National Research Ethics Committee

NREC-CT Meeting

03 July 2024

Attendance

Name	Role
Dr Cliona McGovern	Chairperson, NREC-CT B
Dr John Hayden	Deputy Chairperson, NREC CT-B
Prof. Colm O'Donnell	Deputy Chairperson, NREC-CT B
Ms Serena Bennett	Committee Member, NREC-CT B
Dr Karina Halley	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
Dr Niall McGuinness	Committee Member, NREC-CT B
Prof. Seamus O'Reilly	Committee Member, NREC-CT B
Mrs Ann Twomey	Committee Member, NREC-CT B
Acting Head, National Office for RECs	
Ms Patricia Kenny	Project Officer, National Office for RECs
Dr Jane Bryant	Project 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
Ms Megan O'Neill*	Project Officer, National Office for RECs

Apologies: Prof. Michaela Higgins, Dr Åine de Róiste, Ms Evelyn O'Shea

Quorum for decisions: Yes

Agenda

- Welcome & Apologies
- 2023-506229-12-00
- 2023-508818-42-00
- 2023-508165-33-00
- 21-NREC-CT-068_Mod-4
- 2023-506987-15-00
- 2023-505699-31-00
- 2023-507353-15-00
- 2023-506091-27-00
- 2023-508734-34-00
- AOB

- The Chair welcomed the NREC-CT B.
  - The minutes from the previous NREC-CT B meeting on 29th May 2024 were approved.
  - The NREC Business Report was discussed and noted.

Applications

2023-506229-12-00

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

  - NREC-CT Decision:
- Request for more information

  - Additional Information Required

Part II Considerations

1. **Compliance with national requirements on data protection**

- No Considerations

2. **Compliance with use of biological samples**

- No Considerations

3. **Financial arrangements**

- No Considerations

4. **Proof of insurance**

- The NREC-CT requested assurance that the necessary insurance policies will be in place for the full duration of the trial.

5. **Recruitment arrangements**

- The NREC-CT requested clarification as to whether paediatric participants will be recruited in this study in Ireland. The appropriate documentation for the PI and site working with this cohort should be submitted for NREC review if participants under 16yrs old are to be included. If paediatric participants are not partaking in this study in Ireland the NREC-CT requested that documents specific to paediatric participants are not submitted for review, or that the cover letter clearly sets out the ethical review requirements of the submission.

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

- The NREC-CT noted reference to “reuse of data” on pg. 17 of the Caregiver PISCF and requested that this language is changed to clearly set out that this refers to future research.
- The NREC-CT noted the use of terms the “reuse of data” and “future research outside the protocol” on pg. 21 of the Caregivers PISCF and requested that this is modified so they are readily understandable by the lay population.
- The NREC-CT considered the following statement on pg. 17 of the Caregivers PISCF, “Ipsen may share your child’s coded data with Ipsen’s services providers, business and research partners” and requested that this is modified to clearly set out who the data may be shared with.
- The NREC-CT requested that the PISCFs are modified to clearly set out that the risks associated with exposure to ionising radiation in participating in this study exceeds that of standard care, noting that information on this was not provided in the Assent forms, particularly for participants aged 11-15yrs or the Switch Over Assent form for participants aged 11-15yrs old.
- The NREC-CT noted that the section on future research and biobanking in the Main PISCF and Caregiver PISCF is not described in line with regulations and best practice. Further it was noted that no explanation is provided in the Assent Form for 11-15 year olds. 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
- There should be a separate PISCF dealing with future research

- The NREC-CT noted that pg.6 of the Main PISCF refers to post-trial follow up every 3 months and queried whether there is a final cut-off date for follow up. The PISCF should be modified to reflect this cut-off point and this should be harmonised across the relevant documents.
- The NREC-CT noted that the Biological Samples Compliance form refers to genetic testing and requested that clarity is provided in the PISCF regarding genetic testing and requested the following:

- It should be made clear to participants whether these tests are optional or mandatory
- The genetic testing requested must be restricted and defined in line with the Data Protection Act 2018 (Section 36(2) (Health Research) Regulations 2018) and clearly explained clearly to the participant,
- Clarification should be provided on 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/HSE-National-Policy-for-Consent-in-Health-and-Social-Care-Research-compressed.pdf

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

7. **Suitability of the clinical trial sites facilities**

- The NREC-CT requested further information regarding the facilities in place for paediatric participants, as the proposed site for this study is St Vincent's University Hospital (SVUH) which does not care for patients with cancer or other conditions aged < 16 years old. If the Sponsor intends to recruit participants under 16 years old, as set out in the protocol and the PISCFs submitted, the NREC-CT requested that the Site Suitability Form of an appropriate site is submitted for paediatric participants, clearly setting out their involvement.

