National Research Ethics Committee

NREC-CT A Meeting

5th February 2025

Attendance

Name	Role
Prof. Alistair Nichol	Chairperson, NREC-CT A
Ms Caoimhe Gleeson	Deputy Chairperson, NREC-CT A
Prof. Gene Dempsey	Deputy Chairperson, NREC-CT A
Dr Brian Bird	Committee Member, NREC-CT A
Dr Maeve Kelleher	Committee Member, NREC-CT A
Dr Dawn Swan	Committee Member, NREC-CT A
Dr Darren Dahly	Committee Member, NREC-CT A
Prof. Aisling McMahon	Committee Member, NREC-CT A
Mrs Erica Bennett	Committee Member, NREC-CT A
Dr David Byrne	Committee Member, NREC-CT A
Ms Margaret Cooney	Committee Member, NREC-CT A
Dr Sean Lacey	Committee Member, NREC-CT A
Ms Mandy Daly	Committee Member, NREC-CT A
Ms Muireann O'Briain	Committee Member, NREC-CT A
Ms Dympna Devenney	Committee Member, NREC-CT A
Dr Emily Vereker	Head of Office, National Office for RECs
Dr Jane Bryant	Programme Officer, National Office for RECs
Dr Laura Mackey	Programme Officer, National Office for RECs
Dr Susan Quinn	Programme Manager, National Office for RECs

Apologies:

Quorum for decisions:

Agenda

- Welcome & Apologies
- 2024-516030-35-00
- 2023-505616-38-00 SM-3
- 2022-501105-12-00 SM-4
- 2022-502972-22-00 SM-1
- 2022-501417-31-01 SM-14
- 2023-508922-83-00 SM-1
- 2023-508818-42-00 SM-6
- 2023-504918-29-00 SM-8
- 2023-507963-20-00 SM-1
- AOB

- The Chair welcomed the NREC-CT A.
  - The minutes from the previous NREC-CT A meeting on 8th January 2025 were approved.
  - The NREC Business Report was discussed and noted.

Applications

2024-516030-35-00

Institutions: Beaumont Hospital, Galway University Hospital, University Hospital Waterford

Study title: A Phase 3, randomized, open-label study of belantamab mafodotin administered in combination with lenalidomide and dexamethasone versus daratumumab,

lenalidomide, and dexamethasone in participants with newly diagnosed multiple myeloma who are ineligible for autologous stem cell transplantation (TI-NDMM)-DREAMM-10

Dossiers Submitted: Part I & II

- **NREC-CT Decision:**

- Request for Further Information

- **Additional Information Required RFI**

Part I Considerations (RFI) for addition to CTIS

1. It is noted that the case where a participant develops liver toxicity and treatment is suspended, the participant can be rechallenged, the sponsor is requested to provide further information to clarify whether there is a dose modification involved in the rechallenge phase.

Part II Considerations

1. Compliance with national requirements on data protection

- The NREC-CT noted the use of a third party concierge service, ICON, and that personal data will be transferred to this company. The NREC-CT requests more information about steps taken to prevent the increased risk of participants being identifiable outside the hospital site using this service.
- The NREC-CT noted that for the optional recorded telephone interviews, there are no specifics regarding where these recordings will be kept and the data protection measures taken to secure this personal data. The NREC-CT noted that on page 2 of the optional telephone ICF it contains the text “contact the study doctor or data privacy officer to retain your anonymity”. This text should be removed and the steps taken to protect the data should be explained to the participants.
- The NREC-CT noted in the main PIS-ICF page 27 it states that in the event that study staff cannot contact the participant, the trial will use an independent company to check publicly available records. The NREC-CT requested clarification on how the fidelity of the participant identity will be ensured. NREC-CT requests that this is added as a specific consent item in the PIS-ICF, that the participant will sign/initial beside. The NREC-CT requests that the vendor and public databases being accessed be identified to NREC and/or in the PIS-ICF.

2. Financial arrangements

- The NREC-CT noted that regarding reimbursements per visit, is not stated what that amount will be, only that “reasonable amounts” will be covered. The NREC-CT noted that in the compensation document, a country specific cap on amount of reimbursement is present. The NREC-CT requests that the PIL provide details about what is covered (for example travel, meals, accommodation, childcare, contraception, out of pocket expenses) to highlight what the participant should retain receipts for, and if there is a maximum limit for compensation (either per visit or total over lifetime of study), this should be specified.

3. Proof of insurance

- The NREC-CT noted that the insurance cover expired 31st December 2024. Please provide update insurance details.

4. Subject information and informed consent form

- 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.
- The NREC-CT noted that for the optional qualitative telephone interviews, no information was provided regarding the interview questions. The NREC-CT requests that telephone transcripts are provided for review by the NREC-CT.
- The NREC-CT noted the use of the abbreviations PFS and OS in the main PIS-ICF on pages 7-10. The NREC-CT requests that these abbreviations be removed and just referred to as follow-up.
- The NREC-CT noted in the main PIS-ICF page 17 in the "Side effects" section the following sentence: "The side effects described below are from 95 people with relapsed/refractory multiple myeloma who received at least 1 dose of belantamab mafodotin in 1 study, at a dose of 2.5 mg/kg." The NREC-CT requests that this sentence be rewritten in simplified language.
- The NREC-CT noted in the main PIS-ICF in the section "Women who can become pregnant" on page 23, it stated that some methods of contraception will not be allowed in this study. The NREC-CT requests that the list of approved contraception methods be added to the PIS-ICF in the relevant sections.
- The NREC-CT noted that in the optional future research PIS-ICF on page 2 the text: "opting out of optional future research does not exclude the sponsor from undertaking biomarker research": The NREC-CT requests that this sentence be made clearer to the participant with simpler language. The Committee requested that future use of samples throughout the study PIS-ICFs is sufficiently explained 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 the 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 future research will be ethically reviewed once clearly defined.
    - For further 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/HSE-National-Policy-for-Consent-in-Health-and-Social-Care-Research-compressed.pdf

- The NREC-CT noted that the PIS-ICFs is well written, however the NREC-CT requests a review of acronyms across all Ireland PIS-ICF's to ensure that they remove acronyms where possible for easier comprehension and where not possible to remove the acronym should be written out in full at first usage. For example, "this PIS-ICF" could be replaced on page 3 with "this document" and on Page 7 the acronym ECOG is used in only one place and the acronym OSDI is used in two places and is not needed.
- The NREC-CT noted the sentence on page 20 "refer to the lenalidomide Patient Information Leaflet (PIL)/package insert", "refer to the dexamethasone PIL/package insert." And on page 22 "refer to the daratumumab PIL/package insert." These documents can be very technical in nature. The NREC-CT notes the PIS-ICF should contain the relevant information related to the study drugs, and requests clarification on what supports are in place to explain these documents to the participant if required.
- The NREC-CT noted on page 10 of the Main PIS-ICF that a sedative is given pre-BMAT. The NREC-CT considered that this is not routine practice in some Irish sites. This should be explained if it not part of the standard of care to the participant in the PIS-ICF.
- The NREC-CT noted that in optional interview study PIS-ICF it states that the doctor will discuss further including details of the designated vendor. The vendor information should be provided to the NREC and included in the PIS-ICF.
- The NREC-CT noted the use of the terminology "vital status" on pages 13, 30, 38 in the main PIS-ICF. The NREC-CT request this terminology to be made clearer to the participant, please ensure that this is aligned in all of the Irish study PIS-ICF.
- The NREC-CT request clarification on the section on home visits, home therapy and courier services and if this is applicable to Ireland. If this is not applicable, the NREC-CT requests that it be removed. If this section is relevant to Ireland, the NREC-CT requests that this section be updated to be specific to the Irish site.
- The NREC-CT noted in the main PIS-ICF on page 16 it states "Some people who have received belantamab mafodotin in clinical studies developed problems in the front part of the eye called the cornea". The NREC-CT also noted that 79% of participants in DREAMM-7 study had some degree of keratopathy. THE NREC-CT requests that the frequency and severity of keratopathy is detailed in lay terms for the participant in PIL in the relevant sections.
- The NREC-CT noted that there are two specific PIS-ICFs for restarting belantamab in the event of significant liver-related safety event, however in the Main PIL, hepatic impairment is mentioned only briefly in the >10% of participants category. The NREC-CT requests clarity on why liver impairment is a significant risk that warrants a specific PIS-ICF. If it is a significant risk to the participant this should be highlighted with more details in the PIS-ICF.
- The NREC-CT noted the use of the third partner vendor ICON concierge, can the use of this vendor in Ireland be confirmed. If this vendor is not being used, can information relating to ICON concierge be removed.
- The NREC-CT noted that none of the ICF's provided leave a placeholder for the qualification of the person performing the interview. The NREC-CT requests that a placeholder for the qualification of the person performing the interview be added to all study ICFs.

5. Suitability of the clinical trial sites facilities

- The NREC-CT noted that none of the sites have provided information regarding access to ophthalmology, which is required at a minimum prior to each dose of belanatamab. The NREC-CT requests details on how ophthalmology exams will be conducted at the study sites.

2023-505616-38-00 SM-3

Institutions: Mater Hospital, Beaumont Hospital, Cork University Hospital, St. James Hospital, University Hospital Galway, St. Vincent's Hospital

Study title: A Multicenter, Global, Interventional, Open label Study of Trastuzumab Deruxtecan (T-DXd), an Anti-HER2-Antibody Drug Conjugate (ADC), in Subjects who Have Unresectable and/or Metastatic HER2-low or HER2 Immunohistochemistry (IHC) 0 Breast Cancer (BC) (DESTINY-Breast15)

Dossiers Submitted: Part I & II

- **NREC-CT Decision:**

- Request for Further Information

- **Additional Information Required RFI**

Part II Considerations

1. Subject information and informed consent form

- The NREC-CT requests that the Main Cohort 1 PISCF and Main Cohort 2 PISCF be updated with a placeholder for the qualification of the person performing the consent interview.
- The NREC-CT noted that several contraception methods have been removed as options from the PIS-ICF. The NREC-CT is requesting clarification on why these methods are no longer options for participants.
- The NREC-CT noted that in biomarker tumor PIS_ICF on page 4 *"your sample may be stored and used for the development and commercialisation of companion diagnostics (CDx) tests".* The NREC-CT requests clarification so that it is clear that consent is confined to the disease 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: HSE National Policy for Consent in Health and Social Care Research (V1.1, 2023) 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 in biomarker tumour on page 5 PIS_ICF it states that stored sample (including microscope images) *"may be shared globally by the Sponsor (organisation funding this research), the Sponsor's commercial or research partners, the Sponsor's authorised representatives or collaborators, or other commercial organisations or drug companies".* The NREC-CT requests that more details be provided in the PIC_ICF who exactly these samples will be shared with.
- The NREC-CT noted on page 13 the Main Cohort 1 PISCF and page 14 Main Cohort 2 PISCF the information about optional PET scan does not include any information about the risks. The NREC-CT requests that information about the qualitative risks of a PET scan in lay terms be added to these sections.

2022-501105-12-00 SM-4

Institutions: Tallaght University Hospital, Cork University Hospital

Study title: An Open-label, Randomized, Controlled Phase 3 Study of Disitamab Vedotin in Combination with Pembrolizumab Versus Chemotherapy in Subjects with Previously Untreated Locally Advanced or Metastatic Urothelial Carcinoma that Expresses HER2 (IHC 1+ and Greater)

Dossiers Submitted: Part I & II

- **NREC-CT Decision:**

- Favourable

2022-502972-22-00 SM-1

Institutions: Beaumont Hospital, Our Lady of Lourdes Hospital

Study title: A Randomized, Double-Blind, Placebo-Controlled Phase 3 Study of VE303 for Prevention of Recurrent Clostridioides difficile Infection: The RestoratiVE303 Study

Dossiers Submitted: Part I & II

- **NREC-CT Decision:**

- Request for Further Information

- **Additional Information Required RFI**

Part II Considerations

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

- The NREC-CT noted on page 4, page 26, 28 the Parent Information Sheet and Informed Consent Form, “if you have not already consented to the open-label” and “If you would like to continue into the open label”. The NREC-CT notes that it is best practice for re-consent to occur after explanation to and discussion with any child participant. When pre-consent occurs it is also best practice is for any child participant to be involved it is best practice for re-consent to occur after explanation to and discussion with any child participant. The NREC-CT requests revision of these sections to reflect the involvement of the child in the discussion and consent process.
- The NREC-CT notes that page 6 and 7 of the Parent Information Sheet the text references to “Pregnancy test (if you are able to become pregnant)”, The NREC-CT requests that this be updated to reflect the child becoming pregnant, not the parent.
- The NREC-CT notes on page 9 of the Parent Information Sheet the text “Certain regional areas can offer services to courier the stool samples you collect at home to the site or the lab on your behalf. If this option is available in your area” The NREC-CT requests clarification if this service available for the Irish sites. If this is not available, please remove from the Parent information sheet.

2022-501417-31-01 SM-14

Institutions: St. James Hospital

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)

Dossiers Submitted: Part I & II

- **NREC-CT Decision:**

- Favourable

2023-508922-83-00 SM-1

Institutions: University Hospital Galway, Tallaght University Hospital, Beaumont Hospital, St. James Hospital

Study title: A Phase 2 Trial of Adagrasib Monotherapy and in Combination with Pembrolizumab and a Phase 3 Trial of Adagrasib in Combination with Pembrolizumab versus Pembrolizumab in Patients with Advanced Non Small Cell Lung Cancer with KRAS G12C Mutation

Dossiers Submitted: Part I & II

- **NREC-CT Decision:**

- Request for Further Information

- **Additional Information Required RFI**

Part II Considerations

1. Subject information and informed consent form

- The NREC-CT noted in PIS-ICF for Phase 2(Page 39) and Phase 3(Page 36) the following “If your study doctor needs to follow up with you but cannot find you, <he/she> may try to learn your new address, telephone number or current health status by calling or writing to the person(s) named as your secondary contacts. If your study doctor cannot obtain information through your secondary contacts, he or she may ask for the assistance of a third-party representative and may share with that representative limited information about you” The NREC-CT requests clarification on who the secondary contacts are, how their personal contact information will be stored, how consent for contacting them will be recorded. In regard to both the secondary contacts and the third-party vendor the NREC-CT also requests clarification on how the fidelity of the participant identity will be ensured. NREC-CT requests that this is added as a specific consent item in the PIS-ICF, that the participant will sign/initial beside. The NREC-CT requests that the vendor details and public databases being accessed be identified to NREC and/or in the PIS-ICF.
- The NREC-CT noted in PIS-ICF for phase 2(Page 39) and Phase 3 (Page 34) the following ‘The Sponsor is responsible for deciding what personal data needs to be collected during the study’. This should be amended to reflect article 5 of the GDPR guidelines and updated in all relevant PIS-ICFs.
- The NREC-CT noted on page 4 of the Optional Tumour PIS-ICF, that a blood sample will be collected if the participant is in Phase 3. The NREC-CT request clarification if there are any additional samples collected during phase 2.
- The NREC-CT noted on page 2 of the Pregnant partner PIS-ICF and pregnancy PIS-ICF, “and, if clinically possible that additional investigations will be performed”. The NREC-CT requested that a specific consent for the additional investigations be sought and this consent process reflected in the PIS-ICF.
- The NREC-CT requests that the all relevant PIS-ICFs be updated with a placeholder for the qualification of the person performing the consent interview.

2023-508818-42-00 SM-6

Institutions: Children's Health Ireland

Study title: An International, Multicenter, Randomized, Double-Blind, Parallel Group, Vehicle-Controlled, Phase 2/3 Study with Open-Label Extension Evaluating the Efficacy and Safety of Diacerein 1% Ointment for the Treatment of Generalized Epidermolysis Bullosa Simplex (EBS)

Dossiers Submitted: Part II

- **NREC-CT Decision:**

- Favourable

2023-504918-29-00 SM-8

Institutions: St Vincent's University Hospital, Bon Secours Hospital Cork, Mater Hospital

Study title: An Open-label, Randomized Phase 3 Study of MK-2870 as a Single Agent and in Combination with Pembrolizumab Versus Treatment of Physician's Choice in Participants with HR+/HER2- Unresectable Locally Advanced or Metastatic Breast Cancer

Dossiers Submitted: Part I & II

- **NREC-CT Decision:**

- Request for Further Information

- **Additional Information Required RFI**

Part II Considerations
1. Suitability of the investigator
• The NREC-CT is requesting clarification on the current sites and PI's. If a change in PI has occurred, the NREC-CT is requesting to review the CV, COI and GCP. If there has been a change in site, the NREC-CT is requesting a site suitability form.

2023-507963-20-00 SM-1

Institutions: Cork University Hospital, Trinity College Dublin, Tallaght University Hospital, Beaumont Hospital

Study title: A Phase 3, Multicenter, 2-Arm Randomized, Open-Label Study of Trastuzumab Deruxtecan in Subjects with HER2 Positive Metastatic and/or Unresectable Gastric or Gastro Esophageal Junction (GEJ) Adenocarcinoma Subjects who have Progressed on or After a Trastuzumab-Containing Regimen (DESTINY-Gastric04)

Dossiers Submitted: Part I & II

- **NREC-CT Decision:**

- Request for Further Information

- **Additional Information Required RFI**

Part II Considerations

1. Subject information and informed consent form

- The NREC-CT noted on page 13 of the Main ICF the text “Patient acknowledged that the patient has received and understood a separate patient information guide regarding the risk of lung problem.” The NREC-CT has not received this separate patient information guide and requests it be submitted for review.

- AOB:
  - XXX
  - XXX