National Research Ethics Committee

NREC-CT A Meeting

18th September 2024

Attendance

Name	Role
Prof. Gene Dempsey*	Deputy Chairperson, 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
Ms Margaret Cooney	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
Mrs Patricia Kenny	Project Officer, National Office for RECs
Dr Emma Heffernan	Project Officer, National Office for RECs
Ms Rachel McDermott	Project Administrator, National Office for RECs
Mr Ciarán Horan	Administrative Assistant, National Office for RECs

*Chaired Meeting

Apologies: Prof. Alistair Nichol, Dr Brian Bird, Dr Seán Lacey, Ms Caoimhe Gleeson, Dr David Byrne

Quorum for decisions: Yes

Agenda

- Welcome & Apologies
- 2023-509632-26-00
- 2022-501709-11-00 SM-9
- 2023-503765-37-00 SM-4
- 22-NREC-CT-172_Mod-2
- 2023-509908-15-00 SM-1
- 2023-505268-12-00 SM-2
- 2022-500536-11-01 SM-16
- 2024-511553-22-00 SM-1
- 2022-500699-76-00 SM-14
- AOB

- The Chair welcomed the NREC-CT A.
  - The minutes from the previous NREC-CT A meeting on 14th August 2024 were approved.
  - The NREC Business Report was discussed and noted.

Applications

2023-509632-26-00

Institutions: St Vincent's University Hospital, START Dublin, Mater Misericordiae University Hospital, Cork University Hospital, Galway University Hospital, Tallaght University Hospital

Study title: A Phase 1b/2 Pan-tumor, Open-label Study to Evaluate the Efficacy and Safety of Ifinatamab Deruxtecan (I DXd) in Subjects with Recurrent or Metastatic Solid Tumors (IDeate-Pantumor02)

Dossiers Submitted: Part I and II

- **NREC-CT Decision:**

- Request for Further Information

Part I Considerations

1. Protocol

- The Sponsor is asked to give further information or clarification on the Statistical Design, specifically in relation to the following:
    - The Protocol states that no statistical hypotheses will be tested, but it is noted that the statistical considerations includes many references to statistical tests estimates, and confidence intervals. Please clarify what statistical tests will be used.
    - The Sponsor is requested to clarify whether the study is powered to observe sufficient effects to meet the endpoints.
    - The Protocol states that data in Stage 1 will be used to make decisions around futility and/or dosing for Stage 2. Please clarify how these decisions will be made.
    - With respect to futility and the decision to move to stage 2, further explanation is required for how the table of assumed ORRs under standard of care were calculated, and the rationale as to why there is a different anticipated ORR for each cohort.
    - Further justification is required as to why the data from each cohort will be analysed separately. This will have the same effect as discarding the data from some number of patients, even if there is considerable between-cohort heterogeneity.

2. DSMB Charter

- The Sponsor is recommended to add an independent statistician to the IDMC.

Part II Considerations

1. Compliance with national requirements on data protection

- The NREC-CT noted that explicit consent is not detailed in the DPIA as a legal basis for data processing, and requested clarification on whether this is applicable.

2. Financial arrangements

- The NREC-CT noted that participants may be unwell during the trial and require accompaniment from a carer for site visits, and requested further information on whether carers may also be reimbursed for out-of-pocket expenses.

3. Recruitment arrangements

- The NREC-CT noted that the participant study guide states: ‘the study doctor may need to take a small piece of tissue from your tumour. If this has already been done, you will need to provide this sample to the study team’. The NREC-CT requested that this is reworded as it may be confusing for the participant, implying the participant will have their sample in their possession (Participant Study Guide, Page 7).
- The NREC-CT requests clarification on whether participants who require the use of an Impartial Witness will be included in the trial, as contradictory statements are detailed in the Recruitment Arrangements form, stating that those who cannot read

or write are not anticipated to be included (Recruitment Arrangements template, Section 4.1).

4. Subject information and informed consent form

- The NREC-CT requests the participant is given more detail on how the IMP works (Main PISCF, Page 2).
- The NREC-CT notes the following sentence: 'An investigational drug is a drug that is not approved for your disease' and requested that this is further clarified for participants that while it is not approved by regulators, it has previously been tested in human participants. (Main PISCF, Page 2).
- The NREC-CT noted the use of technical language through the PISCF documents, including 'immunogenicity analyses, SAEs, ctDNA, PBMC', and requested that these be explained to participants in lay language.
- The NREC-CT notes that the participant is asked to consent in relation to incidental findings, and requests that this is fully explained to participants in the main body of the PISCF (Main PISCF, Page 10).
- The NREC-CT requested that the number of participants/studies that have been treated with the IMP is added to the section on Side Effects, and additionally referenced when describing previous benefit observed in previous studies (Main PISCF, Pages 10-12).
- The NREC-CT noted that the potential side effects from similar drugs have been included in the PISCF, and requested that further detail is included on what types of drugs are being referenced, and how likely these side effects are to affect participants in this trial (Main PISCF, Page 14).
- The NREC-CT noted the following sentence in relation to the risk of interstitial lung disease: 'The study doctor will provide you with a separate patient information guide regarding the risk of lung problems' and requested that if this patient guide is available, to please submit it for review. Furthermore, further information on the frequency and severity of this risk should be detailed in the PISCF (Main PISCF, Page 12).
- The NREC-CT requested that the participant is given information on who to contact out-of-hours if the study doctor is not available.
- The NREC-CT advised that the section on HIV testing and reporting of same is not in line with Irish law, and while HIV is a notifiable infection, the information provided does not identify the individual, using a coding system for anonymity. The NREC-CT requests that this section is amended to comply with Irish law (Main PICSF, Page 15).
- The NREC-CT noted the consent section that states 'If the study doctor is not my GP', and requests this is removed or reworded, as in Ireland the study doctor would not be the participant/participant's partner's GP (Main ICF, Page 26 and Pregnant Partner ICF, Page 7).
- The NREC-CT noted the following sentence in relation to genetic data: 'If identifiable genetic or health information is disclosed to unauthorised persons, there is the possible risk of discrimination by employers, insurance providers or others', and requested that this is amended to reflect Irish law (Main PISCF, Page 16/17).
- The NREC-CT noted inconsistencies between the PISCF documents and the DPIA, and requested that these be corrected as applicable:

- The sub-study PISCF references masked data, however this is not explained in the Main PISCF and is not mentioned in the DPIA.
- The DPIA details that the Sponsor will ensure that participant data is protected, however in the Main PISCF consent section it contradicts this, asking participants to acknowledge that these safeguards are not in place.
- GDPR requirements should be referenced in the Main PISCF, pages 20/21.

- The Sponsor is requested to submit any Part II documentation that require updates as a result of the Part I Assessment.

5. Suitability of the clinical trial sites facilities

- The NREC-CT noted that ophthalmology examinations will form part of the schedule of assessments, and requested further information on where these examinations will take place, if not already present at site.

2022-501709-11-00 SM-9

Institutions: St James's Hospital, Cork University Hospital

Study title: A single arm, open-label Phase 3b study to describe the safety and tolerability of ivosidenib in combination with azacitidine in adult patients newly diagnosed with IDH1m acute myeloid leukemia (AML) ineligible for intensive induction chemotherapy

Dossiers Submitted: Part I and II

- **NREC-CT Decision:**

- Request for Further Information

Part II Considerations

1. Subject information and informed consent form

- The NREC-CT requested clarification on whether all participants will be reconsented to the new ICF document.
- The NREC-CT noted that continued access to the IMP will be facilitated through commercial means should the IMP become available commercially, and requested further information on whether participants will then be charged for this access.
- The NREC-CT noted that while the language in the new ICF document is very clear, the layout could lead to participants signing to give their consent without having fully read the contents. The NREC-CT requested that the consent page be placed at the end of the document to avoid this possibility. Additionally, the NREC-CT requested that consent for the male partner be separated from the main consent section.

2023-503765-37-00 SM-4

Institutions: St James's Hospital

Study title: An Extension Study Assessing the Long-term Safety and Efficacy of Etranacogene Dezaparvovec (CSL222) Previously Administered to Adult Male Subjects with Haemophilia B

Dossiers Submitted: Part I and II

- **NREC-CT Decision:**

- Request for Further Information

Part II Considerations

1. **Subject information and informed consent form**
   - The NREC-CT noted technical language in the Optional Future Research ICF document, including 'molecular analysis' and 'genome', and requested that these are explained in lay terminology.

22-NREC-CT-172_Mod-2

Institutions: St James's Hospital

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

Dossiers Submitted: N/A

- **NREC-CT Decision:**

- Request for Further Information

- **Additional Information Required:**
- The NREC-CT noted that the Sponsor will assign a unique identifier to each participant, and queried whether this should take place at the site, by site staff (Protocol, Page 60).
- The NREC noted the following sentence: "biopsies will be collected in a subset of consenting patients to measure pharmacoynamic parameters, cancer genetic profiling..", and requested that this be rephrased in lay language (Main PISCF, Page 5).

2023-509908-15-00 SM-1

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

- **NREC-CT Decision:**

- Request for Further Information

Part II Considerations

1. **Subject information and informed consent form**
   - The NREC-CT noted the following sentence: “Grapefruit or bitter oranges should be consumed with caution around the time you take zanubrutinib” and requested better clarity is given to participants on this instruction; for example, advising that participants completely omit these foods from their diet (Main PISCF, Page 25)
   - The NREC-CT noted the long list of prohibited medications/ concomitant medications, and requested further information on whether the participant’s GP is informed of these requirements. If a GP letter is available, please submit it for review. (Main PISCF, Pages 24/25)
   - The NREC-CT noted the list of possible central labs for storage of participant samples, and requested further information on which lab is relevant for Irish participants. (Main PISCF, Page 35)

2023-505268-12-00 SM-2

Institutions: La Nua Hospital Mental Health Centre, Sheaf House

Study title: A Phase III, multicentre, randomised, double-blind, controlled study to investigate the efficacy, safety, and tolerability of two initial administrations of COMP360 in participants with treatment-resistant depression

Dossiers Submitted: Part I and II

- NREC-CT Decision:

- Favourable

2022-500536-11-01 SM-16

Institutions: Our Lady of Lourdes Hospital, Portiuncula Hospital, Connolly Hospital, Beaumont Hospital, St Vincent’s University Hospital, Regional Hospital Mullingar

Study title: A randomized, double-blind, placebo-controlled, multicenter, phase III study to evaluate the efficacy and safety of ABX464 once daily for induction treatment in subjects with moderately to severely active ulcerative colitis

Dossiers Submitted: Part I and II

- **NREC-CT Decision:**

- Request for Further Information

Part II Considerations

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

- The NREC-CT notes the reference to the study doctor or 'his' delegated staff, and requested that this is changed to 'their' delegated staff. (Main PISCF, Page 4)

2024-511553-22-00 SM-1

Institutions: Beaumont Hospital

Study title: A Phase 3, Multicenter, Open-Label Extension Study of Oral Ozanimod for Moderately to Severely Active Crohn's Disease

Dossiers Submitted: Part I and II

- NREC-CT Decision:

- The initial decision was Request for Further Information, with the consideration to be raised below. However, the study was concluded in Ireland shortly after the submission of this Substantial Modification, and as such, no further action was required and no decision was issued.

Part II Considerations

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

- The NREC-CT noted the termination of the study, and requested further information on how this will be communicated to the participants.

2022-500699-76-00 SM-14

Institutions: Our Lady's Hospital Manorhamilton, Cork University Hospital, St James's Hospital, Connolly Hospital

Study title: A Phase 3, Randomized, Double-Blind, Placebo-Controlled Study to Evaluate the Efficacy and Safety of Deucravacitinib in Participants with Active Systemic Lupus Erythematosus (SLE) (POETYK SLE-1)

Dossiers Submitted: Part I and II

- **NREC-CT Decision:**

- Request for Further Information

Part II Considerations

1. **Recruitment arrangements**

- The NREC-CT requested further detail of the new recruitment vendor: AutoCruitment, specifically in relation to the following:
    - The privacy policy of the platform, in terms of security of the data transferred outside of the EU;
    - How the platform determines participant eligibility for the trial (is there human involvement or is it determined through AI);
    - The use of a potential participant's phone number in a follow up text message, and how a potential participant can opt out of that if they are no

longer interested in completing their screening through the platform; Furthermore, the NREC-CT considered that it may be undue inducement to follow up with a participant via text message who has decided not to complete the process,
    - The equity of this being an online platform, and whether there are alterative options for recruitment of participants who may not have access to a computer or the internet;
    - Whether the platform is paid on a per-participant basis.

2. Subject information and informed consent form

- The NREC-CT noted that the monetary amounts detailed for participant payment or reimbursement 'may have tax implications' and requests that this is clarified for participants, or removed if not applicable to the Irish setting.

- AOB:
    - An update on the recent CTR Collaborate Stakeholder's Meeting was given by Dr Jane Bryant.