National Research Ethics Committee

NREC-CT B Meeting

8th November 2023

Attendance

Name	Role
Dr Cliona McGovern	Chairperson, NREC-CT B
Dr Jean Saunders	Deputy Chairperson, NREC CT-B
Ms Paula Prendeville	Committee Member, NREC-CT B
Ms Susan Kelly	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
Dr Mary McDonnell Naughton	Committee Member, NREC-CT B
Ms Jasmine Joseph	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 Geraldine O'Dea	Committee Member, NREC-CT B
Prof Deirdre Murray	Committee Member, NREC-CT B
Ms Caoimhe Gleeson	Committee Member, NREC-CT B

Dr Lina Zgaga	Committee Member, NREC-CT B
Dr Steve Meaney	Committee Member, NREC-CT B
Ms Aileen Sheehy	Programme Manager, 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 Manager, National Office for RECs
Ms Rachel McDermott	Project Officer, National Office for RECs

*Drafted minutes

Apologies: Dr Mark Robinson, Prof Abhay Pandit, Ms Mandy Daly, Prof. John Faul, Ms Serena Bennett

Quorum for decisions: Yes

Conflicts of Interest: The following Committee Members declared Conflicts of Interest, and were not in attendance for the discussion of the respective applications:

Dr Cliona McGovern: 2023-506967-33-00, 22-NREC-CT-124_Mod_2, 22-NREC-CT-115_Mod_3

Prof. Colm O'Donnell: 2023-503993-19-00

Ms Jasmine Joseph: 21-NREC-CT-155_Mod-4

Agenda

- Welcome & Apologies
- 2023-506967-33-00
- 2023-504993-40-00
- 2023-503993-19-00
- 22-NREC-CT-124_Mod_2
- 22-NREC-CT-138_Mod-4
- 21-NREC-CT-155_Mod-4
- 22-NREC-CT-105_Mod_4
- 22-NREC-CT-115_Mod_3
- 22-NREC-CT-155_Mod_2
- 2022-501943-34-00 SM-1
- 22-NREC-CT-116_Mod-3
- 21-NREC-CT-036_Mod-7
- 23-NREC-CT-029_Mod-2
- 21-NREC-CT-173_Mod-4

- 22-NREC-CT-034_Mod-3
- AOB

- The Chair welcomed the NREC-CT B, including the new Committee Members.
  - The minutes from the previous NREC-CT B meeting on 11th October 2023 were approved.
  - The NREC Business Report was discussed and noted.

Applications

2023-506967-33-00

Principal Investigators & Institutions: Mater Misericordiae University Hospital (Prof. Peter Kelly)

Study title: CONCISE COlchicine iN Circulating Inflammatory markers after StrokE

EudraCT: 2023-506967-33-00

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.

NREC-CT Decision:

- Request for Further Information

Additional Information Required:

Part I

- The Sponsor was requested to clarify whether all WOCBP are to be excluded, as specified in the eligibility criteria (Protocol pages 8 and 9), or pregnant participants only, as specified in the participant-facing information. Furthermore, clarification was requested on whether breastfeeding women are to be included or excluded.
- Patients participating in another clinical trial within the previous 3 months (particularly the CONVINCE trial) should be added to the exclusion criteria.
- The Sponsor was requested to give further details on how long blood samples will be retained, given the data associated with those samples will be retained for 25 years.

- The Sponsor was requested to provide further details regarding the determination of population size (91) and whether this size was needed to provide estimates of CRP levels.
- Inconsistent terminology was noted regarding the duration of the study, varying between 4 weeks, 30 days, and 1 month. The sponsor was requested to clarify the duration and edit the documents for consistency.
- It was noted that similar studies to the trial proposed have already been undertaken and published using this medicinal product and similar patient cohorts. The Sponsor was requested to provide further information and justification on what are the anticipated therapeutic and public health benefits as a result of this study.

Part II

- The NREC-CT requested confirmation that the study will have insurance in place for the entirety of its duration.
- The NREC-CT noted that the information given in this template for recruitment of participants does not match that detailed in the Protocol. Clarification was requested on which approach is correct.
- The NREC-CT requested clarification on whether provision for translation services will be given for participants who may require them. If so, please outline the process for recruiting participants who may require translation services.
- The NREC-CT requested clarification on whether all WOCBP are to be excluded, as per eligibility criteria (Protocol pages 8 and 9), or pregnant participants only, as per the Informed Consent Form. Furthermore, clarification was requested on the inclusion of breastfeeding women. This should be clarified in the relevant participant materials.
- The NREC-CT requested further details on how long blood samples will be retained, given the data associated with those samples will be retained for 25 years.
- The NREC-CT noted that Dr Sarah Corey is listed as a PI in some of the submitted documentation, and requested clarification on whether Dr Corey is a PI or sub-investigator. If Dr Corey is a PI, the NREC-CT requests submission of a CV, Declaration of Interest, and confirmation that GCP training has been completed and is in date.

2023-504993-40-00

Principal Investigators & Institutions: Mater Misericordiae University Hospital (Dr John Lambert), Beaumont Hospital (Dr Samual McConkey)

Study title: A Phase 3b, multi-center, randomized, parallel-group, open-label, non-inferiority study evaluating the efficacy, safety, and tolerability of oral dolutegravir/lamivudine once-daily as a first-line regimen compared to oral bictegravir/emtricitabine/tenofovir

alafenamide once daily for virologic suppression and maintenance in antiretroviral therapy naïve adults living with HIV

EudraCT: 2023-504993-40-00

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.

NREC-CT Decision:

- Request for Further Information

Additional Information Required:

Part I

- The Sponsor was requested to give further information on the statistical design of the study, specifically in relation to further information on why multiplicity adjustment will not be performed. The validity of the results may be affected through the increased chance of Type I error associated with multiplicity analysis.

Part II

- The NREC-CT requested clarification on why there is provision for a legally designated representative in the consent section, given that all participants will have capacity to consent (Main ICF, Pregnant Partner ICF, Treatment Restart ICF). If this is not required, the Committee suggested removing it from the patient materials.
- The NREC-CT noted that the Main ICF is seeking blanket consent for future use of samples/ data, for unspecified purposes, without further consent. This type of consent is not in line with best practice, the Declaration of Taipei 2016 and not in compliance with the Data Protection Act 2018 (Section 36(2) (Health Research) Regulations 2018), where informed participant consent is a mandatory safeguard. The NREC-CT requested i) consent can only be obtained for the purpose of specified health research, either in relation to a particular area or more generally in that area or a related area of health research, and/or ii) that an option is provided to enable participants to consent to be contacted, and/or (iii) confirmation that subsequent research ethics review will be sought for specific research once clearly defined.
- The NREC-CT noted that participants both ‘may’ and ‘will’ be reimbursed, and requests this section is clarified for participants (Main ICF, page 26).

2023-503993-19-00

Principal Investigators & Institutions: Royal Victoria Eye and Ear Hospital (Prof. Conor Murphy)

Study title: Perioperative treatment of high immunological risk corneal transplant patients with allogeneic adipose-derived mesenchymal stem cells.

EudraCT: 2023-503993-19-00

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.

NREC-CT Decision:

- Request for Further Information

Additional Information Required:

Part I

- A Data Safety Monitoring Committee should be established to support analysis of this study. A charter for this Committee and details of its membership should be submitted as part of the RFI.
- It was noted that the different cell doses will be delivered in increasing volumes of carrier, ranging from 0.5 to 1.0 ml. Further information is requested whether these different volumes could have different impacts on the target tissue and whether the cells can be delivered in the same volume by using preparations of increasing cell density?
- Further clinical evidence is required around the tolerability and safety from prior studies. Any limitations from these studies should also be included in this assessment. This information should be expanded on in both the Protocol and the PIL.
- The Protocol would benefit significantly from a schema outlining the study process.
- It was noted that one of the primary aims of the study is '*the effect on the profile of conjunctival inflammatory cells.'*. This should be recategorized as an exploratory endpoint.
- Little information was provided on how the analysis of safety information will take place. Specifically, further information is required on which timepoints are used for endpoint analysis, how will the Sponsor determine if the doses administered are both safe and well-tolerated.
- The current rationale for dosage proposed was considered inadequate and further information is required to support the proposed dosages.
- Given that the MSCs are allogeneic, clarification was required on whether there is an increased risk that the use of MSCs could sensitise the recipient were a further corneal graft needed, increasing the risk of graft rejection in subsequent grafts? If so, this should be captured in the protocol and adequately addressed in the relevant participant materials.
- The protocol states that the efficiency of ASC therapy prior to corneal transplant will be measured by the absence of graft rejection episodes and graft failure during

follow up (52 weeks), but what if failure occurs independently or by a study confounding variable?

- The description of the phase of clinical trial was inconsistent, with the proposal using “Initiation, Phase 1b feasibility, feasibility, Phase 1b feasibility”. Phase 1b and feasibility are not equivalent study designs. It was requested that this is corrected.
- Although a formal sample size is not required for a Phase 1B study, it was queried whether sufficient evidence will be obtained from 3 patients at each dosage to conclude on safety and tolerability given potential variables. Further information was required to support the proposed sample size.
- The protocol proposes to increase recruitment to mitigate any potential dropouts but did not describe how the data from dropouts will be treated and /or analysed.
- The protocol states that they will investigate “Long term” survival with a follow up for 52 weeks, however, Fig 1 (B) in the proposal shows failure rates decline rapidly after 1.5 years. Further information is required to support the long-term survival period.
- Subjects should not be identified by both initials and study ID number, only study ID number.
- Exclusion criteria stated, “inability to understand potential risks and benefits”. This should be rephrased to “Unable to provide informed consent”.
- Further information was required on how the study end points will be analysed.
- It was noted that the *in vitro* and *in vivo* effects on cardio myopathy are well established, however based on the IB, little information is available to non-clinical pharmacology in the context of corneal transplant. Further information was requested on evidence for the presence pro-angiogenic potential in transplanted cornea to support the justification of the study.
- It was noted that there is limited information on the safety aspects of the study. Further information was required to understand what would constitute an adverse event during this study, and how would this be addressed? Further information was also required as to what a potential unexpected adverse event might be and how will this be managed?
- It was noted that the release criteria on page 11 of the IB states that the release of VEGF was “above the acceptance criteria”. Data on page 18 of the IB also shows that the ASC drives angiogenesis. A risk benefit statement was required to support the information provided in the IB.

Part II

- The NREC-CT noted that blood samples, tear samples and inflammatory cells will be obtained as part of the study. The submitted template was not submitted with information regarding these samples. The NREC-CT requested that this template is completed and re-submitted for review.
- The NREC-CT noted that there is no insurance certificate provided from the supplier for the cell product submitted, or agreements with the site and supplier of

the cell product. The NREC-CT requested that this information be submitted for review.

- The NREC-CT requested further information on how the cost of the cell therapy will be covered. This information needs to be clarified and where relevant, information included in the participant materials.
- The NREC-CT requested that insurance details from the supplier of the cell therapy is shared with the NREC for review in the event that there is an issue with the therapy.
- The NREC-CT noted that a generic PIL template was used for this study with many sections included not relevant to the overall study design. The Committee requested that a trial specific revised consent form should be resubmitted.
- The NREC-CT considered that limited information around the risks associated with the study were included in the PIL. The Committee recommended that the Subject Information and Consent Form include further information on the purpose of the study, and the risks and safety/tolerability information for the study.
- The NREC-CT requested further information be provided on contingency and safety measures for the participants for the day of surgery, for example in the event that adverse events are experienced.
- The NREC-CT noted that PIL indicates that a participant can withdraw at any time. However, once they receive the MSC injection, they may withdraw from follow up, but the study intervention has taken place. This needs to be clarified in the participant materials.
- The NREC-CT noted Page 4 of the PIL states that there is evidence that the patient would benefit from MSC therapy. The Committee requested that the information is updated to ensure that participants are informed that any evidence is only from animal studies.
- The NREC-CT noted that the PIL describes the safety results for other studies but does not directly address the risks of the procedure, such as complications of any sub conjunctival injection, nor the outcomes that are being measured such as pain or inflammation. The Committee requested that this information is updated in the PIL.
- The NREC-CT requested that the use of Yes / No boxes in the consent section are limited to when participants have a choice.
- The NREC-CT requested that information on the Data Protection Officer and the Data Commissioners Office are included in the PIL.
- The NREC-CT considered the study title in the PIL as misleading. The primary aim of this study is not to prevent corneal transplant rejection but to assess the safety and tolerability of MSCs. The Committee requested that this is corrected.
- The NREC-CT requested that the section on ‘Other treatment’ is revised to ensure participants are fully informed of their options.

- The NREC-CT requested that complex terminology used such as ‘coded’ and ‘early phase study’ are explained in lay language.
- The NREC-CT requested that further information on the collection, use and retention of biological samples is captured in the PIL.
- The NREC-CT requested that the NREC template for Site Suitability Assessment is completed and submitted for review. This template can be found here: https://www.nrecoffice.ie/submit-under-the-clinical-trial-regulation/
- The NREC-CT requested that the site suitability is updated to include further detail on the specific requirements for this study including database (RedCap) management, Biobanking facilities, SAE & AE recording/reporting, Statistical analysis, and any other requirements as relevant.
- The NREC-CT requested that an EMA or NREC CV template for Prof. Murphy is completed and submitted for review. The NREC template can be found here: https://www.nrecoffice.ie/submit-under-the-clinical-trial-regulation/

22-NREC-CT-124_Mod_2

Principal Investigator: Prof Alistair Nichol

Study title: Randomised, Embedded, Multi-factorial, Adaptive Platform Trial for Community Acquired Pneumonia (REMAP-CAP)

EudraCT: 2015-002340-14

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.

NREC-CT Decision:

- Request for more information

Additional Information Required:

- The NREC-CT requested clarification on how and when Telephone Assent will be used, and further information on the consent process associated with same.
- The NREC-CT considered that the currently options provided to participants in the Telephone Assent form may be too binary for questions related to the Advanced Care Act and co-decision making agreement. The Committee recommended the addition of other options for binary Yes/No boxes in the Telephone Assent Form, for example, ‘Unsure’ or similar wording.
- The NREC-CT requested confirmation that the additional Investigators have completed GCP training.

22-NREC-CT-138_Mod-4

Principal Investigator: Dr Philip Murphy

Study title: A Phase 3 Open-Label, Randomized Study of pirtobrutinib (LOXO-305) versus Investigator's Choice of Idelalisib plus Rituximab or Bendamustine plus Rituximab in BTK Inhibitor Pretreated Chronic Lymphocytic Leukemia/Small Lymphocytic Lymphoma (BRUIN CLL-321)

EudraCT: 2020-004554-30

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.

NREC-CT Decision:

- Request for Further Information

Additional Information Required:

- The NREC-CT noted that the Main ICF is seeking blanket consent for future use of samples/ data, for unspecified purposes, without further consent. This type of consent is not in line with best practice, the Declaration of Taipei 2016 and not in compliance with the Data Protection Act 2018 (Section 36(2) (Health Research) Regulations 2018), where informed participant consent is a mandatory safeguard. The NREC-CT requested i) consent can only be obtained for the purpose of specified health research, either in relation to a particular area or more generally in that area or a related area of health research,, and/or ii) that an option is provided to enable participants to consent to be contacted, and/or (iii) confirmation that subsequent research ethics review will be sought for specific research once clearly defined.
- The NREC-CT requested further detail is added for participants on what out-of-pocket costs will be reimbursed.

21-NREC-CT-155_Mod-4

Principal Investigator: Prof Sean Kennelly

Study title: A randomised double-blind placebo-controlled clinical trial investigating the effect and safety of oral semaglutide in subjects with early Alzheimer´s disease (Evoke)

EudraCT: 2020-004848-29

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.

NREC-CT Decision:

- Request for Further Information

Additional Information Required:

- The NREC-CT noted that the Main ICF is seeking blanket consent for future use of samples/ data, for unspecified purposes, without further consent. This type of consent is not in line with best practice, the Declaration of Taipei 2016 and not in compliance with the Data Protection Act 2018 (Section 36(2) (Health Research) Regulations 2018), where informed participant consent is a mandatory safeguard. The NREC-CT requested i) consent can only be obtained for the purpose of specified health research, either in relation to a particular area or more generally in that area or a related area of health research, and/or ii) that an option is provided to enable participants to consent to be contacted, and/or (iii) confirmation that subsequent research ethics review will be sought for specific research once clearly defined.
- The NREC-CT noted that participants will be offered an item for their participation, and requests further details of what this item is. This information should also be added to the ICF document.
- The NREC-CT noted that the option for Legally Authorised Representative signatures has been removed from the Direct to Patient ICF document, but remains on other ICF documents, and requested clarification on this inconsistency.
- Although not part of the Amendment, The NREC-CT requested clarification on whether provision for a meal or refreshment for the participant and their study partner will be made or reimbursed. The NREC-CT strongly recommended that the provision of refreshments, and meals where appropriate, is provided to participants and study partners.

22-NREC-CT-105_Mod_4

Principal Investigator: Dr Elisabeth Vandenberghe

Study title: A Phase 3 Open-Label, Randomized Study of LOXO-305 versus Investigator Choice of BTK Inhibitor in Patients with Previously Treated BTK Inhibitor Naïve Mantle Cell Lymphoma (BRUIN MCL-321)

EudraCT: 2020-004553-72

NREC-CT comments:

- Based on the above, the NREC-CT B agreed that this substantial amendment application be designated as favourable, subject to additional conditions being met.

NREC-CT Decision:

- Favourable with Conditions

Additional Conditions:

- The NREC-CT noted that the Main ICF is seeking blanket consent for future use of samples/ data, for unspecified purposes, without further consent. This type of consent is not in line with best practice, the Declaration of Taipei 2016 and not in compliance with the Data Protection Act 2018 (Section 36(2) (Health Research) Regulations 2018), where informed participant consent is a mandatory safeguard. The NREC-CT requested i) consent can only be obtained for the purpose of specified health research, either in relation to a particular area or more generally in that area or a related area of health research, and/or ii) that an option is provided to enable participants to consent to be contacted, and/or (iii) confirmation that subsequent research ethics review will be sought for specific research once clearly defined.
- The NREC-CT noted references to the US jurisdiction throughout the ICF document, and requests that these are changed for the Irish setting.
- Although not part of the Amendment, The NREC-CT requested clarification on whether provision for a meal or refreshment for the participant and their study partner will be made or reimbursed. The NREC-CT strongly recommended that the provision of refreshments, and meals where appropriate, is provided to participants and study partners.

22-NREC-CT-115_Mod_3

Principal Investigator: Prof. Patrick Mallon

Study title: An International Multicentre, Phase 2, Randomised, Adaptive Protocol to determine the need for, optimal timing of and immunogenicity of administering a booster mRNA vaccination dose against SARSCoV-2 in the general population (18+ years) already vaccinated against SARS-CoV-2 (EU-COVAT-2 BOOSTAVAC)

EudraCT: 2021-004889-35

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-155_Mod_2

Principal Investigator: Prof. Edward McKone

Study title: A Phase 3, Open-label Study Evaluating the Long-term Safety and Efficacy of VX-121 Combination Therapy in Subjects With Cystic Fibrosis

EudraCT: 2021-000713-17

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.

NREC-CT Decision:

- Request for Further Information

Additional Information Required:

- The NREC-CT noted the wording in Row 10 of the Fact Sheet related to when the participant should take their dose of IMP. It is unclear as to whether the two tablets should be taken at approximately the same time as each other, or approximately the same time each day. This clarity request also pertained to the Visit Guide.
- The NREC-CT noted that the adolescent assent form provides information around the potential risks in the event of pregnancy. In the event of pregnancy in a minor, the NREC-CT requested confirmation that adequate safeguards are in place at Irish sites.

2022-501943-34-00

Principal Investigator: Prof. Noel G. McElvaney

Study title: A Randomized, Double-Blind, Placebo-Controlled, Phase 3 Study to Evaluate the Efficacy and Safety of Fazirsiran in the Treatment of Alpha-1 Antitrypsin Deficiency–Associated Liver Disease With METAVIR Stage F2 to F4 Fibrosis

EudraCT: 2022-501943-34-00

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.

NREC-CT Decision:

- Request for Further Information

Additional Information Required:

- The NREC-CT requested that the videos arising from the scripts are submitted for review (Patient videos from the Landing Page Script, eConsent video). If this is not possible through CTIS, these videos should be submitted by email to clinicaltrials@nrec.ie , referencing the trial and RFI details in the email.

22-NREC-CT-116_Mod-3

Principal Investigator: Dr Adrian Murphy

Study title: An Open-label Randomized Phase 3 Study of Tucatinib in Combination with Trastuzumab and mFOLFOX6 versus mFOLFOX6 given with or without either Cetuximab or Bevacizumab as First-line Treatment for Subjects with HER2+ Metastatic Colorectal Cancer

EudraCT: 2021-002672-40

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.

NREC-CT Decision:

- Request for Further Information

Additional Information Required:

- The NREC-CT requested clarification on the length of retention time for archival material, and if this changes when samples are transported to the U.S.
- In relation to archival samples, the NREC-CT also requested clarification on whether an archival sample will be required for all participants, or only if HER2 status is unknown.
- The NREC-CT noted an increase in the number of diagnostic scans, and requests further information on any risk of increased exposure to radiation for participants. If so, this additional risk should be captured in the participant materials.
- The NREC-CT requested that additional information is provided to participants in the ICF documents on what symptoms they may expect in the case of elevated levels of enzymes as this may not be familiar terminology.
- The NREC-CT noted that third parties will have access to participants' medical records and uncoded data, and requested further information on what data will be accessible, by whom, and under what circumstances and whether a DPIA has been carried out.
- While not part of the Amendment, The NREC-CT recommended that the ICF document would benefit from a short summary Patient Information Leaflet at the beginning of the main document, or as an additional document, for ease of comprehension.

21-NREC-CT-036_Mod-7

Principal Investigator: Prof. Ray McDermott

Study title: Phase 3 Multicenter, Randomized, Double-blinded, Active-controlled, Clinical Study to Evaluate the Safety and Efficacy of Lenvatinib (E7080/MK-7902) in Combination with Pembrolizumab (MK-3475) Versus Lenvatinib in First-line Therapy of Participants with Advanced Hepatocellular Carcinoma (LEAP-002)

EudraCT: 2018-002983-26

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.

NREC-CT Decision:

- Request for Further Information

Additional Information Required:

- The NREC-CT noted that Pembrolizumab will no longer be made available after conclusion of the study, and requested further information on the reason for this. The NREC-CT also requests that this information is made clear to participants in the ICF document.

23-NREC-CT-029_Mod-2

Principal Investigator: Prof. Maeve Lowery

Study title: Phase 3 Multicenter, Randomized, Double-blinded, Active-controlled, Clinical Study to Evaluate the Safety and Efficacy of Lenvatinib (E7080/MK-7902) in Combination with Pembrolizumab (MK-3475) Versus Lenvatinib in First-line Therapy of Participants with Advanced Hepatocellular Carcinoma (LEAP-002)

EudraCT: 2021-003461-35

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.

NREC-CT Decision:

- Request for Further Information

Additional Information Required:

- The NREC-CT requested clarification on why male contraception measures have been removed from the ICF document, and why this is inconsistent with the section directly underneath it, which contains details of male contraception requirements.

21-NREC-CT-173_Mod-4

Principal Investigator: Prof. Valerie Byrnes

Study title: A phase IIb, double-blind, randomised, placebo-controlled trial to evaluate the efficacy and tolerability of ZED1227 in celiac disease subjects experiencing symptoms despite gluten-free diet

EudraCT: 2020-004612-97

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-034_Mod-3

Principal Investigator: Prof. Patrick Morris

Study title: CA209-7FL: A Randomized, Multicenter, Double-blind, Placebo-controlled Phase 3 Study of Nivolumab Versus Placebo in Combination With Neoadjuvant Chemotherapy and Adjuvant Endocrine Therapy in Patients With High-risk, Estrogen Receptor-Positive (ER+), Human Epidermal Growth Factor Receptor 2-Negative (HER2-) Primary Breast Cancer

EudraCT: 2019-002469-37

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.

NREC-CT Decision:

- Request for Further Information

Additional Information Required:

- The NREC-CT noted that depression is now a common side effect, and requested clarification on whether questionnaires or supports will be available to participants in relation to this side effect.
- The NREC-CT noted the updates to Section 19 as detailed on Page 3 of the ICF Addendum, and requested further detail on how this data will be kept confidential, and whether it will be coded data.

- **AOB:**
  - None