National Research Ethics Committee

NREC-CT B

27th of July 2022

Attendance

Name	Role
Dr Jean Saunders	Chairperson, NREC-CT B
Ms Serena Bennett	Committee Member, NREC-CT B
Mr Philip Berman	Committee Member, NREC-CT B
Dr Lorna Fanning	Committee Member, NREC-CT B
Dr John Hayden	Committee Member, NREC-CT B
Mr Gavin Lawler	Committee Member, NREC-CT B
Ms Paula Prendeville	Committee Member, NREC-CT B
Dr Mary McDonnell Naughton	Committee Member, NREC-CT B
Dr Eimear McGlinchey	Committee Member, NREC-CT B
Ms Mandy Daly	Committee Member, NREC-CT B
Ms Susan Kelly	Committee Member, NREC-CT B
Ms Deirdre MacLoughlin	Committee Member, NREC-CT B
Dr Christina Skourou	Committee Member, NREC-CT B
Dr Susan Quinn*	Programme Manager, National Office for RECs
Dr Emma Heffernan*	Project Officer, National Office for RECs
Dr Jane Bryant	Project Officer, National Office for RECs
Ms Ayesha Carrim	Project Officer, National Office for RECs
Ms Rachel McDermott	Project Administrator, National Office for RECs

*Drafted minutes

Apologies: Prof. John Faul, Dr Cliona McGovern, Dr Mark Robinson,

Dr Enda Dooley, Prof Seamus O'Reilly, Prof. Abhay Pandit, Ms Caoimhe Gleeson, Prof Colm O'Donnell, Prof Andrew Green, Prof David Smith.

Quorum for decisions: Yes

Agenda

Welcome & Apologies

Application 22-NREC-CT-127

Application 22-NREC-CT-128

Application 22-NREC-CT-129

Application 22-NREC-CT-130

Application 22-NREC-CT-131

AOB

- The Chair welcomed the NREC-CT B.
    - The Minutes from the NREC-CT B meeting on 22nd June 2022 were approved
    - The NREC Business Report was noted.
    - Declarations of interest: Mr Philip Berman (22-NREC-CT-128). Mr Berman left the meeting for the review of 22-NREC-CT-128.

Applications

22-NREC-CT-127

Principal Investigator: Prof Orla Hardiman

Study title: A Phase 2, Multicenter, Randomized, Double-Blind, Placebo-Controlled Study Evaluating Safety and Efficacy of CORT113176 (Dazucorilant) in Patients with Amyotrophic Lateral Sclerosis (DAZALS)

Lead institution: Beaumont Hospital

EudraCT No.: 2021-005611-31

- NREC-CT comments:

- The Committee noted this clinical trial application represents a Phase 2, Multicenter, Randomized, Double-Blind, Placebo-Controlled Study Evaluating Safety and Efficacy of Dazucorilant in Patients with Amyotrophic Lateral Sclerosis

- The Committee agreed that additional information was required to inform its deliberations and therefore, was not yet in a position to return a final ethics decision

- NREC-CT Decision:

- Request for further information

- Additional Information Required

- The Committee noted that section 4.5 Patient Discontinuation or Withdrawal of the protocol (pg. 39) states, '*the Investigator and/or Sponsor terminates the patient's participation before completion of the study and permanently withdraws the patient from the study, ceasing administration of study drug, procedures, and assessments, without further follow*-up' and requests that clarification whether existing participants will be followed up if the study is terminated early by the sponsor.
- The Committee noted that the Protocol states that participants who drop out from the trial will be replaced. With a stated expectation of 20% dropout rate, the Committee requested clarification on how the randomization 1:1:1 will be maintained, if data from participants who drop out is not unblinded to facilitate the recruitment of a new participant into the same category.
- The Committee noted that Pg 8 of the Protocol refers to Statistical Analysis Plan. As an SAP was not included as part of the submission and the sponsor appears to be located in the UK and US, the Committee requested that clarification is provided regarding where statistical analysis will be carried out.
- The Committee requested justification is provided for the use of two different doses of Dazucorilant during the trial.
- The Committee requested clarification as to how PK testing will be carried out in the PK sub-group, and specific information is provided regarding how it will be ensured that participants selected for PK testing are not receiving the placebo.
- The Committee noted reference to the use of an *'impartial witness'* on pg. 20 of the PIS/CF. As it is not legal within the Irish jurisdiction to provide consent on behalf of someone else, the Committee requested that the sentence '*I, the impartial witness, confirm that the participant is physically not able to consent, therefore I am consenting on behalf of them'* is removed from the PIS/CF.
- The Committee noted that the section on risks of trial participation in the PIS/CF is limited and requested that the potential risks of taking part in the trial is expanded to include all trial related risks, and not just pregnancy related risk
- The Committee noted that pg. 8 of the PIS/CF states '*You may also request that no new tests are performed on your information or samples after you withdraw consent. However, information that has already been collected for the study will still be used'* and requested clarity is provided for participants on what will happen to their information and samples should they withdraw from the study, specifically regarding new tests on their data.
- The Committee requested that the word 'risks' is added to pg. 9 of the PIS/CF in the section referring to *'any new information, findings or changes.'*
- The Committee requested that use of the word *'explicit'* in relation to data processing on pg. 19 of the PIS/CF is explained.

- The Committee noted that Pg 9 of the ICF states that '*you will be reimbursed up to [TBD] per visit for reasonable costs associated with study participation…*' The NREC-CT B requested that the text on travel and expenses is amended to provide clarity on the maximum amount of compensation provided to participants for travel and refreshments and that this be further elucidated in the PIS/CF.
- Given the nature of ALS and / or potential drug side effects of the trial drug (tiredness, dizziness etc), the Committee requested that costs associated with trial participation are also allocated for a travel companion / assistant, to accompany participants for on-site visits, and the maximum amount of compensation provided to traveling companions/ assistants for travel and refreshments is elucidated in the PIS/CF.
- The Committee noted that Section G.1 of the NREC Application From under Financial Arrangements, states, *"The NHS insurance/indemnity will cover liability of site staff for negligence*" and requested that this is adapted to the Irish jurisdiction.

22-NREC-CT-128

Principal Investigator: Dr Desmond Murphy

Study title: A multi-centre, single arm, open-label extension study to evaluate the long-term safety of GSK3511294 (Depemokimab) in adult and adolescent participants with severe asthma with an eosinophilic phenotype from studies 206713 or 213744

Lead institution: Cork University Hospital

EudraCT No.: 2020-004334-38

- NREC-CT comments:

- The Committee noted this clinical trial application represents a multi-centre – 18 countries single arm open label extension study to evaluate the long-term safety of Depemokimab (GSK3511294) in adult and adolescent participants with severe asthma
- The Committee agreed that additional information was required to inform its deliberations and therefore, was not yet in a position to return a final ethics decision

- NREC-CT Decision:

- Request for further information

- Additional Information Required:

- The Committee noted references to the UK Data Protection Act and requested that these references are removed, and study materials are amended for the Irish jurisdiction.

- The Committee noted a discrepancy between the cover letter, NREC application form and the study documentation provided regarding adolescents participating in the trial and requested clarification in this regard.
- The Committee noted that it is not clear from the submission which studies were conducted at which sites and by which clinical leads and requested further clarification on the details of studies conducted to date.
- The Committee noted that section D1 of the NREC Application Form states that 750 participants will be recruited to the trial and section C9 and C10 states that 'in this open-label extension study, all participants will receive GSK3511294 100 mg SC for 52 weeks', whereas later in section C10 states that 'the study will include approximately 375 participants in a 2:1 ratio to GSK3511294 (n=250) and matching placebo (n=125)'. The Committee requested clarification on the number of participants taking part in the trial and confirmation that all participants will be enrolled in the OLE and given the trial drug and not a placebo.
- The Committee noted that the information on transfer of data from EU and non-EU in the PIS/CF (pg. 13) is overly legalistic and requested that this is simplified into plain English suitable for lay audiences.
- The Committee noted several links relating to contractual clauses in the PIS/CF (pg. 14) and requested that all information participants require to make an informed decision about participating in the trial is included in the PIS/CF document itself.
- The Committee requested justification for the collection of race and ethnicity data from participants.
- The Committee requested that a Financial Disclosure is provided.

22-NREC-CT-129

Principal Investigator: Dr John Quinn

Study title: A Phase 3, Randomized, Multicentre, Double-Blind, Placebo-Controlled, Efficacy and Safety Study of Birtamimab Plus Standard of Care vs. Placebo Plus Standard of Care in Mayo Stage IV Participants with Light Chain (AL) Amyloidosis

Lead institution: Beaumont Hospital

EudraCT No.: 2021-000037-14

- NREC-CT comments:

- The Committee noted this clinical trial application represents a A Phase 3, Randomized, Multicentre, Double-Blind, Placebo-Controlled, Efficacy and Safety Study of Birtamimab Plus Standard of Care vs. Placebo Plus Standard of Care in Mayo Stage IV Participants with Light Chain (AL) Amyloidosis

- The Committee commended the high quality of the study design and the well written application.
- The Committee agreed that additional information was required to inform its deliberations and therefore, was not yet in a position to return a final ethics decision

- NREC-CT Decision:
- Request for further information

- Additional Information Required:
- The Committee noted that the box ‘incentives’ is ticked in the Application Form (D10), and requested this is corrected/clarified
- The Committee noted the box (D11) regarding notification of GP is unticked and requested this is corrected
- The Committee requested that the language in / or terms used in Table 1 and Table 2 (p6 – 10) are harmonised with the rest of the document e.g., use of “paracetamol” rather than “acetaminophen”
- The Committee noted that the section ‘reproductive risks’ (p.17) is not inclusive of participants with same-sex partners and requested this is modified.
- The Committee noted that AL Amyloidosis will be confirmed by scintigraphy (in some participants) and this is noted as a risk in the protocol, but requested that this is also added to the PIL/CF under procedure risks.
- The Committee requested an outline is provided of the procedures proposed for handling responses received to digital advertising materials
- The Committee noted that the PIS/CF includes ‘pregnancy consent’ (p28), including consent on behalf of the baby for storage of data. Although this is an unlikely event to occur, clarification is requested regarding this proposed data retention and alignment with legislation and GDPR, including reconsent of the baby at adulthood and right to withdrawal.
- The Committee noted that languages including sign language are mentioned as available options for disseminating patient information and requested that Braille should also be considered, if required.
- The Committee notes that the recruitment advert suggests that participants may be invited to a follow up extension study and requests that it is clarified if both participants taking the placebo and the trial drug will be eligible to take part.
- The Committee noted that PI CV is brief and does not list any research experience and requested a more comprehensive CV is provided

22-NREC-CT-130

Principal Investigator: Prof Brian Kirby

Study title: Phase 2, randomized, parallel-group, double-blind, placebo-controlled study of sonelokimab in patients with active moderate to severe hidradenitis suppurativa

Lead institution: St Vincent's Hospital

EudraCT No.: 2021-005928-38

- NREC-CT comments:

- The Committee noted this clinical trial application represents a phase 2, randomised, parallel group, double blind, placebo-controlled study of sonelokimab in patients with active moderate to severe hidradenitis suppurativa.
- The Committee commended the high quality of this submission and the clear information, accessible language, and clear consent for participants.
- The Committee agreed that additional information was required to inform its deliberations and therefore, was not yet in a position to return a final ethics decision

- NREC-CT Decision:

- Request for further information

- Additional Information Required:

- The Committee noted there are reference to the study length as 28 weeks in the cover letter and as 32 weeks throughout documentation and requested this is corrected if it is an error. Furthermore, the dates of study (21/10/22 – 21/07/23) in the NREC Application Form appear to be incorrect and requested this is corrected throughout.
- The Committee requested details are provided regarding the pathway of referral should a participant score highly on the C-SSRS (Protocol p.80).
- The Committee noted that Page 9 of PIS/ICF adequately addresses future medical research, limiting it to "can be kept as exploratory research blood samples for future testing related to understanding HS, or how sonelokimab works". The Committeee requested that this sentence is also included on p21, to ensure alignment with the Health Research Regulations (2018).

