National Research Ethics Committee

NREC-CT A Meeting

25th June 2025

Attendance

Name	Role
Prof. Alistair Nichol	Chairperson, NREC-CT A
Ms Caoimhe Gleeson	Deputy Chairperson, NREC-CT A
Prof. Gene Dempsey	Deputy Chairperson, NREC-CT A
Dr Brian Bird	Committee Member, NREC-CT A
Dr Maeve Kelleher	Committee Member, NREC-CT A
Dr Dawn Swan	Committee Member, NREC-CT A
Dr Darren Dahly	Committee Member, NREC-CT A
Prof. Aisling McMahon	Committee Member, NREC-CT A
Mrs Erica Bennett	Committee Member, NREC-CT A
Dr David Byrne	Committee Member, NREC-CT A
Ms Margaret Cooney	Committee Member, NREC-CT A
Dr Sean Lacey	Committee Member, NREC-CT A
Ms Mandy Daly	Committee Member, NREC-CT A
Ms Muireann O'Briain	Committee Member, NREC-CT A
Ms Dympna Devenney	Committee Member, NREC-CT A
Dr Emily Vereker	Head of Office, National Office for RECs
Dr Jane Bryant	Programme Officer, National Office for RECs
Dr Laura Mackey	Programme Officer, National Office for RECs
Dr Susan Quinn	Programme Manager, National Office for RECs

Apologies:

Quorum for decisions:

Agenda

- Welcome & Apologies
- 2025-521040-37-00
- 2024-519827-16-00
- 2022-501707-27-01 SM-7
- 2022-502629-16-00 SM-5
- 2023-509908-15-00 SM-3
- 2023-507698-16-00 SM-2
- 2022-500758-41-00 SM-20
- 2023-503630-44-00 SM-2
- 2022-501895-25-00 SM-23
- 2023-506327-29-00 SM-2
- AOB

- The Chair welcomed the NREC-CT A.
  - The minutes from the previous NREC-CT A meeting on 21st May 2025 were approved.
  - The NREC Business Report was discussed and noted.

Applications

2025-521040-37-00

Institutions: University Hospital Waterford, Cork University Hospital

Study title: DEFINITIVE: Diagnostic HER2DX-guided treatment for patients with early-stage HER2-positIve breast cancer

Dossiers Submitted: Part I & II

- **NREC-CT Decision:**

- Request for Further Information

- **Additional Information Required RFI**

Part I Considerations (RFI) for addition to CTIS

1.

- It is noted that the “HER2DX will be centrally determined at Hospital Clinic of Barcelona (HCB) prior to beginning of study treatment. The result will be sent to the eCRF within 7-10 business days from the sample reception at the central referral laboratory.” The risk score and pCR Likelihood score are applied to participants which will determine the treatment they receive. Therefore, it is requested that the sponsor clarifies how the score is verified or double-checked.

- It is noted in the protocol Section 6.6 (Patient Follow-Up) that it states, 'survival follow-up information might be collected', implying that in some instances, the participant will not be followed up. It is requested that the sponsor justifies instances where participants are not followed up.

- It is noted adjuvant therapy options include trastuzumab emtansine. In Ireland, this is approved under very specific reimbursement criteria. It is requested that the sponsor confirms access to trastuzumab emtansine for participants, or what plan is in place for participants if they cannot receive trastuzumab emtansine.

- Several issues regarding formatting, language and grammar have been noted, which may lead to problems executing the protocol. It is requested that the sponsor reviews the protocol in detail to correct these issues. The following are examples of such:

    - Protocol Section 2.2.3 (Exploitation Committee). The word “exploitation” has connotations that could be misconstrued. The sponsor is requested to reconsider the title of this committee to better reflect its purpose.

    - Protocol Section 3.2 (Independent Ethics Committee). The last sentence “at least annually DSUR” would benefit from review for clarification

    - Protocol Section 3.5 (Patient Information and Informed Consent). Contains the abbreviation 'LOPD' which should be preceded with the full text. Also, assuming this refers to the Spanish Organic Law on Data Protection, it is

requested that the sponsor confirms whether all relevant MS local regulations will be referred to?

- Protocol Section 3.7 (Premature termination…). “Decided by the Investigator”. It is requested the sponsor clarifies the purpose of this sentence.

- Protocol Section 3.9 (Deviation from the Clinical Performance Study Plan). This section refers to classification of subjects as 'protocol violators'. It is requested that this is updated to the following: 'protocol violations by participants'.

- Protocol Section 6.6 (Follow-up). It is requested that the sponsors notes the duplicated text in section 6.7 (End if Study) and removes duplicated text.

- Protocol Section 8 (Trial Treatments). The section under this is noted as 9.1 Summary of Trial Treatments which should be 8.1. Also, all remaining subheadings start with 9 instead of 8 and this continues to 10. It is requested that the sponsor reviews the protocol formatting and revise accordingly.

- Appendix 8 (EuroQOL) It is noted that there are multiple misspellings and font changes throughout this questionnaire It is requested the original validated version of this questionnaire is included in the protocol.

- It is noted throughout the protocol that the use of CPSP, CSP, Clinical Performance Study Plan, Clinical Performance Study Protocol, Clinical Study Plan, and Clinical Study Protocol are used interchangeably. It is requested that the sponsor align terminology and all ensure abbreviations and terminology are consistent throughout document.

- Multiple spelling mistakes are noted - examples include on page 29 “Allocationof” and on page 55 “Medicial”. It is requested that the sponsor reviews the protocol for spelling and grammar mistakes throughout.

Part II Considerations

1. Recruitment arrangements

- The NREC-CT noted in the recruitment arrangements document it states: “The ability to personally sign the study consent document before participating in the study is required, which effectively excludes people under guardianship, conservatorship or in emergency situations.” It also noted that the ICF’s have space for legal representatives to sign and are set up to facilitate potential participants who require legal representation to take part. The NREC-CT requests clarification if potential participants who require legal representatives to sign on their behalf are being recruited and if they are not being recruited, can an explanation on why they are being excluded from the trial be provided.

2. Subject information and informed consent form

- If applicable, the Sponsor is requested to submit any Part 2 documentation that require updates as a result of the Part 1 Assessment.Please include detail of the Part 1 consideration that triggered the update to the Part 2 documentation.
- 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.
- The NREC-CT noted that throughout the ICF's, technical language is used, including but not limited to the following examples listed. The NREC-CT requests that all the ICF's are reviewed and replaced with lay terminology with the technical term in brackets alongside.
    - The NREC-CT noted on page 6 of the Main ICF and throughout the ICF the use of the terms "intraveneously", and "subcutaeneously". The NREC-CT requests that these terms are explained in lay language.
    - The NREC-CT noted on page 9 of the Main ICF in the test and procedures table "MRI" and "MUGA". The NREC-CT requests that an asterix be placed next to these words to link them to the explanations further down the ICF.
    - The NREC-CT noted on page 11 of the Main ICF "neurotoxicity", "Neutrophils", "mucositis", "conjunctivitis", "haematological problems", "neurologic toxicity", "pulmonary fibrosis"," haemoglobin" on page 12 of the Main ICF "erythema" and on page 13 "echocardiogram" and requested these are explained in lay terminology.
    - The NREC-CT noted on page 13 of the Main ICF use of the terms echocardiogram and MUGA. These terms are technical and do not fully convey the procedure to a lay person. The NREC-CT requests that an explanation on what these procedures are, what they entail for the participant and the length of time involved in provided for the participant in the appropriate sections.
    - The NREC-CT noted in Section 3 of the Main ICF reference to chemotherapy and endocrine therapy. The NREC-CT requests that more information is provided about the differences between these two types of treatment in the context of this study.
    - The NREC-CT noted on page 3 of the Main ICF it states "The test looks at 27 genes, grouped into four genomic signatures". The NREC-CT requests that more context and information is provided in non-technical language.
    - The NREC-CT noted on page 4 of the Main ICF it states "is considered not just as an isolated marker" The NREC-CT requests that "is considered not just as an isolated marker" is explained in non-technical language.
- The NREC-CT noted on page 1 of the pregnant partner ICF it states "you or your partner were informed that any pregnancy occurring during your participation in the study at the times indicated in the informed consent that you or your partner signed, and which vary depending on whether the participant is male or female, are times when the foetus could have been exposed to the study medication." The pregnant partner of a participant in a clinical trial might not have been informed by the trial participant. The NREC-CT requests that this section is rewritten to avoid

assuming that the pregnant partner was fully aware of the advice contained in the main ICF.

