National Research Ethics Committee

NREC-CT B Meeting

11th October 2023.

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
Dr Enda Dooley	Committee Member, NREC-CT B
Dr Lorna Fanning	Committee Member, NREC-CT B
Dr John Hayden	Committee Member, NREC-CT B
Prof. Colm O'Donnell	Committee Member, NREC-CT B
Dr Deborah Wallace	Committee Member, NREC-CT B
Dr Niall McGuinness	Committee Member, NREC-CT B
Prof Abhay Pandit	Committee Member, NREC-CT B
Ms Mandy Daly	Committee Member, NREC-CT B
Prof Andrew Green	Committee Member, NREC-CT B
Ms Deirdre MacLoughlin	Committee Member, NREC-CT B
Prof Seamus O'Reilly	Committee Member, NREC-CT B
Dr Christina Skourou	Committee Member, NREC-CT B
Dr Mark Robinson	Committee Member, NREC-CT B
Dr Emily Vereker	Acting Head, National Office for RECs
Ms Patricia Kenny	Project Officer, National Office for RECs

Dr Jane Bryant	Project Officer, National Office for RECs
Dr Laura Mackey	Programme Officer, National Office for RECs
Dr Susan Quinn	Programme Officer, National Office for RECs
Dr Emma Heffernan*	Project Officer, National Office for RECs

*Drafted minutes

Apologies:

Ms Paula Prendeville

Ms Susan Kelly

Dr Mary McDonnell Naughton

Quorum for decisions:

Agenda

- Welcome & Apologies
- 2023-504031-41-00
- 2023-504989-37-00
- 2022-501353-37-00
- 2022-503111-42-00
- 2022-501220-14-00
- 22-NREC-CT-095_Mod-3
- 22-NREC-CT-026_Mod-2
- 23-NREC-CT-021_Mod-1
- 23-NREC-CT-023_Mod-1
- 22-NREC-CT-016_Mod-3
- AOB

- The Chair welcomed the NREC-CT B.
  - The minutes from the previous NREC-CT B meeting on 6th September 2023 were approved.
  - The NREC Business Report was discussed and noted.

Applications

2023-504031-41-00

Principal Investigators & Institutions: Cork University Hospital (Prof Seamus O'Reilly), Beaumont Hospital (Prof. Patrick Morris), Sr Vincent's University Hospital (Prof Michaela Higgins), University Hospital Waterford (Dr Miriam O'Connor), University Hospital Galway (Prof. Maccon Keane), Mater Private Hospital (Prof Catherine Kelly)

Study title: CAMBRIA-2: A Phase III, Open-Label, Randomised Study to Assess the Efficacy and Safety of Camizestrant (AZD9833, a Next Generation, Oral Selective Estrogen Receptor Degrader) vs Standard Endocrine Therapy (Aromatase Inhibitor or Tamoxifen) as Adjuvant Treatment for Patients With ER+/HER2- Early Breast Cancer and an Intermediate-High or High Risk of Recurrence Who Have Completed Definitive Locoregional Treatment and Have No Evidence of Disease

EudraCT: 2023-504031-41-00

NREC-CT comments:

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

NREC-CT Decision:

- Request for more information

Additional Information Required RFI

Part I

- It was noted that not all the recommendations raised by the EMA have been implemented by the Sponsors. Clarity is requested as to when the outstanding recommendations will be implemented.

Part 2

- The NREC-CT notes that in Storage and Use of Biosamples Section 3.2 the question “If samples are to be sent to other organisations how will they be managed after analyses is carried out”, is answered to say these are to be returned to AZ Biobank. The Committee comments that it is not appropriate that samples would be sent to a Biobank without the explicit consent of participants.
- The NREC-CT notes that no compensation will be provided to carers. The Committee requests that this is amended so that carers of participants are entitled to reasonable out of pocket expenses.
- The NREC-CT notes that there is a space on the Main SIS and ICF for an impartial witness to sign, however, the Recruitment Informed Consent Procedure template

supplied is missing the relevant section related to the impartial witness. The Committee requests the updated Recruitment Informed Consent Procedure template be supplied for review.

- If participants require the assistance of carers to attend visits, the NREC-CT requests confirmation that carers will also be entitled to compensation for reasonable out of pocket expenses.'
- The NREC-CT requests further information on what will happen to any data/samples obtained during the screening process including the data/samples for those participants who are ineligible to participate in the study having been screened? This information should also be clarified for participants in the participant materials.
- The NREC-CT notes that the Main SIS and ICF, while necessary, is long and complex. The Committee requests that the PIL be restructured using headings to improve accessibility and readability of the participant information.
- The NREC-CT notes that the language and terminology on pg 4 Main SIS and ICF “Understanding ER+/HER2- early breast cancer with an intermediate or high risk of recurrence” is not accessible to a lay audience. The Committee requests that this section of the SIS and ICF is revised to be more accessible and simplified into plain English, to ensure that participants are fully informed.
- The NREC-CT requests that the section on Luteinizing Hormone Releasing Hormone (LHRH) on p7 of Main SIS and ICF should be moved to a later section of the SIS and ICF as it interrupts the flow of Section 3 - “What will happen if I join the study".
- The NREC-CT notes there is reference to re-screening and to the signing of a new informed consent form on pg 7 Main SIS and ICF however there was no consent form for screening provided in the initial application. The Committee requests that Screening SIS and ICF be provided for review.
- As this is a Phase 3 study, the NREC-CT requests confirmation if the detail included in the section on p13 of Main SIS and ICF on potential risks associated with animal models is necessary? If so, the Committee requests that it be updated in lay language to refer directly to the related risk for participants in this study.
- The NREC-CT requests more information on why the participants health insurance number is required as stated on pg 17 of Main SIS and ICF. If this is not relevant to Ireland, the Committee requests that this be removed.
- The NREC-CT notes that the Main SIS and ICF pg 22 states that “. If your insurance does not cover all costs for the standard endocrine therapy, LHRH agonists or specific tests required for this study, you will be reimbursed by the study sponsor for these expenses” The NREC- CT requests that the SIS and ICF be updated to confirm that neither participants nor their health insurance are charged for their participation in the study or any study specific procedures.
- The NREC-CT requests that the Main SIS and ICF consent statements on pg 27 and pg 28 be placed in a table with separate boxes for each statement to enable participants to initial each statement to show understanding and consent.
- The NREC-CT notes Main SIS and ICF pg 29 has a section for completion by participants’ legally accepted representative. The Committee requests information in

relation to what circumstances would a legally accepted representative sign the SIS/ICF.

- The NREC-CT requests the Main SIS and ICF pg 29 “Impartial Witness” section be updated to clarify in which circumstances the impartial witness signature can be used. Please ensure that this is in line with GCP guidelines for impartial witnesses.
- The NREC-CT notes that the section on future research in the Main SIS and ICF (pg. 25) and Optional Genetic Research SIS and ICF is not described in line with regulations and best practice. The Committee requests 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,
    - 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,
    - 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 NREC-CT notes that the Optional Genetic Research SIS and ICF states that “Any data generated from your biosamples will be stored as long as necessary for scientific research objectives and allowed by law” and requests that the maximum data retention period is clearly stated in the ICF.
- The NREC-CT requests the sentence on pg 3 Pregnant Partner SIS and ICF pg 3 “You are asked to contact the study doctor if you have a miscarriage or if you decide to have an abortion.” be removed
- The NREC-CT requests that further information on Prof Kelly previous clinical trial experience is added to the CV.
- The NREC-CT notes the Dr O’Sullivan has not fully completed the Declaration of Interest Form. The Committee requests that a fully completed Declaration of Interest Form be submitted for Dr O’Sullivan.

2022-503111-42-00

Principal Investigators & Institutions: Children’s Health Ireland (Dr Declan O’Rourke)

Study title: A Phase 3, Randomized, Double-blind, Placebo-controlled, Multicenter Study with a Treatment and Observation Period to Evaluate the Safety and Efficacy of

Vesleteplirsen (SRP-5051) in Ambulatory Subjects with Duchenne Muscular Dystrophy Amenable to Exon-51 Skipping Treatment (MOTIVATE)

EudraCT: 2022-503111-42-00

NREC-CT comments:

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

NREC-CT Decision:

- Request for more information

Additional Information Required RFI

Part I

- Further information is requested on whether study participants will have access to the study drug once the trial has ended or if the option of a study extension will be in place.
- "The Protocol pg 47 Inclusion criteria states that participants must be "ambulatory, ie, able to independently walk 10 meters in < 30 seconds" Confirmation is requested as to if a participant suffers a loss of ambulation during the trial, will they be allowed to remain on the trial.

Part II

- The NREC-CT requests submission of Statement of Funding as this was not provided in the initial application.
- The NREC-CT notes that a patient navigator is listed in the study brochure and flyer. The NREC-CT also notes that the patient navigator works for My tomorrow's website, which appears to be a 'for profit' company. However, there is no detail of this study navigator or My tomorrows in the recruitment procedures template. The Committee has concerns about inclusion of third parties in the recruitment process and would prefer their exclusion, otherwise a comprehensive description of their role should be provided. If they are to be included, the Committee requests further information in relation to the study navigator and My tomorrows such as:
    a) what exact role will they have in the study?
    b) what information will they be collecting and giving to participants?
    c) are they being paid every time a patient is recruited?
    d) is there any oversight from the PI?
- The Committee also requests that the study brochure and flyer be updated to contain more detail on the role of the patient navigator.

- The NREC-CT requests confirmation that the branded items listed in the Welcome Kit which are to be provided to participants will not have the study logo or branding on them to protect the confidentiality of research participants taking part in the trial.
- The NREC-CT notes the Recruitment template mentions the HCP Fact Sheet, HCP Letter and GP Letter however they were not provided in the initial application. The Committee requests that they are provided for review.
- The NREC-CT requests that the Flyer be updated to provide more information in lay language on what PPMOs and exon 51 skipping are rather than just referring the participant to a website.
- The NREC-CT requests that the study brochure and handbook be updated to contain more information about the purpose of the study and the risks involved.
- The NREC-CT notes that the Recruitment Informed Consent Procedure section 4.3 states that “Impartial witness will sign on behalf of patient´s parent / legal representative”. The Committee requests that this be updated as an impartial witness cannot consent on behalf of a patients’ parent / legally designated representative. As per ICH GCP an Impartial Witness “attests that the information in the consent form and any other written information was accurately explained to, and apparently understood by, the subject or the subject's legally acceptable representative, and that informed consent was freely given by the subject or the subject’s legally acceptable representative.” The PISCF should also reflect the Recruitment Informed Consent Procedure and include a placeholder for the signature and date of a potential impartial witness.
- The NREC-CT notes that the Main ICF Parental is long and dense and agrees with the DPO comments in their letter of 23/08/2023 that because of the length of the document there is a risk that guardians/participants will not gain an adequate understanding of the activities of the trial. The NREC-CT requests information on how this risk will be mitigated.
- The NREC-CT requests that the length of the Main ICF Parental is reduced while ensuring that sufficient information is provided to potential participants.
- The NREC-CT notes errors on pg 7 of Main ICF Parental with numerous references to “your” instead of “your child’s” and pg 35 reference to “your medical record” instead of “your child’s medical record”.
- The NREC-CT notes that pg 12 of Main ICF Parental “Your child may not be able to get the study drug after the study is over.” The Committee requests additional information here on any plans for extension studies if available.
- The NREC-CT requests that the Main ICF Parental pg 18 be updated to caution participants to stop using the supplements in the event of serious issues or serious side effects or language to seek immediate advice.
- The NREC-CT requests the Main ICF Parental pg 20 be updated to detail how the risk of Rhabdomyolysis will be mitigated to reassure participants.
- The NREC-CT requests that the Main ICF Parental pg 21 be updated to provide more explanation to participants around the statement “Please note that Sarepta will not

cover the cost of port removal if medicines other than the study drug have been infused via the port".

- The NREC-CT noted the reference to a reference to a travel policy pg 25 in the Main ICF. This was not included in the documentation for review. The Committee requests that this document is shared with the committee for review.
- The NREC-CT advises that there is a duplication of information on pages 26 and 27 of Main ICF Parental in relation to compensation.
- The NREC-CT advises that the information on compensation pg 27 of Main ICF Parental is contradictory and confusing "There are no plans to pay you or give you other compensation for an injury to your child, should one occur" and "The sponsor will provide compensation for any injury caused by taking part in this study in accordance with the Irish Pharmaceutical Healthcare Association (IPHA) guidelines. In the EU, there may be compensation for damages resulting directly from participation in this clinical study in the form of insurance, guarantee or similar arrangement" The Committee requests that the section on compensation be shortened and a statement added to confirm that insurance is in place to provide compensation for injuries as a result of participation in the research study,
- The NREC-CT notes that the section on future research in the Main ICF Parental (pg. 28) is not described in line with regulations and best practice. The NREC requests that future research be updated to be limited to the disease area or specific drug research. 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 NREC-CT requested the Main ICF Parental be updated to include detail around the risks of IV and infections.
- The NREC-CT notes that the Sub Study M - Cardiac and Musculoskeletal MRI ICF pg 2 refers to a central reader called Clario and requested the PIL be updated to advise where this reader is based.
- The NREC-CT notes that the Sub Study B ICF - Open muscle biopsy sub study states that if the child "declines to participate in this sub study, or you decide not to allow your child to take part in this sub study, they may not be able to continue to be a part of in the main study" which contradicts the information on pg 9 of Main ICF Parental which indicates it is optional to take part in the sub studies "Your child may be asked to participate in a sub-study. If you agree to allow your child to participate in a sub-study, you will need to consent individually to each sub-study by signing a separate sub-study ICF provided to you". The NREC-CT requests that the Sub Study B ICF be updated to give a consistent message on how sub-study participation affects the child's participation in the main trial.
- The NREC-CT noted that Sub Study P ICF pg 3 states "After the sub-study tests are completed, some of your child's samples may be stored for up to 20 years, in case any samples need to be re-tested". The Committee requested the ICF be updated with information to participants on the purpose of the retest.

- The NREC-CT welcomes the assent procedures and assent forms however the Committee also notes that some of the language and terminology in the ICF Age Range 1 - Assent form 6-11, was not child friendly. The Committee requests that the ICF be revised to ensure the language is more accessible and simplified for the age of the participant and explanations given for words such as 'Regulatory authorities', 'standard of care', 'ICF'. The NREC-CT also notes that the individual sub studies are not explained in the ICF Age Range 1 and requests that a paragraph on each sub study to be added to the ICF in order for the participants aged 6-11 to be able to give assent for them.
- The NREC-CT notes a typo on pg 10 of ICF Age Range 1 - Assent form 6-11 the first tick box "YES, I would like my to participate in the Open muscle biopsy sub study".
- The NREC-CT requests that the ICF Age Range 1 - Assent form 6-11 be updated to be consistent with terminology used for parent/legal guardian. Please note in Ireland a Carer cannot consent on behalf of a child unless they have legal authority to do so.
- The NREC-CT notes that the ICF Age Range 2 – Assent form 12-15 language and terminology is not appropriate for the age range and requests that the ICF Age Range 2 be revised to include more age-appropriate language throughout.
- The NREC notes the Study diary for magnesium data was not supplied with the initial application. The Committee requests this is submitted for review.

2023-504989-37-00

Principal Investigators & Institutions: Beaumont Hospital (Dr Jarushka Naidoo), St James's Hospital (Dr Sinead Cuffe)

Study title: A Randomized, Controlled, Multiregional Phase 3 Study of Ivonescimab Combined with Chemotherapy Versus Pembrolizumab Combined with Chemotherapy for the First-line Treatment of Metastatic Squamous Non-small Cell Lung Cancer (HARMONi-3)

EudraCT: 2023-504989-37-00

NREC-CT comments:

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

NREC-CT Decision:

- Request for more information

Additional Information Required RFI

Part 2

- The NREC-CT notes in the Pregnancy Follow-up PIL, the inclusion of consent from parents of a pregnant adolescent under 16, who would be partner of a trial participant.

The NREC-CT considers that such an outcome would be very unlikely and requests that this section is removed from the consent form.

- The NREC-CT notes that the Main SIS and ICF (pg 23 and 30) is seeking blanket consent for “new medical research, developing new medical products or procedures and other business purposes”. This type of consent is currently too broad and not described in line with national regulations and best practice. where informed participant consent is a mandatory safeguard. The NREC-CT requests that future research be confined to lung cancer and/or the drug/s under study in this trial and that this be amended in the Main SIS and ICF.

2022-501353-37-00

Principal Investigators & Institutions: Mater Misericordiae University Hospital (Dr Frank Lyons), St Vincent’s University Hospital (Dr Andrea Haren)

Study title: A Randomized Study of Andexanet Alfa Compared to Usual Care in Patients Receiving a Factor Xa Inhibitor who Require Urgent Surgery or Procedure (ANNEXA-RS).

EudraCT: 2022-501353-37-00

NREC-CT comments:

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

NREC-CT Decision:

- Request for more information

Additional Information Required RFI

Part 2

- The NREC-CT notes reference to “Optional Future Research Consent Form” on pg 4 of Main ICF however this was not submitted with the initial application. The Committee requests the Optional Future Research ICF be submitted for review.
- The NREC-CT requests that the Main ICF be updated to include more information around the role and designation of the legally designated representative as defined in the S.I. No. 99 / 2022.).
- The NREC-CT notes that if a legal representative signs the consent on behalf of a participant in an emergency situation, that on D1, D2 or D7 visits the participants consent will be obtained to take part in the study and for future use of collected samples. The Committee requests information on what would happen to the data and samples collected in the situation that the participant does not survive to D1, D2 or D7 visits to give consent.

- The NREC-CT requests that all reimbursed expenses that participants are entitled to should be clearly stated in the Main ICF document pg 5, and that the wording is changed from ‘may be reimbursed’ to ‘will be reimbursed’.

2022-501220-14-00

Principal Investigators & Institutions: Beaumont Hospital (Prof. Patrick Morris), Bon Secours Hospital Cork (Prof. Conleth Murphy)

Study title: Multicenter, open-label, phase 2 study of carboplatin plus mirvetuximab soravtansine followed by mirvetuximab soravtansine continuation in folate receptor-alpha positive, recurrent platinum sensitive, high-grade epithelial ovarian, primary peritoneal, or fallopian tube cancer following 1 prior line of platinum-based chemotherapy

EudraCT: 2022-501220-14-00

NREC-CT comments:

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

NREC-CT Decision:

- Request for more information

Additional Information Required RFI

Part 1

- Due to the number of CT scans involved in the study, the exposure to ionizing radiation is considered to be a potential risk to participants. Justification is required to support the number of scans involved as part of trial participation. It is also requested that the sponsor clarify whether it is possible to use alternative scans such as MRIs to reduce the exposure to ionizing radiation to participants.

Part 2

- The NREC-CT notes that (pg 6) Section 4.8 Answers ‘No’ to the question “If secondary future use of samples – will Ethics Committee or Biobanking Committee be contacted”. The NREC-CT requests justification why subsequent research ethics review will not be sought for secondary future use of samples.
- The NREC-CT notes that the Pre-Screening ICF (pg8) Optional Consent for Conduct of Secondary Research states “… and to be able to find the best way to treat patients with ovarian cancer and other cancers”. The Committee would consider this definition too broad and advises that this is not in line with national legislation and HSE guidelines - Health Research Regulations (Data Protection Act 2018 (Section 36(2) (Health Research) Regulations 2018) and HSE National Policy for Consent in Health and Social Care Research (V1.1, 2023). The Committee

requests that future research be confined to ovarian, peritoneal, or fallopian tube cancer and other cancers and that this be amended in the relevant ICF.

- The NREC-CT noted that the Pre-Screening ICF pg 4 and 6 be updated to remove reference to NREC having access to 'personal data'. The Committee requests that this is amended to 'coded or pseudonymized data'.
- The NREC-CT notes that eye related adverse events are common and requests that the Main ICF be updated to include information for participants on what to do or who to call if they experience issues with their eyes outside of office hours.
- The NREC-CT requests that the sentence on pg3 "it is possible that after the screening tests have been reviewed, you would not be able to take part in the study" be removed from the Main ICF as someone that has failed the inclusion criteria (determined through screening) would not be considered eligible for the CT and would not be given this ICF.
- The NREC-CT requests that phrase "If you are a woman" on pg 9 Main ICF Reproductive Risks be removed or updated to "woman of childbearing potential or breast feeding ….."
- The NREC-CT notes that Main ICF pg 4 states "Your eyes may need to be dilated for the eye exams in this study, which may cause blurred vision". Please clarify if this indicates that the participant will need a companion to accompany them to the study site on the days of planned eye tests. If yes, the NREC-CT requests the ICF be updated to include requirement for a companion to accompany the participant on days of planned eye tests and that compensation for reasonable out of pocket expenses such as travel and meals for the companion are also provided and detailed in the ICF.
- The NREC-CT notes the phrase on Main ICF pg 9 Reproductive Risks "If you are a woman". The Committee requests that this phrase be removed or changes to "If you are a woman of childbearing potential or breast feeding".
- The NREC-CT notes the refence to a travel assistance policy on pg 17 of Main ICF. This was not included for review. The Committee requests that this document is shared with the Committee for review.
- The NREC-CT notes the refence to a travel assistance policy on pg 17 of Main ICF. This was not included for review. The Committee requests that this document is shared with the Committee for review.
- The NREC-CT requests that Main ICF pg 19 be updated to remove reference to NREC having access to 'personal data' / medical records. The Committee requests that this is amended to 'coded or pseudonymized data'.
- The NREC-CT notes reference on pg19 of the Main ICF to "pseudonymized data" and requests that this be explained further in the body of the ICF.
- The NREC-CT requests that the GP letter pg 2 reference to "Ethics Committee" be updated to National Research Ethics Committee

- The NREC-CT notes an old version of the Site Suitability Form has been completed for Bon Secours. The Committee requests that the updated Version 2.0 be completed for Bon Secours and submitted for review.
- The NREC-CT notes that Beaumont Site Suitability Form pg4 Item 5 states exposure to Ionising Radiation at the site is not above what is required for standard of care, however the Main ICF pg12 states "you may have more CT scans than you would normally have for your medical treatment. CT scans expose you to radiation, which may increase your risk of getting a new cancer and/or cause harmful changes to your genes……. Your risk of harm might be as high as 1 in 1000". The NREC-CT requests that the Site Suitability Form be updated to correct this contradiction and justification provided on pg 4 item 5 for the increased exposure.

22-NREC-CT-095_Mod-3

Principal Investigator: Dr Kelly

Study title: Efficacy and safety of COMP360 psilocybin therapy in anorexia nervosa: a proof-of-concept study

NREC-CT comments:

- Based on the above, the NREC-CT B agreed that this substantial amendment application be designated as favourable.

NREC-CT Decision:

- Favourable

22-NREC-CT-026_Mod-2

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)

NREC-CT comments:

- 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 on this Substantial Amendment.

NREC-CT Decision:

- Request for further information

Additional Information Requested:

- The NREC-CT noted the introduction of the Happify App and consider it to be well intentioned. However, the NREC-CT believe that the introduction of this app has the potential for negative impacts on the well-being of participants. As the app is not included in the study procedures and is an additional add-on for participants, the Committee requests the app is removed from the study.
- The NREC-CT noted that tracked change version of the 6.a. Participants Study Guide and 6. b. the Patient Brochure were not included in the application and requested that these documents are provide for ease of review.

23-NREC-CT-021_Mod-1

Principal Investigator: Prof Ken McDonald

Study title: The impact of Empagliflozin on Left atrIal Volume and the feasibility of using Fitbit and mHealth to prescribe Exercise in non-diabetic Pre- Heart Failure (ELIVE pre-HF)

NREC-CT comments:

- 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 on this Substantial Amendment.

NREC-CT Decision:

- Request for further information

Additional Information Requested:

- The NREC-CT requested that the reconsenting strategy is detailed on pg. 6 of the Substantial Modification Form.
- The NREC-CT requested that the sentence on pg. 3 of the Genetics PISCF *'Following on from this, your genetic code will be fully de-identified'* is removed, as genetic sequences cannot be fully de-identified.
- The NREC-CT noted that the text on pg.5 of the Genetics PISCF states that *'we will keep your pseudonymised personal data for up to 15 years, after this data will be fully anonymized and data stored indefinitely'* and requested that the original sentence informing participants that their data will be stored for up to 15 years is reinstated, as genetic sequences cannot be fully de-identified / anonymized and therefor this data should be deleted, and not retained indefinitely and also participants should be fully informed as to the maximum retention periods for their data.
- The NREC-CT noted that the PIL/ICF states "We will apply for further review by the National Office for Research Committees if the study team plan to undertake any further research using collected samples". As consent for recontact/future use is not included in the study, the Committee suggests that this is removed.

23-NREC-CT-023_Mod-1

Principal Investigator: Dr Jarushka Naidoo

Study title: A Phase 3 Study to Evaluate Zimberelimab (AB122) Combined with Domvanalimab (AB154) Compared to Pembrolizumab in Front-Line, PD-L1-High, Locally Advanced or Metastatic Non-Small Cell Lung Cancer

NREC-CT comments:

- Based on the above, the NREC-CT B agreed that this substantial amendment application be designated as favourable

NREC-CT Decision:

- Favourable

22-NREC-CT-016_Mod-3

Principal Investigator: Prof Ray McDermott

Study title: A Phase 3, Open-label, Randomized, Noninferiority Trial of Subcutaneous Formulation of Nivolumab Versus Intravenous Nivolumab in Participants With Advanced or Metastatic Clear Cell Renal Cell Carcinoma Who Have Received Prior Systemic Therapy

NREC-CT comments:

- Based on the above, the NREC-CT B agreed that this substantial amendment application be designated as favourable

NREC-CT Decision:

- Favourable

- **AOB:**
  - None