National Research Ethics Committee

NREC-CT A Meeting

22 February 2023

Attendance

Name	Role
Prof. Alistair Nichol	Chairperson, NREC-CT A
Prof. Mary Donnelly	Deputy Chairperson, NREC-CT A
Ms. Erica Bennett	Committee Member, NREC-CT A
Prof. Tina Hickey	Committee Member, NREC-CT A
Dr Dervla Kelly	Committee Member, NREC-CT A
Prof. John Wells	Committee Member, NREC-CT A
Prof. Catherine Hayes	Committee Member, NREC-CT A
Ms Muireann O'Briain	Committee Member, NREC-CT A
Prof. David Brayden	Committee Member, NREC-CT A
Prof. Patrick Dillon	Committee Member, NREC-CT A
Dr John O'Loughlin	Committee Member, NREC-CT A
Dr Darren Dahly	Committee Member, NREC-CT A
Prof. Gene Dempsey	Committee Member, NREC-CT A
Prof. Austin Duffy	Committee Member, NREC-CT A
Mr Gerald Eastwood	Committee Member, NREC-CT A
Dr John O'Loughlin	Committee Member, NREC-CT A
Ms Ann Twomey	Committee Member, NREC-CT A
Dr Emily Vereker	Head, National Office for RECs
Dr Jane Bryant	Programme Officer, National Office for RECs
Dr Susan Quinn	Programme Manager, National Office for RECs

Dr Emma Heffernan*	Project Officer, National Office for RECs

*Drafted minutes

Apologies: Dr Geraldine Foley, Mr Gerard Daly, Dr Heike Felzmann, Dr Jimmy Devins, Prof. Donal Brennan, Ms Evelyn O'Shea

Quorum for decisions: Yes

Agenda

- Welcome & Apologies
- 2022-500587-35-01
- 2022-500699-76-00
- 2022-501939-16-00
- 2022-501943-34-00
- 23-NREC-CT-011
- AOB

- The Chair welcomed the NREC-CT A.
  - The minutes from the previous NREC-CT A meeting on 25 January 2023 were approved.
  - The NREC Business Report was discussed and noted.

Applications

2022-500587-35-01

Principal Investigators: Prof Karl Boyle, Dr Liam Healy, Dr Margaret O'Connor, Prof Peter Kelly, Dr Tim Cassidy, Prof. Ronan Collins, Dr George Pope

Study title: Tranexamic acid for hyperacute spontaneous IntraCerebral Haemorrhage (TICH-3)

EudraCT: 2022-500587-35-01

Lead institutions: Beaumont Hospital, Cork University Hospital, Limerick University Hospital, Mater Misericordiae University Hospital, St Vincent's University Hospital, Tallaght University Hospital, University Hospital Waterford

- NREC-CT comments:

- The NREC-CT A agreed that additional information was required to inform its deliberations before a final ethics position could be returned.

- NREC-CT Decision:

- Request for more information

- Additional Information Required

- Part I Considerations
- It is noted that an independent doctor may play a role in the consent process. Further details are requested on whether the particular grade of doctor to be consulted needs to be specified in this case, and how they would be identified.
- For inclusion in the Member State-specific Appendix on pregnancy testing requirements; IE EC accepted the rationale provided by the investigational team regarding the feasibility of pregnancy testing and agree that this decision is to be made at the discretion of the treating physician and/or study investigator. This should be included in appendix 2 and communicated clearly to members of the study team in each jurisdiction.
- It was noted that though patients taking anti-coagulation are not eligible for the study with the exception of those taking direct anticoagulants. The rationale for this needs to be clearly explained.
- The eligibility criteria state that patients with active seizures are excluded. On p27 it also states that ‘we will be excluding patients with active seizures and/or epilepsy.’ The investigators need to clarify if a history of epilepsy is allowed if patient not actively having seizures.
- Part II Considerations
- The NREC-CT notes the insurance certificate is out of date, and requests an updated certificate.
- The NREC-CT notes that the initial recruitment process gives detail on the UK setting but not the Irish setting. Given the different context, further specifics should be added to this document (Section 1.0)
- The NREC-CT notes that staff ‘should’ have training in assessing capacity, and requests further information on the usual process for assessing capacity in an emergency situation, and confirmation that all study staff will receive capacity assessment training as necessary (Section 2.2, 2.3)
- The NREC-CT requests that the Irish definition of Legal Representative is taken into account in the event the participant does not have capacity to consent (Section 2.4). This is defined in the context of clinical trials as follows in SI 99/2022, reg. 3:
- *A person, other than a person connected with the conduct of the trial, who by virtue of his or her family or other personal relationship with the individual*

    - *can provide the best interpretation of the will and preferences of the individual based on their knowledge of the individual*
    - *is available and willing to act for that purpose, or*
    - *if there is no such person, the medical practitioner primarily responsible for the medical treatment provided to the individual where he or she*
    - *can provide the best interpretation of the will and preferences of the individual based on their knowledge of the individual*
    - *is not involved in the conduct of the trial,*
    - *is of the view that participation in the trial will not prejudice the health and wellbeing of the individual, and*
    - *is available and willing to act for that purpose*
- The NREC-CT notes that UK terminology and NHS references are found throughout the participant information leaflets and consent forms, and requests that this terminology be amended for the Irish setting.
- The NREC-CT requests inclusion of information relating to CTR (EU Regulation No 536/2014) Article 35(3), where the participant needs to be informed that they can object to the use of their data. This may be particularly relevant to participants who have not regained capacity and have no next of kin who can inform the study investigator of the participants' will and preferences.
- The NREC-CT recommends that a separate participant information leaflet and informed consent form for optional future biological research is given to participants/their legal representative as appropriate.
- The NREC-CT noted that short information sheets are provided for emergency consent and requested that the full length PISCF should clearly explain to participants that consent to participate in the trial has already taken place.
- The NREC-CT requests confirmation that GDPR-level protections will apply when participants' data is moved outside the EU, and that this is communicated in the Information Sheets (Participant Information Sheet Page 4, and other participant-facing documents as necessary).
- The NREC-CT recommends that a sub-heading be applied to the first page of the Participant Information Leaflet and Informed Consent Form, adding information that the forms pertain to consent to continue in the study.
- The NREC-CT notes that the EU CT number across the Participant-facing documentation varies between 35-00 and 35-01, and requests all documents are updated to the correct version of 35-01
- The NREC-CT requests confirmation that local arrangements allow that a member of the study team will always be available to consent a participant, or if not, confirmation that a process is in place, such as a delegation log, through which the study team would be alerted in the event that a participant need to be consented

2022-500699-76-00

Principal Investigator: Dr Miriam O'Sullivan

Study title: A Phase 3, Randomized, Double-Blind, Placebo-Controlled Study to Evaluate the Efficacy and Safety of Deucravacitinib in Participants with Active Systemic Lupus Erythematosus (SLE) (POETYK SLE-1)EudraCT: 2022-500699-76-00

Lead institution: Our Lady's Hospital Manorhamilton

- NREC-CT comments:

- The NREC-CT A agreed that additional information was required to inform its deliberations before a final ethics position could be returned.

- NREC-CT Decision:

- Request for more information

- Additional Information Required

- The The NREC-CT recommend removal of the Participant number from the front page of the PISCF and Participant Appointment Card to avoid making them a linking sheet with the Participant's name.
- The NREC-CT note that no contraceptive measures are required to be used by male participants, and requests further rationale as to why this is the case. Furthermore, the Committee requests appropriate advice on contraception is added to the PISCF to male participants, in line with the advice for female participants (Page 2, 23).
- The NREC-CT note the following sentence "the safety was acceptable and no new safety concerns were found" and suggests that this may be misinterpreted as it based on prior knowledge that has not yet been made available to readers. The Committee requests more clarity in the wording and suggests the sentence states "The safety was acceptable and this information is summarised in section 3 of this leaflet" (Page 12 Section 2.9).
- The NREC-CT notes that in the list of acceptable methods of contraception, tying of fallopian tubes is listed as the first option. The Committee suggests that hormonal contraception should be listed first (Page 24).
- The NREC-CT requests that the maximum amount of reimbursement for travel expenses is detailed (Page 25 Section 4.3).
- The NREC-CT requests further explanation of the phrase "serious research injuries" for the participant (Page 27 Section 5.1).
- The NREC CT requests that details of who to contact in the hospital complaints department are added to the end of Section 5 (Page 27)
- The NREC-CT requests additional context is added to Section 6.5 on why a participant might contact the DPC, for example "You have the right to file a complaint with the Irish

data protection commission whose contact details are available on their website" (Page 30)

2022-501939-16-00

Principal Investigators: Prof. Robert Byrne, Prof. Kenneth McDonald, Prof. Niall Mahon, Prof. Ross Murphy

Study title: HERMES: Effects of ziltivekimab versus placebo on morbidity and mortality in patients with heart failure with mildly reduced or preserved ejection fraction and systemic inflammation

EudraCT: 2022-501939-16-00

Lead institutions: Mater Private, Heartbeat Trust, St Michael's Hospital, Mater Misericordiae University Hospital, St James's Hospital

- NREC-CT comments:

- The NREC-CT A agreed that additional information was required to inform its deliberations before a final ethics position could be returned.

- NREC-CT Decision:

- Request for more information

- Additional Information Required

- The NREC-CT requests clarification on how the exact process of recruitment will be performed, and how the recruitment materials submitted will be used in this process.
- The NREC-CT notes the number of participant information and informed consent documents, and requests further detail on how long the participants will have to consider their enrolment in the study.
- The NREC-CT notes that the participant is required to discuss reimbursement for expenses with the study doctor, and requests instead that the doctor introduces this subject with the participant during the consent process (Main PISCF, Section 7, Page 12).
- The NREC-CT requests that a comprehensive list of appropriate contraception options is detailed in the Main PISCF, to reflect the Protocol (Main PISCF, Page 11).
- The NREC-CT notes that there is no requirement or consent to inform the participant's GP, and requests that this be added to the relevant PISCF documents, in addition to submission of a GP Letter for review.
- The NREC-CT requests clarification on the format of the information to be shared with other researchers outside of the study; whether this data will be pseudonymised or fully

anonymised. Additional information on the purpose of sharing this data should also be added to the Main PISCF (Section 8, Page 14).

- The NREC-CT requests that it is made clear that participants will not be informed of the results from genotyping studies (Genotyping PISCF).
- The NREC-CT requests emphasis be placed on if information on a child born to a participant during the study is provided, that it will be for information purposes only. No benefit or treatment if necessary, will given as a result of this information (Pregnant Partner PISCF).

2022-501943-34-00

Principal Investigator: Prof Noel McElvaney

Study title: A Randomized, Double-blind, Placebo-Controlled, Phase 3 Study to Evaluate the Efficacy and Safety of Fazirsiran in the Treatment of Alpha-1 Antitrypsin Deficiency-Associated Liver Disease With METAVIR Stage F2 to F4 Fibrosis

EudraCT: 2022-501943-34-00

Lead institution: Beaumont Hospital

- NREC-CT comments:

- The NREC-CT A agreed that additional information was required to inform its deliberations before a final ethics position could be returned.

- NREC-CT Decision:

- Request for more information

- Additional Information Required

- The Sponsor is requested to confirm the timepoints for the liver biopsies, and to make these timepoints clear across all relevant documentation in Part II
- The NREC-CT requests further detail on provision for payments to the hospital from the Sponsor for tests including imaging, blood draws and liver biopsies.
- The NREC-CT notes that the insurance certificate expires in 2024, before the end of the trial, and requests confirmation that the trial will be insured for its full duration.
- The NREC-CT recommend that the participant information and consent for optional Future Biological Research be separated from the Main PISCF into a new document, to enhance understanding.
- The NREC-CT requests further details on Prof. McElvaney's clinical trials experience, if available. The Committee also requests confirmation that expertise in hepatology will

also be available on site to complement Prof McElvaney's expertise in pulmonary medicine, given the nature of the trial.

23-NREC-CT-011

Principal Investigator: Dr Declan O'Rourke

Study title: A Randomized, Double-Blind, Placebo-Controlled, Multiple Ascending Dose Study Assessing Safety, Tolerability, Pharmacodynamics, Efficacy, and Pharmacokinetics of DYNE-251 Administered to Participants with Duchenne Muscular Dystrophy Amenable to Exon 51 Skipping

EudraCT: 2021-005478-24

Lead institution: Children's Health Ireland at Temple Street

- NREC-CT comments:

- The NREC-CT A agreed that additional information was required to inform its deliberations before a final ethics position could be returned.

- NREC-CT Decision:

- Request for more information

- Additional Information Required

- The NREC-CT noted that a flyer was submitted as part of the application and requested detail is provided as to the purpose of this document.
- The NREC-CT noted that some participants will be consented for cardiac MRI and requested details on how these participants will be recruited.
- The NREC-CT considered the PIL to be comprehensive but lengthy and requested that a lay summary PIL is made available for participants, highlighting the pertinent issues that trial participation will involve. This NREC guide may be useful: https://www.nrecoffice.ie/pil-summary-guidance/
- The NREC-CT noted that the proposed trial is to take place in St James's Hospital and requested the following:
    - Confirmation from the Director at the CRF at St James's Hospital that the necessary supports are in place to safely manage a first-in-human phase 1/2 paediatric clinical trial.
    - A detailed account of the level of support available, including the required clinical expertise, to manage a potentially critically ill child in the case of anaphylaxis or other emergency situations.
    - A detailed account of the provisions in place, including level of clinical expertise available, and transfer arrangements, should the child require transfer to a paediatric hospital.

    - Confirmation that appropriately trained staff are in place during trial drug administration.
    - Confirmation that the PI will be present during trial drug administration.
- The NREC-CT requested that evidence of up-to date ICH-GCP certification is provided for the PI, Dr O'Rourke.
- The NREC-CT noted that pg.17 of the PISCF states that 'You have the right to require that any previously retained samples are destroyed' and requested that participants are advised that their samples will be destroyed.
- The NREC-CT noted that the consent for data processing is not line with Irish data protection legislation and Health Research Regulations 2018, whereby the age of consent is 18 years of age. It is requested that participants under the age of 18 will need to provide assent for the processing of their data and their parents /guardians will need to provide consent for the processing of data.
- The NREC-CT noted that Pregnant Partner PISCF suggests retaining data on a pregnancy or child for up to 30 years and requested that the processes in place for obtaining the consent of the child, on reaching the age of 18, for the retention of their personal data is described in line with Irish data protection law (Data Protection Act 2018 (Section 36(2)) (Health Research) Regulations 2018
- The NREC- noted that the study insurance certificate provided does not cover the whole trial duration and requested that the insurance policy is updated to provide cover for the full duration of the trial

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- AOB: