# National Research Ethics Committee

## NREC-CT Meeting

**11th September 2024**

### Attendance

| Name | Role |
|---|---|
| Prof David Brayden | Chairperson, NREC-CT D |
| Prof David Smith | Deputy Chairperson, NREC-CT D |
| Dr Christina Skourou | Deputy Chairperson, NREC-CT D |
| Prof Andrew Green | Committee Member, NREC-CT D |
| Prof Cathal Walsh | Committee Member, NREC-CT D |
| Prof Deirdre Murray | Committee Member, NREC-CT D |
| Dr Geraldine O'Dea | Committee Member, NREC-CT D |
| Prof Lina Zgaga | Committee Member, NREC-CT D |
| Ms Deirdre McLoughlin | Committee Member, NREC-CT D |
| Prof Tina Hickey | Committee Member, NREC-CT D |
| Dr Mary McDonnell Naughton | Committee Member, NREC-CT D |
| Prof Geraldine O'Sullivan Coyne | Committee Member, NREC-CT D |
| Ms Chanel Watson | Committee Member, NREC-CT D |
| Dr Jeff Moore | Committee Member, NREC-CT D |
| 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 |
| Ms Patricia Kenny* | Project Officer, National Office for RECs |
| | |

**Apologies:** Gerry Daly

**Quorum for decisions:** Yes

## Agenda

- Welcome & Apologies
- 2023-508138-33-00
- 2022-500031-37-00
- 2023-507536-21-00
- 22-NREC-CT-157_Mod-6
- 2022-500237-92-00_SM-1
- 22-NREC-CT-058_Mod-3
- 2022-501417-31-01 SM-13
- 2022-501939-16-00 SM-15
- 2022-501763-40-00 SM-3
- AOB

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- The Chair welcomed the NREC-CT D.
  - The minutes from the previous NREC-CT D meeting on 31st July were approved.
  - The NREC Business Report was discussed and noted.

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## Applications

**2023-508138-33-00**

Institutions: Beaumont Hospital

Study title: Phase 1/2 Multicenter, Open-label Study to Evaluate Safety, Tolerability, Pharmacokinetics, and Pharmacodynamics of NTLA-3001 in Participants with Alpha-1 Antitrypsin Deficiency (AATD)-Associated Lung Disease

Dossiers Submitted: Part I and II

- **NREC-CT Decision:**

- Request for Further Information

- **Additional Information Required**

**Part I**

| Part I Considerations (RFI) for addition to CTIS |
|---|
| 1. The Sponsor is requested to update the protocol to include a list of prohibited medications. |

**Part II**

| Part II Considerations |
|---|
| **1. Compliance with national requirements on data protection** |
| • No Considerations raised by the NREC |
| **2. Compliance with use of biological samples** |
| • No Considerations raised by the NREC |
| **3. Financial arrangements** |
| • No Considerations raised by the NREC |
| **4. Proof of insurance** |
| • No Considerations raised by the NREC |
| **5. Recruitment arrangements** |
| • The NREC-CT noted that the Protocol pg. 60 a key inclusion criterion is "Participants must have a negative cotinine test and agree to the smoking and nicotine restrictions" however neither the pre-screening checklist or the study reference card refer to smoking status/history. The Committee requested that the Pre-screening Checklist and Study Reference Card be updated to include reference to smoking status/history |
| **6. Subject information and informed consent form** |
| The NREC-CT noted that some of the sections on future research in the SIS and ICF Optional Future research pg. 2 and SIS and ICF Optional Tissue Research pg. 2 is seeking blanket consent for future use of samples for unspecified purposes without further consent. This consent is not described in line with regulations and best practice as it is not confined to the disease or drug under study ie. "To see if |

