National Research Ethics Committee

NREC-CT Meeting

4th December 2024

Attendance

Name	Role
Prof Mary Donnelly	Chairperson, NREC-CT C
Prof John Faul	Deputy Chairperson, NREC-CT C
Dr Jean Saunders	Deputy Chairperson, NREC-CT C
Prof Austin Duffy	Committee Member, NREC-CT C
Prof Fionnuala Breathnach	Committee Member, NREC-CT C
Mr Gerry Eastwood	Committee Member, NREC-CT C
Prof Andrew Smyth	Committee Member, NREC-CT C
Dr Steve Meaney	Committee Member, NREC-CT C
Prof Anne Mathews	Committee Member, NREC-CT C
Ms Paula Prendeville	Committee Member, NREC-CT C
Dr Emily Vereker	Head of Office, National Office for RECs
Mr Ciaran Horan	Administrative Assistant, National Office for RECs
Dr Jane Bryant	Programme Officer, National Office for RECs
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
Dr Emma Heffernan*	Project Officer, National Office for RECs

Apologies: Mr Philip Berman, Dr Deborah Wallace, Ms Susan Kelly, Dr Dervla Kelly, Dr Susan Finnerty

Quorum for decisions: Yes

Conflict of Interest: 2022-502785-25-00 SM-9 Steve Meaney – was not present for discussion of trial at meeting

Agenda

- Welcome & Apologies
- 2024-516248-24-00
- 2023-509256-34-00
- 2022-502785-25-00 SM-9
- 2023-506924-94-00 SM-1
- 2023-510351-31-00 SM-1
- 2023-506229-12-00 SM-1
- 2023-506669-70-00 SM-5
- 2023-507881-19-00 SM-4
- 2023-508522-95-00 SM-3
- AOB

- The Chair welcomed the NREC-CT C.
  - The minutes from the previous NREC-CT C meeting on 6th November were approved.
  - The NREC Business Report was discussed and noted.

Applications

2024-516248-24-00

Institutions: St James's Hospital

Study title: A Long-term, Open-label Study to Evaluate the Safety and Efficacy of Orally Administered Deucrictibant Extended-Release Tablet for Prophylaxis Against Angioedema Attacks in Adolescents and Adults with Hereditary Angioedema

Dossiers Submitted: Part I & II

- **NREC-CT Decision:**

- Request for Further Information

- **Additional Information Required**

Part II Considerations

1. Financial arrangements

- The NREC-CT noted that participants will receive a payment of 25 euro for 'accurate' completion of study diaries on Pg. 10 of the PISCF. This payment is only mentioned in the PISCF and is not captured in the compensation template. The committee requests that a rationale is provided for this payment as it may result in completion bias. The committee also requests that all payments are equitable across all participants without conditions. This should clearly be reflected in the PISCF.

2. Proof of insurance

- The NREC-CT noted that the insurance runs until November 1st, 2026, and that the length of the study would exceed this date, the NREC-CT requests that the sponsors provides confirmation that comprehensive insurance will be in place for the full duration of the study.

3. Subject information and informed consent form

- The NREC-CT noted that the Main PISCF has used a bundled approach to consent in the Informed Consent Section of the PISCF and requested that a layered approach to consent is used (in that each consent item is listed and a box for participants to provide their initials is included alongside each consent item) in line with HSE policy. 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
- The NREC-CT noted that on page 11, pregnant participants are expected to provide information on the outcome of the pregnancy. The NREC-CT requests that this should be made more explicit, detailing what information will be requested, stored and access to that information, and that it is included as a separate Pregnancy PISCF.
- The NREC-CT noted 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.
- The NREC-CT noted that on page 6, participants are given information about an optional biomarker sub-study. The NREC-CT requests that that inclusion or exclusion from this optional sub-study should be made more explicit, detailing what

information will be requested, stored and access to that information, and that it is included as a separate Biomarker PISCF.

- The NREC-CT noted that the Invitation letter contains the phrase to “you and your child”. As minors will not be recruited in Ireland, this letter should adapted to reflect Irish recruitment setup.
- 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.

2023-509256-34-00

Institutions: Beaumont Hospital

Study title: A Phase 1/2 Dose-Exploration and Dose-Expansion Study to Evaluate the Safety and Efficacy of BEAM-302 in Adult Patients with Alpha-1 Antitrypsin Deficiency (AATD)-Associated Lung Disease and/or Liver Disease

Dossiers Submitted: Part II

- **NREC-CT Decision:**

Request for Further Information

- **Additional Information Required**

Part II Considerations

1. Compliance with use of biological samples

- The NREC-CT noted that pg. 5 of the S1_Compliance with use of biological samples_IE_Beam Therapeutics states that ‘No secondary future use is intended as of this moment’ which is potentially ambiguous, in that it implies that samples could be used at another ‘moment’ in time. The NREC-CT requested that a more robust and clear statement is included to make it clear whether biological samples will only be used for the purposes of this study and stored for the duration of the study. If the Sponsor plans to retain samples beyond the duration of the study, a clear rationale should be provided.

2. Proof of insurance

- The NREC-CT noted that the insurance expires on 16 March 2026 and requested confirmation that insurance is in place for the duration of the trial.

3. Subject information and informed consent form

- The NREC-CT noted that the Main PISCF document includes the use of appendices to convey important information. The Committee requested that it is made clear to participants that all sections of the Main PISCF should be read, including the appendices, before agreeing to take part in the study. Participants should be informed of this on pg. 1 of the PISCF.

- The NREC-CT requested that participants are given more information in the main body of the Main PISCF regarding of the make-up / composition of BEAM302. This should be described in plain English suitable for a lay audience.
- The NREC-CT requested that the rationale for needing to meet the study requirements for inclusion should be explained to participants on pg. 4 of the Main PISCF.
- The NREC-CT noted that the Compliance with use of biological samples_IE_Beam Therapeutics document states that up to 4 liver tissue samples will be taken from participants and requested that participants are informed of this in the Main PISCF. The following should be explained to participants in the main body of the Main PISCF using plain English suitable for a lay audience:
    - what tests they will need to undergo to collect the liver samples
    - the reason why liver samples are required. If the liver samples are being taken solely for research purposes and not to guide treatment, then this should be clearly stated to participants.
    - Whether these tests are an optional or mandatory component of the trial.
    - All procedure-related risks associated with taking liver tissue samples
- The NREC-CT requested that the use of 'Day -2, Day-1 and Day 1' terminology to describe the dosing period on pg. 4 of the Main PISCF is revised for clarity and replaced with more patient friendly accessible terminology suitable for a lay audience.
- The NREC-CT requested that the meaning of 'dose limited toxicity' on pg. 4 of the Main PISCF should be explained to the participants using plain English suitable for a lay audience, noting that at present it appears as a potentially worrying statement about 'toxicity' from a participant's perspective.
- The NREC-CT requested that the '12-month pregnancy test' is explained in more detail to participants on pg. 5 of the Main PISCF.
- The NREC-CT noted that pg. 5 of the Main PISCF states that LT follow up will last more than 13 years and requested that participants are informed of the exact length of time LT follow up will last (15 years).
- The NREC-CT noted the differences between changes in blood tests and liver damage should be noted/explained to participants using plain English suitable for a lay audience.
- The NREC-CT requested that the text 'No changes to DNA were detected except those in identifiable locations' on pg. 8 of the Main PISCF may be confusing for participants and requested that this phrase is revised for clarity.
- The NREC-CT noted that the reversible nature of the QTc changes are described on pg. 8 of the Main PISCF and requested that the transient nature in the pre-clinical / animal models is explained to participants.
- The NREC-CT noted that there is a very brief description of potential safety investigations on pg. 9 of the Main PISCF which is not well explained to participants. The NREC-CT requested that the rationale for potential safety investigations, including how their existing blood samples may be used by the study team for additional testing, is explained in more detail to participants using plain English suitable for a lay audience.
- The NREC-CT noted that participants are provided with advice on what happens if they withdraw from the study, they may be asked to partake in follow-up visits on

pg. 10 of the Main PISCF. The NREC-CT requested that participants are advised that if they withdraw from the study, they are not required to take part in study follow up visits, as they are no longer taking part in the study.

- The NREC-CT noted that pg. 12 of the Main PISCF states that participants may not be eligible to take part in the study if they do not consent to genetic testing which seems to conflict with earlier statements in the Main PISCF (for example pg. 17) which states that genetic testing is a mandatory component of the study. The NREC-CT requested that it is clarified in the Main PISCF whether the genetic component of the study is mandatory, and that this is reflected throughout the Main PISCF including the informed consent section on pg. 12.
- The NREC-CT suggested that there are separate spaces/boxes for the printed name and the signature in the informed consent section on pgs. 12 & 14 of the Main PISCF, to ensure that both are plainly captured and to support legibility and the research record.
- In line with GDPR requirements, the NREC-CT requested justification is provided for the need to collect gender data to avail of the PCS on pg. 13 of the Main PISCF.
- The NREC-CT noted that participants urine samples may be used for a drug panel and alcohol test, and this is not well foregrounded in the Main PISCF (detailed on pg. 16 of the appendix) and requested that the requirement for these tests features more prominently in the main body of the Main PISCF.
    - The rationale for the drug panel and alcohol test should be provided to the participants in the Main PISCF.
- The NREC-CT noted that participants can take part in optional samples for exploratory analysis on pg. 17 Main PISCF optional samples for exploratory analysis' and requested that it is made clear to participants that this will be done in line with Health Research Regulations (Data Protection Act 2018 (Section 36(2) (Health Research) and will be confined to a specified disease area or drug such as the disease area / IMP under investigation as part of the trial.
- The NREC-CT noted that pg. 17 of the main PISCF states that participants are to undergo genetic testing and requested the following is explained to participants using plain English suitable for a lay audience:
    - detail as to the type of genetic testing involved, including information regarding the purposes of this testing.
    - detail outlining the potential risks entailed in such analysis being performed.
    - the possible ownership of such data by private or commercial interests and that this elucidated in the PISCF.
    - the right to withdraw genetic data, the mechanism for anonymisation, storage and security and transfer of genetic material and its associated data. For 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/HSENational-Policy-for-Consent-in-Health-and-Social-Care-Researchcompressed.pdf
- The NREC-CT noted that pg. 20 of the Main PISCF states that 'The study doctor may also check your health information on public records if allowed by local law' and requested that detail is provided to participants what is meant by 'public records'.

- The NREC-CT noted that pg. 21 of the Main PISCF included a discussion about the sharing of anonymous data and requested that participants are given more information about this.
    - Consent to data anonymisation should also be added as a separate consent item in the informed consent section on pg. 11 of the Main PISCF.
- The NREC-CT noted that pg. 4 of the Pregnant Partner PISCF states that NREC will have access to pregnant partners medical records and requested that this is reworded so it is clear that NREC will only have access to non-identifiable personal information. This should also be amended on pgs. 9 and 10 of the PISCF.
- The NREC-CT requested that the scope of the future use of data / samples on pg. 3 of the Optional Future Research PISCF is made clearer for participants i.e. that the future use of data / samples (including genetic research) is described in line with regulations / best practice on pg. 3 of the PISCF. 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 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 Optional Future Research 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 NREC-CT noted that pg. 2 of the Optional Future Research PISCF references ‘combine coded personal data’ and requested that it is made clear to participants whether this data is to be pseudonymised or anonymised.
- The NREC-CT noted that pg.2 of the Optional Future Research PISCF states that the sponsor will limit the number of people with access to data, which seems to conflict with the statement that it will be shared ‘with other scientists or partner companies’ and requested that it is made clear to participants exactly who their data will be shared with.
- The NREC-CT noted that participants may be confused by the statement regarding future use of samples / data should they withdraw from the study on pg.3 of the Optional Future Research PISCF and requested that it is made clear to participants the relationship between withdrawal from the main study and future use of samples and requested that it is made to clear to participants what will happen to their samples and data should they withdraw from the study.
- The NREC-CT noted a difference in the scope of the consent table on pg. 4 of the Optional Future Research PISCF – e.g. there are no elements such as having the opportunity to ask questions etc. and requested that this aligned with the consent section in the Main PISCF.

- The Sponsor is requested to submit any Part 2 documentation should they 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-CT noted that that the Site Suitability Assessment for Beaumont Hospital states that participants are to undergo liver biopsy and requested clarification as this is not specified in the PISCF.

2022-502785-25-00 SM-9

Institutions: Beaumont Hospital, St James's Hospital

Study title: A Phase 3, Open label, Randomized Study Comparing the Efficacy and Safety of Odronextamab, an anti-CD20 × anti-CD3 bispecific antibody, in Combination with CHOP (O-CHOP) versus Rituximab in Combination with CHOP (R-CHOP) in Previously Untreated Participants with Diffuse Large B-cell Lymphoma (DLBCL) (OLYMPIA-3)

Dossiers Submitted: Part I & II

- **NREC-CT Decision:**

- Favourable

2023-506924-94-00 SM-1

Institutions: Mater Misericordiae University Hospital, St James's Hospital, St Vincent's University Hospital, Connolly Hospital, National University of Ireland

Study title: The cardiovascular safety and efficacy of cagrilintide 2.4 mg s.c. in combination with semaglutide 2.4 mg s.c. (CagriSema 2.4 mg/2.4 mg s.c.) once-weekly in participants with established cardiovascular disease

Dossiers Submitted: Part I & II

- **NREC-CT Decision:**

- Favourable

2023-510351-31-00 SM-1

Institutions: Children's Health Ireland

Study title: A Randomized, Double-Blind, Placebo-Controlled, Multiple Ascending Dose Study Assessing Safety, Tolerability, Pharmacodynamics, Efficacy, and Pharmacokinetics of DYNE-251 Administered to Participants with Duchenne Muscular Dystrophy Amenable to Exon 51 Skipping

Dossiers Submitted: Part I & II

- **NREC-CT Decision:**

Request for Further Information

- **Additional Information Required**

Part II Considerations

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

- The NREC-CT noted that the future use of data / samples is not described in line with regulations / best practice on pg. 3 of L1_DYNE251-DMD-201_Biomarker-Substudy-ICF_IE_English PISCF. 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 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 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 NREC-CT requested that the wording on pg. 17 of the L1_DYNE251-DMD-201_Main-ICF_IE_English_TC_NotPublic is amended to state that NREC will only have access to non-identifiable data, and not participant's personal data

2023-506229-12-00 SM-1

Institutions: St Vincent's University Hospital

Study title: A phase II, randomized, open-label study to assess the efficacy, safety, and pharmacokinetics (PK) of maintenance cabozantinib (XL184) plus best supportive care (BSC) versus BSC in children, adolescents and young adults (AYA) with unresectable residual osteosarcoma either at diagnosis or at first relapse after standard treatment.

Dossiers Submitted: Part I & II

- **NREC-CT Decision:**

Request for Further Information

- **Additional Information Required**

Part II Considerations

1. **Financial arrangements**

1. The NREC-CT noted that the the proposed future use of data/samples is not in line with regulations on pg. 16 and 20 of the Main PISCF. 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, in line with best practice, the Declaration of Taipei 2016 and as required under the Health Research Regulations (Data Protection Act 2018 (Section 36(2) (Health Research) Regulations 2018). In line with explicit consent under the Health Research Regulations, future use should be confined to the purpose of specified health research (e.g, research into unresectable residual osteosarcoma) and/or the 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.

- An option should be provided to enable current participants to be reconsented should updates in future use of biological samples /data occur
- 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/

2. The Switch PISCF should also specify details on future use of samples/data to align with the main PISCF and provide a consent option to this.

2023-506669-70-00 SM-5

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

Study title: A Phase 3, Randomized, Double-blind, Placebo-controlled, Multicenter Study to Evaluate the Efficacy and Safety of Amyloid Depleter ALXN2220 in Adult Participants with Transthyretin Amyloid Cardiomyopathy (ATTR-CM)

Dossiers Submitted: Part I & II

- **NREC-CT Decision:**

- Request for Further Information

- **Additional Information Required**

Part II Considerations

1. Subject information and informed consent form

- The NREC-CT noted that the future use of PK samples is not described in line with regulations / best practice on Pg. 16 of the Main PISCF. 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 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 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/

- 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 main ICF page 6, stated that "an observation period of at least 30 minutes replaces 2 hours but that the patient information video refers to an observation period of 2 hours. The NREC-CT requests that these materials align.
- The NCRE-CT notes that participant information video on page 2 the study duration is given as between 2.5 and 4.5 years and that the PICSF gives a a study duration of between 4 to 5 years on page 4. The NREC-CT requests that these materials align.
- The NREC-CT notes that on page 5 of the video text the word die is used. The NREC-CT suggest that this be corrected to the word dice for clarity.

2. Suitability of the clinical trial sites facilities

- The NREC-CT noted that the site suitability form references St. James's Hospital on page 1, and that it is not signed. The NREC-CT requests that the site suitability form be updated to only refer to the site where the study will be conducted and be signed by a suitable person from that site.

2023-507881-19-00 SM-4

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

Study title: Vaccination to prevent Mpox Infection (MPOX-VAX Study)

Dossiers Submitted: Part II

- **NREC-CT Decision:**

- Favourable

2023-508522-95-00 SM-3

Institutions: Children's Health Ireland

Study title: EPIK-P3: A phase II study to evaluate the long-term safety and efficacy of alpelisib in patients with PIK3CA Related-Overgrowth Spectrum (PROS) who previously participated in Study CBYL719F12002 (EPIK-P1)

Dossiers Submitted: Part II

- **NREC-CT Decision:**

  Request for Further Information

- **Additional Information Required**

Part II Considerations

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

- The NREC-CT requested clarification as to whether participants will be reconsented as a result of this modification.
- The NREC-CT noted that pg. 24 of the parent / guardian PISCF states 'a meaningful number of participants did show lasting positive response (≥ 20% shrinkage in their lesions) on their scans' .and requested that this 'meaningful' number is quantified, e.g. XX out of the number of participants or XX in so many participants, so parents / guardians are fully informed.
- The NREC-CT noted that pg. 23 of the adolescent assent form states 'a meaningful number of participants did show ≥ 20% shrinkage of their lesions on scans' and requested that this 'meaningful' number is quantified, e.g. X out of the number of participants or XX in so many participants, so participants are fully informed.

- AOB:
  - N/A