National Research Ethics Committee

NREC-CT Meeting

28th August 2024

Attendance

Name	Role
Colm O'Donnell	Acting Chairperson, NREC-CT B
Ms Serena Bennett	Committee Member, NREC-CT B
Dr Åine de Róiste	Committee Member, NREC-CT B
Dr Karina Halley	Committee Member, NREC-CT B
Prof. Michaela Higgins	Committee Member, NREC-CT B
Ms Jasmine Joseph	Committee Member, NREC-CT B
Dr Ciaran Lee	Committee Member, NREC-CT B
Dr Andrew Lindsay	Committee Member, NREC-CT B
Dr Niall McGuinness	Committee Member, NREC-CT B
Ms Evelyn O'Shea	Committee Member, NREC-CT B
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 Megan O'Neill	Project Officer, National Office for RECs
Mr Ciaran Horan*	Administrative Assistant, National Office for RECs

*Drafted minutes

Apologies: Dr Cliona McGovern, Dr John Hayden, Dr Karina Halley, Prof Seamus O'Reilly, Ann Twomey

Quorum for decisions: Yes

Agenda

- Welcome & Apologies
- 2024-511458-32-00
- 2023-503188-40-00
- 2024-513009-30-00
- 2023-504993-40-00 SM-2
- 2023-508884-59-00 SM-1
- 2022-502442-27-00 SM-2
- 23-NREC-CT-020_Mod-2
- 22-NREC-CT-050_Mod-5
- 21-NREC-CT-086_Mod-5
- AOB

- The Chair welcomed the NREC-CT B.
  - The minutes from the previous NREC-CT B meeting on 3rd July 2024 were approved.
  - The NREC Business Report was discussed and noted.

Applications

2024-511458-32-00

Institutions: CHI Crumlin

Study title: A multicenter study to evaluate the efficacy, safety, tolerability, and pharmacokinetics of filgotinib, with single arm induction and maintenance, in pediatric subjects (8 to <18 years of age) with moderately to severely active ulcerative colitis

Dossiers Submitted: Part I & Part II

- NREC-CT Decision:

Request for more information

Part II Considerations

1. **Compliance with national requirements on data protection**
   - No Considerations
2. **Compliance with use of biological samples**
   - No Considerations
3. **Financial arrangements**
   No Considerations
4. **Proof of insurance**
   No Considerations
5. **Recruitment arrangements**
   - No Considerations
6. **Subject information and informed consent form**
   - The NREC-CT would like to commend the Sponsor on the high quality of participant materials submitted for assessment.

The NREC-CT noted that the section on future research in the Parental PISCF (pg. 18) “to help improve the design of research studies in the future”, and Future Scientific Research PISCF (pg. 2), “your information then contributes to more and broader science”, is not described in line with regulations and best practice. The NRECT-CT noted that the Future Scientific Research PISCF (page 2) also stated, "If you can allow re-use of your information, that may help us to learn about:

● the way filgotinib and drugs of the same group work,

● ulcerative colitis."

However, these statements are contradictory, and it is not clear that the future research would only take place in the area of the disease or drug under study.

- 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,
    1. 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,

2. 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: NREC guidance on use of biological samples and associated data - Use of biological samples and associated data - NREC (nrecoffice.ie)

- The NREC-CT noted that the Quality of Life Questionnaire could cause some participants distress due to the nature of the questions, and requested that additional information is included in the PISCF to outline the safeguards and processes in place if a participant demonstrates levels of anxiety or mental distress.
- The NREC-CT requested that the Parental PISCF is modified to clearly set out that their child has been offered Filgotinib either because other therapies are not working or not appropriate for the participant.
- The NREC-CT the language on pg. 9 of the PISCF, "It is not certain that these will happen to you while you are taking filgotinib", and requested that this information regarding the risk of side effects is modified, making it clear to participants that it is not expected that filgotinib will cause effects that are not yet known.
- 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.

7. Suitability of the clinical trial sites facilities

- No Considerations

8. Suitability of the investigator

- No Considerations

2023-503188-40-00

Institutions: CHI Crumlin

Study title: An Open-label, Phase 3 Study to Evaluate the Pharmacokinetics, Safety, and Immunogenicity of Vedolizumab Subcutaneous in Pediatric Subjects With Moderately to Severely Active Ulcerative Colitis or Crohn's Disease Who Achieved Clinical Response Following Open–label Vedolizumab Intravenous Therapy

Dossiers Submitted: Part I & Part II

- NREC-CT Decision:

Request for more information

Part II Considerations

9. Compliance with national requirements on data protection

- No Considerations

10. Compliance with use of biological samples

- No Considerations

11. Financial arrangements

- No Considerations

12. Proof of insurance

- No Considerations

13. Recruitment arrangements

- The NREC-CT considered that some of the language used in the advocacy email may not be appropriate for an Irish audience. The Committee requested clarification as to whether the advocacy email and letter submitted will be used in Ireland, and if so, requested that the language in these documents is modified to take on a more neutral tone.

14. Subject information and informed consent form

- The NREC-CT would like to commend the Sponsor on the quality of participant materials submitted for assessment.
- The NREC-CT noted that the Quality of Life Questionnaire could cause some participants distress due to the nature of the questions, and requested that additional information is included in the PISCF to outline the safeguards and processes in place if a participant demonstrates levels of anxiety or mental distress.
- The Sponsor is requested to submit any Part II 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.

15. Suitability of the clinical trial sites facilities

- No Considerations

16. Suitability of the investigator

- No Considerations

2024-513009-30-00

Institutions: Portiuncula University Hospital, St. Vincent's University Hospital, OLOL Hospital, Beaumont Hospital, Midland Regional Hospital Mullingar, Connolly Hospital

Study title: A Phase 2a Multicenter, Randomized, Platform Study of Targeted Therapies for the Treatment of Adult Subjects with Moderate to Severe Crohn's Disease

Dossiers Submitted: Part I & Part II

- NREC-CT Decision:

Request for more information

Part II Considerations

17. Compliance with national requirements on data protection

- No Considerations

18. Compliance with use of biological samples

- No Considerations

19. Financial arrangements

- Please submit a brief description of the financing of the clinical trial. This document must be provided in an accessible and searchable format (Word document 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 clarification as to who the “Budget for Submission” document and payment schedule referred to, does this pertain to the local hospital?

20. Proof of insurance

- No Considerations

21. Recruitment arrangements

- The NREC-CT noted that the Recruitment and informed consent procedures document states that subjects may be identified through the use of digital advertisement on social media, however these have not been submitted for NREC review. The NREC-CT requested clarification as to whether digital advertising through social media would be used, and if so that this material is submitted for NREC review.

22. Subject information and informed consent form

- The NREC-CT noted that the primary and secondary study endpoints are at 12 weeks, with no study endpoints beyond this period. The Committee requested further information of the endpoint/purpose of treatment beyond this time 12-week period, including the long-term extension study? The NREC-CT requested that this be explained to the participant in the PISCF.
- The NREC-CT noted that TB screening may be required “according to local guidelines” (pg. 6 PISCF). The NREC-CT queried whether TB screening is required in Ireland and that the PISCF is updated so it is clear to participants in Ireland if so.
- The NREC-CT requested that the PISCF is modified to explicitly communicate the potential risk of progressive multifocal leukoencephalopathy (PML) and the severity of this potential side effect, noting that PML after treatment with natalizumab has a 2-year mortality rate of 25-30% and those who survive often have severe disability. The NREC-CT questioned what additional processes are in place to ensure the safety of participants and requested that this is elucidated in the PISCF.
- The NREC-CT noted that three colonoscopies are scheduled in the Study Activity Table provided in the protocol, though the Study Activity Table given in the Main PISCF suggests that there will be eight “Blood and biopsy samples for biomarkers”. The NREC-CT requested that the PISCF is modified to align with the protocol.
- The NREC-CT queried whether male participants who may be sexually active with a woman of childbearing potential are required to use birth control measures and for how long after last dose of the study drug. The PISCF should be modified to reflect this information.
- The NREC-CT requested that the PISCF is modified to clearly set out to participants that those with a prior inadequate response to risankizumab will not be randomised to Group 1 (risankizumab only), as described in the protocol.
- The NREC-CT requested that the PISCF is updated to provide information for participants regarding continuation or inclusion in the long-term extension study, including details that risankizumab is the only drug that will be available in the long-term study.
- The NREC-CT requested that the information regarding the Long-Term Extension Study given on pg.4 of the PISCF is modified to give the name of the study drug involved, as it has been set out for the other groups (i.e. ➢ Long-Term Extension study: risankizumab alone).
- The NREC-CT noted that pg.4 of the PISCF refers to IV infusion for the delivery of risankizumab and that self-injection of risankizumab is later described for the long-term extension study. The NRECT-CT requested that the PISCF is updated to provide an explanation to participants of these alternative administration routes.

- The NREC-CT requested that the details regarding the “rescue therapy” that participants may commence at week 12 (pg. 5 Main PISCF) are further elucidated, clarifying whether participants will continue with the treatment arm, continue to participate in the study or may be withdrawn from the study.
- The NREC-CT requested that the Study Screening Procedure item “Biomarker and exploratory research samples will be collected (blood, stool and biopsy)” on pg.5 of the PISCF is modified, clearly setting out for participants that the exploratory research blood sample is optional.
- The NREC-CT requested pg.2 of the PISCF (What is the purpose of this study & why have I been invited?) is modified to include the potential participant’s consent, “If you are selected to be in this study, **and consent”.**
- The NREC-CT requested that the participant-facing materials are reviewed and modified as appropriate to ensure that the information provided is consistent and legible, noting some typographical errors in the PISCF.
- The NREC-CT requested that the PISCF is modified to use the term “participant” instead of “subject”.
- 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.

23. Suitability of the clinical trial sites facilities

- No Considerations

24. Suitability of the investigator

- No Considerations

2023-504993-40-00 SM-2

Institutions: Mater Misericordiae University Hospital, Beaumont Hospital

Study title: A Phase 3b, multi-center, randomized, parallel-group, open-label, non-inferiority study evaluating the efficacy, safety, and tolerability of oral dolutegravir/lamivudine once-daily as a first-line regimen compared to oral bictegravir/emtricitabine/tenofovir alafenamide once daily for virologic suppression and maintenance in antiretroviral therapy naive adults living with HIV

Dossiers Submitted: Part I & Part II

- NREC-CT Decision:

Request for more information

Part II Considerations

25. Compliance with national requirements on data protection

- No Considerations

26. Compliance with use of biological samples

- The NREC-CT requested further information explaining the increase in volume of the blood draws.

27. Financial arrangements

- No Considerations

28. Proof of insurance

- No Considerations

29. Recruitment arrangements

- No Considerations

30. Subject information and informed consent form

- The NREC-CT noted reference to eConsent material in the cover letter, however this has not been submitted for Ireland. The NREC-CT requested clarification as to whether eConsent material will be used in Ireland and if so, that this is submitted for ethical review.
- The NREC-CT noted that assessments have been added to the Withdrawal Visits and requested that these additional assessment activities are set out clearly in the PISCF, as described in the SoA in the protocol.
- The NREC-CT noted that in the Pregnant Participant PISCF the Participant is directed to the main PISCF to learn who has access to data. This is not considered sufficient for the purposes of informed consent. The NREC-CT requested that the Pregnant Participant PISCF is modified throughout to include data protection information to provide sufficient detail instead of referring to the main PISCF.
- The NREC-CT requested that the monetary amounts for reimbursement are removed from the **Main PISCF** (**Page 34).**
- 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.

31. Suitability of the clinical trial sites facilities

- No Considerations

32. Suitability of the investigator

- No Considerations

2023-508884-59-00 SM-1

Institutions: St James's Hospital, Our Lady's Children's Hospital

Study title: ATLAS-OLE: An Open-label, Long-term Safety and Efficacy Study of Fitusiran in Patients with Hemophilia A or B, with or without Inhibitory Antibodies to Factor VIII or IX

Dossiers Submitted: Part I & Part II

- NREC-CT Decision:

Request for more information

Part II Considerations

33. Compliance with national requirements on data protection

- No Considerations

34. Compliance with use of biological samples

- No Considerations

35. Financial arrangements

- No Considerations

36. Proof of insurance

- No Considerations

37. Recruitment arrangements

- No Considerations

38. Subject information and informed consent form

- The NREC-CT noted that the section on future research in the **Main PIS/CF (pg. 54)** 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,
    1. 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,
    2. 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 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.

39. Suitability of the clinical trial sites facilities

- No Considerations

40. Suitability of the investigator

- No Considerations

2022-502442-27-00 SM-2

Institutions: Conolly Hospital, St Vincent's University Hospital, University Hospital Galway

Study title: A Phase 3, randomised, double-blind, parallel-group, event-driven, cardiovascular safety study with BI 456906 administered subcutaneously compared with placebo in participants with overweight or obesity with established cardiovascular disease (CVD) or chronic kidney disease, and/or at least two weight-related complications or risk factors for CVD

Dossiers Submitted: Part I & II

- NREC-CT Decision:

Favourable

23-NREC-CT-020_Mod-2

Institutions: Tallaght University Hospital

Study title: Randomised phase 3 trial of enzalutamide in first line androgen deprivation therapy for metastatic prostate cancer: ENZAMET.

Dossiers Submitted: N/A

- NREC-CT Decision:

  Favourable

22-NREC-CT-050_Mod-5

Institutions: University Hospital Waterford

Study title: A randomized, double-blind, parallel-group, multicentre, phase II study to compare the efficacy and tolerability of fulvestrant (FaslodexTM) 500mg with placebo and fulvestrant (FaslodexTM) 500mg in combination with PD-0332991 (Palbociclib) as first line treatment for postmenopausal women with hormone receptor-positive metastatic breast cancer, who have completed at least 5 years of adjuvant endocrine therapy and remained disease free for more than 12 months following its completion or have “de novo” metastatic disease “The FLIPPER Study”

Dossiers Submitted: N/A

- NREC-CT Decision:

- Favourable

21-NREC-CT-086_Mod-5

Institutions: Trinity College Dublin

Study title: A Phase 1/2 Trial of the Synthetic Cannabinoid ART27.13 in Patients with Cancer Anorexia and Weight Loss

Dossiers Submitted: N/A

- NREC-CT Decision:

- Favourable

- No AOB