National Research Ethics Committee

NREC-CT D Meeting

15th May 2024

Attendance

Name	Role
Prof David Brayden	Chairperson, NREC-CT D
Prof David Smith	Deputy Chairperson, NREC-CT D
Dr Christina Skourou	Deputy Chairperson, NREC-CT D
Dr Enda Dooley	Committee Member, NREC-CT D
Prof Andrew Green	Committee Member, NREC-CT D
Prof Cathal Walsh	Committee Member, NREC-CT D
Dr Geraldine O'Dea	Committee Member, NREC-CT D
Prof Lina Zgaga	Committee Member, NREC-CT D
Mr Gerry Daly	Committee Member, NREC-CT D
Ms Deirdre McLoughlin	Committee Member, NREC-CT D
Prof Tina Hickey	Committee Member, NREC-CT D
Dr Mary McDonnell Naughton	Committee Member, NREC-CT D
Prof Geraldine O'Sullivan Coyne	Committee Member, NREC-CT D
Ms Chanel Watson	Committee Member, NREC-CT D
Ms Aileen Sheehy	Programme Manager, National Office for RECs
Dr Laura Mackey	Programme Officer, National Office for RECs
Dr Susan Quinn	Programme Manager, National Office for RECs
Ms Patricia Kenny*	Project Officer, National Office for RECs

*Drafted minutes

Apologies: Deirdre Murray

Quorum for decisions:

Agenda

- Welcome & Apologies
- 2023-505678-14-00
- 2023-506288-33-00
- 22-NREC-CT-153_Mod-3
- 2022-502122-41-00_SM-2
- 2023-505543-39-00_SM-12
- 22-NREC-CT-013_Mod-3
- 22-NREC-CT-107_Mod-2
- 22-NREC-CT-177_Mod-3

- The Chair welcomed the NREC-CT D.
  - The minutes from the previous NREC-CT D meeting on 10th April 2024 were approved.
  - The NREC Business Report was discussed and noted.

Applications

2023-505678-14-00

Principal Investigators & Institutions: Beaumont Hospital (Dr Aoibhlinn O'Toole), St Vincent's University Hospital (Prof. Glen Doherty)

Study title: A Multicenter, Randomized Study to Evaluate the Safety and Efficacy of Lutikizumab for Induction and Maintenance Therapy in Subjects with Moderately to Severely Active Ulcerative Colitis

Dossiers Submitted: Part I and II

- **NREC-CT Decision:**
- Request for more information

- **Additional Information Required RFI**

Part I Considerations (RFI) for addition to CTIS

1. It was noted that the Investigator Brochure for Lutikizumab is dated 2021. The Sponsor is requested to confirm that the safety profile has not changed in the past three years and to report when the Investigator Brochure will be next updated.
2. Rationale is requested to be provided regarding assignment to open-label lutikizumab maintenance dose 1 for those participants who do not achieve clinical response.
3. The rationale for participants continuing to inject two subcutaneous injections (one being a placebo) after the induction period was unclear, as this is considered burdensome for participants. The Sponsor is requested is provide rationale for this.

Part II Considerations

1. Compliance with national requirements on data protection

- The NREC-CT would advise that it is a requirement to submit either a DPIA or the NREC-CT National Statement of Data Compliance as part of Ireland Part II requirements. The Committee, while noting your response to validation consideration regarding Compliance with national requirements on data protection regarding not providing your DPIA, stated that the NREC-CT National Statement of Data Compliance template must then be submitted. Further information can be found on our website, including the National Statement of Data Compliance template www.nrecoffice.ie/submit-under-the-clinical-trial-regulation.

2. Compliance with use of biological samples

- No considerations raised by NREC

3. Financial arrangements

- The NREC-CT requested that the Compensation for trial participants document be updated to include compensation for expenses for legally designated representatives also.

