National Research Ethics Committee

NREC-CT A Meeting

6th of April 2022

Attendance

Name	Role
Prof. Alistair Nichol	Chairperson, NREC-CT A
Dr Heike Felzmann	Deputy Chairperson, NREC-CT A
Prof. Mary Donnelly	Deputy Chairperson, NREC-CT A
Prof. Tina Hickey	Committee Member, NREC-CT A
Dr Dervla Kelly	Committee Member, NREC-CT A
Prof. John Wells	Committee Member, NREC-CT A
Mr Gerard Daly	Committee Member, NREC-CT A
Ms Ann Twomey	Committee Member, NREC-CT A
Prof. Catherine Hayes	Committee Member, NREC-CT A
Ms Muireann O'Briain	Committee Member, NREC-CT A
Prof. David Brayden	Committee Member, NREC-CT A
Prof. Patrick Dillon	Committee Member, NREC-CT A
Dr John O'Loughlin	Committee Member, NREC-CT A
Dr Darren Dahly	Committee Member, NREC-CT A
Ms Aileen Sheehy*	Programme Manager, National Office for RECs
Dr Laura Mackey*	Project Officer, National Office for RECs
Dr Susan Quinn	Programme Manager, National Office for RECs

*Drafted minutes

Apologies: Dr Jimmy Devins, Prof. Gene Dempsey, Dr Geraldine Foley

Quorum for decisions: Yes

Agenda

- Welcome & Apologies
- 22-NREC-CT-071
- 22-NREC-CT-172
- 21-NREC-CT-168_AMEND-1
- 21-NREC-CT-169_AMEND-1
- 21-NREC-CT-044_AMEND-3
- 21-NREC-CT-167_AMEND-1
- AOB

- The Chair welcomed the NREC-CT A.
  - The minutes from the previous NREC-CT A meeting on 9th of March 2022 were approved.
  - The NREC Business Report was discussed and noted.

Applications

22-NREC-CT-071

- Principal Investigator: Prof. Brian Kirby

Study title: A Phase 3, open-label, parallel group, multicenter, extension study evaluating the long-term treatment of bimekizumab in study participants with moderate to severe hidradenitis suppurativa

Lead institution: St Vincent's University Hospital

  - NREC-CT comments:

- The NREC-CT A noted that this study represents a Phase 3, open-label, parallel group, multicenter, extension study evaluating the long-term treatment of bimekizumab in study participants with moderate to severe hidradenitis suppurativa
- The NREC-CT A commented positively on this application overall, with some minor clarifications noted throughout.

- The NREC-CT A agreed that additional information was required to inform its deliberations before a final ethics position could be returned.

  - NREC-CT Decision:

- Request for Further Information

  - Further Information Requested:

- The NREC-CT A requested clarity whether women of childbearing age will be included in the study.
- The NREC-CT A noted that this study would take place within a non-psychiatric cohort and that an invasive PHQ questionnaire around suicidality would be administered at frequent intervals over the course of the trial. It is the understanding of the Committee that this measure is predictive in psychiatric populations rather than non-psychiatric populations. The Committee suggested the use of the less invasive questionnaire as a screen test at frequent intervals and the implementation of the more invasive PHQ questionnaire if negative emotions are identified through the less invasive questionnaire.
- In relation to the increase risks to participant's mental health, the NREC-CT A requested further information on:
    - What the process would be for psychological assessment during the trial?
    - How the red flag would be raised when participants indicated they were having negative emotions?
    - What the process would be for referral to a mental health facility?
    - What are the qualifications of the team member to analyse these data?
    - Who in the team / site would take responsibility for this aspect of the trial?
- The NREC-CT A requested a rationale for the sample size in Ireland.
- The NREC-CT A considered the PIL to be comprehensive but lengthy and requested a plain English executive summary of the salient points of the study is included at the beginning of the PIL.
- The NREC-CT A noted that participation in the trial may lead to an increased risk of Tuberculosis infection and requested that this increased risk is further elucidated in the participant materials.
- The NREC-CT A requested that within the participant materials the risks related to vaccinations are further elucidated.
- The NREC-CT A considered the information around alternatives to self-administration of the drug to be unclear and requested further information on this element and that the participant materials are amended also to reflect this clarification.
- The NREC-CT A considered that the link between mental health problems and the study was unclear and requested that this information is further elucidated in the participant materials.
- The NREC-CT A considered that the section 'What happens when the research study stops?' does not address the pertinent question around what happens if the participant's

participation in the study is stopped and requested that the participant materials are adapted to include this information.

- The NREC-CT A noted that 'legitimate interest' is used as the legal basis for this study. However, in Ireland, the basis for data processing in research is participant consent. The NREC-CT A requested that consent is identified as the basis for data protection elements of this study and the Health Research Regulations 2018 are also referenced in any text related to data protection.
- The NREC-CT A noted that data would be transferred outside of the jurisdiction and requested that a clear statement ensuring that any personal data would be managed and processed in line with GDPR is adapted to clarify this.
- The NREC-CT A noted that biological samples collected as part of the study but not processed before the participant has withdrawn consent may continue to be processed after the participant has withdrawn their consent. The Committee requested a rationale for this.
- Owing to the large number of study visits, the NREC-CT A requested that the text on expenses is adapted to include a clear statement that travel, parking and refreshment expenses will be reimbursed and how this will be done.
- The NREC-CT A noted that the Site Suitability template was submitted but lacked the necessary detail and requested that a more comprehensive template is submitted as part of the response to the request for further information.
- The NREC-CT A noted that the study insurance certificate provided would not cover the whole trial duration and requested assurance that the trial would be adequately insured for the whole duration and will cover all sites.
- The NREC-CT A requested that the participant's General Practitioner would be included in discussions around the trial due to restrictions on concomitant medications.

22-NREC-CT-072

- Principal Investigator: Prof. Sean Kennelly

Study title: A Phase III, multicenter, randomized, parallel-group, double-blind, placebo-controlled study to evaluate the efficacy and safety of gantenerumab in participants at risk for or at the earliest stages of Alzheimer's disease

Lead institution: Tallaght University Hospital

- NREC-CT comments:

- The NREC-CT A noted that this study represents a Phase III, multicenter, randomized, parallel-group, double-blind, placebo-controlled study to evaluate the efficacy and safety of gantenerumab in participants at risk for or at the earliest stages of Alzheimer's disease
- The NREC-CT A recognised that this is a highly important area of research and commended the quality of the participant materials in particular.

- The NREC-CT A agreed that additional information was required to inform its deliberations before a final ethics position could be returned.

  - NREC-CT Decision:

- Request for Further Information

  - Further Information Requested:

- The NREC-CT A noted the significant burden placed on the potential study partner and requested further information on the supports available to this person over the duration of the trial and the process in place if the study partner cannot commit to the full duration of the trial or needs to withdraw their services.
- The NREC-CT A noted the expected high volume of Irish-based participants required for the study and requested a rationale why the sample size is limited to Ireland.
- • The NREC-CT A requested further information on the numbers of participants who may be eligible for screening, how many participants are likely to pass screening and how this is expected to be broken down across the 4 sites.
- • The NREC-CT A noted the use of mobile nurses and requested further information on where these nurses will be recruited from.
- The NREC-CT A noted that the precise number of scans required as part of the trial was not readily found in the documentation and requested further information related to this point and requested that the participant materials are adapted to include this information.
- • The NREC-CT A considered the criteria for crossover unclear, and requested further information related to this aspect of the trial. In particular, how will that decision be made and how will it be communicated to participants.
- • The NREC-CT A considered the description provided of the process for unblinding to be inconsistent across the documentation provided and requested clarification at what stage does unblinding happen. The Committee also requested that the documentation is revised to ensure the description of this process is consistent.
- The NREC-CT A requested further information around the criteria for progressing to a clinical diagnosis of MCI or dementia and how this will be applied to the trial.
- The NREC-CT A requested further information on who from the study team will be taking responsibility for the Statistical Analysis Plan.
- • The NREC-CT A noted that disease progression is identified as a secondary outcome and requested further information around how the planned sample size related to this analysis of this particular outcome.
- The NREC-CT A noted that some of the language used in the brochure may be ‘over-selling’ the benefits of the trial e.g. ‘patients can take control of their lives’ and requested that such language is adapted accordingly.
- The NREC-CT A requested that the PIL is furnished with further information on how participants can claim expenses.

- The NREC-CT A considered the information in the PIL around the study partner to be limited and requested that the PIL includes further information around the role of this person and how trial participation can be facilitated in the event that a study partner cannot be identified.
- In relation to the future use of biological samples, the NREC-CT A requested confirmation that further research using participant samples or data from this study would undergo full ethics review and that this is outlined in participant materials.
- In the event of injury or harm, the NREC-CT A 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 A requested further information related to data monitoring over the course of the trial.
- The NREC-CT A requested further information related to the clinical trial experience of the site investigators.
- The NREC-CT A raised operational concerns around each site managing 300 participants. The Committee requests further information around how each site is equipped to manage this volume of participants and all related procedures.

21-NREC-CT-168_AMEND-1

- Principal Investigator: Dr Janice Walshe

Study title: An Open-label, Randomized, Phase 2/3 Study of Olaparib Plus Pembrolizumab Versus Chemotherapy Plus Pembrolizumab After Induction of Clinical Benefit With First-line Chemotherapy Plus Pembrolizumab in Participants With Locally Recurrent Inoperable or Metastatic Triple Negative Breast Cancer (TNBC) (KEYLYNK-009).

Lead institution: St. Vincent's University Hospital

- NREC-CT comments:

- The NREC-CT A noted that this application represents a substantial amendment to an Open-label, Randomized, Phase 2/3 Study of Olaparib Plus Pembrolizumab Versus Chemotherapy Plus Pembrolizumab After Induction of Clinical Benefit With First-line Chemotherapy Plus Pembrolizumab in Participants With Locally Recurrent Inoperable or Metastatic Triple Negative Breast Cancer
- The NREC-CT A commented this a was a clear and comprehensive substantial amendment submission.
- Based on the above, the NREC-CT A agreed that this substantial amendment application be designated as favourable.

- NREC-CT Decision:

Favourable

21-NREC-CT-169_AMEND-1

- Principal Investigator: Dr Patrick Hayden

Study title: Phase 3, Multicenter, Randomized, Open-label Study to Compare the Efficacy and Safety of Pomalidomide, Bortezomib and Low-Dose Dexamethasone versus Bortezomib and Low-Dose Dexamethasone in Subjects with Relapsed or Refractory Multiple Myeloma

Lead institution: St James's Hospital

- NREC-CT comments:

- The NREC-CT A noted that this application represents a substantial amendment to a Phase 3, Multicenter, Randomized, Open-label Study to Compare the Efficacy and Safety of Pomalidomide, Bortezomib and Low-Dose Dexamethasone versus Bortezomib and Low-Dose Dexamethasone in Subjects with Relapsed or Refractory Multiple Myeloma.
- The NREC-CT A commented this a was a straightfroward and comprehensive substantial amendment submission.
- Based on the above, the NREC-CT A agreed that this substantial amendment application be designated as favourable.

- NREC-CT Decision:

- Favourable

21-NREC-CT-044_AMEND-3

- Principal Investigator: Dr Cliona Mary Grant

Study title: A Phase 3, Randomized, Double-blind, Placebo-controlled Study to Evaluate Pembrolizumab Versus Placebo as Adjuvant Therapy Following Surgery and Radiation in Participants with High-risk Locally Advanced Cutaneous Squamous Cell Carcinoma (LA cSCC) (KEYNOTE-630)

Lead institution: St James's Hospital

- NREC-CT comments:

- The NREC-CT A noted that this application represents a substantial amendment to a Phase 3, Randomized, Double-blind, Placebo-controlled Study to Evaluate

Pembrolizumab Versus Placebo as Adjuvant Therapy Following Surgery and Radiation in Participants with High-risk Locally Advanced Cutaneous Squamous Cell Carcinoma.

- The NREC-CT A commented this substantial amendment submission was comprehensive and clearly laid out.
- Based on the above, the NREC-CT A agreed that this substantial amendment application be designated as favourable.

- NREC-CT Decision:

Favourable

21-NREC-CT-167_AMEND-1

- Principal Investigator: Prof Sherif El-Masry

Study title: Phase III, Prospective, Multinational, Multicenter, Randomized, Controlled, Two-arm, Double Blind Study to Assess Efficacy and Safety of D-PLEX Administered Concomitantly with the Standard of Care (SoC), Compared to a SoC Treated Control Arm, in Prevention of Post Abdominal Surgery Incisional Infection

Lead institution: Our Lady of Lourdes Hospital

- NREC-CT comments:

- The NREC-CT A noted that this application represents a substantial amendment to a Phase III, Prospective, Multinational, Multicenter, Randomized, Controlled, Two-arm, Double Blind Study to Assess Efficacy and Safety of D-PLEX Administered Concomitantly with the Standard of Care (SoC), Compared to a SoC Treated Control Arm, in Prevention of Post Abdominal Surgery Incisional Infection.
- The NREC-CT A commented this a was a clear and comprehensive substantial amendment submission.
- Based on the above, the NREC-CT A agreed that this substantial amendment application be designated as favourable.

- NREC-CT Decision:

Favourable

- AOB:
  - Prof. Alistair Nichol provided an update to the Committee regarding the establishment of a dedicated substantial amendment subcommittee to alleviate the high volume of substantial amendments submitted and awaiting review.