- The NREC-CT noted on page 1 of the pregnancy partner ICF “In these cases, your pregnancy would be followed until its outcome to understand the possible effects of the treatment on your pregnancy and your baby. You were also informed that, if you have the baby, the baby's health will be followed.” This section reads that it is mandatory to follow the pregnancy and the health of the baby. The NREC-CT requests that this is rewritten to ask for permissions to follow the pregnancy outcome, to detail why the clinical team is asking for this permission, and to detail any mandatory reporting requirements under the Clinical Trial Regulation.
- The NREC-CT noted on page 2 of the pregnancy partner ICF “We will ask you about your pregnancy, including when it started and how it progressed. We will also keep track of your baby's health” The NREC-CT requests that the type of information that is collected is detailed in the ICF in non-technical language.
- The NREC-CT noted on page 2 of the pregnancy partner ICF “We will also keep track of your baby's health until your local doctor or specialist confirms their well-being. Typically, these health checks happen soon after your baby is born.” The NREC-CT requests the maximum length of time for the collection of information about the baby’s health is included in this section.

2024-519827-16-00

Institutions: Beaumont Hospital, University Hospital Limerick, Cork University Hospital, University Hospital Galway

Study title: Flamboyant: A Randomized, Open-Label, Controlled Phase 3 Study Comparing Daratumumab, Lenalidomide and Dexamethasone Induction followed by Linvoseltamab Versus continued Daratumumab, Lenalidomide, and Dexamethasone in Newly Diagnosed Transplant Ineligible Multiple Myeloma Patients

Dossiers Submitted: Part I & II

- **NREC-CT Decision:**

- Request for Further Information

- **Additional Information Required RFI**

Part II Considerations

1. Financial arrangements

- The NREC-CT noted on page 6 the Main ICF “There are no additional costs to you” and “You will be compensated for reasonable travel expenses”. Participants should be clear what they might be able to claim for, and from whom, and the process for reimbursement. The NREC-CT requests that more details on who the participant talks to about compensation and how compensation can be claimed to be added to the ICF and the “Compensation for Trials Participants” form, such that the burden of finding out the information is not placed on the participant.

2. Recruitment arrangements

- The NREC-CT noted in the “Recruitment Procedure” form that an impartial witness signature might be required, however the Main ICF, pregnant partner ICF, withdrawal ICF and optional future research ICF do not contain space for an impartial witness signature. The NREC-CT requests that a placeholder for an impartial witness is added to the relevant ICFs along with text explaining where a witness signature would be needed.

3. Subject information and informed consent form

- If applicable, the Sponsor is requested to submit any Part 2 documentation that require updates as a result of the Part 1 Assessment.Please include detail of the Part 1 consideration that triggered the update to the Part 2 documentation.
- 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.
- The NREC-CT noted on page 1 of the main ICF, the introductory paragraph could be improved. The NREC-CT requests that more information on multiple myeloma is added to the introduction section of the Main ICF on page 1 in non-technical language, followed by an explanation of the treatments being tested.

- The NREC-CT noted the following statements on page 1 of the ICF: ‘multiple myeloma is considered to be an incurable disease’, ‘the standard treatment is effective’, and ‘linvoseltamab is effective’. These statements may be seen as contradictory to patients and should be re-worded.
- The NREC-CT requests that the section “What is the purposed of this study” is rewritten for clarity for the participant, with a reduction in technical language.
- The NREC-CT noted “Multiple myeloma is also known as Kahler's disease” This term is not commonly used in Ireland and may be confusing. The NREC-CT requests that this sentence is removed from the main ICF.
- The NREC-CT noted on page 2 of the Main ICF “Bone Marrow tests” are referenced in the Screening Section. This test is not explained to the participant. The NREC-CT requests that more context is given to “Bone marrow tests”, including the type of tests to be performed and the length of time the test will take.
- The NREC-CT noted on page 3 of the Main ICF “Further medical examination may be done by your own General Practitioner or a specialist. The costs of these examinations will be charged to your own insurance.” The NREC-CT requests that the ICF is reviewed for the Irish healthcare context and that “The costs of these examinations will be charged to your own insurance” is removed from the Main ICF.
- The NREC-CT noted on page 5 of the Main ICF “Treatment: DRd (control arm): approximately up to 750 ml based on average treatment duration of 60 cycles. DRd +linvoseltamab (experimental arm): approximately 1100 ml based on average treatment duration of 85 cycles.” The NREC-CT requests that the frequency of the blood sampling is explained in this section.
- The NREC-CT noted on page 5 of the Main ICF “You will be asked to collect 24-hour urine samples to measure the myeloma proteins as part of standard care.” The NREC-CT request information is added to the ICF including the type of tests to be performed and the frequency of samples to be collected.
- The NREC-CT noted on page 5 of the Main ICF “At 26 specific timepoints blood samples will be drawn for immunogenicity analyses” This is not sufficiently explained to the participant. The NREC-CT requests that more context is provided in this section, including the frequency of timepoints, the volume of blood to be drawn and the type of tests to be performed.
- The NREC-CT noted on page 6 of the Main ICF “This means that there is no additional cost for you or your health insurance on top of the cost of standard treatment that you would get if you do not participate in the study. Only the components of treatment in this study which are the same as the standard treatment are declared to your health insurance, as would otherwise also happen.” The NREC-CT requests that the ICF should be reviewed for the Irish healthcare context and that references to charging or declaring to a participants health insurance is removed.
- The NREC-CT noted on page 6 of the Main ICF “There are no additional costs for you….You will be compensated for reasonable travel expenses” The NREC-CT requests that more context is provided for participants about reimbursement for costs, including but not limited to how expenses can be claimed, what information is needed for an expenses claim, who they contact regarding expenses and what type of expenses can be claimed. The NREC-CT also requests clarification, due to

the protocol stating that the participant has to be within 30 minutes of the hospital or be hospitalised for 24 hours after receiving a dose, will expense costs to carers, and accommodation costs for participants/carers who have to travel long distance be reimbursed.

- The NREC-CT noted on page 8 of the Main ICF “Leg pain (which could be a symptom of thrombosis)” The NREC-CT requests that thrombosis is explained to participants in non-technical language.
- The NREC-CT noted on page 12 of the Main ICF the sections “Pregnancy Risks” and “Harm to the unborn child”. The two sections contain a lot of duplicated information. The NREC-CT requests that these two sections are combined and condensed, and duplicated information is reduced.
- The NREC-CT noted on page 12 of the Main ICF “Female participants of childbearing potential must use at least one highly effective method of contraception.” The NREC-CT requests that the ICF list the acceptable methods of “highly effective methods of contraception”.
- The NREC-CT noted on page 13 of the Main ICF “You cannot continue to use the medicinal products you were taking during the study after the study has finished.” The NREC-CT requests clarification that for participants who have had a successful response to the medication, whether continued access to the medicinal products could be provided after the trial has ended.
- The NREC-CT noted on page 13 of the Main ICF “You may have to complete a withdrawal of consent form for withdrawal of treatment or for withdrawal from the study.” The NREC-CT requests that this is rewritten as to be clear to the participant that completing the withdrawal of consent form is not a condition for withdrawal.
- The NREC-CT noted that the Protocol requires that patients are within a short distance (30 mins) of the treatment centre or an emergency department for a minimum of 24 hours after administration of Linvoseltamab, and willing to be hospitalised after treatment if not capable of being nearby. This is not explained in sufficient detail in the Main ICF. The NREC-CT requests that this is explained in further detail in the Main ICF, so that it is clear to the participant that they will be required to be close to the hospital, or hospitalised if more than 30 minutes away from the hospital, and any appropriate supports that will be in place to facilitate this.
- The NREC-CT noted on page 2 of the Main ICF “Correlatives studies - Exploratory analyses (research) of blood and bone marrow specimens will be conducted to learn more about the multiple myeloma cells and understand the details of how the treatments work, including effects on the immune system.” Furthermore, the NREC-CT noted on page 5 “including exploratory test in bone marrow and blood: at screening, certain times during the study treatment, and at suspected progression of disease.” The NREC-CT requests clarification of the type of correlative studies and exploratory tests and noted it is unclear to the participant whether these tests are part of the trial, or of optional future research studies. If these are referring to future research, it is not described in line with regulations / best practice. The NREC-CT requested that future use of samples / personal data is sufficiently explained to participants in the PISCF documents so as to constitute broad informed consent, as required under the Health Research Regulations (Data

Protection Act 2018 (Section 36(2) (Health Research) Regulations 2018). Furthermore,

- it should be made optional
- it should be confined to a specified disease, related diseases or drug under study in this trial. Consent can only be obtained where future use of samples and data is defined such that participants are fully informed,
- and/or that an option is provided to enable participants to consent to be contacted in the future about other research studies,
- optional future research is made into a separate and explicit consent item in the Informed Consent section of the Main PISCF, with separate participant information section and signatures section, so it is distinct from the main consent to participate in the research.

The PISCF should also make it clear to participants that subsequent research ethics review will be sought for specific research once clearly defined. For further guidance, please see: NREC guidance on use of biological samples and associated data - https://www.nrecoffice.ie/guidance-on-use-of-biological-samples-and-associated-data/

- The NREC-CT noted on page 4 of the Future Research ICF "Discontinuation of participation will not have any negative consequences for me and will not affect my position as a healthcare customer." The phrase "healthcare customer" is not an appliable term and the NREC-CT requests that this is rewritten into language more appropriate for the Irish healthcare context.
- The NREC-CT noted on page 1 of the Pregnancy ICF "In this information sheet, we request your permission for the collection of (medical) data on your pregnancy and the pregnancy outcome." The NREC-CT requests that the length of time that data will be collected for, and the type of data being collected on the child and pregnancy be added to the "Why have I been given this form" section.
- The NREC-CT noted on page 1 of the Pregnancy ICF "The decision to do this is yours and your baby's biological father. Both your consents are voluntary. If you both decide now to consent, you can withdraw this at any moment, without having to give a reason" and on page 5 of the Pregnancy ICF that there is space for the signature for both parents of the child. The NREC-CT notes that one parent can provide consent for their child's participation (as per the HSE National Policy for Consent in Health and Social Care Research, section 5: (https://www2.healthservice.hse.ie/files/157/) and requests that the pregnancy ICF is reviewed and amended.
- The NREC-CT noted on page 1 of the Pregnancy ICF "you will receive the best possible care, whether you take part or not". This phrasing gives the implication that the "care" relates to the pregnancy, The NREC-CT requests that this phrase is rewritten so that is clear to the participant that this is in reference to their multiple myeloma treatment.
- The NREC-CT noted on page 8 of the Pregnancy ICF a section for withdrawal of consent. The NREC-CT requests that a date box placeholder is added for the withdrawal of consent and that a placeholder for the witness of the withdrawal of consent should be added to this section.
- The NREC-CT noted a minor typographical error on page 8 of the Pregnancy ICF "I withdraw my consent to collection of data about my health status, my pregnancy

and my baby status of health". The NREC-CT requests that this is rewritten as "I withdraw my consent to collection of data about my health status, my pregnancy and my baby's status of health.

2022-501707-27-01 SM-7

Institutions: Crescent Medical Centre (Galway), Moycullen Medical Centre (Galway), Gorey Medical Centre (Wexford), Moyview Family Practice (Mayo), Main Street Clinic (Loughrea), Tramore Primary Care Centre, The Heights Medical Centre

Study title: European Clinical Research Alliance on Infectious Diseases – primary care adaptive platform trial for pandemics and epidemics (ECRAID-Prime)

Dossiers Submitted: Part I & II

- **NREC-CT Decision:**

- Request for Further Information

- **Additional Information Required RFI**

Part II Considerations raised

1. Subject information and informed consent form

- If applicable, the Sponsor is requested to submit any Part 2 documentation that require updates as a result of the Part 1 Assessment. Please include detail of the Part 1 consideration that triggered the update to the Part 2 documentation
- 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.
- The NREC-CT noted that the future use of data and samples (including genetic research) is not described in line with regulations / best practice on pg 5 and page 14 of the LTX-109 ICF. The NREC-CT requested that future use of samples / personal data is sufficiently explained to participants in the PISCF documents so as to constitute broad informed consent, as required under the Health Research Regulations (Data Protection Act 2018 (Section 36(2) (Health Research) Regulations 2018). Furthermore,
    - it should be confined to a specified disease, related diseases or drug under study in this trial. Consent can only be obtained where future use of samples and data is defined such that participants are fully informed,
    - and/or that an option is provided to enable participants to consent to be contacted in the future about other research studies,
    - The PISCF should also make it clear to participants that any future research will also be subject to ethical approval, once clearly defined.
    - For further guidance, please see: NREC guidance on use of biological samples and associated data - https://www.nrecoffice.ie/guidance-on-use-of-biological-samples-and-associated-data/
- The NREC-CT noted on page 12 of the LTX-109 ICF "*I understand that data collected during the trial may be looked at by authorised individuals such as monitors, auditors or supervisory authorities, members of the coordinating team, members of a committee monitoring data and safety of the trial, regulatory*

authorities, and individuals of ECRAID-Prime for research purposes. I allow these individuals access to my personal health information." The NREC-CT noted that this list is overly broad and does not contain enough context. The NREC-CT requests that the list should be divided into two lists which of these authorised individuals will be accessing coded data and which will be accessing personal non-coded data.The NREC-CT requests that context for why authorised individuals will be accessing the data to the section "Who can see your personal information?" on page 5 of the LTX-109 ICF.

2022-502629-16-00 SM-5

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:**

- Request for Further Information

- **Additional Information Required RFI**

Part II Considerations raised

1. Subject information and informed consent form

- If applicable, the Sponsor is requested to submit any Part 2 documentation that require updates as a result of the Part 1 Assessment. Please include detail of the Part 1 consideration that triggered the update to the Part 2 documentation
- 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.
- The NREC-CT noted the Addendum to IB edition 9 for JNJ-80202135 (nipocalimab) contains updated risks pertaining to DVT and PE, Hemophagocytic and serious adverse events such as myocardial infarction. The NREC-CT requests clarification as to why the PIL was not updated with these risks.
- The NREC-CT noted on Maternal ICF Page 25 and 26 the addition of the text “An optional collection of an additional 0.04 cup (10 ml) cffDNA blood sample for diagnostic test development may also be considered. The optional additional cffDNA samples collected in this study will be preserved for long-term use, potentially for a duration of up to 15 years or as required by local regulations. These samples may be utilized for the development of diagnostics and/or companion diagnostic tests related to nipocalimab in HDFN that extend beyond the parameters of this study. ”The NREC-CT requested that the term “extend beyond the parameters of this study” is better explained such that the participant is informed that future research will be confined to nipocalimab in HDFN. Consent can only be obtained where future use of samples and data is defined such that participants are fully informed.
- The NREC-CT requests that “Potential future diagnostic test development” on page 5, should be revised to “potential future HDFN diagnostic test development”
- The NREC-CT requests that “An optional collection of an additional 0.04 cup (10 ml) Cell Free-Fetal DNA (cffDNA) blood sample for diagnostic test development may also be considered in this period” should be revised to “An optional collection

of an additional 0.04 cup (10 ml) Cell Free-Fetal DNA (cffDNA) blood sample for HFDN diagnostic test development may also be considered in this period."

2023-509908-15-00 SM-3

Institutions: Mater Misericordiae University Hospital, University Hospital Limerick

Study title: A Phase 3 Randomized, Open-Label, Multicenter Study Comparing Zanubrutinib (BGB-3111) plus Rituximab Versus Bendamustine plus Rituximab in Patients with Previously Untreated Mantle Cell Lymphoma Who Are Ineligible for Stem Cell Transplantation

Dossiers Submitted: Part I & II

- **NREC-CT Decision:**

- Request for Further Information

- **Additional Information Required RFI**

Part II Considerations raised

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

- If applicable, the Sponsor is requested to submit any Part 2 documentation that require updates as a result of the Part 1 Assessment. Please include detail of the Part 1 consideration that triggered the update to the Part 2 documentation
- 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.
- The NREC-CT noted "the study doctor may check publicly available records until the end of the study to confirm your vital status" The NREC-CT requests clarification on what public databases will be checked for vital status and if the participants personal information will be disclosed on the public databases and/or registers during the search.

2023-507698-16-00 SM-2

Institutions: University Hospital Waterford, Mater Misericordiae University Hospital

Study title: A Phase 3 Open-Label, Randomized Study of Fixed Duration Pirtobrutinib (LOXO-305) plus Venetoclax and Rituximab versus Venetoclax and Rituximab in Previously Treated Chronic Lymphocytic Leukemia/Small Lymphocytic Lymphoma (BRUIN CLL-322)

Dossiers Submitted: Part I & II

- NREC-CT Decision:

- Favourable

2022-500758-41-00 SM-20

Institutions: St. James's Hospital

Study title: A Multi-Center, Randomized, Double-Blind, Placebo-Controlled Multiple Ascending Dose Study to Evaluate the Safety and Tolerability of QRL-201 in Amyotrophic Lateral Sclerosis

Dossiers Submitted: Part I & II

- **NREC-CT Decision:**

Request for Further Information

- **Additional Information Required RFI**

Part II Considerations raised

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

- If applicable, the Sponsor is requested to submit any Part 2 documentation that require updates as a result of the Part 1 Assessment. Please include detail of the Part 1 consideration that triggered the update to the Part 2 documentation
- 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.
- The NREC-CT noted the submission of the "K2_ANQUR Clinical Trial Backgrounder" and the "K2_ANQUR Fact Sheet". The NREC-CT requests clarification if these information sheets will be given to potential participants or current participants. The NREC-CT requests that if these information sheets are to be given to potential participants or participants, that acronyms such as CRF, ALS, PK, ASO and CSF be avoided and the technical language should be rewritten into lay language.
- The NREC-CT noted "K2_ANQUR Clinical Trial FAQ" the NREC-CT requests clarification if this information sheet will be given to potential participants or participants. If this will be given to potential participants or participants, information for healthcare practitioners should not be included.
- The NREC-CT noted that throughout the new advertising materials supplied, use of terminology which may be considered an inducement for participants to take part in the study, for example (but not limited to) "ground breaking", "most advanced", "precision medicine". The NREC-CT requests that the advertising materials supplied are reviewed for use of appropriate and balanced language.
- The NREC-CT requests for clarification on how each of the advertising materials submitted (listed below) will be used, in what format, how will they be presented to the intended audience, and what is the makeup of the intended audience.
    - K2_ANQUR Clinical Trial Backgrounder
    - K2_ANQUR Clinical Trial FAQ
    - K2_ANQUR Followup Letter to Referring Physicians

- K2_ANQUR Local Site Template Release
- K2_ANQUR Overview PPT
- K2_ANQUR Pt Flyer
- K2_ANQUR RNR PSA
- K2_Fact Sheet

2023-503630-44-00 SM-2

Institutions: Cork University Hospital, Children's Health Ireland

Study title: A Phase 3 multi-center trial to evaluate the efficacy and safety of tralokinumab in combination with topical corticosteroids in children (age 2 to <12 years) and infants (age 6 months to <2 years) with moderate-to-severe atopic dermatitis. The trial is randomized, double-blind, placebo-controlled, and parallel-group for children (age 2 to <12 years) and open label and single-group for infants (age 6 months to <2 years)

