National Research Ethics Committee

NREC-CT Meeting

20 March 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
Prof. Catherine Hayes	Committee Member, NREC-CT B
Prof. Michaela Higgins	Committee Member, NREC-CT B
Ms Jasmine Joseph	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
Ms Evelyn O'Shea	Committee Member, NREC-CT B
Mrs Ann Twomey	Committee Member, NREC-CT B
Ms Aileen Sheehy	Programme Manager, National Office for RECs
Dr Laura Mackey	Programme Officer, National Office for RECs
Ms Megan O'Neill*	Project Officer, National Office for RECs

Apologies: Ms Serena Bennett, Dr Katherine Benson, Prof. Abhay Pandit, Prof. John Wells

Quorum for decisions: Yes

Agenda

- Welcome & Apologies

- 2023-510117-26-00
- 21-NREC-CT-013_Mod-4
- 23-NREC-CT-006_Mod-2
- 23-NREC-CT-012_Mod-2
- 22-NREC-CT-085_Mod-2
- 2022-501576-25-00
- 23-NREC-CT-005_Mod-3
- 22-NREC-CT-103_Mod-1
- 22-NREC-CT-097_Mod-4
- AOB

- The Chair welcomed the NREC-CT B.
  - The minutes from the previous NREC-CT B meeting on 21 February 2024 were approved.
  - The NREC Business Report was discussed and noted.
  - The Chair stepped out of the discussion of one of the trials due to a declared COI. The Deputy Chair chaired the discussion for this study.

Applications

2023-510117-26-00

Principal Investigators & Institutions: Mater Misericordiae University Hospital, Dublin

Study title: Phase 2 Study of Tremelimumab (Day 1 only), Durvalumab (MEDI4736) and Trans-arterial catheter chemoembolization (TACE) in patients with advanced Hepatocellular Carcinoma (HCC)

- **NREC-CT Decision:**

- Request for further information

Part I Additional Information Required RFI
1. Overall, the protocol document would benefit significantly from a revision to more clearly elucidate the key parameters and rationale of the study – particularly the rationale for the regimen selected in the study. Specifically, this revision should include clear language related to the rational of the selected regimen for the study further, starting with where the investigators are at now, brief discussion of how we got there and why the study rationale was selected.

2. It was not clear in the Protocol what the anticipated timeline is for the conduct of the recruitment procedures. Please clarify whether this "preliminary discussion" will take place in advance of the screening visit and collection of baseline evaluations, and define this time period. Without compromising clinical need for early treatment, the participant should have a reasonable amount of time to make their decision on participation before undergoing Day 1 treatment, and the timeframe for the recruitment procedure described in the Protocol should reflect this.

3. Please set out clearly in the Protocol the time period between the initial baseline evaluations visit and Day 1.

4. It is noted that telephone call may replace in person visits in exceptional circumstances for screening an informed consent. Please set out in the Protocol what processes will take place in the telephone calls proposed for participant convenience. The rationale and timelines for these processes should also be elucidated.

5. It is queried how long is the study follow-up period. Clarification is also required whether the requirement to complete a follow-up period may mean a participant is not eligible for existing or potentially new SOC treatments for progressed disease.

6. Please comment on the comparability of the populations of this trial and the recently presented HIMALAYA study presented by Abou-Alfa et al. at GI ASCO 2022. Clarification is required whether these participants were ineligible for TACE should be further elucidated.

7. Please provide further information on the study database the research team will access to complete their analysis. Is it sufficiently detailed for the analysis to be completed?

8. Please provide further details on the plans in place to publish the study results to the scientific community and/or patients.

9. The protocol should be updated to align with the study compensation plan as it is set out in the Patient Information Leaflet, in that participants may be eligible to claim for compensation if injured as a result of participation in the study.

10. Please provide the SmPCs (or equivalent product information for both the drug eluting beads (i.e., doxorubicin) and the contrast agents (unspecified)) used during the TACE procedure

Part II Considerations

1. Compliance with national requirements on data protection

- The NREC-CT requested that the DPO statement regarding the data protection risks and mitigating safeguards are shared with the committee for review.

2. Compliance with use of biological samples

- The NREC-CT requested that the time period storage of biological samples is harmonised across the PIL (25 years), Protocol (20 years) and the Biological Samples (15 years), as they currently provide conflicting time periods. If samples are stored for the longer time periods (20 or 25 years), the NREC-CT requests that justification is provided if samples are to be stored for a longer period of time.

3. Financial arrangements

No Considerations

4. Proof of insurance

The NREC-CT requested assurance that the insurance policy in place for this study will be renewed upon its expiration.

5. Recruitment arrangements

- The NREC-CT requested further details for the recruitment procedure, clarifying whether the investigators will reach out to other centres for potential participants and whether it will be possible to recruit the whole cohort from the MMUH.
- It is noted that telephone call may replace in person visits in exceptional circumstances for screening an informed consent. Please set out in the Recruitment Arrangements, aligning with the process set out in the Protocol, what

processes will take place in the telephone calls proposed for participant convenience. The rationale and timelines for these processes should also be elucidated.

6. Subject information and informed consent form

- The NREC-CT requested that the PIL should explain that all patients on the study will get the same treatment.
- The NREC-CT considered the following statement on pg 3 of the PIL, "During the screening period, you may learn that you may not proceed to take part in the study. If this occurs, your study doctor will discuss the reasons for this with you". The NREC-CT requested that this is modified to state that "your study doctor will discuss the reasons for this with you and other options available to you".
- The NREC-CT noted that ethnicity data will be collected in this trial. As this is counted as special category data under the GDPR, the Committee requested that the PIL is updated to include the justification for collection of this data as per GDPR requirements.
- The NREC-CT noted that the PIL describes a long follow-up period until the study ends, and the protocol describes a 3-month follow-up period. The NREC-CT requested that the follow-up period is harmonised across the Protocol and PIL, clarifying when participants leave the study and return to off-study clinical care, and whether the requirement to complete a follow-up period may mean a participant is not eligible for existing or potentially new SOC treatments for progressed disease.
- The NREC-CT recommended that a chart is added to the PIL setting out the treatment and visit schedule for participants clearly.
- The NREC-CT requested that the PIL is modified to include the list of medications and herbal treatments that cannot be used in conjunction with the trial drugs, as detailed in the Protocol.
- The NREC-CT noted that the section on future research in the PIL (What will happen to your samples that are collected in the study, pg 7) 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 noted that aspects of the Consent for Optional Future Research is seeking blanket consent for future / additional 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 'specified health research, either in relation to a particular area or more generally in that area or a related area of health research, or part thereof' and this is clearly stated in the main body and informed consent section of the PISCF.

- The NREC-CT requested that the Consent for Optional Future Research PISCF is provided as a separate document. The PISCF should also make it clear to participants that subsequent research ethics review will be sought for specific research once clearly defined.
- The NREC-CT noted that the PIL states on pg 7 that genetic analysis will not be done on any of the blood samples or other tissue samples that are collected, however pg 20 of the PIL (What will happen if you agree to optional future research?) states " Future research may involve genetic tests using DNA or RNA obtained from your samples. This may include whole exome or whole genome sequencing". The NREC-CT requested that the information regarding optional future genetic research is harmonised and aligns with requirements under the Health Research Regulations 2018. The NREC-CT recommended that information regarding optional future research is moved to a new, separate PIL so that it is set out clearly for participants.
- The NREC-CT requested that the terms whole genome sequencing and exome sequencing are explained in the PIL.
- The NREC-CT noted that the PIL does not state whether or not participants will be informed of DNA/RNA findings (if any). The NREC-CT requested that the PIL is modified to inform participants of the process for these findings.
- The NREC-CT requested that the time period storage of biological samples is harmonised across the PIL (25 years), Protocol (20 years) and the Biological Samples (15 years), as they currently provide conflicting time periods. If samples are stored for longer time periods (20 or 25 years), the NREC-CT requests that justification is provided if samples are to be stored for a longer period of time.
- The NREC-CT noted that pg 7 (What will happen to your samples that are collected in the study?) of the PIL indicates that participants will not be contacted about future research after they initially consent, however the ICF presents five options, including re-consenting. The NREC-CT requested that this is modified to harmonise the PIL and ICF.
- The NREC-CT noted the following consent item in the ICF; "I consent and authorize that my study data may be transferred within and outside the European Union, to countries, including the United States, where data may not have the same level of data protection as in Ireland or in the European Union". The PIL should be updated to clearly set out this transfer of data, including details of what data is being shared, to whom and where.
- The NREC-CT considered that information provided to participants around their biological samples to be limited. The Committee requested that the PIL is modified to clearly set out how long participant samples and data will be stored for, where they will be stored and when they will be destroyed.
- 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 as these documents are composed of

images, rather than searchable text, and cannot be optimised for use with assistive software.

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

- No Considerations

8. **Suitability of the investigator**

- The NREC-CT appreciated the detail given regarding the experience of the Investigator and their suitability, however they noted that the Declaration of Interest had not been submitted and request that this is provided.

21-NREC-CT-013_Mod-4

Principal Investigators & Institutions: Dr John Quinn (Beaumont Hospital), Dr Janusz Krawczyk (University Hospital Galway), Dr Vitaliy Mykytiv (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)

- **NREC-CT Decision:**

- Request for further information

Additional Information Required RFI

- The NREC-CT considered that the language in the main PILCF (pg 32-33) regarding clinical trial liability and IPHA research injury guidelines was overly complex and queried whether this information was required. The NREC-CT requested that this language is simplified and suggested that adding a link to the relevant IPHA webpage may simplify the process for participants.

