National Research Ethics Committee

NREC-CT B Meeting

21st February 2024

Attendance

Name	Role
Dr Cliona McGovern	Chairperson, NREC-CT B
Dr John Hayden	Deputy Chairperson, NREC CT-B
Prof. Colm O'Donnell	Deputy Chairperson, NREC-CT B
Ms Serena Bennett	Committee Member, NREC-CT B
Dr Katherine Benson	Committee Member, NREC-CT B
Prof. Catherine Hayes	Committee Member, NREC-CT B
Prof. Michaela Higgins	Committee Member, NREC-CT B
Ms Jasmine Joseph	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
Prof. Abhay Pandit	Committee Member, NREC-CT B
Mrs Ann Twomey	Committee Member, NREC-CT B
Dr Emily Vereker	Acting Head, National Office for RECs
Ms Patricia Kenny*	Project Officer, National Office for RECs
Dr Laura Mackey	Programme Officer, National Office for RECs
Dr Susan Quinn	Programme Manager, National Office for RECs
Aileen Sheehy	Programme Manager, National Office for RECs

Apologies: Prof. John Wells

Quorum for decisions: Yes

Agenda

Welcome & Apologies

2023-506669-70-00

2023-509780-25-00

2023-508165-33-00

2023-508084-76-00

23-NREC-CT-015_Mod-3

2022-500121-33-01 SM-9

22-NREC-CT-186_Mod-4

AOB

The Chair welcomed the NREC-CT B.

The minutes from the previous NREC-CT B meeting on 17th January 2024 were approved.

The NREC Business Report was discussed and noted.

Applications

2023-506669-70-00

Principal Investigators & Institutions: Mater Misericordiae University Hospital (Dr Gerard Giblin), St James's Hospital (Dr Ross Murphy)

Study title: A Phase 3, Randomized, Double-blind, Placebo-controlled, Multicenter Study to Evaluate the Efficacy and Safety of Amyloid Depleter ALXN2220 in Adult Participants with Transthyretin Amyloid Cardiomyopathy (ATTR-CM)

EudraCT: 2023-506669-70-00

- **NREC-CT comments:**

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

- **NREC-CT Decision:**

Request for more information

- **Additional Information Required RFI**

Part II Considerations (RFI) for addition to CTIS
1. **Compliance with national requirements on data protection**
• No Considerations
2. Compliance with use of biological samples
• No Considerations
3. Financial arrangements
• No Considerations
4. Proof of insurance
• The NREC-CT noted that the current insurance certificate submitted expired on 29/02/2024. The Committee requested assurances that adequate insurance coverage will be in place for the duration of the trial.
5. Recruitment arrangements
• No Considerations
6. **Subject information and informed consent form**
• The NREC-CT requested that the SIS and ICF's Adult Subject and Pregnant Partner be updated to include the EU trial number for participants. • The NREC-CT noted that the SIS and ICF for Adult Subject are seeking blanket consent for future use of samples/data for unspecified purposes without further consent. This type of consent is not in line with best practice, the Declaration of Taipei 2016 and not in compliance with the Data Protection Act 2018 (Section 36(2) (Health Research) Regulations 2018), where informed participant consent is a mandatory safeguard. The NREC-CT requested that future research is restricted to research in the area of Transthyretin Amyloid

Cardiomyopathy and/or the study drug and this is clearly stated in the main body and consent declaration/form sections of the SIS and ICF. The Committee also requests that any future use of samples or data is reviewed by an ethics committee and requested that this is captured in the PISCFs. Consent for optional future research should also be clearly distinct in the consent for participation on the study trial.

