National Research Ethics Committee

NREC-CT Meeting

31st July 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
Prof Andrew Green	Committee Member, NREC-CT D
Prof Cathal Walsh	Committee Member, NREC-CT D
Prof Deirdre Murray	Committee Member, NREC-CT D
Dr Geraldine O'Dea	Committee Member, NREC-CT D
Mr Gerry Daly	Committee Member, NREC-CT D
Ms Deirdre McLoughlin	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
Lina Zaga	Committee Member, NREC-CT D
Dr Jeff Moore	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
Rachel McDermott	Admin, National Office for RECs

Apologies: Tina Hickey

Quorum for decisions:

Agenda

- Welcome & Apologies
- 2022-502825-17-00
- 2022-502972-22-00
- 2024-512412-22-00
- 2023-508929-27-00 SM-2
- 2022-500758-41-00 SM-16
- 2023-504899-25-00 SM-4
- 2023-504931-42-00 SM-2
- 2023-504957-11-00 SM-1
- 2023-507294-18-00 SM-3
- 2022-501352-28-00 SM-7
- AOB

- The Chair welcomed the NREC-CT D.
  - The minutes from the previous NREC-CT D meetings on 15th May 2024 and 12th June 2024 were approved.
  - The NREC Business Report was discussed and noted.

Applications

2022-502825-17-00

Institutions: Beaumont Hospital, St Vincent's University Hospital, Tallaght University Hospital, University Hospital Waterford

Study title: A Phase 2 and Phase 3 Peri-operative Trial of Fianlimab and Cemiplimab Compared with Anti-PD1 Alone in Patients with Resectable Stage III and IV Melanoma

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 Considerations raised by NREC
2. Compliance with use of biological samples
• The NREC-CT noted the wording in that Compliance with Use of Biological Samples document pg 4 Q 5.1 that if the study doctor learns information related to the participants health during the course of the study, the study doctor may discuss this information with the participant. The Committee requested that this be updated to the study doctor **will** discuss this information with the participant.
3. Financial arrangements
• No Considerations raised by NREC
4. Proof of insurance
• No Considerations raised by NREC
5. Recruitment arrangements
• The NREC-CT noted the wording pg 131 Protocol ""A third party vendor may assist in recruitment efforts, such as the development of recruitment materials". It was unclear to the Committee if a third-party vendor may also be involved in the actual recruitment of participants. Please update the recruitment and informed consent document pg 1 to clarify. Please note if a third-party vendor will be involved in the actual recruitment of participants, then the ICF's must also be updated to include this information.
6. Subject information and informed consent form
• The NREC-CT noted that the SIS-ICF FBR sub-study for future research is seeking blanket consent for future use of samples, for unspecified purposes, without further consent on pg. 2 of the SIS-ICF FBR. This consent is not described in line with regulations and best practice as it is not confined to the disease or drug under study ie. "different types of diseases and how to diagnose, treat, or prevent them", "linked to certain diseases or disorders" and "studying different types of diseases". This type of consent is not in line with best practice, the Declaration of Taipei 2016 and not in compliance with the Data Protection Act 2018 (Section 36(2) (Health Research) Regulations 2018), where informed participant consent is a mandatory safeguard. The NREC-CT requested that future research is restricted

to ‘specified health research, either in relation to a particular area or more generally in that area or a related area of health research, or part thereof’ and this is clearly stated in the main body and informed consent section of the PISCF. The NREC-CT requested

i) that consent for future use of samples is provided on a separate consent form and not bundled

ii) is made optional, and

iii) consent can only be obtained where future use of samples and data is defined such that participants are fully informed,

and/or iv) that an option is provided to enable participants to consent to be contacted is provided in a separate consent form.

Furthermore, the NREC request confirmation that subsequent research ethics review will be sought for specific research once clearly defined.

- 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 (including documents modified using Optical Character Recognition) as these documents cannot be optimised for use with assistive software.
- The NREC-CT noted the wording pg 20 SIS-ICF Main under personal data that may be collected includes ‘sexual habits or behaviour’. The Committee were unclear as to the relevance/requirement for the collection of this information as part of this clinical trial. Please remove reference to this or update the SIS-ICF Main pg 20 to clarify/provide justification for its collection.
- The NREC-CT requested that the SIS-ICF Main pg 19 “Will I be paid for being in the study” be updated to provide more details around the reimbursement process including reference to accommodation and meal expenses, requirement for providing receipts, travel services partner etc.
- The NREC-CT requested that SIS-ICF Main consent form pg 25 bullet point 5 be updated to include a specific statement that the participant understands that if they leave the study their samples will continue to be used for exploratory research as described in the SIS-ICF Main, unless they separately withdraw their consent for this.
- The NREC-CT noted the wording SIS-ICF Main pg 16 Unknown Risks which states *‘You should also report any new medications or supplements you start taking”.* The Committee suggested that it would be more appropriate to request that the participant consult their study doctor before they start taking any new medications or supplements. The Committee advised that this should also be detailed in the GP letter.

7. Suitability of the clinical trial sites facilities

- No Considerations raised by NREC

8. Suitability of the investigator

- No Considerations raised by NREC

2022-502972-22-00

Institutions: Our Lady of Lourdes Hospital, Beaumont Hospital

Study title: A Randomized, Double-Blind, Placebo-Controlled Phase 3 Study of VE303 for Prevention of Recurrent Clostridioides Difficile Infection: The RestoratiVE303 Study

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 Considerations raised by NREC

2. Compliance with use of biological samples

- No Considerations raised by NREC

3. Financial arrangements

- The NREC-CT noted that Q2 on compensation for trial participant document mentions a monetary payment to participants, parent/caregiver and legal representatives. Please provide justification for the monetary payment.

4. Proof of insurance

- No Considerations raised by NREC

5. Recruitment arrangements

- No Considerations raised by NREC

6. Subject information and informed consent form

- The NREC-CT noted that the ICF Main Adult pg 17 and ICF Caregiver pg 17 for are seeking blanket consent for future use of samples, for unspecified purposes, without further consent. This consent is not described in line with regulations and best practice as it is not confined to the disease or drug under study ie. “Data may be shared with collaborators at other institutions for future purposes” and “perform additional unknown future research”. This type of consent is not in line with best practice, the Declaration of Taipei 2016 and not in compliance with the Data Protection Act 2018 (Section 36(2) (Health Research) Regulations 2018), where informed participant consent is a mandatory safeguard. The NREC-CT requested that future research is restricted to ‘specified health research, either in relation to a particular area or more generally in that area or a related area of health research, or part thereof’ and this is clearly stated in the main body and informed consent section of the PISCF. The NREC-CT requested

i) that consent for future use of samples is provided on a separate consent form and not bundled

ii) is made optional, and

iii) consent can only be obtained where future use of samples and data is defined such that participants are fully informed,

and/or iv) that an option is provided to enable participants to consent to be contacted is provided in a separate consent form.

Furthermore, the NREC request confirmation that subsequent research ethics review will be sought for specific research once clearly defined.

- The NREC-CT requested that ICF Main Adult pg 21 and ICF Caregiver pg 21 Optional consent section should be separated out from the consent for the main trial. The Committee requested that the optional section pg 21 be moved to a separate page from the Main consent form and signature pages. The Optional section should have its own separate signature sections to ensure explicit consent.
- The NREC-CT requested that the ICF Main Adult pg 21 consent form for main trial be updated to remove the consent statement *"I understand that the coded information collected about me will be used to support other research in the future and may be shared pseudo-anonymously with other researchers*" as this is an optional component.
- The NREC-CT requested that the ICF Caregiver pg 21 consent form for main trial be updated to remove the consent statement *"I understand that the coded information collected about my child will be used to support other research in the future and may be shared pseudo-anonymously with other researchers."* as this is an optional component.
- 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 (including documents modified using Optical Character Recognition) as these documents cannot be optimised for use with assistive software.
- The NREC-CT requested that the ICF Main Adult pg 12 and ICF Caregiver pg 12 be updated to replace "you may be reimbursed for any reasonable travel" to "you will be reimbursed for any reasonable travel"
- The NREC-CT advised that the language in the ICF Assent 12–15-year-old is not age appropriate and should contain greater communication materials for this age group. The Committee requested that the ICF Assent be updated to be in more age-appropriate language.
- The NREC-CT noted the wording on Protocol page 56: "If a participant chooses to withdraw… tests and evaluations listed for W8 will be carried out within 7 days". The Committee requested that the ICF Main Adult pg 4-5 be updated to clarify the

rationale for requiring participants who have withdrawn from the study to continue to have test/evaluations after they have withdrawn. The Committee also requested that the ICF Main Adult pg 4-5 be updated to make it clear that it optional for participants who have withdrawn to take part in these tests and evaluations.

7. **Suitability of the clinical trial sites facilities**
   - No Considerations raised by NREC
8. **Suitability of the investigator**
   - No Considerations raised by NREC

2024-512412-22-00

Institutions: CHI Temple St

Study title: A Phase III study to evaluate the efficacy of INM004 (Shiga antitoxin) in pediatric patients with Shiga toxin-producing Escherichia coli-associated Hemolytic Uremic Syndrome

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 Considerations raised by NREC
2. **Compliance with use of biological samples**
   - No Considerations raised by NREC
3. **Financial arrangements**
   - No Considerations raised by NREC
4. **Proof of insurance**
   - No Considerations raised by NREC
5. **Recruitment arrangements**
   - No Considerations raised by NREC
6. **Subject information and informed consent form**
   - The NREC-CT requested that the SIS and ICF Adults, SIS and ICF Parents/Guardian pg 1 be updated to include the EU trial number for participants.
   - The NREC-CT requested that the SIS and ICF Adults and SIS and ICF Parents/Guardians consent pages 11-13 be updated as follows:
     - remove the no tick boxes from the mandatory consent statements as participants/parents/guardians cannot tick no if they wish to participate.
     - the additional consent statements on pg 13 such as *"I understand that any review of my original medical records will be done with the assistance of the Study Doctor"* also require a box for the participant to initial or tick to consent

    - The optional consent statement for future research “I understand that the storage and processing of my personal data and/or blood samples may be used for the purpose of future research, once approved by a relevant research ethics committee” and the yes/no tick boxes should be separated out from the consent for the main trial. The Committee requested that the optional section pg 13 be moved to a separate page from the Main consent form and signature pages. The Optional component section should have its own separate signature sections to ensure explicit consent.
- The NREC-CT noted wording on SIS and ICF Adults and SIS and ICF Parents/Guardians pg 9 that the study doctor will ask you for permission if your/your child’s samples are to be used in future for a purpose not described in this document”. The Committee requested that SIS and ICF Adults and SIS and ICF Parents/Guardians consent form optional component section be updated to include consent statement for the participant to consent to be contacted in the future.
- 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 (including documents modified using Optical Character Recognition) as these documents cannot be optimised for use with assistive software.
- The NREC-CT requested that the Patient ID Card be updated to include the name of the trial.
- The NREC-CT requested that the SIS and ICF 12-15 yr pg 2 be updated to replace “sign this consent form” with “sign this assent form”.
- The NREC-CT noted the SIS and ICF 12-15 yr pg 5 states “please mark the box” however there are no tick boxes. The Committee advised that there should only be a yes tick box as participants would only sign the form if they assent to take part The Committee requested that the SIS and ICF 12-15 yr pg 5 be updated to include tick box for yes.
- The NREC-CT requested that the SIS and ICF 6 yr be updated to include further detail to explain the study to the child, including referencing the child being in hospital, and why they are being invited to participate in this study.
- The NREC-CT advised that the assent form does not need to countersigned by the parents/guardian as there is a separate ICF for parents/guardians to sign. The Committee requested that the signature space for parents to countersign be removed from pg 3 of the SIS and ICF 6yr.
- The NREC-CT noted Yes/No options on pg 3 of the SIS and ICF 6 yr assent form to mark the participants choose to take part or not and advised that there should only be a yes option as participants would only sign the form if they assent to take part. The Committee requested that the SIS and ICF 6 yr pg 3 be updated remove the No option.
- The NREC-CT advised that the SIS and ICF Adults and SIS and ICF Parents/Guardians should start with an invitation and description of the trial and not a discussion of legal terms and consent. The Committee requested that SIS and ICF Adults and SIS and ICF Parents/Guardians be updated to move the “Why am I/is my child being invited to participate?” and “What is the purpose of the study” sections to ICF’s to the start of the ICF ahead of the discussion on legal terms etc.
- The NREC-CT requested that the SIS and ICF Parents/Guardians pg 3 “Your child is being invited to participate in this Study because they are a patient between 9 months and 17 years of age” be updated to “between 9 months and 15 years of

age" as participants aged 16yrs+ may consent themselves to both participation in a regulated study and associated data processing.

- The NREC-CT noted the SIS and ICF Parents/Guardians pg 5 lists a series of responsibilities for the child while taking part in the study, The Committee requested that this section be updated to reflect these are responsibilities for parents/guardians and not the child.
- The NREC-CT requested that the SIS an ICF Parents and Guardians pg 10 be updated to remove reference to parents contacting the NREC to discuss their child's rights as this is incorrect.
- The NREC-CT requested the SIS and ICF Adults p 9 be updated to remove reference to parents contacting the NREC if you have any questions, complaints or concerns about the research.
- The NREC-CT requested that SIS and ICF Adults pg 16/17, SIS and ICF Parents/Guardians pg 16/17 *"How can you exercise your/your child's data protection rights"* be updated to explicitly refer to GDPR and Irish legislation and to detail what will happen to the samples and data already collected if participant withdraws.
- The NREC-CT requested that the SIS and ICF Adults pg 7 and SIS and ICF Parents/Guardians pg 7 be updated to include detail around the mechanism for reimbursement.

7. Suitability of the clinical trial sites facilities

- No Considerations raised by NREC

8. Suitability of the investigator

- No Considerations raised by NREC

2023-508929-27-00 SM-2

Institutions: Children's Health Ireland

Study title: A Phase 3 open-label, multicenter study of the long-term safety and efficacy of intravenous recombinant coagulation factor VIII Fc-von willebrand factor-XTEN fusion protein (rFVIIIFc-VWF-XTEN; BIVV001) in previously treated patients with severe hemophilia A

Dossiers Submitted: Part I and II

- **NREC-CT Decision:**

Request for more information

- **Additional Information Required RFI**

Part II Considerations

1. Compliance with use of biological samples

- This document represents information already approved under CTD

2. Proof of insurance

- No Considerations raised by NREC

3. 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 (including documents modified using Optical Character Recognition) as these documents cannot be optimised for use with assistive software.
- The NREC-CT requested that SIS ICF Parent/ Guardian is updated to include reference to prohibition of FVIII products during the study apart from in emergency or limited accidental situations

4. Suitability of the investigator

- This document represents information already approved under CTD

2022-500758-41-00 SM-16

Institutions: St James's Hospital

Study title: A multi-center, randomized, double-blind, placebo-controlled multiple ascending dose study to evaluate the safety and tolerability of QRL-201 in Amyotrophic Lateral Sclerosis

Dossiers Submitted: Part I and II

- **NREC-CT Decision:**

Request for more information

- **Additional Information Required RFI**

Part II Considerations

1. 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 (including documents modified using Optical Character Recognition) as these documents cannot be optimised for use with assistive software.
- The NREC-CT requested that the Main ICF Risk section 6 be updated to include information around the risk of seizures.
- The NREC-CT requested clarification as to whether existing participants will be re-consented with this updated Main ICF and when this will occur. Reconsent is recommended by the NREC due to the risk of seizures identified.
- The NREC-CT noted the half life of CSF is approximately 100 days (Protocol, page 30). The NREC-CT requested that participants are informed in the Main ICF regarding any risks for interactions with concomitant medications in this period.

2023-504899-25-00 SM-4

Institutions: St Vincent's University Hospital, Tallaght University Hospital

Study title: A Phase 3 Randomized, Open-label Study of MK-5684 Versus Alternative Abiraterone Acetate or Enzalutamide in Participants With Metastatic Castration-resistant Prostate Cancer (mCRPC) Previously Treated With Next-generation Hormonal Agent (NHA) and Taxanebased Chemotherapy

Dossiers Submitted: MSC Part I and II

- **NREC-CT Decision:**

Request for more information

- **Additional Information Required RFI**

Part II Considerations
1. Compliance with use of biological samples
• No Considerations raised by NREC
2. Financial arrangements
• The NREC-CT notes from Compensation for trial participants document that participants will be provided with branded tote bag designed with the study logo. The Committee requests that the logo be omitted from the bag to avoid the participants' participation in the study and/or condition being shown publicly
3. Recruitment arrangements
• No Considerations raised by NREC
4. 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 (including documents modified using Optical Character Recognition) as these documents cannot be optimised for use with assistive software.
• The NREC-CT noted the following duplication of risks/SE's in the ICF Main and requested that they be updated to clarify: ○ pg 12 and 13. Sudden and hot flushes appear to be listed both as very common and common side effects – please clarify. ○ pg 14 and 15. Abdominal pain and upper abdominal pain are listed separately ○ pg 15 Duplication of SE – lab test finding of high cholesterol levels in the blood (blood cholesterol increased) and high levels of cholesterol in the blood (hypercholesterolaemia)
• The NREC-CT noted that compensation to participants is being added as part of this Substantial Modification in the form of a monetary stipend, and requested clarification as to how participants already enrolled in the study will be informed of this change, and how they can claim expenses for their time on the study to date.

2023-504931-42-00 SM-2

Institutions: University Hospital Limerick, Beaumont Hospital

Study title: A Phase 2 Study to Evaluate the Efficacy and Safety of MK-1026 in Participants with Hematologic Malignancies

Dossiers Submitted: Part I and II

- **NREC-CT Decision:**

  Request for more information

- **Additional Information Required RFI**

Part II Considerations
1. Compliance with use of biological samples
• This document represents information already approved under CTD
2. Financial arrangements
• This document represents information already approved under CTD
3. Recruitment arrangements
• This document represents information already approved under CTD
4. 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 (including documents modified using Optical Character Recognition) as these documents cannot be optimised for use with assistive software. • The NREC-CT noted addition of wording on pg 2 on Summary PIS and pg 6 on Main Adult Consent to extra-nodal sampling for participants with marginal zone lymphoma. The Committee requested that both documents be updated to provide a lay language explanation for extra-nodal sampling. • The NREC-CT requested clarification if existing participants will be re-consented with this updated Main ICF and Summary PIS and when this will occur.
5. Suitability of the investigator
• This document represents information already approved under CTD

2023-504957-11-00 SM-1

Institutions: Tallaght University Hospital, St Vincent's University Hospital

Study title: A Phase 3, Randomized, Open-label Study of MK-5684 Versus Alternative Abiraterone Acetate or Enzalutamide in Participants with Metastatic Castration-resistant Prostate Cancer (mCRPC) That Progressed On or After Prior Treatment with One Next generation Hormonal Agent (NHA)

Dossiers Submitted: Part I and II

- **NREC-CT Decision:**

  Favourable

2023-507294-18-00 SM-3

Institutions: Mater Misericordiae University Hospital, Tallaght University Hospital, Mater Private Hospital

Study title: A Phase III Randomized, Open-label Study to Evaluate Efficacy and Safety of Pembrolizumab (MK-3475) in Combination with Axitinib versus Sunitinib Monotherapy as a First-line Treatment for Locally Advanced or Metastatic Renal Cell Carcinoma (mRCC) (KEYNOTE-426)

Dossiers Submitted: Part I and II

- **NREC-CT Decision:**

  Request for more information

- **Additional Information Required RFI**

Part II Considerations

1. **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 (including documents modified using Optical Character Recognition) as these documents cannot be optimised for use with assistive software.
- The NREC-CT requested that the ICF Main Addendum be updated to include additional detail around the rationale for the updates. The Committee also requested that ICF Main Addendum pg 2 be updated to provide rationale as why the second course is no longer going to be available.

2022-501352-28-00 SM-7

Institutions: St Vincent's University Hospital, St James's Hospital, Beaumont Hospital, University Hospital Galway

Study title: A randomized, placebo-controlled, double-blind, multi-center, phase III trial to assess the efficacy and safety of trimodulin (BT588) in adult hospitalized subjects with severe community-acquired pneumonia (sCAP)

Dossiers Submitted: Part I and II

- **NREC-CT Decision:**

  Favourable

- **AOB:**
    - Two stage consent process was discussed