National Research Ethics Committee

NREC-CT Meeting

26th March 2025

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
Dr Åine de Róiste	Committee Member, NREC-CT B
Prof. Michaela Higgins	Committee Member, NREC-CT B
Ms Jasmine Joseph	Committee Member, NREC-CT B
Dr Ciaran Lee	Committee Member, NREC-CT B
Dr 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
Prof. John Wells	Committee Member, NREC-CT B
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
Chita Murray	Programme Manager, National Office for RECs
Deirdre Ni Fhloinn	Project Officer, National Office for RECs
Peadar Rooney	Project Officer, National Office for RECs
Ciaran Horan	Administrative Assistant, National Office for RECs

Apologies: Andrew Lindsay, Karina Halley, Serena Bennett

Quorum for decisions: Yes

Agenda

- Welcome & Apologies
- 2024-515698-85-00
- 2024-513547-82-00
- 2024-511126-31-00 SM1
- 2024-512749-18-00 SM1
- 2023-509877-22-00 SM4
- 2024-510620-39-00 SM6
- 2023-507263-19-00 SM1
- 2023-506334-75-00 SM3
- 2023-507353-15-00 SM-2
- 2022-500395-57-00 SM-7
- AOB

- The Chair welcomed the NREC-CT B.
  - The minutes from the previous NREC-CT B meeting on 12th February 2025 were approved.
  - The NREC Business Report was discussed and noted.

Applications

2024-515698-85-00

Institutions: Mater Private Hospital, St James's Hospital, Cork University Hospital, Beacon Hospital, Beaumont Hospital

Study title: A Randomized, Double-Blind, Phase 3 Trial of Adagrasib plus Pembrolizumab plus Chemotherapy vs. Placebo plus Pembrolizumab plus Chemotherapy in Participants with previously Untreated, Locally Advanced or Metastatic Non-squamous Non-small Cell Lung Cancer with KRAS G12C Mutation (KRYSTAL-4)

Dossiers Submitted: MSC Part I & II

- NREC-CT Decision:
- Request for Further Information

- Additional Information Required

Part II Considerations

1. Financial arrangements

- The NREC- CT noted that carers of participants have not been included for travel, accommodation and meal expense reimbursement in the Compensation Form (p1). The Committee requested that reimbursement of travel, accommodation and meal expenses are considered for carers of participants and, if included, that it is elucidated in the Compensation Form and PISCF's.

2. Subject information and informed consent form

- The NREC-CT noted discrepancies in the scope of future research described in the Protocol (pg 43), the Compliance with Biological Samples Form (pg 7), Optional Future Research PISCF (pg 2) and the Main PISCF (pg 33). The Committee requested confirmation that the scope of future research will be limited to that which is outlined in the Main PISCF and Future Research PISCF for the Republic of Ireland.
- The NREC-CT noted that the Sponsor will not seek additional external ethics approval for future research (Biological Samples Form pg9). The Committee requested that subsequent research ethics review will be sought for specific future research once clearly defined and that this is elucidated in the Main PISCF and Optional Future Research PISCF. 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 requests that all PISCF's be updated with a placeholder for the qualification/dated signature of the person performing the consent interview
- The NREC-CT noted that all PISCF's submitted include a witness signature line. The NREC-CT requests information be added to each PISCF explaining the context where a witness signature would be needed.
- The NREC- CT noted that the consent section in all PISCF's consists of bullet points with one signature area. The Committee requests that the PISCFs are amended to include specific tick box consent options that the participant can sign/initial separately.
- 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.

3. Suitability of the clinical trial sites facilities

- The NREC-CT noted that in the Site Suitability Forms, three of the five participating sites report that patients will be exposed to an ionising radiation burden greater than the normal standard of care. The Committee request clarification on why the level of ionising radiation that participants are exposed does not appear to be standardised across all sites and recommends that this information is also elucidated in the PISCF's as applicable.

2024-513547-82-00

Institutions: Tallaght University Hospital, Mater Misericordiae University Hospital

Study title: A Phase 3, Randomized, Multicenter, Double-Blind, Placebo-Controlled Study of Acoramidis for Transthyretin Amyloidosis Prevention in the Young (ACT-EARLY Trial)

Dossiers Submitted: Add MSC 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 storage duration of samples did not align between the with Main ICF (pg 16), the Optional genetic ICF (pg2) and the Biological Samples Form (pg3). The Committee requests that the duration for which samples will be stored reflects the CTR and is aligned across all documentation.
- The NREC noted a reference to social security numbers (Main ICF pg 14). The Committee requested the removal of this reference, and an amendment made to relate to the Irish context, as applicable.
- The NREC noted reference to participants being billed for emergency treatment or treatment if they become injured or ill as a direct result of receiving study medicine (Main ICF pg 15). The NREC-CT requested that these references are removed and that it is clarified that there will be no expense to the participant for inclusion in the study.
- The NREC-CT requests that the Main ICF (pg 24) and Optional Genetic ICF (pg8) be updated with a placeholder for the qualification of the person performing the consent interview.
- 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 would like to commend the sponsor on patient advocate integration and noted that the patient handbook was excellent.

