National Research Ethics Committee

NREC-CT A Meeting

22nd May 2024

Attendance

Name	Role
Ms Caoimhe Gleeson*	Deputy Chairperson, NREC-CT A
Prof. Gene Dempsey	Deputy Chairperson, NREC-CT A
Dr Darren Dahly	Committee Member, NREC-CT A
Ms Muireann O'Briain	Committee Member, NREC-CT A
Dr Dawn Swan	Committee Member, NREC-CT A
Dr Maeve Kelleher	Committee Member, NREC-CT A
Mrs Dympna Devenney	Committee Member, NREC-CT A
Dr Sean Lacey	Committee Member, NREC-CT A
Dr Brian Bird	Committee Member, NREC-CT A
Mrs Erica Bennett	Committee Member, NREC-CT A
Dr Emily Vereker	Head of Office, 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 Manager, National Office for RECs
Ms Aileen Sheehy	Programme Manager, National Office for RECs
Ms Rachel McDermott	Project Administrator, National Office for RECs

*Chaired Meeting

**~~Drafted Minutes~~

Apologies: Prof. Alistair Nichol, Dr Lorna Fanning, Dr Geraldine Foley, Prof. Aisling McMahon, Ms Mandy Daly

Quorum for decisions: Yes

Agenda

- Welcome & Apologies
- 2023-505617-24-00
- 2023-510128-66-00
- 2022-501007-28-00
- 2023-505457-40-00
- 22-NREC-CT-035_Mod-4
- 22-NREC-CT-129_Mod-3
- 21-NREC-CT-028_Mod-3
- 23-NREC-CT-027_Mod-1
- AOB

- The Chair welcomed the NREC-CT A.
  - The minutes from the previous NREC-CT A meeting on 17th April 2024 were approved.
  - The NREC Business Report was discussed and noted.

Applications

2023-505617-24-00

Institutions: START Dublin, Beaumont Hospital

Study title: A Randomized Phase 2 Study of Ocular Toxicity Evaluation and Mitigation During Treatment with Mirvetuximab Soravtansine in Patients with Recurrent Ovarian Cancer with High Folate Receptor-Alpha Expression

Dossiers for Review: Part II

NREC-CT Decision: Request for Further Information

Part II Considerations
1. Recruitment arrangements
• The NREC-CT noted that participants will have as much time as they need to decide whether to enrol in the study, and requested clarification on whether there is a minimum or maximum allowable time in place. • The NREC-CT noted that the PISCF documents will be available in the local language, and requested clarification on whether participants who may not have English as a first language will also be accommodated.
2. Subject information and informed consent form

- The NREC-CT requested that terms such as ‘platinum-sensitive’ and ‘platinum-resistant’ are explained in lay language in the Main PISCF (page 3).
- The NREC-CT requested further details are given to participants on the potential implications of MIRV being an investigational medicinal product, and how this may impact participants who enrol in the study (Main PISCF, page 4).
- The NREC-CT requested that the duration of the study is added to the section entitled ‘How long will I be in this study’ (Main PISCF, page 7).
- The NREC-CT requested that further details on the frequencies of expected side effects are given in relation to the eye drops (Main PISCF, page 13).
- The NREC-CT noted that participants are requested to contact the ‘study doctor on call’ in the event of an emergency after regular hospital hours, and requested further details on who this might be in the Irish setting, and that participants are directed to the appropriate emergency services in the event that there is no 24-hour study doctor assigned (Main PISCF, page 20).
- The NREC-CT noted that ‘Personal Data’ and ‘Coded Data’ are used interchangeably throughout all PISCF documents, and requests that this discrepancy is clarified or better explained. Two examples of this are on pages 16 and 22 of the Main PISCF.
- The NREC-CT noted the following sentence on page 18 of the Main PISCF: “*In some cases, employers could use your genetic information to decide whether to hire or fire you.”,* and requested that this is amended or removed in line with Irish law.
- The NREC-CT requested that references to U.S. law are amended to EU law (Main PISCF, page 19).
- The NREC-CT requested that all references to the participant not being billed for tests or studies as part of the trial, or deductibles and co-payments from health insurers should be amended for the Irish setting throughout all PISCF documents. Two examples can be found on page 20 of the Main PISCF and page 6 of the Ocular Sub-Study PISCF.
- The NREC-CT noted that participants ‘may’ be reimbursed, and requested that this be amended to ‘will’ be reimbursed in all PISCF documents, in line with sections 1 and 2 of the Compensation for Trial Participants document submitted. The Committee also requested clarification on whether an upper limit of reimbursement is in place.

3. Suitability of the clinical trial sites facilities

- The NREC-CT noted that the SSA document for Beaumont Hospital states that no scans above standard of care will be required, however in the ‘Imaging Risks’ section of the Main PISCF (page 13), it states that a participant may have more scans that would be required for standard of care. The NREC-CT requested that this discrepancy be clarified and updated in the relevant documentation.

2023-510128-66-00

Institution: St James Hospital

Study title: A Phase 3 Study of Pembrolizumab in Combination With Carboplatin/Taxane (Paclitaxel or Nab-paclitaxel) followed by Pembrolizumab With or Without Maintenance MK-2870 in the First-line Treatment of Metastatic Squamous Non-small Cell Lung Cancer

Dossiers for Review: Part I and II

NREC-CT Decision: Request for Further Information

Part II Considerations

1. Recruitment arrangements

- The NREC-CT noted that planned advertisement materials have not been submitted for review, and requested that these be submitted once available.
- The NREC-CT requested that the Recruitment Summary Document be reworded to further emphasise the risks and potential lack of benefit for the trial, and to de-emphasise the list of payments that the participant could receive, such as to give better balance to the document and reduce the risk of undue incentivisation for participants.

2. Subject information and informed consent form

- The NREC-CT noted discrepancies between the Main PISCF and the Compliance with Biological Samples Template, where the following statement is given; "*tissue maybe used to improve and develop tests. This tissue may be completely used and not available for future testing*" (page 5) and "*genetic and biomarker samples kept for up to 15years…to answer questions about the way drugs work in this trial"* (page 7). There is no indication for future use in the PISCF, however the Compliance with Use of Biological Samples states that samples are used for future research, stored for 20 years, and that participants will not be contacted to give further consent. The NREC-CT requests clarification on which information is correct, and that the respective documents are updated to correct this discrepancy. If updated, the PISCF needs to clearly outline future use and seek participant explicit consent for this.
- The Sponsor is requested to submit any participant-facing documentation that require updates as a result of the Part I Assessment.

2022-501007-28-00

Institutions: Bon Secours, St Vincent's University Hospital, Beacon Hospital, Sligo University Hospital, Beaumont Hospital, Cork University Hospital

Study title: EMBER-4: A Randomized, Open-Label, Phase 3 Study of Adjuvant Imlunestrant vs Standard Adjuvant Endocrine Therapy in Patients who have Previously Received 2 to 5 years of Adjuvant Endocrine Therapy for ER+, HER2- Early Breast Cancer with an Increased Risk of Recurrence

Dossiers for Review: Part I and II

NREC-CT Decision: Request for Further Information

- The Sponsor is requested to confirm whether the new CTCAE PRO questionnaire for female participants will be used in Ireland, and if so, to please submit it for review.

2023-505457-40-00

Institution: St Vincent's University Hospital, St James's Hospital, Cork University Hospital

Study title: Randomized, Multi-center, Double-blind, Placebo-controlled Phase 3 Study of Bemarituzumab plus Chemotherapy versus Placebo plus Chemotherapy in Subjects with Previously Untreated Advanced Gastric or Gastroesophageal Junction Cancer with FGFR2b Overexpression (FORTITUDE 101)

Dossiers for Review: Part I and II

NREC-CT Decision: Favourable

22-NREC-CT-035_Mod-4

Principal Investigator: Dr Ross Murphy, St James Hospital

Study title: HELIOS-B: A Phase 3, Randomized, Double-blind, Placebo-controlled, Multicenter Study to Evaluate the Efficacy and Safety of Vutrisiran in Patients with Transthyretin Amyloidosis with Cardiomyopathy (ATTR Amyloidosis with Cardiomyopathy)

EudraCT: 2019-003153-28

NREC-CT Decision: Favourable

22-NREC-CT-129_Mod-3

Principal Investigator: Dr John Quinn, Beaumont Hospital

Study title: A Phase 3, Randomized, Multicenter, Double-Blind, Placebo-Controlled, Efficacy and Safety Study of Birtamimab Plus Standard of Care vs. Placebo Plus Standard of Care in Mayo Stage IV Subjects with Light Chain (AL) Amyloidosis

EudraCT: 2021-000037-14

NREC-CT Decision: Favourable

21-NREC-CT-028_Mod-3

Principal Investigator: Dr Catherine Flynn, St James's Hospital

Study title: HO150/AMLSG 29-18: A phase 3, multicenter, double-blind, randomized, placebo-controlled study of ivosidenib or enasidenib in combination with induction therapy and consolidation therapy followed by maintenance therapy in patients with newly diagnosed acute myeloid leukemia or myelodysplastic syndrome with excess blasts-2, with an IDH1 or IDH2 mutation, respectively, eligible for intensive chemotherapy.

EudraCT: 2018-000451-41

NREC-CT Decision: Request for Further Information

- The NREC-CT A requested that the cover letter is updated to provide rationale for the updates to the Protocol, for example the addition of sections 18.3-18.9, such that it can be fully reviewed by the NREC.

23-NREC-CT-027_Mod-1

Principal Investigator: Dr Beatrice Nolan, CHI Crumlin

Study title: A Phase 3, Prospective, Open-label, Uncontrolled, Multicenter Study on Efficacy and Safety of Prophylaxis with rVWF in Children Diagnosed With Severe von Willebrand disease

EudraCT: 2020-003304-13

NREC-CT Decision: Request for Further Information

- The NREC-CT noted the clinical commitment of approval that “In the event of an anaphylactic reaction, fast access to hospital care is considered critical and before the trial commences, patients/carers should be provided with clear instruction on how to access hospital care without delay”. The Committee requested further information on whether the IMP will be administered to participants at home, and further details on the potential risk of anaphylaxis , the proposed mitigation strategies in terms of time to onset, and whether an adrenaline pen will be given to parents. The NREC-CT requested that this information is made clear to parents and participants in the PIL.
- The NREC-CT noted the use of Greenphire for reimbursement of expenses, and requested further information on whether there is an alternative process for reimbursement, should participants and their parents/guardians not wish to use Greenphire.
- The NREC-CT noted the updated ICF section on receipt of study notifications, and requested further information on whether there is any impact on appointment reminders if Parents/Guardians do not wish to consent to this.
- The NREC-CT noted that there are no details on withdrawal from the study or information on how participant data will be stored during the study in the following documents (Parent Brochure, Assent Guide - 12-17 Years, Caregiver Study Guide and Talking Points Guide), and requested that brief sections on same be added for participants.

- AOB:
  - The ongoing Expression of Interest campaign was noted to the Committee.
  - The process and timing of Assessment Report submission was noted to the Committee.