of the PISCF is too technical and requested that this is simplified to be more patient friendly and use plain English suitable for a lay audience.
- The NREC-CT noted that the term placebo ('Placebo is a substance that looks like efgartigimoid but is not active') is not well explained to participants on pg. 2 of the PISCF and requested that the term placebo is explained to participants using plain English suitable for a lay audience.
- The NREC-CT requested that it is clarified in the PISCF whether the placebo is saline or a gamma globulin infusion on pg. 2 of the PISCF.

- The NREC-CT noted that it is incorrect to refer to a placebo as a ‘study drug’ and requested that this is amended on pg. 2 of the PISCF.
- The NREC-CT requested that the risk data in the section ‘What are the possible risks of participating in the study?’ on pg. 3 of the PISCF is updated to include detail as to the likelihood / chance of each risk occurring, i.e. 1 in 1000 or 10% etc.
- The NREC-CT requested that it is made clearer to participants on pg. 3 of the PISCF that prior ITP therapies, except those allowed as concurrent, will be discontinued on enrolment to the trial.
- The NREC-CT requested that the PISCF explicitly states on pg. 5 in the section ‘what will happen when the study ends’ that efgartigimod will not be available to participants after the study has ended (if that is the case).
- The NREC-CT requested that the following statement on pg. 5 ‘check with your insurance company that participating in this study will not affect your policy’ is made more explicit / prominent in the PISCF.
- The NREC-CT requested that it is explained to participants in the section ‘What will happen to any samples I give?’ on pg. 7 of the PISCF how their samples are being used and specifically for what purpose including detail as to whether their samples are related to routine purposes, related to the trial or being retained for optional future research. Please use plain English suitable for a lay audience.
- The NREC-CT noted that the future use of data / samples (including genetic research) in not described in line with regulations / best practice on pg. 7 of the Main PISCF. The NREC-CT requested that future use of personal data is sufficiently explained to participants in the PISCF documents so as to constitute broad informed consent, as required under the Health Research Regulations (Data Protection Act 2018 (Section 36(2) (Health Research) Regulations 2018). Furthermore,
    - it should be made optional
    - it should be confined to a specified disease area or drug under study in this trial. Consent can only be obtained where future use of samples and data is defined such that participants are fully informed,
    - and/or that an option is provided to enable participants to consent to be contacted in the future about other research studies,
    - optional future research is made into a separate and explicit consent item in the Informed Consent section of the Main PISCF, with separate participant information section and signatures section, so it is distinct from the main consent to participate in the research

  The PISCF should also make it clear to participants that subsequent research ethics review will be sought for specific research once clearly defined. For further guidance, please see: NREC guidance on use of biological samples and associated data - https://www.nrecoffice.ie/guidance-on-use-of-biological-samples-and-associated-data/
- The NREC-CT requested that further detail of the ‘apps or other devices used in the study’ are described to participants on pg. 8 of the PISCF, including the data protection arrangements in place for such apps and devices.
- The NREC-CT requested that it is made clear to participants on pg. 10 of the PISCF if their data is being sent outside the EU, for what purpose and what safeguards are in place to protect their data.

- The NREC-CT noted that the Informed Consent section of the PISCF states 'I understand that relevant sections of my medical notes will be reviewed by representatives of argenx BV, auditors and national and foreign regulatory authorities where it is relevant to my taking part in the study. I give permission for these individuals to have access to my medical records' and requested that it is made clear to participants in the main body of the PISCF who and for what purpose will have access to their medical notes. The Committee requests that the PISCF specifies the rationale why such bodies may require access to medical notes.
- The Sponsor is requested to submit any Part 2 documentation that require updates as a result of the Part 1 Assessment. Please include detail of the Part 1 consideration that triggered the update to the Part 2 documentation.
- 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.

2024-513958-29-00

Institutions: St James's Hospital, Griffin Daly Medical Centre, Turloughmore Medical Centre, University Hospital Galway

Study title: Semaglutide for people with obesity and resistant hypertension (SUPPORT): a pilot, randomized, parallel-group, integrated, multicentre clinical trial

Dossiers Submitted: Part I & II

- **NREC-CT Decision:**

- Request for Further Information

- **Additional Information Required**

Part I Considerations (RFI) for addition to CTIS

- It is noted on pg. 13 of the protocol and pg. 6 of the protocol synopsis that the trial is described as 'double blinded', which seems incongruent with the description of the administration of the IMP and placebo which suggests that the administrator of the IMP/ placebo is not blinded (i.e. it is not a matched placebo (the placebo syringe is empty), with the research nurse generating a 'click, to replicate the sound of the pre-filled pen' with an accompanying 'training pen'). Please clarify this in the protocol and align across all relevant documentation, including relevant part 2 documents.
- The combined oral contraceptive pill should not be listed as a protocol-recommended contraceptive method for this cohort of trial participants (resistant hypertension). Please provide an alternative to this contraceptive method and align across all relevant documentation, including relevant part 2 documents.

Part II Considerations

1. Recruitment arrangements

- The NREC-CT noted that the description of the Step 3 Randomization Visit on the SUPPORT Trial recruitment webpage document does not include a description of the placebo ('If you are (suitable to continue) we will then either start you on the trial drug, Semaglutide, or you will continue with your current management plan. You will have a 50% chance of being on the trial drug'). The NREC-CT requested that potential participants are informed that they may be randomised to the placebo.
- The NREC-CT noted that the SUPPORT Trial recruitment webpage document does not include answers to the questions in the 'my rights' section including questions related to data protection and other questions and requested that this section is updated to include answers.

2. Subject information and informed consent form

- The NREC-CT requested that the PISCF documents are updated to include the brand names Ozempic or Wegovy alongside Semaglutide, in line with the recruitment materials.
- The NREC-CT requested that it is made clearer to participants in the PISCF that if they wish to discuss trial participation with their family, friends or GP, that they do so in advance of the screening visit, where they will be consented to take part in the trial.
- The NREC-CT noted that the protocol states that there is a risk to the mental health of participants on the placebo arm associated with lack of weight loss when participating in the trial. The NREC-CT requested that participants are informed of this is the PISCF. Participants should also be informed of the support pathways in place, should they experience mental health issues when participating in the trial.
- The NREC-CT noted recent reports in the media regarding side-effects related to muscle loss (sarcopenia) associated with weight loss / Semaglutide/ GLP-1 agonists in clinical trials. The NREC-CT requested clarification if this potential risk is relevant to this trial and therefore should be relayed to participants in the PISCF with appropriate advice to participants on how to mitigate this risk (to increase protein intake and increase strength and resistance training). Please see example of study identifying this risk - A systematic review of the effect of Semaglutide on lean mass: insights from clinical trials - PubMed
- The Sponsor is requested to submit any Part 2 documentation that require updates as a result of the Part 1 Assessment.Please include detail of the Part 1 consideration that triggered the update to the Part 2 documentation.
- 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.

3. Suitability of the investigator

- The NREC-CT requested confirmation that nurses consenting participants to the trial have undertaken sufficient training to perform this task

2024-512477-27-00 SM-1

Institutions: St James's Hospital, Cork University Hospital, University Hospital Galway, Mater Misericordiae University Hospital

Study title: REFRaME-O1: A Phase 2/3 Open-label Study Evaluating the Efficacy and Safety of Luveltamab Tazevibulin (STRO-002) versus Investigator's Choice (IC) Chemotherapy in Women with Relapsed Platinum-resistant Epithelial Ovarian Cancer (Including Fallopian Tube or Primary Peritoneal Cancers) Expressing Folate Receptor Alpha (FOLR1)

Dossiers Submitted: Part I & II

- **NREC-CT Decision:**

- Request for Further Information

- **Additional Information Required**

Part II Considerations

1. **Subject information and informed consent form**
   - The NREC-CT noted that updates to the PISCF include changing the word 'patient' to 'subject' and requested that the word 'participant' is used instead of the word 'subject'.

2024-513168-24-00 SM-2

Institutions: Mater Misericordiae University Hospital, St Vincent's University Hospital

Study title: A randomized, controlled, parallel group, open-label trial evaluating the impact of treatment with GLP-1 analogue Semaglutide on weight loss in people living with HIV and obesity (SWIFT)

Dossiers Submitted: Part I & II

- **NREC-CT Decision:**

- Request for Further Information

- **Additional Information Required**

Part II Considerations

1. **Subject information and informed consent form**
   - The NREC-CT noted that there are multiple PIs listed on pg. 1 of the PISCF requested that the PISCF only lists PIs relevant to the study in Ireland are listed, so it is clear to participants.

- The NREC-CT noted that pg. 7 of the PISCF states that the Danish Medicines Agency and the Italian Medicines Agency will have access to study records and requested clarification as to why Danish and Italian agencies would have access to participants study records in Ireland.
- The NREC-CT noted that pg. 4 of the PISCF states that participants are to undergo genetic testing and requested the following is explained to participants using plain English suitable for a lay audience:
    - detail as to the type of genetic testing involved, including information regarding the purposes of this testing.
    - detail outlining the potential risks entailed in such analysis being performed. the possible ownership of such data by private or commercial interests and that this elucidated in the PISCF.
    - the right to withdraw genetic data, the mechanism for anonymisation, storage and security and transfer of genetic material and its associated data. For guidance, please see HSE National Policy for Consent in Health and Social Care Research (V1.1, 2023) https://hseresearch.ie/wp-content/uploads/2023/02/HSENational-Policy-for-Consent-in-Health-and-Social-Care-Researchcompressed.pdf
- The NREC-CT noted that the future use of data / samples (including genetic research) in not described in line with regulations / best practice in the section 'What will happen to my samples?' on pg. 5 of the Main PISCF. The NREC-CT requested that future use of personal data is sufficiently explained to participants in the PISCF documents so as to constitute broad informed consent, as required under the Health Research Regulations (Data Protection Act 2018 (Section 36(2) (Health Research) Regulations 2018). Furthermore,
    - it should be made optional
    - it should be confined to a specified disease area or drug under study in this trial. Consent can only be obtained where future use of samples and data is defined such that participants are fully informed,
    - and/or that an option is provided to enable participants to consent to be contacted in the future about other research studies,
    - optional future research is made into a separate and explicit consent item in the Informed Consent section of the Main PISCF, with separate participant information section and signatures section, so it is distinct from the main consent to participate in the research

  The PISCF should also make it clear to participants that subsequent research ethics review will be sought for specific research once clearly defined. For further guidance, please see: NREC guidance on use of biological samples and associated data - https://www.nrecoffice.ie/guidance-on-use-of-biological-samples-and-associated-data/

2023-507698-16-00 SM-1

Institutions: Mater Misericordiae University Hospital, University Hospital Waterford

Study title: A Phase 3 Open-Label, Randomized Study of Fixed Duration Pirtobrutinib (LOXO-305) plus Venetoclax and Rituximab versus Venetoclax and Rituximab in

Previously Treated Chronic Lymphocytic Leukemia/Small Lymphocytic Lymphoma (BRUIN CLL-322)

Dossiers Submitted: Part I & II

- **NREC-CT Decision:**

- Request for Further Information

- **Additional Information Required**

Part II Considerations

1. **Subject information and informed consent form**
   - The NREC-CT requested that the potential severity of the skin rash (i.e. the likelihood of experiencing grade 3+ rash or rash so significant it meets the criteria for a Serious Adverse Event) is described in the PISCF in line with the description in the Investigator letter, so participants are fully informed of this common ADR. This should be described using plain English suitable for a lay audience.

2024-515198-91-00 SM-1

Institutions: St Vincent's University Hospital

Study title: Phase II/III Multicenter Randomized, Double-Blind, Placebo-Controlled Platform Trial of Potential Disease Modifying Therapies Utilizing Biomarker, Cognitive, and Clinical Endpoints in Dominantly Inherited Alzheimer's Disease

Dossiers Submitted: Part I & II

- **NREC-CT Decision:**

- Request for Further Information

- **Additional Information Required 0**

Part II Considerations

1. **Subject information and informed consent form**
   - The NREC CT requested that experience of potential TEAEs and AEs (as described in the protocol and safety reports) related to the combined treatment are better reflected on pg. 23 of the PISCF in section 'Combination Use of Investigational Drugs', especially in the context of the revised consent for dose escalation.
   - The NREC-CT noted that pg. 30 of the L1_ SIS and ICF_E2814 ICF_TC states that future use of data will be used 'to develop a better understanding of a disease, or to improve the design of future research studies' and requested future use of data / samples is confined to a particular area of health research such as the related disease or drug under study in this trial as required under the Health

Research Regulations (Data Protection Act 2018 (Section 36(2) (Health Research) Regulations 2018).

- AOB:
    - N/A