

# National Research Ethics Committee

## NREC-CT A Meeting

17<sup>th</sup> April 2024

### Attendance

Name	Role
Prof. Alistair Nichol	Chairperson, NREC-CT A
Prof. Gene Dempsey	Deputy Chairperson, NREC-CT A
Dr Darren Dahly	Committee Member, NREC-CT A
Ms Mandy Daly	Committee Member, NREC-CT A
Dr Geraldine Foley	Committee Member, NREC-CT A
Ms Muireann O'Briain	Committee Member, NREC-CT A
Dr Dawn Swan	Committee Member, NREC-CT A
Dr Maeve Kelleher	Committee Member, NREC-CT A
Mrs Dympna Devenney	Committee Member, NREC-CT A
Dr Sean Lacey	Committee Member, NREC-CT A
Dr Lorna Fanning	Committee Member, NREC-CT A
Dr Brian Bird	Committee Member, NREC-CT A
Prof. Aisling McMahon	Committee Member, NREC-CT A
Dr Emily Vereker	Head of Office, 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 Rachel McDermott	Project Administrator, National Office for RECs

**Apologies:** Ms Caoimhe Gleeson, Mrs Erica Bennett

**Quorum for decisions:** Yes

## Agenda

- Welcome & Apologies
- 2023-503699-25-00
- 2023-508383-29-00
- 2022-501020-19-01
- 22-NREC-CT-046\_Mod-4
- 21-NREC-CT-048\_Mod-4
- 21-NREC-CT-172\_Mod-4
- 2022-502936-38-00
- 22-NREC-CT-032\_Mod-6
- 2022-502123-21-00
- AOB

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

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## Applications

### 2023-503699-25-00

Institutions: Connolly Hospital, Our Lady of Lourdes Hospital, Tallaght University Hospital

Study title: A Multicenter, Randomized, Double-blind, Placebo-controlled, Phase 3 Study to Evaluate the Efficacy, Safety, and Tolerability of BMS-986278 in Participants with Progressive Pulmonary Fibrosis

Dossiers for Review: Part I and II

NREC-CT Decision: Request for Further Information

### Part II Considerations

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

- The NREC-CT noted that the DPIA does not explain risk mitigation for identified risks, and requested that this be added to the document, particularly for data that will be transferred outside of the EEA (Table 2). This should also be explicitly detailed in the ICF documents for participants (Section 6).

#### 2. Financial arrangements

- The NREC-CT noted that participants will be given a tote bag, and requested that this bag be free of any trial logo, such as to maintain the privacy of the participants.

### **3. Recruitment arrangements**

- The NREC-CT requested clarification on how many participants will be recruited in IE, with discrepancies noted between CTIS, the Main ICF and Site Suitability Assessment Forms.

### **4. Subject information and informed consent form**

- The NREC-CT noted that the section on future research in the Main ICF (Section 11.1, page 37) 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.
  - The NREC-CT noted that the Main ICF used a bundled approach to consent and requested that a layered approach to consent is used (in that each consent item is listed and a box for participants to provide their initials is included alongside each consent item) in line with HSE policy (Page 32).
  - 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 participants may be reimbursed for expenses incurred 'with the Sponsor's written approval' and requested that this be amended to be consistent with the information given in the Compensation for Trial Participants document. Further information should also be given to participants on the schedule of reimbursement, what expenses can and can't be reimbursed and for whom, and whether receipts can be submitted at any time throughout the trial (Main ICF, Page 22).
- The NREC-CT noted that a stipend will be provided to participants, as detailed in the Compensation for Trial Participants document, however it is stated in the Main ICF (page 22) that no monetary payment will be made. The NREC-CT requested that this discrepancy is clarified, however that the monetary value of the stipend should not be added to the ICF document.
- The NREC-CT noted that in the Protocol, participants must come off the IMP at two years, even if they are deriving benefit. The Committee strongly encourage the sponsor to provide access to the IMP for participants who derive benefit, requested a rationale in the case of not providing continued access, and that this is communicated in the Main ICF under this section (Main ICF, page 9).

- The NREC-CT noted that alternative treatments may be available outside of the trial and requested that details of Standard of Care in Ireland are added to the Main ICF, to give participants further information (Main ICF, Page 2).
- The NREC-CT noted the following typo in the Summary ICF (Page 3); ‘....*at least on highly effective method of contraception*’. The Committee requested clarification on whether this should read ‘one’, and if so, that this should be amended due to the importance of conveying this information correctly to participants.
- The Sponsor is requested to submit any participant-facing documentation that require updates as a result of the Part I Assessment.

## 5. Suitability of the investigator

- The NREC-CT requests further detail is provided on the trial experience of the PI at Our Lady of Lourdes Hospital.

### 2023-508383-29-00

Institution: Children’s Health Ireland, Temple St

Study title: A Phase 2, Randomized, Double-Blind, Placebo-Controlled, Multiple-Ascending Dose Study of PGN-EDO51 with a Long-Term Extension in Participants with Duchenne Muscular Dystrophy Amenable to Exon 51-Skipping Treatment (CONNECT2-EDO51)

Dossiers for Review: Part I and II

NREC-CT Decision: Request for Further Information

## Part II Considerations

### 1. Recruitment arrangements

- The NREC-CT noted in the Recruitment material (K2 documents) that given this is a Phase 2 study, the following sentence does not adequately explain that this is the first time the drug has been administered to this participant cohort, and that it will only be available to others if the trial is successful; “*a drug is investigational when it is allowed to be studied in a select group of volunteers before it becomes available to more people*”
- The NREC-CT noted that excessively emotive language in the Recruitment material should be avoided where possible, for example “*Do you or someone you love have DMD*”

### 2. Subject information and informed consent form

- The NREC-CT requested that the monetary amounts for the stipend are removed from the ICF documents (Main Adult ICF, Page 17).
- The NREC-CT noted the financial compensation provided (Main Adult ICF, Page 17), and queried how this compensation is paid in the case of minors participating in the study, whether it will be paid directly to their caregivers, and that this is clearly explained in the ICF documents. The NREC-CT note discrepancies in the length of time for site visits and infusions, between 2-3 days (Page 4) and 5 hours (Page 7). The Committee requests these inconsistencies are explained to participants, such that they are aware that the initial infusion may involve an overnight stay (Main Adult ICF, Assent Forms).

- The NREC-CT request that more detail or explanation is added to the wording ‘Changes to Kidney Labs’ (Main Adult ICF, Page 13, Section 10). Other technical language throughout the ICF documents, such as ‘placebo’ and ‘IV infusion’ should also be explained for participants.
- The NREC-CT note that participants may be asked to sign a separate consent form for the biopsy anesthesia, and requested clarification on whether this additional ICF is for both the biopsy and the anesthesia, or the anesthesia only (Main Adult ICF, Page 14)
- The NREC-CT note that participants can consent to being contacted for future biological research once that research becomes clear, and requested that it is clarified that further consent can be given at that time, if the participant wishes to do so (Optional Future Research ICF).
- The NREC-CT noted the description of the IV as a ‘...small, soft, plastic straw’ and requested that the description include the fact that a needle will also be involved in this process (Assent Form, Ages 6-11, Page 2).
- The NREC-CT noted that the EC listed is the National Office for Research Ethics Committees, and advised that this should be the National Research Ethics Committee for Clinical Trials of Investigational Medicinal Products (NREC-CT) (ICF and Assent documents).
- The Sponsor is requested to submit any participant-facing documentation that require updates as a result of the Part I Assessment.

## 2022-501020-19-01

Institutions: Cork University Hospital, Mater Misericordiae University Hospital, St Vincent’s University Hospital

Study title: A Multicenter, Adaptive, Randomized, Controlled Trial Platform to Evaluate Safety and Efficacy of Strategies and Treatments for Hospitalized Patients with Respiratory Infections: Strategies and Treatments for Respiratory Infections & Viral Emergencies (STRIVE) - Shionogi Protease Inhibitor (S-217622)

Dossiers for Review: Part I and II

NREC-CT Decision: Request for Further Information

### Part II Considerations

#### 1. Financial arrangements

- The NREC-CT noted that reasonable travel expenses will be reimbursed, however there is no mention of meal or refreshment reimbursement in the Compensation for Participants form, whereas this is mentioned in the Main PISCF (Page 9). The NREC requested that this be clarified across both documents.

#### 2. Recruitment arrangements

- The NREC-CT noted that participants will be given ‘adequate time’ to consider their participation in the study, and requested further detail on how much time this would entail.

- The NREC-CT requested clarification on whether participants who do not have English as a first language will be included in this study, and if not, that a justification is given (Section 1.8).
- The NREC-CT noted that while participants who lack capacity or who are in an emergency situation will not be recruited, patients who require ventilation or ECMO may become eligible at a later stage. The Committee requested further information on whether these participant groups will be recruited, and if so, what the processes around capacity assessment and consent will be.

### 3. Subject information and informed consent form

- The NREC-CT notes differences across the ICF documents in regard to how long data will be stored, where in some places it is designated at 25 years, and in others it is less clear. The NREC-CT requested clarity on this, and that this is reflected across all ICF documents.
- The NREC-CT noted that although the website link for the DPC on Page 11 of the Main PISCF does work when clicked on using an electronic copy, participants will be given a paper copy and as such, this website address should be simplified for easy use.
- The NREC-CT noted that only SVUH is mentioned in the section detailing processing of personal data, and requested clarification on whether this section is applicable to all sites (Main PISCF, Page 11, Section 4).
- The NREC-CT noted that participant data will be sent to both the UK and US, and requested further information on whether sites in IE will send data to both the UK and US, or to the UK only, who will then send the data to the US. Participants should also be made aware that there may be reduced or different levels of data security outside of the EEA and EU (Main PISCF, Page 12).
- The NREC-CT noted that the PISCF documents do not mention co-enrollment within the STRIVE platform, and requested clarification on whether participants recruited to this specific study will be eligible for co-enrollment.
- The NREC-CT noted that Future Biological Research is mentioned in the Main PISCF, and requested that reference be made in this section to the separate optional consent form that participants will be given (Page 7).
- The NREC-CT noted that the Pregnant Partner PISCF used a bundled approach to consent and requested that a layered approach to consent is used (in that each consent item is listed and a box for participants to provide their initials is included alongside each consent item) in line with HSE policy. Please see HSE National Policy for Consent in Health and Social Care Research (V1.1, 2023): Health Service Executive <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 Sponsor is requested to add the EU CT number to all participant-facing materials.

### 4. Suitability of the investigator

- The NREC-CT requests further detail on the trial experience of the PI at the Mater Misericordiae University Hospital.

## **22-NREC-CT-046\_Mod-4**

Principal Investigator: Dr Declan O'Rourke, Children's Health Ireland, Temple St

Study title: A Double-Blind, Placebo-Controlled, Multicenter Study With an Open-Label Extension to Evaluate the Efficacy and Safety of SRP4045 and SRP-4053 in Patients With Duchenne Muscular Dystrophy

EudraCT: 2015-002069-52

NREC-CT Decision: Request for Further Information

- The NREC-CT requests clarification on why the following sentence has been removed from 2 of the Parental Main ICF: SRP-4045 and SRP-4053 are not approved by the European Medicines Agency (EMA), the Health Products Regulatory Authority (HPRA) or similar government agencies abroad.
- The NREC-CT noted the use of the word 'subjects' throughout the PISCF documents and requested that this be amended to 'patients' or 'participants'.
- The NREC-CT noted reference to race and ethnicity data being collected, and requested justification for same is added to the ICF, in line with GDPR (Parental Main ICF, page 28; Pregnant Partner Assent, page 3; Pregnant Partner Adult ICF, page 2).
- The NREC-CT noted removal of "for 25 years" for length of time coded list will be kept at the study site, and requested clarification on how long this data will be stored (Parental Main ICF, page 29).
- The NREC-CT requested that the optional consents should be made into a separate consent section, and not part of the main trial consent.
- The NREC-CT noted that an optional stipend will be provided to participants, as detailed in the Compensation for Trial Participants document, however it is stated in the Main Parental ICF (page 17) that no monetary payment will be made. The NREC-CT requested that this discrepancy is clarified, however that the monetary value of the stipend should not be added to the ICF document.
- The NREC-CT noted that the Pregnant Partner ICF and Assent forms use a bundled approach to consent and requested that a layered approach to consent is used (in that each consent item is listed and a box for participants to provide their initials is included alongside each consent item) in line with HSE policy. Please see HSE National Policy for Consent in Health and Social Care Research (V1.1, 2023): Health Service Executive <https://hseresearch.ie/wp-content/uploads/2023/02/HSE-National-Policy-for-Consent-in-Health-and-Social-Care-Research-compressed.pdf>.

## **21-NREC-CT-048\_Mod-4**

Principal Investigator: Prof. Jarushka Naidoo, 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

EudraCT: 2020-003645-11

NREC-CT Decision: Favourable

## **21-NREC-CT-172\_Mod-4**

Principal Investigator: Prof. Janice Walshe, St Vincent's University Hospital

Study title: EPIK-B5: A Phase III, randomized, double-blind, placebo-controlled study of alpelisib (BYL719) in combination with fulvestrant for men and postmenopausal women with HR-positive, HER2-negative advanced breast cancer with a PIK3CA mutation, who progressed on or after aromatase inhibitor and a CDK4/6 inhibitor

EudraCT: 2021-001966-39

NREC-CT Decision: Request for Further Information

- The NREC-CT noted that the information provided for access of medical records remotely is for a UK site, and requested clarification on whether there is an Irish equivalent for Irish medical records (Main PISCF, Page 11)
- The NREC-CT noted references to the UK and NHS on pages 11 and 31 of the Main PISCF, and requested that these be amended for the Irish sites.
- Although not part of this substantial modification, the NREC-CT noted that the section on future research in the Main ICF (Pages 27 and 36) 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,
  - o 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,
  - o 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.
  - o 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>

## **2022-502936-38-00**

Institution: St James's Hospital, University Hospital Galway

Study title: A Phase 3 Randomized, Placebo-Controlled, Double-Blind Study to Evaluate Upadacitinib in Adolescent and Adult Subjects with Moderate to Severe Atopic Dermatitis

Dossiers for Review: Part I and II

NREC-CT Decision: Request for Further Information

- The NREC-CT noted typos throughout the ICF document, and recommended it is proof-read before giving to participants.



- The NREC-CT noted that the section on contraception and pregnancy is complicated, contains technical language and is not accessible for participants, for example: 'Contraception recommendations related to the use of concomitant therapies prescribed per standard of care should be based on the local label'. The NREC-CT requests that this section be improved for participant understanding, and either omit or explain jargon and technical language.
- The NREC-CT noted the use of the word 'subjects or female subjects' throughout the Main ICF and requested that this be amended to 'patients/female patients', 'participants/female participants', or 'participants who can get pregnant'.
- The NREC-CT noted that participants may be able to participate in a long-term extension study, and requested that it is made clear that this will be a separate trial with a separate consent process. The participants should also be given details on who they can speak to for more information on this separate trial.

## **22-NREC-CT-032\_Mod-6**

Principal Investigator: Prof. Niamh O'Connell, St James's Hospital

Study title: Phase III, open-label, single-dose, multi-center multinational trial investigating a serotype 5 adeno-associated viral vector containing the Padua variant of a codon-optimized human factor IX gene (AAV5-hFIXco-Padua, AMT-061) administered to adult subjects with severe or moderately severe hemophilia B

EudraCT: 2017-004305-40

NREC-CT Decision: Request for Further Information

- The NREC-CT noted that numbers of patients who have already been treated with the IMP are detailed on page 2 of the Main ICF, and requested clarification on whether these numbers represent global patient numbers, or those in IE.
- The NREC-CT requested that the optional tissue sample in the event of development of a tumour, be designated as 'tumour' tissue sample to distinguish from the liver tissue sample previously mentioned, to avoid any confusion for participants (Main ICF, page 26)

## **2022-502123-21-00**

Principal Investigator: Cork University Hospital, Tallaght University Hospital

Study title: Phase 2 Study of MK-6482 in Participants With Advanced Renal Cell Carcinoma

Dossiers for Review: Part I and II

NREC-CT Decision: Request for Further Information

- The Sponsor is requested to add the EU CT number to the ICF documents.
- The NREC-CT noted inclusion of technical language, such as 'monotherapy' in the Main ICF, and requested that this is explained for participants (Main ICF, Page 9).

- The NREC-CT requested that the reference to potential fertility problems for men and women be expanded, with more detail given to participants on what potential problems may occur and their impacts (Main ICF, page 11).
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- AOB:
  - None