National Research Ethics Committee

NREC-CT Meeting

10 May 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 Lorna Fanning	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
Prof. Colm O'Donnell	Committee Member, NREC-CT B
Ms Mandy Daly	Committee Member, NREC-CT B
Prof Andrew Green	Committee Member, NREC-CT B
Ms Susan Kelly	Committee Member, NREC-CT B
Prof Seamus O'Reilly	Committee Member, NREC-CT B
Dr Christina Skourou	Committee Member, NREC-CT B
Ms Byrony Milner	Administrative Assistant, National Office for RECs
Rachel McDermott	Project Administrator, National Office for RECs
Dr Susan Quinn	Programme Officer, National Office for RECs
Dr Emma Heffernan*	Project Officer, National Office for RECs

Apologies: Prof Abhay Pandit, Dr Eimear McGlinchey, Ms Deirdre MacLoughlin, Ms Mandy Daly, Dr Mark Robinson

Quorum for decisions: Yes

Agenda

- Welcome & Apologies
- 2023-503209-13-00
- 2022-501417-31-01
- 21-NREC-CT-079_Mod-7
- 21-NREC-CT-177_Mod-3
- 22-NREC-CT-148_Mod-1
- 22-NREC-CT-007_Mod-3
- 22-NREC-CT-018_Mod-4
- 21-NREC-CT-021_Mod-4

- The Chair welcomed the NREC-CT B.
  - The minutes from the previous NREC-CT B meeting on 12 April 2023 were approved.
  - The NREC Business Report was discussed and noted.

Applications

2023-503209-13-00

Principal Investigator: Prof. Afif EL-Khuffash

Study title: Co-administration of Acetaminophen With Ibuprofen to Improve Duct-Related Outcomes in Extremely Premature Infants

EudraCT: 2023-503209-13-00

Lead institution: Rotunda Hospital

- **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. RFI

- **NREC-CT Decision:**

- Request for more information

- **Additional Information Required**

Part 1

- The Committee requested clarification regarding the sample size calculation and whether it is powered sufficiently to meet the trial objectives.
- The Committee noted that pg.21 of the protocol states that '*For families who refuse to participate in the study, consent will be sought to collect de-identified demographic and study outcome data during the NICU stay. This is important to collect to identify differences between recruited and not recruited patients and conform the representative nature of study population at the end of the trial. No data will be collected for patients in the absence of explicit signed consent'* and requested the following:
    - requested clarification as to how study outcome data will be collected from participants who refuse to participate in the trial, noting that in line with legislation and best practice, data cannot be collected from participants who refuse to take part in the trial. Please see HSE National Policy for Consent in Health and Social Care Research (2022)
    - confirmation that data will not be collected from participants who have not been consented to participate in the trial.

Part 2

- The Committee requested that medical terminology in the PISCF is explained using lay language, specifically the terms 'Ultrasound' and 'Drip' on pg. 4 of the PISCF and Intravenous, Plasma Acidity, Concomitantly and Flucloxacillin on pg. 6 of the PISCF.
- The Committee requested the statement on pg.8 of the PISCF regarding NREC being able to access the study data base is removed as NREC will not have access to the study database.
- The Committee requested the statement on pg. 12 of the PISCF regarding NREC being able to access to participant's medical records, as NREC do not have access to participant's medical records.
- The Committee noted that the protocol states that data will be collected from neonates enrolled in the trial, whereas the submitted PIL suggests that data will be collected from both the enrolled child and their parents/ guardians and requested the following:
- clarification as to whether data will be collected from parents / guardians.
- If data is to be collected from parents / guardians, then they will each need to separately sign an adult PISCF. This will need to be provided for NREC review.
- If data is being collected from parents / guardians, then the DPIA will need to be updated to take account of this and submitted for NREC review.
- The submitted PIL needs to be amended so that it is clear that this form is only to be used for enrolling the participating child in the trial and all references to collection of data from parents / guardians is removed (i.e., this PISCF should only reference 'your child's data' and not 'your data').

- The Committee requested that it is clarification how long data will be retained for and if data is to be used for secondary research, the process for obtaining consent for data processing from the neonates once they reach 18 years of age. Please see HSE National Policy for Consent in Health and Social Care Research (2022)

2022-501417-31-01

Principal Investigator: Prof. Fergal Kelleher

Study title: A Phase 3, Randomized, Double-blind, Active-Comparator-Controlled Clinical Study of Adjuvant MK-7684A (Vibostolimab with Pembrolizumab) Versus Adjuvant Pembrolizumab in Participants with High-risk Stage II-IV Melanoma (KEYVIBE-010)

EudraCT: 2022-501417-31-01

Lead institution: St James' 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**

Part 1

- Favourable / Favourable with conditions / Request for more information /Unfavourable
- There are concerns regarding the statistical design of the study. Specifically, that the trial was powered with 1 sided alpha, which may not be powered sufficiently to look for negative treatment outcome. A rationale is requested for use of this statistical method.
- There remain concerns regarding patient safety and quality of survival. More information is requested regarding how the study safety signals will be monitored, and regarding the duration of surveillance.
- The follow up of three months is deemed insufficient, and reassurance is requested that participants would be monitored for long term side effects.
- It is requested that data is provided on outcome, survival, quality of life and toxicity in previous melanoma study that included the combination MK-7684A.
- It is requested that rationale is provided for the number of participants, and the trial duration, based on the previous melanoma study.
- Clarification is requested as to whether any minors will be enrolled in this trial in any MSC, and if not, it is requested that the protocol is amended to remove these references.

Part 2

- The Committee expressed concerns regarding patient safety and quality of survival and deemed the response to the RFI request for safety data in the original submission as being inadequate. This has not been sufficiently addressed in the current submission. Further information is requested regarding long term safety monitoring.

21-NREC-CT-079_Mod-7

Principal Investigator: Prof Mc Dermott

Study title: A Randomized Phase 3 Study Evaluating Cystectomy with Perioperative Pembrolizumab and Cystectomy with Perioperative Enfortumab Vedotin and Pembrolizumab versus Cystectomy Alone in Participants who are Cisplatin-Ineligible or Decline Cisplatin with Muscle-Invasive Bladder Cancer (KEYNOTE-905/EV-303).

- **NREC-CT comments:**

- Based on the above, the NREC-CT B Committee agreed that this substantial amendment application be designated as favourable.

- **NREC-CT Decision:**

- Favourable

21-NREC-CT-177_Mod-3

Principal Investigator: Prof Doherty

Study title: A Phase 2b/3, Randomized, Double-blind, Placebo-controlled, Parallel-group, Multicenter Protocol to Evaluate the Efficacy and Safety of Guselkumab in Participants with Moderately to Severely Active Ulcerative Colitis.

- **NREC-CT comments:**

- Based on the above, the NREC-CT B Committee agreed that this substantial amendment application be designated as favourable.

- **NREC-CT Decision:**

- Favourable

22-NREC-CT-148_Mod-1

Principal Investigator: Prof Orla Hardiman

Study title: A PHASE 3, OPEN-LABEL EXTENSION OF COURAGE-ALS (CY 5031)

- **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 Further Information

Additional Information Required:

- The committee note the inclusion of 'remote labs' on pg. 2 and that the PT will be attending "another location outside of the clinic" or "arrange for another method with your study doctor that is approved by the Sponsor to have your Week 6 and/or Week 18 remote laboratory visits performed if arrangements cannot be made with the home health vendor." The committee would like confirmation that the sponsor will cover any costs incurred by the PT attending other sites/ clinics.
- The Committee note on pg. 14 under "How will your personal data be used?" that ethics committee is listed as a reason to collect personal data. The committee request for this to be removed as ethics committees will not have access to personal data.
- The Committee also note on pg. 14 under "Who will have access to your personal data?", there is mention of 'Competent Authorities' that will have access to your personal data. The committee would like to know who the 'competent authorities' will be?
- On pg. 2 of the ICF, under point 4, future studies are mentioned, however the committee recognise that there is no mention of future research within the PIL. Please clarify.

22-NREC-CT-007_Mod-3

Principal Investigator: Dr Clodagh Keohane

Study title: A Phase 3, Double-Blind, Randomized Study to Compare the Efficacy and Safety of Luspatercept (ACE-536) Versus Placebo in Subjects with Myeloproliferative Neoplasm-Associated Myelofibrosis on Concomitant JAK2 Inhibitor Therapy and Who Require Red Blood Cell Transfusions. The "INDEPENDENCE" Trial.

- **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 Committee noted the protocol distinguishes between *additional research* (6.9.1.1) on pg. 76– i.e., research related to the study drug and/or the disease – and *optional research (6.9.1.2)* – i.e., research not related to the study drug and/or disease. The PISCF however does not make this distinction. Please note, seeking blanket 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 Data Protection Act 2018 (Section 36(2) (Health Research) Regulations 2018) where informed participant consent is a mandatory safeguard. The Committee requested that the section regarding optional research is removed within the protocol.
- On pg. 10, the Committee queried whether it is necessary to include the bullet points regarding blood samples and biomarkers that will not be collected.
- The Patient Information Leaflet does not indicate potential exclusion from the trial due to Covid-19. The Committee queried whether this should be included. Please clarify.

22-NREC-CT-018_Mod-4

Principal Investigator: Dr Jarushka Naidoo

Study title: Clinical trial of MK-7684A with chemotherapy for extensive-stage small cell lung cancer (ES-SCLC)

- **NREC-CT comments:**

- The NREC-CT 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

- On pg.17 under, ‘Expenses and Payments’- the committee suggested this should include information on how to request reimbursement. Greenphire, is one option but there are no alternative options provided. The Committee requested that the PIL should clarify how participants will be reimbursed if they choose not to use Greenphire.
- The consent form on pg. 22 stated, “I agree to provide samples for use in this trial under the conditions described in the information sheet”. However, the information sheet on pg. 6 states that “Your tissue may be used to improve and develop tests to help people with cancer”. The committee found this wording is too vague and should be limited to the specific disease area. The consent and the ICF must be more specific and should only refer to research related to the study.
- The Committee noted a statement on pg. 3 of the Optional PIS that, “the trial team will share some of your personal information with Greenphire, such as your name, address,

telephone number, date of birth, email address, and coded participant identification number for the trial." The Committee required justification for providing Greenphire with the coded participant ID, as they believe this would appear to increase the risk of breaking patient confidentiality. Please clarify.

21-NREC-CT-021_Mod-4

Principal Investigator: Prof Douglas Veale

Study title: POETYK PsA-1 (054) - A Phase 3, Randomized, Double-Blind, Placebo-Controlled Study to Evaluate the Efficacy and Safety of BMS-986165 in Participants with Active Psoriatic Arthritis who are Naïve to Biologic Disease Modifying Anti-rheumatic Drugs.

- **NREC-CT comments:**

- 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

Additional Information Required

- The Committee noted on pg. 13 states "Your consent to this biomarker testing is mandatory to participate in this study due to the important nature of the information obtained from this type of testing." However, the consent form on pg. 25 does not include biomarker testing. Please amend or clarify.
- The Committee noted the total volume of blood collected on pg. 11. However, the committee requested including a breakdown of the approximate number of teaspoons of blood that will be taken on each occasion.
- The Committee noted the introduction of adjudication committees. It is suggested that these groups are given anonymized data and are under the same strict confidentiality agreements as the study doctors. The Committee would like to know how their confidentiality is protected/ managed and will they be required to sign confidentiality forms.