National Research Ethics Committee

NREC-CT A Meeting

10th January 2024

Attendance

Name	Role
Prof. Alistair Nichol	Chairperson, NREC-CT A
Ms Caoimhe Gleeson	Deputy Chairperson, NREC-CT A
Prof. Gene Dempsey	Deputy Chairperson, NREC-CT A
Dr Brian Bird	Committee Member, NREC-CT A
Dr Darren Dahly	Committee Member, NREC-CT A
Dr Lorna Fanning	Committee Member, NREC-CT A
Dr Maeve Kelleher	Committee Member, NREC-CT A
Dr Sean Lacey	Committee Member, NREC-CT A
Ms Muireann O'Briain	Committee Member, NREC-CT A
Dr Dawn Swan	Committee Member, NREC-CT A
Mrs Erica Bennett	Committee Member, NREC-CT A
Dr Emily Vereker	Head of Office, National Office for RECs
Ms Patricia Kenny	Project Officer, National Office for RECs
Ms Megan O'Neill	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 Manager, National Office for RECs
Ms Aileen Sheehy	Programme Manager, National Office for RECs

Apologies: Mrs Dympna Devenney, Ms Mandy Daly, Dr Geraldine Foley, Dr Heike Felzmann

Quorum for decisions: Yes

Agenda

- Welcome & Apologies
- 2022-501980-42-00
- 2022-502503-30-00
- 22-NREC-CT-183_Mod-2
- 22-NREC-CT-011_Mod-2
- 22-NREC-CT-102_Mod-3
- 2022-501007-28-00 SM
- 2023-503661-28-00 SM
- 23-NREC-CT-035_Mod-2
- AOB

- The Chair welcomed the NREC-CT A.
  - The minutes from the previous NREC-CT A meeting on 23rd November 2023 were approved.
  - The NREC Business Report was discussed and noted.

Applications

2022-501980-42-00

Principal Investigators & Institutions: Dr Michael Riordan, Children's Health Ireland at Temple Street

Study title: A Phase 3, Open-label, Uncontrolled Study to Evaluate theActivity, Safety, Pharmacokinetics and Pharmacodynamics of Roxadustat for the Treatment of Anemia in Pediatric Participants with Chronic Kidney Disease

EudraCT: 2022-501980-42-00

Dossiers for Review: Part II

1. Compliance with national requirements on data protection

- The NREC-CT requested clarification on whether there is a data processing role for the PI.

2. Compliance with use of biological samples

- No Considerations

3. Financial arrangements

- The NREC-CT noted that reimbursement for meal expenses will not cover the carer for the participant, and recommended that meal-related expenses be extended to both the participants and their carer given the extensive time required on site for trial visits.

4. Proof of insurance

- No Considerations

5. Recruitment arrangements

- The NREC-CT requested clarification on who will have access to medical records for screening purposes, and confirmation that the following guidelines will be followed: https://hseresearch.ie/data-protection-and-research/#Access-to-patient-personal-data

6. Subject information and informed consent form

- The NREC-CT requested confirmation that there are procedures in place for supportive and sensitive discussions on contraception and pregnancy with participants.
- While the letter from the DPO in the Data Protection section of the Dossier details Future Biological Research, this is not detailed in the Consent or Assent forms. The NREC-CT requested clarification on whether Future Biological Research will occur, and if so, further clarity and optional consent is provided for participants regarding what will happen to their sample and the associated data.
- The NREC-CT requested clarification on what additional study procedures or assessments will be in place for the first ten participants in each cohort being enrolled in the PK analysis, and requested that this is updated in the relevant Consent and Assent Forms.
- The NREC-CT noted that severe risk language has been omitted from the 13-15 year old Assent Form, and requested that this is reinstated.
- The NREC-CT noted that the Study Overview section of the Main and Parent Consent forms states that the study medicine has not been approved in this participant group, and requested that participants are given more information on what exactly that means for them in the context of this study.

7. Suitability of the clinical trial sites facilities

- No Considerations

8. Suitability of the investigator

- The NREC-CT noted that Dr Riordan's CV does not list extensive clinical trial experience and requested confirmation that Dr Riordan will have access to mentorship or supports during the trial, if required.

2022-502503-30-00

Principal Investigators & Institutions: Prof. Owen Smith, CHI Crumlin

Study title: International Collaborative Treatment Protocol for Infants Under One Year with KMT2A – rearranged Acute Lymphoblastic Leukemia or Mixed Phenotype Acute Leukemia

EudraCT: 2022-502503-30-00

Dossiers for Review: Part I and II

NREC-CT Decision: Request for Further Information

1. **Compliance with national requirements on data protection**
   - No Considerations
2. **Compliance with use of biological samples**
   - No Considerations
3. **Financial arrangements**
   - The NREC-CT noted that no reimbursement of expenses is available for participants, and requested justification for this.
4. **Proof of insurance**
   - No Considerations
5. **Recruitment arrangements**
   - No Considerations
6. **Subject information and informed consent form**

- The NREC-CT requested clarification regarding the number of study visits, and that this is made clear to participants in the assent and consent forms.
- The NREC-CT requested clarity as to whether assent forms will be developed for children as they age within the study.
- The NREC-CT requested that clarity is provided in the PIL on page 1 regarding what to do in an emergency while taking part in the study. It was unclear to the Committee whether the contact details (page 17, Questions and Complaints) in the PIL were available 24/7.
- The NREC-CT requested that the same size box is provided for both ‘yes’ and ‘no’ options in the optional consent section, to allow use of initials in both options.
- The NREC-CT noted that the Participant Information Leaflet (page 9) states that no extra punctures are needed, but subsequently states that extra blood will be taken for PK studies. The NREC requested clarification that these samples will be taken from a central line, and in addition clarification as to whether additional visits are required for PK studies.
- The NREC-CT considered it was not clear from the PIL, how frequent the follow-up visits are, and what is entailed in each visit. The NREC-CT noted that an appendix detailing all study visits and what they entail would be helpful for participants.

- The NREC-CT requested rewording of text within the Participant Information Leaflet, including Page 1 “We ask that you participate in these scientific studies”, and page 4 “and therefore receive appropriate treatment”. The Committee requested that this be rephrased to ensure participants do not feel undue pressure to enroll.
- The NREC-CT queried whether participants are informed as to what the current standard treatment for this patient cohort is, and how this differs from the trial intervention.
- The NREC-CT noted that Section B (sub-studies, page 10) contains details of standard chemotherapy involved for each treatment phase. The NREC-CT requested that this be added to Part A, page 5 of the PIL, as it is not exclusive to the sub-study.
- The NREC-CT requested clarity on whether participants who withdraw from the IMP or the study would be permitted to undergo safety follow up visits.
- The NREC-CT noted that participants’ samples may be used for optional future biological research, and requested more specific details on the disease area(s) within the field of cancer for this future research.

7. Suitability of the clinical trial sites facilities

- No Considerations

8. Suitability of the investigator

- No Considerations

22-NREC-CT-183_Mod-2

Principal Investigator: Prof. Iracema Leroi

Study title: A Phase 3, multicenter, randomized, double-blind, placebo-controlled study to assess the efficacy, safety, and tolerability of AVP-786 (deudextromethorphanhydrobromide [d6-DM]/quinidine sulfate [Q]) for the treatment of agitation in patients with dementia of the Alzheimer’s type

EudraCT: 2020-000799-39

NREC-CT Decision: Request for Further Information

- The NREC-CT noted that Patient Facing Documents are dated from 2020. The Sponsor is requested to justify the delayed submission.
- The NREC-CT noted that the GP Letter refers to Appendix 2, but this appendix was not attached to the letter.
- The NREC-CT requested further information on how participants will be reconsented with the updated PISCF versions.
- The NREC-CT requested removal of any trial logo from the study participant pack, such as not to breach confidentiality for participants.
- The NREC-CT requested that the versioning of the PISCF is updated on pages 16/18 of the Legal Rep ICF document.

22-NREC-CT-183_Mod-2

Principal Investigator: Dr Darren Cowzer

Study title: PaTcH Trial: A phase 2 study to explore primary and emerging resistance mechanisms in patients with metastatic refractory Pancreatic cancer treated with Trametinib and Hydroxychloroquine

EudraCT: 2021-006276-16

NREC-CT Decision: Favourable

22-NREC-CT-183_Mod-2

Principal Investigator: Prof. Christopher Bacon

Study titleA Phase 3 Randomized Study Comparing Bortezomib, Lenalidomide and Dexamethasone (VRd) followed by Ciltacabtagene Autoleucel, a Chimeric Antigen Receptor T cell (CAR-T) Therapy Directed Against BCMA versus Bortezomib, Lenalidomide, and Dexamethasone (VRd) followed by Lenalidomide and Dexamethasone (Rd) Therapy in Participants with Newly Diagnosed Multiple Myeloma for Whom Hematopoietic Stem Cell Transplant is Not Planned as Initial Therapy

EudraCT: 2021-001242-35

NREC-CT Decision: Favourable

2022-501007-28-00

Principal Investigators: Dr Deirdre O'Mahony, Prof. Janice Walshe, Dr Jennifer Westrup, Dr Michael Martin, Prof. Patrick Morris, Prof Seamus O'Reilly

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

EudraCT: 2022-501007-28-00

Dossiers for Review: Part II

NREC-CT Decision: Favourable

2023-503661-28-00

Principal Investigators: Prof. Alan Irvine, Prof. Michelle Murphy, Dr Michael O'Connell, Dr Trevor Markham, Prof. Brian Kirby.

Study title: A Phase 3 Randomized, Placebo-Controlled, Double-Blind Study to Evaluate Efficacy and Safety of Upadacitinib in Adult and Adolescent Subjects with Moderate to Severe Hidradenitis Suppurativa Who Have Failed Anti-TNF Therapy

EudraCT: 2023-503661-28-00

Dossiers for Review: Part II

NREC-CT Decision: Favourable

23-NREC-CT-035_Mod-2

Principal Investigator: Dr Andrea Malone

Study title: A randomized phase 3 trial of fludarabine/cytarabine/gemtuzumab ozogamicin with or without venetoclax in children with relapsed AML

EudraCT: 2021-00212-11

NREC-CT Decision: Request for Further Information

- The NREC-CT requests that the PISCF documents further emphasise that HIV, Hep A, Hep C positive results must be reported to the health authorities.
- The NREC-CT requests that the 'optional consent section' of the PISCF document should start on a new page, and not follow on from the preceding page.
- The NREC-CT requests justification for collection of D.O.B. data for all participants.
- The NREC-CT requests clarification on whether 'participant data' transfer to AbbVie entails personal data or other participant data. This should be made clear in the PISCF document.
- The NREC-CT requests that terms such as pyrexia, thrombocytopenia, stomatitis, neutropenia and encoded are explained in the PISCF documents in lay language.
- The NREC-CT requests clarification on whether race and ethnicity data are being collected in Ireland, and if so, justification for its collection.

- AOB:
  - None