National Research Ethics Committee

NREC-CT Meeting

03 April 2024

Attendance

Name	Role
Prof Mary Donnelly	Chairperson, NREC-CT C
Dr Jean Saunders	Deputy Chairperson, NREC-CT C
Dr Susan Finnerty	Committee Member, NREC-CT C
Prof Andrew Smyth	Committee Member, NREC-CT C
Dr Dervla Kelly	Committee Member, NREC-CT C
Ms Susan Kelly	Committee Member, NREC-CT C
Dr Deborah Wallace	Committee Member, NREC-CT C
Ms Paula Prendeville	Committee Member, NREC-CT C
Mr Philip Berman	Committee Member, NREC-CT C
Prof Anne Mathews	Committee Member, NREC-CT C
Ms Aileen Sheehy	Programme Manager, National Office for RECs
Ms Rachel McDermott	Project Administrator, National Office for RECs
Dr Susan Quinn	Programme Manager, National Office for RECs
Dr Emma Heffernan*	Project Officer, National Office for RECs

*Drafted minutes

Apologies: Prof Fionnuala Breathnach; Prof Austin Duffy; Prof John Faul; Mr Gerry Eastwood; Dr Steve Meaney

Quorum for decisions: Yes

Agenda

- Welcome & Apologies
- 2023-506817-23-00
- 2023-505989-29-00
- 2023-508398-10-00
- 2022-501895-25-00
- AOB

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

Applications

2023-506817-23-00

Institutions: Beacon Hospital; Tallaght University Hospital; St James's University Hospital; Cork University Hospital; University Hospital Limerick, Mater Misericordiae University Hospital; St Vincent's University Hospital; Mater Private Hospital.

Study title: EORTC-2238-GUCG: Intermittent Androgen deprivation Therapy in the era of AR pathway inhibitors; a phase 3 pragmatic randomized trial (DE-ESCALATE)

Dossiers Submitted: Part 1 & 2

- **NREC-CT Decision:**

- Request for more information

- **Additional Information Required**

Part I Considerations

- When looking at disease progression in trial participants, please provide justification as to why a PSA level of 5 ng/mL is being used to indicate that a participant should restart treatment.
- Given the potential toxicity, please provide justification as to why cross-over to the other intermittent arm is limited at the end of protocol treatment for participants randomized to the intermittent trial arm only (Protocol pg. 42)

Part II Considerations

- **Compliance with national requirements on data protection**
- No Considerations
- **Compliance with use of biological samples**
- The NREC-CT noted that a document detailing Compliance with the applicable rules for the collection, storage and future use of biological samples from clinical trial subjects has not been submitted. The NREC-CT requested that this document is submitted for committee review on the appropriate templates from the NREC or European Commission websites. The NREC template can be found here: https://www.nrecoffice.ie/submit-under-the-clinical-trial-regulation/.
- The NREC-CT requested that the Compliance with the applicable rules for the collection, storage and future use of biological samples from clinical trial subjects document aligns with updates requested in the PISCF documents.
- **Financial arrangements**
- The NREC-CT noted that participants will not be reimbursed for out-of-pocket expenses and requested that to ensure equity in access to clinical trials across all socioeconomic groups that participants are reimbursed for all reasonable out of pocket expenses and this is detailed in the P1_Compensation trial participants document.
- The NREC-CT requested that a brief description of the financing of the clinical trial is provided for committee review.
- **Proof of insurance**
- No Considerations
- **Recruitment arrangements**
- The NREC-CT requested that further detail is added to the K1_Recruitment arrangements document explaining how participants will be recruited to the trial.
- Please explain what 'discuss with the Tumour Board' means in section 1.1. of the K1_Recruitment arrangements document.
- **Subject information and informed consent form**

- The NREC-CT deemed the PISCF documents as inadequate, as they do not provide the required clear and accessible information for participants to make a fully informed decision about participating in the trial. The NREC-CT requested that the PISCF documents are thoroughly revised to ensure that trial participants are provided with sufficient information to make a fully informed decision about participating in the trial, in line with ICH-GCP. This information should be presented in a clear concise manner, using plain English suitable for a lay audience.
- The NREC-CT requested that the purpose of the trial is explained to participants in the PISCF. This should include details of the experimental aspects of the trial and the rationale for testing the alternative dosage / regimen.
- The NREC-CT requested that it is explained clearly to participants in the PISCF that there are two study arms.
- The NREC-CT requested that it is explained to participants in the PISCF what each study arm consist of.
    - This should include an explanation of the two treatment arms and what treatment regimens they will be expected to follow.
    - This should include an explanation detailing what the modification group will be asked to do i.e. take a break from their medication.
    - It need to be made clearer in the PISCF that a decision not to participate in the intermittent arm could allow patients to continue in the continuous study arm.
- The NREC-CT requested that the trial related activities (such as site visits, physical exams, questionnaires, imaging etc) associated with each arm are clearly presented in the PISCF documents.
- The NREC-CT requested that it is explained to participants in the PISCF that they may be randomized to either treatment arm.
- The NREC-CT requested that detail is added to the PISCF documents as to the implications of what being randomised to each of the two trial arms entails (i.e. while patients randomised for the intermittent treatment arm can refuse consent and continue on the continuous arm, patients randomised on the continuous arm cannot opt for the intermittent arm).
- The NREC-CT requested that in the section ‘what will happen to me if I participate, and what will I have to do’ on pg. 4 of the Enrolment PISCF, the sentence ‘you will continue on the same treatment as before...’ is misleading, as two thirds of patients will be asked to take a break and requested that this is explained in the PISCF.
- The NREC-CT noted that the tables (pg. 5 of the Enrolment PISCF and pg.5 of the experimental PISCF) are not presented using a patient friendly approach and may be confusing for participants. The NREC-CT requested that these tables are revised so they clearly and concisely describe what will happen in each arm of the trial.
- The NREC-CT noted that section ‘What are the possible advantages of participating’ pg. 5 of the Enrolment PISCF states ‘taking part in the study will not have an impact on your health’ and requested that this is removed, as the treatment regimen may influence outcomes/progression.
- The NREC-CT noted that both the PISCF documents do not detail the potential risks associated with trial participation and requested that this is amended so participants are fully informed. This should include details of the IMP and potential side effects and discomforts (ranging from mild to serious), contraceptive risks, risks associated with trial related activities and other potential risks specific to the trial.
- The NREC-CT requested that participants are informed of the potential alternative treatments to trial participation in the PISCF documents.

- The NREC-CT noted that pg. 4 of the Enrolment PISCF states ‘As per standard of care, your study doctor can refer you for a certain type of imaging…’ and requested that the PISCF explicitly states what imaging is likely to be required.
    - The NREC-CT requested that reference to ‘standard of care’ is explained using lay terminology.
- The NREC-CT noted that pg. 4 of the Experimental PISCF states ‘… possibly imaging’ and requested that the PISCF explicitly states what imaging is likely to be required.
- The NREC-CT noted that participant are to complete questionnaires and requested that PISCF documents detail whether this will be done electronically or verbally or by other means other means (e.g. post)
    - The NREC-CT requested if consideration has been given to privacy/confidentiality and how this will be managed.
- The NREC-CT noted that pg. 6 of the states ‘Am I insured when I participate in this study?’ and requested that this reworded as it could be seen as implying personal health insurance to individual participants is provided during the trial. It should be explained to participants that insurance covers injuries that arise as a result of participation in the trial.
- The NREC-CT noted that pg. 10 of the Enrolment PISCF states that data will be kept for 25 years and ‘at 25 years and every 5 years thereafter, EORTC will assess whether they can still keep your data for further research’ and requested that this is amended in line with regulations and states the maximum length of time participant’s data will be stored for. This should be aligned across all relevant documents.
- The NREC-CT noted that the PISCF 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 ‘specified health research, either in relation to a particular area or more generally in that area or a related area of health research, or part thereof’ (i.e. Prostate Cancer) and this is clearly stated in the main body and informed consent section of the PISCF.The NREC-CT requested
    - i) that consent for future use of samples is provided on a separate consent form and not bundled
    - ii) is made optional, and
    - iii) consent can only be obtained where future use of samples and data is defined such that participants are fully informed,
    - and/or iv) that an option is provided to enable participants to consent to be contacted is provided in a separate consent form.
    - The NREC request confirmation that subsequent research ethics review will be sought for specific research once clearly defined.
- The NREC-CT noted that participants will not be reimbursed for out-of-pocket expenses and requested that to ensure equity in access to clinical trials across all socioeconomic groups and that participants are not left out of pocket as a result of participating in a clinical trial that participants are reimbursed for all reasonable out of pocket expenses, including travel, meal/ refreshments, and overnight accommodation ,if required and this is detailed in the PISCF.
    - The NREC-CT requested that the process for reimbursement is explained in the PISCF.
- The Sponsor is requested to submit any participant-facing documentation that requires updates as a result of the Part I Assessment.

- The National Office requests that all documentation provided in response to RFI is presented in an accessible and searchable format (Word or original PDF). We are unable to accept scanned documents (including documents modified using OCR) as these documents are composed of images, rather than searchable text, and cannot be optimised for use with assistive software.
- **Suitability of the clinical trial sites facilities**
- No Considerations.
- **Suitability of the investigator**
- No Considerations.

2023-505989-29-00

Institutions: Beaumont Hospital

Study title: A Phase 3, Open-label, Multicenter, Randomized Study of Tarlatamab in Combination with Durvalumab vs Durvalumab Alone in Subjects with Extensive Stage Small Cell Lung Cancer Following Platinum, Etoposide and Durvalumab (DeLLphi 305)

Dossiers Submitted: Part 1 & 2

- **NREC-CT Decision:**

- Request for more information

- **Additional Information Required**

Part I Considerations

- Please provide justification for undertaking the interim analysis
- Please confirm whether the volume of PRO assessments to be completed by participants has been reduced. If not, please provide the rationale for this.

Part II Considerations

- **Compliance with national requirements on data protection**
- No Considerations
- **Compliance with use of biological samples**
- The NREC-CT requested that the S1_ Compliance on the collection use and storage of biological sample document is amended to align with any updates to the PISCF documents regarding future use of biological samples and genetic data.
- **Financial arrangements**
- No Considerations
- **Proof of insurance**
- No Considerations
- **Recruitment arrangements**
- The NREC-CT noted that participants are given a minimum of 24 hours to assess the information provided before deciding to consent. Participants should be advised that they can take the necessary time they need to make a fully informed decision to participate in the research. The Committee recommends that this is rephrased to ensure that participants are given ample time to digest the information and make a truly informed decision.
- The NREC-CT noted that pg. 4, section 4 of the K1_Recruitment arrangements_For Publication document states that an impartial witness is not required and noted that if participants are unable to provide a written signature, then an impartial witness will be required. The NREC-CT recommends that

participants who are unable to provide a written signature are given an equal opportunity to participate in the study.

- **Subject information and informed consent form**
- The NREC-CT noted that both the Pre-screening and Main PISCFs 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 'specified health research, either in relation to a particular area or more generally in that area or a related area of health research, or part thereof' (ie. Lung Cancer) and this is clearly stated in the main body and consent declaration sections of the Pre-screening, Main and Optional Future Research PISCFs.The NREC-CT requested the following:
    - i) that consent for future use of samples is provided on a separate consent form (details regarding future research listed in Table 2 on pg. of the Main PISCF need to be moved to a separate document that includes both a patient information section and an informed consent section, placeholders for the signatures of the person taking consent and the participant) and not bundled (a tick box for participant initials should be provided along each consent item)
    - ii) is made optional
    - iii) consent can only be obtained where future use of samples and data is defined such that participants are fully informed, and/or
    - iv) that an option is provided to enable participants to consent to be contacted is provided in a separate consent form.
    - The NREC request confirmation that subsequent research ethics review will be sought for specific research once clearly defined, and this is captured in the PISCFs.
- The NREC-CT noted that the 'Study Product Monitoring Information', section 2, on pg. 3 of the PISCF is not written using clear language and may be confusing for participants. The NREC-CT requested that this section is revised to be participant friendly and written in a clear, concise manner, suitable for a lay audience.
- The NREC-CT noted that Table 2, 'For this Study You Will Have these Tests or Procedures Done' on pg. 7 of the PISCF is difficult to follow (particularly the column 'Treatment Period') and requested that this is presented in a clear, concise patient friendly approach.
- The NREC-CT requested that it is made clear to participants in the Pre-screening and Main PISCFs the location where the infusions will take place.
- The NREC-CT requested that the symptoms of Tumour Lysis Syndrome are added to the 'Other Possible Risks' section on pg. 16 of the PISCF under the heading 'Tumour Lysis Syndrome'.
- The NREC-CT noted that pg. 29 of the Main PISCF states that participants information 'may' be anonymised and requested that it is made clear which data will be anonymised.
- The NREC-CT requested confirmation that only hospital and study site staff and not the trial sponsor, will have access to a participant's identity. This should be clearly stated on pg. 17 of the Pre-screening PISCF and pg. 28 of the Main PISCF.
- The NREC-CT noted that participants have the option to take part in a genetic research sub-study and requested the following:
    - Further detail as to the nature of the genetic tests to be undertaken. This should be explained using plain English suitable for a lay audience.

- Further detail 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 Optional Genetic Sub-study 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 (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 reference is made to the NHS ('These organisations may be universities, NHS organisations or companies involved in health and care studies in this country or abroad') on pg. 17 of the Pre-screening PISCf and pg. 29 of the Main PISCF and requested that all references to UK based entities such as the NHS are removed and replaced with Ireland specific references, where appropriate.
  - The NREC-CT also requested that it is made clear in the PISCFs that the reference to 'this country' is a reference to Ireland, and not the UK.
- The Sponsor is requested to submit any participant-facing documentation that requires updates as a result of the Part I Assessment.
- The National Office requests that all documentation provided in response to RFI is presented in an accessible and searchable format (Word or original PDF). We are unable to accept scanned documents (including documents modified using OCR) as these documents are composed of images, rather than searchable text, and cannot be optimised for use with assistive software.
- **Suitability of the clinical trial sites facilities**
- No Considerations
- **Suitability of the investigator**
- No Considerations

2023-508398-10-00

Institutions: N/A

Study title: Discontinuation of rituximab compared with rituximab maintenance in ANCA-associated vasculitis – a randomized non-blinded controlled trial (DISRITUX)

Dossiers Submitted: Part 1

- **NREC-CT Decision:**

- Request for more information

- **Additional Information Required**

Part I Considerations (RFI) for addition to CTIS

- It is noted that an interim analysis is being conducted for the primary outcome (relapse) at 24 months. Please confirm if the alpha level for the primary outcome at the end of trial (36 months) will be adjusted due to this interim analysis.
- Please confirm that the use of any data from Irish participants for research purposes will be in line with the Health Research Regulations 2018.
- The protocol states that even if the results from the interim analysis are significant at 24 months, the trial will not terminate, as the authors are keen to evaluate

secondary hypotheses at 36 months. Please provide justification for continuing to expose participants to further rituximab with the potential for adverse events (or vice versa, if the rituximab should be continued in all) for an additional year to explore secondary hypotheses.

2022-501895-25-00

Institutions: St Vincent's University Hospital; Cork University Hospital; St James's Hospital; Beaumont Hospital; Galway University Hospital; Our Lady's Hospital; Connolly Hospital.

Study title: A randomized, parallel-group, double-blind, placebocontrolled, 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 1 & 2

- **NREC-CT Decision:**

- Request for more information

- **Additional Information Required**

Part I Considerations (RFI) for addition to CTIS

- Please provide justification for the rapid steroid tapering (24 weeks), where in Standard of Care Treatment steroid tapering takes place over 1-2 years (as per pg. 8 EMA scientific advice).
- Please provide justification as to why a phase 2 trial was not undertaken.

Part II Considerations

- **Compliance with national requirements on data protection**
- No Considerations
- **Compliance with use of biological samples**
- The NREC-CT requested that the S1_CAIN457C22301_Compliance use of Biological Samples Declaration_IRE documents is amended to align with updates to the PISCF documents.
- **Financial arrangements**
- No Considerations
- **Proof of insurance**
- The NREC-CT noted that the potential numbers of participants detailed in the SSA documents, and the insurance certificate do not tally and requested confirmation that there is insurance for all participants taking part in the trial. The Committee requested confirmation that as per the insurance policy, recruitment will be limited to 16 participants in Ireland.
- **Recruitment arrangements**
- The NREC-CT noted that pg. 4 section 4.1 states that an impartial witness may be required for older patients and requested that this is amended to incorporate participants of any age who are unable to provide a signature.
- The NREC-CT requested clarification as to whether participants lacking capacity will be recruited to the trial. If so, please provide detail in section 2 of the K1_CAIN457C22301_Recruitment_Consent_Procedure_IRE form.
- **Subject information and informed consent form**

- The NREC-CT noted that the summary PIL on pg. 3 of the PISCF is not patient friendly with excessive use of technical language and requested that the lay summary PIL is simplified and further expanded for participants, highlighting the pertinent issues that trial participation will involve. This NREC guide may be useful: https://www.nrecoffice.ie/pil-summary-guidance/
- The NREC-CT requested that the EU Trial Number is added to pg. 1 of the PISCF documents.
- The NREC-CT noted that participants will undergo rapid steroid tapering (24 weeks), where in Standard of Care Treatment steroid tapering takes place over 1-2 years (as per pg. 8 EMA scientific advice in Part 1 dossier) and requested that participants are informed of the implications of this on pg. 5 of the PISCF.
- The NREC-CT noted that the IMP has been linked to exacerbations of pre-existing inflammatory bowel disease and new-onset inflammatory conditions of the colon and small intestine and requested that this potential risk is given more emphasis in the risk section (section 8) of the PISCF.
    - The NREC-CT requested that the potential risk exacerbations of pre-existing inflammatory bowel disease and new-onset inflammatory conditions of the colon and small intestine linked with the IMP, is also included in the GP letter.
- The NREC-CT noted the significant burden placed on the placebo group in terms of regular placebo injections and requested that this is further highlighted in the PISCF.
- The NREC-CT noted that the Optional Consent for Additional Research using your Coded Data or Samples PISCF is seeking blanket consent for future / additional 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 polymyalgia rheumatica, and this is clearly stated in the main body and informed consent section of the Optional Consent for Additional Research using your Coded Data or Samples PISCF.
    - The Committee also requested that any future use of biological samples is reviewed by an ethics committee and requested that this is explained to participants in the PISCF.
    - The NREC-CT requested that the S1_CAIN457C22301_Compliance use of Biological Samples Declaration_IRE is amended to align with updates to the Optional Consent for Additional Research using your Coded Data or Samples PISCF.
- The NREC-CT noted that the use of the terms ‘coded’ and ‘coded data’ are used throughout the PISCF documents and requested that the terms ‘pseudonymised data’ and ‘anonymised data’ are used instead, where relevant, and that both these terms are explained to participants.
- The NREC-CT requested that it is made clear to participants who has access to their pseudonymised data in section 13.1 of the Main PISCF.
- The NREC-CT noted that participants are to undergo genetic testing (pg. 10 of the Main PISCF) and requested the following:
    - that explicit consent obtained for genetic testing is sought in the informed consent section of 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 (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 requested that the S1_CAIN457C22301_Compliance use of Biological Samples Declaration_IRE is amended to align with updates to the PISCF.
- The NREC-CT noted that section of the PSCF states 'I agree to my GP being informed of my participation in the study…' and requested that this is amended to 'I agree that my GP *will* be informed of my participation in the study…'.
- The NREC-CT requested that section 15 (detailing what happens if a member of hospital staff is exposed to blood, tissue or bodily fluids) on pg. 22 of the PISCF is removed, as it may cause unnecessary distress to participants.
- The NREC-CT noted that pg. 3, section 2.1 of the K1_CAIN457C22301_Recruitment_Consent_Procedure_IRE form regarding the recruitment of incapacitated adults, states 'N/A', whereas the Main PISCF (pg. 26) includes a placeholder for a signature from a legally designated representative. The NREC-CT requested the following:
    - Clarification as to whether participants lacking capacity will be recruited to the trial.
    - If participants lacking capacity are to be recruited to the trial, then K1_CAIN457C22301_Recruitment_Consent_Procedure_IRE form requires updating.
    - If If participants lacking capacity are not to be recruited to the trial, then the placeholder for a signature from a legally designated representative should be removed from the PISCF.
- The NREC-CT noted that in the event of pregnancy, the Sponsor will collect data related to the baby and retain the information for 25 years. The NREC-CT requests further information on whether any process for reconsent will be implemented when the child turns 16.
- The NREC-CT noted that pg. 18 of the PISCF places a limit on the amount of compensation participants can claim for when attending study visits, which may not be adequate to cover all reasonable out-of-pocket expenses in an Irish context. To ensure that participants are not left out-of-pocket as a result of participating in the trial, the NREC-CT requested that participants are reimbursed for all reasonable expenses including travel, meals / refreshments, and accommodation, if required, and this is clearly stated in the PISCF.
    - The NREC-CT requested that the process for claiming reimbursement is also clearly stated in the PISCF.
    - The NREC-CT requested that the exact values are omitted from the PISCF, so as not to constitute any inducement to participation.
- The Sponsor is requested to submit any participant-facing documentation that requires updates as a result of the Part I Assessment.
- The National Office requests that all documentation provided in response to RFI is presented in an accessible and searchable format (Word or original PDF). We are unable to accept scanned documents as these documents are composed of images, rather than searchable text, and cannot be optimised for use with assistive software.
- **Suitability of the clinical trial sites facilities**
- The NREC-CT noted that the SSAs for Beaumont Hospital and Cork University Hospital state that the exposure to ionising radiation at these sites is above what is required for standard of care and requested clarification as to why this is not the case for the other participating sites.

- The NREC-CT noted that both the ‘yes’ and ’no’ boxes are completed on pg. 3, section 5 in the SSA for Beaumont Hospital and requested that this is corrected, so that only one box is completed.
- **Suitability of the investigator**
- No Considerations

- AOB:

N/A