

National Research Ethics Committee

NREC-CT D Meeting

31st January 2024

Attendance

Name	Role
Prof David Brayden	Chairperson, NREC-CT D
Prof David Smith	Deputy Chairperson, NREC-CT D
Dr Christina Skourou	Deputy Chairperson, NREC-CT D
Dr Enda Dooley	Committee Member, NREC-CT D
Prof Cathal Walsh	Committee Member, NREC-CT D
Prof Deirdre Murray	Committee Member, NREC-CT D
Dr Geraldine O'Dea	Committee Member, NREC-CT D
Dr Mark Robinson	Committee Member, NREC-CT D
Prof Lina Zgaga	Committee Member, NREC-CT D
Mr Gerry Daly	Committee Member, NREC-CT D
Ms Deirdre McLoughlin	Committee Member, NREC-CT D
Prof Tina Hickey	Committee Member, NREC-CT D
Dr Mary McDonnell Naughton	Committee Member, NREC-CT D
Prof Geraldine O'Sullivan Coyne	Committee Member, NREC-CT D
Ms Aileen Sheehy	Programme Manager, National Office for RECs
Dr Laura Mackey	Programme Officer, National Office for RECs
Dr Susan Quinn	Programme Manager, National Office for RECs
Ms Patricia Kenny*	Project Officer, National Office for RECs

*Drafted minutes

Apologies: Prof Andrew Green

Quorum for decisions:

Agenda

- Welcome & Apologies
- 2023-504655-27-00
- 2022-502276-23-00
- 2023-507353-15-00
- 2022-502122-41-00 SM-1
- 2022-502886-71-00 SM-3
- 21-NREC-CT-090_Mod-6
- 22-NREC-CT-012_Mod-5
- 2023-503209-13-00 SM-3
- 2023-505023-31-00 SM-2
- 2022-502425-18-00 SM-6
- AOB

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- The Chair welcomed the NREC-CT D.
 - The NREC Business Report was discussed and noted.
 - Declarations of Interest – None noted
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Applications

2023-504655-27-00

Principal Investigators: Royal Victoria Eye and Ear Hospital (Mr Noel Horgan)

Study title: A Phase 3 Randomized, Masked, Controlled Trial to Evaluate Efficacy and Safety of Belzupacap Sarotalocan (AU-011) Treatment Compared to Sham Control in Subjects with Primary Indeterminate Lesions or Small Choroidal Melanoma

EudraCT: 2023-504655-27-00

Dossiers for Review: Part I and II

- **NREC-CT Decision:**
- Request for more information

- **Additional Information Required RFI**

Part II Considerations

1. Compliance with national requirements on data protection

- No considerations raised by NREC

2. Compliance with use of biological samples

- No considerations raised by NREC

3. Financial arrangements

- The NREC-CT noted a contradiction in information regarding reimbursement of travel/meals/accommodation as the Main ICF states they will be reimbursed however the Compensation for Trial Participants document states they will not be. The Committee requested that the Compensation for Trial Participant be updated to confirm that reimbursement for travel/meal/accommodation is covered.

4. Proof of insurance

- No considerations raised by NREC

5. Recruitment arrangements

- The NREC-CT requested that the Recruitment brochure (pg 2) be updated to make it clearer to participants that no active drug will be delivered in this treatment arm.
- The NREC-CT notes that participants will be provided with branded items designed with the study logo, and requests that the logo be omitted from these items to maintain the privacy of participants taking part in the trial.

6. Subject information and informed consent form

- The NREC-CT noted that the Main ICF (pg 16) has a section for legally authorized representative, if applicable. The Committee queried under what circumstances would the legally acceptable/authorised representative sign the PIS/ICF.
- The NREC-CT requested that the Main ICF pg 1 be updated to include the EU trial number for participants.

