National Research Ethics Committee

NREC-CT EEA Meeting

05 April 2023

Attendance

Name	Role
Prof. Alistair Nichol	Chairperson, NREC-CT
Ms. Serena Bennett	Committee Member, NREC-CT
Ms Susan Kelly	Committee Member, NREC-CT
Dr Lorna Fanning	Committee Member, NREC-CT
Mr Gavin Lawler	Committee Member, NREC-CT
Mr Philip Berman	Committee Member, NREC-CT
Ms Erica Bennett	Committee Member, NREC-CT
Dr Christina Skourou	Committee Member, NREC-CT
Ms Mandy Daly	Committee Member, NREC-CT
Prof. Austin Duffy	Committee Member, NREC-CT
Dr Darren Dahly	Committee Member, NREC-CT
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 Susan Quinn	Programme Officer, National Office for RECs
Dr Emma Heffernan*	Project Officer, National Office for RECs
Bryony Milner	Administration Assistant, National Office for RECs

*Drafted minutes

Apologies:

Conflict of Interest: Mr. Gavin Lawler (23-NREC-CT-030) & Dr Lorna Fanning (23-NREC-CT-027)

Quorum for decisions: Yes

Agenda

- Welcome & Apologies
- 23-NREC-CT-012
- 23-NREC-CT-028
- 23-NREC-CT-031
- 23-NREC-CT-036
- 23-NREC-CT-033
- 23-NREC-CT-027
- 23-NREC-CT-030
- 23-NREC-CT-029
- 23-NREC-CT-035
- 23-NREC-CT-032
- AOB

- The Chair welcomed the NREC-CT.

Applications

23-NREC-CT-012

Principal Investigator: Dr Janusz Krawczyk

Study title: Phase 3 Study of Teclistamab in Combination With Lenalidomide and Teclistamab Alone versus Lenalidomide Alone in Participants With Newly Diagnosed Multiple Myeloma as Maintenance Therapy Following Autologous Stem Cell Transplantation

EudraCT: 2021-002531-27

Lead institution: Galway University Hospital

- NREC-CT comments:

- The NREC-CT 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 noted that participants on Arm C of the trial will not receive standard maintenance treatment and requested a risk benefit analysis of not receiving standard of care treatment and outcome is added to the PISCF.
- The NREC-CT requested confirmation, due to the potential risks of participating in the trial, that the PI in each site will consent participants to the study, and that this task will not be delegated to other members of the study team.
- The NREC-CT noted that potential participants are to be identified through the normal hospital clinics and referrals from outside local hospitals and requested further detail is provided in the NREC Application Form on how participants will be made aware of the trial in the first instance.
- The NREC-CT noted that participants are not being recruited from St James's Hospital in Dublin, and queried why this is the case considering that St James's is likely to treat the majority of patients with this condition in the country. Please clarify whether there is perhaps a competing trial that may hamper accrual.
- The NREC-CT noted that section E7 of the NREC Application Form states that 'There are no plans to provide specific translations to subjects who do not speak the local language. Therefore, it may not be possible to include those subjects who do not speak the local language' and requested the following:
    - Clarification as to whether participants who speak the Irish language are included.
    - Justification for the exclusion of participants who do not speak the local language.
- The NREC-CT requested that section D8 of the NREC Application Form is corrected, as women of childbearing potential are being recruited to the trial.
- The NREC-CT noted multiple spelling and grammatical errors in the NREC Application Form and requested that these are corrected.
- The NREC-CT requested that section F1 of the NREC Application Form, regarding the retention of biological material, is completed.
- The NREC-CT noted that participants are to undergo genetic testing and requested that explicit consent be obtained for genetic testing, requested in the ICF.
- The NREC-CT noted that pg. 122 of the protocol states that 'Additionally, whole genome and gene expression profiling may be performed for exploratory studies', though this is not mentioned in the main or optional PISCF under the section 'samples collected for scientific/ genetic research'. The NREC-CT requested clarification as to whether participants in Ireland will undergo whole genome and gene expression profiling.

- If participants taking part in the trial in Ireland are to undergo whole genome and gene expression profiling, then the NREC-CT requested the following:
- Explicit consent, including outlining the risks entailed in such analysis being performed is added to the PISCF.
- The possible ownership of such data by private or commercial interests and that this elucidated in the PISCF.
- The right to withdraw genetic data, and clear information on how to do so, must also be provided in the PISCF.
- Clarification is provided in the PISCF on the mechanism for anonymisation, storage and security and transfer of genetic material and its associated data. For guidance 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 that risks/side effects that are life threatening and occur in the majority of those exposed to the IMP are highlighted early in the PISCF and all potential risks / side effects are integrated into the PISCF and not included as an appendix, so participants are fully informed of the potential risks involved in trial participation.
    - The NREC-CT requested that the risk language indicating the risks of Lenalidomide to the unborn baby is amended to be less ambiguous i.e., remove use of the word ‘may’ and replace with ‘will’ or ‘most likely will’’.
- The NREC-CT noted that the consent material layout is not in line with best practice and requests that the applicant provides participants with a layered/unbundled approach to consent. Please see HSE National Policy for Consent in Health and Social Care Research (2022)
- The NREC-CT noted that pg. 11 of the PISCF notes the danger of pregnant women coming into contact with the trial drug and requested that this is highlighted in bold in the PISCF.
- The NREC-CT noted that the consent for future research is not in line with regulations / best practice and requested that this is amended - i) consent for future use of samples should be provided on a separate consent form and not bundled with general consent to data processing ii) it should be made optional, and iii) consent can only be obtained where future use of samples and data is defined such that participants are fully informed, and/or iv) that an option is provided to enable participants to consent to be contacted to provide fresh consent to future use is provided in a separate consent form. Please see HSE National Policy for Consent in Health and Social Care Research (2022)
    - The NREC requested confirmation that subsequent research ethics review will be sought for specific research once clearly defined.

- The NREC-CT noted that the pregnant partner PISCF states that data will be retained for 25 years and requested justification for this.
    - The NREC-CT requested details of the process in place for obtaining the consent of the child, on reaching the age of 18, for the retention of their personal data is described in line with Irish data protection law (Data Protection Act 2018 (Section 36(2)) (Health Research) Regulations 2018.
- The NREC-CT noted that the use of impartial witness in the pregnant partner PISCF where the witness is being asked to consent on behalf of the pregnant partner, is not in line with Irish legislation and requested that this is amended.
- The NREC-CT requested submission of CVs for Prof Siobhan Glavey and Dr Vitaliy Mykytiv, detailing previous clinical trial experience and evidence of up-to-date ICH-GCP certification.
- The NREC-CT requested a more detailed CV is provided for Dr Janusz Krawczyk outlining previous clinical trial experience.
- The NREC-CT requested confirmation that agreements are in place with parties in third countries that provide for equivalent GDPR protections and that this is elucidated across all PISCFs.
- The NREC-CT noted that PISCF Appendix B: insurance information states that 'The insurance policy does not cover the following damage: damage as a result of a risk that you were informed about in the written information. This does not apply if the risk occurs in a more severe form than envisaged, or if the risk was very unlikely to occur;' and also 'damage to your health that would also have occurred if you had not participated in the study'. The NREC-CT requested clarification of these statements.
- The NREC-CT noted that pg. 14 of the NREC Application Form states that participants will not be reimbursed for trial related expenses, which seems to conflict with information in the PISCF which states, 'there are no additional costs for you' and requested confirmation that participants will be reimbursed for all reasonable out-of-pocket expenses.
- The NREC-CT requested further detail is provided in the PISCF regarding reimbursement, including:
    - The process involved in submitting receipts and claiming reimbursement,
        - The level of reimbursement permissible per day
        - Whether all meals are included
        - What travel arrangements are included.
        - Whether overnight accommodation can be claimed
        - Whether a person accompanying the participant to site visits can also claim out-of-pocket expenses

23-NREC-CT-028

Principal Investigator: Dr Desmond Murphy

Study title: A Two-part Phase IIa Randomised, Double-blind, Placebo-controlled, Dose-ranging, Multi-centre Study to Assess Efficacy and Safety of Inhaled AZD1402 Administered as a Dry Powder Twice Daily for Four Weeks in Adults with Asthma on Medium-to-High Dose Inhaled Corticosteroids

EudraCT: 2020-002828-37

Lead institution: Cork University Hospital

- NREC-CT comments:

- The NREC-CT 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 noted that participants are to undergo genotyping and requested justification for this type of analysis.
- The NREC-CT noted that race and ethnicity data will be collected from participants and requested justification for this.
- The NREC-CT noted that participants are required to use an e-diary and requested clarification as to how participants who cannot / or would prefer not to use an e-diary will be catered for.
- The NREC-CT requested that an emergency contact is provided in the GP letter.
- The NREC-CT noted that participants will undergo training through the use of a training video and requested that the video is submitted for NREC review.
- The NREC-CT requested that an estimated length of time of study visits, various assessments and completion of the ediary is added to the PISCF, so participants are fully informed about the potential burden of trial participation.
- The NREC-CT noted that males are required to undergo a vasectomy and requested that this is clarified / reworded in the PISCF.
- The NREC-CT noted that participants are to undergo genetic testing and requested that clarity is provided in the optional genetic sample PISCF regarding genetic testing including:
    - The genetic testing requested must be restricted and defined.

    - The type of genetic testing to be undertaken must be clearly explained to participant.
    - The NREC-CT noted that pg. 23 of the main consent includes an optional consent for human leukocyte antigen (HLA) genotyping which may be confusing for participants and requested that the optional consent for the HLA genotyping is removed from the main PISCF and added to the optional genetic sample PISCF.
    - The NREC-CT requested that *human leukocyte antigen genotyping* is explained using lay terminology in the PISCF.

- The NREC-CT noted that the optional genetic sample PISCF states that results of genetic testing may be shared with insurance companies and requested justification for this.
- The NREC-CT noted that, in the pregnant partner PISCF, pregnant partners are asked to contact the study doctor if they decide to undergo an abortion and requested justification for this.
- The NREC-CT noted that the PISCF is seeking blanket consent for future use of samples / data, for unspecified purposes, without further consent. This type of consent 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 requests i) that consent for future use of samples is provided on a separate consent form and not bundled ii) is made optional, and iii) consent can only be obtained where future use of samples and data is defined such that participants are fully informed, and/or iv) that an option is provided to enable participants to consent to be contacted is provided in a separate consent form.
    - The NREC requested confirmation that subsequent research ethics review will be sought for specific research once clearly defined.
    - The NREC-CT also requested that the reference to future research in the NREC Application Form is amended throughout to reflect the above (point 3.7).
- The NREC-CT requested that the intense pharmacokinetic sampling study is provided on a separate PISCF, as it is potentially confusing to participants in its current format.
- The NREC-CT requested that the ‘Thank you’ card is amended to remove the text ‘millions of others’, as it suggests taking part in a clinical trial is a routine event.
- The NREC-CT also requested that the word ‘brave’ is also removed from the ‘Thank you’ card, as it suggests that those who chose not to take part in a clinical trial are not brave.
- The NREC-CT noted that the smoking cessation period(s) (listed as eligibility criteria in the digital add and the poster) are for different lengths of time and requested that this is clarified and corrected on relevant documents.

- The NREC-CT requested that a CV is provided for Dr Brian Kent detailing previous clinical trial experience and evidence of up-to-date ICH-GCP certification.
- The NREC-CT noted that the DPIA does not reference the data being collected from the participant's pregnant partner and details of the birth and baby. The NREC-CT requested that the DPIA must incorporate this data and ensure a data protection risk assessment is conducted and mitigating safeguard actions are implemented.
- The NREC-CT noted that the study insurance certificate provided does not cover the whole trial duration and requested that the insurance policy is updated to provide cover for the full duration of the study.
- The NREC-CT noted that participants are being offered €83 per visit and requested that the monetary amounts are not stated in the PISCF, as this could be seen as a financial inducement to participate. It is sufficient to reassure participants that all reasonable out-of-pocket expenses *will* be covered.
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23-NREC-CT-031

Principal Investigator: Dr Omar Elsherif

Study title: A Phase 2A, Randomized, Double-Blind, Placebo-Controlled, Clinical Trial Evaluating the Safety and Efficacy of CM-101 in Subjects with Primary Sclerosing Cholangitis

EudraCT: 2019-002945-39

Lead institution: St. Vincent's University Hospital

- NREC-CT comments:

- The NREC-CT 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 RFI

- The NREC-CT noted that the DMC charter differs from the protocol in terms of design of the study and requested that this is clarified and aligned across relevant documentation (see study diagram in charter).
- The NREC-CT requested clarification as to how many participants are taking part in the placebo arm of the trial.

- The NREC-CT noted that the participants are being recruited via a recruitment vendor and that the information regarding the trial is overly positive and requested that this is amended to provide a more balanced description of the potential risks involved in taking part in a phase 2 clinical trial.
- The NREC-CT noted that details of a recruitment website was included in the submission and requested the following:
    - Clarification as to whether this website will be used to identify and recruit participants in Ireland.
    - Clarification as to whether the website will collect personal data and how this will be aligned with the Health Research Regulations 2018.
    - The recruitment website says that participants will be compensated for their time, but this was not mentioned in the Application Form or in the protocol. The NREC requested that is clarified and corrected where necessary.
    - The percentage of patients receiving a placebo noted on the recruitment website does not match what is mentioned in the protocol and the NREC requested that this is corrected and aligned.
    - The NREC-CT noted that the website mentions US study sites and requested that Irish sites are also included, if the website is to be used for recruitment in Ireland.
- The NREC-CT noted that the intended use of samples / data is not well described in the PISCF and requested that this is amended so participants are fully informed what samples will be taken, what they will be used for, how their samples and data will be stored, including details of maximum retention periods.
- The NREC-CT noted that details regarding the potential future use of samples / data is not provided in the PISCF and requested clarification as to whether future research will take place. The NREC-CT noted that seeking blanket consent for future use of samples / data, for unspecified purposes, without further 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), in which informed participant consent is a mandatory safeguard. The NREC-CT requests i) that consent for future use of samples is provided on a separate consent form and not bundled ii) is made optional, and iii) consent can only be obtained where future use of samples and data is defined such that participants are fully informed, and/or iv) that an option is provided to enable participants to consent to be contacted, provided in a separate consent form.
    - The NREC requested confirmation that subsequent research ethics review will be sought for specific research once clearly defined.
    - If future research includes genetic research, then this needs to be explained to participants in the PISCF. Please see HSE-National-Policy-for-Consent-in-Health-and-Social-Care-Research.

- The NREC-CT requested that the risk section in the PISCF includes details on how many participants to date have received the study drug.
- The NREC-CT requested that the sponsor amends the signatories to ICF so that 'next of kin' is removed and 'impartial witness' is documented in line with the HSE-National-Policy-for-Consent-in-Health-and-Social-Care-Research.
- The NREC-CT noted that some participants are to undergo a liver biopsy and that this procedure is not well described in the PISCF and requested that this is amended so participants are fully informed as to the nature of this procedure and the potential risks involved.
- The NREC-CT requested that details of who participants should contact out of hours is added to the SSA and detailed in the PISCF.
- The NREC-CT requested that the SSA for SVUH details the qualifications of other site staff members.
- The NREC-CT requested that a more detailed CV is provided for Dr El Sherif outlining clinical trial experience and evidence of up-to-date ICH GCP certification.
- The NREC-CT noted that section B13 of the DPIA states that study data will be anonymised only and requested clarification.
- The NREC noted that the Application Form and the PISCF states that generating a patient ID requires sending age, sex, race, site and initials to sponsor/ service provider in order to create a unique ID and requested justification for this, as this is not typically required for generating unique IDs (which are typically pre-coded into electronic data capture systems) and the data could potentially make participants identifiable.
- The NREC-CT noted that the PatientWing document states that participants will be 'compensated for time' and requested that this is clarified.
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23-NREC-CT-036

Principal Investigator: Prof Iracema Leroi

Study title: Phase 1, Randomized, Double-Blind, Placebo-Controlled, Multiple Ascending Dose Study to Evaluate the Safety, Tolerability, Immunogenicity, Pharmacokinetics, and Pharmacodynamics of PRX012 in Subjects with Alzheimer's Disease

EudraCT: 2022-001774-61

Lead institution: St James's Hospital

- NREC-CT comments:

- The NREC-CT 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

- The NREC-CT noted that the proposed trial is to take place in St James's and Tallaght University Hospitals and requested the following:
    - Confirmation from the Director at the Clinical Research Facility at St James's Hospital that the necessary supports are in place to safely manage a phase 1 clinical trial.
    - Confirmation from the Director at the Clinical Research Facility Tallaght University Hospital that the necessary supports are in place to safely manage a phase 1 clinical trial.
    - A detailed account of the level of supports available at each site, including the required clinical expertise, to manage a potentially critically ill participant in the case of anaphylaxis or other emergency situations.
    - Confirmation that appropriately trained staff are in place during trial drug administration.
    - Confirmation that the PI will be present during trial drug administration.
- The NREC-CT requested justification for the placebo arm of the trial.
- The NREC-CT notes that participants may take part in optional CSF collection by way of a lumbar puncture and requested the following:
    - clarification as to whether participants in Ireland will be taking part of this aspect of the trial.
    - if participants in Ireland are taking part in this aspect of the trial the NREC-CT requested that this procedure is detailed in the Application Form and submitted for NREC review.
    - if participants in Ireland are taking part in this aspect of the trial the NREC-CT requested that the suitability of the facilities, suitability of equipment, and clinical expertise required to undertake this procedure is detailed in the SSA for St James's Hospital and Tallaght University Hospital and both SSAs are resubmitted for NREC review.
    - details of the procedure involved including the potential risks of a lumbar puncture are explained in greater detail to participants in the optional CSF sub study PISCF.
- The NREC-CT noted that this study involved participants with Alzheimer's Disease and noted that the Application Form did not outline the process involved in consenting participants to a trial when they may lack decision making capacity and requested the following:

    - clarification regarding the consent process. Specifically, a ‘legally authorised representative’ cannot lawfully consent for the processing of personal data for health research, on behalf of a participant who lacks decision-making capacity to consent but can provide assent as a safeguard. The applicant must therefore specify whether a consent declaration from the HRCDC will be applied for to ensure compliance with the Regulations, or rationale as to why a consent declaration is not required.
    - The sponsor should ensure that any involvement of a representative or proxy individual in the consent protocol, is in accordance with all applicable legislative frameworks. The sponsor should give consideration to:
    - procedures that can be implemented to seek assent from the legally designated individual, or a proxy individual who understands the will and preference of the participant.
    - the HSE-National-Policy-for-Consent-in-Health-and-Social-Care-Research.
    - the Health Research Regulations
    - the Application From is amended taking into consideration the above and submitted for NREC review.
- The NREC-CT noted that a ‘legally authorised representative’ signature is included on the main PISCF on behalf of a person that lacks decision-making capacity. As there was no reference in the Application Form to participants that lack-decision making capacity, the NREC-CT queried under what circumstances would legally acceptable/authorised representative sign the PISCF’s. The sponsor should ensure that any involvement of a representative or proxy individual in the consent protocol, is in accordance with all applicable legislative frameworks. Specifically, under Irish data protection law, a legally authorised representative cannot lawfully consent on behalf of another individual for the processing/use of personal data for health research but can provide assent as a safeguard. The sponsor should give consideration to:
    - procedures that can be implemented to seek assent from the legally designated individual, or a proxy individual who understands the will and preference of the participant.
    - the HSE-National-Policy-for-Consent-in-Health-and-Social-Care-Research.
    - the Health Research Regulations

- The NREC-CT noted that the PISCF was not written in an accessible format and suggested that the applicant seeks the involvement of a public or patient reviewer/PPI in the development of participant materials to ensure that they are accessible to participants.
- The NREC-CT requested that the risks need to be clearly explained to participants and clearly laid out in the PISCF, so they are fully aware of the potential risks involved in a phase 1 trial.
- The NREC-CT requested that further detail is added to the PISCF with regard to the safety data of this class of monoclonal antibodies that target amyloid in the brain.
- The NREC-CT requested that the number of participants who have received the trial drug to date, is detailed in the PISCF.
- The NREC-CT requested that the requirement to undertake 5 extra PET scans is made clearer in the PISCF.
- The NREC-CT requested that details regarding standard of care are provided in the 'are there any alternative treatments?' section the PISCF.
    - Furthermore, it needs to be made clear to participants how standard of care treatment compares to potential involvement in this trial.
- The NREC-CT noted the inclusion of a C-SSRS and requested the following:
    - details of provisions in place to support participants, should the questionnaire indicate a mental health issue.
    - Acknowledgement in the PIL/ICF that completion of this assessment may cause distress, and clarification as to the pathway of care and referral offered to participants displaying a mental health issue.
- The NREC-CT noted that the PISCF 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 requests that consent for future use of samples is i) provided on a separate consent form and not bundled and ii) consent can only be obtained where future use of samples and data is defined such that participants are fully informed, and/or iv) that an option is provided to enable participants to consent to be contacted is provided in a separate consent form.
    - The NREC request confirmation that subsequent research ethics review will be sought for specific research once clearly defined.

- The NREC-CT noted that participants are advised in the PISCF that their samples might undergo ‘anticipated research’ and requested that is made clear to participants what tests their samples will undergo in this trial.
- The NREC-CT requested that clarification is provided on the care of participants during out of office hours and requested that this is detailed in the PISCF, including contact numbers for staff.
- The NREC-CT noted that the study insurance certificate provided does not cover the whole trial duration and requested that the insurance policy is updated to provide cover for the full duration of the study.

23-NREC-CT-033

Principal Investigator: Prof Karen Cadoo

Study title: A Randomized Phase III, Two-Arm Trial of Paclitaxel/Carboplatin/Maintenance Letrozole Versus Letrozole Monotherapy in Patients with Stage II-IV, Primary Low-Grade Serous Carcinoma of the Ovary or Peritoneum

EudraCT: 2022-002877-27

Lead institution: St James's Hospital

- NREC-CT comments:

- The NREC-CT 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 notes that pg.2 of the main PISCF states that ‘Women must not become pregnant while on this study. Suitable contraceptive measures will be discussed with you’ while the eligibility criteria listed in the protocol states that all patients must have undergone a bilateral salpingo-oophorectomy to participate in the trial and requested that this is clarified.

- The NREC-CT noted that section C12 of the Application Form regarding adverse events, risks, hazards etc was not completed and requested that this is amended.

- The NREC-CT noted that there is conflicting information in the Application Form regarding the participation of participants lacking decision-making capacity and requested the following:
    - clarification as to whether participants lacking capacity will be recruited to the trial and that this made clear in the Application Form – please note that the Application Form states that sections E10 to E13 should not be completed if the clinical trial does not involve participants lacking decision-making capacity.
    - if participants lacking capacity are taking part in the trial, then the consent process will need to be clarified. Specifically, a 'legally authorised representative' cannot lawfully consent for the processing of personal data for health research, on behalf of a participant who lacks decision-making capacity to consent but can provide assent as a safeguard. The applicant must therefore specify whether a consent declaration from the HRCDC will be applied for to ensure compliance with the Regulations, or rationale as to why a consent declaration is not required.
- The NREC-CT noted that section E13 of the Application Form makes reference to the use of a legal representative and queried under what circumstances would legally acceptable/authorised representative be required. The sponsor should ensure that any involvement of a representative or proxy individual in the consent protocol, is in accordance with all applicable legislative frameworks. The sponsor should give consideration to:
    - procedures that can be implemented to seek assent from the legally designated individual, or a proxy individual who understands the will and preference of the participant.
    - the HSE-National-Policy-for-Consent-in-Health-and-Social-Care-Research.
    - the Health Research Regulations
- The NREC-CT noted that section D.7 of the Application From states 'The criteria for enrolment must be followed explicitly. If a patient who does not meet enrolment criteria is inadvertently enrolled, that patient should be discontinued from the trial treatment, but can be allowed to continue in the trial in order to provide the follow-up data needed for the analysis of the entire population. An exception may be granted if the patient, in the opinion of the investigator, is having benefit from the trial treatment. In these rare cases, the investigator must obtain documented approval from Cancer Trials Ireland to allow the patient to continue receiving the trial treatment provided by the Sponsor' and requested the following:

    - clarification as to how ineligible participants could be enrolled into the trial.
    - confirmation that only participants who meet the eligibility criteria for the trial will be enrolled on the trial.
    - confirmation that data will not continue to be collected on participants who are deemed ineligible to take part in the trial.
    - confirmation that the PI will not approach Cancer Trials Ireland to approve a participant into a clinical trial that they are not eligible to take part in.
    - section D7 of the Application Form needs to be revised and resubmitted for NREC review, taking into consideration the Health Research Regulations 2018, ICH-GCP and the HSE-National-Policy-for-Consent-in-Health-and-Social-Care-Research.
- The NREC-CT requested clarification as to the signatory on section 4.3 the 'NREC Appendix Form clinical trials of investigational medicinal production in combination with exposure to radiation', as the signature is present, but the printed name has been omitted.
- The NREC-CT noted that this study is also funded by the Irish Cancer Society and requested that this is added to the PISCF.
- The NREC-CT noted that the PISCF states that the Department of Health receives study data as supervisor of NREC and requested that this is removed, as the Department of Health does not receive study data.
- The NREC-CT noted that the intended use of samples / data is not well described in the PISCF and requested that this is amended so participants are fully informed what samples will be taken, what they will be used for, how their samples and data will be stored, including details of maximum retention periods.
- The NREC-CT noted that details regarding the potential future use of samples / data is not provided in the PISCF and requested clarification as to whether future research will take place is stated in the PISCF.
    - If samples are to be retained for future use, then this must be done in line with best practice, the Declaration of Taipei 2016 and the Data Protection Act 2018 (Section 36(2) (Health Research) Regulations 2018), in which informed participant consent is a mandatory safeguard. The NREC-CT requested i) that consent for future use of samples is provided on a separate consent form and not bundled ii) is made optional, and iii) consent can only be obtained where future use of samples and data is defined such that participants are fully informed, and/or iv) that an option

is provided to enable participants to consent to be contacted, provided in a separate consent form.
    - The NREC requested confirmation that subsequent research ethics review will be sought for specific research once clearly defined.
    - If future research includes genetic research, then this needs to be explained to participants in the PISCF. Please see HSE-National-Policy-for-Consent-in-Health-and-Social-Care-Research.
- The NREC-CT noted that the PISCF has some issues with typography (i.e., very small font, some sections difficult to read etc) and requested that this is amended to be more accessible to participants.
- The NREC-CT deemed that it is not appropriate for participants taking part in a clinical trial to be expected to pay for the trial drug and requested confirmation that participants will not have to pay for the study drug and that this is elucidated in the PISCF.
- The NREC-CT noted that participants travel expenses will not be reimbursed and requested that in order to ensure equity in access to clinical trials for all socio-economic groups, participants are reimbursed for reasonable out-of-pocket expenses and that this is elucidated in the PISCF.
- The NREC-CT noted that the study insurance certificate provided does not cover the whole trial duration and requested that the insurance policy is updated to provide cover for the full duration of the study.

23-NREC-CT-027

Principal Investigator: Dr Beatrice Nolan

Study title: A Phase 3, Prospective, Open-label, Uncontrolled, Multicenter Study on Efficacy and Safety of Prophylaxis with rVWF in Children Diagnosed With Severe von Willebrand disease

EudraCT: 2020-003304-13

Lead institution: CHI Crumlin

- NREC-CT comments:

- The NREC-CT 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 noted that participants may undertake administration of the trial drug at home and requested the following:
    - confirmation that this approach has been deemed safe and acceptable from a clinical perspective.
    - further explanation in the PISCF regarding the potential burden for parents / guardians to undertake home administration, considering that twice weekly administration is required.
    - further explanation in the PISCF regarding the potential burden of multiple site visits if the drug cannot be administered at home.
- The NREC-CT noted that section E12 of the Application Form states that 'Where a participant is aged 16 or older and has borderline capacity to consent, information will be explained in a manner that is understandable to the individual. This will be done with support of the participant's parent/legal guardian. A decision about who should give consent will be made by the Investigator performing the consent procedure in collaboration with the family'.
    - Furthermore, the NREC-CT requested clarification as to whether participants who lack decision-making capacity will be taking part in the trial.
    - The NREC-CT requested that participants who are 16 years of age and have decision-making capacity are accommodated to consent for their participation in the study, in accordance with legislation.
    - It is also requested that the line 'A decision about who should give consent will be made by the Investigator performing the consent procedure in collaboration with the family' should be amended to clarify that the Investigator is not deciding who can or cannot give consent. This should be decided based on decision-making capacity and the in accordance with legislation.
- In accordance with Irish data protection legislation and Health Research Regulations 2018, the age of consent for data processing of personal data, is 18 years of age. The NREC-CT requested details of the process in place for consenting participants upon reaching the age of 18 years of age for the processing of their personal data.

- The NREC-CT noted that the assent forms are not in line with best practice and requests that the applicant provides participants with a layered/unbundled approach to consent. Please see HSE National Policy for Consent in Health and Social Care Research (2022)
- The NREC-CT noted that the that future use of biological samples and data will be used for research 'related to the study drug and your child's disease'.
    - The NREC request that the description of the future research to be carried out is elucidated further, if possible, to ensure the participants is fully informed.
    - The NREC request confirmation that subsequent research ethics review will be sought for specific research once clearly defined.
- The NREC-CT also requested that information regarding future use of biological samples and data is included in the assent forms.
- The NREC-CT noted that pg.25 of the Main Parent Legal Guardian ICF states that the 'child's video or audio records that will be collected for the study in case of the Global Health Emergency, e.g. your child's study interviews etc. being video or audio recorded and sent in a secure way to third parties working with the Sponsor for analysis', and requests that this is further explained in the PISCF, in terms of how the video's will be used, transferred and safeguarded appropriately.
- The NREC-CT noted that potential confusing information is provided in the PISCF regarding infusions and whether some of the infusions are administered at study visits - the documentation currently states that infusions are twice weekly at visits 2, 3, 4, 5, 6, 7, and 8, but that scheduled study visits occur in months 1, 2, 3, 6, and 9. The NREC-CT requested that this is clarified in the PISCF.
- The NREC-CT noted assent forms were provided for 6–11-year-olds and for over 12-year-olds and requested that these are disaggregated into more appropriate age brackets to ensure readability and comprehension. Please see https://hseresearch.ie/wp-content/uploads/2023/02/HSE-National-Policy-for-Consent-in-Health-and-Social-Care-Research-compressed.pdf (5.3.1 Obtaining the assent of a child)
- The NREC-CT requested that evidence of up-to-date ICH-GCP is provided for Dr Nolan
- The NREC-CT noted that the section F2 of the Application Form states that in relation to the retention of data "the initials and date of birth may also be collected if permitted under local laws governing privacy" and requested clarification as to whether the principle of data minimisation is being applied and consideration given as to whether initials and full date of birth are necessary to retain.

23-NREC-CT-030

Principal Investigator: Prof Sinéad Brennan

Study title: NRG-HN009: Randomized Phase II/III Trial of Radiation With High-Dose Cisplatin (100 mg/m2) Every Three Weeks Versus Radiation With Low-Dose Weekly Cisplatin (40 mg/m2) For Patients With Locoregionally Advanced Squamous Cell Carcinoma Of The Head And Neck (SCCHN)

EudraCT: 2022-004130-19

Lead institution: St. Luke's Radiation Oncology Centre at St. James's Hospital

- NREC-CT comments:

- The NREC-CT 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 noted that pharyngeal constrictor muscles are not included in the organs at risk listed and requested clarification as to why this is the case considering the dose to these tissues has been correlated with numerous side-effects / toxicities in head and neck cancer patients recently.
- The NREC-CT noted that participants are given the option of completing a patient history form and note that sensitive health data, such as sexual preferences, is being requested. The NREC-CT requested the following:
    - justification for the type of questions being asked re salary and sexual preferences.
    - clarification in the PISCF as to why this data is being collected and how it will be used or requested that this optional form is removed for participants in Ireland.
- The NREC-CT noted that participants are undergoing radiotherapy and requested clarification as to whether participants swallowing muscles will be assessed.
- The NREC-CT requested further detail regarding the involvement of the medical oncology team in the trial including the following:
    - detail as to whether the IMP will be prescribed and monitored by the medical oncology team.
    - clarification as to who will perform the assessment prior to administration of cisplatin and ensure the patient is fit to receive this in compliance with the trial protocol.

    - clarification as to whether a medical oncologist will be a co-investigator on the trial.
- The NREC-CT that the text 'risk of second cancer' is added as a serious effect of radiation therapy both in the PISCF and the GP letter.
- The NREC-CT noted that participants travel expenses will not be reimbursed and requested that in order to ensure equity in access to clinical trials for all socio-economic groups, participants who are attending site visits outside standard of care treatment are reimbursed for reasonable out-of-pocket expenses and that this is elucidated in the PISCF.
- The NREC-CT noted that Cancer Trials Ireland public liability insurance letter expired on February 8th, 2023, and requested confirmation that this has been renewed and that there is adequate insurance in place.

23-NREC-CT-029

Principal Investigator: Prof Maeve Lowery

Study title: A Randomized, Multi-center, Double-blind,Placebo-controlled Phase 3 Study of Bemarituzumab plus Chemotherapy versus Placebo plus Chemotherapy in Subjects with Previously Untreated Advanced Gastric or Gastroesophageal Junction Cancer with FGFR2b Overexpression (FORTITUDE-101)

EudraCT: 2021-003461-35

Lead institution: St James's Hospital

- NREC-CT comments:

- The NREC-CT 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 that the process involved in withdrawing from the trial is described in the PISCF, so participants are fully informed of the process involved should they wish to withdraw from the trial.
- The NREC-CT noted that participants are not advised what to do in the event they experience life threatening side effects (such as allergic reaction) while participating in the trial and requested that this is added to the PISCF.

- The NREC-CT noted that pg. 6 of the PISCF advises participant to “come to your visits and do what doctor tells you to do” and requested that this is rephrased to be more patient friendly.
- The NREC-CT requested that participants are advised in the PISCF that by signing the consent form they are not giving up their legal rights.
- The NREC-CT requested submission of CVs for Prof Ray McDermott and Dr Derek Power, detailing previous clinical trial experience and evidence of up-to-date ICH-GCP certification.
- The NREC-CT requested evidence of up-to-date ICH-GCP certification is submitted for Prof Lowery.
- The NREC-CT noted that the legal basis for processing of personal data is not well described in the PISCF and requested that this is amended. Legal basis for data processing is not stated in the PISCF; in the DPIA (Section 3.1) various legal bases are recorded for processing data “explicit consent” and the legal justification is “it is necessary for compliance with a legal obligation”. The correct legal bases for data processing of personal data of the participant must correctly set out in accordance with GDPR and Health Research Regulations, and clearly described in the PISCF.
- The NREC-CT requested further detail is provided to participants in the PISCF regarding the process involved in claiming reimbursement for out-of-pocket expenses.
- The NREC-CT requested that the insurance policy is updated to provide cover for the full duration of the study.

23-NREC-CT-035

Principal Investigator: Dr Andrea Malone

Study title: A randomized phase 3 trial of fludarabine/cytarabine/gemtuzumab ozogamicin with or without venetoclax in children with relapsed AML

EudraCT: 2021-003212-11

Lead institution: CHI Crumlin

- NREC-CT comments:

- The NREC-CT 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 noted that the screening process is potentially burdensome on participants and requested clarification as to whether the screening process takes place on the same day and if any alternatives could be provided.
- The NREC-CT queried whether parents / guardians would be present during site visits and requested that this added to the Assent Forms to reassure children.
- The NREC-CT deemed the statement about insurance in 12-15 Assent Form as not appropriate for this age group and requested that this is removed, or a justification is provided for its inclusion.
- The NREC-CT noted that some participants are to undergo a lumbar puncture and that this procedure is not well described in the PISCF for Parents/ Guardians and requested that this is amended so participants are fully informed as to the nature of this procedure and the potential risks involved.
    - The NREC-CT requested that the lumbar puncture is also described in sufficient detail in the relevant assent forms including potential risks involved using lay language / age-appropriate terms.
- The NREC-CT noted that pg. 7 of the 12-15 Assent Form states, 'If you want to know more about exactly what we do with your data, you can ask your parents (it's in their information sheet), or you can also ask the study doctor' and deemed that this places an unacceptable additional burden on parents. The NREC-CT requested that information regarding what happens to the study data is added to the Assent Form using lay language / age-appropriate terms.
- The NREC-CT noted that pg. 5 of the Young Adult PISCF (Figure 1) indicates that participants may undergo bridging treatment and requested that a description of bridging treatment takes place earlier in the PISCF, so the diagram is more accessible to participants.
- The NREC-CT requested that the language in the 12-15 Assent Form is adapted to be warmer and more child friendly.
- The NREC-CT noted that pg. 4 of the 12-15 Assent Form states, 'There is more information about the side effects in your parent's information sheet.' and deemed that this places an unacceptable additional burden on parents. The NREC-CT requested that information regarding side effects is added to the Assent Form using lay language / age-appropriate terms.
- The NREC-CT noted that the timeframe for visits is not clear and requested that this is clearly laid out in the PISCF for parents/ guardians and details the projected length of each site visit etc.

- The NREC-CT noted that the dosing instructions as laid out in the Participant Dosing Instructions are complicated and requested that this is separated out (such as 2 pages instead of 1) and simplified so that it is clear.
- The NREC-CT noted that participants are reimbursed for travel / transportation and requested that participants will be reimbursed for all reasonable out-of-pocket expenses, including refreshments and this is clearly stated in the PISCF.
    - The NREC-CT requested that participants are advised on the process involved in claiming expenses and reimbursement in the PISCF.

23-NREC-CT-032

Principal Investigator: Prof Roisin Connolly

Study title: De-Escalation of adjuvant ChemotheRapy in HER2-positive, EStrogen reCEptor-negative, Node-negative early breast cancer patients who achieved pathological complete response after neoadjuvant chemotherapy and Dual HER2 blOckade. DECRESCENDO.

EudraCT: 2020-002918-41

Lead institution: Cork University Hospital

- NREC-CT comments:

- Based on the above, the NREC-CT Committee agreed that this application be designated as favourable with conditions.

- NREC-CT Decision:

- Favourable with conditions

- Conditions of Approval

- Participants are reimbursed for reasonable out-of-pocket expenses and that the process involved in reimbursement is clearly elucidated in the PISCF. It is important that there is equity of access to clinical trial for all prospective participants, and participants are not unduly disadvantaged by not receiving expenses.

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- AOB: