National Research Ethics Committee

NREC-CT B Meeting

30th April 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
Ms Serena Bennett	Committee Member, NREC-CT B
Dr Åine de Róiste	Committee Member, NREC-CT B
Dr Karina Halley	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 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
Dr Emily Vereker	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 Chita Murray	Programme Manager, National Office for RECs
Ms Deirdre Ni Fhloinn*	Project Officer, National Office for RECs

*Drafted minutes

Apologies: Prof John Wells, Mrs Ann Twomey

Quorum for decisions: Yes

Agenda

- Welcome & Apologies
- 2025-521523-73-00
- 2024-517869-16-00
- 2024-514435-20-00
- 2024-517729-20-00
- 2023-503772-24-00 SM3
- 2023-507536-21-00 SM3
- 2024-513087-26-00 SM13
- AOB.

- The Chair welcomed the NREC-CT B.
  - The minutes from the previous NREC-CT B meeting on 26th March 2025 were approved.
  - The NREC Business Report was discussed and noted.

Applications

2025-521523-73-00

Institutions: Mater Misericordiae University Hospital (Prof. Austin Duffy)

Study title: A Phase 1/1b First-in-Human, Multi-Part, Open-Label Study to Investigate the Safety, Tolerability, Pharmacokinetics, Biological, and Clinical Activity of DF9001 as a Monotherapy and in Combination Therapies in Patients with Advanced (Unresectable, Recurrent, or Metastatic) Solid Tumors, and Expansion in Selected Indications (Constellation)

Dossiers Submitted: MSC Part I & II

- **NREC-CT Decision:**

- Request for Further Information – Trial subsequently withdrawn

2024-517869-16-00

Institutions: Mater Misericordiae University Hospital (Prof. Austin Duffy)

Study title: C5991001_A Phase 1 Open-label, Multicenter Study to Evaluate the Safety, Tolerability, Pharmacokinetics, and Antitumor activity of PF-08052666 /SGN-MesoC2 in Participants with Advanced Solid Tumors (Dazzle)

Dossiers Submitted: RMS Part I & II

- **NREC-CT Decision:**

- Request for Further Information

- **Additional Information Required RFI**

Part II Considerations

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

- 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 requests that the PISCF's be updated with a placeholder for the qualification/dated signature of the person performing the consent interview
- The NREC-CT noted references to anonymised data in the PISCF (pg19/20) but not in the Compliance with Biological Samples Form. The Committee requested that if data is to be anonymised that the ICF be updated to include a consent statement for the participant to explicitly consent to the processing of their personal data from pseudonymised /coded data to anonymised data as per General Data Protection Regulation (GDPR). An explanation of the process is provided to participants in the PISCF using plain English suitable for a lay audience. This should include an explanation of the term 'anonymised'. In addition, the PISCF and Biological Samples Form should be aligned.
- The NREC-CT noted that the future use of data / samples (including genetic research) is not listed in the Biological Samples Form (pg 5) but is outlined in the Main PISCF (pg19), where it is not described in line with regulations / best practice. The NREC-CT requested that if future use of samples / personal data is planned that it is outlined in the Biological Samples Form and also 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 made optional
- 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/

2024-514435-20-00

Institutions: Children's Health Ireland (Dr. Joanne Hughes)

Study title: A Phase 3b Open-Label Study of Long-Term Neurocognitive Outcomes in Children With Phenylketonuria Treated With Sepiapterin (Epiphany)

Dossiers Submitted: RMS Part I & II

- **NREC-CT Decision:**

- Request for Further Information

- **Additional Information Required RFI**

Part I Considerations (RFI) for addition to CTIS
1.

- It is noted that the drug dosing described in Figure 1 of the protocol (p19) is exact (i.e., 7.5mg/kg every day for 0-6 months old); however, earlier in the protocol (p16) the dose is described as a range (i.e., 'up to' 7.5mg/kg every day for 0-6 months old). Please clarify the dose of Sepiapterin for all age groups and ensure it is aligned throughout the protocol.
- It is noted that there are no details in the protocol on how to prepare and administer exact doses of Sepiapterin to children of different weights if only 250mg and 1000mg sachets of the IMP are provided. Please clarify the following: i) how exact doses will be measured by parents, ii) the reproducibility of these doses if the IMP is to be mixed in water/juice/soft food, and iii) how the risk of over or underdosing will be mitigated.

- It is noted that in the study protocol (pg13), participants will be administered 2g protein/kg (or 100mg Phe/kg). Please comment on the risk of this leading to an adverse event in the protocol and also in the PISCF, if applicable.

Part II Considerations

1. Recruitment arrangements

- The NREC-CT noted that in the Patient Recruitment Form (Q1.6), no timeframe is outlined for how long the participant will be given to consider participating in the study. The Committee requested that sufficient time is given to the participant to consent to participate in the study and that this is outlined in the Patient Recruitment Form and all relevant PISCF's.
- The NREC-CT noted that participants who reach the age of 16 can consent to continued participation in the study but that there is no consent form for them (Recruitment Form, pg 5). The Committee requested confirmation that if participants 16 years old or older plan to be recruited, that a relevant PISCF will be submitted in advance for review.

2. Subject information and informed consent form

- 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 information regarding pregnancy is included in the PISCF for 6–11-year-olds. The Committee request that the age ranges for the PISCF's are amended to reflect guidance from the EMA (e.g. a PISCF for 6-9 year olds and a PISCF for 10-15 year olds) and that reference to pregnancy/contraception is also removed from the PISCF for 6-9 yr olds as per EMA guidance (https://www.ema.europa.eu/en/documents/other/assent-informed-consent-guidance-paediatric-clinical-trials-medicinal-products-europe_en.pdf)
- The NREC-CT noted that the language related to pregnancy and contraception was not suitable for child participants (e.g. 'female of childbearing potential', 'barrier method', 'abstinence', 'sexually active') in the Parent PISCF (pg11) and PISCF for 12–15-year-olds (pg 5). The Committee requested that the PISCF's are amended to include age-appropriate language and/or lay language.
- The NREC-CT noted that some wording in the PISCF for 6–11-year-olds needs to be amended. The Committee requests that the final sentence of pg.4 is amended to "we will make sure that you get the help to deal with anything bad that might happen".
- The NREC-CT noted that the Parent PISCF is 25 pages in length. The Committee requests that the Sponsor gives due consideration to the overall length of the

document and evaluates whether there is an appropriate opportunity to reduce its length.

- The NREC-CT noted that no details were included in the Parent PISCF on how to prepare and administer exact doses of Sepiapterin to children of different weights if only 250mg and 1000mg sachets of the IMP are provided. The Committee requested clarification on how exact doses will be measured by parents and that this is elucidated in the Parent PISCF.
- The NREC-CT noted that reference to the future use of data / samples (including genetic research) on pg. 25 of the Parent PISCF is not in line with regulations / best practice (Health Research Regulations (Data Protection Act 2018 (Section 36(2) (Health Research) Regulations 2018)). The Committee request:
    - optional future research should be made into a separate and explicit consent item in the Informed Consent section of the Main PISCF, with separate signatures section, so it is distinct from the main consent to participate in the research
    - please clarify in all relevant documentation whether biological samples will be used for future research as there is conflicting information in the Parent PISCF (pg20) and the Biological samples form (pg4)
    - 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/

2024-517729-20-00

Institutions: St Vincent's University Hospital (Prof. John Crown)

Study title: Extended Follow-up of Patients with Melanoma Treated with Fianlimab Plus Cemiplimab in Expansion Cohorts from R3767-ONC-1613 (Apollo)

Dossiers Submitted: RMS Part I & II

- **NREC-CT Decision:**

- Request for Further Information

- **Additional Information Required RFI**

Part II Considerations

1. Financial arrangements

- The NREC-CT noted that participants will not be paid for taking part in the study (PISCF pg5) however the Compensation for Participant Form states that the participant will be reimbursed for travel and will also receive a monetary payment

(pg 1, 2). The Committee requested that the PISCF and Compensation Form are aligned and the monetary payment to participants is quantified if applicable.

- The NREC-CT noted that meals and accommodation for both participants and carers will not be reimbursed (Compensation Form pg 1, 2). The Committee requested that participants are reimbursed for all reasonable out of pocket expenses, to ensure equity in access to clinical trials across all socioeconomic groups. This information must be provided in the PISCF with clear guidance regarding how these expenses can be claimed, and in the Compensation Form. Additionally, the Sponsor is also requested to give due consideration to the reimbursement of the expenses of carers.

