National Research Ethics Committee

NREC-CT A Meeting

13th August 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
Ms Chita Murray	Programme Manager, National Office for RECs

Dr Peadar Rooney*	Project Officer, National Office for REC’s

*Drafted minutes

Apologies:

Quorum for decisions:

Agenda

- Welcome & Apologies
- 2025-521188-11-00
- 2024-519901-36-00
- 2024-520407-27-00
- 2024-517131-52-00
- 2024-519654-37-00
- 2023-507482-26-00 SM-1
- AOB

- The Chair welcomed the NREC-CT A.
  - The minutes from the previous NREC-CT A meeting on 25th June 2025 were approved.
  - The NREC Business Report was discussed and noted.

Applications

2025-521188-11-00

Institutions: University Hospital Galway, Connolly Hospital

Study title: A Phase III double-blind, randomised, parallel-group superiority trial to evaluate efficacy and safety of the combined use of oral vicadrostat (BI 690517) and empagliflozin compared with placebo and empagliflozin in participants with type 2 diabetes, hypertension and established cardiovascular disease

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 there are no details as to what options are available if a potential participant is already taking empagliflozin. Please clarify in the protocol if they would be restricted from taking part in the trial.
- It is noted that there are no details as to what options are available if a patient discontinues the IMP empagliflozin and returns to prescription empagliflozin e.g. whether the participant would be able to remain in the trial. This is not strictly called out in the protocol at Section 4.2.2.1: Restrictions regarding concomitant treatment. Please clarify.
- It is noted that there are no details as to what options are available of a participant discontinues the IMP empagliflozin and begins treatment with a different SGLT2i. This is not strictly called out in the protocol at Section 4.2.2.1: Restrictions regarding concomitant treatment. Please clarify.

Part II Considerations

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 there is a lack of information for participants who are already on the empagliflozin. The NREC-CT requests that a paragraph is added to

pg5 of the Main PIL in the section “what is the study medicine?” regarding how participation in this study would work for potential participants already who are already on the drug.

- The NREC-CT noted on page 5 of the Main PIL use of the term “Etc”. The NREC-CT requests removal of the term “Etc”.
- The NREC-CT noted that page 9 of the Main PIL states “Pays the study doctor” The NREC-CT requests that this is replaced with “pays the study site”.
- The NREC-CT noted that page 9 of the Main PIL states “But you may benefit from the additional care and attention from the study staff.” The NREC-CT requests that this is rewritten so as not to imply that any benefit above the standard of care may come from being in this clinical trial.
- The NREC-CT noted on page 18 and 19 of the Main ICF inconsistency in the presentation of the side effects. The NREC-CT requests that the side effects for vicadrostat and empagliflozin are presented in similar styles and include the number of people who have taken the drug in studies and the percentage who reported side effects.
- The NREC-CT noted that the Compliance of Biological Samples form, section 4 regarding the future use of samples states that samples will be destroyed. The NREC-CT requests that it should be explicitly stated that samples will not be used for future research and will be destroyed at the end of the study.
- The NREC-CT noted on page 8 of the Main ICF that “Scout Clinical” will provide compensation and travel services. The NREC-CT requests that information about what a participant will do if they do not want to use “Scout Clinical” be detailed on page 8 of the Main ICF.
- The NREC-CT noted on page 8 of the Main ICF that “Scout Clinical” will provide compensation and travel services. The NREC-CT requests clarification whether Scout Clinical will be sent any data related to the participants in this trial outside of the EEA.
- The NREC-CT noted on page 24 of the Main PIL, the use of the terms “anonymised”, “securing reimbursement”, “legitimate interests in maximising the outputs”. The NREC-CT requests that these terms be replaced with language accessible to a layperson.
- The NREC-CT noted on page 24, page 25 and page 26 of the Main PISCF the use of the phrase “coded data”. The NREC-CT requests that an explanation of coded data is added to page 25, and/or that the image of page 24 is updated to include reference to code data.
- The NREC-CT noted on page 12 of the Main PIL, that there are five options of withdrawal with different follow-up options in case of treatment discontinuation. The NREC-CT requests clarification on where the participants consent and signature will be recorded in the event a participant selects one of these options when withdrawing.
- The NREC-CT noted that page 59 of the protocol states “Patient finder service may be used if allowed by local legislation for lost to follow-up participants.” The NREC-CT requests that this option for following up using a third-party vendor service is detailed in the Main ICF

    - The NREC-CT requests clarification if the sharing of personal information with a “lost to follow up” third party vendor is optional. If this is optional this should be made clear in the PISCF.
    - The NREC-CT requests that the vendor details (if available) be identified in the PISCF. If the vendor details are not currently available, when vendor details are available, that the PISCF be amended with the information and the participants informed of this change.
- The NREC-CT noted in Section 6.2 of the protocol that home visits are possible. The NREC-CT requests that if this option is to be made available to participants in Ireland, that it is detailed in the Main ICF and that this an optional service that participants can opt into.
- The NREC-CT noted in section 1.8 of the recruitment documentation that a translation of the Main ICF could be used. The NREC-CT requests a witness signature placeholder is added to the Main ICF and that information be added to all relevant ICFs explaining the context where an impartial witness signature would be needed (as per CTR: Annex I,L 62(b)).

2024-519901-36-00

Institutions: Beaumont Hospital, St. James’s Hospital

Study title: ETOP 27-23 ARCH – A randomised phase III trial of adjuvant cemiplimab in patients with resected stage II-IIIA NSCLC who have not received prior adjuvant chemotherapy.

Dossiers Submitted: Part I & II

- **NREC-CT Decision:**

- Request for Further Information

- **Additional Information Required RFI**

Part II Considerations

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 page 11 of the Master ICF states “This is where cancer samples are collected from all study participants. The samples will be used and stored in coded form. This means that the cancer sample does not contain any personal information that could be used to identify you (see →Section 9). A

collection of coded samples is called a 'biobank'. The samples will be kept at the research laboratory in Milan for 25 years and will be destroyed at the end of that period unless the samples are used up before then”. The NREC-CT also noted on the ‘Compliance with applicable rules for biological samples’ form that “No future research” was ticked. The NREC-CT requests clarification is added to the relevant section of the Master ICF on page 11 that samples stored in the biobank will be used for this study as detailed in the ICF and no other study.

- The NREC-CT noted that page 3 of the Master ICF states “The first 4 infusions will be given at 3-week intervals. After that, they will receive a further 6 infusions at 6-week intervals.” The NREC-CT requests that the total number of visits and the total length of time is added to this sentence.
- The NREC-CT noted that page 3 of the Master ICF includes the term “intravenous infusion”. The NREC-CT requests that “intravenous infusion” is explained using language accessible to a layperson.
- The NREC-CT noted that page 11 of the Master ICF states “Research on lung cancer and blood samples may include methods such as targeted gene sequencing or whole exome sequencing” The NREC-CT requests that a lay explanation of ‘exome’ is added to this paragraph.
- The NREC-CT noted that page 11 of the Master ICF states that participants may undergo whole genome/whole exome sequencing and requested the following:
    - Sequencing is confined to genes involved in the disease being treated or related diseases and /or genes involved in the metabolism of the medicines being used in the trial and this is elucidated in the PISCF.
    - Explicit consent, including outlining the risks entailed in such analysis being performed, is added to the PISCF.
    - The possible ownership of such data by private or commercial interests and that this elucidated in the PISCF.
    - The right to withdraw genetic data, and clear information on how to do so, must also be provided in the PISCF.
    - Clarification is provided in the PISCF on the mechanism for anonymisation, storage and security and transfer of genetic material and its associated data.
    - For guidance, please see HSE National Policy for Consent in Health and Social Care Research (V2.0, 2024). Dublin: Health Service Executive https://www2.healthservice.hse.ie/organisation/national-pppgs/hse-national-policy-for-consent-in-health-and-social-care-research
- The NREC-CT noted the use of technical language on the patient card. The NREC-CT requests clarification whether the language used is intended for the participant to reference or for healthcare providers.

2024-520407-27-00

Institutions: Children's Health Ireland

Study title: APOLLO: A Randomized, Double-Blind, Placebo-Controlled Study of Bitopertin to Evaluate the Efficacy, Safety, and Tolerability in Participants with Erythropoietic Protoporphyria (EPP) or X-Linked Protoporphyria (XLP)

Dossiers Submitted: Part I & II

- **NREC-CT Decision:**

- Request for Further Information

- **Additional Information Required RFI**

Part II Considerations

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 page 13 of the Main Participant ICF and page 14 of the Parent/Guardian ICF state "…is paying the Study Doctor and study staff for their work in this study." The NREC-CT requests that this is changed to "…is paying the Hospital and the Study site to conduct this trial"
- The NREC-CT noted that page 15 of the Main Participant ICF and page 15 of the Parent/Guardian ICF state "Vendors are service providers that process data on behalf of the sponsor. All service providers on the study have been assessed and approved by the sponsor and have signed appropriate contracts to protect your data. These include: Scout (travel), PCM Trials (home health), Clario (ePRO), Suvoda (IRT). These vendors help manage the clinical trial". The NREC-CT requests clarification whether all these vendors will be used in Ireland. If they are not being used in Ireland, they should be removed from this list of vendors. If they are being using in this study in Ireland, please include information about what role they play, what information they receive, how that information is being stored and for how long, and whether that service is optional in the Main Participant ICF and the Parent/Guardian ICF.
- The NREC-CT noted that page 15 of the Main Participant ICF and page 15 of the Parent/Guardian ICF state **"**Service providers who assist in managing, administering, or delivering reimbursement services". The NREC-CT requests clarification on who the service providers are. If they are a vendor, they should be specifically named in the ICF along with information about what role they play, what information they receive, how that information is being stored and for how

long and whether that service is optional in the Main Participant ICF and the Parent/Guardian ICF. If the vendor details are not currently available, when vendor details are available, that the Main Participant ICF and the Parent/Guardian ICF be amended with the information and the participants informed of this change.

- The NREC-CT noted that page 3 of the Assent 12-15 years ICF states “Participation in the study is not that different from the care you have already been receiving. Therefore, it will not affect your daily life” The NREC-CT notes that this sentence is misleading as the participant will be attending clinic and on some days those visits will be up to seven hours. The NREC-CT requests that this sentence is rewritten to more accurately reflect the experience of participation in the study, or deleted.
- The NREC-CT noted that page 5 of the Assent 12-15 years ICF and page 7 of the Main Participant ICF and page 7 of the parent/guardian ICF state “These will be about how EPP affects your quality of life, about your physical, mental (including any thoughts you may have about suicide), and social health, and if you experience being avoided, excluded, detached, disconnected from, or unknown by others.” The NREC-CT requests that more details are included in all of the ICFs about what will happen if a participant has an identified suicide risk or if the PHQ-8 score is less than 10.
- The NREC-CT noted on page 4 of the Assent 12-15 years ICF that the participants will be undergoing a pregnancy test. The NREC-CT requests that a section about pregnancy and contraception with appropriate language should be included inthe Assent 12-15 years ICF.
- The NREC-CT noted the future use of data/samples (including genetic research) is not described in line with regulations/best practice on page 10 of the Parent/Guardian ICF and page 9 of the Main Participant ICF which state “Samples for future exploratory research will be stored for 10 years after the end of the study at Resolian Bioanalytics or a Sponsor-designated long-term storage facility and then destroyed.” The NREC-CT requested that future use of samples 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,
    - That consistent terminology is used to refer to future research. The terms ‘biological research’, ‘optional biobanking’ and ‘future exploratory research’ are used. The NREC-CT requests that single consistent term is used.
    - and/or that an option is provided to enable participants to consent to be contacted in the future about other research studies,
    - The current consent for future research in the Adult/Guardian ICF is limited to the storage of samples. The NREC-CT requests that optional future research is made into a separate and explicit consent item in the Informed Consent section of the Main PISCF so that the future use of samples is restricted to research in 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
    - The PISCF should also make it clear to participants that subsequent research ethics review will be sought for specific research once clearly

Formatted: Font: Arial, Not Bold

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 that the Assent 12-15 years ICF does not include information on the future use of samples. The NREC-CT requests that more information in appropriate language about storage of samples is included in the Assent 12-15 years ICF.
- The NREC-CT request clarification of the consenting procedure which will occur for participants who reach the age of 16, regarding the continued storage and/or processing of their data (including samples) for future research. Note that the applicable age of consent to both data processing and participation in clinical trials in Ireland is 16 years of age.

2024-517131-52-00

Institutions: St. James's Hospital, University Hospital Limerick, University Hospital Galway, Mater Misericordiae University Hospital

Study title: A Phase 3 Randomized, Open-Label, Multicenter Study of Sonrotoclax Plus Anti-CD20 Antibody Therapies Versus Venetoclax Plus Rituximab in Patients With Relapsed/Refractory Chronic Lymphocytic Leukemia/Small Lymphocytic Lymphoma

Dossiers Submitted: Part I & II

- **NREC-CT Decision**:

- Request for Further Information

- **Additional Information Required RFI**

Part II Considerations

1. Compliance with use of biological samples

- The NREC-CT noted that page 2, section 2.1 of the "compliance with applicable rules for biological samples" form states "The following blood volumes in ml are taken as a part of standard patient care and analysed by local laboratories." The NREC-CT requests clarification if the site hospital laboratories will be performing the analysis, as they have not been explicitly detailed in the site suitability assessment form for the hospital sites, and that this information is added to the 'compliance with applicable rules for biological samples' form.

2. Financial arrangements

- The NREC-CT noted in the "P1 Compensation for trial participants" that the "Legal representative" can claim for loss of earnings. The NREC-CT requests clarification on why this has been provided for these participants and their legal representatives.

Commented [CM1]: Can we add the name of the form here, where this information has been presented? Is it the Recruitment Arrangements form?

3. Recruitment arrangements

- The NREC-CT noted that the “Recruitment Arrangements” document in sections 1.5 and 1.11 states that recruitment is limited to a single location in the investigator’s clinics. The NREC-CT requests clarification on why the informed consent can only be performed in a single location.

4. 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 page 42 of the Main Adult ICF includes a witness signature line. The NREC-CT requests that information be added to all relevant PISCFs explaining the context where an impartial witness signature would be needed (as per CTR: Annex I,L 62(b)).
- The NREC-CT noted that page 2 of the Main Adult ICF states “In Ireland, around 19 participants/patients will take part across approximately 4 of study centres” The NREC-CT requests that this is rewritten to “In Ireland, around 19 participants/patients will take part across 4 study centres”
- The NREC-CT noted on page 3 and 4 of the Main Adult ICF, that several options for continuing to consent for the collection of personnel information are detailed. The NREC-CT requests clarification on where the participants consent and signature will be recorded in the event a participant selects one of these options when withdrawing from the main study and where withdrawal of optional future or additional research is recorded.
- The NREC-CT noted the figure on page 2 of the “Summary Participant Information Sheet”. The NREC-CT requests that this is revised to include information that the first cycle of treatment is ramp-up of the BCL2 inhibitor alone, followed by 6 cycles of combination therapy and then 18 cycles of monotherapy. The current formatting implies that dual therapy commences from cycle 1.
- The NREC-CT noted reference on page 5 of the Main adult ICF to “biomarker testing”. The NREC-CT requests that the details of all biomarkers that are being tested for are explained in the Main Adult ICF.
- The NREC-CT noted that page 15 of the Main Adult ICF states “Cases of TLS and changes in blood test results were reported in patients treated with sonrotoclax or venetoclax.” The NREC-CT requests that more context to this risk is made available to the participant, including the frequency of occurrence and the number of times this has occurred.
- The NREC-CT noted that a separate informed consent form for pregnant participants was not provided. The NREC-CT requests that a separate optional consent form, including the collection of data related to a participant’s pregnancy, is provided.
- The NREC-CT noted that page 26 of the Main Adult ICF states “Your study doctor will medically follow your pregnancy until its completion to monitor you and your baby’s health status. The sponsor will continue to collect information about your

pregnancy, the birth of your baby, and the health of your baby for up to 8 weeks after birth, even if study treatment is stopped." This statement implies that the study doctor is providing obstetric care. It should be clear in the Main Adult ICF that the study doctor will be providing the participant with an optional consent form for the collection of information regarding pregnancy, the birth of the baby and the health of the baby for up to 8 weeks after birth. The NREC-CT requests that this is rewritten so that it is clear that the study doctor and sponsor will collect data only, provided explicit consent is provided to do same, and have no role in providing obstetric care.

- The NREC-CT noted on page 27 of the Main Adult ICF in "Blood for Safety laboratories" a wide range of volume(s) in the amount of blood taken. The NREC-CT requests a brief layperson explanation is provided explaining the reason for such a large range.
- The NREC-CT noted that page 29 of the Main Adult ICF states "If a third party needs to be engaged to help you with any logistics, you may need to share your personal data with them, and this will be done always following the local regulations.", which is repeated on page 30. The NREC-CT requests that the duplicated information is removed.
- The NREC-CT noted that page 29 of the Main Adult ICF states "If a third party needs to be engaged to help you with any logistics, you may need to share your personal data with them, and this will be done always following the local regulations." while on page 30, this third party is named as Scout Clinical. If Scout Clinical is providing these services, please remove references to "third party" and replace with the named vendor Scout Clinical.
- The NREC-CT noted that an ICF for Scout Clinical was not included with the submitted documents. The Committee requests to review the Scout Clinical ICF for consent of participants regarding use of their data.
- The NREC-CT noted that page 2 of the optional future research ICF states "BeiGene would like to retain/archive/save any leftover biological samples from the study, for use in additional research to help better understand how certain medications may work and to help develop new ways to monitor and treat patients with your condition" which 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 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.

Commented [CM2]: Is some text missing?

    - 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 that page 3 of the optional future research ICF states “This optional research may examine all the genes in your disease cells” and the NREC-CT requests the following:
    - Genomic sequencing is confined to genes involved in the disease being treated or related diseases and /or genes involved in the metabolism of the medicines being used in the trial and this elucidated in the ICF.
    - Explicit consent, including outlining the risks entailed in such analysis being performed, is added to the optional future ICF.
    - The possible ownership of such data by private or commercial interests and that this elucidated in the ICF.
    - The right to withdraw genetic data, and clear information on how to do so, must also be provided in the ICF.
    - Clarification is provided in the ICF on the mechanism for anonymisation, storage and security and transfer of genetic material and its associated data.
    - For guidance, please see HSE National Policy for Consent in Health and Social Care Research (V2.0, 2024). Dublin: Health Service Executive https://www2.healthservice.hse.ie/organisation/national-pppgs/hse-national-policy-for-consent-in-health-and-social-care-research

2024-519654-37-00

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

Study title: A Multicenter, Randomized, Double-blind, Phase 2/3 Study of Ficerafusp Alfa (BCA101) or Placebo in Combination with Pembrolizumab for First-Line Treatment of PD-L1-positive, Recurrent or Metastatic Head and Neck Squamous Cell Carcinoma

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.
• In order to address the concerns raised by committee members about participants receiving suboptimal doses in phase 3, The NO office has supported the consideration raised by Belgium (the Reporting Member State): "In the section 3 of protocol, "Subjects receiving the ficerafusp alfa dose that was deselected at the end of Phase 2 will continue treatment at the same dose as assigned at randomization." There is an ethical concern about the number of patients that will be exposed to a potentially suboptimal treatment in the non-selected BCA101 dose arm, whose data will not be considered neither for OBD selection nor for confirmatory analyses". This has been supported with the following text "Ireland EC would support the raising of a consideration regarding the continuation of participants continuing on suboptimal dosing in phase 3 and requests justification of the trial design if this cannot be changed"

Part II Considerations
1. Financial arrangements
• The NREC-CT noted that financial reimbursement is said to cover travel and meal costs for patient and carer. The NREC-CT requests that any limits on travel/meal costs should be specified in the financial reimbursement form and explained in the Main ICF.
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 large sentences and technical language were used frequently in the Main ICF, the Pre-screening ICF, pregnant partner ICF and the Pharmacogenomic ICF. The NREC-CT requests all of the ICFs are reviewed to use lay language and reduce sentence length.
- NREC-CT noted that item 6 of the Pregnant Partner ICF includes five permissions for the collection of personal information to be used for the follow-up of a pregnancy. The NREC-CT noted there is only one ‘tick’ area, giving the impression that it is an ‘all or nothing’ list. The NREC-CT requests separate boxes for each consent item in that section.
- The NREC-CT noted that page 2 of the Main ICF states “It is estimated that approximately 687 participants will be enrolled into this study.” The NREC-CT requests that more context is added to this statement to avoid confusion. The NREC-CT requests that the total worldwide number of participants and the number of participants planned for Ireland be provided.
- The NREC-CT noted that page 3 of the Main ICF states “The study consists of 2 phases, Phase 2 and Phase 3”. The NREC-CT requests that more context is added to this paragraph to avoid confusion. The NREC-CT requests that a small summary of Phase 1 to be added to this section.
- The NREC-CT noted on pages 6 to 16 of the Pre-screening ICF and on pages 20 to 23 of the Main ICF that Greenphire vendor services are offered for the payment of participants’ expenses. Placing the consent for an optional service in the middle of a consent details for a clinical trial is inappropriate and could potentially confuse the participants about what they are agreeing to. The NREC-CT requests that the details of the Greenphire services, data transfer and personal information required and associated risks are detailed in a separate and optional consent section or after the consent section for the clinical trial.
- The NREC-CT noted that page 23 of the Main ICF states “If you choose to opt out of these services, it will not impact your participation in the study and alternative options will be provided to you”, referring to the use of Greenphire services. The NREC-CT requests that that alternative options for reimbursement are detailed in the Main ICF.
- The NREC-CT noted on page 2 of the Pre-screening ICF, the “Purpose of the Study” section has several complex sentences, with one of the sentences over sixty words long. The NREC-CT requests that this section is rewritten in clear, simple lay language.
- The NREC-CT noted that page 2 of the Pre-screening ICF includes the term “oropharynx squamous cell cancer”. The NREC-CT requests that this terminology is explained in lay language.
- The NREC-CT noted on page 4 of the Pre-screening ICF that the section “What are the costs and payments for taking part in the study” includes technical language and long sentences such as “This may include delivering reimbursement payments, arranging travel, replacing your card, providing sponsor or site requested reports, providing customer service support to you or the site staff, communicating with you or your caregiver about reminders and the status of your reimbursement requests and/or travel itinerary and complying with any legally required financial or compliance reporting obligations, including conducting identity

verification to issue you a ClinCard." The NREC-CT requests that this section is rewritten in clear, simple lay language.

- The NREC-CT noted on page 4 of the Pre-screening ICF that the section "What are the cost and payments for taking part in the study" mentions verification of the participant identity for a Clincard. The NREC-CT requests that an explanation of the Clincard be added to this section, including what it is, and what it is used for.
- The NREC-CT noted on page 6 of the Pre-screening ICF "For transfers to the US, your information is protected by the GDPR required agreements and legally required supplementary measures, where applicable." The NREC-CT noted that GDPR is not explained and requests that a brief summary be included indicating that this EU regulation concerns data protection and what the legally required supplementary measures aim to do and why they are required.
- The NREC-CT noted that there is no Pregnant Participant ICF and noted that page 19 of the Main ICF states "If you become pregnant, your study doctor will collect information on your pregnancy, including the outcome and the health of the baby for up to 12 months following the delivery date." It does not detail the risks or details for collecting data on the pregnancy or the participants child, and it is assumed that the participant will participate. The NREC-CT request that a separate optional Pregnant Participant ICF is submitted for review.
- The NREC-CT noted in the Main ICF, the Pre-screening ICF and the Pharmacogenomic ICF that the risks associated with data collection and storage are not detailed. The NREC-CT requests that these risks are detailed in all applicable ICFs.
- The NREC-CT noted that page 27 of the Main ICF states "All study data will be kept for a minimum of 2 years after the study drug has been approved or development of the study drug has ended, whichever comes later." The NREC-CT requests that an approximate minimum timeframe should be indicated.
- The NREC-CT noted that the Main ICF does not include reference to the legal basis of data processing or to GDPR legislation, except in reference to travel reimbursement. There is no statement to indicate transferring data outside the EU may have additional risks. The Committee requests that the applicable information be included.
- The NREC-CT noted that page 10 of the Main ICF, under the headings "Biomarker Research" and "On treatment Biopsy (Optional), and page 3 of the Prescreening ICF state "In addition to the testing performed on your samples for this study, with your permission, future biomedical research may be performed". The NREC-CT notes that the future use of data/samples (including genetic research) 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 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 that Pharmacogenomic ICF states that participants may undergo genetic sequencing and requested the following:
  - Sequencing is confined to genes involved in the disease being treated or related diseases and /or genes involved in the metabolism of the medicines being used in the trial and this elucidated in the Pharmacogenomic ICF.
  - Explicit consent, including outlining the risks entailed in such analysis being performed, is added to the Pharmacogenomic ICF.
  - The possible ownership of such data by private or commercial interests and that this elucidated in the Pharmacogenomic ICF
  - The right to withdraw genetic data, and clear information on how to do so, must also be provided in the Pharmacogenomic ICF.
  - Clarification is provided in the Pharmacogenomic ICF on the mechanism for anonymisation, storage and security and transfer of genetic material and its associated data.
  - For guidance, please see HSE National Policy for Consent in Health and Social Care Research (V2.0, 2024). Dublin: Health Service Executive https://www2.healthservice.hse.ie/organisation/national-pppgs/hse-national-policy-for-consent-in-health-and-social-care-research

3. Suitability of the clinical trial sites facilities

- The NREC-CT noted that the site suitability assessment form (SSA) for St. James's Hospital (SJH) names the 'site' as Trinity College Dublin. The NREC-CT requests that this SSA is amended to reflect that the study will be performed in the Clinical Research Facility at SJH.
- The NREC-CT noted that the site suitability assessment form (SSA) for Beaumont Hospital indicates that the study radiation is above the Standard of Care National Comprehensive Cancer Network guidelines; in the St. James's Hospital and Cork University Hospital SSAs, it states that the study radiation is not above the Standard of Care National Comprehensive Cancer Network Guidelines. The NREC-CT requests that this is clarified and aligned.

2023-507482-26-00 SM-1

Institutions: Tallaght University Hospital, Mater Private Hospital, Bon Secours Hospital

Study title: PEACE 8: Combination of darolutamide and stereotactic body radiation therapy in patients with castration resistant prostate cancer and oligometastases on functional imaging

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 page 7 of the Main ICF states “NB: If you are allergic to contrast agents…”. The NREC-CT request removal of the Latin abbreviation NB and request the use of lay terminology instead. • The NREC-CT noted that page 7 of the Main ICF states “An electrocardiogram (ECG). To be performed only during the selection phase, to be repeated during following visits if the result shows an abnormality.” The NREC-CT requests that the word electrocardiogram be added to the section ‘PART 3: Glossary’ of the Main ICF.

- AOB:
  - XXX
  - XXX