National Research Ethics Committee

NREC-CT Meeting

17 Jan 2024

Attendance

Name	Role
Dr Cliona McGovern	Chairperson, NREC-CT B
Dr John Hayden	Deputy Chairperson, NREC CT-B
Prof Colm O'Donnell	Deputy Chairperson, NREC-CT B
Prof Seamus O'Reilly	Committee Member, NREC-CT B
Prof Catherine Hayes	Committee Member, NREC-CT B
Prof Michaela Higgins	Committee Member, NREC-CT B
Dr Andrew Lindsay	Committee Member, NREC-CT B
Ms Evelyn O'Shea	Committee Member, NREC-CT B
Dr Niall McGuinness	Committee Member, NREC-CT B
Prof Abhay Pandit	Committee Member, NREC-CT B
Dr Katherine Benson	Committee Member, NREC-CT B
Prof John Wells	Committee Member, NREC-CT B
Ms Ann Twomey	Committee Member, NREC-CT B
Mrs Jasmine Joseph	Committee Member, NREC-CT B
Ms Serena Bennett	Committee Member, NREC-CT B
Ms Aileen Sheehy	Programme Manager, National Office for RECs
Dr Susan Quinn	Programme Officer, National Office for RECs
Dr Laura Mackey	Programme Officer, National Office for RECs
Dr Jane Bryant	Project Officer, National Office for RECs
Ms Megan O'Neill*	Project Officer, National Office for RECs

Apologies: Prof Michaela Higgins, Prof John Wells

Quorum for decisions: Yes

Agenda

- Welcome & Apologies
- 2022-501606-35-01
- 2023-503614-80-00
- 2022-501463-40-01
- 2022-500395-57-00
- 21-NREC-CT-089_Mod-6
- AOB

- The Chair welcomed the NREC-CT B.
  - The minutes from the previous NREC-CT B meeting on 21 January 2024 were approved.
  - The NREC Business Report was discussed and noted.

Applications

2022-501606-35-01

Principal Investigators & Institutions: Cork University Hospital (Dr Dearbhaile Collins), University Hospital Waterford (Dr Paula Calvert), University Hospital Galway (Dr Michael McCarthy), Bon Secours Hospital Cork (Prof. Conleth Murphy), St James's Hospital (Prof Karen Cadoo), Sligo University Hospital (Dr Lore Komanyane), Beaumont Hospital (Dr Megan Greally)

Study title: Randomized, multicenter, open-label, Phase 3 study of mirvetuximab soravtansine in combination with bevacizumab versus bevacizumab alone as maintenance therapy for patients with FRα-high recurrent platinum-sensitive epithelial ovarian, fallopian tube, or primary peritoneal cancers who have not progressed after second-line platinum-based chemotherapy plus bevacizumab (GLORIOSA)

EudraCT: 2022-501606-35-01

NREC-CT Decision:

- Request for more information

Additional Information Required:

Part II

- The NREC-CT noted that participants will not be compensated for accommodation and meal expenses, and that carers will not be reimbursed. The NREC-CT recommended that such out-of-pocket expenses are captured in the PIS. If this is not possible, the NREC-CT requested justification for this and that this is set out clearly in the PIS.
- The NREC-CT requested further details of the process for participants to obtain reimbursement, and ask that these details are provided in the PIS.
- The NREC-CT requested that where relevant advice regarding contraception is set out clearly in the PISCF as the risks to a pregnant participant and their child are not known.
- The NREC-CT considered that information provided on COVID-19 in the patient materials may be outdated. The NREC-CT requested that Exhibit 2 (Supplementary Subject Informed Consent to Enable Remote Data Verification) of the Main PISCF is updated to reflect the current processes in place in the context of COVID-19. Remote data verification may be required, however it should not be specified or limited to the COVID-19 pandemic.
- The NREC-CT noted that the Main PIS describes optional future research that pertains to ovarian cancer. The NREC-CT requested that this is specified in the informed consent for optional future research.
- The NREC-CT noted the following statement on pg.18 of the Main PISCF regarding Optional Consent for Conduct of Secondary Research; “In the context of future research, Sponsor may share your Coded Data with other researchers or partners, such as companion diagnostics companies, to better understand your disease and develop new tests or therapies for the treatment of cancer.” The NREC-CT requested that this is modified to specify ovarian cancer.
- The NREC-CT noted that the participants’ samples “may be stored and analysed at other 3rd party vendors engaged by the Sponsor that are not listed here”. These 3rd party vendors must be specified in the PIL.
- The NREC-CT noted in the Main PISCF and Pre-Screening PISCF, the consent form limits future use to coded data but the information in the PISCF covers the use coded data and patient samples. The NREC-CT requested clarity over this point.
- The NREC-CT’s position is that any future research that uses the coded data or samples from participants require the approval of an Ethics Committee. The NREC-CT requested that this is captured in all the relevant PISCFs.
- The NREC-CT requested that the Pre-Screening PISCF is modified to provide further specific details of the future use of participants’ samples and data.
- The NREC-CT noted that some of the language used in the Pre-screening PISCF does not reflect the process of pre-screening e.g. ‘I voluntarily agree to be part of this research

study'. The Committee requested that the Pre-Screening PISCF is updated and tailored in certain sections to align with the purpose of the document i.e. to determine eligibility.

- The NREC-CT noted the following statement regarding Use of Remaining Samples (pg.3 of the Pre-Screening PISCF); "This will allow Sponsor and other research centres to better understand ovarian cancer, how MIRV works, and to be able to find the best way to treat patients with ovarian cancer or other cancers." Please specify the other cancers.
- Similarly, the NREC-CT requested that pg.12 of the Pre-Screening PISCF is updated to specify the "other cancers".
- The Pre-Screening PISCF indicates that samples will initially be sent to and stored in CellCartaNV, Belgium but may be transferred to, tested at or stored at other third-party testing labs or facilities. The NREC-CT requested that these third-party labs or facilities are specified in the Pre-Screening PISCF.
- The NREC-CT noted that the duration of the follow-up study has not been given in the Pregnancy Follow-Up PISCF. The NREC-CT requested that the cut-off date for data collection in the pregnancy follow-up study is specified in the Pregnancy Follow-Up PISCF.
- The NREC-CT requested that pg.26 of the Run-In Study PISCF is updated to specify the "other cancers" that the optional future research may include.
- The NREC-CT noted that the GCP certification for Dr Paula Calvert is dated 21st October 2020. The NREC-CT requested that an updated GCP certificate is submitted.

2023-503614-80-00

Principal Investigators & Institutions: Mater Misericordiae University Hospital (Prof. Sean Gaine)

Study title: A Phase 3, Randomized, Double-Blind, Placebo-Controlled Study to Evaluate the Efficacy and Safety of Oral Inhalation of Seralutinib for the Treatment of Pulmonary Arterial Hypertension (PAH)

EudraCT: 2023-503614-80-00

NREC-CT Decision:

- Request for more information

Additional Information Required:

Part II

- The NREC-CT noted that the collection, storage and future use of human biological samples form refers to the use of a "third party biorepository vendor" in sections 3.2 and 4.3. The NREC-CT requested clarification of whether this is a biobank and request that the documentation is updated accordingly.

- The NREC-CT noted that the declaration states ‘samples from analysis may be destroyed’. The Committee requested that the wording is changed to confirm that samples will not be kept beyond the retention period and will be destroyed at that point.
- The NREC-CT noted that study staff may access the participant’s medical chart if they cannot make follow-up telephone calls, as described on pg.6 of the Main PISCF. This should be modified to clarify the distinction between participants who have been lost to follow-up and those that have withdrawn from the study. The NREC-CT requested assurance that if participants have withdrawn from the study their personal medical records would no longer be accessible to the study team without their explicit consent.
- The NREC-CT noted the processes in place for an impartial witness to engage in the informed consent procedure as described in Section 4.0 of the Recruitment and informed consent procedure form however it is not captured in the participant materials. The NREC-CT requested that this is provisioned for in the Main ICF and the Pharmacogenetics ICF.
- The NREC-CT requested that whole genome sequencing is explained in the Pharmacogenetics ICF. Information should also be given to explain what genomic sequencing will be performed if not whole genome sequencing.
- The NREC-CT noted that the Main ICF states (pg.4) “The assessment of biomarkers in this study includes an optional test to see if there are any variations in your genes (pharmacogenetics)”. Pg.8 of the Main ICF specifically distinguishes between ‘biomarkers’ (i.e. RNA tests [proteomics & transcriptomics) and ‘pharmacogenetics’ (i.e. DNA tests) and has a separate ICF for pharmacogenetics. The NREC-CT requested clarification of what is being consented to with regard to RNA & DNA testing as optional and mandatory.
- The NREC-CT noted the following statement in the Main ICF; “Study data, including your coded medical information, may be retained and later used for further research into your medical indication, unless you object.” It is not clear whether this future research is separate to the sample’s additional research and pharmacogenetic research. The NREC-CT requested that it is clarified and that the scope of this research is set out clearly in the PISCF. The NREC-CT also requested that the phrasing of this consent item in the ICF is modified so that participants may opt-in, in line with GDPR, and not opt-out (“unless you object”). If the research team do plan to use biological samples for future research, broad consent must be obtained in line with requirements under the Health Research Regulations 2018 and participants must be made aware that any future research using the participants data or samples will be assessed by an Ethics Committee.
- The NREC-CT noted that information including the participant’s race and ethnicity will be collected as part of the study procedure, as described in both the Main PISCF and Pregnant Partner PISCF. Justification under GPDR for the collection of this special category data must be provided to the participants in the PISCF.
- The NREC-CT noted that the Main PISCF (pg.20) states that samples will be stored in a laboratory in Belgium, however the Use of Biological Samples Declaration (pg.4) states that samples will “then with the third party biorepository vendor located in the United States.” The NREC-CT requested that this is clarified and that the documentation is updated accordingly to reflect this.

- The NREC-CT requested that clarification is provided regarding the transfer of participant's data for payments made through Greenphire, whether this data will be transferred to the UK or the US and the protections in place for this.
- The NREC-CT appreciate that participants will be reimbursed for expenses, however the Committee request that the amount of money available for reimbursement is not specified in the recruitment and participant materials.

2022-501463-40-01

Principal Investigators & Institutions: St Vincent's University Hospital (Prof Sean McDermott), Cork University Hospital (Dr Derek Power), St James's Hospital (Prof. Maeve Lowery)

Study title: An Open-Label Early Access Phase 3b Study of Ivosidenib in Patients With a Pretreated Locally Advanced or Metastatic Cholangiocarcinoma

EudraCT: 2022-501463-40-01

NREC-CT Decision:

- Request for more information

Additional Information Required:

Part I

- A Steering Committee was due to be established for this study. What is the update to the status of the Steering Committee establishment?

Part II

- The NREC-CT requested assurance that the insurance policy provided would be extended to cover the entirety of the study period.
- The NREC-CT noted that the Sponsor may transfer or share samples "with its delegates, partners and/or other investigators inside or outside the European Economic Area (EEA)", as set out in sections 4.5 and 4.9 of the Compliance with Member State Applicable Rules for the Collection, Storage, and Future Use of Human Biological Samples form. This information should be set out clearly in the PISCF and the NREC-CT requested that it is updated accordingly.
- The NREC-CT noted that two questionnaires have been submitted that participants will complete. These questionnaires appear to be completed via an online app, however the Main PISCF (pg.4) states that these are received at the study centre. The NREC-CT requested clarification of where this activity takes place and that it is described clearly in the PISCF.
- Considering the following statement: "Your GP or the study doctor can answer any questions that you have about other treatments", the NREC-CT noted that a sample of the GP letter had not been submitted for review. The NREC-CT requested clarification as

to whether such a letter will be sent to participants' GPs. If so, NREC-CT requested that it is submitted for review.

- The NREC-CT noted that tumor assessments or evaluations will be conducted according to local standards as described in the Main PISCF and requested that what is entailed and the frequency of these assessments is further elucidated in the PISCF.
- The NREC-CT noted that candidates who do not meet the inclusion criteria at their first screening could be screened again at the discretion of the PI. The NREC-CT requested that this is set out in the PISCF.
- The NREC-CT requested that the wording on pg.3 of the Main PISCF, "to know about anticancer therapies that you could have taken", is reworded to make it clearer for participants what is involved.
- The NRECT-CT noted that participants' study information of data may be sent to other countries and requested that it is clearly defined in the PISCF which countries these are, in addition to whether they are inside or outside the European Economic Area (EEA).
- The NREC-CT requested that the language on pg.4 of the Main PISCF, detailing the blood and urine samples collected for laboratory tests, is reconsidered so it is clear to participants what is required. The statement regarding the "amount of blood given for a typical blood donation" may lead to misinterpretation by participants that a blood donation is required.
- The NREC-CT noted that the table on pg.6 of the Main PISCF detailing the schedule of activities is from the protocol and requested that is modified for a layperson to understand.
- The NREC-CT requested that the term "overall survival follow up" used in the table on pg.6 of the Main PISCF is amended with more sensitive language.
- The NREC-CT requested that the language on pg.10 of the Main PISCF (What if I get harmed or injured during the study?) is simplified. The NREC-CT requested that the language is modified to clearly set out what is and what is not covered by the Sponsor's compensation.

2022-500395-57-00

Principal Investigators & Institutions: St James's Hospital (Dr Cliona Grant)

Study title: A Phase 3, Randomized, Double-blind, Placebo-controlled Study to Evaluate Pembrolizumab Versus Placebo as Adjuvant Therapy Following Surgery and Radiation in Participants with High-risk Locally Advanced Cutaneous Squamous Cell Carcinoma (LA cSCC) (KEYNOTE-630)

EudraCT: 2022-500395-57-00

NREC-CT Decision:

- Request for more information

Additional Information Required:

Part I

- The Summary of Changes table given in the Protocol included tracked changes to the initial Summary of Changes table in addition to an "Additional Changes" table. It was difficult to discern the changes between these two tables spread out over a number of pages. Please consider an alternative format to present these modifications going forward.

Part II

- The NREC-CT noted that pg.5 of the Main PISCF describes the procedure for pregnancy testing under Treatment Visits as follows; "To perform a pregnancy test if you are a woman able to have children. This test will be done at your hospital." The NREC-CT requested that this is modified to align with Section 10.7.3 of the protocol which states that "monthly pregnancy testing throughout study treatment and at end of treatment is required for women of childbearing potential." Information about how this will be conducted should also be given in the Main PISCF.
- The NREC-CT noted that Section 8.1.13 of the protocol states "If the participant provides documented informed consent for Future Biomedical Research, any leftover tissue that would ordinarily be discarded at the end of the main study will be retained for Future Biomedical Research". The NREC-CT requested that the Main PISCF is modified to inform participants of this.

21-NREC-CT-089_Mod-6

Principal Investigators & Institutions: Cork University Hospital (Dr Dearbhaile Collins), St James's Hospital

Study title: A Randomized, Phase 3, Double-Blind Study of Chemoradiotherapy With or Without Pembrolizumab for the Treatment of High-risk, Locally Advanced Cervical Cancer (KEYNOTE-A18 / ENGOT-cx11/ GOG-3047)

EudraCT: 2019-003152-37

NREC-CT Decision:

- Favourable

- AOB:
  - None