National Research Ethics Committee

NREC-CT Meeting

06 September 2023

Attendance

Name	Role
Dr Cliona McGovern	Chairperson, NREC-CT B
Dr Jean Saunders	Deputy Chairperson, NREC CT-B
Ms Serena Bennett	Committee Member, NREC-CT B
Mr Philip Berman	Committee Member, NREC-CT B
Dr Enda Dooley	Committee Member, NREC-CT B
Dr John Hayden	Committee Member, NREC-CT B
Dr Mary McDonnell Naughton	Committee Member, NREC-CT B
Ms Paula Prendeville	Committee Member, NREC-CT B
Prof Andrew Green	Committee Member, NREC-CT B
Ms Susan Kelly	Committee Member, NREC-CT B
Ms Deirdre MacLoughlin	Committee Member, NREC-CT B
Ms Caoimhe Gleeson	Committee Member, NREC-CT B
Prof Seamus O'Reilly	Committee Member, NREC-CT B
Dr Christina Skourou	Committee Member, NREC-CT B
Ms Aileen Sheehy	Programme Manager, National Office for RECs
Ms Patricia Kenny	Project Officer, National Office for RECs
Rachel McDermott	Programme Administrator, National Office for RECs
Dr Laura Mackey	Programme Officer, National Office for RECs
Dr Emma Heffernan*	Project Officer, National Office for RECs

*Drafted minutes

Apologies: Dr Mark Robinson, Ms Mandy Daly, Prof Abhay Pandit, Dr Lorna Fanning, Mr Gavin Lawler, Prof John Faul, Prof Colm O'Donnell

Quorum for decisions: Yes

Agenda

- Welcome & Apologies
- 2022-501453-36-00
- 2022-502215-10-00
- 2022-501709-11-00
- 2022-501707-27-00
- 23-NREC-CT-024_Mod-1
- AOB

- The Chair welcomed the NREC-CT B.
  - The minutes from the previous NREC-CT B meeting on 12 July 2023 were approved.
  - The NREC Business Report was discussed and noted.

Applications

2022-501453-36-00

Principal Investigators & Institutions: St James's Hospital (Dr Ciara O'Hanlon Brown), University Hospital Waterford (Dr Miriam O'Connor), Beacon Hospital (Dr Lisa Prior), MMUH (Dr Geraldine O'Sullivan Coyne), Mater Private Hospital (Dr Catherine Kelly).

Study title: An international, multicenter, randomised, superiority phase III, open label, 2-arm study to investigate distant metastasis free survival with elacestrant compared with standard endocrine therapy patients with ctDNA+ ER+/HER2- early breast cancer

- **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**

Part 1

- The EC: The EC noted that pg. 72 and 74 of the protocol states that data and samples may be used for undefined future research and requested that future research is confined to breast cancer research only and this is explained in the protocol.

Part 2

- The NREC-CT noted that section 4.1 of the S1_Compliance on the Collection Use and Storage of Biological Samples form states that the further usage of clinical trial data and samples is undefined and requested that future research is confined to breast cancer research only and this is explained in relevant PISCF.
- The NREC-CT requested that all sections of the S1_Compliance on the Collection Use and Storage of Biological Samples form are fully completed with the required information, rather than state 'refer to protocol or PIL' for ease of assessment by the committee.
- The NREC-CT noted that a statement confirming the source of funding was not provided in the initial application and requested that this statement is provided.
- The NREC-CT noted that participants are not reimbursed for out of expenses and requested that to ensure equitable access to clinical trials across all socio-economic groups that trial participants are reimbursed for reasonable out-of-pocket expenses, including meals / refreshments and travel, and this is detailed in the P1_Compensation Trial Participants Investigator Funding and Other Arrangements form.
- The NREC-CT noted that some of the language and terminology used in the PISCF was not participant friendly. The Committee requested that the PISCF is revised to ensure the language is more accessible and simplified into plain English, so participants are fully informed. The NREC-CT also requested that the following are addressed:
    - The NREC-CT noted that the risk section (Appendix 2) of the PISCF is not sufficiently clear and understandable to a lay person (e.g., using medical terminology such as 'Stevens Johnson Syndrome' without further explanation) and requested that this section is simplified into plain English for a lay audience with all potential side effects listed and explained.
    - The NREC-CT noted that the terminology describing the various phases of the trial (such as screening phase, testing phase, treatment phase) may be confusing for potential participants and requested that the various phases are simplified, listed and explained in a table.
    - The NREC-CT noted that the length of time participants will be involved in the trial, including to attend treatment/testing visits, attend study visits and follow up, is not clearly described and requested that this is made clearer for participants.
- The NREC-CT noted that participants are not reimbursed for out of expenses and requested that to ensure equitable access to clinical trials across all socio-economic

groups that trial participants are reimbursed for reasonable out-of-pocket expenses, including meals / refreshments and travel, and this is detailed in the PISCF, so participants are reassured that they will not be out of pocket as a result of participating in the trial.

