National Research Ethics Committee

NREC-CT Meeting

18th December 2024

Attendance

Name	Role
Prof David Brayden	Chairperson, NREC-CT D
Prof David Smith	Deputy Chairperson, NREC-CT D
Dr Christina Skourou	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
Ms Deirdre McLoughlin	Committee Member, NREC-CT D
Dr Mary McDonnell Naughton	Committee Member, NREC-CT D
Prof Geraldine O'Sullivan Coyne	Committee Member, NREC-CT D
Ms Chanel Watson	Committee Member, NREC-CT D
Mr Gerry Daly	Committee Member, NREC-CT D
Dr Jeff Moore	Committee Member, NREC-CT D
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
Ms Patricia Kenny*	Project Officer, National Office for RECs

*Drafted minutes

Apologies: Tina Hickey

Quorum for decisions:

Agenda

- Welcome & Apologies
- 2024-512828-12-00
- 2024-513621-23-00
- 2022-502202-33-00 SM-4
- 2023-509569-19-00 SM-1
- 2024-513992-42-00 SM-1
- 2023-507889-89-00 SM-1
- 2023-508137-14-00 SM-1
- 2024-516582-36-00 SM-1
- 2023-503280-42-00 SM-1
- 2023-505242-25-00 SM-3
- AOB

- The Chair welcomed the NREC-CT D.
  - The minutes from the previous NREC-CT D meeting on 13th November 2024 were approved.
  - The NREC Business Report was discussed and noted.

Applications

2024-512828-12-00

Institutions: Children's Health Ireland

Study title: An open-label study to collect safety and effectiveness information on long-term treatment with vamorolone in boys with Duchenne Muscular Dystrophy who have completed prior studies with vamorolone (The GUARDIAN Study)

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 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 Parents ICF page 6, that the NREC-CT is listed as the contact point for research participants rights. The NREC-CT requests that this is revised, as the NREC-CT is not a contact points for research participants rights. If a participant or carer of a participant in a clinical trial wants to discuss their rights, they should be advised to contact the study doctor, their GP, appropriate patient advocacy groups, country or site patient advocacy groups or country or site patient liaisons as appropriate.
- The NREC-CT noted minor typographical errors for correction:
    - Parents PICSF page 11, there is a in last sentence which states "6the".
    - Parents PICSF page 12 section 2.5, has the numbers 6.1 at the end of the paragraph. The NREC-CT requests that these be amended for clarity.
- The NREC-CT notes the use of the word "secret" in the PICSF for 6-11 years, and 12-15 years old PICSF. The NREC-CT requested that the word "private" be used instead.
- The NREC-CT notes that the font in the 6-11 PICSF is different from the rest of the documents and difficult to read. The NREC-CT requests that the same font be used across all patient facing documents.
- The NREC-CT noted that it was not clear whether the study will include participants over the age of 16, and the reconsenting procedure in place for

participants who reach the age of 16 during the study. The NREC-CT requests that clarity is provided, and that the PISCFs are amended to provide this detail.

- The NREC-CT notes that the parent PICSF section 3.3, page 13, contains the words “cushingoid features” without explanation. The NREC-CT requests that the parent PICSF provides context and lay language explanation for “cushingoid features”.
- THE NREC-CT requests that the adult and parent guardian PICSF provides information about whether enrolling in this study would preclude participants from participating in any other study.

2024-513621-23-00

Institutions: Beaumont Hospital

Study title: TACTI-004, a double-blinded, randomized phase 3 trial in patients with advanced/metastatic non-small cell lung cancer (NSCLC) receiving eftilagimod alfa (MHC class II agonist) in combination with pembrolizumab (PD-1 antagonist) and chemotherapy.

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**

- The NREC-CT noted that in Section 1.3 there is a reference to a Biomarker blood sample, however the Main ICF does not contain details of biomarker blood samples. The Committee requested that Main ICF be updated to include specific details around biomarker blood samples being taken during the study, and their use.
- The NREC-CT noted Pg 4 Section 3.2 it is stated that “Samples analysed and stored centrally will be anonymised”. The Committee were unclear if this should be pseudonymised rather than anonymised, please clarify and update as necessary. If samples will be stored anonymously, this should be clearly stated in the Main ICF and specific consent sought to process pseudonymised samples to anonymised samples as per GDPR.

2. **Recruitment arrangements**

- The NREC-CT noted Section 1.3 of Recruitment Arrangement document “In addition, all data collected from participants will be kept anonymous and records that can identify them will be kept confidential”. The Committee were unclear if this should be pseudonymous rather than anonymous, please clarify and update as necessary. If data will be stored anonymously this should be clearly stated in the

Main ICF and specific consent sought to process pseudonymised data to anonymised data as per GDPR.

- The NREC-CT noted the Recruitment arrangements document has multiple mentions of "legally authorized representative (if applicable)". The Committee requested that the Main ICF be updated to include reference to legally authorised representative and a signature section for the legally authorised representative to sign, if the situation arises.
- The NREC-CT noted that the recruitment arrangements document states that the person can allow a GP or family member to be contacted to get follow up information, and requested that this is captured in the SIS and ICF Main
- The NREC-CT noted Section 1.1 of the Recruitment arrangement document states "Potential patients … will be identified through clinical practice at selected sites" and Section 1.2 states "In addition, they could be informed via paper advertisement in the Clinics/Hospitals, but also in an electronic format through social media", however the Committee were unclear on a number of issues:
    - Whether either or both of these approaches will be used in Ireland. The Sponsor should confirm and update the Recruitment arrangement document as necessary.
    - In the Advocacy Outreach Text document there is wording for social media posts and an Email to Potential Participant. It was not clear to the Committee who would be sending this email and how they would have the details of the person to email them. Please clarify and update the email template as necessary.

3. Subject information and informed consent form

- 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 reference on pg. 3 SIS and ICF Main "Blood may be collected in your home by a mobile nurse.". The Committee requested that the SIS and ICF Main be updated to include more detail in relation to mobile nurse service including if it is optional or not and what information will be sent to them. The consent form should also be updated to include a specific consent statement for participants to consent to their information being passed to mobile nurse service.
- The NREC-CT requested that the wording SIS and ICF Main pg 2 IRB/IEC Review section *"The Irish National Research Ethics Committee (NREC) has also given a favourable opinion that the study can take place. This organization is responsible for making sure that the rights of people who take part in clinical research studies are protected. The favourable opinion should not be thought of as an encouragement for you to take part in this study"* be deleted and replaced with *"The National Research Ethics Committee (NREC) has approved the study."*
- The NREC-CT noted the wording on pg. 3 of the SIS and ICF Main *"If required per Irish law, blood will be collected to test for human immunodeficiency virus (HIV)*

and hepatitis B and C. If your test results are positive, you will be told. The results of your tests will be kept confidential and reported to authorities only as needed by law." The Committee requested clarification regarding the reason for HIV or Hep B an C testing as there is not requirement under the study for this and Ireland has no legal requirement for it. The Committee requested that this wording be updated or deleted from the SIS and ICF Main as required.

- The NREC-CT noted that pg 7 of the SIS and ICF Main is not described in line with regulations and best practice as it is not confined to the disease or drug under study ie. "If you give your consent, your leftover samples will be kept for potential further exploratory and/or preliminary laboratory testing in the future, including but not limited to additional analyses related to your cancer and efti".
  The NREC-CT requested that future use of samples/personal data is sufficiently explained to participants in the 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 specified disease area or drug under study in this trial (non-small cell lung cancer (NSCLC) and/or eftilagimod), and this is clearly stated in the main body of PIS pg 7 and informed consent section of the ICF pg 21. 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 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 SIS and ICF Main be updated to include:
    - detail on the duration of the treatment phases given in weeks rather than cycles.
    - indicate how many questionnaires participants will be expected to complete and an estimate of how long completion of the questionnaires should take
    - Section 4 pg. 8 Side effects of eftilagimod be updated to include information on how many people have been treated with eftilagimod to date
    - Pg. 9 Side effects of pembrolizumab be updated to present the descriptor of side effect frequencies as presented in the Pembrolizumab patient information leaflet (EMA), using the descriptors for the range of frequencies as very common, common, rare etc.. For example very common side effects in the study SIS and ICF Main are described as having a frequency of 20% or more and common side effects having a frequency of 5 to 19% which the Committee determined did not align with the EMA descriptors of frequency.

