National Research Ethics Committee

NREC-CT Meeting

12 July 2023

Attendance

Name	Role
Dr Cliona McGovern	Chairperson, NREC-CT B
Dr Jean Saunders	Deputy Chairperson, NREC CT-B
Prof. John Faul	Deputy Chairperson, NREC-CT B
Ms Serena Bennett	Committee Member, NREC-CT B
Mr Philip Berman	Committee Member, NREC-CT B
Dr Enda Dooley	Committee Member, NREC-CT B
Dr John Hayden	Committee Member, NREC-CT B
Dr Mary McDonnell Naughton	Committee Member, NREC-CT B
Mr Gavin Lawler,	Committee Member, NREC-CT B
Ms Paula Prendeville	Committee Member, NREC-CT B
Ms Susan Kelly	Committee Member, NREC-CT B
Ms Deirdre MacLoughlin	Committee Member, NREC-CT B
Prof Seamus O'Reilly	Committee Member, NREC-CT B
Dr Christina Skourou	Committee Member, NREC-CT B
Ms Ayesha Carrim	Project Officer, National Office for RECs
Dr Jane Bryant	Project Officer, National Office for RECs
Dr Laura Mackey	Programme Officer, National Office for RECs
Dr Susan Quinn	Programme Manager, National Office for RECs
Dr Emma Heffernan*	Project Officer, National Office for RECs
Ms Aileen Sheehy	Programme Manager, National Office for RECs

Ms Rachel McDermott	Project Administrator, National Office for RECs

*Drafted minutes

Apologies: Dr Lorna Fanning, Prof. Colm O'Donnell, Dr Mark Robinson, Prof Andrew Green, Ms Mandy Daly

Conflict of Interest: Dr John Hayden and Dr Cliona McGovern for 2022-501157-36-00

Quorum for decisions: Yes

Agenda

- Welcome & Apologies
- 2022-501157-36-00
- 2023-504487-41-00
- 2022-500121-33-01
- 22-NREC-CT-138_Mod-3
- 22-NREC-CT-173_Mod-1
- AOB

- The Chair welcomed the NREC-CT B.
  - The minutes from the previous NREC-CT B meeting on 14/06/2023 were approved.
  - The NREC Business Report was discussed and noted.

Applications

2022-501157-36-00

Principal Investigators & Institutions: St Vincent's University Hospital (Prof Alistair Nichol), Tallaght University Hospital (Dr Yvelynne Kelly), Beaumont Hospital (Prof Gerard Curley)

Study title: Early Sedation with Dexmedetomidine vs. Placebo in Older Ventilated Critically Ill Patients (SPICE IV)

EudraCT: 2022-501157-36-00

- **NREC-CT comments:**

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

- **NREC-CT Decision:**

- Request for more information

- **Additional Information Required**

Part 1

- The NREC-CT noted that the constitution of the DMC is made up of members from the same University (i.e., Tufts in Maine and Boston) and requested the justification for this. As this is an international trial, the NREC-CT recommends that the DMC includes additional members from varied locations to avoid the potential for institutional / location bias.

Part 2

- The NREC-CT requested justification for the questions listed on pg.1 of the Telephone assent SPICE IV V1.0 1 and on pg.13 of the SPICE IV Assent Generic Master forms.
- The NREC-CT requested clarification as to what actions will be undertaken based on the information provided by a respondent to the questions listed in the Telephone assent SPICE IV V1.0 and the SPICE IV Assent Generic Master forms.
- The NREC-CT noted that 'living wills' are referred to as 'Advanced Healthcare Directives' in Ireland and requested that this is amended in the SPICE IV Assent Generic Master and Telephone assent Generic Master forms to reflect Irish legislation.
- The NREC-CT requested that the IE-SPICE IV Telephone Assent Generic Master V1.0 and the SPICE IV Assent Generic Master includes a question asking if the participant has either a co-decision-making agreement or decision-making representation order in place (as per the provisions of the Assisted Decision Making (Capacity) Act 2015).
- Furthermore, the NREC-CT requested further clarification as to the procedure in place to determine and follow the participants' will and preference should they have an Advanced Healthcare Directive in place.
- The NREC-CT noted that an 'Enduring Power of Attorney' cannot consent to medical treatment under the 1996 Act or the Assisted Decision Making (Capacity) Act 2015 and requested that this question is removed from the Telephone assent SPICE IV V1.0 and the SPICE IV Assent Generic Master forms.
- The NREC-CT noted that if a person is a 'Ward of Court', only the High Court through the Office of the Ward of Court can provide consent to participate in the research and requested that the consent process reflects this legal requirement.
- The NREC-CT noted that pg. 2 of the IE-SPICE IV Telephone Assent Generic Master V1.0 PISCF and pg. 13 of the SPICE IV Assent Generic Master states 'I give permission for data to be stored for possible future research related to the current study without further consent being required but only if the research is approved by a Research Ethics

Committee' and requested that this is amended to make it clear that participants will provide their own consent for future use of samples / data once they are in a position do so.

- The NREC-CT requested that the language in the Consent to Continue Generic Master form is updated to ensure that participants are aware that they have already been enrolled in the study and that they have since received the study intervention.

2023-504487-41-00

Principal Investigators & Institutions: University Hospital Galway (Prof. John Laffey), St Vincent's University Hospital (Prof. Jane O'Halloran)

Study title: A Multicenter, Adaptive, Randomized, Controlled Trial Platform to Evaluate Safety and Efficacy of Strategies and Treatments for Hospitalized Patients with Respiratory Infections: Strategies and Treatments for Respiratory Infections & Viral Emergencies (STRIVE) - Immune Modulation Strategy Trial

EudraCT: 2023-504487-41-00

- **NREC-CT comments:**

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

- **NREC-CT Decision:**

- Request for more information

- **Additional Information Required**

- NREC-CT comments:

Part 1

- The NREC-CT requested clarification whether the scientific advice regarding endpoints, as suggested by the EMA and FDA has been implemented.
- The NREC-CT requested clarification as to how quickly participants can be unblinded, should there be a need to do so.
- The NREC-CT requested clarification whether the scientific advice regarding study design and co-enrolment, as suggested by the EMA and FDA has been implemented.

Part 2

- The NREC-CT noted that participants' data will be transferred outside of the EU. The Committee requested that this is made clear to participants in the PISCF, including any safeguards in place.

- The NREC-CT requested that the Data Protection Commissioner of Ireland's contact details are added to the Main PISCF
- The NREC-CT noted that participants can be co-enrolled to multiple trials simultaneously. This may be confusing to participants, given the complexity of their treatment and what is involved in trial participation. The Committee requested that details of learning and support measures in place to educate participants on the various aspects of the trial are described in the recruitment document.
- The NREC-CT noted that the study title may be confusing, in that it is not immediately clear to participants what the study is about (the title does not mention either abatacept or Covid 19). The Committee requested that a plain English language title suitable for a lay audience is added to the PISCF, so participants are clear what the trial is about.
- The NREC-CT requested that it is made clearer to participants at the point of entry to the trial which aspects of the trials they may be randomized to. This also needs to be included in the PISCF.
- The NREC-CT requested that details regarding the standard of care treatment for this condition is explained in the Main PISCF.
- The NREC-CT requested that additional information around the previous studies related to this trial is added to the PISCF.
- The NREC-CT noted that the section on future research in the Main PISCF (pg. 5 and pg. 7) is not described in line with regulations. The Committee requested that future use of samples is sufficiently explained 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,
    - consent for future use of samples should be provided on a separate consent form.
    - it should be made optional, and
    - 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 is provided in a separate consent form.
    - 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: 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
    - Any updates should also be reflected in the STRIVE_E2_compliance with rules for samples form and the flipbook.
- The NREC-CT noted that the information on pg. 12, section 4.3 of the Main PISCF regarding withdrawal is not explained clearly and requested that it is made clear to participants what will happen to their information should they withdraw from the study.

- The NREC-CT noted that the Main PISCF (particularly section 4) uses abbreviations / acronyms, such as 'PMH', 'PROMS', 'CTU and 'UCL' and terms, such as 'sponsor' and 'platform trials' which may be confusing for participants and requested that all abbreviations / acronyms are written in long form in the first instance and medical terminology is simplified into plain English for a lay audience.
- The NREC-CT noted that pg. 4 of the Main PISCF states that participants are to undergo a 'physical exam' and requested that a clear explanation of what is involved in a physical exam is clearly explained in the PISCF.
- The NREC-CT noted that pg. 53, section 12.3 of the master protocol states that that participants lacking decision making capacity may be recruited to the trial, yet this has not been included in the PISCF and requested clarification as to whether participants lacking decision making capacity will be recruited in Ireland.
- The NREC-CT noted that pg. 19 of the Main PISCF includes a translator signature and requested that this is removed in instances where a translator is not required.
- The NREC-CT noted that the Main PISCF references the FDA when referring to regulators and requested that this is changed to the EMA, where relevant.
- The NREC-CT requested that a lay summary PIL is made available 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 noted that the footnote on the Main PISCF references 'STRIVE Trial 2 Pregnant Partner IS-ICF' and requested that this is corrected.
- The NREC-CT noted that pg. 4 of the Main PISCF mentions future research in a table without a prior description of future research or that future research is optional and requested that future research is described in a section before the table, and it is made clear that it is optional.
- The NREC-CT noted that pg. 14, section 8 of the Main PISCF states 'we will keep your personal data for 25 years. This may mean that some information is held for longer than other information' and requested that the maximum retention periods for all data are clearly stated in the PISCF.
- The NREC-CT commended the applicant for the quality of the flip book but noted that it presents the trial in an overly positive manner and requested that participants are also advised that participating in the trial might not make a difference to their condition.
- The NREC-CT noted that pg. 17 of the flipbook states that NREC may be able to see personal information and requested that this is removed.
- The NREC-CT noted that pg. 8 of the Genomics PISCF states that participants must write a letter to the PI to withdraw from the study and requested that this is removed, as it places an additional barrier on participants to withdraw from the study.
- The NREC-CT noted that pg. 2 of the Genomics PISCF states that Ownership of blood sample will "become the property of INSIGHT" and requested that this is removed, as it does not tally with the right to withdraw.
- The NREC-CT noted that pg. 1 of the Genomics PISCF includes the following text "International Strategic Initiatives in Global HIV Trials" which may be distressing /

confusing for participants and requested that it is clarified in the PISCF why the 'International Strategic Initiatives in Global HIV Trials' are involved in the study when it is not a HIV research study.

- The NREC-CT noted that pg. 3 of the Genomics PISCF states that blood samples will be stored 'for as long as funding is available for storage and testing' and requested that the maximum retention periods that samples will be stored for is clearly stated in the Genomics PISCF.
- The NREC-CT requested that the destruction procedure for samples and the underlying data is clearly stated in the Genomics PISCF once the retention period has ended.
- The NREC-CT noted that pg. 9 of the PISCF states that 'the study will provide some funding towards the costs of travelling to clinic appointments on Day 14 where you will be asked to attend in person only because of the study, which would not happen if you were being treated outside of the study'. The Committee requested confirmation that participants will be reimbursed for all reasonable out of pocket expenses, including travel and meals / light refreshments and that this is clearly explained in the PISCF.
- The NREC-CT requested that the process for claiming reimbursement is clearly stated in the PISCF.
- The NREC-CT noted the Dr O'Halloran has declared an interest in that she was given a grant by Janssen for an unrelated study and requested clarification for this declaration, specifically clarification as to whether Janssen is involved in the STRIVE trial.

2022-500121-33-01

Principal Investigators & Institutions: Cork University Hospital (Prof. Michael Clarkson)

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

EudraCT: 2022-500121-33-01

- **NREC-CT comments:**

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

- **NREC-CT Decision:**

- Request for more information

- **Additional Information Required**

- The NREC-CT requested clarification on whether samples are to be retained for future use, with discrepancies noted between Sections 4.0, 4.2 and 4.8 of Compliance on use of Biological Samples. The Sponsor is requested to update this template with this clarification, and to reflect any updates in the relevant participant-facing documents as

appropriate and taking into account local regulations (including the Health Research Regulations 2018) and best practice.

- The NREC-CT noted that participants are reimbursed for travel expenses but not for meals / light refreshments and requested that participants are also reimbursed for meals / light refreshments. This should also be updated in the PISCF.
- The NREC-CT noted that participants may be approached to participate in the study after they present in emergency care and requested clarification on when potential participants will be approached for recruitment to the study. The Committee also requested clarification on whether potential participants will be approached for consent if they are acutely unwell at the time of recruitment.
- The NREC-CT requested that it is clarified in the PISCF when the questionnaires will be administered.
- The NREC-CT noted the section for Participant ID to be recorded on the PISCF and commented that the inclusion of this information would make the PISCF a linking sheet and would compromise pseudonymization of the participant data. The NREC-CT requested that the Participant ID number is removed (or redacted if applicable) on copies of the PISCF and confirmation is provided that the Participant ID number will only to be recorded on the site/master file PISCF copy. Specifically, the Participant ID should not be recorded (or else redacted) on the copy that is placed in the medical record file, to maintain pseudonymization of trial data.
- The NREC-CT noted that there is conflicting information provided on pg. 6 of the DPIA, pg. 8 of the PISCF and on pg. 3 of the Compliance on Biological Samples form regarding maximum retention periods for data, including biological samples and requested that the maximum data retention periods are clearly stated and aligned across all relevant documents.
- The NREC-CT noted that pg. 8 of the Main PISCF states that ‘anonymized samples will be used for methodology development’ and requested that the term ‘methodology development’ is clarified in the PISCF, so participants are fully informed as to what will happen to their anonymized samples.
- The NREC-CT noted that participants are to undergo PROMIS-29 questionnaire and requested details of the provisions in place, including referral pathways, should the questionnaire indicate a mental health issue is clearly described in the PISCF.
- The NREC-CT noted that the consent items on pg. 11 of the PISCF are bundled and requested that a tiered / unbundled approach to consent is used in all PISCF forms, in that each consent item is listed (it is not sufficient to say ‘’to that information about me is handled as described in this information,’ consent must be specific with each item listed). A box for participants to provide their initials must be included alongside each consent item. Please see: HSE National Policy for Consent in Health and Social Care Research (V1.1, 2023) https://hseresearch.ie/wp-content/uploads/2023/02/HSE-National-Policy-for-Consent-in-Health-and-Social-Care-Research-compressed.pdf
- The NREC-CT noted that pg. 8 of the main PISCF and pg., 2 of the Pregnancy Follow Up PISCF states that NREC will have access to participants medical records and requested that this is removed, as NREC do not have access to participants medical records.

- The NREC-CT noted that pg. 11 of the PISCF states '…can stop my participation in the clinical trial without my decision affecting my future medical care', whereas pg. noted that this is not the case for participants who receive imlifidase, as described on pg. 4 of the PISCF. The Sponsor is requested to amend the PISCF to take the potential risks of taking imlifidase into account.
- The NREC-CT requested reassurance that the consent for data collection on behalf of the newborn as described on pg. 9, section 9.4 of the Protocol_Summary of changes v3 to v4, and pg.1 sections 3 of the L1_SIS and ICF_IE_Pregnancy follow-up is carried out in line with Irish regulations and best practice. Please see: pgs. 58 & 59 of the 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

22-NREC-CT-138_Mod-3

Principal Investigator: Dr Philip Murphy

Study title: A Phase 3 Open-Label, Randomized Study of LOXO-305 versus Investigator's Choice of Idelalisib plus Rituximab or Bendamustine plus Rituximab in BTK Inhibitor Pretreated Chronic Lymphocytic Leukemia/Small Lymphocytic Lymphoma (BRUIN CLL-321)

EudraCT: 2020-004554-30

- **NREC-CT comments:**

- The NREC-CT B agreed that it was unable to give a favourable ethics opinion.

- **NREC-CT Decision:**

- Unfavourable

- **Key Reasons for Unfavourable Decision**

- The NREC-CT were unable to adequately assess the substantial amendment based on the information provided by the Sponsor. The Committee requested that the entire submission undergoes review and revision before resubmission. The NREC-CT noted the following:
    - The Cover Letter and Application Form did not provide a clear description of the SM under review.
    - The PISCF was deemed inadequate and did not provide the required clear and accessible information to participants, particularly in relation to consent for future research.
- The NREC-CT requested that all study documents are proofread for accuracy and the submission is presented in a coherent format.

- For any future submission, the following is recommended:
    - the cover letter clearly states the nature of the SM and provides justification for the proposed changes.
    - the SM is clearly described in the application form.
    - All submitted documents should be listed in the cover letter as ‘for review’, ‘for notification’ (in the case of a non-substantial modification) or ‘for reference’.
    - The main and optional future research PISCFs are presented in an accessible plain language format for participants to be able to comprehend and make an informed decision about trial participation and in line with regulations and best practice, the Data Protection Act 2018 (Section 36(2)) (Health Research) Regulations 2018), the HSE National Policy for Consent in Health and Social Care Research and ICG-GCP.
    - Mandatory and exploratory research are clearly defined and described in the PISCF in line with regulations. For guidance, please see the HSE National Policy for Consent in Health and Social Care Research (V1.1, 2023).
- The following information in relation to the Happify app is added to the PISCF:
    - justification for the use of this App
    - details of the data protection / data security arrangements in place for participants using the app are explained in the PISCF.
    - details of the training provided for participants is described in the PISCF.
    - details of the referral pathways in place should the app indicate a mental health issue.
    - details of how participants who do not have a smart phone will be accommodated is described in the PISCF.
- The NREC-CT recommends that any aspect of the substantial amendment that requires imminent approval for the trial to continue is separated out, resubmitted in a clear and coherent format that can be assessed by Committee members and marked as urgent in the subject line.

22-NREC-CT-173_Mod-1

Principal Investigator: Prof. Bryan Hennessy

Study title: Single arm phase 2 trial of neoadjuvant trastuzumab deruxtecan (T-DXd) with response directed definitive therapy in early stage HER2- positive breast cancer:. a standard chemotherapy-sparing approach to curativeintent treatment – SHAMROCK study

EudraCT: 2022-002485-32

- **NREC-CT comments:**

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

- **NREC-CT Decision:**

- Request for more information

- **Additional Information Required**

- The The NREC-CT requested that the reference to NREC accessing medical records is removed from the PISCF as NREC do not have access to medical records.
- The NREC-CT requested clarification as to whether participants will be given the results of scans and tests carried out during the study and that this explained in the PISCF.
- The NREC-CT noted that only participants in Beaumont Hospital will undergo additional biopsies (PISCF pg. 13 & 24) and requested that it is clarified in the PISCF why these additional biopsies are being carried out in Beaumont Hospital only.
- The NREC-CT note that pg. 30 of the PISCF states '*In the event that you do not attend scheduled visits, your study doctor will contact you, or your named next of kin, or your General Practitioner to obtain follow-up information'* and requested that this is changed to '*In the event that you do not attend scheduled visits, your study doctor will contact you, or your named next of kin, or your General Practitioner to ascertain if you are intending on continuing in the trial'*.
- The NREC-CT noted that it is not clear in pg. 48 of the Protocol whether radiotherapy is part of SoC treatment or as a result of trial involvement and requested that it is clearly stated in the PISCF whether radiotherapy is part of SoC, and if any radiotherapy will be administered as a result of trial participation.
- Furthermore, if participants are to be exposed to radiation above the SoC then this needs to be explained in the PISCF.

- AOB: N/A