- The NREC-CT also requested that the process for claiming expenses is clearly explained in the PISCF.
- The NREC-CT noted that some of the language and terminology used in the PISCF was not participant friendly. The Committee requested that the PISCF is revised to ensure the language is more accessible and simplified into plain English, so participants are fully informed. The NREC-CT also requested that the following are addressed:
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- The NREC-CT noted that the length of time participants will be involved in the trial, including to attend treatment/testing visits, attend study visits and follow up, is not clearly described and requested that this is made clearer for participants.
- The NREC-CT noted that participants are not reimbursed for out of expenses and requested that to ensure equitable access to clinical trials across all socio-economic groups that trial participants are reimbursed for reasonable out-of-pocket expenses, including meals / refreshments and travel, and this is detailed in the PISCF, so participants are reassured that they will not be out of pocket as a result of participating in the trial.
- The NREC-CT also requested that the process for claiming expenses is clearly explained in the PISCF.
- The NREC-CT noted that the section on future research in the Main PISCF is not described in line with national regulations and best practice. The Committee requested that future use of samples is sufficiently explained so as to constitute broad informed consent, as required under the Health Research Regulations (Data Protection Act 2018 (Section 36(2) (Health Research) Regulations 2018). Furthermore,
    - consent for future use of samples should be provided on a separate PISCF.
    - it should be made clear that this is optional, and
    - consent can only be obtained where future use of samples and data is defined such that participants are fully informed, and/or:
    - that an option is provided to enable participants to consent to be contacted is provided in a separate consent form.

- The PISCF should also make it clear to participants that subsequent research ethics review will be sought for specific research once clearly defined. For further guidance, please see: HSE National Policy for Consent in Health and Social Care Research (V1.1, 2023) https://hseresearch.ie/wp-content/uploads/2023/02/HSE-National-Policy-for-Consent-in-Health-and-Social-Care-Research-compressed.pdf
- The NREC-CT noted that participants are to complete quality of life questionnaires which may be triggering for some participants and requested details of the supports available for participants including referral pathways, should the questionnaires indicate a mental health issue and that this is elucidated in the PISCF.
- The NREC-CT requested that future research on data and samples is restricted to breast cancer research only and this is explained in the relevant PISCF.
- The NREC-CT noted that pg. 33 of the PISCF states 'at 25 years and every 5 years thereafter EORTC will assess whether they can still keep your data for further research' and requested that the maximum data retention periods for all data is clearly stated in the PISCF.
- The NREC-CT noted that pg. 35 of the PISCF states that 'Further use of remaining samples After completion of the circulating tumour DNA tests, remaining samples will be stored at Natera in the USA who can then use it for their internal research in cancer and requested that it is made clear to participants on pg. 5 of the PISCF that samples collected at screening will be retained whether they do or not progress to the treatment phase of the trial.
    - It also needs to be made clear to participants that this will be restricted to breast cancer research.
    - consent for future use of samples should be provided on a separate PISCF.
    - It should be made clear that this is optional for participants.
    - The PISCF should also make it clear to participants that subsequent research ethics review will be sought for specific research once clearly defined. For further guidance, please see: HSE National Policy for Consent in Health and Social Care Research (V1.1, 2023) https://hseresearch.ie/wp-content/uploads/2023/02/HSE-National-Policy-for-Consent-in-Health-and-Social-Care-Research-compressed.pdf
- The NREC-CT noted that participants block / surgical tissue used for breast cancer diagnosis (pg. 13 of the PISCF) will be used during the study. The Committee requested clarification as to whether the entire sample will be used or whether the remainder sample may be used by the participant in the event they wish to use the sample for alternative research studies. If the entire sample is being used in this study and not available for any future alternative research studies, then this should be clarified in the PISCF.
- The NREC-CT noted that participants' data will be transferred outside of the EU. The Committee requested that this is made clear to participants in the PISCF, including any safeguards in place.

- The NREC-CT requested that Dr Kelly's CV is updated to include details of relevant clinical trial / study experience

2022-502215-10-00

Principal Investigators & Institutions: St James's Hospital (Dr Niamh O'Connell)

Study title: Open-label, long-term safety and efficacy study of Mim8 in participants with haemophilia A with or without inhibitors

- **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**

Part 2

- The NREC-CT noted that a statement confirming the source of funding was not provided in the initial application and requested that this statement is provided.
- The NREC-CT noted that participants will be offered non-monitory payment items as detailed in section 2 of the Compensation to Trial Subjects form and requested that to protect the confidentiality of research participants taking part in the trial, the name of the trial is not displayed on these items.
- The NREC-CT noted that section 1.6 of the Recruitment and Informed Consent Procedure form states that participants will be given 'ample time' to consider whether to participate in the trial and requested that the minimum amount of time participants will be given to decide whether to participate in the trial is clearly stated.
- The NREC-CT noted that section 1.1 of the Recruitment and Informed Consent Procedure form that sites will be offered a 'communication package' for participants and requested that the contents of this package are provided for review.
- The NREC-CT noted that pg. 11 of the main PISCF states that the study has been reviewed, appraised, and approved by 'the national health authority in your country' and requested that the name of the national health authority is provided.
- The NREC-CT noted that the Main PISCF (pgs.13 & 17) and Future Research PISCF (pg. 8) state that information collected by Novo Nordisk during the study is stored in a database and may be shared with researchers who are not part of the study and requested that it is explained to participants in both PISCFs that this data is anonymised.

- The NREC-CT noted that the Future Research PISCF states that samples may be used for research into 'haemophilia A or related diseases' and requested that future research is confined to haemophilia A only and this is amended in the Future Research PISCF.
- The NREC-CT noted that participants will need to use an email address to access the study app and requested details of the provisions in place should participants not wish to use email are outlined in the PISCF.
- The NREC-CT noted that pg. 11 of the PISCF states that participants will be reimbursed for reasonable travel and if necessary, accommodation expenses whereas the Compensation to Trial Subjects form states that participants will also be reimbursed for meals and requested that it is stated in the PISCF that participants will also be reimbursed for meals.
- The NREC-CT noted that pg. 11 of the PISCF states that 'reasonable travel expenses, and if necessary, accommodation will be reimbursed if local law allows' and requested the words 'if local law allows' is removed from this sentence.
- The NREC-CT noted that a pen injector (DV3407-C1 pen-injector) may be used by trial participants and requested clarification as to whether a submission to NREC-MD is required.

2022-501709-11-00

Principal Investigators & Institutions: Cork University Hospital (Dr Vitaliy Mykytiv) & St James's Hospital (Dr Nina Orfali)

Study title: A single arm, open-label Phase 3b study to describe the safety and tolerability of ivosidenib in combination with azacitidine in adult patients newly diagnosed with IDH1m acute myeloid leukemia (AML) ineligible for intensive induction chemotherapy

- **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**

Part 2

- The NREC-CT noted that an NREC-CT National Statement of Data Compliance template or a study specific DPIA was not submitted and requested that either a NREC-CT National Statement of Data Compliance template or a study specific DPIA is submitted for review. Further information can be found on our website, including the National Statement of Data Compliance template www.nrecoffice.ie/submit-under-the-clinical-trial-regulation

- The NREC-CT noted that the Greenphire Customer Statement of Disputed Transaction form contains references to US contacts details and dollar signs and requested that this form is adapted to the Irish context and revised to include Irish contact details and Euro signs.
- The NREC-CT noted that a statement confirming the source of funding was not provided in the initial application and requested that this statement is provided.
- The NREC-CT commended the applicant on the quality of their video (K2_Recruitment material video transcript_IRL).
- The NREC-CT noted that participants and caregivers are reimbursed for out-of-pocket expenses for travel and accommodation and requested that participants and caregivers are also reimbursed for reasonable out-of-pocket expenses for meals / refreshments and that this is elucidated in the Main and Caregiver PISCFs.
- The NREC-CT requested confirmation that caregivers will be reimbursed for out-of-pocket expenses should they accompany the participant to study visits.
- The NREC-CT noted that pg. 4 of the Pregnant Partner Informed Consent form requests 'permission for my and my baby's personal information to be collected…' and requested that these are separated out into two separate points, one for the pregnant partner's personal information and one for the baby's personal information.
- The NREC-CT noted that the caregiver is required to conduct a Family Reported Outcome Measure assessment which requires use of the participant's personal data and requested that explicit permission is sought from the participant on pg. 21/22 of the Main PISCF for the caregiver to use their data.
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2022-501707-27-00

Principal Investigators & Institutions: The Heights Medical Centre (Dr Virag Feher), Moyview Family Practice (Dr Scott Walkin), The Crescent Medical Centre (Dr Sinead Feeney), Tramore Primary Care Centre (Dr Dermot Nolan), Main Street Clinic (Dr Cathal Nugent), Moycullen Medical Centre (Dr Eva Flynn)

Study title: European Clinical Research Alliance on Infectious Diseases – primary care adaptive platform trial for pandemics and epidemics (ECRAID-Prime)

- **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**

Part 2

- The NREC-CT noted that a statement on the course of trial funding was not submitted in the initial application and requested that this statement is submitted.
- The The NREC-CT noted that the risk section (including scientific information related to the IMP) is not well described in the PISCF and requested that this is amended so participants can make a fully informed decision about participating in the trial. This information should be explained in plain English suitable for a lay audience.
- The NREC-CT noted that the term nitric oxide is not well explained in the PISCF and requested that this is explained in plain English with a lay audience in mind in the PISCF.
- The NREC-CT noted that contraindicated / prohibited medications are not described in the PISCF and requested that this is amended.
- The NREC-CT noted that participants are required to take their own swabs and requested that the instructions are made clearer in the L2_Other subject information material Instructions swab document to ensure that all participants are carrying out the procedure in the same way.
- The NREC-CT requested that the infographic on pg. 2 of L2_Other subject information material Instructions medical product document is amended so that the instructions asking participants to ensure the spray is held vertically, precedes step 4, where participants are instructed to insert the bottle tip into their nostril.
- The NREC-CT noted that participants are requested to contact their GP should they experience an adverse reaction and requested that details of the pathway in place for participants contacting their GP practice is explained in the PISCF. Please include the following:
    - Details on how participants' calls will be handled / prioritized i.e., they could be contacting a busy GP practice.
    - Clarification as to whether there is a nominated person in each practice / site dedicated to dealing with these calls.
    - Details as to how they can contact their GP should they need to contact their GP outside of practice opening hours.
- The NREC-CT noted that the section on future research in the PISCF (pg. 4) is not described in line with regulations and best practice. The Committee requested that future use of samples is sufficiently explained so as to constitute broad informed consent, as required under the Health Research Regulations (Data Protection Act 2018 (Section 36(2) (Health Research) Regulations 2018). Furthermore,
    - consent for future use of samples should be provided on a separate consent form.
    - it should be made optional, and
    - consent can only be obtained where future use of samples and data is defined such that participants are fully informed, and/or:
    - that an option is provided to enable participants to consent to be contacted is provided in a separate consent form.

- The PISCF should also make it clear to participants that subsequent research ethics review will be sought for specific research once clearly defined. For further guidance, please see: HSE National Policy for Consent in Health and Social Care Research (V1.1, 2023) https://hseresearch.ie/wp-content/uploads/2023/02/HSE-National-Policy-for-Consent-in-Health-and-Social-Care-Research-compressed.pdf

- The NREC-CT noted that pg.10 of the PISCF states 'I consider the swabs a gift to Ecraid' and requested that this sentence is removed from the PISCF.

23-NREC-CT-024_Mod-1

Principal Investigator: Prof John Crown

Study title: A Phase 1/1b Open-label, Multicenter Study to Investigate the Safety, Tolerability, Pharmacokinetics, and Antitumor Activity of KIN-2787 in Participants with BRAF and/or NRAS Mutation-positive Solid Tumors

- **NREC-CT comments:**

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

- **NREC-CT Decision**:

- Request for more information

- **Additional Information Required**

- The NREC-CT noted that a consenting strategy was not outlined in section D. 6 of the Substantial Modification Form and requested that the consenting strategy is detailed in this section.
- The NREC-CT noted that the additional table, labelled 'Part A1 Crossover from KIN-2787 Monotherapy to KIN-2787 + binimetinib Combination (A2)' on pg. 12 of the tracked changes PISCF may be confusing for participants and requested that this table is moved to the Crossover PISCF.
- The NREC-CT noted a typo on pg. 3 of the tracked changes Crossover PISCF ('These procedures will occur during while you are taking the KIN-2787 study drug') and requested that this is corrected.

- AOB: