National Research Ethics Committee

NREC-CT A Meeting

9th of March 2022

Attendance

Name	Role
Dr Heike Felzmann	Acting (Deputy) Chairperson, NREC-CT A
Prof. Mary Donnelly	Deputy Chairperson, NREC-CT A
Prof. Tina Hickey	Committee Member, NREC-CT A
Dr Dervla Kelly	Committee Member, NREC-CT A
Dr Jimmy Devins	Committee Member, NREC-CT A
Mr Gerard Daly	Committee Member, NREC-CT A
Ms Ann Twomey	Committee Member, NREC-CT A
Prof. Catherine Hayes	Committee Member, NREC-CT A
Ms Muireann O'Briain	Committee Member, NREC-CT A
Prof. David Brayden	Committee Member, NREC-CT A
Prof. Gene Dempsey	Committee Member, NREC-CT A
Dr John O'Loughlin	Committee Member, NREC-CT A
Dr Geraldine Foley	Committee Member, NREC-CT A
Ms Aileen Sheehy*	Programme Manager, National Office for RECs
Dr Laura Mackey*	Project Officer, National Office for RECs
Dr Marta Pisarska	HRB Postdoctoral Intern, National Office for RECs

*Drafted minutes

Apologies: Prof. Alistair Nichol, Prof. John Wells, Prof. Patrick Dillon, Dr Darren Dahly

Quorum for decisions: Yes

Agenda

- Welcome & Apologies
- 22-NREC-CT-009
- 21-NREC-CT-153_AMEND-1
- 21-NREC-CT-067_AMEND-2
- 21-NREC-CT-157_AMEND-1
- 21-NREC-CT-158_AMEND-1
- 21-NREC-CT-001_AMEND-2
- 21-NREC-CT-159_AMEND-1
- AOB

- The Chair welcomed the NREC-CT A.
  - The minutes from the previous NREC-CT A meeting on 9th of February 2022 were approved.
  - The NREC Business Report was discussed and noted.

Applications

22-NREC-CT-009

- Principal Investigator: Prof. Sean Murphy

Study title: TENECTEPLASE IN CENTRAL RETINAL ARTERY OCCLUSION STUDY (TenCRAOS): A Prospective, randomised-controlled, double-dummy, double-blind phase 3 multi-centre trial of TNK 0.25 mg/kg + placebo vs. ASA + placebo (2 arms with 1:1 block randomisation)

Lead institution: Mater Misericordiae University Hospital

- NREC-CT comments:

- The NREC-CT A noted that this study represents a prospective, randomised-controlled, double-dummy, double-blind phase 3 multi-centre trial of TNK 0.25 mg/kg + placebo vs. ASA + placebo
- The NREC-CT A recognised that this is a highly important area of research.

- 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 NREC-CT A noted that the start date for the trial in the application form is 01 February and requested that this is corrected.
- As the trial would involve participants with likely visual impairment, the NREC-CT A requested further information on the supports available to participants who may not be in a position to read the participant materials.
- The NREC-CT A requested that the contact details of Irish-based PIs are included in the participant materials rather than the Norwegian-based project manager.
- The NREC-CT A noted that the flowchart provides inconsistent information from the participant materials in relation to the administration of the study design with respect to ASA tablets. Specifically, the consent form seems to imply that all participants will be administered ASA tablets, and this does not tally with the flow chart where half the subjects will be getting placebo tablets. The Committee requested clarification on this point and requested that the relevant documents are amended accordingly.
- The NREC-CT A requested further information on the recruitment processes and timelines in place between a participant being notified of the trial and then having to provide informed consent.
- The NREC-CT A requested further clarification if women of childbearing age would be excluded from the study and justification to support the rationale
- The NREC-CT A noted the long list of exclusion criteria, including those lacking decision-making capacity and those with no fixed abode. While the Committee understands that inclusion may be necessarily restrictive for this study due to the emergency circumstances in which participants will be recruited, it supports the principles that capacity should always be presumed until proven otherwise and requested further information on the process in place to assess capacity, as well as further justification for the extensive exclusion criteria.
- The NREC-CT A requested further information on whether there would be provision of translators for non-English speakers to support recruitment on to the trial.
- The NREC-CT A noted that one inclusion criterion was that ‘a woman of childbearing potential, must confirm, that in her opinion, she cannot be pregnant…’ and requested justification for the approach taken. In addition, it is at odds from the application form where women of childbearing age seem to be excluded from the study
- The NREC-CT A noted that the CV for the national PI was submitted, however requested that the CVs for the three PIs at other sites are submitted.

- The NREC-CT A noted that limited information was provided around the storage, protection, use and retention / destruction of blood samples obtained from participants, and requested further information on this aspect of the study.
- The NREC-CT A would consider that the reimbursement of reasonable expenses is best practice for clinical trials and requested rationale for the decision not to cover out of pocket expenses for participating in this study.
- The NREC-CT A noted that a translated version of the DPIA was included with the submission but considered that the document lacked information related to the potential data protection risks to Irish participants and the measures in place to mitigate against those risks. The NREC-CT A requested further information on data protection aspects of the study directly related to Irish participants.
- The NREC-CT A requested a copy of the relevant insurance policy from the Sponsor and assurances that adequate cover is in place to protect both participants and trial staff.

21-NREC-CT-153_AMEND-1

- Principal Investigator: Prof. Ian Flitcroft

Study title: Childhood Atropine for Myopia Progression (CHAMP): A 3-Arm Randomized, Double-Masked, Placebo-Controlled, Phase 3 Study of Atropine Sulfate Ophthalmic Solution 0.01 % and 0.02 %

- Lead institution: The Greenway Hub, Technological University Dublin

  - NREC-CT comments:

- The NREC-CT A noted that this application represents a substantial amendment to a 3-arm randomized, double-Masked, placebo-controlled, phase 3 study of aftropine sulfate ophthalmic solution 0.01 % and 0.02 % for childhood myopia progression.
- The NREC-CT A commented this a was a clear and comprehensive substantial amendment submission.
- Based on the above, the NREC-CT A agreed that this substantial amendment application be designated as favourable.

  - NREC-CT Decision:

- Favourable

21-NREC-CT-067_AMEND-2

- Principal Investigator: Prof. Maeve Lowery

Study title: A Phase 3, Randomized Study to Evaluate the Efficacy and Safety of Lenvatinib (E7080/MK-7902) plus Pembrolizumab (MK-3475) plus Chemotherapy Compared with Standard of Care Therapy as First-line Intervention in Participants with Advanced/Metastatic Gastroesophageal Adenocarcinoma (LEAP-015)

Lead institution: St James's Hospital

- NREC-CT comments:

- The NREC-CT A noted that this application represents a substantial amendment to a Phase 3, Randomized Study to Evaluate the Efficacy and Safety of Lenvatinib plus Pembrolizumab plus Chemotherapy Compared with Standard of Care Therapy as First-line Intervention in Participants with Advanced/Metastatic Gastroesophageal Adenocarcinoma.
- The NREC-CT A commented this a was a straightforward and comprehensive substantial amendment submission.
- Based on the above, the NREC-CT A agreed that this substantial amendment application be designated as favourable.

- NREC-CT Decision:

- Favourable

21-NREC-CT-157_AMEND-1

- Principal Investigator: Dr Emma Tuohy

Study title: An Open-Label, Multicenter, Extension Study of AG-348 in Adult Subjects with Pyruvate Kinase Deficiency Previously Enrolled in AG-348 Studies

Lead institution: St James's Hospital

- NREC-CT comments:

- The NREC-CT A noted that this application represents a substantial amendment to an Open-Label, Multicenter, Extension Study of AG-348 in Adult Subjects with Pyruvate Kinase Deficiency Previously Enrolled in AG-348 Studies.
- The NREC-CT A commented this substantial amendment submission was comprehensive and clearly laid out.
- Based on the above, the NREC-CT A agreed that this substantial amendment application be designated as favourable.

- NREC-CT Decision:

- Favourable

21-NREC-CT-158_AMEND-1

- Principal Investigator:

Study title: A Phase 3 study comparing Daratumumab, Lenalidomide, and Dexamethasone (Drd) versus Lenalidomide and Dexamethasone (Rd) in subjects with previously untreated multiple myeloma who are ineligible for high dose therapy.

Lead institution: University Hospital Galway

- NREC-CT comments:

- The NREC-CT A noted that this application represents a substantial amendment to a Phase 3 study comparing Daratumumab, Lenalidomide, and Dexamethasone (Drd) versus Lenalidomide and Dexamethasone (Rd) in subjects with previously untreated multiple myeloma who are ineligible for high dose therapy.
- The NREC-CT A commented this substantial amendment submission was clear and straightforward.
- Based on the above, the NREC-CT A agreed that this substantial amendment application be designated as favourable.

- NREC-CT Decision:

- Favourable

21-NREC-CT-001_AMEND-2

- Principal Investigator: Professor Sean Raymond McDermott

Study title: Phase Ib/II Trial of Pembrolizumab (MK-3475) Combination Therapies in Metastatic Castration-Resistant Prostate Cancer (mCRPC) (KEYNOTE-365)

Lead institution: Tallaght University Hospital

- NREC-CT comments:

- The NREC-CT A noted that this study represents a Phase Ib/II Trial of Pembrolizumab (MK-3475) Combination Therapies in Metastatic Castration-Resistant Prostate Cancer.

- 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 NREC-CT A noted that the amendment included the addition of a blood pressure check which can be done by participants at home or through the pharmacy. The Committee requested further information on how participants would be able to check their blood pressure at home and any additional supports provided to participants. If blood pressure is checked at the pharmacy, would participants be reimbursed for the cost?

22-NREC-CT-159_AMEND-1

- Principal Investigator: Professor Suzanne Norris

Study title: The effect of semaglutide in subjects with non-cirrhotic nonalcoholic steatohepatitis

Lead institution: St James's Hospital

  - NREC-CT comments:

- The NREC-CT A noted that this study examines the effect of semaglutide in subjects with non-cirrhotic nonalcoholic steatohepatitis.
- 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 NREC-CT A noted numerous issues and inconsistencies related to the Participant Information Leaflet (PIL) and requested that all of these are addressed and a revised PIL is resubmitted to the Committee:
    - The Committee requested that all formatting in the document is revised and corrected,

  - Under Section 2 ‘Deciding if you want to take part’, the Committee requested that participants are provided with a specific time period between being informed about the study and consenting,
  - Under ‘Taking part in other studies’, the Committee noted it states that participants cannot participate in other studies while on the trial, yet elsewhere in the PIL it discusses participants partaking in COVID-related trials. The Committee requested that this is clarified for participants.
- The Committee noted that no information is provided to participants around the route in which reasonable expenses will be reimbursed and requested that this is clarified in the participant materials.
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- AOB:
  - Ms Aileen Sheehy informed the Committee that the Department of Health will present on the Clinical Trials Regulation and its transposition into Irish Legislation. A meeting date is yet to be set.
  - There was discussion regarding the Committee meetings moving to in-person events. Ms Aileen Sheehy informed the Committee members that no plans were currently in place to move to in-person meetings but that this decision would be re-visited in summer.
- The Chair closed the meeting.