- Pg. 8 The description of the frequency of “flu-like symptoms” as “few” may minimize the side effect for participants. The Committee requested that this be updated to replace the descriptor “few” with “some” or instead remove the descriptor altogether and just refer to the frequency.
- The NREC-CT noted that some side effects for eftilagimod including alopecia 41%, neuropathy 18% as detailed in the Investigators Brochure are not accurately reflected in the SIS and ICF Main.

- The NREC-CT noted an SIS and ICF Pregnant Partner has been submitted for review however no SIS and ICF has been submitted for the pregnant participant to sign to consent to collecting of data on the pregnancy. The Committee requested an SIS and ICF for pregnant participants be submitted for review.
- The NREC-CT requested that statement pg. 14 SIS and ICF Main “To receive reimbursement for these costs, you will need to obtain upfront approval and provide proper receipts” be updated to provide more detail around what this upfront approval will involve.
- The NREC-CT requested that the SIS and ICF Main clearly states whether access to the study drug will be available to participants after the study has ended.

4. Suitability of the clinical trial sites facilities

- The NREC-CT were unclear on the number of participants that will take part in the study as the Site Suitability Form for Beaumont Hospital states that the planned number of trial participants is three, however the other study paperwork states that the planned number of participants in Ireland is 11. Please clarify.

2022-502202-33-00 SM-4

Institutions: CHI Temple St

Study title: AttaCH: A Phase 2, Multicenter, Long-Term, Open Label Extension Trial Evaluating Safety, Tolerability, and Efficacy of Subcutaneous Doses of TransCon CNP Administered Once Weekly in Children and Adolescents with Achondroplasia

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 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 all ICF documents are seeking blanket consent for future use of samples/data for unspecified purposes without further consent. This type of consent is not in line with best practice, the Declaration of Taipei 2016 and not in compliance with the Data Protection Act 2018 (Section 36(2) (Health Research) Regulations 2018), where informed participant consent is a mandatory safeguard. The NREC-CT requested that future research is restricted to research in the area of achondroplasia and/or the study drug and this is clearly stated in the main body and informed consent sections. The NREC-CT also requests that any future use of biological samples is reviewed by an ethics committee and requested that this is captured in the PISCFs.
- The NREC-CT noted that the EU CT number is not on the front page of any of the PISCFs - The NREC-CT requested that all PISCFs page 1 be updated to include the 14 digit EU CT trial number.
- The NREC-CT noted on page 9 of the Parent PIS the following text “Throughout the entire study your child may receive up to 7,424 mSv from x-ray and an additional 0,002 mSv from the DXA scanning.” The format of the 0,002 mSV could be misleading to participants (as it could be interpreted as 0.002 mSV) and is more easily comprehended if written as 2mSV. The NREC-CT requested that this sentence be updated.

2023-509569-19-00 SM-1

Institutions: Mater Misericordiae University Hospital, Beaumont Hospital, Cork University Hospital, University Hospital Limerick, Bon Secours Hospital Cork

Study title: A multicenter, randomized, open-label, blinded endpoint evaluation, phase 3 study comparing the effect of abelacimab relative to apixaban on venous thromboembolism (VTE) recurrence and bleeding in patients with cancer associated VTE (ASTER)

Dossiers Submitted: Part I & II

- **NREC-CT Decision:**

- Favourable

2024-513992-42-00 SM-1

Institutions: Bon Secours Hospital Cork, Beaumont Hospital, Cork University Hospital

Study title: A multicenter, randomized, open-label, blinded endpoint evaluation, phase 3 study comparing the effect of abelacimab relative to dalteparin on venous thromboembolism (VTE) recurrence and bleeding in patients with gastrointestinal (GI)/genitourinary (GU) cancer associated VTE (Magnolia)

Dossiers Submitted: Part I & II

- **NREC-CT Decision:**

- Favourable

2023-507889-89-00 SM-1

Institutions: Cork University Hospital, St Vincent's University Hospital, Beaumont Hospital, Wexford General Hospital, University Hospital Waterford, Tallaght University Hospital, Galway University Hospital

Study title: Randomized, Embedded, Multifactorial Adaptive Platform trial for Community-Acquired Pneumonia (REMAP-CAP)

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 the wording on pg 3 of EU RSA Country Appendix regarding withdrawal of consent/assent and queried if this aligns with the withdrawal options on Main ICF pg 21.
   - 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.

2023-508137-14-00 SM-1

Institutions: Beaumont Hospital

Study title: A Phase 2, Single-Arm, Open-Label Extension Study, Evaluating the Long-Term Safety and Clinical Efficacy of SAR447537 (INBRX-101) in Adults with Alpha-1 Antitrypsin Deficiency (AATD) Emphysema

Dossiers Submitted: Part I & II

- **NREC-CT Decision:**

- Request for Further Information

- **Additional Information Required RFI**

Part I Considerations (RFI) for addition to CTIS

1. The Sponsor is requested to update the Layman Protocol Summary pg 5 to remove the sentence “The risk of a side effect from this level of radiation exposure is low compared to the potential benefits of taking part in the study” as this is not a valid assumption given the first sentence of this section reads “It is currently unknown if SAR447537 will help to treat AATD emphysema”

Part II Considerations

1. Subject information and informed consent form

- 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 Main ICF Cohort 1 pg. 14, pg. 27-/28, pg. 41 and Main ICF Cohort 2 and 3 pg. 14, pg. 26-28 and pg. 40 is seeking blanket consent for future use of samples/data for unspecified purposes without further consent. This type of consent is not in line with best practice, the Declaration of Taipei 2016 and not in compliance with the Data Protection Act 2018 (Section 36(2) (Health Research) Regulations 2018), where informed participant consent is a mandatory safeguard. The NREC-CT requested that future research including genetic analyses is restricted to research in the disease and/or drug under study and this is clearly stated in the main body and informed consent sections of the Main ICF Cohort 1 27-/28, pg. 41 and Man ICF Cohorts 2 and 3 pg. 26-28 and pg. 40. The Committee also requests that any future use of biological samples is reviewed by an ethics committee and requested that this is captured in the PISCFs.

2024-516582-36-00 SM-1

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

Study title: Single arm phase 2 trial of neoadjuvant trastuzumab deruxtecan (T-DXd) with response-directed definitive therapy in early stage HER2-positive breast cancer: a standard chemotherapy-sparing approach to curative-intent treatment – SHAMROCK study

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 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 the EU CT number listed the study documents is not the full 14 digit EU-CT number. The Committee requested that the SIS and ICF Main be updated to list the full 14 digit EU-CT number 2024-516582-36-00 to enable participants to find the trial on EU Clinical Trials Registry.
- The NREC-CT requested the SIS and ICF Main, page 2, be updated to provide a lay language explanation for the word “taxane” when it is first used.

2023-503280-42-00 SM-1

Institutions: Tallaght University Hospital

Study title: A Phase 3, Open-label, Randomized, Noninferiority Trial of the Subcutaneous Formulation of Nivolumab Versus Intravenous Nivolumab in Participants With Advanced or Metastatic Clear Cell Renal Cell Carcinoma Who Had Received Prior Systemic Therapy

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 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 the addition of wording on pg. 24-25 of the SIS an ICF Main in relation to what will happen if a participant withdraws their consent. The Committee stated that if a participant withdraws from a study, then it is not appropriate:
    - to contact their primary care physician to obtain health information unless the participant has explicitly consented to this.
    - to share personal information with a third party representative in order to determine health status without the participant explicitly consenting to this
    - to contact participants family without their explicitly consenting to this.

  The Committee requested that the SIS and ICF Main pg 24 be updated to remove reference to above or to update the wording to be clear to participants that they will be specifically asked if they consent to the above when withdrawing and they can choose not to consent to this if they wish.

2023-505242-25-00 SM-3

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

Study title: Phase 2 Dose-Ranging and Interception Study of Linvoseltamab in Patients with High-Risk Monoclonal Gammopathy of Undetermined Significance or Non-High-Risk Smoldering Multiple Myeloma

Dossiers Submitted: Part II

- **NREC-CT Decision:**

- Favourable

- AOB:
    - None