National Research Ethics Committee

NREC-CT B

6th of October 2021

Attendance

Name	Role
Dr Cliona McGovern	Chairperson, NREC-CT B
Dr Jean Saunders	Deputy Chairperson, NREC CT-B
Prof. John Faul	Deputy Chairperson, NREC-CT B
Ms Serena Bennett	Committee Member, NREC-CT B
Mr Philip Berman	Committee Member, NREC-CT B
Ms Mandy Daly	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
Ms Caoimhe Gleeson	Committee Member, NREC-CT B
Ms Paula Prendeville	Committee Member, NREC-CT B
Prof. Colm O'Donnell	Committee Member, NREC-CT B
Prof. David Smith	Committee Member, NREC-CT B
Ms Aileen Sheehy*	Programme Manager, National Office for RECs
Dr Laura Mackey*	Project Officer, National Office for RECs
Dr Jennifer Ralph James	Head, National Office for RECs

*Drafted minutes

Apologies: Prof. Abhay Pandit, Mr Gavin Lawler, Dr Mark Robinson

Quorum for decisions: Yes

Agenda

- Welcome & Apologies
- Conflict of Interest Presentation by Dr Jennifer Ralph James.
- Application 21-NREC-CT-095
- Application 21-NREC-CT-100
- Application 21-NREC-CT-101
- Application 21-NREC-CT-089_AMEND-1
- Application 21-NREC-CT-090_AMEND-1
- AOB

- The Chair welcomed the NREC-CT B.
  - The Minutes from the NREC-CT B meeting on the 1st of September were approved.

Applications

21-NREC-CT-095

Principal Investigator: Professor Laurence Egan

- Study title: Multi-center, double-blind, randomized, placebo-controlled, phase IIa trial to evaluate Spesolimab (BI 655130) efficacy in patients with fibrostenotic Crohn's Disease

Lead institution: University Hospital Galway

  - NREC-CT comments:
- The NREC-CT B noted that the clinical trial application represents a Multi-center, double-blind, randomized, placebo-controlled, phase IIa trial to evaluate Spesolimab (BI 655130) efficacy in patients with fibrostenotic Crohn's Disease.
- The NREC-CT B praised the quality of the submission and considered the documentation well-presented and comprehensive.
- The NREC-CT B agreed that additional clarification regarding specific aspects of the study was required to inform its deliberations.

- NREC-CT Decision:

- Request for Further Information

- Additional Information Required:

- The NREC-CT B required further information on the trial extension and how participants will be chosen to participate.
- On Page 3 of the Participant Information Leaflet (PIL), the NREC-CT B requested that the term ‘computer generated’ is added before ‘random choice’.
- The NREC-CT B requested that an additional sentence is added in relation to male contraception not being required, to outline the rationale for this statement.
- The NREC-CT B suggested that the Emergency Contacts section on Page 18 of the PIL is updated to include information on out-of-hours contacts as per the Trial Identification Card.
- The NREC-CT B requested further information on circumstances where the personal data of participants may continue to be processed for purposes other than the health research where there is a legal basis to do so
- The NREC-CT B requested that the DPIA is submitted as part of the response to the request for further information.
- The NREC-CT B requested that any additional financial compensation, by way of a gesture for the participant’s time, is given at the end of their involvement in the study and not included in the participant materials or mentioned as part of the recruitment processes.
- The NREC-CT B requested further information on how participants who may not have the technical knowledge to use the online tools provided (i.e., e-diary and smart phone app) will be supported as part of participating in the trial.
- The NREC-CT B requested that the separate consent form for future research is submitted as part of the response to the request for further information.

21-NREC-CT-100

Principal Investigator: Professor Edward McKone

- Study title: A Phase 3, Randomized, Double-blind, Controlled Study Evaluating the Efficacy and Safety of VX-121 Combination Therapy in Subjects With Cystic Fibrosis Who Are Homozygous for F508del, Heterozygous for F508del and a mGating (F/G) or Residual Function (F/RF) Mutation, or Have At Least 1 Other Triple Combination Responsive CFTR Mutation and No F508del Mutation

Lead institution: St Vincent’s University Hospital

- NREC-CT Comments:

- The NREC-CT B noted this clinical trial application represents a Phase 3, Randomized, Double-blind, Controlled Study Evaluating the Efficacy and Safety of VX-121 Combination Therapy in Subjects with Cystic Fibrosis Who Are Homozygous for F508del, Heterozygous for F508del and a mGating (F/G) or Residual Function (F/RF) Mutation, or Have At Least 1 Other Triple Combination Responsive CFTR Mutation and No F508del Mutation.
- The NREC-CT B agreed that it is not in a position to return a final ethics opinion based on the information and documentation received thus far. In this regard, the Committee required additional information to inform its deliberations.
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  - NREC-CT Decision:

- Request for Further Information

  - Additional Information Required:

- The NREC-CT B requested further information on how the standard of care will be maintained throughout the trial and after the trial has completed.
- The NREC-CT B requested a rationale for the decision not to provide participants with access to the study drug after the trial has completed.
- The NREC-CT B requested further information on the supports in place in the event of an adverse outcome related to an infant or foetus, and that this information is also included in the Pregnancy PIL.
- The NREC-CT B requested clarity on the number of Irish sites involved in the study and the number of participants due to be recruited at each site.
- The NREC-CT B requested that that participants are given more than 24 hours to assess the information provided before deciding to consent, and suggested that materials are provided to participants in advance of the clinic visit.
- The NREC-CT B considered that all participant materials require considerable revision ahead of being used in the trial.
- The NREC-CT B requested that a separate PIL and consent form is developed for Parents and Guardians as under national consent requirements, i.e., that Parents or Guardians must sign a consent form on behalf of a minor.
- The NREC-CT B requested that the applicant defines what an adult is in line with national legislation.
- The NREC-CT B noted that in the adolescent forms, no information is provided on what the biological samples will be used for. The Committee requested that this is elucidated further.
- The NREC-CT B requested that where blood tests are referenced in the materials, the amount of blood intended to be drawn in teaspoons is included.
- The NREC-CT B requested further information on whether ongoing technical support will be provided to participants for at home spirometry.

- The NREC-CT B requested that on both the Adult and Adolescent PILs, potential risks should be presented more clearly, and serious risks should be further highlighted.
- In the Adolescent Assent Form and Addendum, the NREC-CT B requested that the word 'Mom' or 'Dad' is removed and replaced with 'Parent or Guardian'.
- The NREC-CT B requested that the relevant information leaflets should allow for Parents and Guardians to support minors in the completion of the questionnaire.
- The NREC-CT B requested that reference to pregnancy and OCP is removed from the adolescent materials and included in the Parent / Guardian materials instead.
- In the Adult PIL, the NREC-CT B requested that the requirement for follow-up visits after immediate withdrawal is explained to participants.
- The NREC-CT B considered the statement in the Pregnancy PIL that confidentiality may not be maintained to be potentially harmful to the participant and requests that confidentiality is strictly maintained for this cohort of participants.
- The NREC-CT B requested that all risks are included in the GP letter.
- The NREC-CT B requested that all questionnaires are adapted to an Irish readership.
- 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.

  Further to the above, NREC-CT B requested confirmation that any future research project using samples or data from participants involved in this study will undergo full ethics review.
- The NREC-CT B noted that data will be pseudonymised and requested further information on who will hold the key to the data.
- The NREC-CT B noted that in the DPIA specifies that there is '*insufficient de-identification of participant data'.* The Committee requested further information on how this risk will be mitigated.
- The NREC-CT B requested further information about storage of and access to biological samples, and requested that further information is provided to participants on this.
- The NREC-CT B requested assurance that adequate insurance will be in place for the duration of the trial.

21-NREC-CT-101

Principal Investigator: Professor Edward McKone

- Study title: A Phase 3, Randomized, Double-blind, Controlled Study Evaluating the Efficacy and Safety of VX-121 Combination Therapy in Subjects With Cystic Fibrosis Who Are Heterozygous for F508del and a Minimal Function Mutation (F/MF).

Lead institution: St Vincent's University Hospital, Dublin 4.

- NREC-CT Comments:

- The NREC-CT B noted that the clinical trial application represents a Phase 3, Randomized, Double-blind, Controlled Study Evaluating the Efficacy and Safety of VX-121 Combination Therapy in Subjects with Cystic Fibrosis Who Are Heterozygous for F508del and a Minimal Function Mutation.
- The NREC-CT B agreed that additional information and clarifications were required in several documents included in the applications is not in a position to return a final ethics opinion. In this regard, the Committee required additional information to inform its deliberations.

- NREC-CT Decision:

- Request for Further Information

- Additional Information Required

- The NREC-CT B requested further information on how the standard of care will be maintained throughout the trial and after the trial has completed.
- the NREC-CT B requested a rationale for the decision not to provide participants with access to the study drug after the trial has completed.
- The NREC-CT B requested further information on the supports in place in the event of an adverse outcome related to an infant or foetus, and that this information is also included in the Pregnancy PIL.
- The NREC-CT B requested clarity on the number of Irish sites involved in the study and the number of participants due to be recruited at each site.
- The NREC-CT B requested that that participants are given more than 24 hours to assess the information provided before deciding to consent, and suggested that materials are provided to participants in advance of the clinic visit.
- The NREC-CT B requested further information on whether participants lacking decision making capacity will be in the study. If so, what supports will be available to this cohort of participants?
- The NREC-CT B considered that all participant materials require considerable revision ahead of being used in the trial.
- The NREC-CT B requested that a separate participant information leaflet and consent form is developed for Parents and Guardians as under national consent requirements, i.e., that Parents or Guardians must sign a consent form on behalf of a minor.
- The NREC-CT B requested that the applicant defines what an adult is in line with national legislation.
- The NREC-CT B noted that in the adolescent forms, no information is provided on what the biological samples will be used for. The Committee requested that this is elucidated further.

- The NREC-CT B requested that a rationale for conducting intimate examinations is included in both the Adult and Adolescent PILs, as well as providing the participant with the option to attend such examinations with a third party of their choice.
- The NREC-CT B requested further information on whether ongoing technical support will be provided to participants for at home spirometry.
- The NREC-CT B requested that on both the Adult and Adolescent PILs, potential risks should be presented more clearly, and serious risks should be further highlighted.
- The NREC-CT B requested that the relevant information leaflets should allow for Parents and Guardians to support minors in the completion of the questionnaire.
- The NREC-CT B requested that reference to pregnancy and OCP is removed from the adolescent materials and included in the parent / guardian materials instead.
- In the Adult PIL, the NREC-CT B requested that the requirement for follow-up visits after immediate withdrawal is explained to participants.
- The NREC-CT B considered the statement in the Pregnancy PIL that confidentiality may not be maintained to be potentially harmful to the participant and requested that confidentiality is strictly maintained for this cohort of participants.
- The NREC-CT B requested that all risks are included in the GP letter.
- The NREC-CT B requested that all questionnaires are adapted to an Irish readership.
- 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 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.

  Further to the above, NREC-CT B requested confirmation that any future research project using samples or data from participants involved in this study will undergo full ethics review.
- The NREC-CT B noted that data will be pseudonymised. The Committee requested further information on who will hold the key to the data.
- The NREC-CT B noted that in the DPIA specifies that there is '*insufficient de-identification of participant data'.* The NREC-CT B requested further information on how this risk will be mitigated.
- The NREC-CT B noted that samples will be stored in Boston and archive staff will have access. This Committee requested further information on the storage and access to samples and requests that further information is provided to participants on this.
- The NREC-CT B requested assurance that adequate insurance will be in place for the duration of the trial.
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21-NREC-CT-089_AMEND-1

Principal Investigator: Dr Dearbhaile Collins

- Study title: A Randomized, Phase 3, Double-Blind Study of Chemoradiotherapy With or Without Pembrolizumab for the Treatment of High-risk, Locally Advanced Cervical Cancer (KEYNOTE-A18 / ENGOT-cx11/ GOG-3047)

Lead institution: Cork University Hospital

- NREC-CT Comments:

- The NREC-CT B noted that the substantial amendment application represents an update to the Protocol and Participant Materials of a Randomized, Phase 3, Double-Blind Study of Chemoradiotherapy With or Without Pembrolizumab for the Treatment of High-risk, Locally Advanced Cervical Cancer (KEYNOTE-A18 / ENGOT-cx11/ GOG-3047).
- The NREC-CT B considered this a well-presented application and that the substantial amendments made were reasonable.
- The NREC-CT B agreed that while additional revisions to the patient materials were required, this application can be designated Favourable with Conditions.

- NREC-CT Decision:

- Favourable with Conditions

- Associated Conditions

- The NREC-CT B noted that the consent statement was altered to '*the participant provides documented informed consent'*. The NREC-CT B requested clarification as to why this statement has been altered.

21-NREC-CT-090_AMEND-1

Principal Investigator: Dr Jarushka Naidoo

- Study title: A Phase 2 Randomized Double-blind Study of Relatlimab plus Nivolumab in Combination with Chemotherapy vs. Nivolumab in Combination with Chemotherapy as First Line Treatment for Participants with Stage IV or Recurrent Non-small Cell Lung Cancer (NSCLC).

Lead institution: Beaumont Hospital

- NREC-CT Comments:

- The NREC-CT B noted that this substantial amendment application represents an update to the Protocol, Participant Materials, and Investigator Brochure of a A Phase 2 Randomized Double-blind Study of Relatlimab plus Nivolumab in Combination with

Chemotherapy vs. Nivolumab in Combination with Chemotherapy as First Line Treatment for Participants with Stage IV or Recurrent Non-small Cell Lung Cancer (NSCLC).

- The NREC-CT B agreed that the substantial amendments were acceptable with some minor clarifications required.

  - NREC-CT Decision:

- Favourable with Conditions

  - Associated Conditions

- The NREC-CT B noted that the cover letter states *'participants will be reconsented as deemed appropriate'.* The NREC-CT B requests further information on the proposed reconsenting process.

- AOB: None
- The Chair closed the meeting.