certain genes are associated with certain diseases or disorders, To better understand the causes of diseases and how to diagnose, treat, or prevent them (how your response is affected by your genes), To see how gene mutations (changes) may be linked to your disease/condition or other related diseases, To assist with the development of diagnostic tests."
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' and this is clearly stated in the main body and informed consent section of the PISCF. The NREC-CT advised that consent can only be obtained where future use of samples and data is defined such that participants are fully informed. If future research is not able to be clearly defined at present, then an option should be provided to enable participants to consent to be contacted when the research is further defined. Furthermore, the NREC request confirmation 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 Sponsor is requested to submit any Part II documentation that requires updates as a result of the Part I Assessment. Please include details of the Part 1 Consideration responsible for triggering update to Part 2 documents in your submission.
- 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 the Pregnancy ICF pg. 4 refers to Medpace being a data processer. The Committee requested clarification as to whether Medpace will be available as a travel partner for Irish participants, and if not, that all references to Medpace are removed from the ICF. If Medpace will be used in Ireland, the Committee requested clarification as to why information in relation to pregnancy would be shared with Medpace who are a travel partner. The Committee also requested that the ICF be updated to remove reference to data being shared with Medpace or include detail around why it is being shared.
- The NREC-CT noted that Phase 1 patients would remain as inpatients for 24 hours post infusion and Phase 2 patients would remain as inpatients for 8 hours. The Committee requested that the Adut Main ICF be updated to clarify for participants if they would be in a room with a bed for the duration of their inpatient observation rather than in an infusion chair.
- The NREC-CT requested that the Summary ICF be updated to include text which states that this treatment cannot be undone, as is highlighted in the Main ICF (Page 15 and 23).

**7. Suitability of the clinical trial sites facilities**

- No Consideration raised by NREC

**8. Suitability of the investigator**

- Please submit an accessible and searchable version (Word document or original PDF) of Declaration of Interest (DOI) for Noel McElvaney. 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.

**2022-500031-37-00**

Institutions: University Hospital Galway St James's Hospital St Vincent's University Hospital

Study title: RADAR: A randomised phase III trial with a PET response adapted design comparing ABVD +/- ISRT with A2VD +/- ISRT in patients with previously untreated stage IA/IIA Hodgkin lymphoma

Dossiers Submitted: Part I and II

- **NREC-CT Decision:**

- Request for Further Information

- **Additional Information Required**

**Part II Considerations**

**1. Compliance with national requirements on data protection**

- No Considerations raised by the NREC

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

- No Considerations raised by the NREC

**3. Financial arrangements**

- The NREC-CT noted that participants will not be reimbursed for expenses and requested that participants are reimbursed for all reasonable out of pocket expenses, to ensure equity in access to clinical trials across all socioeconomic groups. This information must be provided in the Participant information leaflet with clear guidance regarding how these expenses can be claimed, and in the document P1_Compensation trial participants investigator funding and other arrangements.

**4. Proof of insurance**

- No Considerations raised by the NREC

**5. Recruitment arrangements**

- No Considerations raised by the NREC

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

- The NREC-CT noted that the reference to future research in the SIS and ICF PIS Adult pg. 2 "future research" and pg.19 "future research projects" and SIS and ICF Adults ICF .pg. 2 "support other research in the future" is not described in line with

regulations and best practice. The Committee requested that future use of samples 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 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 Sponsor is requested to submit any Part II documentation that requires updates as a result of the Part I Assessment. Please include details of the Part 1 Consideration responsible for triggering update to Part 2 documents in your submission.
- 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 requested that the SIS and ICF PIS Adults pg.20 be updated to include the website address for EU database and trials registry website where the study results will be published.
- The NREC-CT requested that the consent page for PIS Adult and PM Partner Adults be updated to include boxes beside each statement for the participant to initial to show their explicit consent.
- The NREC-CT noted the statement on consent page for PIS Adult “I agree to use effective contraception as described in the patient information sheet, throughout trial treatment and for at least 6 months after completing treatment” is worded for female participants of childbearing potential. The Committee requested this be updated to also reflect contraception requirements for male participants with female partners.
- The NREC-CT noted pg. 6 of the PIS Adult mentions Hepatitis B and C and HIV testing. The Committee requested that page 6 be updated to add a statement to inform participants that the study team are required to report any positive HIV, Hep test result to the relevant authority as they are mandatory notifiable diseases. (Infectious Diseases (Amendment) Regulations 2022 (S.I. No. 258 of 2022) May 2022).
- The NREC-CT requested that the ICF and PIS be combined in one document to ensure the documents do not have different versions and dates on them.

**7. Suitability of the clinical trial sites facilities**

- No Considerations raised by the NREC

**8. Suitability of the investigator**

- No Considerations raised by the NREC

Institutions: Mater Misericordiae University Hospital

Study title: A Phase 1/2 Open Label, Dose Escalation and Expansion Study of MDNA11, IL-2 Superkine, Administered Alone or in Combination with Immune Checkpoint Inhibitor in Patients with Advanced Solid Tumors (ABILITY-1 STUDY)

Dossiers Submitted: Part I and II

- **NREC-CT Decision:**

- Request for Further Information

- **Additional Information Required / Favourable with Conditions**

## Part II Considerations

**1. Compliance with national requirements on data protection**

- No Considerations raised by the NREC

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

- No Considerations raised by the NREC

**3. Financial arrangements**

- The NREC-CT noted that the Compensation for Trial Participants document shows that travel, and meal expenses will be offered to participants. The Committee requested that the Compensation for Trial Participants document be updated to include expenses for carer/legal representative. The Committee also requested that the SIS and ICF Main pg. 16 be updated to include reference to expenses for carer/legal representatives being covered.

**4. Proof of insurance**

- No Considerations raised by the NREC

**5. Recruitment arrangements**

- The NREC-CT requested that the Recruitment and Informed Consent Procedure document be updated to describe the recruitment process as follows
    - 1.2 – please describe the format of the resources used for recruitment, e.g. paper or electronic and how these will be presented to potential participants e.g. in the clinic, via the post, through social media or on the radio). Who will initially approach potential participants? Please provide clarity as to whether there will be posters, leaflets, letters to participant's GP's etc.
    - 1.3 - Will identification of potential participants involve access to identifiable information? – Coding will be done by study team at the site (as per ICF pg.. 20) not by the sponsor, please update to clarify.

- 1.11 Please provide a clear indication of what the first step of recruitment is. The Committee noted that the first step of recruitment would not be the signing of ICF, as stated in the informed consent procedure document.

## 6. Subject information and informed consent form

- The Sponsor is requested to submit any Part II documentation that requires updates as a result of the Part I Assessment. Please include details of the Part 1 Consideration responsible for triggering update to Part 2 documents in your submission.
- 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 SIS and ICF Main covers the different arms of the study which means there is a lot of irrelevant information for patients for whom the detail does not apply, for example pg. 5 Fresh tumour tissue – Depending on the part of the study you are being enrolled in, biopsies to collect fresh tumour tissue are optional or required. The Committee requested that a separate ICF be developed for each strand/arm of the study to ensure the participants can understand what the study is about and give explicit consent. If it is not possible to obtain consent via separate consent documents, the Committee requested that a study schema or diagram of the study design is added to ensure clarity for participants.
- The NREC-CT requested that the SIS and ICF Main pg. 9 be updated to remove the Yes/No consent statements for tumour tissue collection and analysis and the initial section for acknowledging that “I have been informed that I am being considered to participate in a part of the study that requires fresh tumour tissue collection and analysis, and I agree to this.” These statements should all be detailed on the consent form at the end of the SIS and ICF Main and not in the middle of the document.
- The NREC-CT requested that the consent page for SIS and ICF Main pg. 23 be updated to list each consent statement separately and to include boxes beside each statement for the participant to initial to show their explicit consent.
- The NREC-CT requested that the consent page for SIS and ICF Main pg. 23 be updated to move the optional future research and fresh tumour tissue collection to the following page with a signature box separate to that for consent to the main study to enable participants to explicitly consent, or not, to these optional components.
- The NREC-CT noted that SIS and ICF Main pg. 8 states that participants will have MRI/CT scans every 8 weeks (or more frequently if needed). The Committee requested that SIS and ICF Main risk section pg. 15 be updated to detail how this frequency of use differs from standard of care and associated background radiation people are exposed to in daily life. The Committee also commented that the frequency of these scans does not constitute a “small exposure to radiation” and requested this text is amended to reflect this. The NREC-CT requested that the consent page for SIS and ICF Main pg. 23 be updated to move the optional components to a separate page

- The NREC-CT requested that the SIS and ICF Main pg. 17 section on Insurance be rewritten in lay language and to provide more detail of what is covered rather than what is not covered.
- The NREC-CT requested that SIS and ICF Main pg. 10 be updated to include the frequency of the side effects such as very common, common, uncommon etc.
- The NREC-CT requested that the SIS and ICF Main pg. 12 Common side effect of loss of skin colour & hypothyroidism be updated to give more detail such as uniform/patchy, temporary/permanent etc.
- The NREC-CT requested that the SIS and ICF Main pg. 1 be updated to include a statement that this is a phase 1 trial, what a phase 1 trial is, and how many people have received this drug so far.
- The NREC-CT requested that the GP Letter be updated to provide an explanation for all acronyms used.
- The NREC-CT noted that the Compensation for Trial Participants document shows that travel, accommodation and meal expenses will be offered to participants. The Committee also requested that the SIS and ICF Main pg. 16 be updated to include reference to accommodation and meal expenses.

**7. Suitability of the clinical trial sites facilities**

- The NREC-CT noted the response to Q5 stating that the exposure to ionizing radiation is not above standard of care. The Committee requested clarification on what is normal for standard of care and how this exposure is not above that threshold.

**8. Suitability of the investigator**

- No Considerations raised by NREC

**22-NREC-CT-157_Mod-6**

Institutions: Sheaf House, Tallaght Adult Mental Health Services

Study title: A randomized, double-blind, placebo-controlled, Phase 2b trial with an open-label extension to determine the safety and efficacy of GH001 in patients with treatment-resistant depression

Dossiers Submitted: N/A

- **NREC-CT Decision:**

- Request for Further Information

- **Additional Information Required**
- The NREC-CT requested that the consent pages of Pregnancy Follow up ICF pg. 4 and Pregnant Partner ICF pg. 6 be updated to include a statement that the pregnant person gives consent for the study investigator to contact their obstetrician, to obtain independent information about their pregnancy and the outcome.
- The NREC-CT noted that Pregnancy Follow up ICF pg. 5 and Pregnant Partner ICF pg. 6 are requesting consent for future use of data for unspecified purposes including

sharing anonymous data with other researchers. The Committee advised that the future use of data for pregnancy follow up and pregnant partner should be optional. The Committee requested that the Pregnancy Follow up ICF and Pregnant Partner ICF be updated to move the consent statement for future use to a separate page from the Main consent form with its own signature box for optional components and yes/no tick boxes for the pregnant person to tick and sign to request explicit consent.

- The NREC-CT also noted that Pregnancy Follow up ICF pg. 5 and Pregnant Partner ICF pg. 6 are seeking blanket consent for future use of 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 research in the area of depression and/or the study drug and this is clearly stated in the main body and informed consent sections of the Pregnancy Follow up ICF and Pregnant Partner ICF. 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 Pregnancy Follow up ICF pg. 5 and Pregnant Partner ICF pg. 6 state that information may be “shared anonymously with other researchers”. The Committee requested that the Pregnancy Follow up ICF and Pregnant Partner ICF be updated to have a separate consent statement for the participant to explicitly consent to the processing of their personal data from coded to anonymised data it as per Article 4 (2) and (6) General Data Protection Regulation (GDPR). The Committee requested that the Pregnancy Follow up ICF and Pregnant Partner ICF be updated to have a separate consent statement for the participant to explicitly consent to the processing of their personal data from coded to anonymised data it as per Article 4 (2) and (6) General Data Protection Regulation (GDPR). The Committee would advise this should also be an optional component and requested that the Pregnancy Follow up ICF and Pregnant Partner ICF be updated to move the consent statement for anonymising data to a separate page along with optional future use component with yes/no tick boxes for the pregnant person to tick and sign to request explicit consent.

**2022-500237-92-00 SM-1**

Institutions: St Vincent's University Hospital

Study title: A phase 3, multicenter, randomized, double-blind, placebo-controlled trial comparing the efficacy and safety of tafasitamab plus lenalidomide in addition to R-CHOP versus R-CHOP in previously untreated, high-intermediate and high-risk patients with newly-diagnosed diffuse large B-cell lymphoma (DLBCL) [frontMIND]

Dossiers Submitted: Part I and II

- **NREC-CT Decision:**

- Request for Further Information

- **Additional Information Required**

| Part II Considerations |
|---|

1. **Compliance with national requirements on data protection**
   - This document represents information already approved under CTD
2. **Compliance with use of biological samples**
   - This document represents information already approved under CTD
3. **Financial arrangements**
   - This document represents information already approved under CTD
4. **Proof of insurance**
   - No Considerations raised by NREC
5. **Subject information and informed consent form**
   - The NREC-CT noted that the sponsor has changed from Morphosys AG, to Incyte Corporation. The Committee where unclear how existing participants will be informed of this change of sponsor. Please clarify.
   - The Sponsor is requested to submit any Part II documentation that requires updates as a result of the Part I Assessment. Please include details of the Part 1 Consideration responsible for triggering update to Part 2 documents in your submission.
   - 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.
6. **Suitability of the clinical trial sites facilities**
   - This document represents information already approved under CTD
7. **Suitability of the investigator**
   - This document represents information already approved under CTD

**22-NREC-CT-058_Mod-3**

Institutions: St James Hospital, Bon Secours Hospital Cork, Beaumont Hospital, Mater Misericordiae University Hospital, University Hospital Waterford

Study title: PICCOLO: A Phase 2, Single Arm Study of Mirvetuximab Soravtansine in Recurrent Platinum-Sensitive, High-Grade Epithelial Ovarian, Primary Peritoneal, or Fallopian Tube Cancers with High Folate Receptor-Alpha Expression

Dossiers Submitted: N/A

- **NREC-CT Decision:**

  Favourable

- **Additional Information Required**
- None

**2022-501417-31-01 SM-13**

Institutions: St James Hospital, Beaumont Hospital

Study title: Phase 3, Randomised, Double-blind, Active-ComparatorControlled Clinical Study of Adjuvant MK 7684A (Vibostolimab with Pembrolizumab) Versus Adjuvant Pembrolizumab in Participants with High-risk Stage II-IV Melanoma (KEYVIBE010)

Dossiers Submitted: Part I and Part II

- **NREC-CT Decision:**

- Request for further information

- **Additional Information Required /**

**Part I Considerations (RFI) for addition to CTIS**

1. The Sponsor is requested to update Protocol pg. 89 Section 8.4.3 to replace “The investigator will also make every attempt to follow all nonserious AEs that occur in randomized participants for outcome” with “The investigator will also make every attempt to follow all nonserious AEs that occur in randomized participants for outcome even if the participant has withdrawn consent”

**Part II Considerations**

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

- No Considerations raised by NREC

**2022-501939-16-00 SM-15**

Institutions: The Heartbeat Trust, Mater Private Network, Mater Private Hospital, University College Dublin

Study title: HERMES: Effects of ziltivekimab versus placebo on morbidity and mortality in patients with heart failure with mildly reduced or preserved ejection fraction and systemic inflammation.

Dossiers Submitted: Part I and II

- **NREC-CT Decision:**

- Request for Further Information

- **Additional Information Required / Favourable with Conditions**

**Part II Considerations**

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

- The NREC-CT noted that the cover letter Pg..1 states that the “Background for Substantial Mod-15” was “to incorporate a new potential risk associated with Ziltivekimab …. Retained placenta in non-clinical trials …. Necessitating ….”implement testing with highly sensitive urine pregnancy tests”. The NREC-CT requested that the SI-IC Main pg. 11/12 be updated to include the placenta retention risk.
- The NREC-CT requested that the SI-IC Main pg. 12 and 13 sentence regarding syringe/pens not being left in reach of children under 3 be updated to replace “children under 3” with just “children”
- The Sponsor is requested to submit any Part II documentation that requires updates as a result of the Part I Assessment. Please include details of the Part 1 Consideration responsible for triggering update to Part 2 documents in your submission.
- 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.

**2022-501763-40-00 SM-3**

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

Study title: A Phase 3, Randomized, Double-blind Study to Evaluate the Safety and Efficacy of Emtricitabine and Tenofovir Alafenamide (F/TAF) Fixed-Dose Combination Once Daily for Pre-Exposure Prophylaxis in Men and Transgender Women Who Have Sex with Men and Are At Risk of HIV-1 Infection.

Dossiers Submitted: Part I and II

- **NREC-CT Decision:**

- Favourable

- **Additional Information Required**

**Part II Considerations**

1. **Compliance with national requirements on data protection**
   - This document represents information already approved under CTD
2. **Subject information and informed consent form**
   - No Considerations raised by NREC

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- AOB:
- Member Forum 6th December was mentioned.