2024-511126-31-00 SM1

Institutions: University Hospital Galway, St James's Hospital

Study title: A multi-center, randomized, double-blind, placebo controlled, parallel-group Phase IIIb study evaluating the effect of inclisiran on atherosclerotic plaque progression assessed by coronary computed tomography angiography (CCTA) in participants with a diagnosis of non-obstructive coronary artery disease without previous cardiovascular events (VICTORION-PLAQUE)

Dossiers Submitted: MSC Part 1 & 2

- NREC-CT Decision:
- Favourable

- Additional Information Required
- None

2024-512749-18-00 SM1

Institutions: Mater Private Hospital, University Hospital Waterford, Mater Misericordiae University Hospital, University Hospital Galway, St James's Hospital, Beaumont Hospital, University Hospital Limerick

Study title: Isa-RVD Study: Phase II, Multi-centre, Single-Arm, Open-Label Study to evaluate the efficacy and safety of the combination regimen Isatuximab, Lenalidomide, Bortezomib, and Dexamethasone in Patients with Newly Diagnosed Multiple Myeloma

Dossiers Submitted: RMS Part 1 & 2

- NREC-CT Decision:

- Request for Further Information

- Additional Information Required

Part II Considerations

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

- The NREC-CT noted reference to a 'risk management programme for Lenalidomide' in the Main PISCF (pg7). The Committee requests that further details of this programme are elucidated in the PISCF to facilitate participant understanding and informed consent.

- The NREC-CT noted that the future use of data / samples (including genetic research) is not described in line with regulations / best practice on pg. 30 and 38 of the Main PISCF. The NREC-CT requested that future use of samples / 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, related diseases 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 once fully defined (on pg 38 the removal of the middle tick box option 'Yes' would facilitate compliance with best practice)
- 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.

2023-509877-22-00 SM4

Institutions: Children's Health Ireland

Study title: A Phase 3, Prospective, Open-label, Uncontrolled, Multicenter Study on Efficacy and Safety of Prophylaxis with rVWF in Children Diagnosed With Severe von Willebrand disease.

Dossiers Submitted: MSC Part 1 & 2

- NREC-CT Decision:

- Request for Further Information

- Additional Information Required

Part II Considerations
1. Subject information and informed consent form

- The NREC-CT noted references to "your child" and "your child's medicine" in the Turning 16 PISCF (pg26). The committee requested that this is amended to address the participant directly.

- The NREC-CT noted that participants are recommended to speak to the study doctor if additional support for remote visits is required (Main ICF, Pg18). The committee requested that this option of additional support for remote visits is recommended rather than offered.
- The NREC-CT noted that the future use of data / samples (including genetic research) is not described in line with regulations / best practice on pg.25/26 of the Main PISCF and pg 12/24/25 of the Turning 16 PISCF. The NREC-CT requested that future use of samples / 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, related diseases 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.

2024-510620-39-00 SM6

Institutions: Tallaght University Hospital

Study title: An Open-label, Randomized, Phase 3 Study of MK-6482 in Combination with Lenvatinib (MK-7902) vs Cabozantinib for Treatment in Participants with Advanced Renal Cell Carcinoma Who Have Progressed After Prior Anti-PD-1/L1 Therapy

Dossiers Submitted: MSC Part 1 & 2

- NREC-CT Decision:

- Favourable

- Additional Information Required
- None

2023-507263-19-00 SM1

Institutions: St James's Hospital, University Hospital Limerick, Tallaght University Hospital, Beaumont Hospital

Study title: A Randomized Phase 3 Study of MRTX849 versus Docetaxel in Patients with Previously Treated Non-Small Cell Lung Cancer with KRAS G12C Mutation

Dossiers Submitted: MSC Part 1 & 2

- NREC-CT Decision:

- Request for Further Information

- Additional Information Required

Part II Considerations

1. Subject information and informed consent form

- The NREC-CT noted, despite withdrawal of participant consent for further follow-up or contact, that 'the study doctor may continue to collect information on your health status where the law allows' (Main ICF pg 14). The Committee requests that reference to study follow-up after participant withdrawal is clarified, and/or removed if not in line with legislation in the Republic of Ireland.