4. Proof of insurance

- No considerations raised by NREC

5. Recruitment arrangements

- The NREC-CT noted contradictory information in the Recruitment and informed consent procedure template pg 1 Section 1.1 states that *"Subjects may be identified through site local practice/patient database, or referred to the site by other clinicians"* however on pg 2 Section 1.4 it states that "*Appropriately trained site staff (i.e., Investigator, Study Nurse, Study Coordinator) will be responsible for identifying potential participants and will contact by phone, written communication (letter or email), or during a routine clinic visit.".* The Committee requested that the Recruitment and informed consent procedure template section 1.4 be updated to reflect the fact that other local clinicians may identify and refer the participant.
- It was unclear to the NREC-CT who the Biomarker educational material will be given to. The Committee felt that this document indicates to participants that their treatment plan will be personalised, which is not the case. The Committee requested that if the Biomarker education material is to be given to participants that the language be amended to make this clear such as from "will be" to "would be" or "could be" as this would communicate to participants that this relates to research investigating possibilities of personalised treatments that might be developed in the future.

6. Subject information and informed consent form

- The Sponsor is requested to submit any participant-facing documentation that requires updates as a result of the Part I Assessment.
- The National Office requests that all documentation provided in response to RFI is presented in an accessible and searchable format (Word or original PDF). We are unable to accept scanned documents as these documents are composed of images, rather than searchable text, and cannot be optimised for use with assistive software.
- The NREC-CT requested that the ICF Main pg 23 be updated to include a specific statement for participants to give explicit consent for future use of biological samples being collected and used for the development of diagnostic tests for the drug or disease that is being studied which is separate to the consent for the optional biomarker research.
- The NREC-CT noted that the information on withdrawing/declining participation does not indicate that this can be done without negative consequences until part 2 of the ICF Main pg 19 and 23. The Committee requested that ICF Main pg 9 'Do I have to take part?' be updated to include this information early on in the ICF.
- The NREC-CT noted that the ICF Main does not indicate whether the number of endoscopies over the course of the study (n=3) is more than would be undertaken in the normal course of treatment. The Committee requested that ICF Main pg 2 be updated to include this information for participants and also to include the number of specimens being taken each time.
- The NREC-CT noted a typographical error on ICF Main pg 19 2nd paragraph, pg 19 "The results of this study could be used to identify you will not be included in such reports, presentations and publications".
- The NREC-CT requested that ICF Main pg 2, 2nd paragraph be updated to provide a lay language explanation for participants of what is meant by *"blind"* in *"maintain the blind"* sentence.

- The NREC-CT commented that the paragraphs on ICF Main pg 2 paragraphs 4 and 5 are conflicting/confusing to the participant as one states that study is double blind but the other says if the participant is non responder, they will receive a known (open-label) drug. The Committee requested that these be updated to be less confusing for participants.
- The NREC-CT requested that the ICF Main pg 9 risks section be updated to include details around the risk of chest x-ray, the Committee commented it is not appropriate to advise the participant they should *"ask the doctor".*
- The NREC-CT requested that the ICF Main be updated to include information about what will be used for placebo such that the participant is informed regarding what substance will be injected.
- The NREC-CT advised that the ICF Main pg 10-16 side effects is verbose and repetitive. The Committee requested that this be edited and redesigned to remove the repetition and be written in more lay language.
- The NREC-CT requested that the ICF Main pg 19 be updated to provide information about the availability of the clinical trial results at the end of the trial in the EU database with link to database provided as well.
- The NREC-CT requested that the ICF Main pg 23 be updated to move the consent for optional biomarker research to the following page with a separate signature box to enable participants to explicitly consent to this optional component separate to consent for the main study.
- The NREC-CT requested that the ICF Main and Compliance of Biological Samples form be updated to include details of what country/countries the participant's data and biological samples may be transferred to/stored, and the details of this storage duration.
- The NREC-CT commented that the ICF Main was long with multiple repetitions. The Committee requested that the ICF Main be reviewed and updated to shorten it; remove any duplication such as pregnancy is mentioned on pg 12 and again on pg 16; and delete reference to any items that are not relevant to the study such as video/voice recording (pg 18 and 19).
- The NREC-CT requested that ICF Main pg 14 be updated to include the frequency of Myocardial Infarction and Stroke cases.
- The NREC-CT noted the ICF Main pg 2 makes reference to an iPhone being provided to participants to assist with the electronic diary completion. The Committee were unclear of the following:
    - Is the iPhone only capable of being used for diary completion or can it be used as a phone as well. The Committee requested that the ICF be updated to clarify.
    - Will the participant keep the iPhone at the end of the trial. The Committee requested that the ICF Main be updated to clarify for participants if the iPhone will be returned at the end of the trial.
- The NREC-CT requested that the ICF Main pg 2 be updated to clarify how long the completion of the diary will take the participant each day.
- The NREC-CT noted that participants have to complete a paper record of the drugs they have taken. The Committee queried if this could be done via the iPhone that the participants are being provided with.

- The NREC-CT requested that the ICF Main pg 2 be updated to clarify for participants that the long-term extension study will be a sperate study that participants would have to consent to.
- The NREC-CT requested that the ICF Main pg 16 be updated to include compensation for expenses for legally designated representatives also.

7. Suitability of the clinical trial sites facilities

- No considerations raised by NREC

8. Suitability of the investigator

- No considerations raised by NREC

2023-506288-33-00

Principal Investigators & Institutions: Tallaght University Hospital (Prof Ray McDermott), Cork University Hospital (Prof Richard Bambury), St Vincent's University Hospital (Prof Ray McDermott)

Study title: MK-5684-01A Substudy: A Phase 1/2 Umbrella Substudy of MK-5684-U01 Master Protocol to Evaluate the Safety and Efficacy of MK-5684-based Treatment Combinations or MK-5684 Alone in Participants with Metastatic Castration-resistant Prostate Cancer (mCRPC)

Dossiers Submitted: Part I and II

- **NREC-CT Decision:**
- Request for more information

- **Additional Information Required RFI**

Part II Considerations

1. Compliance with national requirements on data protection

- No NREC-CT considerations raised

2. Compliance with use of biological samples

- The NREC-CT noted that tumour samples from earlier biopsy will be used in the study if available The Committee requested that the "Compliance with biological samples" form Section 2 be updated to include detail around the collection of archival samples.

3. Financial arrangements

- No NREC-CT considerations raised

4. Proof of insurance

- No NREC-CT considerations raised

5. Recruitment arrangements

- No NREC-CT considerations raised

6. Subject information and informed consent form

- The Sponsor is requested to submit any participant-facing documentation that require updates as a result of the Part I Assessment.
- The National Office requests that all documentation provided in response to RFI is presented in an accessible and searchable format (Word or original PDF). We are unable to accept scanned documents as these documents are composed of images, rather than searchable text, and cannot be optimised for use with assistive software.
- The NREC-CT requested that the ICF Main Consent pg 20 be updated to include specific statement that the participant confirms that a copy of the signed and dated Informed Consent Form will be provided to them and that a copy will be retained by the study doctor.
- The NREC-CT requested that the ICF Main be updated to include a statement that the study has been approved by NREC-CT (National Research Ethics Committee for Clinical Trials of Investigational Medicinal Products).
- The NREC-CT requested that the ICF be updated to include detail of approximately how much additional time a participant will give by participating in the study such as hospital visit for additional tumour biopsies, compared to standard of care.

7. Suitability of the clinical trial sites facilities

- No NREC-CT considerations raised.

8. Suitability of the investigator

- No NREC-CT considerations raised

22-NREC-CT-153_Mod-3

Principal Investigators & Institutions: Beaumont Hospital (Prof Orla Hardiman)

Study title: Randomised Double-Blind Placebo-Controlled Phase 3 Trial of Triumeq in Amyotrophic Lateral Sclerosis

Dossiers Submitted: N/A

- **NREC-CT Decision:**
- Favourable

- **Additional Information Required RFI**
- None

2022-502122-41-00_SM-2

Principal Investigators & Institutions: Prof Sean McDermott (Tallaght University Hospital), Dr Jarushka Naidoo (Beaumont Hospital)

Study title: An Open-label, Randomized Phase 3 Study to Evaluate Efficacy and Safety of Pembrolizumab (MK-3475) in Combination with Belzutifan (MK-6482) and Lenvatinib (MK-7902), or MK-1308A in Combination with Lenvatinib, versus Pembrolizumab and

Lenvatinib, as First-line Treatment in Participants with Advanced Clear Cell Renal Cell Carcinoma (ccRCC

Dossiers Submitted: Part I and Part II

- **NREC-CT Decision:**
- Request for more information

- Additional Information Required RFI

Part II Considerations

1. **Subject information and informed consent form**

- The NREC-CT noted the addition of Weight Gain as a side effect in Investigator Brochure Table 57: Patients with VHL-disease-associated RCC, which lists weight gain as Very Common and IB-Table 58: Patients with advanced RCC which lists weight gain as Common (same dosage). The Committee also noted the addition of "Weight gain" as a Common side effect in ICF Main, pg 9. It was unclear to the Committee if the participants on the trial would be those with VHL-disease-associated RCC or with advanced RCC or both, and clarification is requested to ensure the classification in relation to weight gain on the ICF Main is correct.

2023-505543-39-00_SM-12

Principal Investigators & Institutions: Tallaght University Hospital (Dr Patrick Mitchell), Cork University Hospital (Prof. Desmond Murphy), University Hospital Galway (Dr M.J. Harrison)

Study title: A Phase III, Multicentre, Randomised, Double-blind, Chronic-dosing, Parallel-group, Placebo-controlled Study to Evaluate the Efficacy and Safety of Tozorakimab in Participants with Symptomatic Chronic Obstructive Pulmonary Disease (COPD) with a History of COPD Exacerbations (MIRANDA).

Dossiers Submitted: Part I and Part II

- **NREC-CT Decision:**
- Request for more information

- **Additional Information Required RFI**

Part II Considerations

1. **Recruitment arrangements**

- The NREC-CT noted that Recruitment material Poster English has IE-enUK in the footer however both Recruitment material_Patient Study Guide_Proposed and Recruitment material_Study Summary Tool_Proposed have UK-enUK in the

footer. The Committee requested that both these documents are updated to replace UK-enUK with IE-enUK.

2. **Suitability of the investigator**

- The NREC-CT requested that Dr Harrison's CV is updated to include details of relevant clinical trial / study experience and be provided for review.

22-NREC-CT-013_Mod-3

Principal Investigators & Institutions: Prof Maeve Lowery

Study title: Randomized, Multicenter, Phase 3 Study of Zanidatamab in Combination with Chemotherapy with or without Tislelizumab in Subjects with HER2-positive Unresectable Locally Advanced or Metastatic Gastroesophageal Adenocarcinoma (GEA)

Dossiers Submitted: N/A

- **NREC-CT Decision:**
- Favourable

- **Additional Information Required RFI**
- None

22-NREC-CT-107_Mod-2

Principal Investigators & Institutions: Dr Jane Peter

Study title: CH-IV: International Collaborative Treatment Protocol for Children and Adolescents with LANGERHANS CELL HISTIOCYTOSIS

Dossiers Submitted: N/A

- **NREC-CT Decision:**
- Request for more information

- **Additional Information Required RFI**
- The NREC-CT requested the SM form and cover letter be updated to provide justification for the protocol updates.
- The NREC-CT noted that the consent form is not included in the submission. The Committee requested that the consent form for use with this information sheet be updated to show the same date and version as the PIL and that it be provided for review. The Committee commented that the information sheet and consent form should be one document and not separate to ensure the documents do not have different versions and dates on them.

22-NREC-CT-177_Mod-3

Principal Investigators & Institutions: Prof Jarushka Naidoo

Study title: A Phase II, Open-label, Multicentre, Randomised Study of Neoadjuvant and Adjuvant Treatment in Patients with Resectable, Early-stage (II to IIIB) Non-small Cell Lung Cancer (NeoCOAST-2)

Dossiers Submitted: N/A

- **NREC-CT Decision:**
- Favourable

- **Additional Information Required RFI**
- None

- **AOB:**
  - None