- The NREC-CT requested that the Other Pregnant Partner ICF pg 1 be updated to include the EU trial number for participants.
- The NREC-CT noted that the Protocol (pg 61/62) refers to a separate ICF for enrolling patients to a long-term follow-up registry which was not provided for review. The NREC-CT requested that further information on this registry and the associated ICF be provided for review.
- The NREC-CT noted that the short study title CoMpass only appears in the recruitment brochures. The Committee requested that all ICFs be updated to include the short study title.
- The NREC-CT requested that the explanation of the sham treatment in the Main ICF (pg 2) be updated to make it clearer to participants that no active drug will be delivered in this treatment arm.
- The NREC-CT requested confirmation that the Irish site will be utilising Greenphire services. The Committee stated that if Greenphire services are being utilised, it must be optional for participants to use the services and that an alternative method of reimbursement also be offered. The Committee requested that the Main ICF (pg 6 section 6) be updated to be clear on the reimbursement options for Irish participants.
- The NREC-CT requested the Main ICF (pg 6) be updated to include more detail around the timing/intervals of the reimbursement process for participants (i.e. whether participants can claim their reimbursement after each visit).
- The NREC-CT noted that Main ICF (pg 10 section 17) refers to UK GDPR regulations. The NREC-CT requested that this be updated to reflect Irish GDPR regulations.
- The NREC-CT requested clarification as to whether the sharing of the pathology results with the sponsor is optional. The Committee noted the Main ICF pg 15 has a yes/no tick box. If the sharing of the pathology results is mandatory, the Committee requested that the no tick box be removed and an explanation of the requirement. If the sharing of the results with the sponsor is optional, it should appear on a separate page from the Main consent form with its own signature box to request explicit consent. The NREC-CT noted that the Main ICF (pg 15) has a Yes/N/A box for PK testing, but that testing will not occur at every site. The Committee requested that this be updated to be specific to the Irish site, to remove the N/A if PK testing will take place or remove the statement completely if PK testing will not take place.
- The NREC-CT noted that Other Pregnant Partner ICF (pg 10 section 9) refers to UK GDPR regulations. The NREC-CT requested that this be updated to reflect Irish GDPR regulations.
- The NREC-CT noted that Other Pregnant Partner ICF (pg 3) states that data will be kept for 25 years. The Committee requested clarification on the process for obtaining consent for data processing from the child once they reach the age of consent (18 years of age). Please see HSE National Policy for Consent in Health and Social Care Research (2022).

7. Suitability of the clinical trial sites facilities

- The NREC-CT noted the Site Suitability Form submitted for Royal Victoria Eye and Ear Hospital was signed by the Principal Investigator which is not appropriate under the Clinical Trial Regulations. The Committee requested that an updated

Site Suitability Template be provided which is signed by the CEO, Head of Clinic / institution, Director of Research, Clinical Director, or delegate of the hospital.

8. Suitability of the investigator

- The NREC-CT requested that an updated CV be provided for Prof Horgan to provide more detail on Prof Horgan's previous research experience and current training (including GCP), as these sections were not completed in the form.

2022-502276-23-00

Principal Investigators & Institutions: Mater Misericordiae University Hospital (Dr Anne Fortune), Cork University Hospital (Dr Clodagh Keohane), Connolly Hospital (Prof. Patrick Thornton)

Study title: Randomized, open-label, multicenter phase 3 study to assess the efficacy and safety of GIVinostat versus hydroxyurea IN JAK2V617F-positive high-risk Polycythemia Vera patients: the GIV-IN PV TRIAL

EudraCT: 2022-502276-23-00

Dossiers for Review: Part I and II

- **NREC-CT Decision:**
- Request for more information

- **Additional Information Required RFI**

Part II Considerations

1. Compliance with national requirements on data protection

- No considerations raised by NREC

2. Compliance with use of biological samples

- The NREC-CT noted the response in Use of Biological Samples Declaration Section 4.10 regarding unsolicited findings. The Committee requested clarification on when and how participants would be contacted regarding the unsolicited findings.

3. Financial arrangements

- No considerations raised by NREC

4. Proof of insurance

- No considerations raised by NREC

5. Recruitment arrangements

- The NREC-CT requested clarification if advertising materials would be used to recruit participants for this study. If so, please provide for review.

6. Subject information and informed consent form

- The NREC-CT noted that the Main ICF pg 1, 9, 22 and 24 has references to legally acceptable representative/legal representative. The Committee queried under what circumstances would a legally authorized representative sign the PIS/ICF.

- The NREC-CT noted the Pregnant Partner ICF pg 1, 5, 7 and 9 has references to legally acceptable representative/legal representative. The Committee queried under what circumstances would a legally authorized representative sign the PIS/ICF.
- The NREC-CT noted the Optional Genetic Testing ICF pg 5 and 6 has references to legally acceptable representative/legal representative. The Committee queried under what circumstances would a legally authorized representative sign the PIS/ICF.
- The NREC-CT requested that the Optional Genetic ICF pg 1 be updated to include the EU trial number for participants.
- The NREC-CT noted that the Protocol pg 20 refers to blood being taken to test for hepatitis and HIV infections at screening however there is no reference to this in the Main ICF. The Committee requested that Main ICF be updated to add a statement informing participants that they will be tested for these virus at screening and that the study team are required to report any positive HIV, Hep A or Hep C test result to the relevant authority as they are mandatory notifiable diseases. (Infectious Diseases (Amendment) Regulations 2022 (S.I. No. 258 of 2022) May 2022)
- The NREC-CT note for Mater Misericordiae University Hospital and Connolly Hospital that the MRI/CT scans may be performed at a site other than the study site. The Committee requested that the Main ICF be updated to contain a statement advising participants from these sites that they may need to travel to a separate site for some MRI/CT scans.
- The NREC-CT requested that the Main PIL be updated to specify that this trial is primarily for high-risk patients (>60 yo), for whom HU is the standard of care.
- The NREC-CT queried how incidental findings will be managed. The Committee requested information on the process for incidental findings from the study, and the details of communicating these to participants. The Committee stated that this information should be included in ICFs.
- The NREC-CT noted that the Master Dosing instructions Patient Diary specifies very specific storage temperatures for the two drugs however this is not detailed in the Main ICF. The Committee requested that the Main ICF be updated to include instructions on how these drugs need to be stored.
- The NREC-CT stated that the two-stage nature of the trial is not adequately explained in the main PIL, especially the nature of the escalating dosage in Treatment phase, where dosages will be increased until TEAEs occur. The Committee requested that the Main ICF (pg 3) be updated to provide a lay language explanation of the two-stage nature of the trial.
- The NREC-CT noted the statement on Main ICF pg 3 “You may also undergo phlebotomies and blood transfusions.” The Committee requested that this be updated to clearly identify when a blood transfusion might be required.
- The NREC-CT advised that the placement of paragraph on mutations pg 10 Main ICF is confusing as immediately after this paragraph participants are asked to report ‘any of these’ side effects. The Committee requested that the paragraph on mutations be moved to the information on contraception (pg 13).
- The NREC-CT noted that the pregnancy precautions for male participants treated with GIVinostat are not clear in the Main ICF. The Committee requested that the

Main ICFpg 13 be updated to clarify if contraception is required for males treated with GIVinostat.

- The NREC-CT noted pg 16 of Main ICF states “A list of companies to whom your coded information is transferred is available from Italfarmaco via your study doctor”. The Committee requested that the Main ICF be updated to advise participants that a transfer agreement will be in place with each company. This information should also be provided in the Pregnancy Partner ICF and the Optional Genetic Testing ICF.
- The NREC-CT noted the wording on Main ICF (pg 17) that “If you should withdraw from the study, data collected prior to your withdrawal may still be processed along with other data collected as part of the study”. The Committee requested that the Main ICF be updated to provide justification for possible processing of data after withdrawal.
- The NREC-CT noted that in the Optional Genetic ICF (pg 3) it states “Genetic research studies may present unique risks to you and your relatives.” The Committee requested that the risks be explained in more detail and information provided about how incidental findings arising from the genetic study will be communicated or managed.
- The NREC-CT noted that while the consent form (pg 5) of the Optional Genetic Testing ICF is clear regarding future use of samples, the references to future use on page 2 are considered by the Committee to be vague. The Committee requested that the Optional Genetic Testing ICF (pg 2) be updated to use the wording on page 5, to ensure it is clear that sample(s) will only be used for future research related to polycythemia vera.

7. Suitability of the clinical trial sites facilities

- The NREC-CT noted the Site Suitability Forms submitted for Mater Misericordia University Hospital and Mater Private Network were signed by the Principal Investigator which is not appropriate under the Clinical Trial Regulations. The Committee requested that an updated Site Suitability Template be provided which is signed by the CEO, Head of Clinic / institution, Director of Research, Clinical Director, or delegate of the relevant hospital.

8. Suitability of the investigator

- No considerations raised by NREC

2023-507353-15-00

Principal Investigators & Institutions: Connolly Hospital (Dr Eoin Judge), Mater Misericordiae University Hospital (Dr Kate O'Reilly)

Study title: An open-label extension trial of the long-term safety and efficacy of BI 1015550 taken orally in patients with idiopathic pulmonary fibrosis (IPF) and progressive pulmonary fibrosis (PPF) (FIBRONEER™-ON)

EudraCT:2023-507353-15-00

- **NREC-CT Decision:**
- Request for more information /Unfavourable

- **Additional Information Required RFI**

Part II Considerations

1. Compliance with national requirements on data protection

- No considerations raised by NREC

2. Compliance with use of biological samples

- No considerations raised by NREC

3. Financial arrangements

- The NREC-CT requested that the Compensation for Trial participants document be updated to be clear that accommodation costs may be covered to align with the Greenphire ICF.

