National Research Ethics Committee

NREC-CT A Meeting

07 December 2022

Attendance

Name	Role
Prof. Alistair Nichol	Chairperson, NREC-CT A
Ms. Erica Bennett	Committee Member, NREC-CT A
Prof. Tina Hickey	Committee Member, NREC-CT A
Dr Dervla Kelly	Committee Member, NREC-CT A
Ms Muireann O'Briain	Committee Member, NREC-CT A
Prof. David Brayden	Committee Member, NREC-CT A
Dr Darren Dahly	Committee Member, NREC-CT A
Prof. Gene Dempsey	Committee Member, NREC-CT A
Prof. Donal Brennan	Committee Member, NREC-CT A
Prof. Austin Duffy	Committee Member, NREC-CT A
Dr Geraldine Foley	Committee Member, NREC-CT A
Ms Evelyn O'Shea	Committee Member, NREC-CT A
Dr Emily Vereker	Acting Head, National Office for RECs
Ms Patricia Kenny	Project Officer, National Office for RECs
Dr Jane Bryant	Programme Officer, National Office for RECs
Dr Anne Costello	Programme Manager, National Office for RECs
Dr Susan Quinn	Programme Manager, National Office for RECs
Dr Emma Heffernan*	Project Officer, National Office for RECs

Apologies: Dr Heike Felzmann, Dr John O'Loughlin, Mr Gerard Daly, Prof. Catherine Hayes, Ms Evelyn O'Shea, Mr Gerald Eastwood, Prof. Patrick Dillon, Prof. John Wells, Dr Jimmy Devins, Ms Ann Twomey, Prof. Mary Donnelly

Quorum for decisions: Yes

Agenda

- Welcome & Apologies
- 22-NREC-CT-180
- 22-NREC-CT-181
- 22-NREC-CT-177
- 22-NREC-CT-178
- AOB

- The Chair welcomed the NREC-CT A.
  - The minutes from the previous NREC-CT A meeting on 09 November 2022 were approved.
  - The NREC Business Report was discussed and noted.

Applications

22-NREC-CT-180

Principal Investigator: Prof John Reynolds

Study title: NEoadjuvant chemoradiotherapy for Esophageal squamous cell carcinoma versus Definitive chemoradiotherapy with salvage Surgery as needed (NEEDS Trial)

EudraCT: 2020-000149-15

Lead institution: St. James's Hospital

  - NREC-CT comments:
- The NREC-CT A 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

- It was noted during the discussion that the standard of care for these patients continues to evolve with recent data suggesting a role for immune checkpoint inhibitors, in particular nivolumab. The NREC-CT acknowledges issues related to patient access of new and promising drugs but do request clarification on whether participation in this clinical trial would preclude patients accessing any available compassionate access programs for immunotherapy.
- Furthermore, the NREC-CT requested clarification as to the process which would be followed for participants on this trial, if immunotherapy was to become standard of care in Ireland during the course of the study.
- The NREC-CT notes that private patients are advised to contact their insurer about the trial. The Committee recommended that the participants are provided with a letter by the investigators relaying the exact information required, which can be provided to their insurer.
- The NREC-CT noted that the PISCF was very complex with technical language, which was considered unreadable in parts, and requests the following:
    - That the document is restructured and undergoes considerable revisions, to improve accessibility.
    - That the applicant seeks the involvement of a public or patient reviewer/PPI in the restructuring of participant materials to ensure that they are accessible.
    - That the applicant considers where lay language could be used, and whether e.g., doses of radiation are required, such as in this statement: “For the Control arm, patients will receive Neoadjuvant Chemoradiotherapy, with weekly carboplatin and paclitaxel and radiation in 1.8 fractions to 41.4 Gy followed by pre-planned oesophagectomy.”
- The NREC-CT requested confirmation as to the pathway of care for participants who score highly on the QoL questionnaires, or who may experience distress answering the questions posed which include reference to anxiety, depression, feeling less attractive etc.
- The NREC-CT considered the GP letter to be overly long, and requested that it be clarified to the GP what role (if any), they may have in side effect management and participant comfort while under their care, including what medication can be prescribed by the GP
- The NREC-CT noted that data will be kept for by Karolinska hospital for “At least 25 years“ and requested that the length of time data will be stored for is clearly stated.

22-NREC-CT-181

Principal Investigator: Dr Eugene Ng

Study title: ORACLE: A long-term follow-up study to evaluate the safety and durability of GT005 in participants with geographic atrophy, secondary to age-related macular degeneration treated in a Gyroscope-sponsored antecedent study.

EudraCT: 2020-003987-22

Lead institution: UPMC Whitfield Hospital

- NREC-CT comments:

- The NREC-CT A 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 A asked that the study team ensure the participants are aware they are not obliged to continue into this study and to ensure that the approach at the last site visit by a study team member who is familiar to the participant does not create any aspect of coercion to participate.
- The NREC-CT A requested confirmation as to the pathway of support which will be provided to participants who experience distress when completing the Visual Function Questionnaire which includes references to embarrassment of self and giving up driving etc.
- The NREC-CT A noted that the Participant Information Leaflet (PIL) is very well written. The Committee recommended that a recorded version of the PIL could be made available, due to participants on the trial having reduced visual function.
- The NREC-CT A requested explanations are provided in the PIL for the tests “Colour fundus photography” and “fundus autofluorescence”. The Committee requested that the word antecedent should be replaced with previous.
- The NREC-CT A requested that *Section G: Are there alternative treatments?* is reworded as it may be confusing to participants: “There are currently no approved therapies for GA secondary to AMD” which is followed by “You may also choose to discuss alternative therapies for GA with the study doctor”.
- The NREC-CT A noted that as there are several tests detailed at each visit, it would be helpful to participants to indicate how long will each visit is expected to take

- The NREC-CT A recommended that all patient facing material have enlarged font, including the Scout Clinical Informed Consent Form. The NREC-CT A deemed that the financial compensation arrangements were excellent in this study.

22-NREC-CT-177

Principal Investigator: Dr Jarushka Naidoo

Study title: A Phase II, Open-label, Multicentre, Randomised Study of Neoadjuvant and Adjuvant Treatment in Patients with Resectable, Early-stage (II to IIIB) Non-small Cell Lung Cancer (NeoCOAST-2)

EudraCT: 2021-003369-37

Lead institution: Beaumont Hospital

- NREC-CT comments:

- The NREC-CT A 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 noted that the study design diagram on pg. 2 of the Safety Management Plan does not include Arm 3 of the trial and requested that this is corrected.
- The NREC-CT noted discrepancies in the number of participants anticipated to be recruited to the trial in Ireland and requested that this is clarified and harmonised across all documentation.
- The NREC-CT noted reference to 'NHS Trust' in several documents and requested that these are removed, and all documents instead include relevant Irish references.
- The NREC-CT deemed in the PISCF to be overly long, too technical, and poorly written in parts and requested that this document is thoroughly revised. The NREC-CT suggested that the PISCF would benefit from PPI input. The following guidelines may be of benefit in drafting a PISCF: https://www.nrecoffice.ie/pil-summary-guidance/
- The NREC-CT requested reference to GDPR, and the Data Protection Act 2018 (Section 36(2)) (Health Research) Regulations 2018 is added to the PISCF regarding the legal basis for data use.
- The NREC-CT noted that is not clear from the submitted documentation which specific genetic analyses are essential (i.e., required for enrolment into the trial) and which are

optional - pg. 13/14 of the Application Form specifically references *'essential'* genetic analyses that *'may involve all or part of participant genetic information'*, whereas the DPIA seems to indicate that all genetic analyses are optional.

- The NREC-CT requests that is clarified which genetic tests are mandatory for trial participation and which are optional, and that this is clearly explained in the PISCF.
    - Furthermore, the NREC-CT requested that detail is provided as to which specific procedures, and the specific genetic information associated with them is elucidated in the PISCF.
- The NREC-CT deemed that the further use of genetic information is considered too vague. The NREC-CT notes that seeking consent for future use of samples / data, for unspecified purposes, without further 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 notes i) that consent for future use of samples must be 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 v) that subsequent research ethics review will be sought for specific research once clearly defined
- The NREC-CT noted that pg.14 of the ICF states that *'the analysis will be part of your coded data which will also include genetic data'* and requested that participants are informed that genetic information can directly identify a person and their data cannot be considered truly anonymous/coded and this is elucidated the PIL.
    - Furthermore, the NREC-CT requested that analysis of genetic samples will not attempt to re-identify the data subject
- The NREC-CT noted that there is contradictory information on pg. 17 of the ICF regarding additional bio samples for future use and requested that this is corrected
- The NREC-CT noted that pg. 4 of the optional ICF references *'listed authorised people'* and requested that it clarified in the ICF who these people are.
- The NREC-CT noted that Pg.5 of the Pregnant Partner ICF includes the statement *'I agree that my and my baby's coded personal data can be used for other medical, healthcare, or scientific related research purposes'* and requested that further detail (if available) is provided in the ICF as to the nature of *'other medical, healthcare, or scientific related research'*. Please see point 3.4 above re consent for future use.
- The NREC-CT requested that a more detailed account of the suitability of the facilities and equipment available is provided in the SSA for Beaumont Hospital
- The NREC-CT requested a more detailed CV is provided for Dr Naidoo, detailing previous clinical trial experience and evidence of up-to-date ICH-GCP certification**.**
- The NREC-CT noted that the language suggests that participants *'may'* be reimbursed for trial related expenses and requested that this is more clearly stated as *'can'* or *'will',* so participants are reassured that trial participation will not leave them out of pocket

- The NREC-CT A requested a more detailed account of the compensation arrangements in place for participants is provided in the PISCF including information of the process involved in process involved in reimbursement of trial related expenses.

22-NREC-CT-178

Principal Investigator: Prof Sean Gaine

Study title: IMPAHCT-FUL: A Long-Term Extension, Multi-Center Safety Study of AV-101 in Subjects With Pulmonary Arterial Hypertension (PAH) Who Have Completed Study AV-101-002

EudraCT: 2021-006864-25

Lead institution: Mater Misericordiae University Hospital

- NREC-CT comments:

- The NREC-CT A 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 noted that participants are required to undergo right heart catheterisation as part of the trial and requested clarification if this procedure is additional to the Standard of Care. If this procedure is an addition to Standard of Care, then this needs to be elucidated in the PIL, with the risks of the procedure clearly highlighted to the participant.
- The NREC-CT deemed the PIL to be exceptionally long, overly complex, and with frequent use of abbreviations and legalistic language. The Committee requested that the PIL should be revised to be more patient-friendly and simplified into plain language for a lay audience.
- The NREC-CT noted that it is not made clear in the PIL why the extension study is being carried out and requested that this is clarified in the PIL at the outset.
- The NREC-CT requested that male participants are also given advice re pregnancy avoidance in the PIL
- The NREC-CT requested that the summary PIL states the potential side effects of the trial drug
- The NREC-CT requested that the importance of pregnancy avoidance is also mentioned in the summary PIL

- The NREC-CT requested that the pregnancy follow up PIL is amended to include pregnancy in female partners of male participants.
- Pg. 2 of the pregnancy follow up PIL states that *'there is a small risk of loss of confidentiality'* and requested that this is clarified
- Pg. 2 of the Withdrawal document states that *'if you withdraw consent from the study, information about your health status may be obtained from public records such as government vital statistics or obituaries, as allowed by local law'* and requested the reference to public records is clarified.
- The NREC-CT noted that the use and sharing of health data as described in the PIL is vague and requested that clarification as to how data will be used is clarified in the PIL.
- The NREC-CT requested it is made clear in the PIL, the process for revoking permission for use and sharing of data is outlined in the PIL.
- The NREC-CT noted that pg. 1 of the PIL states *"your study doctor is being paid by the study sponsor to perform this research study"* and requested further details of the financial arrangements between the sponsor and the PI.
- Furthermore, the NREC-CT requested that in the interest of full disclosure that this is made clear to participants before they consent to partake in the study
- The NREC-CT requested that it is outlined in the Application Form under potential conflict of interest if there be a financial link between the PI and the sponsor
- The NREC-CT noted that the Scout documents are not geared towards an Irish audience and requested the following:
- The NREC-CT A noted US centric terms such as *'ground transport'* requested the language in this document is adapted to an Irish audience
- The Scout policy document does not list Ireland as one of the participating European countries and requested that this is amended to include Ireland
- The Scout policy document does not include budgetary maximums and approval thresholds / per diem payments for Ireland and requested that this is amended to include Ireland.
- The NREC-CT noted that not all study visits are included and requested that this is amended to include all study related visits.
- The NREC-CT requested that the documents include Irish contact details
- The NREC-CT noted that participants are advised to check with their insurance company that participation in this trial will not affect their policy. NREC-CT requested that information regarding the potential impacts on personal health insurance is elucidated in the PIL.
    - The NREC-CT also requested that the sponsors provide a letter for participants to share with their insurance company detailing the pertinent information

- AOB: