National Research Ethics Committee

NREC-CT Meeting

25/09/2024

Attendance

Name	Role
Dr Cliona McGovern	Chairperson, NREC-CT B
Dr Colm O'Donnell	Deputy Chairperson, NREC-CT B
Dr John Hayden	Deputy Chairperson, NREC-CT B
Ms Serena Bennett	Committee Member, NREC-CT B
Dr Åine de Róiste	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 Karina Halley	Committee Member, NREC-CT B
Dr Laura Mackey*	Programme Officer, National Office for RECs
Dr Susan Quinn	Programme Manager, National Office for RECs
Ms Aileen Sheehy*	Programme Manager, National Office for RECs
Ms Rachel McDermott	Project Administrator, National Office for RECs
Dr Jane Bryant	Programme Officer, National Office for RECs
Mr Ciaran Horan*	Administrative Assistant, National Office for RECs

*Drafted minutes

Apologies: Mrs Ann Twomey, Prof. Michaela Higgins

Quorum for decisions:

Agenda

- Welcome & Apologies
- 2022-502000-73-00
- 2023-506962-30-00 SM1
- 21-NREC-CT-146_Mod-4
- 2023-504923-20-00 SM2
- 2022-502110-85-00 SM4
- 2023-505543-39-00 SM13
- 2023-504031-41-00 SM15
- 2022-502629-16-00 SM4
- 2023-506081-31-00 SM1
- AOB

- The Chair welcomed the NREC-CT B.
  - The minutes from the previous NREC-CT B meeting on 28/08/2024 were approved.
  - The NREC Business Report was discussed and noted.

Applications

2022-502000-73-00

Institutions: Beaumont Hospital

Study title: A Randomized, Double-blind, Placebo-Controlled, Multicenter Phase 3 Study to Evaluate the Safety, Tolerability, and Efficacy of XEN1101 as Adjunctive Therapy in Focal-Onset Seizures

Dossiers Submitted: AMS Part I & Part II

- NREC-CT Decision:
- Request for Further Information

Part II Considerations

1. Compliance with national requirements on data protection

- The NREC-CT noted that very little information has been provided around the data transfer agreements and safeguards in place for the storage and processing of sensitive personal data by the third-party vendor, PatientWing. If Patient Wing is planned to be used in Ireland, the NREC-CT requested a statement of confirmation from the Beaumont Hospital Data Protection Officer that they deem the safeguards in place to maintain potential participants rights and privacy adequate, including in the event of any future use of the sensitive data.

2. Compliance with use of biological samples

- None

3. Financial arrangements

The NREC-CT noted that compensation is not provided for carers of participants enrolled in the study. The NREC-CT recommended that compensation is provided to carers and requested justification as to why this is not provided. This should also be captured in the PISCF

4. Proof of insurance

None

5. Recruitment arrangements

- The NREC-CT noted that PatientWing recruitment will be used during the pre-screening phase, which is a US based technology company. However, no details regarding PatientWing are included in the protocol or the PILs. The NREC-CT requested confirmation that PatientWing will be used to recruit Irish participants. If so, the participant-facing Part II documents must be updated to reflect this procedure.
- If PatientWing is to be used to recruit Irish participants, the NREC-CT requested clarification on the following:
    1. The participant discloses personal details in the online pre-screener questionnaire. What safeguards are in place that align with national data protection legislation and GDPR.
    2. In the phone call script, the placebo is referred to as a ‘sugar pill’. Please amend this to ‘placebo’.
    3. The phone call script refers to a 3-year open-label extension (OLE) which is not described in the PIL. Please clarify whether the OLE will be available to Irish participants and if so, please include details in the PIL.
    4. In the NREC recruitment form, the sponsor states that the first act of recruitment would be the contact between the investigator and the potential participant” yet it also mentions “an online website for interested potential participants to access a prescreening questionnaire with a follow-up phone call. This information is contradictory, please confirm the first act of recruitment for Irish participants and amend the documentation accordingly.
    5. Will posters be displayed at the hospital site related to the use of PatientWing and if so, what data protection agreements are / will be in place with the hospital?
    6. Given that detailed medical questions will be asked during the follow-up phone call, please confirm the type of qualifications and expertise of the person asking the questions and whether they be able to refer the participant to relevant mental health services if required?
    7. What, if any consent processes are in place to confirm that the participant has consented to be contacted in relation to future studies or use of data?

6. Subject information and informed consent form

- The NREC-CT noted that no information about how the study drug works or details about previous trials assessing the study drug is provided in the main PIL. The NREC-CT requested that those details are included in the PIL.

- In addition, the NREC-CT requested that additional information in relation to study drug side effects is included, specifically:
    1. Whether drug interactions or exacerbations of side effects can occur with the study drug and the participant's current medications.
    2. That the severity and burden (e.g., symptom duration, additional management approaches, impact on daily life) of each side effect listed, and not a general statement about all side effects.
- The NREC-CT noted on page 11 of the main PIL, 'there are no anticipated side effects' if the participant is in the placebo group. However, they may already be experiencing significant side effects from their current medications, and it is requested that the sponsor clarifies that no additional side effects alongside those already experienced by the participant may be anticipated if in the placebo group.
- The NREC-CT requested that additional detail regarding 'retinal pigmentary abnormalities' are provided in the main PIL (Pg. 11) to clearly explain what specific changes in the eye could occur.
- The NREC-CT noted that there is an increased risk of suicide associated with seizure medications, and that in the main PIL (Pg. 11) participants are directed to call the study doctor or the local emergency services if they are having suicidal thoughts or are in crisis. However, the study doctor may not be contactable at all times, and therefore, it is requested that further details about the care pathways and site resources for managing a participant in crisis are described. In addition, the sponsor may wish to include details regarding Irish national helplines, such as the Samaritans or Pieta House (https://www.samaritans.org/ireland/samaritans-ireland/ , https://www.pieta.ie/).
- The NREC-CT noted that the investigator may stop the study drug for 2-5 days if the study drug is not tolerated and then resume at a lower doses. Given that this is a double-blind study, it is not clear how the investigator will determine the lower dose, and also, what happens to participants taking the placebo medication. The NREC-CT requested the following:
    1. The sponsor provides additional details on the process for determining lower dose per treatment arm.
    2. That information about temporarily stopping the drug and lower the dose to manage side effects is included in the main PIL.
- The NREC-CT noted that alcohol consumption is not permitted, as described in the PIL (p9), yet in the protocol, alcohol is limited to 2 standard units per day (Pg. 35). It is requested that information regarding alcohol consumption in the PIL and protocol are aligned.
- The protocol states that participants should not drive, operate complex machinery etc., until they have become accustomed to the potential sedative effects of the study drug. However, in the PIL, this is described as 'calming effects' (Pg. 10) which the NREC-CT considered inappropriate/unacceptable and requested it is updated to reflect the description in the protocol.
- Given that many participants may not be able to drive due to their symptoms and medication side effects, but that important information about the study drug side effects are described in this section, the NREC-CT requests that the opening sentence in the PIL (Pg. 10), i.e., 'you will be asked not to drive' is changed to include the side effect first, e.g., 'due to the sedative effects of the study drug, you will be asked not to operate complex machinery such as driving, until you have gotten used to the study medication'.
- The NREC-CT requested in the main PIL, section 'Do I need to participate in this study to receive treatment for my condition? (p14)' that it is made explicit to the participant that they will continue to receive their standard treatment if they participate in the study, and that 'alternatives' are related to the study drug / interventions alone.

- The NREC-CT requested that further clarity is provided in the main PIL regarding the impact on a participant's insurance policy (p15).
- The NREC-CT noted a number of typos throughout the main PIL and recommends that the document is proof-read before resubmission.
- The NREC-CT requested that additional information is needed in the final sentence of section 15 in the main PIL (p20) 'You may be asked to stop being a participant in the research study even if you do not want to stop'.
- The NREC-CT requested that a 'What will happen if I decide to not participate' Q&A section is included in the main PIL, and that it also includes an explanation of the standard of care.
- The NREC-CT noted that the pregnant partner and pregnancy follow-up PILs include results of non-clinical studies regarding the impact of the study drug in unborn rats. It is requested this information is also included in the main PIL so that participants are aware of the potential side effects to a foetus prior to a pregnancy occurring.
- The NREC-CT requested that the APGAR score in the pregnant partner PIL (p4) is explained further.
- The NREC-CT requested that details on how the sponsor will collect data about the pregnancy is included in the pregnant partner PIL and pregnancy follow-up PIL.
- The NREC-CT requested that the following sentence in the pregnant partner PIL (p5) is removed 'make sure that relevant information about the study is recorded for your care ', as it is the responsibility of the study / site staff to ensure any relevant information is recorded.
- The NREC-CT requested that when referring to accessing a pregnant partner's medical record, participants are consenting to allow access to information related to the study only and not their entire medical record.
- The NREC-CT requested confirmation that the pregnant partner will be provided with information that they can share with their obstetrician regarding the risk to their pregnancy, regardless of whether they consent to participate in the study or not.
- The NREC-CT requested that information is included in the pregnancy follow-up PIL regarding the care a pregnant person will receive following their withdrawal/removal from the trial. In addition, will they have an option to take part in an open-label extension of the study drug following the birth?
- In the event of a pregnancy, the NREC-CT requested if possible, that the participant is informed of which arm they were assigned to, which may alleviate significant worry and stress for those assigned to the placebo arm.
- The NREC-CT noted that participants' samples will be sent to York for analysis and requested that further information is provided to participants on the analyses that will take place and the data protection measures in place.
- The NREC-CT requested a number of clarifications or corrections in the section 'Who are the authorised recipients of your personal data' in the pregnant partner PIL (p4) and main PIL (p16):
    1. Remove reference to the REC, as they are not recipients of patients' personal data.
    2. Explain why 'other government agencies including those outside your county of residence' are recipients.
    3. Explain who 'vendors working on this study' are and why they are recipients.
    4. Explain why 'individuals involved in marketing authorisation' are recipients.
- The NREC-CT noted in the pregnant partner PIL (p6) and main PIL (p18) that 'Your personal data will only be shared with and disclosed to authorised third

parties and recipients, if instructed and permitted by the sponsor.' Please provide further details on authorised third parties and recipients.
- The Sponsor is requested to submit any Part II documentation that require updates as a result of the Part I Assessment.
- 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.

7. Suitability of the clinical trial sites facilities

- none

8. Suitability of the investigator

- The NREC-CT noted that the principal investigator's GCP training has expired. Please clarify whether they have updated their GCP training since.

2023-506962-30-00 SM1

Institutions: Beaumont Hospital, St James's Hospital

Study title: The effect of semaglutide in subjects with non-cirrhotic non-alcoholic steatohepatitis

Dossiers Submitted: Part I & Part II

- NREC-CT Decision:

- Request for Further Information

Part II Considerations

1. Subject information and informed consent form

- To align with the other information provided in the PISCF under 'Side effects of semaglutide in NASH,' the NREC-CT requested that further information is provided to participants around the potential signs and symptoms of a bowel obstruction and the steps to take if the participant experiences such symptoms.
- To align with the other information provided in the PISCF, the NREC-CT requests that further information is provided to participants around the post-marketing data on bowel cancer cases e.g. the potential frequency of occurrence.

21-NREC-CT-146_Mod-4

Institutions: Tallaght University Hospital

Study title: A Randomized Open-Label Phase III Study of Sacituzumab Govitecan Versus Treatment of Physician's Choice in Subjects with Metastatic or Locally Advanced Unresectable Urothelial Cancer

Dossiers Submitted: N/A

- NREC-CT Decision:

- Favourable

2023-504923-20-00 SM2

Institutions: Tallaght University Hospital

Study title: A Phase 3, Randomized, Double-blind, Placebo- and Active-Comparator-Controlled Clinical Study of Adjuvant V940 (mRNA-4157) Plus Pembrolizumab Versus Adjuvant Placebo Plus Pembrolizumab in Participants With Resected Stage II, IIIA, IIIB (N2) Non-small Cell Lung Cancer (INTerpath-002)

Dossiers Submitted: Part I & II

- NREC-CT Decision:

- Request for Further Information

Part II Considerations

1. Recruitment arrangements

- The NREC-CT requested that the Figure 1 in the GP letter lists No ALK mutations as a key eligibility criteria as per Figure 1 in the updated protocol.

2022-502110-85-00 SM4

Institutions: Cork University Hospital, Children's Health Ireland

Study title: A Phase 3, Double-blind, Placebo-controlled, Randomized Study to Assess the Efficacy and Safety of Epicutaneous Immunotherapy with DBV712 250 µg in 4-7-year-old Children with Peanut Allergy (VITESSE)

Dossiers Submitted: Part I & II

- NREC-CT Decision:

- Request for Further Information

Part I Considerations (RFI) for addition to CTIS

1. Section 4.1 (study design) states "subjects will be eligible to receive treatment with open-label DBV712 250 µg for up to 2 additional years if they were randomized DBV712 250 µg (VP + VP group) or for 3 years if they were randomized placebo (Placebo + VP group). Treatment allocation during the DBPC period of the study will remain blinded until the Month 12 DBPC Treatment Period ends, and the database is locked. Subjects who elect to roll-over into the Open-label Extension Period will sign the consent form for the Open-label Extension Period prior to any study procedures related to Visit 12."
   Similarly, section 6.1.5 states that "Unblinding for the study will occur once all final clinical data from the DBPC Treatment Period have been entered into the database and all data queries have been resolved, the eCRF and the DBPC Treatment Period database has been signed and locked, and the assignment of subjects to the analysis sets has been completed."
   Since participants are entered to the original study on a staggered basis, by definition, they will complete the study on a staggered basis. The proposed OLE study therefore requires unblinding of the original study on a participant-by-participant basis in order to allocate treatment duration to the active or placebo arms of the OLE study. This breaking of the blind may require a substantial amendment to the original study protocol and potentially jeopardise the validity of the original study data/results.
   Please clarify how treatment allocation will be carried out in the OLE study while maintaining the blind until "all final clinical data from the DBPC treatment period" have been entered and cleaned?