Dossiers Submitted: Part II

- **NREC-CT Decision:**

- Request for Further Information

- **Additional Information Required RFI**

Part II Considerations raised

1. Subject information and informed consent form

- If applicable, the Sponsor is requested to submit any Part 2 documentation that require updates as a result of the Part 1 Assessment. Please include detail of the Part 1 consideration that triggered the update to the Part 2 documentation
- 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.
- The NREC-CT noted on page 14 of the revised ICF, the word optional has been removed from the consent form and the use of participants data for future research is no longer an optional yes/no.
    - The NREC-CT requests that "grant my explicit consent for the processing of my infant's personal data, including my infant's personal health data and my infant's biological samples, for the purposes of the study, as described in the information sheet" is given a yes/no tick box.
    - The NREC-CT requests that "I understand that my child's pseudonymized personal data (including data generated from samples) can be used for future research as described in the participant information sheet" is given a yes/no tick box and is made optional.
- The NREC-CT noted that the future use of data is not described in line with regulations / best practice on page 10 and 11 of the assent 2 to 12 year PISCF. The NREC-CT requested that future use (secondary purposes) of samples / personal data is sufficiently explained to participants in the PISCF documents so as to constitute broad informed consent, as required under the Health Research Regulations (Data Protection Act 2018 (Section 36(2) (Health Research) Regulations 2018). Furthermore,
    - it should be made optional

- it should be confined to a specified disease, related diseases or drug under study in this trial. Consent can only be obtained where future use of samples and data is defined such that participants are fully informed,
- and/or that an option is provided to enable participants to consent to be contacted in the future about other research studies,
- optional future research is made into a separate and explicit consent item in the Informed Consent section of the Main PISCF, with separate participant information section and signatures section, so it is distinct from the main consent to participate in the research.
- The PISCF should also make it clear to participants that any future research will also be subject to ethical approval, once clearly defined
- For further guidance, please see: NREC guidance on use of biological samples and associated data - https://www.nrecoffice.ie/guidance-on-use-of-biological-samples-and-associated-data/

2022-501895-25-00 SM-23

Institutions: St. James's Hospital, Beaumont Hospital, Cork University Hospital, University Hospital Galway

Study title: A randomized, parallel-group, double-blind, placebo-controlled, multicenter Phase III trial to evaluate efficacy and safety of secukinumab administered subcutaneously versus placebo, in combination with a glucocorticoid taper regimen, in patients with polymyalgia rheumatica (PMR)

Dossiers Submitted: Part II

- NREC-CT Decision:

- Favourable

2023-506327-29-00 SM-2

Institutions: St. James's Hospital, Tallaght University Hospital, Cork University Hospital

Study title: A Phase 3 Randomized Double-blind Study of Adjuvant Pembrolizumab With or Without V940 in Participants With Resectable Stage II to IIIB (N2) NSCLC not Achieving pCR After Receiving Neoadjuvant Pembrolizumab With Platinum-based Doublet Chemotherapy (INTerpath-009)

Dossiers Submitted: Part I & II

- **NREC-CT Decision:**

- Request for Further Information

- **Additional Information Required RFI**

Part II Considerations raised

1. Subject information and informed consent form

- If applicable, the Sponsor is requested to submit any Part 2 documentation that require updates as a result of the Part 1 Assessment. Please include detail of the Part 1 consideration that triggered the update to the Part 2 documentation
- 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.
- The NREC-CT noted on page 6 of the Main PISCF the revised text contains repeated text. "After you stop visiting the trial site, the trial doctor or trial staff will contact you about every 12 weeks or more frequently to check on your health." The NREC-CT requested that this section be revised to for clarity and the information on stopping treatment, moved to the withdrawal section on page 18, section 19 of the Main PICSF.
- The NREC-CT noted the 13th consent item on page 24 of the Main PICSF "I understand that I may be given additional medication during the trial to help manage side-effects. I understand that the trial doctor of staff will explain the risks and benefits of any such medication to me before I take them, and I will be provided with the relevant package insert/patient information leaflet where applicable." It is the NREC-CT understanding that the additional medication prescribed to the participant by their doctor, would fall under standard of care treatments. The NREC-CT requests clarification on why this specific item was added to the consent table. If this text remains in place, the NREC-CT requests clarification on what support will be in place to assist participants understand the technical language in the package inserts, if required.

- AOB:
  - XXX
  - XXX