National Research Ethics Committee

NREC-CT A Meeting

13th March 2024

Attendance

Name	Role
Prof. Alistair Nichol	Chairperson, NREC-CT A
Prof. Gene Dempsey	Deputy Chairperson, NREC-CT A
Dr Darren Dahly	Committee Member, NREC-CT A
Ms Mandy Daly	Committee Member, NREC-CT A
Mrs Erica Bennett	Committee Member, NREC-CT A
Ms Muireann O'Briain	Committee Member, NREC-CT A
Dr Dawn Swan	Committee Member, NREC-CT A
Mrs Dympna Devenney	Committee Member, NREC-CT A
Prof. Aisling McMahon	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
Ms Aileen Sheehy	Programme Manager, National Office for RECs

*Drafted minutes

Apologies: Ms Caoimhe Gleeson, Dr Geraldine Foley, Dr Brian Bird, Dr Maeve Kelleher, Dr Sean Lacey, Dr Lorna Fanning

Quorum for decisions: Yes

Agenda

- Welcome & Apologies
- 2023-504918-29-00

- 2022-502629-16-00
- 2023-503697-21-01
- 2022-500439-35-00
- 22-NREC-CT-158_Mod-2
- 22-NREC-CT-011_Mod-3
- 23-NREC-CT-034_Mod-4
- AOB

- The Chair welcomed the NREC-CT A.
  - The minutes from the previous NREC-CT A meeting on 14th February 2024 were approved.
  - The NREC Business Report was discussed and noted.

Applications

2023-504918-29-00

Institutions: Mater Misericordiae University Hospital, Bon Secours Hospital Cork, St Vincent's University Hospital

Study title: An Open-label, Randomized Phase 3 Study of MK-2870 as a Single Agent and in Combination with Pembrolizumab Versus Treatment of Physician's Choice in Participants with HR+/HER2- Unresectable Locally Advanced or Metastatic Breast Cancer

Dossiers for Review: Part I and II

NREC-CT Decision: Request for Further Information

Part II Considerations

1. **Compliance with national requirements on data protection**
   - The NREC-CT requested that data received by vendors outside of the EU, such as identifiable details for reimbursement, be appropriately categorised as a risk (DPIA, Section 15, Page 6).
2. **Subject information and informed consent form**
   - The NREC-CT requested that clarification is given to participants regarding reimbursement for expenses, including whether or not they can avail of any reimbursement if they do not opt to use Greenphire (Optional Greenphire ICF).
   - The NREC-CT requested that the monetary amounts for reimbursement are removed from the Main Consent ICF (Page 16) and Optional Prescreening ICF (Page 4).
   - The NREC-CT noted the sentence in the Main Consent ICF (Section 14, Page 15): *If the drug(s) works and if your cancer gets better, you may receive a health benefit,* and was concerned that a wording which implied a possibility of a cure

could give participants unreal expectations, and suggested a re-phrasing with words giving a realistic potential of the drug combination on trial.

- The NREC-CT noted that there is no information in the Optional Prescreening ICF for participant withdrawal, and requests further information is provided on what will happen to a participant's tumour sample, should they decide to withdraw from the study after signing the consent form.
- The NREC-CT requests that a table or graphic showing the schedule of assessments be added to the Main Consent ICF, to better inform the participant of all tests and scans for each visit (Page 7).
- The Sponsor is requested to submit any participant-facing documentation that require updates as a result of the Part I Assessment.

3. Suitability of the clinical trial sites facilities

- The NREC-CT noted that one of the PIs has stated that there is a possibility of standard of care ionising radiation levels being exceeded (in relation to one site), and seeks confirmation that should such possibility of increased exposure arise, all necessary precautions will be taken (Q5, Site Suitability Assessment Forms).

4. Suitability of the investigator

- The NREC-CT requests further detail on the trial experience of the PI at the Mater Misericordiae University Hospital.
- The NREC-CT noted the GCP certification for the PI at the Bons Secours Cork is dated 2021, and requested it be renewed on expiry.

2022-502629-16-00

Institution: The Rotunda Hospital

Study title: A Phase 3 Randomized, Placebo-Controlled, Double-Blind, Multicenter Study to Evaluate the Efficacy and Safety of Nipocalimab in Pregnancies at Risk for Severe Hemolytic Disease of the Fetus and Newborn (HDFN)

Dossiers for Review: Part I and II

NREC-CT Decision: Request for Further Information

Part II Considerations

1. Compliance with national requirements on data protection

- The NREC-CT noted that gender data was not selected as being collected, and requested clarification on whether this is the case.

2. Recruitment arrangements

- The NREC-CT requested that any references to the FDA, IRB and NHS be replaced with those appropriate to the Irish and European landscape, as applicable.
- The NREC-CT requested that medical terms used in recruitment posters be rephrased in lay language, such as 'randomisation' and 'placebo'.

3. Subject information and informed consent form

- The NREC-CT noted that the sections on future research and collection of samples for same in the Maternal Clinical PISCF (Pages 21, 22) and Parent/Legal

Guardian PISCF (Pages 3, 12 and 13) are not clearly described in line with regulations and best practice. The Committee requested that future use of samples is sufficiently explained so as to constitute broad informed consent, as required under the Health Research Regulations (Data Protection Act 2018 (Section 36(2) (Health Research) Regulations 2018). Furthermore,

- it should be confined to the disease or drug under study in this trial. Consent can only be obtained where future use of samples and data is defined such that participants are fully informed,
- and/or:
  - that an option is provided to enable participants to consent to be contacted in the future about other research studies.
  - The PISCF should also make it clear to participants that subsequent research ethics review will be sought for specific research once clearly defined.
- For further guidance, please see: HSE National Policy for Consent in Health and Social Care Research (V1.1, 2023) https://hseresearch.ie/wp-content/uploads/2023/02/HSE-National-Policy-for-Consent-in-Health-and-Social-Care-Research-compressed.pdf
- The NREC-CT also requested that separate consent be sought for the optional collection of samples.

- The NREC-CT requested that the monetary amounts for reimbursement are removed from the Maternal Clinical PISCF (Page 17) and Parent/ Legal Guardian PISCF (Page 9).
- The NREC-CT requested that any references to the FDA, IRB and NHS be replaced with those appropriate to the Irish and European landscape, as applicable.
- The NREC-CT requested that the advice on anti-natal colostrum detailed in the Maternal Clinical PISCF (Page 8) be amended to be consistent with that detailed in the Protocol (Page 53).
- The NREC-CT noted that standard of care therapies are not permitted during this study, and requested further information is given to participants on any safety implications of this (Maternal Clinical PISCF, Page 17).
- The NREC-CT noted that the Maternal Clinical PISCF (Page 16) states that additional costs may be incurred where the participant uses the Clario eCOA Study App on their own device, and requested clarification as to whether these additional costs will be reimbursed, and that this is made clear to the participant.
- The NREC-CT requested that further detail is given to participants regarding the frequency of occurrence for infusion reactions (Maternal Clinical PISCF, Page 13).
- The Sponsor is requested to submit any participant-facing documentation that require updates as a result of the Part I Assessment.
- The Sponsor is requested to add the trial EU CT number to the PISCF documents.

4. Suitability of the clinical trial sites facilities

- The NREC-CT requested additional details on whether there will be supports available at site in the event of serious adverse events.

2023-503697-21-01

Institutions: Our lady of Lourdes Hospital, Connolly Hospital

Study title: A Multicenter, Randomized, Double-blind, Placebo-controlled, Phase 3 Study to Evaluate the Efficacy, Safety, and Tolerability of BMS-986278 in Participants with Idiopathic Pulmonary Fibrosis

Dossiers for Review: Part I and II

NREC-CT Decision: Request for Further Information

Part II Considerations

1. Recruitment arrangements

- The NREC-CT requested clarification on how the Informed Consent Presentation will be used; for example, whether the potential participant will be given an opportunity to ask questions throughout, or if they will be provided with the slides to look at by themselves. If the case is the latter, the NREC-CT requested that certain slides be updated with further information, such as 'additional eligibility requirements' and 'other IPF option' on slides 6 and 7. The use of graphics or tables would also enhance accessibility for participants.
- The NREC-CT requested further information on how an impartial witness might be identified, in such situations where a witness may be required.
- The NREC-CT noted that excessive enthusiasm in social media posts and other participant-facing material should be avoided where possible, for example "Now recruiting!"

2. Subject information and informed consent form

- The NREC-CT noted that the section on future research in the Main PISCF (Sections 10 and 11, Pages 34-37) and Pregnant Partner PISCF (Page 4) is not described in line with regulations and best practice. The Committee requested that future use of samples is sufficiently explained so as to constitute broad informed consent, as required under the Health Research Regulations (Data Protection Act 2018 (Section 36(2) (Health Research) Regulations 2018). Furthermore,
    - it should be confined to the disease or drug under study in this trial. Consent can only be obtained where future use of samples and data is defined such that participants are fully informed,
    - and/or:
        - that an option is provided to enable participants to consent to be contacted in the future about other research studies.
        - The PISCF should also make it clear to participants that subsequent research ethics review will be sought for specific research once clearly defined.
    - For further guidance, please see: HSE National Policy for Consent in Health and Social Care Research (V1.1, 2023) https://hseresearch.ie/wp-content/uploads/2023/02/HSE-National-Policy-for-Consent-in-Health-and-Social-Care-Research-compressed.pdf
    - The NREC-CT also requested that Section 6.3 of the Main PISCF is updated in line with the above clarifications and changes, including further detail or examples of third party entities who will have access to participants' data.

- The NREC-CT noted that participants 'may' be reimbursed for expenses incurred and requested that this be amended to 'will'. Further information should also be given to participants on the schedule of reimbursement, what expenses can and can't be reimbursed and for whom, and whether receipts can be submitted at any time throughout the trial (Main ICF, Page 22).
- The NREC-CT noted that participants will be given a tote bag, and requested that this bag be free of any trial logo, such as to maintain the privacy of the participants.
- The NREC-CT requested that a table or graphic showing the schedule of assessments be added to the Main Consent ICF, to better inform the participant of all tests and scans for each visit. This section should also include an estimate of approximate lengths of site visit that can be expected.
- The NREC-CT noted language such as 'your best interests' in Section 2.8.1 of the Main PISCF, and in accordance with the Decision Making (Capacity) Act 2015, requested that this be rephrased to language such as 'clinically indicated', or similar language that reflects the Act.
- The NREC-CT requested that medical language and acronyms detailed on Pages 10 and 11 of the Main PIL be explained in lay language.
- The NREC-CT requested more clarity is given to participants in Section 2.5 of the Main PISCF on differences between 'discontinue the study treatment' and 'withdraw from the study'.
- The NREC-CT requested that a sentence is added to Section 3.12, Page 20 of the Main PISCF, to confirm that a pregnant partner's consent and participation is at their own discretion.
- The NREC-CT noted that the PISCF used a bundled approach to consent and requested that a layered approach to consent is used (in that each consent item is listed and a box for participants to provide their initials is included alongside each consent item) in line with HSE policy. Please see HSE National Policy for Consent in Health and Social Care Research (V1.1, 2023): Health Service Executive https://hseresearch.ie/wp-content/uploads/2023/02/HSE-National-Policy-for-Consent-in-Health-and-Social-Care-Research-compressed.pdf.
- The Sponsor is requested to submit any participant-facing documentation that require updates as a result of the Part I Assessment.
- The NREC-CT requested that a definition of an 'excessive' amount of grapefruit be added to the PISCF, such that participants understand quantities and details of foods they should and shouldn't eat.

3. Suitability of the clinical trial sites facilities

- The NREC-CT noted that titration visits could last up to 8 hours, and requested any details on how participants might be comfortably accommodated for these extended visits at site.

4. Suitability of the investigator

- The NREC-CT requested further detail on the trial experience of the PI at Connolly Hospital.

2022-500439-35-00

Institutions: Mater Misericordiae University Hospital, Beaumont Hospital, University Hospital Galway, St James's Hospital, University Hospital Limerick, Cork University Hospital, St Vincent's University Hospital, University Hospital Waterford

Study title: A phase 3 multicenter, randomized, prospective, open-label trial of ibrutinib mono-therapy versus fixed-duration venetoclax plus obinutuzumab versus fixed-duration ibrutinib plus venetoclax in patients with previously untreated chronic lymphocytic leukemia (CLL)

Dossiers for Review: Part I and II

NREC-CT Decision: Request for Further Information

- The Sponsor is requested to submit tracked change versions of the updated ICF documents for review.

22-NREC-CT-158_Mod-2

Principal Investigator: Prof Michael Keane

Study title: A double blind, randomized, placebo-controlled trial evaluating the efficacy and safety of BI 1015550 over at least 52 weeks in patients with Idiopathic Pulmonary Fibrosis (IPF)

EudraCT: 2022-001091-34

NREC-CT Decision: Favourable

22-NREC-CT-011_Mod-3

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

23-NREC-CT-034_Mod-4

Principal Investigator: Prof. Orla Hardiman

Study title: Phase 2, Multicenter, Randomised, DoubleBlind, Placebo-Controlled Study Evaluating Safety and Efficacy of CORT113176 (Dazucorilant) in Patients with Amyotrophic Lateral Sclerosis (DAZALS)

EudraCT: 2021-005611-31

NREC-CT Decision: Favourable

- AOB:
  - None