National Research Ethics Committee

NREC-CT A Meeting

8th of June 2022

Attendance

Name	Role
Prof. Alistair Nichol	Chairperson, NREC-CT A
Dr Heike Felzmann	Deputy Chairperson, NREC-CT A
Prof. Mary Donnelly	Deputy Chairperson, 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
Mr Gerard Daly	Committee Member, NREC-CT A
Mrs Erica Bennett	Committee Member, NREC-CT A
Prof. Catherine Hayes	Committee Member, NREC-CT A
Prof. Donal Brennan	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
Ms Ann Twomey	Committee Member, NREC-CT A
Ms Evelyn O'Shea	Committee Member, NREC-CT A
Prof. Austin Duffy	Committee Member, NREC-CT A
Dr Cliona McGovern	Chairperson, NREC-CT B
Mr Colm O'Loughlin	Department of Health
Dr Emma Heffernan	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

*Drafted minutes

Apologies: Mr Gerard Eastwood, Dr Jimmy Devins, Prof David Brayden, Ms Muireann O'Briain

Quorum for decisions: Yes

Agenda

- Welcome & Apologies
- 22-NREC-CT-101
- 22-NREC-CT-102
- 22-NREC-CT-103
- 2022-500363-12-00
- AOB

- The Chair welcomed the NREC-CT A.
  - The minutes from the previous NREC-CT A meeting on 11th of May 2022 were approved.
  - The NREC Business Report was discussed and noted.

Applications

22-NREC-CT-101

Principal Investigator: Prof Faisal Sharif

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)

Lead institution: NUI Galway

EudraCT Number: 2021-004601-47

- NREC-CT comments:

- The NREC-CT A noted that this trial represents a multi-centre randomised placebo-controlled double-blind trial of inclisiran for participants with non-obstructive coronary artery disease.
- The NREC-CT A commented that this was a good submission, with a clearly defined protocol, and that the graphics in the PIL/ICF were especially helpful.
- 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 Further Information

- Further Information Requested:

- The Committee noted some discrepancies in the description of the length of time that participants will be enrolled in the trial and requests clarity of same.
- The Committee noted a discrepancy between the protocol and the radiation document outlining the potential amount of radiation participants may be exposed to during the trial and requested that this is aligned.
- The Committee requested that information is provided as to when and where consent will be obtained.
- The Committee requested further details of how sites will be selected (i.e. 2 out of the 4 proposed sites).
- The Committee requested details of potential candidate numbers per site, and feasibility of performing the study in the proposed timelines.
- The Committee queried whether there was an error in the PIL/ICF CCTA graphic – depicting an additional visit during the treatment period and request clarity of same.
- The Committee requested that in the case where a participant is deemed ineligible, a line is added to the consent form stating that the reasons for removal from the trial will be discussed with the participant and appropriate follow up with a local clinician will be organised.
- The Committee noted a number of typos in the ICF and requests that these are corrected.
- The Committee requested that reference to the ‘HPRA’ is preplaced with ‘Health Products Regulatory Authority’.
- The Committee noted several references to ‘The Trust’ and ‘NHS’ and requests that these are removed and replaced with participant materials adapted to Irish sites.
- The Committee requested that repeated items and paragraphs are removed from the Genetic consent form.

- The Committee requested further detail is provided to participants for consent for additional research in relation to requiring additional ethical approval.
- The Committee noted that 3 of the 4 site suitability forms are lacking in sufficient detail and requested more comprehensive site suitability forms are submitted.
- The Committee requested that more comprehensive CVs are provided for Drs McAdam and Murphy detailing their clinical trial experience.
- The Committee noted the submission of an incomplete DPIA with an email thread from the DPO, and requested that a comprehensive study specific DPIA is provided, including input from the DPO.
- The Committee requested that clarity is provided in relation to the length of time trial materials will be retained for after the study has ended.

22-NREC-CT-102

Principal Investigator: Professor Christopher Bacon

Study title: A Phase 3 Randomized Study Comparing Bortezomib, Lenalidomide and Dexamethasone (VRd) followed by Ciltacabtagene Autoleucel, a Chimeric Antigen Receptor T cell (CAR-T) Therapy Directed Against BCMA versus Bortezomib, Lenalidomide, and Dexamethasone (VRd) followed by Lenalidomide and Dexamethasone (Rd) Therapy in Participants with Newly Diagnosed Multiple Myeloma for Whom Hematopoietic Stem Cell Transplant is Not Planned as Initial Therapy - CARTITUDE-5

Lead institution: St James' Hospital

EudraCT Number: 2021-001242-35

- NREC-CT comments:

- The NREC-CT A noted that this study represents a Phase 3 randomised study comparing a combination of drugs with and without CAR-T therapy, in patients with multiple myeloma.
- The NREC-CT A noted that PIL is thorough and instructive.
- 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 Further Information

- Further Information Requested:

- The Committee acknowledged receipt of a Notification of Urgent Safety Measure, including Cover Letter and Dear Investigator letter, submitted on 07/06/2022.
- The Committee requested a comprehensive response is provided on the following queries in relation to this Urgent Safety Measure:
    1. The Committee note the rising incidence of Covid-19 in the community in Ireland and request information as to how this will be addressed by the applicants in relation to this Urgent Safety Measure.
    2. The Committee requested confirmation is provided that the Health Products Regulatory Authority (HPRA) have been informed of this Urgent Safety Measure.
    3. The Committee requested that information is provided regarding the outcomes of the investigation into the cases, and the Independent Data Monitoring Committee's safety review, and requested a copy is provided of same.
    4. The Committee requested that updated information is provided as to what the impact is on the safety benefit of the trial.
    5. The Committee requested that the PIL is revised to explain clearly to participants that this is a higher risk treatment than conventional therapy, and to clearly outline the substantial risk versus benefit involved in participation in the trial.
- The Committee noted that the PIL is excessively long and could be overwhelming to potential participants. Additionally, the Committee deemed that the PIL does not lay out the rational for the study well, and that the information regarding the risks of taking part in the trial are not well described for a lay person. The Committee requested that an executive summary is provided to participants. The Committee also requested that the potential benefits, as well as the potential risks of participating in the trial are clearly outlined in plain English to ensure accessibility and comprehension.
- The Committee requested reassurances that due to the complexity of the trial that the PI should conduct all participant counselling
- The Committee noted that in the ICF, it states that the Sponsor will not pay for doctor visits, treatments or tests that are not part of this study. In light of the multiple potential side effects associated with the medicines used in this study including the IMP, and the likelihood that participants being affected by one or more is high, the Committee requested confirmation that any associated related costs will be covered by the Sponsor.
- The Committee requested that a similar statement to that presented for WOCBP (Pg 50 of ICF) needs to be added to the ICF for male participants in relation to informing their study doctor if their partner gets pregnant.
- The Committee requested further detail is provided as to the nature of future use of biological samples, and noted that further ethical approval will need to be obtained before any unrelated research can take place using these samples.
- The Committee requested justification is provided as to why only English-speaking participants will be recruited in Ireland.

- The Committee requested that no data is provided to the flow cytometry company (Flowmetric) being used by the sponsor in the USA until contractual clauses are signed and evidence of the signed clauses are provided to the NREC-CT A.

22-NREC-CT-103

Principal Investigator: Prof Emer Joyce

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)

Lead institution: Mater Misericordiae University Hospital

EudraCT Number: 2020-005643-22

- NREC-CT comments:

- The NREC-CT A noted that this application represents a multicentre, open-label extension study to look at long term safety and efficacy in patients with cardiomyopathy, who participated in a previous Phase 3 trial.
- The NREC-CT A commented that the PIL was largely patient friendly, and that this was overall a positive submission.
- 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 Further Information

- Further Information Requested:

- The Committee deemed that some sections of the PIL were text-heavy and requested that it be simplified into plain English to improve accessibility. The outline of the research activities would also benefit from some additional visual aids to support participants' understanding.
- The Committee requested that the statement regarding the need to allow doctors to confirm 'whether or not you are alive' (PIL, p.4) is rephrased and its rationale explained to participants.
- The Committee requested that the Principal Investigator's CV be resubmitted detailing previous clinical trials experience.
- The Committee requested that all statements regarding participants' data-related rights need to be specific to the Irish context and explicitly reference Irish data protection law (Data Protection Act 2018 (Section 36(2)) (Health Research) Regulations 2018).
- The Committee requested that confirmation that the data transferred outside of the EU will be coded, is clearly stated in the ICF, in line with the information provided in the PIL.

- The Committee noted that a study specific DPIA was not included in the application and requests that a comprehensive DPIA is provided, including input from the site DPO.
- The Committee felt that information provided to participants regarding compensation for trial participation is ambiguous and requests that it is made clear to participants in participant documents that they will not be compensated for taking time off work, but that they will be reimbursed for travel related expenses only.
- The Committee noted that the insurance policy is due to expire soon and requests that the insurance policy is updated to provide cover for the full duration of the study

EudraCT Number: 2022-500363-12-00

Lead Principal Investigator**:** Professor Joe Eustace (Cork CRF is lead site for the SOLIDARITY group of studies in Ireland)

Study title: Efficacy and Safety of AXL-Inhibitor bemcentinib for the Treatment of Moderate COVID-19 (AXL-SolidAct)

- NREC-CT comments:

- The NREC-CT A noted that this application represents a placebo-controlled study examining the use of bemcentinib for the therapeutic intervention of COVID-19.
- The NREC-CT A commented on the suitability of the investigators and site facilities.
- 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 Further Information

- Further Information Requested:

- The Committee requested that the following statement is reflected as specific use in the consent section: '*Your personal data and biosamples may be shared with other research partners with the objective of boosting scientific research on Covid-19 and its treatments, independently of the objectives of the SolidAct trial'*.
- The Committee requested that the statement in the PIL '*Should you get injured as a direct result of participation in this study you will be compensated in accordance with Irish law'* is revised to provide a clear statement of the compensation the participant will be entitled to.
- The Committee requested that an explicit mention of referral to psychological support is provided to participants who experience distress when completing the patient questionnaire 'OSLO COVID-19 QLQ-PW80', specifically Q76 & Q77 regarding concerns of 'abandonment'.

- The Committee noted that participants in the trial may be very ill – and requests information is provided regarding how the participant information will be communicated to participants in these cases.
- The Committee noted that there are a significant number of medications that are contraindicated in this study, and requested that steps are in place to ensure that participation in this trial is highlighted to the participant's medical team both during the hospital stay and into the community following discharge from hospital.
- The Committee requested that the sponsor confirms who the National Coordinating Principal Investigator is and include their CV if not previously submitted.

- AOB:
    - Presentations on the Clinical Trials Regulation (CTR) Legislation were given by Mr Colm O'Loughlin from the Department of Health, and Dr Laura Mackey from the National Office, followed by a discussion on same.