National Research Ethics Committee

NREC-CT Meeting

22nd January 2025

Attendance

Name	Role
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
Ms Paula Prendeville	Committee Member, NREC-CT C
Mr Philip Berman	Committee Member, NREC-CT C
Prof Anne Mathews	Committee Member, NREC-CT C
Ms Chita Murray	Programme Manager, National Office for RECs
Dr Laura Mackey	Programme Officer, 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
Dr Peadar Rooney	Project Officer, National Office for RECs
Mr Ciaran Horan	Administrative Assistant, National Office for RECs
Ms Deirdre Ní Fhloinn	Project Officer, National Office for RECs

Apologies: Prof John Faul, Prof Mary Donnelly, Mr Gerry Eastwood

Quorum for decisions: Yes

Agenda

- Welcome & Apologies
- 2024-516609-22-00
- 2023-506817-23-01
- 2023-510294-34-00
- 2024-511458-32-00 SM-3
- 2023-503630-44-00 SM-1
- 2023-510117-26-00 SM-4
- 2023-510128-66-00 SM-3
- 2023-506987-15-00 SM-3
- 2023-508253-98-00 SM-3
- AOB

- The Chair welcomed the NREC-CT C.
  - The minutes from the previous NREC-CT C meeting on 4th December 2024 were approved.
  - The NREC Business Report was discussed and noted.

Applications

2024-516609-22-00

Institutions: St. Vincent's University Hospital, Cork University Hospital, Connolly Hospital

Study title: A Phase 3 Randomized, Double-Blinded, Placebo-Controlled Multicenter Trial with Open-Label Extension to Evaluate the Efficacy, Safety, and Tolerability of Efgartigimod PH20 Subcutaneous Administered by Prefilled Syringe in Adult Patients with Primary Sjögren's Disease

Dossiers Submitted: Part I & II

- **NREC-CT Decision:**

  Request for Further Information

- **Additional Information Required**

Part II Considerations

1. **Compliance with use of biological samples**

- The NREC-CT noted conflicting statements in the S1_Statement on biological sample handling_IRL document regarding future use of samples. Section 4.1 states that samples left over from tests may be used for future research about Sjogren's disease and the study drug, whereas Section 4.8 states that secondary future use of the samples is not planned. The Committee requested that these sections are aligned. This document should also align with relevant participant facing documents, including the PISCF.

2. **Proof of insurance**

- The NREC-CT noted that the insurance certificate states that six (6) participants will be taking part in the trial, whereas the combined number listed in the site suitability assessments amounts to nine (9) participants. The Committee requested confirmation that all trial participants will be covered by the trial insurance.

3. **Recruitment arrangements**

- The NREC-CT noted that the Doctor-to-Patient letter does not reference participants being placed on the placebo arm during the initial treatment phase of the trial and requested that this is amended.
- The NREC-CT requested that participants are advised on pg. 6 of the Participant Brochure that they *will* be reimbursed for travel expenses, in line with updates to the PISCF.

4. **Subject information and informed consent form**

- The NREC-CT requested that the 14-digit EU Clinical Trial number is added to the PISCF documents.
- The NREC-CT noted that the sentence 'Once the study doctor is satisfied with your or your caregiver's technique and you/they feel confident, you may be able to administer the study medication at home without' on pg. 4 of the L1_SIS and ICF_Main_san is not a complete sentence (missing text after the word 'without') and requested that this is amended.

- The NREC-CT noted conflicting information in the PISCFs regarding the maximum retention period for samples (for example pg. 10 of the L1_SIS and ICF_Main_san states that samples will be kept for 15 years and pg. 21 states that all study data will be kept for 25 years. The NREC-CT requested that the maximum data / sample period is clearly stated and aligned across participant facing documents. This should also be aligned with retention periods stated in the S1_Statement on biological sample handling_IRL.
- The NREC-CT noted that pg. 9 of the PISCF states that optional samples may be taken without explanation as to why these samples are being taken. The NREC-CT requested that the purpose of this optional sampling is explained to participants in the PISCF.
- The NREC-CT noted that pg. 1 of the L1_SIS and ICF_Future Scientific Research_san PISCF states that 'Data used may include selected personal information, results and study data'. The Committee requested that it is clarified to participants exactly what personal information may be provided.
- The NREC-CT noted that the future use of data / samples is not described in line with regulations / best practice in the L1_SIS and ICF_Future Scientific Research_san PISCF (for example pg. 2 states 'This optional future scientific research may provide new scientific information that may help us to better understand, identify, and treat patients with Primary Sjögren's Syndrome *or other diseases* in the future). The NREC-CT requested that future use of samples/ 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 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,

  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 noted that participants are to undergo optional genetic research as described in the L1_SIS and ICF_Pharmacogenomics Research_san PISCF and requested that the purposes of this research is described to participants in line with the Health Research Regulations (Data Protection Act 2018 (Section 36(2) (Health Research) Regulations 2018) in that it should be confined to a specified disease area or drug under study in this trial.
- The NREC-CT noted that pg. 15 of the L1_SIS and ICF_Main_san states 'you '*may'* be compensated / refunded for …' and requested that this is amended to state that participants '*will'* be compensated…, so participants are reassured they will not be out of pocket by taking part in the trial.
- The NREC-CT noted that pg. 15 of the L1_SIS and ICF_Main_san states, 'You may also be asked for permission to be contacted at a later date by your general

practitioner (GP)/family doctor to check on your condition since leaving the study' and requested that this sentence is removed.

- The NREC-CT noted that participants in St Vincent's University Hospital will have to travel to the Royal Victoria Eye and Ear Hospital for salivary gland ultrasounds and requested that they are informed of this in the L1_SIS and ICF_Main_san PISCF.
- The NREC-CT noted that participants in Connolly Hospital will have to travel to the Hermitage Clinic for salivary gland ultrasounds and requested that they are informed of this in the L1_SIS and ICF_Main_san PISCF.
- If applicable, 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.

2023-506817-23-01

Institutions: Beacon Hospital, University Hospital Limerick, Cork University Hospital, Mater Private Hospital, Mater Misericordiae University Hospital, St James's Hospital, St Vincent's University Hospital, Tallaght University Hospital

Study title: EORTC-2238-GUCG: Intermittent Androgen deprivation Therapy in the era of AR pathway inhibitors; a phase 3 pragmatic randomized trial (DE-ESCALATE)

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 that it is clarified in section 1.6 of the K1_Recruitment arrangements document how much time participants randomised to the experimental arm will be given to decide whether they want to participate.
- The NREC-CT noted that section 1.8 of the K1_Recruitment arrangements states that 'Participants who do not speak the national language, will not be eligible for inclusion in the study. Recruitment will be limited to those who are fluent in the national language'. The NREC-CT requested confirmation that where possible, reasonable efforts to accommodate / support participants who do not speak the 'national language' to take part in the trial will be taken and provided with

translation services as required. The NREC-CT requires that any translations of participant materials are completed by a certified translator / translation service.

2. Subject information and informed consent form

- The NREC-CT noted that the statement 'This is the standard of care or best practice and refers to the care/treatment you receive if you do not participate in a clinical study' on pg. 1 (& pg. 3) of the PISCF may be confusing for participants in that it suggests that treatment in the study is different to standard of care treatment. The committee requested that this is rephrased to be clearer.
- The NREC-CT noted that multiple different terms are used in the PISCF documents to describe the treatment break, including 'intermittent' 'experimental' and 'treatment holiday' which may be confusing for participants. The NREC-CT requested that one term is used to describe the treatment break, and this is aligned across all participant-facing materials, including the PISCF documents.
- The NREC-CT noted that the process of randomisation is not well explained to participants on the 'additional research question' section on pg. 6 of the L1_SIS and ICF enrolment PISCF and requested that participants are advised of the following:
    - that they have a 2 in 3 chance of being invited to participate in the additional study
    - the process of randomisation and that they may be randomised to either trial arm.
    - clarification what happens to participants who agree to take part in the experimental arm, and then later change their minds and want to revert to the continuous arm
- The NREC-CT requested that participants are advised on pg. 6 of the enrolment PISCF of the potential risks of taking part in the study, including the potential side effects associated with maximal androgen blockade medications. Although patients will already have received this information when commencing treatment, it is standard practice in an open label efficacy study to highlight key pieces of information related to safety and risk that patients need to be mindful of when taking a medication.
- The NREC-CT requested that participants are advised on pg. 4 of the L1_SIS and ICF experimental PISCF that they have a 2:1 randomisation chance between experimental and control groups.
- The NREC-CT noted that the process of moving between both arms of the study is not well explained to participants on pg. 4 of the L1_SIS and ICF experimental PISCF and requested that this is amended.
- The NREC-CT noted that pg. 4 of the L1_SIS and ICF experimental PISCF states 'If you agree… you will stop the injections and pills' and requested that details of the timeframe involved in stopping their medications is clearly outlined to participants.
    - Detail should also be added regarding how and by whom they will be informed that they need to stop their medications.
- The NREC-CT noted that there could be a possible delay of up to one month from randomisation to the experimental arm and requested that the details of what treatment regime (i.e. continuous or intermittent) is being administered during this timeframe is explained to participants in the L1_SIS and ICF experimental PISCF.