2. Subject information and informed consent form

- 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 a wide range of personal and lifestyle information may be collected by the study team members e.g. eating habits and sexual behaviour (Main PISCF pg 6). The Committee requested that the collection of this sensitive personal information is further justified and explained.
- The NREC-CT noted that the Main PISCF (pg11) includes an impartial witness signature line. The Committee requested that further information be added to the Main PISCF explaining the context where an impartial witness signature would be needed as per ICH GCP Guidelines.

2023-503772-24-00 SM-3

Institutions: University Hospital Galway (Dr Michelle O'Shaughnessy), University Hospital Waterford (Dr Catherine Brown), St Vincent's University Hospital (Dr John Holian), Cork University Hospital (Prof. Michael Clarkson)

Study title: A Phase 2b/3, Multi-part, Randomized, Double-Blinded, Placebo-Controlled Study to Evaluate the Efficacy and Safety of Atacicept in Subjects with IgA Nephropathy (IgAN)

Dossiers Submitted: MSC Part I & II

- **NREC-CT Decision:**

- Favourable

2023-507536-21-00 SM-3

Institutions: Mater Misericordiae University Hospital (Dr Austin Duffy)

Study title: A Phase 1/2 Open Label, Dose Escalation and Expansion Study of MDNA11, IL-2 Superkine, Administered Alone or in Combination with an Immune Checkpoint Inhibitor in Patients with Advanced Solid Tumors

Dossiers Submitted: MSC Part I & II

- **NREC-CT Decision:**

- Request for Further Information

- **Additional Information Required RFI**

Part II Considerations raised

1. Subject information and informed consent form

- 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 information regarding the paired biopsies is incomplete in the Main PISCF (pg. 5/6/11). The committee request that further information on the biopsy process is elucidated in the PISCF, including-
    - That the participant be told whether archival tissue is available for them prior to consenting
    - That the sections outlining the biopsy process are expanded to include whether general anaesthetic will be required
    - An explanation of a 'suitable candidate' for biopsy as per protocol
    - That the option to enrol without consenting to biopsy is made sufficiently clear
    - Clarification that participants do not forego their right to withdraw their consent to biopsies, even after they have opted into the study
- The NREC noted in the Main PISCF that 'samples will be stored for up to 3 years after completion of the study until used for research purposes' (pg 21). The committee requested that the wording is amended such that the meaning is clear and to ensure compliance with data retention periods as per the CTR throughout the PISCF.

- The NREC noted various grammatical and spelling errors in the Main PISCF e.g. “If an archival tumour tissue sample is not available, you may be required to undergo biopsy procedure” (pg 5). The committee requested that the PISCF is checked for grammatical and spelling errors and corrected throughout.

2024-513087-26-00 SM-13

Institutions: St James's Hospital (Dr Sinead Cuffe), University Hospital Galway (Dr Silvie Blazkova), Beaumont Hospital (Dr Jarushka Naidoo)

Study title: Randomized, Double-blind, Multiregional Phase 3 Study of Ivonescimab Combined with Chemotherapy Versus Pembrolizumab Combined with Chemotherapy for the First-line Treatment of Metastatic Non-small Cell Lung Cancer (HARMONi-3)

Dossiers Submitted: MSC Part II only

- **NREC-CT Decision:**

- Request for Further Information

- **Additional Information Required RFI**

Part II Considerations raised
1. Recruitment arrangements
• The NREC-CT noted that the description of overall survival in the patient recruitment brochure (pg2) appears to conflate overall survival with disease progression in stating “Overall survival is also called OS. This means the amount of time after the start of the treatment the cancer does not substantially grow, and the patient is alive”. The Committee requested that the explanation of overall survival is amended to reflect the correct meaning. • The NREC-CT noted that the patient recruitment brochure (pg2) states ‘You will be given ivonescimab, chemotherapy, and pembrolizumab by infusion’. The NREC-CT requested that this sentence is amended to clarify that study participants will be assigned to either ivonescimab + chemotherapy or pembrolizumab + chemotherapy. • The NREC-CT noted that there is no information given in the patient recruitment brochure regarding the duration of the trial. The Committee requested that the recruitment brochure is updated to include information on the duration of the trial. • The NREC-CT noted a footnote in the patient recruitment brochure stating that Ivonescimab is approved in China but not elsewhere. The Committee requested that this information is included in the main body of the text.
2. Subject information and informed consent form
• As per email correspondence from the Sponsor please include any updated information regarding data retention duration and location in the PISCF, ensuring compliance with data retention periods as per the CTR. • As per email correspondence from the Sponsor please submit a patient emergency card, 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.

- AOB:
  - None