22-NREC-CT-131

Principal Investigator: Prof Fionnuala McAuliffe

Study title: Daily versus alternate day oral iron supplementation for the treatment of iron deficiency anaemia in pregnancy -IronWoman

Lead institution: Holles St.

EudraCT No.: 2022-001815-25

- NREC-CT comments:

- The Committee noted this clinical trial application represents a RCT of daily versus alternate day Galfer for the treatment of iron deficiency anaemia in pregnancy
- The Committee agreed that additional information was required to inform its deliberations and therefore, was not yet in a position to return a final ethics decision

- NREC-CT Decision:

- Request for further information

- Additional Information Required:

- The Committee suggested that an extensive review of all documents is carried out to ensure consistency of content across all documentation before the requested documents are resubmitted.
- The Committee noted that the NREC Application Form states that '*There will be no known prior clinical relationship with potential participants*' and that the Electronic Health Record will be the primary method of selecting suitable patients for recruitment. The Committee noted that this method of pre-screening will be carried out prior to consenting and requests that a detailed account of this aspect of recruitment is provided, highlighting safeguards in place in the context of ensuring participant privacy and data protection, including whether power trials (MNCMS tool) will be used to facilitate this. The Committee noted recent guidance on pre-screening under the Health Research Regulations which may be useful as a reference point in this context.
- The Committee requested that the applicants reconsider the use of the term "*anonymised*" which is frequently used (PIL and elsewhere) when it appears that the data will in fact be pseudonymised. This should be changed, and the latter term explained to participants.
- The Committee noted that the protocol refers to essential documents being retained for 15 years, whereas the DPIA states that data will be retained for 5 years and requested clarification is provided on how long essential documents / data will be retained for and amend same in both the protocol and DPIA.
- The Committee noted that the protocol states that *'informed consent will be obtained prior to any study related procedures being undertaken'* however the diagram at 11.1 of the protocol, indicates that pre-screening is carried out before enrolment. The Committee requested clarification as to when written informed consent will be obtained and clarification that no study related activities will be carried out prior to obtaining informed consent.
- The Committee noted that the PIL does not include any reference or request for use of the child's samples and data and requested that this is rectified and aligns with relevant Irish and EU legislation.
- The Committee requested that further information is provided to participants in the PIL regarding the term 'research bloods', including the bloods being collected, the

reasons for collection, and how these will be used. The committee noted that the consent form does not request consent for research bloods to be taken or for reviewing biomarkers and requested that this is included.

- The Committee requested that the participant's GP is informed of their participation in the trial, in line with best practice
- The Committee noted that the consent form states that the purpose of access to medical records is to ensure the study is being carried out correctly, and requested that this is removed as it is considered misleading
- The Committee noted that the consent form does not include the mental health questionnaire and requested that this is amended.
- The Committee noted that the NREC Application Form (Section C.10) provides Reference to the research team accessing electronic health records to collect data about the participants pregnancy, delivery, and the baby's outcomes. The Committee advised that consent must be obtained for this data collection, and details provided on use of this data.
- The Committee noted discrepancies between the DPIA and other submitted documents and requests that these are aligned:
    - The DPIA lists all the risks/ side effects of IDA and of the risk of mild anaemia in alternate day therapy in pregnant women (from a Cochrane review) but this is not indicated in the PIL or the NREC Application Form. The PIL must be amended to ensure participants are informed
    - The DPIA refers to accessing medical records following delivery, to collect delivery and neonatal data as per informed consent, but this is not on the consent document. The Committee requested that this is corrected in the consent document
    - In the 'nature of processing' section of the DPIA, it refers to the specific data that is being collected/ accessed. The Committee requested that this information is added to the Consent Form/PIL
    - The DPIA states that 184 women will be recruited to the study, but other documents state a recruitment target of 230 participants. The Committee requested clarification as to how many participants will be recruited to the study and this number is aligned across all submitted documents.
    - The Committee noted that children are not listed as participants in the DPIA and requested that the DPIA is amended to include children, as access to the data of neonates is being collected as part of the trial
    - The DPIA refers to a data collection sheet and that only the data specified in this sheet will be collected, however this data collection sheet was not included as part of the submission. The Committee requested that a data collection sheet is provided for NREC review.
    - The Committee requested that the exploratory objectives listed in the study protocol should be included in the DPIA and the PIL

- The Committee noted that benefits and risk assessments section of the protocol does not indicate the benefits/risks to the unborn baby or does not adequately identify any risks associated with taking half the recommended dose for IDA in pregnancy. The Committee requested further information is provided regarding Standard of Care, and whether there are risks to the baby/mother from taking a half dose of iron. The risks of reducing intake from daily to alternate days must be documented for both mother and baby.
- The Committee requested that information regarding the potential risks / side effects of participating in the trial is elucidated to participants in the PIL for both the participant and their child.
- The Committee considered that the information provided in the PIL about previous iron studies is misleading, as the benefits were only seen in women who could not tolerate daily iron and requested that this is justified / replaced with relevant studies.
- The Committee requested in the 'What will happen to me if I agree to take part?' section of the PIL there should be some indication of what the participant should do if they cannot tolerate the daily iron during the 4-week period, or if the alternate day iron is not as effective as their daily intake. This information should also be added to the 'what if something goes wrong when I'm taking part in this study 'section.
- The Committee noted that in the WHO-5 Questionnaire, it is not clear what will happen if there is evidence of a mental health issue and requested details of what provisions are in place should the questionnaire indicate a mental health issue.
- The Committee noted that Sections C12 of the NREC Application Form does not refer to mental health issues as a potential side effect of the study and requested that this is amended.
- The Committee noted that participants will be counselled not to take multivitamins and requested that the potential risks to both the mother and baby are elucidated in the PIL.
- The Committee noted that in the study protocol (p.12) there is a difference in which tests/ biomarker measurements are being carried out between the control group and intervention group. The Committee requested justification as to why both groups are not undergoing the same testing.
- The Committee noted that section C10 of the NREC Application Form mentions samples of biomarkers being taken to assess metabolic factors and requested that a detailed explanation as to which biomarkers will be assessed other than *hepcidin* (also indicated in Protocol p16 "and/or other biomarkers")
- The Committee noted that p.21 of the protocol states that the study drug is 'not to be taken with any medication or any other nutritional supplement', whereas p.11 of the protocol states 'Nutritional supplement use will also be recorded'. The Committee requested clarification as to whether participants are permitted to take additional supplements while participating in the trial and amend the protocol accordingly
- The Committee noted that the protocol states that participants will be required to take the study drug with a source of vitamin C such an orange juice (p.21), however this information is omitted from the PIL. The Committee requested that clarification is

provided about taking a source of Vitamin C with the trial drug and an explanation for participants in the PIL.

- The Committee noted that section C10 of the NREC Application Form states that women will be instructed to take the study drug on an empty stomach, which is contraindicative of taking it with food to reduce some of the side effects as per guidance in the SmPC. The Committee requested justification as to why participants will be instructed to take the study drug on an empty stomach, when this conflicts with information in the SmPC.
- The Committee requested that clarity is provided to participants regarding what will happen at the end of the study.
- The Committee requested that the Introduction section of PIL should include information on why the participant is being invited to take part in the study.
- The Committee noted that one of the benefits of participation listed in the PIL is stated "*free supply of iron tablets for first four weeks of treatment*" and was concerned that this may be seen as an inducement to participate and requested that this is removed.
- The Committee noted that participants who are not fluent in English are excluded from participating in the trial and that no interpretation facilities will be provided:
    - Considering the large number of participants to be recruited to the trial, the Committee requests justification for the exclusion of potential participants who are not fluent in English.
    - The Committee also requested clarity as to how English language proficiency will be assessed during screening
    - The Committee noted that in section C10 of the NREC Application Form, participants requiring an interpreter are not listed in the exclusion criteria and requested that this is amended.
- The Committee requested that evidence of current ICH-GCP certification is provided for all trial staff.
- The Committee noted that no compensation is provided to participants for further hospital visits and requested that this is corrected/justified

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- AOB:

The Chair closed the meeting.