23-NREC-CT-006_Mod-2

Principal Investigators & Institutions: Dr. Ciara McDonnell (Temple Street)

Study title: ApproaCH: A Phase 2b, Multicenter, DoubleBlind, Randomized, Placebo-controlled Trial evaluating Efficacy and Safety of Subcutaneous Doses of TransCon CNP Administered Once Weekly for 52 Weeks in Children with Achondroplasia followed by an Open Label Extension period

- **NREC-CT Decision:**

- Request for further information

- **Additional Information Required RFI:**

- The NREC-CT noted the addition of a physical function test at week 52 and 104 and questioned whether a baseline measurement should also be taken. As the Committee considered that the trial design would benefit from a baseline measure, they requested clarification as to why a baseline physical function test is not included in the study design.

23-NREC-CT-012_Mod-2

Principal Investigators & Institutions: Dr Janusz Krawczyk **(**Galway University Hospital)

Study title: Phase 3 Study of Teclistamab in Combination with Lenalidomide and Teclistamab Alone versus Lenalidomide Alone in Participants with Newly Diagnosed Multiple Myeloma as Maintenance Therapy Following Autologous Stem Cell Transplantation

- **NREC-CT Decision:**

- Favourable

22-NREC-CT-085_Mod-2

Principal Investigators & Institutions: Prof Cliona Grant (St James Hospital)

Study title: A Phase 2, Open-Label, Multi-Center Study of PDS0101 (R-DOTAP [Versamune®] + HPVmix) and Pembrolizumab (KEYTRUDA®) Combination Immunotherapy in Subjects with Recurrent and/or Metastatic Head and Neck Cancer and High-Risk Human Papillomavirus-16 (HPV16) Infection

- **NREC-CT Decision:**

- Favourable

2022-501576-25-00

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

Study title: A Phase 3 Trial of Fianlimab (anti-LAG-3) and Cemiplimab versus Pembrolizumab in the Adjuvant Setting in Patients with Completely Resected High-risk Melanoma

- **NREC-CT Decision:**

- Request for further information

- Additional Information Required RFI
- The NREC-CT requested clarification as to whether the participants already recruited will be reconsented to address the potential issues arising from the changes, eg. the exclusion of patients with a history of myocarditis, the addition of immune-mediated cholangitis as a potential risk and the changes to the side effects (eg. vision loss, eye pain on movement, loss of colour vision, dry eye). The NREC-CT requested justification is provided if ongoing participants are not to be reconsented.

23-NREC-CT-005_Mod-3

Principal Investigators & Institutions: Dr Dearbhaile Collins (Cork University Hospital)

Study title: A PHASE 3, RANDOMIZED, PLACEBO CONTROLLED, DOUBLE-BLIND, MULTICENTER TRIAL OF SELINEXOR IN MAINTENANCE THERAPY AFTER SYSTEMIC THERAPY FOR PATIENTS WITH P53 WILDTYPE, ADVANCED OR RECURRENT ENDOMETRIAL CARCINOMA

- **NREC-CT Decision:**

- Request for further information

- **Additional Information Required RFI:**
- The NREC-CT considered the following statement from the Main PISCF; "If you are a public patient taking part in the study this will not involve any extra costs for you. If you are a private patient, you or your private health insurer (if you have one) may only be charged for the costs of routine care and treatments for patients with your cancer type and not the consultations and tests done specifically for the study." The NREC-CT requested clarification as to why private participants may be charged for the costs of routine care in a public hospital.

22-NREC-CT-103_Mod-1

Principal Investigators & Institutions: Dr Emer Joyce (Mater Misericordiae University Hospital, Dublin)

Study title: An Open-Label Extension and Safety Monitoring Study of Acoramidis (AG10) in Participants with Symptomatic Transthyretin Amyloid Cardiomyopathy Who Completed the Phase 3 ATTRibute-CM Trial (AG10-301)

- **NREC-CT Decision:**

- Favourable with conditions

- **Favourable with conditions:**
- The NREC-CT requested that the ATTRibute-CM study logo is removed from the patient bag.

22-NREC-CT-097_Mod-4

Principal Investigators & Institutions: Dr Cormac McCarthy (St. Vincent's University Hospital)

Study title: A randomized, double-blind, placebo-controlled clinical trial of once-daily inhaled molgramostim nebulizer solution in adult subjects with autoimmune pulmonary alveolar proteinosis (aPAP)

- **NREC-CT Decision:**

- Favourable

- AOB: None