National Research Ethics Committee

NREC-CT B

23rd of February 2022

Attendance

Name	Role
Dr Cliona McGovern	Chairperson, NREC-CT B
Dr Jean Saunders	Deputy Chairperson, NREC CT-B
Ms Serena Bennett	Committee Member, NREC-CT B
Mr Philip Berman	Committee Member, NREC-CT B
Dr Enda Dooley	Committee Member, NREC-CT B
Dr Lorna Fanning	Committee Member, NREC-CT B
Dr John Hayden	Committee Member, NREC-CT B
Dr Mary McDonnell Naughton	Committee Member, NREC-CT B
Dr Eimear McGlinchey	Committee Member, NREC-CT B
Mr Gavin Lawler,	Committee Member, NREC-CT B
Ms Paula Prendeville	Committee Member, NREC-CT B
Prof. Colm O'Donnell	Committee Member, NREC-CT B
Ms Aileen Sheehy*	Programme Manager, National Office for RECs
Dr Marta Pisarska*	Postdoctoral Intern, National Office for RECs
Hope Williams	Student Intern, National Office for RECs

*Drafted minutes

Apologies:

Ms Mandy Daly, Ms Caoimhe Gleeson, Prof. Abhay Pandit, Prof. John Faul, Prof. David Smith, Dr Mark Robinson

Quorum for decisions: Yes

Agenda

- Welcome & Apologies
- Application 22-NREC-CT-020
- Application 22-NREC-CT-026
- Application 22-NREC-CT-027
- Application 22-NREC-CT-028
- Application 22-NREC-CT-029
- AOB

- The Chair welcomed the NREC-CT B.
  - The Minutes from the NREC-CT B meeting on the 8th if December were approved.

Applications

22-NREC-CT-020

Principal Investigator: Dr Mark Cahill

Study title: MR42410 A Phase IIIb, Multicenter, Randomized, Visual Assessor-Masked Study Of The Effectiveness And Safety Of A 36-Week Refill Regimen For The Port Delivery System With Ranibizumab Vs Aflibercept Treat & Extend In Subjects With Neovascular Age-Related Macular Degeneration (DIAGRID)

Lead institution: Royal Victoria Eye and Ear Hospital

- NREC-CT comments:

- The NREC-CT B noted this clinical trial application represents a Phase IIIb, Multicenter, Randomized, Visual Assessor-Masked Study of The Effectiveness And Safety Of A 36-Week Refill Regimen For The Port Delivery System With Ranibizumab Vs Aflibercept Treat & Extend In Subjects With Neovascular Age-Related Macular Degeneration (DIAGRID).
- The NREC-CT B commented positively on this trial, praising the supplementary patient facing documents in particular.
- The NREC-CT B agreed that additional information was required to inform its deliberations and therefore, was not yet in a position to return a final ethics decision.

- NREC-CT Decision:

- Request for Further Information

- Additional Information Required

- The NREC-CT B requested further information around contingency plans for the maintenance of the implants in participants in the event that the company ceases operations.
- The NREC-CT B requested further information on what post study care would be provided to participants in instances where the treatment is considered effective and further information on access to the treatment once the trial has terminated. This information would also need to be further elucidated in the participant materials.
- The NREC-CT noted that the CE certification for the device is currently underway and requested an update on this process.
- The NREC-CT B requested further clarification on the underlying effects of adjunct treatments with the implant-host response.
- The NREC-CT B noted that the information around the implant surgery may be limited in the participant materials and requested that this aspect of the trial is further elucidated in the materials.
- The NREC-CT-B requested that the participant materials provide participants with further information around out-of-hours contact information in the event of an emergency.
- The NREC-CT requested that the section on the use, protection and sharing of personal data is adapted in line with the Health Research Regulations 2018 so that explicit consent for the use of data is limited to a specific disease area for future purposes.
- The NREC-CT B requested that the ICF Imaging Certificate is adapted for Irish sites.
- The NREC-CT B requested that the CVs of Dr Ng and Dr Burke are submitted for review.
- In the event of injury or harm, the NREC-CT B noted that compensation may not be given to a participant depending on the competence of the participant or study team to adhere to the protocol. The Committee considered that this is an onerous burden to place on participants and requested further clarity around this caveat and an overview of how this adherence will be assessed.
- The NREC-CT B wanted to bring to the attention of the applicant that the application form contained several copy / paste and referencing errors and requested that for future applications, documents are proofread ahead of submission.

22-NREC-CT-026

Principal Investigator: Dr Anne Fortune

Study title: A Phase 3 Open-Label, Randomized Study of Fixed Duration Pirtobrutinib (LOXO-305) plus Venetoclax and Rituximab versus Venetoclax and Rituximab in Previously Treated Chronic Lymphocytic Leukemia/Small Lymphocytic Lymphoma (BRUIN-CLL-322)

Lead institution: University Hospital The Mater Misericordiae

- NREC-CT comments:

- The NREC-CT B noted this clinical trial application represents a Phase 3 Open-Label, Randomized Study of Fixed Duration Pirtobrutinib (LOXO-305) plus Venetoclax and Rituximab versus Venetoclax and Rituximab in Previously Treated Chronic Lymphocytic Leukemia/Small Lymphocytic Lymphoma (BRUIN-CLL-322).
- The NREC-CT B complemented the scientific design of this study, however, additional clarification regarding a number of inconsistencies in the documentation was required.
- The NREC-CT B agreed that additional information was required to inform its deliberations and therefore, was not yet in a position to return a final ethics decision.

- NREC-CT Decision:

- Request for Further Information

- Additional Information Required:

- The NREC-CT B requested that the frequency of scans and risks associated with exposure to ionising radiation are adequately addressed in the participant materials and that the NREC-CT Ionising Radiation Appendix Form is completed and submitted as part of the response to the request for further information.
- The NREC-CT B noted discrepancies across the documentation around the duration of the trial and requested clarification on this point.
- The NREC-CT B requested that a signed Investigator's Brochure is submitted as part of the response to the request for further information.
- The NREC-CT B considered the content in the Participant Information Leaflet (PIL) too complex for a lay audience and requested it is revised and restructured to ensure that the document is accessible to all participants. The Committee also requested that a brief plain English executive summary of the salient points of the study is included at the beginning of the PIL, outlining the aim of the study.
- The NREC-CT B noted that information related to sites in the US have not been removed from the PIL and requested that all participant materials are adequately adapted for Irish sites.
- The NREC-CT B requested that participants are provided with a minimum time period of 24 hours in which the person can consider participation in advance of consenting.

- The NREC-CT B noted that under Section 9.1 of the PIL, LOXO Oncology will be paying the 'study doctor and/or the study clinic/hospital' and requested that this point is elucidated further to ensure participants are fully informed.
- As the application states that recruitment would be through the direct site research team from a known patient pool, the NREC-CT B requested clarification whether the adverts shared with the Committee for review will be used in Ireland.
- The NREC-CT B considered the information provided on the Mater Hospital site to be limited and requested that a more comprehensive Site Suitability Assessment form is resubmitted as part of the response to the request for further information.
- The NREC-CT B noted that a CV for the national Principal Investigator was submitted, but that the information provided was limited and requested further information on the experience of the site PI.
- The NREC-CT B further requested the CVs for the other site PIs involved with the study.
- The NREC-CT B noted that the insurance certificate provided would not cover the full duration of the trial and requested assurances that cover will be in place for the full duration of the trial.
- The NREC-CT B noted discrepancies across the documentation around the retention period of data and requested clarification on this point.
- The NREC-CT B noted that section 10.7 of the PIL is not in line with national laws on the use of data for research purposes and is inconsistent with the DPIA provided. The Committee required that the text is amended to reflect national legislation and the DPIA.
- The NREC-CT B noted the consent process for the future use of biological samples and data is not in line with national regulations on 'explicit consent' (the Health Research Regulations 2018) and requested that the applicant provides the participant with specific choices as to how their samples and data would be used for future purposes, such as limiting future use to a specific disease area.
- Further to the above, NREC-CT B requested confirmation that any future research project using samples or data from participants involved in this study would undergo full ethics review. This should also be captured in the participant materials.
- The NREC-CT B requested that consent for future biomedical research is separated out from the main consent form.

22-NREC-CT-027

Principal Investigator: Dr John Quinn

Study title: A Phase 2, Randomized, Parallel, Open-Label Study to Investigate the Safety, Efficacy, and Pharmacokinetics of Various Dosing Regimens of Single-Agent Belantamab Mafodotin (GSK2857916) in Participants with Relapsed or Refractory Multiple Myeloma (DREAMM-14)

Lead institution: Beaumont Hospital

- NREC-CT comments:

- The NREC-CT B noted this clinical trial application represents a Phase 2, Randomized, Parallel, Open-Label Study to Investigate the Safety, Efficacy, and Pharmacokinetics of Various Dosing Regimens of Single-Agent Belantamab Mafodotin (GSK2857916) in Participants with Relapsed or Refractory Multiple Myeloma.
- The NREC-CT B commented that a number of documents included in this application required revision.
- The NREC-CT B agreed that additional information was required to inform its deliberations and therefore, was not yet in a position to return a final ethics decision.

- NREC-CT Decision:

- Request for Further Information

- Additional Information Required:

- The NREC-CT B noted that as part of the trial participants would need to undergo frequent eye tests, but limited information is available on this. The Committee requested further information on how this would be managed and arranged, and if participants would be financially supported as part of this aspect of the study. This information should also be captured in the participant materials.
- The NREC-CT B requested further information on supports in place to assist visually impaired participants accessing sites. This information should also be included in the participant materials.
- The NREC-CT B noted that some of the language in the consent form does not align with free, autonomous consent requested that such statements are amended to ensure that consent is not dependent on the permission of others.
- The NREC-CT B requested that the consent section of the Main ICF is only relevant to the participant in the trial proposed and anything separate from the core study is separated from the main consent.
- The NREC-CT B noted that the layout for consent is not in line with best practice and requested that participants are provided with layered consent offering participants specific choices with initial boxes.
- The NREC-CT B requested that all information related to the ‘Genetic Research – Participant Information Sheet and Consent Form’ is included in this document and any references to the main PIL are removed.
- The NREC-CT B considered that the separation of withdrawal process for the core study and the genetic research aspect may be unclear to participants and requested that the withdrawal process for the genetic research is further elucidated in the main PIL.
- The NREC-CT B noted that consent in the Pregnant Partner PIL seeks consent for the retention and use of data relating to the pregnancy and birth ‘for further research …once

the study is complete' … for other research uses not directly related to this study.' This is not in line with national legislation on explicit consent for the use of data in health research. The Committee required that this is amended in line with national legislation.

- Due to the time commitment required by participants and potential carer, the NREC-CT B considered that the financial supports provided to participants would be insufficient for this study and requested that participants and potential carers are supported further in regards meal expenses, travel expenses and potential loss of earnings related to participation in this study.
- The NREC-CT B noted discrepancies across the documentation around the retention period of data and requested clarification on this point.
- The NREC-CT B noted that the insurance certificate provided does not cover the full duration of the trial and requested assurances that cover would be in place for the full duration of the trial.
- The NREC-CT B noted that a CV for the national Principal Investigator was submitted, but that the information provided was limited, and requested further information on the experience of the site PI.
- The NREC-CT B further requested the CVs for the site PIs involved with the study.
- The NREC-CT B noted the consent process for the future use of biological samples and data is not in line with national regulations on 'explicit consent' (the Health Research Regulations 2018) and requested that the applicant provides the participant with specific choices as to how their samples and data would be used for future purposes, such as limiting future use to a specific disease area.
- Further to the above, NREC-CT B requested confirmation that any future research project using samples or data from participants involved in this study would undergo full ethics review. This should also be captured in the participant materials.
- The NREC-CT B requested that consent for future biomedical research is separated out from the main consent form.
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22-NREC-CT-028

Principal Investigator: Dr Richard Costello

Study title: CONNected Electronic Inhalers Asthma Control Trial 3 ("CONNECT 3"), a 24-Week Treatment, Multicenter, Open-Label, Randomized, Parallel Group Comparison Study of Standard of Care Treatment Versus the Budesonide/Formoterol Digihaler Digital System, to Optimize Outcomes in Adult Patients with Asthma

Lead institution: Beaumont Hospital

- NREC-CT comments:

- The NREC-CT B noted this clinical trial application represents a CONNected Electronic Inhalers Asthma Control Trial 3 (“CONNECT 3”), a 24-Week Treatment, Multicenter, Open-Label, Randomized, Parallel Group Comparison Study of Standard of Care Treatment Versus the Budesonide/Formoterol Digihaler Digital System, to Optimize Outcomes in Adult Patients with Asthma.
- The NREC-CT B agreed that it was unable to give a favourable ethics opinion on the application.

  - NREC-CT Decision:

- Unfavourable

  - Key Reasons for Unfavourable Decision:

- The NREC-CT B considered that the presentation of the documentation submitted was too complicated and the information included did not align. For this reason, the Committee was unable to make an informed decision on the study. In any future application, the NREC-CT B requested that the presentation and communication of all documents are revised to ensure that the Committee would be easily able to review the study and suggested that the cover letter includes a summary and rationale for each document provided.
- The NREC-CT B considered the presentation of the device and its function to be overly complicated and requested that the presentation of this information is revised to make the information understandable to the broad spectrum of Committee members.
- The NREC-CT B considered that the process of consent was unclear, particularly consent for the use of data, and therefore concluded it would be difficult for participants to comprehend. In any future application, the Committee requested that this aspect of the trial is completely revised.
- The NREC-CT B considered the description of data protection related to the use of the digital application to be too vague, with very little information provided around the potential of risks to participants. In any future application, the Committee requested that this whole aspect of the submission is completely revised to ensure that risks and protections associated with the study are communicated adequately to both the NREC-CT and participants.

22-NREC-CT-029

Principal Investigator: Dr Karen Cadoo

Study title: A Phase 3 Randomized, Open-label, Active-comparator Controlled Clinical Study of Pembrolizumab versus Platinum Doublet Chemotherapy in Participants With Mismatch Repair Deficient (dMMR) Advanced or Recurrent Endometrial Carcinoma in the First-line Setting (KEYNOTE-C93/GOG-3064/ENGOT-en15)

Lead institution: St James’s Hospital

- NREC-CT comments:

- The NREC-CT B noted this clinical trial application represents a A Phase 3 Randomized, Open-label, Active-comparator Controlled Clinical Study of Pembrolizumab versus Platinum Doublet Chemotherapy in Participants With Mismatch Repair Deficient (dMMR) Advanced or Recurrent Endometrial Carcinoma in the First-line Setting (KEYNOTE-C93/GOG-3064/ENGOT-en15).
- The NREC-CT praised the overall quality and clarity of the submission, and participant materials in particular.
- The NREC-CT B agreed that additional information was required to inform its deliberations and therefore, was not yet in a position to return a final ethics decision.

- NREC-CT Decision:

- Request for Further Information

- Additional Information Required:

- The NREC-CT B noted that the Cover Letter refers to the reconsenting of parents/guardians of minors and requested clarification around this point.
- The NREC-CT B requested further information on how the process of ‘cross-over’ will work and what would be the criteria for ‘cross-over’.
- The NREC-CT B requested further information on the process for incidental findings and how would they be communicated to participants.
- The NREC-CT B noted that samples will be stored in the US and Belgium but requested that this is elaborated on in the participant materials.
- The NREC-CT B noted that some references to organisations in other jurisdictions remain in the participant materials and requested that all participant materials are revised to ensure that the correct Irish organisations or institutions are referenced.
- The NREC-CT B considered that the separation of the withdrawal process for the core study and the future biomedical research may be unclear to participants and requested that the withdrawal process for the future biomedical research is further elucidated in the main PIL.
- The NREC-CT B noted the submission of an ‘Optional archival tumour tissue information sheet’. As this step is a requirement to participate in this study, the Committee considered the ‘optional’ terminology misleading and requested clarification why this is not part of the screening stage of the study.
- The NREC-CT B noted that those lacking decision-making capacity will be excluded from the study. The Committee supports the principles that capacity should always be presumed until proven otherwise and requested further information on the process in place to assess capacity.

- The NREC-CT B noted that recruitment would take place through multi-disciplinary team meetings in the UK and requested further information around the recruitment process within Ireland.
- The NREC-CT B noted the consent process for the future use of biological samples and data is not in line with national regulations on 'explicit consent' (the Health Research Regulations 2018) and requested that the applicant provides the participant with specific choices as to how their samples and data will be used for future purposes, such as limiting future use to a specific disease area. This information should be consistent throughout all of the application material/documents.
- The NREC-CT B noted that the FBR will be based on leftover samples, however the FBR PIL refers to injury and harm as a result of participation in the FBR and requested clarification related to this point. If this is an error in the PIL, then the text should be corrected.
- The NREC-CT B noted that the insurance certificate provided does not cover the full duration of the trial and requested assurances that cover will be in place for the full duration of the trial.
- The NREC-CT B noted that it was stated in the application that the financial budget for this study has not been finalised and requested an update on this.
- The NREC-CT B requested that the CV for Dr Murphy is submitted as part of the response to the request for further information.

- AOB:

- It was suggested that an 'advice to applicants document could be designed and published on NREC website describing the recurring issues encountered by the NREC during the review process, such as the cutting and pasting of incorrect information, common problems with PILs etc.
- Regarding internal processes, the National Office will approach NREC members with surveys to gain more information regarding which processes could be improved.
- NREC member also suggested that additional guidelines could be written for the research community, such as guidelines on recruiting prisoners in clinical trials, as no such guidelines have been published in Ireland to date.
- The NREC members suggested the website toolkit area could include examples of good applications, for example, a well-written PIL.

- The Chair closed the meeting.