- The NREC-CT noted SIS and ICF Adult Subject pg 11 refers to a separate consent form that a female participant or female partner of a male participant will complete if they become pregnant however only the SIS and ICF for Pregnant Partner has been submitted for review. The Committee requested that the SIS and ICF for female participant who becomes pregnant be submitted for review.
- The NREC-CT noted that the Protocol pg 95 refers to blood being taken to test for hepatitis and HIV infections at screening however there is no reference to this in the SIS and ICF Adult Subject. The Committee requested that SIS and ICF Adult Subject be updated to add a statement informing participants that they will be tested for these viruses at screening and that the study team are required to report any positive HIV, Hep A or Hep C test result to the relevant authority as they are mandatory notifiable diseases. (Infectious Diseases (Amendment) Regulations 2022 (S.I. No. 258 of 2022) May 2022).
- The NREC-CT noted that the information on insurance on Pg. 11 of the SIS and ICF Adult Subject pg 11 is very limited and requested that further information is provided to participants.
- The NREC-CT noted on SIS and ICF Adult Subject pg 12 and pg 13 reference to “health insurance number”. The Committee requested that this is removed from the ICF as this is not relevant in Ireland.
- The NREC-CT noted on pg 12 of the SIS and ICF Adult Subject that data on participants education level, occupation, marital status, and household income would be collected. The Committee were unclear why this data would be required as part of the study and requested justification for the collection of same.
- The NREC-CT noted that SIS and ICF Adult Subject pg 14 states an “anonymised set of your data collected in the study” may be generated and shared by the sponsor. The Committee requested that the SIS and ICF Adult pg 19 be updated to include a specific statement for the participant to explicitly consent to the processing of their personal data from coded to anonymised data it as per Article 4 (2) and (6) General Data Protection Regulation (GDPR).
- The NREC-CT requests that the contact details of the Irish Data Protection Commission details be listed on the ICF in relation to the processing of personal data.
- The NREC-CT recommended that the SIS and ICF Adult Subject Pg 20 consent page would benefit from an initial or tick box to confirm understanding of each statement rather than just a list of bullet points.
- The NREC-CT requested that the SIS and ICF Adult Subject pg 20 consent declaration/form for optional components of the study be moved to a separate page from the Main consent declaration/form. The optional components should also have their own signature box to show explicit consent.

- The NREC-CT noted a number of grammatical and typographical errors throughout the PIS-ICF and requested that all patient facing materials are proofread.
- The NREC-CT considered that the terms safety and efficacy on pg.3 of the SIS and ICF Adult Subject may not be clear to participants and requested that the purpose is captured in more accessible terminology.
- The NREC-CT requested that the SIS and ICF Adult Subject Section 3 pg 4 *"The study intervention will be administered via IV infusion every 4 weeks for up to 24 months to a maximum of 48 months"* is updated to clarify that it is for *"at least 24 months up to a max of 48 months.*
- The NREC-CT requested that SIS and ICF Adult Subject pg 5 reference to "DNA (genetic) testing" is updated to provide more detail of what this means/what the testing is for in lay language.
- The NREC-CT noted that Section 6 pg 8 of SIS and ICF Adult Subject states that 3 participants suffered a mild to moderate severity infusion-related reaction. The Committee requested that the SIS and ICF Adult Subject is updated to specify the total number of participants who received the drug/ drug at that dose and the percentage of participants who suffered mild to moderate severity reactions. This should also be reflected in the subsequent risk sections related to adverse events.
- The NREC-CT noted reference on Section 6 pg 9 of the SIS and ICF Adult Subject and allergic reaction risk. The Committee requested that the SIS and ICF Adult Subject be updated to provide assurances that all participants will be monitored for at least 2 hours after infusion to mitigate against this risk.
- The NREC-CT requested the SIS and ICF Adult Subject Section 10 pg 12 be updated to provide more detail on what is meant by "provided that the costs are reasonable".
- The NREC-CT considered that Section 11a page 12 – "Data collected via i.e., smartphone or websites devices and apps would benefit from further elaboration.
- The NREC-CT noted that the SIS and ICF Adult Subject Section 11a pg 12 states *"your answers to questionnaires using a smartphone or handheld device will also be collected"*. The PIL makes reference also to paper questionnaires. The Committee requests clarification over this discrepancy.
- The NREC-CT noted that on Section 12 page 14, the Sponsors outlined the trial related costs that will be covered while participating in the study. The Committee requested clarity whether radiology investigations, pregnancy tests, blood and urine tests will be covered for participants also?
- The NREC-CT requested that Section 12 pg 14 SIS and ICF Adult Subject is updated to clarify that all reasonable travel and meal expenses for the participant and carer/companion will be reimbursed in line with the participant compensation template. The SIS-ICF currently states they "may be" compensated.
- The NREC-CT noted that pg 7 SIS and ICF Adult Subject states that the "genetic analyses" is optional however consent to samples being collected and transferred to laboratory is not optional on pg 19. The Committee requested that the SIS and ICF Adult Subject pg 19 is updated to move consent for collection and transfer of genetic analyses samples out of the consent section

for the main study and move to the page for optional components of the clinical trial.

- The NREC-CT considered that is not clear to participants that choosing not to opt for the additional optional consent (Pg 20) will not impact their participation in the over all trial and requests that this is further elucidated in the PIL.
- The NREC-CT noted that SIS and ICF Adult Subject pg 20 states *"additional blood sample in the event of treatment-related side effects described in section 5"* however Section 5 is the optional procedures section. The Committee requested that this be updated to reflect the correct section and that the optional blood sample may be collected for optional genetic testing only if the patient experiences side effects that are thought to be related to the study drug.
- The NREC-CT noted reference on pg 20 SIS and ICF Adult Subject to optional courier service. It was unclear to the Committee why a courier service would be required as there is no reference to it in the ICF. The Committee requested that the SIS and ICF Adult Subject be updated to provide more information for participants around when and why a courier service may be required.
- The NREC-CT noted reference on pg 20 SIS and ICF Adult Subject to optional reimbursement service however reimbursement is not an optional component of the study and there is no reference to a company providing reimbursement services in the ICF. The Committee requested that the SIS and ICF Adult Subject be updated to confirm reimbursement is not optional and if a reimbursement company will be an option for participant that the SIS and ICF is updated to provide more information for participants around this optional service.
- The NREC-CT noted that the SIS and ICF Adult Subject pg 21 has section for completion by participants legally acceptable/authorised representative and an impartial witness. The Committee requests further clarification under what circumstances would legally acceptable/authorised representative sign the SIS and ICF.
- The NREC-CT requested that the SIS and ICF Adult Subject pg 21 is updated to provide explanation of the situations when an impartial witness would sign the SIS and ICF.
- The NREC-CT noted refence to ATTRv-CM on pg 23 SIS and ICF Adult Subject and requested that this is updated to provide a lay language explanation.
- The NREC-CT requested that additional information is provided to participants around the expected standard of care.
- The NREC-CT noted that Pg. 32 of the protocol specifies that participants with pre-existing risk factors for bleeding, infection or impaired would healing are not eligible to participate in the optional procedures. The Committee requests that this information is captured in the SIS Adult Subject.
- The NREC-CT requested that the SIS and ICF Adult Subject is updated to include information on the number of participants expected in Ireland.
- The NREC-CT requests that further information is added to the SIS and ICF Adult Subject in the event that a participant misses a clinic visit due to hospitalisation elsewhere.

- Due to the volume of questionnaires / surveys mentioned in the protocol, the NREC-CT requested that further information on these is captured in the SIS and ICF Adult Subject.
- The NREC-CT noted that compensation for overnight accommodation is not captured in the patient materials. The Committee advised that for participants that may live a long distance from the hospital accommodation costs should be covered. The Committee requested that the Compenstion for trial participants and the SIS and ICF Adult Subjects be updated to reflect this.

Pregnant partner of study subjects ICF:

- The NREC-CT requested that the SIS and ICF Pregnant Partner pg 6 be updated to include a box for Pregnant Partner to provide their initials alongside each consent item to confirm their understanding and consent to each item. 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 SIS and ICF Pregnant Partner pg 4 and pg 6 is seeking blanket consent for future use of samples/data for unspecified purposes without further consent. This type of consent is not in line with best practice, the Declaration of Taipei 2016 and not in compliance with the Data Protection Act 2018 (Section 36(2) (Health Research) Regulations 2018), where informed participant consent is a mandatory safeguard. The NREC-CT requested that future research is restricted to research in the area of Transthyretin Amyloid Cardiomyopathy and/or the study drug and this is clearly stated in the main body and consent declaration/form sections of the SIS and ICF.
- The NREC-CT noted that the SIS and ICF Pregnant Partner pg 7 has section for completion by participants legally acceptable/authorised representative and an impartial witness. The Committee queried under what circumstances would legally acceptable/authorised representative sign the SIS and ICF.
- The NREC-CT requested that the SIS and ICF Pregnant Partner pg 7 be updated to provide explanation of the situations when an impartial witness would sign the SIS and ICF.

- The NREC-CT request confirmation that a letter to the participant's GP informing them of the trial.

7. Suitability of the clinical trial sites facilities

- The NREC-CT requested that an updated site suitability form for St James Hospital be provided as Section 3 has some information marked as "xx" which is awaiting completion.

8. Suitability of the investigator

- The NREC-CT requested that an updated CV is provided for Prof Murphy to provide more detail on Prof Murphys current GCP training, as this section was not completed in the form.

2023-509780-25-00

Principal Investigators & Institutions: Cork University Maternity Hospital (Prof. Eugene Dempsey)

Study title: Does the use of higher versus lower oxygen concentration improve neurodevelopmental outcomes at 18-24 months in very low birthweight infants

EudraCT: 2023-509780-25-00

- **NREC-CT comments:**

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

- **NREC-CT Decision:**

Request for more information

- **Additional Information Required RFI**

Part II Considerations (RFI) for addition to CTIS
1. **Compliance with national requirements on data protection**
• No Considerations
2. Compliance with use of biological samples
• No Considerations
3. Financial arrangements
• No Considerations
4. Proof of insurance
• No Considerations
5. Recruitment arrangements
• No Considerations
6. **Subject information and informed consent form**
• The NREC-CT requested that the HiLo ICF updated to include the EU trial number for participants. • The NREC-CT requested that the HiLo ICF be updated to provide information about the availability of the clinical trial results at the end of the trial and location of same. • The NREC-CT noted a contradiction in the information provided. The Recruitment Arrangements document Section 1.7 pg 3 states that parents will be approached after a minimum of 72 hours following delivery, however section 5.2 pg 6 states that consent to use the already collected data will be completed within 72 hours of delivery. The Committee requested that this be updated to clarify the timing. • The NREC-CT requested that the HiLo ICF pg 1 be updated to be clear from the start that both 30% and 60% oxygen are SOC at CUMH. The current wording 'at CUMH we generally start at 30% oxygen' suggests that participants who were given oxygen at 60% are receiving something other than the usual standard of care (which is described later as still within the range of normal care).

- Query: The Consent form asks for the ‘mother’s name’ and ‘mother’s signature’. This should be changed to parent/guardian’s signature to account for non-traditional family units and cases where the father is providing consent.
- The NREC-CT queries whether including mother’s MRN could potentially compromise her privacy and confidentiality.

7. Suitability of the clinical trial sites facilities

- No Considerations

8. Suitability of the investigator

- No Considerations

2023-508165-33-00

Principal Investigators & Institutions: St James’s Hospital (Dr Aoife Mahony)

Study title: An Open-Label Extension Study to Assess the Long-Term Safety and Tolerability of ZYN002 Administered as a Transdermal Gel to Children, Adolescents and Young Adults with Fragile X Syndrome

EudraCT: 2023-508165-33-00

- **NREC-CT comments:**

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

- **NREC-CT Decision:**

Request for more information

- **Additional Information Required RFI**

Part I

1. General
2. 1. It is requested that the word “patient(s)” is changed to “participant(s)” in line with the current re-iteration of the Declaration of Helsinki which is planned for adoption later this year.
3. 2. It was noted that copies of the ABC-CFXS Questionnaire and all other scoring assessment tools have not been included in the submission. It is requested that all are appended to the protocol along with their scoring methodology. Confirmation is also requested that all questionnaires are adequately validated.
4. Extension Study or 2 Different Studies:
5. 3. It was noted that this study is entitled an extension study. Generally, this type of study is where an IMP, or comparator, has been given to a patient during a study, a risk/benefit profile has been established and it is considered that patients could benefit from extended use of the IMP. Here, IMP-naïve patients (i.e. screening failures from study ZYN2-CL-033) are planned to be recruited and it is queried whether this can be considered an extension study for these patients. It is planned to use a lower social avoidance (SA) score at screening ($\geq$3) than was used in the

ZYN2-CL-033 study (≥5). This approach has raised concerns as part of the assessment. It is requested that the sponsor justifies why this study should be considered an extension study and not two separate cohort studies.

6. Sample Size:
7. 4. It was noted that an expected sample size should be included rather than a maximum number. As of June 2023, 206 pts were recruited to the ZYN2-CL-033 study. It would appear that the rationale for changing Incl. #5 and thus rescreening the original screening failures is due to a high number of patients failing this criterion. Similarly, withdrawals at visit 3 of the original study are to be rescreened for this study (also IMP-naïve). This would indicate that approx. 200 pts (~50% of screened pts) were lost from the original study due to these criteria not being met. It is requested that these data are provided to determine if the envisaged 450 pts in this extension study is achievable (i.e. please present the numbers of screening failures due to Incl. #5 & drop-outs at visit 3), particularly in respect of EU (i.e. Irish) patients. (note, the expected number of EU/Irish patients was to be approx. n=2 to 4 (<1% of total n); to date 1 EU patient has entered study ZYN2-CL-033).
8. Inclusion/Exclusion Criteria:
9. 5. It was noted that assent is an important part of the consent process in this population however incl. #9 refers to consent only unlike study ZYN2-CL-033. It is requested that clarification as to why assent has been omitted from the entry criteria is provided.
10. 6. It was noted that incl. #1 states that patients must have an ABC-CFXS SA score of at least 3. The max score for this domain appears to be 3 (see section 7.7.15.1). Incl. # 5 of the ZYN2-CL-033 study indicates a possible score of ≥ 5. Clarification is requested on how the ABC-CFXS SA is scored.
11. 7. It was noted that the entry criterion regarding pt BMI has changed from study ZYN2-CL-033 (from 12 to <30 and now 12 to <40kg/m2). Rationale for this change is requested.
12. 8. It was noted that excl. #19 refers to specific questions in the C-SSRS but the assessment tool is not appended. It is requested that a copy of the C-CCRS is included with the protocol.
13. PK Sampling:
14. It was noted that sections 13, 14.1 & 14.4 and Table 10 indicate there will be PK samples/assays for valproic acid. As this is not a standard clinical laboratory test the Committee requested that Table 8 & 9 is clarified in a footnote. In addition, the NREC noted that the collection days in section 7.7.14 do not match the schedule in Table 10. It is requested that the timing of samples is clarified.
15. 10. It was that serum valproic acid measurements do not seem to add much to the study other than confirming the use of anti-epileptic drugs (AEDs). A rationale for these samples is requested.

Part II Considerations (RFI) for addition to CTIS

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

- No Considerations

2. Compliance with use of biological samples

- No Considerations

3. Financial arrangements

- No Considerations

4. Proof of insurance

- No Considerations

5. Recruitment arrangements

- The NREC-CT required explanation why individuals excluded from ZYN2-CL-033 at Visit 2 or Visit 3 are eligible for this study.

6. **Subject information and informed consent form**

- The NREC-CT noted that the Protocol pg 7 refers to blood being tested for hepatitis and HIV infections at re-screening however there is no reference to this in the SIS and ICF Parent/Legal Representative. The Committee requested that SIS and ICF Parent/Legal Representative be updated to add a statement informing parents that their child's blood will be tested for these viruses at re-screening and that the study team are required to report any positive HIV, Hep A or Hep C test result to the relevant authority as they are mandatory notifiable diseases. (Infectious Diseases (Amendment) Regulations 2022 (S.I. No. 258 of 2022) May 2022)
- The NREC-CT queried why travel and other expenses except for meals and parking onsite will only be paid until month 12. The NREC-CT would expect that all expenses would be covered for the full duration of the trial, including expenses incurred by study withdrawals, irrespective of reason for withdrawal.
- The NREC-CT noted SIS and ICF Parent/Legal Rep of Child pg 13 refers to a separate consent form that a female participant or female partner of a male participant will complete if they become pregnant however only the SIS and ICF for Pregnant Partner has been submitted for review. The Committee requested that the SIS and ICF for female participant who becomes pregnant be submitted for review.
- The NREC-CT requested that the SIS and ICF Parent/Legal Rep of Child pg 21 and SIS and ICF Young Adults pg 21 consent declaration/form for optional components of the study be moved to a separate page from the Main consent declaration/form. The optional components should also have their own signature box to show explicit consent.
- The NREC-CT noted that the SIS and ICF Child & Young Person pg 2 states: *"You are being asked to take part in this research study because you are already taking part in the main RECONNECT (Protocol ZYN2-CL-033) research study*" however the inclusion criteria in Protocol pg 63 states that they must have "*completed Protocol ZYN2-CL-033 OR did not qualify for ZYN2-CL-033 at Visit 3 OR patient was a screen failure at Screening or Visit 2 in ZYN2-CL-033 due to an ABC-CFXS Social Avoidance subscale score that did not meet inclusion criterion number 4, but in the Investigator's opinion, may benefit from participation in the study".* The Committee requested that the SIS and ICF Child & Young Person is updated to clarify.
- The NREC-CT requested that the SIS and ICF Child & Young Person pg 4 is updated to include a sentence regarding urine samples that will be required.

- The NREC-CT requested that the SIS and ICF's Young Adult pg 3 & Parent-Legal Rep. pg 3 is updated to provide a lay language description of 22Q deletion syndrome.
- The NREC-CT requested that the SIS and ICF Parent/Legal Rep SIS and ICF Young Adult is updated to include Drug screening in list of rescreening tests.
- The NREC-CT stated that it was not clear what age group the SIS and ICF Child and Young Person was aimed at. The Committee advised that there should be a single page pictorial version of the study for the very young group (3-6yrs) such as the document "K2_Recruitment material Information sheet" incorporated into the child and young person.
- The NREC-CT requests that the information related to contraception measures in SIS and ICFs are further elucidated.

7. Suitability of the clinical trial sites facilities

- No Considerations

8. Suitability of the investigator

- No Considerations

2023-508084-76-00

Principal Investigators & Institutions: Beaumont Hospital (Prof. Noel McElvaney)

Study title: A Phase 2, Double-blind, Randomized, Active-control, Parallel Group Study to Assess the Pharmacokinetics, Pharmacodynamics, Immunogenicity, and safety of INBRX-101 Compared to Plasma Derived Apha1-Proteinase Inhibitor (A1PI) Augmentation Therapy in Adults with Alpha-1 Antitrypsin Deficiency (AATD) Emphysema

EudraCT: 2023-508084-76-00

- **NREC-CT comments:**

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

- **NREC-CT Decision:**

Request for more information

- **Additional Information Required RFI**

Part II Considerations (RFI) for addition to CTIS

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

- No Considerations

2. Compliance with use of biological samples

- No Considerations

3. Financial arrangements

- No Considerations

4. Proof of insurance

- No Considerations

5. Recruitment arrangements

- The NREC-CT requested that the Clinical Study leaflet is updated to provide a lay language explanation of ‘augmentation therapy’ ‘Proslastin’ and ‘emphysema’.
- The NREC-CT requested that the Email template for outreach be updated to provide a lay language explanation of ‘augmentation therapy’.
- The NREC-CT noted that the GP letter has not been furnished with a list of side effects (Pg. 1 paragraph 5). The Committee requests that this is incorporated into the letter.
- The NREC-CT requested that the GP letter be updated to provide detail on study duration and likely end date.
- The NREC-CT requested that the Phone and email script be updated to provide a lay language explanation of ‘augmentation therapy’ and to provide examples of highly effective forms of contraception.

6. **Subject information and informed consent form**

- The NREC-CT noted that Main ICF pg 6 refers to testing for hepatitis and HIV. The Committee requested that Main ICF pg 6 be updated to add a statement informing participants that the study team are required to report any positive HIV, Hep A or Hep C test result to the relevant authority as they are mandatory notifiable diseases. (Infectious Diseases (Amendment) Regulations 2022 (S.I. No. 258 of 2022) May 2022)
- The NREC-CT requested that the Main, sub study Pregnant Participant and Pregnant Partner ICF’s be updated to include the EU trial number for participants.
- It was unclear to the NREC-CT from Main ICF pg 15 if the Irish site will be taking part in Bronchoscopy sub study. The Committee requested the Main ICF pg 15 be updated to clarify this.
- The NREC-CT requested that participants are provided with a list of organisations that will have access to their coded data through the Sponsor.
- The NREC-CT noted that data will be used for future research purposes. The Committee recommends that part of the consent process should remain optional for participants and should be clearly distinct from consent to trial participation. The Committee also requests that participant data used in any future research is reviewed by an ethics committee. This should be captured in the Main ICF.
- The NREC-CT requested that the Main ICF be updated to provide a lay language explanation of ‘augmentation therapy’.
- The NREC-CT recommends that the Main ICF would benefit from specific examples of highly effective forms of contraception.
- The NREC-CT requests that the text on pg. 17 of the Main ICF is amended to state that travel expenses ‘will be reimbursed’ rather than ‘may be paid for...’.

7. Suitability of the clinical trial sites facilities

- No Considerations

8. Suitability of the investigator

- No Considerations

23-NREC-CT-015_Mod-3

Principal Investigators & Institutions: Prof Ray McDermott

Study title: A Randomized multicenter phase III trial comparing enzalutamide vs. a combination of Ra223 and enzalutamide in asymptomatic or mildly symptomatic castration resistant prostate cancer patients metastatic to bone. PEACE III

- **NREC-CT comments:**

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

- **NREC-CT Decision:**

Request for more information

- **Additional Information Required RFI**

The processing of personal data of deceased falls outside the scope of GDPR and therefore the Health Research Regulations and reconsent is not applicable. There is no basis for the NREC-CT to provide a 'waiver' as such for the transfer of data to the Sponsor for the purpose of regulatory use. However, the duty of confidentially and right to privacy shall remain applicable to all personal data and the use such data should not fall outside the scope or regulatory requirements. The Sponsor may choose to seek legal advice to ensure that any future use complies with the deceased participant's rights

The NREC-CT noted that this study has changed from Academic Study to Commercial study, that Bayer have requested acquisition of a copy of the complete study data set from academic Sponsor and that Bayer has been granted a licence by EORTC (the Sponsor) to access and use a copy of the study data "for example applying and maintaining marketing authorisation with regulatory authorities." The Committee stated that there is very little detail in the PISC Addendum on the fact that the study has changed from an academic study to a commercial study and the implications of same. The Committee requested that the PISC Addendum be updated to :

- provide more information on the purposes of the data transfer and why it happening,
- provide information on what Bayer will do with the data including confirmation that the study data is only licensed for the purposes of the development of the drug and bringing it to the market etc. The Committee stated that the use of the data should be in keeping with the purposes agreed to by the participants in their original consent forms,
- Ensure language reflects an option to consent and not a 'need to give your consent' [p2/4 PIL ICF].

Principal Investigators & Institutions: Prof Michael Clarke, Cork University Hospital

Study title: A Phase 3 open-label, controlled, randomised, multi-centre trial comparing Imlifidase and standard-of-care with standard-of-care alone in the treatment of severe anti-GBM antibody disease (Goodpasture disease)

EudraCT: 2022-500121-33-01

- **NREC-CT comments:**

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

- **NREC-CT Decision:**

Request for more information

Additional Information Required RFI

Part II Considerations (RFI) for addition to CTIS
1. **Compliance with national requirements on data protection**
• No Considerations
2. Compliance with use of biological samples
• No Considerations
3. Financial arrangements
• No Considerations
4. Proof of insurance
• No Considerations
5. Recruitment arrangements
• No Considerations
6. **Subject information and informed consent form**
• The NREC-CT noted that SIS and ICF Main pg 9 states that samples are only analysed in the EU however the Compliance on Biological Samples form references hospitals in the US. Please clarify and update SIS and ICF or Compliance on Biological Samples document as relevant. • The NREC-CT noted that reference to kidney samples “All stored samples will be destroyed or returned to the local hospital after the end of the clinical trial’ has been removed from SIS and ICF Main and there is now no reference to the kidney samples being destroyed at the end of the trial in the SIS and ICF Main or Compliance on Biological Samples form. The Committee requested the SIS and ICF Main and Compliance on Biological Samples form be updated to provide detail on when and how kidney samples will be destroyed. The NREC-CT requests further information around the process of reconsent of ongoing participants.
7. Suitability of the clinical trial sites facilities
• No Considerations
8. Suitability of the investigator
• No Considerations

22-NREC-CT-186_Mod-4

Principal Investigators & Institutions: Dr Maria Byrne

Study title: The cardiovascular safety and efficacy of Cagrilintide 2.4 mg s.c. in combination with Semaglutide 2.4 mg s.c. (CagriSema 2.4 mg/2.4 mg s.c.) once-weekly in participants with established cardiovascular disease.

EudraCT:

- **NREC-CT comments:**

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

- **NREC-CT Decision:**

Request for more information

- **Additional Information Required RFI**

The NREC-CT noted the collection of data on race in Main Consent Form pg 15. In line with GDPR special category data requirements, the NREC-CT requested justification regarding collection of race and ethnicity data. The Committee also requested that the Main Consent Form be updated to include this justification in line with GDPR requirements.

The NREC-CT noted that the Participant Exercise video leaflet lists QR codes to access the exercise videos however were unable to access the videos as it requires the payment of a fee to access. The Committee requested links to the exercise videos that do not require payment of a fee in order to review them and also to ensure participants are not required to pay a fee to access study related documents/videos. The Committee requests clarification whether these videos are for review or for notification.

The NREC-CT noted some grammar/typos in the recruitment material e.g. Advertisement Recruitment poster v1.0-2.0 track changes.pdf – the applicant needs to delete ‘and’ before cardiovascular disease, and also include ‘to’ ahead of ‘impact’ in the text, and PIL p4 extra ‘medicine’ in the third bullet point. The Committee requests that all materials are checked for accuracy in the clean versions.

AOB:

- None