8. **Suitability of the investigator**

- The NREC-CT questioned whether a suitable PI with Paediatric Oncology experience was working with participants under 16 yrs old as it noted that the PI CV submitted for review did not detail clinical or research experience in Paediatric

Oncology. If paediatric participants are to be enrolled, as set out in the protocol, Dr Doherty's suitability for working with this population should be set out in the CV or a CV for the Investigator who will be working with this population should be submitted for review.

2023-508818-42-00

Institutions: Children's Health Ireland

Study title: An International, Multicenter, Randomized, Double-Blind, Parallel Group, Vehicle-Controlled, Phase 2/3 Study with Open-Label Extension Evaluating the Efficacy and Safety of Diacerein 1% Ointment for the Treatment of Generalized Epidermolysis Bullosa Simplex (EBS)

- NREC-CT Decision:

- Request for more information

- Additional Information Required RFI

Part II Considerations

1. **Compliance with national requirements on data protection**
   - The NREC-CT noted the transfer of data to non-EU countries in Appendix 1 (Transfer Table) of the CHI DPIA that were not detailed in the other study documents. The NREC-CT requested clarification as to where study samples and data will be transferred to. This information should be harmonised across the study documents and set out clearly in participant-facing materials. The NREC-CT requested that the updated documents are submitted for review.
2. **Compliance with use of biological samples**
   - The NREC-CT requested that the countries involved in the storage and analyses of samples are clarified in the Compliance with Biological Samples form, in line with the information given in Appendix 1 (Transfer Table) of the CHI DPIA. The NREC-CT requested that this information is harmonised across the relevant documentation, including participant-facing materials.
   - The NREC-CT requested that the procedures for the recording, anonymisation and transfer of photos taken on an iPhone are further elucidated and described clearly in the relevant documents.
3. **Financial arrangements**
   - The NREC-CT appreciated that participants & carer/guardians will be reimbursed for costs associated with transport and parking for study visits and requested that the Sponsor consider reimbursement for meals/lunches while attending study visits, as indicated in the 10-15 Years PISCF.
4. **Proof of insurance**
   - No Considerations
5. **Recruitment arrangements**
   - The NREC-CT requested confirmation as to whether recruitment material would be used to recruit participants as they noted the inclusion of the recruitment poster in the submission package, which was not described in the Recruitment Arrangements form.

- The NREC-CT requested confirmation that no participants over the age of 16 will be recruited in Ireland as indicated by the site suitability information.
- The NREC-CT requested confirmation that no participants under 4 years will be recruited until the condition set by the RMS from Part I assessment has been met.

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

- The NREC-CT considered the information given in Section 5 (What are the risks and possible discomforts?) of the PISCFs and the protocol, which states that more than 70 EB or EBS patients have received the ointment in previous clinical trials. This number should be modified to only include participants who received the active ingredient; healthy volunteers or those who received the placebo/vehicle should not be counted.
- The NREC-CT requested that the information regarding the most common AE in the 6-9 Years PISCF is modified to itching instead of diarrhoea, as this is the most common AE for the topical form.
- The NREC-CT requested that the green and red colours used for the consent items in the 6-9 Years PISCF are removed as these could introduce potential bias for participants influencing them to assent. Similarly, the NREC-CT requested that the smiling “thumbs up” emoji is removed as it may also influence the potential participants decision to assent.
- The NREC-CT noted that the 10-15 Years PISCF indicates that lunch will be provided, while other documents state that only travel is covered. The NREC-CT requested clarification on the reimbursement of expenses for participants & carer/guardians and that this is harmonised across all relevant documents.
- The NREC-CT noted that the PISCF directs participants & carer/guardians to the NREC for queries such as those relating to data protection and requested that these contact details are removed. Participants & carer/guardians should not be directed to the NREC for queries related to data protection.
- The NREC-CT requested that the table on pg.4 of the 10-15yrs PISCF is modified to include information pertaining to that particular age group or cohort only. Similarly, the text associated with this table should only provide details relating to that particular age group.
- The NREC-CT noted that the 10-15yrs PISCF details that PK samples will be shipped to the US, whilst the Main PISCF states that the PK samples will be shipped to Japan. The NREC-CT requested that it is clarified where samples will be shipped to and that it is harmonised across the relevant documents. The PISCFs should also clearly set out that the other samples/photographs will be sent to Scotland or the US.
- The NREC-CT noted numerous inaccuracies and typos across the documentation, as well at times, language that is too technical for the proposed age cohort. The Committee requested that all participant materials are proofread to ensure comprehensiveness for potential participants and consistency in the information provided.
- The NREC-CT noted that the Protocol (Section 4.4, pg. 31) states participants “may be given the opportunity to enroll in a 24-week open-label extension study in Part B to receive long-term benefits of diacerein 1% ointment” but the PISCF indicates that participants will be enrolled in the open-label extension (OLE) study. The NREC-CT requested clarification as to whether participation in the OLE is mandatory and that the PISCF is modified to reflect this clarification.
- The NREC-CT requested that age-appropriate PISCFs are provided for participants aged <6 years old to engage in the assent process, in line with the EMA guidance on Assent / Informed Consent Guidance for Paediatric Clinical Trials with Medicinal Products in Europe (2021):

https://www.ema.europa.eu/en/documents/other/assent-informed-consent-guidance-paediatric-clinical-trials-medicinal-products-europe_en.pdf