- The NREC-CT requested that the full 14-digit EU CT number (2023-506817-23-01) is added to all participant facing documents, including the PISCF documents.
- The NREC-CT requested that the Informed Consent section of the PISCF placeholder for the person performing the interview includes a space for the qualifications of the person performing the interview.
- If applicable, 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.

2023-510294-34-00

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

Study title: A phase 3 multicenter, randomised, prospective, open-label trial of fixed-duration (12 cycles) venetoclax/ obinutuzumab vs. fixed-duration (15 cycles) venetoclax/ pirtobrutinib vs. MRD-guided venetoclax/ pirtobrutinib in patients with previously untreated chronic lymphocytic leukaemia (CLL)/ small lymphocytic lymphoma (SLL) aiming to establish measurement of individual residual disease for adjustment of treatment duration to improve outcomes (CLL18/MOIRAI)

Dossiers Submitted: Part I & II

- **NREC-CT Decision:**

- Request for Further Information

- **Additional Information Required**

Part II Considerations

1. **Compliance with use of biological samples**

- The NREC-CT requested that the S1_Compliance on the collection use and storage of biological samples_IE is updated to align with changes to the PISCF documents.

2. **Recruitment arrangements**

- The NREC-CT noted that participants will be given 'at least 48 hours' 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 K1_Recruitment Arrangements_IE

3. Subject information and informed consent form

- The NREC-CT noted that the information detailed in sections 3.6-3.9 of the L1_SIS and ICF_Study Participation_IE PISCF is too detailed and complex and requested that these sections are revised to be more concise, patient friendly and use plain English suitable for a lay audience.
- The NREC-CT noted that the amount of blood taken during blood draws is listed in millilitre (ml) and requested that the number of teaspoons in each draw is also listed.
- The NREC-CT requested that it is made clear to participants which treatment arm of this open-label trial that they have been randomized to.
- The NREC-CT noted that the future use of data / samples (including genetic research) is not described in line with regulations / best practice in both the L1_SIS and ICF_Study Participation_IE PISCF and the L1_SIS and ICF_Data Sample Storage_IE 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 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

  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 noted that pg. 26 of the L1_SIS and ICF_Study Participation_IE PISCF states that 'We therefore ask you to allow us to keep your pseudonymised data indefinitely and to store it permanently in the database'. The committee requested that the maximum retention periods for samples / data are clearly stated in the PISCF documents and aligned in the S1_Compliance on the collection use and storage of biological samples_IE.
- The NREC-CT noted that pg. 8 of the L1_SIS and ICF_Study Participation_IE PISCF and pg. 4 of the L1_SIS and ICF_Data Sample Storage_IE PISCF state that participants may undergo whole genome / whole exome / gene sequencing and requested the following:
  - Genomic sequencing is confined to genes involved in the disease being treated and /or genes involved in the metabolism of the medicines being used in the trial and this elucidated in the PISCF.
  - Explicit consent, including outlining the risks entailed in such analysis being performed, is added to the PISCF.
  - The possible ownership of such data by private or commercial interests and that this elucidated in the PISCF.

  - The right to withdraw genetic data, and clear information on how to do so, must also be provided in the PISCF.
  - Clarification is provided in the PISCF on 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 (V2.0, 2024). Dublin: Health Service Executive https://www2.healthservice.hse.ie/organisation/national-pppgs/hse-national-policy-for-consent-in-health-and-social-care-research/
- The NREC-CT noted that participants are not reimbursed for out of expenses as stated on pg. 23 of the L1_SIS and ICF_Study Participation_IE PISCF. The NREC-CT requested that to ensure equitable access to clinical trials across all socio-economic groups that trial participants are reimbursed for reasonable out-of-pocket trial related expenses (excluding expenses incurred at regular visits), including meals / refreshments and travel, and this is detailed in the PISCF, so participants are reassured that they will not be out of pocket as a result of participating in the trial. Participants may have to pay additional parking charges etc. for extended hospital visits due to trial participation and may also require hospitalization specifically because of participating in the trial.
- If applicable, 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.

2024-511458-32-00 SM-3

Institutions: Children's Health Ireland

Study title: A multicenter study to evaluate the efficacy, safety, tolerability, and pharmacokinetics of filgotinib, with single arm induction and maintenance, in pediatric subjects (8 to <18 years of age) with moderately to severely active ulcerative colitis

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 the layout of the schedule of assessments on pages 4/5 of the L1_Main ICF may be confusing for participants as detail of the treatment visits box is duplicated and requested that this is amended.
- The NREC-CT noted conflicting advice for female participants on pg. 12 of the L1_Main ICF where participants are advised in a text box labelled 'risk' what to do during the study if they are a woman and immediately advised in the text box below that they do not need to take the above actions if they are a woman. The NREC requested that this is corrected.
- The NREC-CT noted that the future use of data / samples is in not described in line with regulations / best practice on pgs. 7 'to re-use your data for reasons other than this study, e.g. new medical and clinical/scientific research, so as to help improve the design of research studies in the future' & 15 'Gaining consent to re-use my and my baby's data for new medical and clinical/scientific research in the future to help improve the design of research studies' of the L1_Pregnancy ICF, pg. 20 'use your data for purposes beyond this study, such as new medical and clinical/scientific research, to contribute to improving the design of research studies in the future' of the L1_Main ICF & pg. 17 'reuse your child's data for purposes beyond this study in this area of health research'. of the L1_Parental ICF. The NREC-CT requested that future use of samples / personal data is sufficiently explained to participants in the above PISCF documents and aligned across all PISCFs 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 confined to a specified disease area (i.e. ulcerative colitis) 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,

    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/

2023-503630-44-00 SM-1

Institutions: Children's Health Ireland, Cork University Hospital

Study title: A randomized, double-blind, placebo-controlled, parallel-group, multicenter, phase 3 trial to evaluate the efficacy and safety of tralokinumab in combination with topical corticosteroids in children (age 2 to <12 years) and infants (age 6 months to <2 years) with moderate-to-severe atopic dermatitis.

Dossiers Submitted: Part I & II

- **NREC-CT Decision:**

- Favourable

2023-510117-26-00 SM-4

Institutions: Mater Misericordiae University Hospital

Study title: A Phase 2 Study of Tremelimumab (Day 1 only), Durvalumab (MEDI4736) and Trans-arterial catheter chemoembolization (TACE)in patients with advanced Hepatocellular Carcinoma (HCC)

Dossiers Submitted: Part I & II

- **NREC-CT Decision:**

- Favourable

2023-510128-66-00 SM-3

Institutions: St James's Hospital

Study title: A Phase 3 Study of Pembrolizumab in Combination With Carboplatin/Taxane (Paclitaxel or Nab-paclitaxel) followed by Pembrolizumab With or Without Maintenance MK-2870 in the First-line Treatment of Metastatic Squamous Non-small Cell Lung Cancer

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 pg. 8 of the L1_ICF_Main consent_IRL_EN_TC_SM03_not pub PISCF states that participants may undergo whole genome / whole exome sequencing and requested the following:
  - Genomic sequencing is confined to genes involved in the disease being treated and /or genes involved in the metabolism of the medicines being used in the trial and this elucidated in the PISCF.
  - Explicit consent, including outlining the risks entailed in such analysis being performed, is added to the PISCF.
  - The possible ownership of such data by private or commercial interests and that this elucidated in the PISCF.
  - The right to withdraw genetic data, and clear information on how to do so, must also be provided in the PISCF.

- Clarification is provided in the PISCF on 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 (V2.0, 2024). Dublin: Health Service Executive https://www2.healthservice.hse.ie/organisation/national-pppgs/hse-national-policy-for-consent-in-health-and-social-care-research/

2023-506987-15-00 SM-3

Institutions: Tallaght University Hospital

Study title: Phase Ib/II Trial of Pembrolizumab (MK-3475) Combination Therapies in Metastatic Castration-Resistant Prostate Cancer (mCRPC) (KEYNOTE-365)

Dossiers Submitted: Part I & II

- **NREC-CT Decision:**

- Favourable

2023-508253-98-00 SM-3

Institutions: St James's Hospital, Beaumont Hospital, Tallaght University Hospital

Study title: A Phase III, Randomized, Double-blind Trial Comparing Trastuzumab Plus Chemotherapy and Pembrolizumab With Trastuzumab Plus Chemotherapy and Placebo as First-line Treatment in Participants With HER2 Positive Advanced Gastric or Gastroesophageal Junction Adenocarcinoma (KEYNOTE 811)

Dossiers Submitted: Part I & II

- **NREC-CT Decision:**

- Favourable

- AOB:
  - N/A