- The NREC-CT noted that the future use of data / samples (including genetic research) is not described in line with regulations / best practice on pg. 6 of the Main PISCF. The NREC-CT requested that future use of samples / 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, related diseases 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,
  - 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 noted that pg. 7 of the Main PISCF states that participants are to undergo genetic testing. The NREC requested that the following is clarified in the PISCF:
    - 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 mechanism for anonymisation of genetic material and its associated data. This should be described using plain English suitable for a lay audience.
    - For guidance, please see HSE National Policy for Consent in Health and Social Care Research (V2.0, 2024). Dublin: Health Service Executive https://www2.healthservice.hse.ie/organisation/national-pppgs/hse-national-policy-for-consent-in-health-and-social-care-research/

- The NREC-CT noted a reference to data anonymization on pg 30 of the Main PISCF. The committee requested that if some or all data is anonymised that the ICF be updated to include a consent statement for the participant to explicitly consent to the processing of their personal data to anonymised data as per Article 4 (2) and (6) General Data Protection Regulation (GDPR).

- 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.

2023-506334-75-00 SM3

Institutions: Mater Misericordiae University Hospital

Study title: An Open-label Extension Study Evaluating the Long-term Safety and Efficacy of Seralutinib Orally Inhaled for the Treatment of Pulmonary Arterial Hypertension (PAH)

Dossiers Submitted: MSC Part 1 & 2

- NREC-CT Decision:

- Request for Further Information

- Additional Information Required

Part II Considerations raised

1. Financial arrangements

- The NREC-CT noted that an undisclosed stipend will be provided after each study visit (Main ICF pg 17) as well as a 33e stipend for each sample submitted in the Fertility Sub Study (Fertility Sub Study ICF pg4). However, the Participant Compensation Form refers only to the 33e stipend for each sample provided in the Fertility Sub Study (pg2). The NREC-CT requested that reference to the stipend in the Main ICF is removed or quantified if applicable and aligned with the Participant Compensation Form.
- The NREC-CT noted that participants will be reimbursed for travel-related expenses, including laboratory fees (p16 Main PISCF and pg 2 Compensation for Participants Form). The Committee requested clarification on whether participants are obliged to pay for certain tests and if so whether these costs are disclosed before enrollment. Any cost to the participant should be outlined and aligned across all PISCF's.

2. Subject information and informed consent form

- The NREC-CT noted that blood sampling could be done in the clinic or a nearby laboratory (Main PISCF pg1/pg10) and that personal information will be included on samples according to local guidelines (Biological Samples Form, pg4). The Committee requested
  - clarification on which laboratories would be eligible
  - further details on who would arrange appointments, sample requests, sample collection etc to be elucidated in the PISCF.
  - Whether including personal information on samples was necessary and if so, that data protection procedures are outlined in the PISCF.

- The NREC-CT noted that no information is provided on whether samples from the fertility substudy will be used for future research. The Committee requested confirmation that samples from the fertility substudy will be not be used for future research.

- The NREC-CT noted that the liklihood of incidental findings are not mentioned in the Fertility Substudy PISCF. The Committee requested clarification on the process for managing incidental findings from the fertility substudy along with details of how these will be communicated to participants if applicable. This information should be included in the PISCF's.

- The NREC-CT noted a new Fertility Substudy referenced on pg 7 of the Main PISCF. The Committee requested further clarification on participant eligibility and exclusion criteria for this Fertility Substudy and that this is elucidated in the Main PISCF and Fertility Substudy PISCF if applicable.

- 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.

2023-507353-15-00 SM-2

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)

Dossiers Submitted: MSC Part 1 & 2

- NREC-CT Decision:

- Request for Further Information

- Additional Information Required

Part II Considerations raised
1. Subject information and informed consent form

- The NREC-CT noted that on Pg 3 of the Main ICF, in the section For IPF patients, the rationale for the lower dose of nerandomilast when given with nintedanib (i.e. the proven safety and efficacy at this dose) is not provided in the opening paragraph. To provide further clarity to participants the Committee request that the rationale for the dose reduction of nerandomilast when given with nintedanib is explained in the opening paragraph of this section.
- 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.

2022-500395-57-00 SM-7

Institutions: St James's Hospital

Study title: A Phase 3, Randomized, Double-blind, Placebo-controlled Study to Evaluate Pembrolizumab Versus Placebo as Adjuvant Therapy Following Surgery and Radiation in Participants with High-risk Locally Advanced Cutaneous Squamous Cell Carcinoma (LA cSCC) (KEYNOTE-630)

Dossiers Submitted: MSC Part 1 & 2

- NREC-CT Decision:

- Request for Further Information

• Additional Information Required

Part II Considerations raised
1. Subject information and informed consent form

- The NREC-CT noted the sentence ‘When you joined the study, neither you, the study doctor and study team did not know which treatment group you were assigned to’ on pg 2 of the Main ICF Addendum. The NREC-CT requests that the phrase ‘did not know’ is replaced with the word ‘knew’ within this sentence, if this is the intended meaning of this sentence, to provide clarification to the participant on the blinding process.
- 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.

- AOB:
  - CTIS demonstration