NATIONAL OFFICE FOR RESEARCH ETHICS COMMITTEES

National Research Ethics Committee

NREC-CT A

11th August 2021

Attendance

Name	Role
Prof Alistair Nichol	Chairperson, NREC CT-A
Dr Heike Felzmann	Deputy Chairperson, NREC-CT A
Dr John O'Loughlin	Committee Member, NREC-CT A
Prof Tina Hickey	Committee Member, NREC-CT A
Dr Dervla Kelly	Committee Member, NREC-CT A
Dr Darren Dahly	Committee Member, NREC-CT A
Prof Mary Donnelly	Committee Member, NREC-CT A
Dr Jimmy Devins	Committee Member, NREC-CT A
Mr Gerard Daly	Committee Member, NREC-CT A
Prof Patrick Dillon	Committee Member, NREC-CT A
Dr Geraldine Foley	Committee Member, NREC-CT A
Ms Aileen Sheehy*	Programme Manager, National Office for RECs
Dr Jane Bryant*	Project Officer, National Office for RECs
Dr Laura Mackey*	Project Officer, National Office for RECs

*Drafted minutes

Apologies: Ms Ann Twomey, Prof Catherine Hayes, Ms Muireann O'Briain, Prof David Brayden, Prof John Wells, Prof Mark Sherlock

Quorum for decisions: Yes

Agenda

- Welcome & Apologies
- Application 21-NREC-CT-046-NCP
- Application 21-NREC-CT-047
- Application 21-NREC-CT-048
- Application 21-NREC-CT-049
- AOB

- The Chair welcomed the NREC-CT A.
  - The minutes from the previous NREC-CT A meeting on 21st July 2021 were approved.
  - The NREC Business Report was discussed and noted.

Applications

21-NREC-CT-046-NCP

Principal Investigator: Professor Elisabeth Vandenberghe

Study title: A Phase 3, Randomized, Open-Label, Controlled, Multicenter Study of Zandelisib (ME-401) in Combination with Rituximab Versus Standard Immunochemotherapy in Patients with Relapsed Indolent Non-Hodgkin's Lymphoma (iNHL) (the COASTAL study)

Lead institution: St James's Hospital

  - NREC-CT comments:
- The NREC_CT A noted that the study was a multicentre study investigating whether zandelisib in combination with rituximab is a more effective treatment than rituximab in combination with chemotherapy
- The NREC-CT A highlighted that the trial was submitted through the National Collaboration Project, a jointly run initiative with the HPRA to pressure test systems ahead of the Clinical Trial Regulation.
- Overall, the NREC-CT A considered that the clinical trial was well considered and the participant materials were very well presented.

- NREC-CT Decision:

- Request for Further Information

- Further Information Requested:

Part I assessment:

- The NREC-CT A noted that the interim analysis will be undertaken at the 70% completion mark of the study. As these analyses are generally completed at the halfway point of a study, the NREC-CT A requested justification for it to be undertaken later in the trial.
- The NREC-CT requested confirmation that standard care will continue for participants recruited to the study.
- The NREC-CT A noted discrepancy in the retention of biological samples and requested clarity on how the samples will be handled.

Part II assessment:

- The NREC-CT A considered the PIL to be comprehensive but lengthy and in parts difficult to read. The Committee requested that a brief plain English executive summary of the salient points of the study is included at the beginning of the PIL outlining the aim of the study.
- The NREC-CT A requested that more information is provided to the participant on the measures taken to ensure confidentiality of the data collected.
- The NREC-CT A requested that the PIL for pregnancy includes information on the follow-up period to assess potential foetal abnormalities.
- The NREC-CT A noted that that follow-up procedures may include a biopsy or a PET scan. The NREC-CT A requested clarity if the choice sits with the participant on whether they opt for a biopsy or a PET scan.
- The NREC-CT A notes that hospital databases will be searched to identify suitable participants. It is the NREC-CT A's understanding that this practice is not permitted under Irish law and should be removed from the process.
- The NREC-CT A sought assurance that data transferred outside of the EEA will be stored and processed in line with GDPR.
- The NREC-CT A noted that the legal basis for data processing used for this study is legitimate interest. As Irish legislation focuses on explicit consent, the NREC-CT A requested that reference to the Health Research Regulation is included in the participant materials and is clearly included in consenting process.
- The NREC-CT A requested clarity for the period for which participant data will be retained as part of the study. This retention period should be highlighted in the participant materials.
- The NREC-CT A requested further information on who within the study team will undertake the consenting process.

- The NREC-CT A noted that participants are only given a maximum of 24 hours to decide whether to participate in the study and requested that this is changed to a minimum of 24 hours.
- The NREC-CT A noted that hotel costs would not be covered under expenses. The NREC-CT A requested justification for this cost not being covered as participants may need to travel to trial site, both of which are based in Dublin.
-

21-NREC-CT-047

Principal Investigator: Dr Larry Bacon

- Study title: A comparison of reduced dose total body irradiation (TBI) and cyclophosphamide with fludarabine and melphalan reduced intensity conditioning in adults with acute lymphoblastic leukaemia (ALL) in complete remission
- Lead institution: St James' Hospital, Dublin 8

  - NREC-CT comments:

- The NREC-CT A noted that the clinical trial application represents a multicentre study comparing total body irradiation and cyclophosphamide, with fludarabine and melphalan reduced intensity conditioning in adults with ALL.
- The NREC-CT A were overall very impressed with the application and considered the documentation to be well presented and comprehensive.
- The NREC-CT A agreed that while some clarifications across the documentation were required, this application can be designated as Favourable with Conditions.

  - NREC-CT Decision:

- Favourable with Conditions

  - Associated Conditions:

- The NREC-CT A requested clarification on duration of contraception required post-transplant.
- The NREC-CT A requested clarification on the definition of the end of trial as opposed to end of treatment.
- The NREC-CT A requested further information on the Legal Representative, a summary of their qualifications and the organisation they are employed by.
- The NREC-CT A requested confirmation that participants, both female and male, will be routinely reminded of the risks related to pregnancy at various intervals over the course of their participation in the trial. The Committee also requested that these risks are elucidated in the PIL and in executive summary of the PIL.

- The NREC-CT requested that the PIL is amended to distinguish between harm as a result of the treatment (side effects), and serious adverse events.

21-NREC-CT-048

Principal Investigator: Dr Jarushka Naidoo

- Study title: A Randomized Phase 3 Study of MRTX849 versus Docetaxel in Patients with Previously Treated Non-Small Cell Lung Cancer with KRAS G12C Mutation
- Lead institution: Beaumont Hospital, Dublin 9

  - NREC-CT Comments:

- The NREC-CT A noted that this application represents Phase III parallel arm trial, comparing MRTX849 and docetaxel in patients with NSCLC with the KRAS G12C Mutation.
- The NREC-CT A commented favourably on the application and considered the trial to be well justified and aspects on monitoring and preclinical evidence to be comprehensively communicated.
- The NREC-CT A agreed that while some clarifications across the documentation were required, this application can be designated as Favourable with Conditions.

  - NREC-CT Decision:

- Favourable with Conditions

  - Associated Conditions:

- The NREC-CT A requested further clarity on the description and division of treatment regiments, participant groupings and associated conditions.
- The NREC-CT A requested confirmation that docetaxel is the acceptable standard of care in this patient group, and if so, justification for why the patients enrolled in the active arm won't receive it in addition to MRTX849.
- The NREC-CT A sought clarification on whether potentially participants will be missing out on other available treatment options, such as additional immunotherapy, by participating in this trial.
- The NREC-CT A requested justification for the exclusion of those lacking capacity, those with psychiatric illness and those with a life expectancy of 3 months.
- The NREC-CT A requested further information on allocation concealment protocols used throughout the study.
- The NREC-CT A requested further justification for the 2:1 allocation protocol.
- The NREC-CT A requested further understanding of randomisation, in terms of stratification, and sequence or concurrence with first-line therapy.

- The NREC-CT A requested clarity on why the MUGA test is not an option in Germany.
- The NREC-CT A requested confirmation that review of the list of medications to be avoided while participating in the trial will be part of the recruitment screening process. The Committee noted that it should be incumbent on the participant's oncologist that the experimental treatment does not impact on the participant's ongoing care.
- The NREC-CT A requested that participants' General Practitioners (GP) are contacted by phone or video call in addition to the GP letter.
- The NREC-CT A requested further information on how patients who are identified as not having the mutation as part of the screening process, are treated following the screening.
- The NREC-CT A requested information on whether food and / or accommodation costs will be covered.
- The NREC-CT requested confirmation that those without the genetic mutation will be excluded from the trial if the trial offers no potential benefit to them.
- The NREC-CT A requested that a brief plain English executive summary of the salient points of the study is included at the beginning of the PIL outlining the aim of the study.
- The NREC-CT A noted that the participant materials indicate that participants will be forgoing other treatments. If this pertains to permanently forgoing future treatments, the NREC-CT A requests that this is explicitly clear in the participant materials.
- The NREC-CT A requested confirmation that participants will be routinely reminded of the risks of pregnancy at various intervals over the course of their participation in the trial.
- The NREC-CT A requested that the risks linked to pregnancy are further elucidated in the PIL, are clearly captured in an executive summary of the PIL, and highlighted in the GP letter.
- The NREC-CT A requested further information on whether the care received by the control and active groups will be comparable to standard care, and that this is also highlighted in the participant materials.
- The NREC-CT A noted that only 'women of child-bearing age' are selected under vulnerable groups and questioned whether 'patients with terminal illness' should also be selected.
- The NREC-CT A requested further information on the facilities available at the Cork site in relation to the trial and completion of the correct site-specific documentation.
- The NREC-CT A sought assurance that data transferred outside of the EEA will be stored and processed in line with GDPR.
- The NREC-CT A requested justification for the indefinite storage of blood sample results.
- The NREC-CT A requested justification for the storage of bank details for 25 years. If feasible, the Committee requested that bank details are deleted once the participant has been reimbursed.
- The NREC-CT A requested confirmation on how long biological samples will be retained for.

21-NREC-CT-049

Principal Investigator: Prof Raymond McDermott

Study title: A Randomized Phase 3 Study of MRTX849 in Combination with Cetuximab Versus Chemotherapy in Patients with Advanced Colorectal Cancer with KRAS G12C Mutation with Disease Progression On or After Standard First-Line Therapy

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

- NREC-CT Comments:

- The NREC-CT A noted that the clinical trial application represents a randomised phase III study investigating the use of the medicinal product MRTX849 in combination with cetuximab, compared to chemotherapy for treatment of patients with advanced colorectal cancer with the KRAS G12C Mutation.
- The NREC-CT A 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 requires additional information to inform its deliberations.

- NREC-CT Decision:

- Request for Further Information

- Additional Information Required:

- The NREC-CT A sought further reassurance that tolerance to the drug combination has been adequately assessed and requested further information on what point the study is currently at and how many participants are currently enrolled.
- The NREC-CT A requested confirmation that the treatment is currently used in Ireland.
- The NREC-CT A requested reassurance that prospective participants will be made aware of the commitment of completing the patient diary in advance of consenting.
- The NREC-CT A requested clarity on how long participants will be on the treatment.
- The NREC-CT A requested further information on the qualifications of those involved in assessing participants' capacity.
- The NREC-CT A requested further information on the supports available to the participant when removed from the study.
- The NREC-CT A requested that the participants' General Practitioners (GP) are contacted by phone or video call in addition to the GP letter.
- The NREC-CT A requested that a brief plain English executive summary of the salient points of the study is included at the beginning of the PIL outlining the aim of the study.
- The NREC-CT A requested that the duration of the study is included in the participant materials.

- The NREC-CT A noted that the PIL states participation could have an impact on personal insurance, and requested that this is either established in advance of the prospective participant agreeing to participate in the trial, or is clearly highlighted in the participant materials.
- The NREC-CT A sought reassurance that participants will be given a hard copy of the PIL.
- The NREC-CT A noted that the address for Tallaght University Hospital is incorrect in some of the materials provided and requested that this is corrected.
- The NREC-CT A requested confirmation that participants will be routinely reminded of the risks of pregnancy at various intervals over the course of their participation in the trial.
- The NREC-CT A requested that the risks linked to pregnancy are further elucidated in the PIL, are clearly captured in an executive summary of the PIL, and highlighted in the GP letter.
- The NREC-CT A requested that reference to the Health Research Regulations 2018 is included in the participant materials and is clearly included in the consenting process.
- The NREC-CT A requested that a justified time limit is included on the retention of personal data.
- The NREC-CT A recommended that the applicant reapplies for ethics approval for the reuse of data for future research studies.
- The NREC-CT A noted the provision for open-ended consent for the future use of left-over samples from the pre-screening process. The Committee considered this open-ended consent to be unacceptable, and requested that the applicant amends this to offer participants a more suitable and informed option for future use of their samples and data.

- AOB:
  - The NREC-CT A discussed the Committee's remit regarding future research consent.

- The Chair closed the meeting.