# National Research Ethics Committee

## NREC-CT Meeting

**5th March 2025**

### Attendance

| Name | Role |
|---|---|
| Prof David Brayden | Chairperson, NREC-CT D |
| Prof David Smith | 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 |
| Mr Gerry Daly | Committee Member, NREC-CT D |
| Ms Deirdre McLoughlin | Committee Member, NREC-CT D |
| Prof Geraldine O'Sullivan Coyne | Committee Member, NREC-CT D |
| Dr Jeff Moore | Committee Member, NREC-CT D |
| 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 |
| Ms Patricia Kenny* | Project Officer, National Office for RECs |
| Ms Rachel McDermott | Project Administrator, National Office for RECs |
| Ms Robyn Ennis | Observer |

*Drafted minutes

**Apologies:** Mary McDonnell Naughton, Christina Skourou, Chanel Watson

**Quorum for decisions:** Yes

## Agenda

- Welcome & Apologies
- 2024-517812-31-00
- 2023-504807-94-00
- 2023-509908-15-00 SM-2
- 2022-501238-52-00 SM-24
- 2024-518177-33-00 SM-1
- 2024-517500-11-00 SM-2
- 2023-504684-16-00 SM-3
- 2022-500439-35-00 SM-8
- 2023-506288-33-00 SM-3
- 2023-506081-31-00 SM-2
- AOB

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- The Chair welcomed the NREC-CT D.
  - The minutes from the previous NREC-CT D meeting on 29th January 2025 were approved.
  - The NREC Business Report was discussed and noted.

## Applications

**2024-517812-31-00**

Institutions: Children's Health Ireland Crumlin

Study title: A low-interventional study to evaluate long-term effectiveness of real-world prophylactic treatment with efanesoctocog alfa on joint health in people with haemophilia A (ALTITUDE)

Dossiers Submitted: Part I & II

- **NREC-CT Decision:**

- Request for Further Information

- **Additional Information Required RFI**

| Part II Considerations |
|---|
| **1. Compliance with national requirements on data protection** |
| • No Considerations raised by NREC |
| **2. Compliance with use of biological samples** |
| • No Considerations raised by NREC |
| **3. Financial arrangements** |
| • The NREC-CT noted that "Meals of reasonable value (or meal vouchers) may be offered in exceptional cases if patients are travelling far, resulting in many hours (>3 hours) away from their home due to a study visit. Compensation for meal expenses will not be offered in general" The Committee requested that this be updated as meals should be offered to everyone regardless of distance they travel. |
| **4. Proof of insurance** |
| • No Considerations raised by NREC |
| **5. Recruitment arrangements** |
| • The NREC-CT noted contradiction in the number of participants in Ireland. The Site Suitability form for CHI Crumlin states 3 participants, however the list of trial sites states 6. The Committee requested confirmation on the number of participants in Ireland and that these documents be updated to align. |
| **6. 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 requested that the SIS and ICF Pregnancy Follow pg 7 *"Parent/legally designated representative's signature for a pregnant person less* |

*than 18 years of age"* be updated to 16 years of age as in Ireland persons over 16 can consent for research themselves.

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

- The NREC-CT noted that section 8 of site suitability form outlines the PI's suitability rather than the suitability of the equipment at the proposed site. The Committee requested that section 8 be updated to address suitability of equipment.

8. **Suitability of the investigator**

- No Considerations raised by NREC

**2023-504807-94-00**

Institutions: Mater Misericordiae University Hospital

Study title: First-in-Human Study of STX-478, a Mutant-Selective PI3Kα Inhibitor as Monotherapy and in Combination With Other Antineoplastic Agents in Participants With Advanced Solid Tumors

Dossiers Submitted: Part I & II

- **NREC-CT Decision:**

- Request for Further Information

- **Additional Information Required RFI**

**Part II Considerations**

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

- No considerations raised by NREC

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

- The NREC-CT notes that question 4.10 on the Form S1_Use of biological samples has not been answered correctly, and the query relating to 'unsolicited findings' should be addressed here.

3. **Financial arrangements**

- No considerations raised by NREC

4. **Proof of insurance**

- No considerations raised by NREC

5. **Recruitment arrangements**

- No considerations raised by NREC

6. **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 requested that the Main Combination ICF pg 33, Main Monotherapy ICF pg 36 and Main Triple combination therapy ICF pg 39 *"I understand that all future research will be reviewed and approved by the NREC before it begins"* be updated to *"I understand that no future research will begin unless it has been reviewed and approved by an ethics committee"*
- The NREC-CT noted that the following statements in the Main Combination ICF pg 10, Main Monotherapy ICF pg 10" and Main Triple Combination Therapy ICF pg 11 "*The Sponsor would like to know if you allow the use of any leftover samples for future research. This means that the samples may be tested to:  Learn more about the effects of STX-478 on advanced solid tumours;  Develop new drugs or devices, tests, or processes, including commercial products; or  Other purposes that are not yet known.*" Main Combination ICF pg 19, Main Monotherapy ICF pg 18 and Main Triple Combination Therapy ICF pg 10 "*to understand the disease better or to review the safety or effectiveness of the study drug, or for other research purposes* "do not describe future research in line with regulations and best practice, as it is not confined to the disease or drug under study.
  The NREC-CT requested that future use of samples/personal data is sufficiently explained to participants and aligned across all relevant sections of SIS and ICF 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 disease, disease area or the drug under study in this trial and this is clearly stated in the main body of PIS and informed consent sections of the ICF. 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 any future research they are consenting to, will also be subject to ethical assessment 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 the following statement in the Pregnancy ICF pg 3 "Triple Combination Therapy, (i.e., STX-478 combined with Fulvestrant and either Ribociclib or Palbociclib*), "When we talk about using your/your baby's coded study data, including your/your baby's coded personal information, it means that Novartis and Pfizer (and parties working with Novartis and Pfizer) will also use this data to develop their drugs and for other research purposes."* does not describe future research in line with regulations and best practice, as it is not confined to the disease or drug under study.
  The NREC-CT requested that future use of samples/personal data is sufficiently explained to participants and aligned across all relevant sections of SIS and ICF 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 disease, disease area or the drug under study in this trial and this is clearly stated in the main body of PIS and informed consent sections of the ICF. 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 any future research they are consenting to, will also be subject to ethical assessment 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 the Main Combination ICF pg 27, Main Monotherapy ICF pg 27 and Triple Combination Therapy ICF pg 33 details that the Ethics Committee will have access to participants' medical records. Please note that the NREC will not request access to medical records of any participants. Please remove reference to this from the PISCF's.
- The NREC-CT noted that Main Combination ICF pg 33, Main Monotherapy ICF pg 36, Main Triple combination therapy ICF pg 39 state that "I understand that the information collected about me will be used to support other research in the future into advanced solid tumours and may be shared anonymously with other researchers. No further consent will be requested to perform this future research." The Committee requested that the Main Combination ICF, Main Monotherapy ICF , Main Triple combination therapy 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 NREC-CT requested that the Main Monotherapy ICF pg 30 be updated to move consent for optional biopsy tumour to a separate page with separate signature sections from the consent for main study to ensure consent for optional components is informed and explicit.
- The NREC-CT noted that the treatment period is not described clearly in the ICF's The Committee requested that Main Monotherapy ICF pg 6, Main Combination Therapy ICF pg 6 ad Main Triple Combination ICF pg 7 be updated to clearly describe the treatment period.
- The NREC-CT noted that the detail on travel expense appears in the appendix of the ICF's. The Committee requested that the Main body of the Monotherapy ICF, Combination Therapy ICF and Triple Combination ICF be updated to provide some detail on the travel expense including specifying (1) what will be reimbursed (travel, food, accommodation) and (2) how (via Colpitts or alternative), and detail of what the alternative is.
- The NREC-CT requested the following statement on page 20/39 of the Main Combination ICF be removed "Irish law requires that you report side effects that you experience even after you leave this study", as this statement is incorrect.

- The NREC-CT requested that all ICF's be updated to clearly state how many visits are needed and include estimated duration of each visit.
- The NREC-CT requested that the statement on Pregnant Partner Participant Newborn Child ICF pg 3 "Your/your baby's general practitioner (GP) or family doctor will be notified of your/your baby's involvement in this study".be updated to include "if you agree"
- The NREC-CT requested that consent pages on Pregnant Partner Participant Newborn Child ICF be updated to include a specific consent statement for follow up 12 months after birth.
- The NREC-CT requested that the Main Combination Therapy ICF pg 10, Main Monotherapy ICF pg 10 and Triple Combination Therapy ICF pg 11 "What happens to the samples collected from you" be updated to replace *"will receive approval by an ethics committee*" with *"will require approval by an ethics committee".*
- The NREC-CT requested that Main Combination Therapy ICF pg 15, Main Monotherapy ICF pg 15 and Triple Combination Therapy ICF be updated to provide a definition and examples of a highly effective method of birth control for use by female partners of male study participants. Furthermore, the NREC requested that clarification is provided regarding the requirement for use of a further method of contraception for participants that have undergone a hysterectomy.
- The NREC-CT requested that the Main Monotherapy ICF pg 27 and Main Combination Therapy ICF pg 33 "Study data, including your coded medical information, may be retained and later used for further research into your medical indication, unless you object" be updated to replace the word *"indication*" with the word *"condition"* which is more appropriate.
- The NREC-CT noted that Main Monotherapy ICF and Main Combination Therapy, and Triple Combination Therapy ICF's only list side effects with a frequency of > 5 in 100. The Committee requested that the ICF's be updated to include all side effects and their frequencies as listed in the patient leaflet for Faslodex (authorised by the EMA).
- The NREC-CT noted that in Triple Combination Therapy ICF there is inconsistency in the way frequencies of side effects are presented between ribociclib and palbociclib. The Committee requested that the Triple Combination Therapy ICF be updated with frequencies of side effects presented for ribociclib and palbociclib being presented in similar way as in the patient leaflet approved by the EMA.

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

- No considerations raised by NREC

**8. Suitability of the investigator**

- No considerations raised by NREC

**2023-509908-15-00 SM-2**

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

Study title: A Phase 3 Randomized, Open-Label, Multicenter Study Comparing Zanubrutinib (BGB-3111) plus Rituximab Versus Bendamustine plus Rituximab in Patients with Previously Untreated Mantle Cell Lymphoma Who Are Ineligible for Stem Cell Transplantation

Dossiers Submitted: Part I & II

- **NREC-CT Decision:**

- Favourable

**2022-501238-52-00 SM-24**

Institutions: Children's Health Ireland Crumlin

Study title: A Phase 2/3 Randomized, Placebo-Controlled, Double-blind, Clinical Study to Evaluate the Efficacy, Safety, and Pharmacokinetics of Vericiguat in Pediatric Participants with Heart Failure due to Systemic Left Ventricular Systolic Dysfunction (VALOR)

Dossiers Submitted: Part I & II

- **NREC-CT Decision:**

- Request for Further Information

- **Additional Information Required RFI**

| Part II Considerations |
|---|
| **1. Compliance with use of biological samples** |
| • As per request from Sponsor, please provide an updated biological samples form if blood volumes are affected. |
| **2. 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<br>• 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.<br>• As per request from Sponsor, please provide updated ICF's if blood volumes are affected. |

**2024-518177-33-00 SM-1**

Institutions: Tallaght University Hospital, Galway University Hospital, St James's Hospital, Sligo University Hospital

Study title: Cancer Appetite Recovery Study (CAReS): a phase 1/2 trial of the synthetic cannabinoid ART27.13 in patients with cancer anorexia and weight loss

Dossiers Submitted: Part I & II

- **NREC-CT Decision:**

- Request for Further Information

- **Additional Information Required RFI**

| Part II Considerations |
|---|
| **1. Compliance with use of biological samples** |
| • This document represents information already approved under CTD |
| **2. Financial arrangements** |
| • This document represents information already approved under CTD |
| **3. Proof of insurance** |
| • No considerations raised by NREC |
| **4. Recruitment arrangements** |
| • This document represents information already approved under CTD |
| **5. 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 the following statement in the SIS Adults pg 19 *"By signing the Consent Form, you agree to allow the study team access to information for the current study and any further research that may be conducted in relation to it, even if you withdraw from the current study."* does not describe future research in line with regulations and best practice, as it is not confined to the disease or drug under study.<br>The NREC-CT requested that future use of personal data is sufficiently explained to participants and aligned across all relevant sections of SIS and ICF 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).<br>Furthermore,<br>o It should be made optional<br>o it should be confined to a disease, disease area or the drug under study in this trial and this is clearly stated in the main body of PIS and informed consent sections of the ICF. 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 any future research they are consenting to, will also be subject to ethical assessment 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 the SIS Adults pg 3 includes the added line *"The sponsor and its representatives will be able to review your treatment assignment but this will not impact how you are being treated".* The Committee requested that this wording be deleted or amended to be clearer about the fact that medical data will be shared with the sponsor

**6. Suitability of the investigator**

- This document represents information already approved under CTD

**2024-517500-11-00 SM-2**

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

Study title: A Phase 1B/2A Dose Escalation Study of BOLD-100 in Combination with Folfox Chemotherapy in Patients with Advanced Solid Tumours

Dossiers Submitted: Part I & II

- **NREC-CT Decision:**

- Favourable

**2023-504684-16-00 SM-3**

Institutions: Mater Misericordiae University Hospital

Study title: A Phase 3, Randomized, Double-Blind, Placebo-Controlled, Multicenter Study to Evaluate the Efficacy and Safety of Tafasitamab Plus Lenalidomide in Addition to Rituximab Versus Lenalidomide in Addition to Rituximab in Patients With Relapsed/Refractory (R/R) Follicular Lymphoma Grade 1 to 3a or R/R Marginal Zone Lymphoma

Dossiers Submitted: Part I & II

- **NREC-CT Decision:**

- Favourable

**2022-500439-35-00 SM-8**

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

Study title: A phase 3 multicenter, randomized, prospective, open-label trial of ibrutinib mono-therapy versus fixed-duration venetoclax plus obinutuzumab versus fixed-duration ibrutinib plus venetoclax in patients with previously untreated chronic lymphocytic leukemia (CLL)

Dossiers Submitted: Part I & II

- **NREC-CT Decision:**

- Favourable

**2023-506288-33-00 SM-3**

Institutions: Tallaght University Hospital, Cork University Hospital, St Vincent's University Hospital

Study title: MK-5684-01A Substudy: A Phase 1/2 Umbrella Substudy of MK-5684-U01 Master Protocol to Evaluate the Safety and Efficacy of MK-5684-based Treatment Combinations or MK-5684 Alone in Participants With Metastatic Castration-resistant Prostate Cancer (mCRPC)

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**

- 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 requested clarification in relation to how this stratification cap will affect Irish participants already screened or if it will only affect those recruited after the pause.
- The NREC-CT requested that the ICF Optional Greenphire Adults pg 2 be updated to replace "laws in the UK." with "laws in Ireland".

**2023-506081-31-00 SM-2**

Institutions: Mater Misericordiae University Hospital, Beaumont Hospital, St Vincent's University Hospital, Tallaght University Hospital, Cork University Hospital

Study title: EPO-TRAUMA

Dossiers Submitted: Part II

- **NREC-CT Decision:**

- Favourable

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- AOB:
  - Overview of interaction with HPRA discussed
  - Overview of CTIS system to be given at next meeting