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

7. **Suitability of the clinical trial sites facilities**

- The NREC-CT noted that the protocol includes both paediatric and adult populations but that the Site Suitability form submitted for review pertain to Children's Health Ireland only. The NREC-CT requested clarification as to whether adult participants will be included in the trial and if so the documents detailing a suitable site should be provided for review.

8. **Suitability of the investigator**

- The NREC-CT noted that the protocol includes both paediatric and adult populations but that the documents submitted for review pertain to a paediatric Principal Investigator only. The NREC-CT requested clarification as to whether adult participants will be included in the trial and if so the documents detailing a suitable PI should be provided for review.

2023-508165-33-00

Institutions: St James's Hospital

Study title: An Open-Label Extension Study to Assess the Long-Term Safety and Tolerability of ZYN002 Administered as a Transdermal Gel to Children, Adolescents and Young Adults with Fragile X Syndrome

- NREC-CT Decision:

- Favourable

21-NREC-CT-068_Mod-4

Institutions: University Hospital Galway

Study title: Phase Ib of Cyclophosphamide, Pomalidomide, Dexamethasone and Daratumumab (CPD-DARA) in patients with relapsed/refractory multiple myeloma (The CPD-DARA Study)

- NREC-CT Decision:

- Favourable

2023-506987-15-00

Institutions: Tallaght University Hospital

Study title: Phase Ib/II Trial of Pembrolizumab (MK-3475) Combination Therapies in Metastatic Castration-Resistant Prostate Cancer (mCRPC) (KEYNOTE-365)

- NREC-CT Decision:

- Favourable

2023-505699-31-00

Institutions: University Hospital Galway

Study title: A Phase 3 Multicenter, Long-Term Extension Study to Evaluate the Safety and Efficacy of Upadacitinib (ABT-494) in Subjects with Ulcerative Colitis (UC)

- NREC-CT Decision:

- Request for more information

- Additional Information Required RFI

Part I Considerations

- The formatting errors on pgs. 10, 11 and 14 of the Investigator's Brochure should be resolved as these pages are currently unreadable.

Part II Considerations

Compliance with national requirements on data protection

- No Considerations

Compliance with use of biological samples

- This document represents information already approved under CTD

Financial arrangements

- This document represents information already approved under CTD

Proof of insurance

- No Considerations

Recruitment arrangements

- This document represents information already approved under CTD

Subject information and informed consent form

- The NREC-CT requested that the PISCF is modified to include details of how long samples will be stored for, as set out in Compliance with the collection, storage and future use of human biological samples form submitted.
- The NREC-CT noted that the section on future research in the **Main PISCF** 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
- The NREC-CT requested that the consent form in the PISCF (pg. 32) is modified in line with regulations and best practice regarding future research. Consent for future research should be separate, clearly defined and confined to the disease or drug under study in this trial.
- 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.

Suitability of the clinical trial sites facilities

- No Considerations

Suitability of the investigator

- This document represents information already approved under CTD

2023-507353-15-00

Institutions: Mater Misericordiae University Hospital, Connolly Hospital

Study title: An open-label extension trial of the long-term safety and efficacy of BI 1015550 taken orally in patients with idiopathic pulmonary fibrosis (IPF) and progressive pulmonary fibrosis (PPF) (FIBRONEER™-ON)

- NREC-CT Decision:

- Favourable

2023-506091-27-00

Institutions: Children's Health Ireland

Study title: A Phase 2, Multicenter, Double-Blind, Randomized, Placebo-controlled Trial, evaluating Safety, Tolerability, and Efficacy of Subcutaneous Doses of TransCon CNP Administered Once Weekly for 52 Weeks in Infants (0 to <2 years of age) with Achondroplasia followed by an Open Label Extension (OLE) period.

- NREC-CT Decision:

- Favourable

2023-508734-34-00

Institutions: Mater Misericordiae University Hospital

Study title: IMPAHCT: A Phase 2b/3, Randomized, Double-Blind, Placebo-Controlled, 24-Week Dose Ranging and Confirmatory Study to Evaluate the Safety and Efficacy of AV-101 in Patients with Pulmonary Arterial Hypertension (PAH)

- NREC-CT Decision:

- Favourable

- AOB:
  - None