National Research Ethics Committee

NREC-CT A Meeting

13 July 2022

Attendance

Name	Role
Prof. Alistair Nichol	Chairperson, NREC-CT A
Dr Heike Felzmann	Deputy Chairperson, NREC-CT A
Prof. Tina Hickey	Committee Member, NREC-CT A
Prof. John Wells	Committee Member, NREC-CT A
Prof. Catherine Hayes	Committee Member, NREC-CT A
Ms Muireann O'Briain	Committee Member, NREC-CT A
Prof. Patrick Dillon	Committee Member, NREC-CT A
Dr John O'Loughlin	Committee Member, NREC-CT A
Dr Darren Dahly	Committee Member, NREC-CT A
Prof. Donal Brennan	Committee Member, NREC-CT A
Mr Gerald Eastwood	Committee Member, NREC-CT A
Dr John O'Loughlin	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*	Project Officer, National Office for RECs
Dr Laura Mackey	Programme Officer, National Office for RECs
Dr Susan Quinn	Programme Officer, National Office for RECs
Dr Emma Heffernan*	Project Officer, National Office for RECs

*Drafted minutes

Apologies: Prof. Mary Donnelly, Ms. Erica Bennett, Ms Evelyn O'Shea, Ms Ann Twomey, Prof. Austin Duffy, Prof. Gene Dempsey, Dr Dervla Kelly, Dr Jimmy Devins, Dr Geraldine Foley, Prof. David Brayden, Mr Gerard Daly

Quorum for decisions: Yes

Agenda

- Welcome & Apologies
- 2022-501132-42-00
- 22-NREC-CT-116
- 22-NREC-CT-117
- AOB

- The Chair welcomed the NREC-CT A.
  - The minutes from the previous NREC-CT A meeting on 8th June 2022 were approved.
  - The NREC Business Report was discussed and noted.

Applications

2022-501132-42-00

Principal Investigators: Dr Aoife Cotter, Prof Eoin Feeney, Prof Fiona Lyons

Study title: Cohort study of human Monkeypox virus disease

Lead institutions: The Mater Hospital, St Vincent's University Hospital, St James's Hospital

- NREC-CT comments:

- The NREC-CT A noted that this application represents a cohort study of human Monkeypox virus disease
- 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 Further Information

- Further Information Requested:

- The Committee requested that a complete DPIA with DPO input is submitted via the CTIS system
- The Committee requested that further detail is provided in the DPIA regarding data security arrangements and additional controls which will be implemented when using email and OxFile for data transfer.
- The Committee requested that specific reference to the Irish Health Research Regulations (2018) is included in the DPIA
- The Committee requested that clarity is provided in the DPIA regarding third party data controller arrangements.
- The Committee noted that in the DPIA, it states that participant data will be collected daily. The Committee requested clarification on this - as to whether participant data is collected daily – or would be only collected daily from day 1-14, and then collected on days 21, 28, at 2 months and at 6 months.
- The Committee requested that reference to Irish Legislation is included in the submitted document regarding the collection, storage and future use of human biological samples.
- The Committee requested that information is provided regarding participant reimbursement.
- The Committee noted that the study insurance certificate provided expires in August 2022 and thus does not cover the whole trial duration and requests assurance that the trial will be adequately insured for the whole duration and will cover all sites.
- The Committee considered that the ICF aimed at age 6-10 is too technical for children of this age group and recommended that the under 6s form is used for this group.
- The Committee noted that the accompanying parent/guardian form details that assent forms are available up to the age of 12 years, however in Ireland Assent is required up to the age of 16 years and requested that this is corrected.

22-NREC-CT-116

Principal Investigator: Dr Adrian Murphy

Study title: An Open-label Randomized Phase 3 Study of Tucatinib in Combination with Trastuzumab and mFOLFOX6 versus mFOLFOX6 given with or without either Cetuximab or Bevacizumab as First-line Treatment for Subjects with HER2+ Metastatic Colorectal Cancer

Lead institution: Beaumont Hospital

EudraCT No.: 2021-002672-40

- NREC-CT comments:

- The Committee noted that this application represents an Open-label Randomized Phase 3 Study of Tucatinib in Combination with Trastuzumab and mFOLFOX6 versus mFOLFOX6 given with or without either Cetuximab or Bevacizumab as First-line Treatment for Subjects with HER2+ Metastatic Colorectal Cancer

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

- NREC-CT Decision:

Request for Further Information

- Further Information Requested:

- The Committee noted that the rational dosage of the study drug is dependent on the final results of the 1b/2 trial, and requested that once confirmation is received regarding final dosing, this information is communicated to the NREC
- The Committee noted that the participant will not have access to the trial treatment following the trial ending, and queried whether access to the study drug could be provided in circumstances where benefit is demonstrated
- The Committee had queries regarding standard of care (SOC) as follows:
    - Noting that crossover from the SOC control arm to the tucatinib experimental arm is not permitted on this trial, the Committee queried whether participants who receive SOC can subsequently be prescribed other HER2 targeting agents on progression. They recommended that the SOC control arm could include the option of prescription of Trastusimab (Herceptin) by the participant's oncologist. They also queried whether the clinician has equipoise in prescribing to these participants
    - The Committee requested that the lack of crossover from the control to the experimental arm is clearly highlighted to participants in the PIL.
- The Committee requested that the list of side effects of standard of care treatments are clearly highlighted to participants in the PIS/ICF as being specific to SOC
- The Committee requested that an additional sentence is added to the PIS/ICF to explain the significance of the statement "HER2 positive means that your cancer cells make extra amounts of a protein called HER2" (p.2 PIS/ICF)
- The Committee requested that further information is provided to participants in the second paragraph (p.2 PIS/ICF) regarding the mechanism of action of the study drug Tucatinib, in targeting HER2
- The Committee requested that the sentence "Your cancer cells make more HER2 than normal which can lead to cancer" (p.3 PIS/ICF) should be reworded to explain more clearly.
- The Committee requested that Clinical Trial Indemnity form is signed by the sponsor and clinical organisation

22-NREC-CT-117

Principal Investigator: Dr Anne Fortune

Study title: A Phase 3, Single-Arm, Open-Label, Multicenter Study to Evaluate the Safety and Efficacy of Tafasitamab Plus Lenalidomide in Participants with Relapsed or Refractory Diffuse Large B-Cell Lymphoma

Lead institution: Mater Hospital

EudraCT No.: 2021-006049-36

- NREC-CT comments:

- The NREC-CT A noted that this application represents a Phase 3, Single-Arm, Open-Label, Multicenter Study to Evaluate the Safety and Efficacy of Tafasitamab Plus Lenalidomide in Participants with Relapsed or Refractory Diffuse Large B-Cell Lymphoma
- 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 Further Information

- Further Information Requested:

- The Committee noted that the exclusion criteria of the study includes those with many co-morbidities, including 'psychiatric disease' (Protocol p.27), and requested that justification is provided for these exclusion criteria, given the level of co-morbidities which may be present in this participant group
- The Committee noted that at end of trial, continuation on the study drug is contingent on "local requirements and commercial availability" (Protocol p.39) and requested clarification about the specific criteria for determining availability and how likely they are to be met.
- The Committee requested that the PIS/ICF is revised to be in line with the Data Protection Act 2018 (Section 36(2)) (Health Research) Regulations 2018) as the legal bases for data processing does not include explicit consent (p.19 PIS/ICF).
- The Committee noted that the participants are requested to participate in genomic research in order to participate in the main trial. The Committee requested that this requirement for trial participation must be removed, and that separate consent must be provided for this future genomic research without any implications for trial participation.
- The Committee noted that as stated in the NREC Application form (p7) the participants in the study have a median survival rate of <1 year, and "The majority of patients will die from this disease". However, the box 'Adults who have a terminal illness' was not ticked in the application form under the section vulnerable participants. The Committee queried

whether this information could be provided sensitively to participants in the PIS/ICF, or if not, requested reassurance that the referring oncologist will discuss with the participants their options at this stage of progression of their disease, and why they are being recruited to this study.

- The Committee requested that the number of study visits is more explicitly stated, i.e. ~31 visits over 2 years.
- The Committee requested that further explanation is provided to participants in relation to some of the "Study Procedures" (p.4 PIS/ICF) which would not be readily understood by a lay person (e.g. Cytomegalovirus (CMV) test) and requested that a brief, plain English description be given for each procedure where it is not immediately obvious what is meant by the procedure name.
- The Committee requested clarity is provided to participants following the statement under 'Leaving the Study' (p.11 PIS/ICF) "Your personal data may in some circumstances continue to be processed". Can this be clarified, with examples of such circumstances.
- The Committee noted that a list of prohibited and permitted medicines must be included in the GP letter, rather than a ban on "any new drug or any therapy whether prescribed or OTC". Currently, the GP letter states that participants must "contact trial personnel" regarding any changes in treatment. The GP must be informed of side effects and have the ability to prescribe medications which could make symptoms or side-effects more comfortable for the participant.
- The Committee requested that a signed copy of the insurance certificate be provided.
- The Committee noted that indemnity forms for the 4 Irish sites (Mater, Vincents, Galway UH, Bon Secours Cork) are not counter signed by site CEO (documents 1.4(b), 1.5(b), 1.6(b), 1.7(b))
- The application form specifies the trial as lasting 30/9/22 to 30/10/26, but the Insurance certificate has the dates 01-May-2022 to 14-Jan-2027, but under 'Policy Expiry' it lists 02-01-2023. These inconsistencies need to be addressed.
- The Committee requested further clarity is provided regarding (p.18 PIS/ICF) - list of persons who may be "recipients of personal data" which includes the category "Payers" (commercial, private and governmental). Please provide further details, including under what Data Protection legislation are these transactions permitted.
- The Committee requested that the DPIA is revised and resubmitted. The Committee noted that parts of the form were incomplete, no risk assessment had been carried out, there were discrepancies between 'personal data'/ 'personally identifiable data', and there was a lack of clarity regarding access to data. Furthermore, there was not sufficient evident of DPO input into the DPIA.
- The Committee requested that regarding reimbursement, the PIS/ICF should state 'will be reimbursed', rather than 'may be… on provision of receipts'. Furthermore, the Committee requested that the PIS/ICF must include a paragraph that addresses how and at what intervals this repayment is to be administered, given the large number of visits involved for each participant, and the burden of collecting and organising multiple receipts for over 30 visits.

- AOB:

The Chair closed the meeting.