National Research Ethics Committee

NREC-CT B

27th of April 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 Lorna Fanning	Committee Member, NREC-CT B
Dr John Hayden	Committee Member, NREC-CT B
Dr Mary McDonnell Naughton	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 Mandy Daly	Committee Member, NREC-CT B
Ms Caoimhe Gleeson	Committee Member, NREC-CT B
Prof. Abhay Pandit	Committee Member, NREC-CT B
Prof. John Faul	Committee Member, NREC-CT B
Dr Mark Robinson	Committee Member, NREC-CT B
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
Dr Marta Pisarska	Postdoctoral Intern, National Office for RECs

*Drafted minutes

Apologies: Dr Eimear McGlinchey, Dr Enda Dooley, Prof. David Smith

Quorum for decisions: Yes

Agenda

- Welcome & Apologies
- Application 22-NREC-CT-084
- Application 22-NREC-CT-085
- Application 22-NREC-CT-086
- Application 22-NREC-CT-087
- AOB

- The Chair welcomed the NREC-CT B.
  - The Minutes from the NREC-CT B meeting on the 27th of March were approved.

Applications

22-NREC-CT-084

Principal Investigator: Professor Elizabeth Mary (Beatrice) Nolan,

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

Lead institution: Children's Health Ireland at Crumlin

  - NREC-CT comments:
- The NREC-CT B noted this clinical trial application represents 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.
- The NREC-CT B commented that this was a well-presented and comprehensive submission, with particular attention to addressing GDPR considerations within the trial.
- The NREC-CT B agreed that while some clarifications were required, this application could be designated as Favourable with Conditions.

- NREC-CT Decision:

- Favourable with Conditions

- Additional Information Required

- The NREC-CT B noted that noted that the study insurance certificate provided has expired (on 30.4.22) and does not cover any period of the proposed study. The Committee requested an updated insurance certificate be provided

22-NREC-CT-085

Principal Investigator: Professor Cliona Grant

Study title: A Phase 2, Open-Label, Multi-Center Study of PDS0101 (R-DOTAP [Versamune®] + HPVmix) and Pembrolizumab (KEYTRUDA®) Combination Immunotherapy in Subjects with Recurrent and/or Metastatic Head and Neck Cancer and High-Risk Human Papillomavirus-16 (HPV16) Infection

Lead institution: St James's Hospital

- NREC-CT comments:

- The NREC-CT B noted this clinical trial application represents a Phase 2, Open-Label, Multi-Center Study of PDS0101 (R-DOTAP [Versamune®] + HPVmix) and Pembrolizumab (KEYTRUDA®) Combination Immunotherapy in Subjects with Recurrent and/or Metastatic Head and Neck Cancer and High-Risk Human Papillomavirus-16 (HPV16) Infection.

- The NREC-CT commended the quality and clarity of the application submitted.

- 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 in the Participant Information Leaflet (PIL) was written in language which was too complex and requested that it be simplified into plain English. Specifically, the Committee requested that the Section in the PIL related to the “Purpose of the study” (pg.3) be rewritten to improve accessibility.

- The NREC-CT B requested that that both the PIL and Patient Recruitment Landing page are updated for Irish study site and participants.

- The NREC-CT-B noted that a statement in the PIL that 'there is no guarantee of privacy' with regard to HLA testing. In line with the Data Protection Act 2018 (Section 36(2) (Health Research) Regulations 2018), the Committee requested it is rewritten in more appropriate language to ensure it is in line with the applicant's commitment to Data Protection.
- The NREC-CT B requested that the pre-screening information sheet should specifically refer to patients contacting their GP when referring to "talking to others."
- The NREC-CT B noted that the PIL under Additional Costs, recommends that patients "speak with your insurance company" and requested clarification on whether the participants/their insurance will be charged for participation in the trial.
- The NREC-CT B noted that participants are directed to the trials page on the clinicaltrial.gov website and requested clarification of whether there is a EudraCT site for EU patients.
- The NREC CT-B noted that the application states that "data will be retained for 30 years after the study ends OR 2 years after approval of the drug OR 2 years after drug development has stopped". The Committee noted that these proposed periods are not mutually exclusive and requested clarification regarding data retention.
- The NREC CT-B noted that the application merely lists PDS Biotechnology Corporation as funding the trial and request that a description is provided that describes the adequacy of the financing.

22-NREC-CT-086

Principal Investigator: Professor Paul Donnellan

Study title: An open-label, randomized, Phase 3 clinical trial of IO102-IO103 in combination with pembrolizumab versus pembrolizumab alone in patients with previously untreated, unresectable, or metastatic (advanced) melanoma

Lead institution: Galway University Hospital,

- NREC-CT comments:

- The NREC-CT B noted this clinical trial application represents an open-label, randomized, Phase 3 clinical trial of IO102-IO103 in combination with pembrolizumab versus pembrolizumab alone in patients with previously untreated, unresectable, or metastatic (advanced) melanoma.
- The NREC-CT commented on the quality of the application overall, with some minor clarifications 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 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 B considered that The Pregnant Partner information consent form provides insufficient information on the study, including the risks to the father. The Committee requested that the participant materials are adapted to include this information.
- The NREC-CT B requested further clarification on the below points in the PIL:
    - Pg 5 states that genetic analysis results will not be provided to participants. Committee notes that an explanation for this must be given, and requests clarification as to where the information will be stored.
    - Pg 5. The committee requested that the section on consent to future research needs to include more detail, and/ or include a link to the detail in the optional future research consent form.
    - Pg 18. “What happens with my data and other personal information? The committee noted that this question is unanswered and requested that this is addressed.
    - Pg 21. The committee requested an explanation as to the purpose of the Impartial witness is provided in the form.

22-NREC-CT-087

Principal Investigator: Dr Paula Calvert

Study title: Randomized, Open-Label, Phase 3 Trial of Tisotumab Vedotin vs Investigator’s Choice Chemotherapy in Second or Third-Line Recurrent or Metastatic Cervical Cancer

Lead institution: University Hospital Waterford

  - NREC-CT comments:

- The NREC-CT B noted this clinical trial application represents a Randomized, Open-Label, Phase 3 Trial of Tisotumab Vedotin vs Investigator’s Choice Chemotherapy in Second or Third-Line Recurrent or Metastatic Cervical Cancer.
- 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 unsatisfactory and were numerous errors in the application form contents that also included typographical and grammatical errors. For this reason, the Committee were unable to make an informed decision on the study and that the presentation and communication of all documents be extensively revised to ensure that the Committee can review the study documentation in any subsequent submission.
- The NREC-CT B had concerns regarding the information for research participants. The Committee noted that the PIL and ICF do not align, and the Committee deemed that they do not inform the patient adequately. There was a lack of clarity and detail provided relating to several elements which must be amended, including but not limited to:
    - The NREC-CT-B noted that the PIL language was too complex and requested that it be simplified into plain English for lay audiences.
    - The NREC-CT B noted that there are references to non-Irish jurisdictions, including but not limited to references to FDA/USA, British sign language, the UK based Human Tissue Authority and the Association of British Pharmaceutical Industry, and requested that all participant materials be adapted for Irish audience/law/sites.
    - The NREC CT-B noted that language stating “you may be eligible for compensation” is not suitable, and clarity must be provided to participants.
    - The Committee deemed there were inconsistencies regarding the length of storage of samples and their movement outside the EU and safeguards for the transfers.
    - The NREC-CT B noted that the proposed consent form, including blanket consent on sharing of all data, including genetic data, is in a direct breach of the Data Protection Act 2018 (Section 36(2)) (Health Research) Regulations 2018).
- Based on the information provided in the application dossier, the NREC-CT B noted that only limited information on the study team and sites was provided.
- The NREC-CT B noted that the Principal Investigator's CV must be updated to adhere to standard CVs for clinical trials.
- The Committee deemed that sufficient information was not provided to ascertain the suitability of the study sites in the Site Suitability Form.
- The NREC CT-B noted that the insurance certificate is for three years rather than for the entire duration of the study – five years.
- Furthermore, the Committee was unclear about the entities referred to in the insurance certificate: Seattle Genetics rather than Seagen. The Committee was not sufficiently assured of the insurance policy to that end

- AOB:

- The Committee discussed potential variances in how Standard of Care is presented in applications, as other authorities involved in the assessment of clinical trials accept a standard of care that acceptable in any EU jurisdiction, as opposed to specific requirements in the Republic of Ireland. This topic will be discussed further in due course.
- The Chair closed the meeting.