2. The procedures for completing the original study and entering the OLE study are unclear in terms of the study visits (EOS visit is not numbered) and logistics. During this phase, participants must complete efficacy and safety assessments at V11 and EOS (which is within 2 weeks of V11 and missing from section 8.2); with the DBPCFC possibly taking 6 hours to conduct. The data must then be queried, cleaned, signed-off, locked, compliance calculated, consent for the OLE study obtained, treatment unblinded and allocated, before V12 (within 4 weeks of V11) and complete a the 5-week progressive increase in system wear time at the start of the OLE. The study schedule footnote also indicates that "Visit 12, the first day of the Open-label Extension Period, may occur on the same day as Visit 11, under the condition that all procedures of both visits and their specific durations are respected".
   Please clarify all procedures, visit numbering, and the timings thereof, for the planned roll-over phase to the OLE study?

Part II Considerations

9. Recruitment arrangements

- The NREC-CT noted that the doctor-to-doctor letter only refers to the original study and does not include information on the open label extension. The Committee requested that this document is amended to better reflect the open label extension.

10. Subject information and informed consent form

- The NREC-CT requested that the 'thumbs-up' emoji is removed from the 4-6yrs assent form and the 6-9yrs assent form to avoid any undue influence.
- The NREC-CT requested clarity on the number of further visits in the 4-6yrs assent form (pg. 2) and the 6-9yrs (pg. 2) assent form. Both documents state there will be 6 more visits, however, there appears to be an additional 5 other visits in during the discontinuation period.
- The NREC-CT raised a number of queries as part of Part I assessment related to lack of clarity over the unblinding process related open label extension. The Committee requested that this is also made clearer to participants in the PISCFs.
- The Sponsor is requested to submit any participant-facing documentation that require updates as a result of the Part I Assessment.
- 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.

2023-505543-39-00 SM13

Institutions: Tallaght University Hospital, Cork University Hospital, University Hospital Galway, Our Lady of Lourdes Hospital

Study title: A Phase III, Multicentre, Randomised, Double-blind, Chronic-dosing, Parallel-group, Placebo-controlled Study to Evaluate the Efficacy and Safety of Tozorakimab in Participants with Symptomatic Chronic Obstructive Pulmonary Disease (COPD) with a History of COPD Exacerbations (MIRANDA)

Dossiers Submitted: Part I & II

- NREC-CT Decision:

- Favourable

2023-504031-41-00 SM15

Institutions: St Vincent's University Hospital, University Hospital Waterford, University Hospital Galway, Mater Private Hospital, Mater Misericordiae University Hospital

Study title: CAMBRIA-2: A Phase III, Open-Label, Randomised Study to Assess the Efficacy and Safety of Camizestrant (AZD9833, a Next Generation, Oral Selective Estrogen Receptor Degrader) vs Standard Endocrine Therapy (Aromatase Inhibitor or Tamoxifen) as Adjuvant Treatment for Patients With ER+/HER2- Early Breast Cancer and an Intermediate-High or High Risk of Recurrence Who Have Completed Definitive Locoregional Treatment and Have No Evidence of Disease

Dossiers Submitted: Part I & II

- NREC-CT Decision:

- Favourable

2022-502629-16-00 SM4

Institutions: Rotunda Hospital

Study title: A Phase 3 Randomized, Placebo-Controlled, Double-Blind, Multicenter Study to Evaluate the Efficacy and Safety of Nipocalimab in Pregnancies at Risk for Severe Hemolytic Disease of the Fetus and Newborn (HDFN)

Dossiers Submitted: Part I & II

- NREC-CT Decision:

Favourable

2023-506081-31-00 SM1

Institutions: Beaumont Hospital, Tallaght University Hospital, Cork University Hospital, Mater Misericordiae University Hospital, St Vincent's University Hospital

Study title: A randomised, double-blind, placebo-controlled trial of erythropoietin alfa versus placebo in mechanically ventilated critically ill patients following traumatic injury

Dossiers Submitted: Part I & II

- NREC-CT Decision:

- Favourable

- AOB:
  - None