# National Research Ethics Committee

## NREC-CT B Meeting

**27th November 2024**

### Attendance

| Name | Role |
|---|---|
| Dr Cliona McGovern | Chairperson, NREC-CT B |
| Dr John Hayden | Deputy Chairperson, NREC CT-B |
| Colm O'Donnell | Deputy Chairperson, NREC-CT B |
| Ms Serena Bennett | Committee Member, NREC-CT B |
| Dr Åine de Róiste | Committee Member, NREC-CT B |
| Dr Karina Halley | Committee Member, NREC-CT B |
| Prof. Seamus O'Reilly | Committee Member, NREC-CT B |
| Ms Evelyn O'Shea | Committee Member, NREC-CT B |
| Mrs Ann Twomey | Committee Member, NREC-CT B |
| Prof. John Wells | Committee Member, NREC-CT B |
| Ms Jasmine Joseph | Committee Member, NREC-CT B |
| 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 |
| Ms Aileen Sheehy | Programme Manager, National Office for RECs |
| Dr Peadar Rooney | Project Officer, National Office for RECs |
| Dr Emma Heffernan | Project Officer, National Office for RECs |
| Mr Ciaran Horan | Administrative Assistant, National Office for REC's |

*Drafted minutes

**Apologies:**

Michaela Higgins,

Niall McGuinness

Ciaran Lee

Andrew Lindsay

**Conflict of Interest:**

Seamus O'Reilly with 2023-507890-17-00 SM4 - was not present for review.

**Quorum for decisions:**

Yes

## Agenda

- Welcome & Apologies
- 2023-508636-61-00
- 2022-502122-41-00 SM-3
- 2023-504694-20-00 SM-3
- 2023-507697-40-00 SM-1
- 2023-510160-12-00 SM-1
- 2023-507890-17-00 SM-4
- 2023-504962-52-00 SM-8
- 2024-512785-33-00 SM-9
- 2023-510289-28-00 SM-1
- AOB

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- The Chair welcomed the NREC-CT B.
  - The minutes from the previous NREC-CT B meeting on 23rd October were approved.
  - The NREC Business Report was discussed and noted.

## Applications

**2023-508636-61-00**

Institutions: Beaumont Hospital, St Vincent's University Hospital

Study title: A Phase 3, Randomized, Double-Blind, Placebo-Controlled Program to Evaluate the Efficacy and Safety of Tulisokibart in Participants with Moderately to Severely Active Crohn's Disease

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 that the proposed future use of data / samples is not described in line with regulations / best practice in the document IRL_MK7240-008_FBR_v.00_English_Site XXXX_24-Oct-2024. 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 made optional
  - 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,
  - optional future research is made into a separate and explicit consent item in the Informed Consent section of the Main PISCF, with separate participant information section and signatures section, so it is distinct from the main consent to participate in the research

  The PISCF should also make it clear to participants that, with regard to subsequent research, ethics committee 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 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, on pg3 of the Main ICF, the four studies groups are detailed. The NREC-CT requested that more detail is included in the Main ICF pg3 about the differences between groups 1,2,3.
- As per the protocol, the NREC-CT requests that the Main ICF provides clarifying information that participants receiving placebo (Group 4) may choose to enter reinduction phases and extension phases upon completion of the initial 52 week study.
- The NREC-CT noted on page 10 of the Main ICF, that “Your pregnancy will be monitored, and the trial doctor will collect health data about your pregnancy and your baby. “The NREC-CT requests that explicit consent for the collection of pregnancy data for the mother and child is included as a separate item in the consent section on page 16 of the Main ICF or as a separate pregnancy ICF to be signed in the event of a pregnancy.
- The NREC-CT noted that on ICF of the optional PK study on page 3 in the monetary payment section, the value of compensation is in GBP. The NREC-CT requests that all monetary compensation should be localised to the country appropriate currency i.e. Euro for the Republic of Ireland.
- The NREC-CT noted that on the optional participant vendor service ICF on page 2 “privacy and data protection laws in the UK” and on page 3 “USA privacy laws may not be the same as in the UK” mentions UK laws, the NREC-CT requests that the forms to be localised to the laws and regulations relevant in the Republic of Ireland.
- The NREC-CT notes that all consent forms do not leave a space for the qualification of the person who obtains consent, the NREC-CT requests that a space is provided for the qualification of the person who is obtaining consent.

**2022-502122-41-00 SM-3**

Institutions: Beaumont Hospital, Adelaide and Meath Hospital

Study title: An Open-label, Randomized Phase 3 Study to Evaluate Efficacy and Safety of Pembrolizumab (MK-3475) in Combination with Belzutifan (MK-6482) and Lenvatinib (MK-7902), or MK-1308A in Combination with Lenvatinib, versus Pembrolizumab and Lenvatinib, as First-line Treatment in Participants with Advanced Clear Cell Renal Cell Carcinoma (ccRCC)

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 rationale why male participants are no longer required to inform the PI if their partner becomes pregnant is provided to the committee.

**2023-504694-20-00 SM-3**

Institutions: Children's Health Ireland

Study title: A phase I/II study of Inotuzumab Ozogamicin as a single agent and in combination with chemotherapy for pediatric CD22-positive relapsed/refractory Acute Lymphoblastic Leukemia

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 that pg. 16 of the IE-en_ICF_Stratum 3_Parents_TC and pg. 13 of the L1_IE-en_ICF_Stratum 3_Adults_TC_ state that future use of data will be used 'for the purposes of scientific research' and requested future use of data / samples is confined to a particular area of health research such as the related disease or drug under study in this trial as required under the Health Research Regulations (Data Protection Act 2018 (Section 36(2) (Health Research) Regulations 2018). This should be aligned across all assent forms.
- The NREC-CT noted that the updated language around future use of samples has been captured in the documentation for the parents / guardians, but has not been included in the assent information for minors. The Committee requests a rationale for this exclusion from the assenting materials.
- The NREC-CT noted that the updated side effects are described using overly technical language and are not suitable for a lay audience. The Committee requested that the updated side effects are explained to parents / guardians on pgs. 12 & 13 of IE-en_ICF_Stratum 3_Parents_TC, and to participants on pgs. 9 & 10 of the L1_IE-en_ICF_Stratum 3_Adults_TC_not for publication using plain English suitable for a lay audience.

2. **Suitability of the investigator**

- The NREC-CT noted that [redacted] has limited clinical trial experience listed in his CV and requested that this section is updated to include a more detailed account of his relevant clinical trial experience. If [redacted] is new to acting as Principal Investigator for trials, the Committee requests further information on additional senior support available at the site for him to be able to fulfil the role.

**2023-507697-40-00 SM-1**

Institutions: Beaumont Hospital, St James's Hospital

Study title: A Phase 3 Open-Label, Randomized Study of LOXO-305 versus Investigator's Choice of Idelalisib plus Rituximab or Bendamustine plus Rituximab in BTK Inhibitor Pretreated Chronic Lymphocytic Leukemia/Small Lymphocytic Lymphoma (BRUIN-CLL-321)

Dossiers Submitted: Part I & II

- **NREC-CT Decision:**

- Request for Further Information

- **Additional Information Required RFI**

| Part II Considerations |
|---|
| **1. Recruitment arrangements** |
| • The NREC-CT requested clarification as to how participants will be informed of the new adverse events reported, given that recruitment has been completed. |
| **2. Subject information and informed consent form** |
| • The NREC-CT noted a number of new TEAEs listed in the updated Investigator's Brochure for Pirobrutinib and, in order to the facilitate informed patient decision-making, the following information is required in the SIS-ICF:<br>▪ On p.2, please provide information on the reported frequency of the additional side effects listed (i.e., Infection of upper respiratory tract and Infection of the structures that carry urine).<br>▪ On p.2, data on relative risk of bleeding for patients with concomitant use of blood thinners.<br>▪ Frequency data on liver injury as per p.96 of IB Pirobrutinib.<br>▪ On p.2, frequency data on "Rituximab Risks".<br>▪ On p.3, frequency data on "Benamustine Risks". |

**2023-510160-12-00 SM-1**

Institutions: Children's Health Ireland

Study title: A randomized phase 3 trial of fludarabine/cytarabine/gemtuzumab ozogamicin with or without venetoclax in children with relapsed AML

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 that the explanation concerning the status change (i.e., updated to IMPs) of the chemotherapy drugs included in the SIS-ICFs for parents/guardians and young adults (p3) is difficult to read, and requests that a clearer explanation using Plain Language is provided. If this paragraph is not required, the Sponsor may decide to remove it.
- As the chemotherapy drugs (i.e., cytarabine, fludarabine, azacitidine) are now considered IMPs, please update the following:
    - Include side effects in the Parents SIS-ICF (p21)
    - Include possible side effects, undesirable effects and inconveniences in the Parents SIS-ICF (p22)
    - Include side effects in the Young Adults SIS-ICF (p20)
    - Include possible side effects, undesirable effects and inconveniences in the Young Adults SIS-ICF (p21)
- The NREC-CT requested that an explanation be included in both the Parents and Young Adults SIS-ICFs as to why racial/ethnicity data is being collected, as per the rationale provided with the FDA Project Equity Initiative.

**2023-507890-17-00 SM-4**

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

Study title: A Phase 3, Double-Blind, Randomized Study to Compare the Efficacy and Safety of Luspatercept (ACE-536) Versus Placebo in Subjects with Myeloproliferative Neoplasm-Associated Myelofibrosis on Concomitant JAK2 Inhibitor Therapy and Who Require Red Blood Cell Transfusions

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 requested that the new text related to common side effects on Page 17 of the PISCF is reworded to ensure that participants clearly understand the terminology. For example, the paragraphs should begin with clear language e.g. 'In participants with MDS, the following symptoms are noticed…'.

- The NREC-CT requested that an additional sentence is added to the informed consent form outlining the role and criteria of the Impartial Witness under the signature line.

**2023-504962-52-00 SM-8**

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

Study title: A Phase 3, Randomized, Open-label, Study to Compare the Efficacy and Safety of Adjuvant MK-2870 in Combination with Pembrolizumab (MK-3475) Versus Treatment of Physician's Choice (TPC) in Participants With Triple-Negative Breast Cancer (TNBC) Who Received Neoadjuvant Therapy and Did Not Achieve a Pathological Complete Response (pCR) at Surgery

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 requested that Section 12 of the Main PISCF is updated to include ILD/pneumonitis as a potential event of clinical interest as per the protocol modification.

**2024-512785-33-00 SM-9**

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

Study title: A Phase 2/3, Randomized, Double-Blinded, Placebo-Controlled, Parallel-Group, 2-Arm, Multicenter, Operationally Seamless Study to Evaluate the Efficacy, Safety, Tolerability, Pharmacodynamics, Pharmacokinetics, and Immunogenicity of Efgartigimod PH20 SC in Participants Aged 18 Years and Older With Active Idiopathic Inflammatory Myopathy

Dossiers Submitted: Part II

- **NREC-CT Decision:**

- Favourable

**2023-510289-28-00 SM-1**

Institutions: St James's Hospital

Study title: A Phase 2, Open-label, Multicenter Study of Mitapivat in Subjects With Sickle Cell Disease and Nephropathy

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 requested that Pg. 27 of the Main ICF related to the Scout Clinical information is amended as follows:
  - Make it explicitly clear that expenses for both participants and carers will be reimbursed as specified in the Compensation template,
  - That the term 'per one-way transfer' is reworded to make it explicitly clear what this term means.
- The NREC-CT noted that on Pg. 7 of the Main ICF there is no information added under the heading 'Checking for Side Effects and Other Medications You Are Taking' and requested clarification whether this is in error.
- The NREC-CT noted the addition of the tote bag for participants and requested confirmation that no trial information will be visible on this merchandise.

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- AOB:
  - N/A