National Research Ethics Committee

NREC-CT B Meeting

15th January 2025

Attendance

Name	Role
Dr Cliona McGovern	Chairperson, NREC-CT B
Dr John Hayden	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. Michaela Higgins	Committee Member, NREC-CT B
Ms Jasmine Joseph	Committee Member, NREC-CT B
Dr Ciaran Lee	Committee Member, NREC-CT B
Dr Andrew Lindsay	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
Dr Emily Vereker	Acting Head, National Office for RECs
Dr Jane Bryant	Project Officer, National Office for RECs
Dr Laura Mackey	Programme Officer, National Office for RECs
Mr Ciaran Horan	Administrative Assistant, National Office for REC's
Dr Susan Quinn	Programme Manager, National Office for RECs
Dr Aileen Sheehy	Programme Manager, National Office for RECs
Ms Deirdre Ní Fhloinn	Project Officer, National Office for RECs
Ms Chita Murray	Programme Manager, National Office for RECs

Apologies: Prof John Wells, Prof Colm O'Donnell, Dr Niall McGuinness

Quorum for decisions: Yes

Agenda

- Welcome & Apologies
- 2023-509391-42-00
- 2024-515162-13-00
- 2024-516009-22-00
- 2023-506842-22-00 SM-1
- 2022-501943-34-00 SM-5
- 2024-510800-35-00 SM-2
- 2022-501463-40-01 SM-3
- AOB

- The Chair welcomed the NREC-CT B.
  - The minutes from the previous NREC-CT B meeting on 27th November 2024 were approved.
  - The NREC Business Report was discussed and noted.

Applications

2023-509391-42-00

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

Study title: A Randomized, Double-blind, Placebo-Controlled Phase 3b Study to Evaluate the Short-and Long-term Efficacy and Safety of Dual Targeted Therapy With Intravenous Vedolizumab and Oral Upadacitinib Compared With Intravenous Vedolizumab Monotherapy for the Treatment of Adult Participants With Moderately to Severely Active Crohn's Disease

Dossiers Submitted: Part I & II

NREC CT Decision

- Request for Further Information

Part II Considerations

1. Compliance with national requirements on data protection

- The NREC noted that criminal record checks may be carried out on study staff (DPIA pg 5) Please clarify if this applies to the Irish context ie Garda Vetting processes.

2. Financial arrangements

- The NREC noted that compensation of meal and travel expenses will not be offered to carers of participants (pg 1 of Payment Compensation Form). The NREC requested that compensation of meal and travel expenses be considered for carers as well as participants of the trial.

3. Recruitment arrangements

- The NREC noted that only three participants were to be recruited in Ireland (one per site as per each site suitability form). The NREC requested clarification on why so few participants were planned to be recruited in Ireland.

4. Subject information and informed consent form

- The NREC noted that that the risk of Progressive Multifocal Leukoencephalopathy (PML) is placed below the section outlining risks with >2% occurrence (p12 Main ICF), which could be confusing to the reader. The NREC requested a clearer separation between these two sections.
- The NREC noted that the risks of Upadacitinib occurring in >2% of participants in Crohn's disease clinical trials are listed on p13 of the Main ICF. However, these risks do not fully correlate with the risks occurring in >3% of participants in Crohn's disease clinical trials according to the SmPC for Upadacitinib. The NREC requested that information on the most common side effects of Upadacitinib and their incidence be updated in the Main ICF.
- The NREC noted that an 'infusion related reaction' is listed as a risk for Upadicitinib in the Main ICF (pg14) and suggested that this may confusing for the reader if Upadicitinib is an oral medication. The NREC requested clarification on the inclusion of 'infusion related reaction' in the risks section for Upadicitinib.
- The NREC noted that reference is made to the NHS in the Main ICF (p17). The NREC requested removal of this reference as it is not applicable to Ireland.
- The NREC noted that questionnaires used in the study were described as potentially upsetting in the main ICF (p14). The NREC requested that appropriate risk mitigation strategies and/or supports for patients be described.
- The NREC-CT noted that the section on future research in the Main PIS/CF (pg22), Future Research ICF (pg1) and Optional Genetic Testing ICF (pg2) is not described 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 in the PIS 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 specified disease area or drug under study in this trial (Crohns disease/Vedolizumab/ Upadacitinib), and this is clearly stated in the main body of PIS/CF p22 and informed consent section of the Future Research ICF p1. 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's 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

2024-515162-13-00

Institutions: Our Lady of Lourdes Hospital, Connolly Hospital, Cork University Hospital, Portiuncula University Hospital

Study title: BRISOTE: A Multicentre, Randomised, Double-blind, Parallel Group, Active-Controlled, Phase 3b Study to Evaluate the Efficacy and Safety of Benralizumab 30 mg SC in Eosinophilic Asthma Patients Uncontrolled on Medium-Dose Inhaled Corticosteroid Plus Long-acting β2 Agonist

Dossiers Submitted: Part I & II

- **NREC-CT Decision:**

- Request for Further Information

Part II Considerations

1. Compliance with the use of biological samples

- The NREC noted that the Main ICF (pg15) and the Biological Samples form (pg4) state that biosamples 'will be destroyed as soon as possible after the tests listed in Part I sections 4 and 5 for the drug development program are completed'. However, the Protocol (pg110) states that 'All appropriately consented samples will be retained for maximum 15 years from last subject last visit'. The NREC requested that the storage period for biosamples is clarified and aligned in all relevant documents.

2. Financial arrangements

- The NREC noted that the Main-ICF states that there will be reimbursement for meals, parking and travel, plus reasonable expenses for carers (pg16). However,

only meals for participants were indicated in the Compensation for Participants form (pg 1). The NREC requested clarification on whether compensation for meals, parking and travel, plus reasonable expenses for both participants and carers will be provided. The NREC requests that the documentation is aligned in all relevant documents.

3. Subject information and informed consent form

- The NREC noted the term 'patient' in informed consent forms (ICFs). The NREC requested that the term patient is replaced with the term 'participant' throughout the Main and Paediatric ICFs.
- The NREC-CT noted that the section on future research in the Main PIS/CF (pg18) 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: 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
- 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.

4. Suitability of the clinical trial sites facilities

- The NREC noted that participants aged between 12-75 years are expected to be recruited in this study, but that no paediatric hospital is listed for Ireland. The NREC requests clarification on whether the hospitals involved have the necessary facilities and experience to care for paediatric participants.

5. Suitability of the investigator

- The NREC noted that participants aged between 12-75 are expected to be recruited in this study, but that no paediatrician is listed. The NREC requests

clarification on whether the investigators are suitably qualified and experienced to care for paediatric participants.

2024-516009-22-00

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

Study title: A Phase 3, Randomized, Double-Blind, Placebo-Controlled Study to Evaluate the Efficacy and Safety of Elritercept (KER-050) for the Treatment of Transfusion-Dependent Anemia in Adult Participants with Very Low-, Low-, or Intermediate-Risk Myelodysplastic Syndromes (MDS) (RENEW)

Dossiers Submitted: Part I & II

- **NREC-CT Decision:**

- Request for Further Information

Part II Considerations

1. Recruitment arrangements

- The NREC-CT noted a lack of age and ethnic-diversity amongst the individuals pictured in the recruitment material. The Committee suggests that the Sponsor may wish to address this when possible.
- The NREC-CT noted that the Patient Letter which will be used as advertisement material, appears to present a positive impression of participation in the study. The Committee suggests that brief additional text is included, to inform the participant that partaking in research is associated with risks that should be discussed with the study team (or similar wording).

2. Subject information and informed consent form

- The Committee requests clarification whether supportive care is clinically appropriate for 24 weeks in the placebo cohort. Can the sponsor elaborate on an Irish Site PI's opinion on its suitability for participants that receive placebo?
- The NREC-CT noted that the possible risks and benefits to the participant of participation in the trial have been included in the Main PIL/ICF (starting at pg.10). The Committee requests that additional information be included with regard to the nature of the study drug, and why the Sponsor has reason to believe that it may prove advantageous/beneficial for the participant (suggest pg.1).
- The NREC-CT noted that participants may undergo bone marrow aspiration. The Committee requests that information be included in the Main PIL/ICF (risk section pg.12) with regard to the likelihood and severity of pain associated with this procedure, and an outline of the applicable pain management plan.
- The NREC-CT noted that pg.14 of the Main PIL/ICF refers to the possibility of optional home nursing visits. The Committee requests confirmation that this service will be available in the Rep. of Ireland and, if not, that reference to home visits be removed from this document.

- The NREC-CT noted that pg.16 of the Main PIL/ICF refers to a third-party vendor (Scout Clinical) which assists with management of out-of-pocket expenses (including meals, transport and lodging) for participants and caregivers. The Committee seeks clarification whether the services of Scout Clinical will be available to participants in the Rep. of Ireland and, if not, that this section of the document be amended while ensuring that such reimbursement is still available and documented.
- The NREC-CT noted that pg.17 of the Main PIL/ICF refers to withdrawal from the study. The Committee requests that additional information be provided which adequately explains that that withdrawal of consent will not affect the results of activities already carried out and the use of data obtained, based on informed consent, before its withdrawal.
- The NREC-Ct noted that pg. 2 of the Optional Future Research PIL/ICF includes the following statement: “In addition, results from the bone marrow tests and blood samples may be used for exploratory analyses” which is not in line with applicable legislation. The NREC-CT requests that future use of personal data is sufficiently explained to participants 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,
- The NREC-CT noted that pg.5 of the Optional Future Research PIL/ICF includes the following statement: “This study has been reviewed and approved by an ethics committee”. The Committee requests that this be amended to indicate that future specified research will be subject to review and approval by an ethics committee.
- The Optional Future Research PIL/ICF 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 NREC-CT noted that the Optional Future Research PIL/ICF does not include any information on genetic testing and suggests that participants should be informed that this type of testing will not occur with their samples.
- The NREC-CT noted that a Pregnancy Follow-up PIL/ICF has been submitted for the study. The Committee requests that the Sponsor comment on whether information could be provided to the pregnant person’s obstetrician/neonatologist with regard to the study arm that the participant (or their partner) took part in.

2023-506842-22-00 SM-1

Institutions: Cork University Hospital, Mater Misericordiae University Hospital, University Hospital Galway

Study title: A Phase 1, First-in-Human, Open-Label, Dose-Escalation and Expansion Study of IMGN151 (anti-FRα antibody-drug conjugate) in Adult Patients with Recurrent Endometrial Cancer and Recurrent, High-Grade Serous Epithelial Ovarian, Primary Peritoneal, or Fallopian Tube Cancers

Dossiers Submitted: Part I & II

- **NREC-CT Decision:**

- Request for Further Information

Part II Considerations

1. **Subject information and informed consent form**
   - While The NREC noted that the cover letter explains the reason for omitting the specific exploratory dosages from the Main ICF, further clarification is required in the Main ICF on how dosage is decided and allocated in the expansion phase of the study (p4).
   - The NREC noted on pg32 of the Main ICF that 'personal information' could be transferred 'to countries that have not been found by the European Commission to provide an adequate level of data protection (including the United States)'. The NREC requested further clarification on this and whether coded data is intended.
   - The NREC noted the term 'subjects' was used in the Pregnant Participant ICF (pg6) and GP Letter (pg1, pg2). The NREC request that the term 'subjects' be subtituted with 'participants".
   - The NREC-CT noted that pg38 of the Main ICF states that the NREC will have access to participants medical records and requested that this is removed, as NREC do not have access to participants medical records.

2022-501943-34-00 SM-5

Institutions: Beaumont Hospital

Study title: A Randomized, Double-blind, Placebo-Controlled, Phase 3 Study to Evaluate the Efficacy and Safety of Fazirsiran in the Treatment of Alpha-1 Antitrypsin Deficiency–Associated Liver Disease With METAVIR Stage F2 to F4 Fibrosis

Dossiers Submitted: Part I & II

- **NREC-CT Decision:**

- Request for Further Information

Part II Considerations

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

- The NREC noted that the Main ICF stated that in the event of the study drug being sold to another company “personal information” will be shared (p25). The NREC requested clarification on what information this entailed and whether ‘coded data’ would be more accurate.
- The NREC commends the sponsor on the quality of the submission.

2024-510800-35-00 SM-2

Institutions: University Hospital Galway, Beaumont Hospital, Cork University Hospital

Study title: A Phase 3, Two-Stage, Randomized, Multicenter, Open-label Study Comparing Iberdomide, Daratumumab and Dexamethasone (IberDd) versus Daratumumab, Bortezomib, and Dexamethasone (DVd) in Subjects with Relapsed or Refractory Multiple Myeloma (RRMM) (EXCALIBER-RRMM)

Dossiers Submitted: Part I & II

- **NREC-CT Decision:**

- Request for Further Information

Part II Considerations

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

- The NREC-CT noted that the following statement appears on pg 20, 21 and 26 of the Main PIS, in relation to the applicable products: “Please refer to current Summary of Product Characteristics (SmPC) for more details on known precautions, warnings, and adverse reactions…”. The Committee requests that relevant information be included in the Main PIS in plain English, such that participants are fully informed with regard to precautions, warnings, and potential adverse reactions without reference to additional documentation which may not be written specifically for participant use.
- The NREC-CT noted that pg 4 of the Main ICF is a blank page. The Committee requests that the document formatting be amended as applicable to remove this blank page, such that there is no separation between the consent statement(s) and the signature section.

2022-501463-40-01 SM-3

Institutions: St Vincent’s University Hospital, Cork University Hospital, St James’s Hospital

Study title: An Open-Label Early Access Phase 3b Study of Ivosidenib in Patients With a Pretreated Locally Advanced or Metastatic Cholangiocarcinoma

Dossiers Submitted: Part I & II

- **NREC-CT Decision:**

- Favourable

- **AOB:**
- None