4. Proof of insurance

- No considerations raised by NREC

5. Recruitment arrangements

- No considerations raised by NREC

6. Subject information and informed consent form

- The NREC-CT noted that the Main ICF pg 12 refers to blood being taken to test for hepatitis and HIV infections. The Committee requested that page 12 be updated to add a statement to inform participants that the study team are required to report any positive HIV, Hep A or Hep C test result to the relevant authority as they are mandatory notifiable diseases. (Infectious Diseases (Amendment) Regulations 2022 (S.I. No. 258 of 2022) May 2022)
- The NREC-CT noted for Connolly Hospital that the MRI/CT scans may be performed at a site other than the study site. The Committee requested that the Main ICF be updated to contain a statement advising participants from Connolly Hospital that they may need to travel to a Hermitage Clinic for some MRI/CT scans.
- The NREC-CT noted that depression, anxiety and suicidality are exclusion criteria for this trial. The Committee requested details of the provisions in place, including referral pathways, should there be an indication of a mental health issue arising.
- It was unclear to the NREC-CT if the investigator intends to contact the clinician caring for the pregnant partner or for her baby, to obtain medical information regarding the pregnancy and baby. The Committee requested that the Pregnant Partner ICF be updated to clarify this.
- The NREC-CT recommended that Main ICF (pg 7), "Your responsibilities" be updated to include a bullet point to highlight the requirement that female participants of child bearing potential must use contraception.
- The NREC-CT noted that the Main ICF pg 12 describes biomarker analysis of gene products, and uses the terms DNA and RNA, which could give the participant the impression that genetic testing is being carried out. The Committee requested that the wording be updated to be clear that biomarker testing is for protein and immunological assays and not genetic testing.

- The NREC-CT requested that the Main ICF pg 13 be updated to provide detail on how and when reimbursement occurs including further detail on travel services which will be used.
- The NREC-CT noted the wording on Main ICF pg 32 consent form “I understand that I can withdraw...but that Boehringer may continue to process my personal data for purposes other than health research where it has a legal basis for doing so”. The Committee requested confirmation regarding the legal basis for processing of the participants personal data in this situation.
- The NREC-CT noted that the Pregnant Partner ICF states that their data protection rights will be limited or not apply if it impairs the achievement of the research, or conflicts with Sponsor's legitimate interest. The Committee would state that this is not consistent with a person's data protection rights and request that this is removed from the ICF.
- The NREC-CT requested that the Optional Sub Study ICF be updated to quantify the risk in relation to HRCT for participants by providing a dose comparator such as comparing the dose to that of a CT scan.

7. Suitability of the clinical trial sites facilities

- No considerations raised by NREC

8. Suitability of the investigator

- No considerations raised by NREC

2022-502122-41-00 SM-1

Principal Investigators: Dr Jarushka Naidoo, Prof Ray McDermott

Study title: An Open-label, Randomized Phase 3 Study to Evaluate Efficacy and Safety of Pembrolizumab (MK-3475) in Combination with MK-6482 and Lenvatinib (MK-7902), or MK-1308A in Combination with Lenvatinib, versus Pembrolizumab and Lenvatinib, as First line Treatment in Participants with Advanced Clear Cell Renal Cell Carcinoma (ccRCC)

EudraCT: 2022-502122-41-00

- **NREC-CT Decision:**
- Favourable
- **Additional Information**
- None

2022-502886-71-00 SM-3

Principal Investigators: Sinead Cuffe, Emer Hanrahan

Study title: A Phase 3, Randomized, Open Label Study to Compare Nivolumab plus Concurrent Chemoradiotherapy (CCRT) followed by Nivolumab plus Ipilimumab or Nivolumab plus CCRT Followed by Nivolumab vs CCRT followed by Durvalumab in Previously Untreated, Locally Advanced Non-small Cell Lung Cancer (LA NSCLC)

EudraCT: 2022-502886-71-00

- **NREC-CT Decision:**
- Favourable

- **Additional Information**
- None

21-NREC-CT-090_Mod-6

Principal Investigators: Dr Jarushka Naidoo, Dr Emer Hanrahan

Study title: A Phase 2 Randomized Study of Relatlimab plus Nivolumab in Combination with Chemotherapy vs. Nivolumab in Combination with Chemotherapy as First Line Treatment for Participants with Stage IV or Recurrent Non-small Cell Lung Cancer (NSCLC)

EudraCT:

- **NREC-CT Decision:**
- Favourable
- **Additional Information**
- None

22-NREC-CT-012_Mod-5

Principal Investigators: Dr Mark Doherty

Study title: A Randomized, Blinded, Placebo-controlled, Phase 2 Study of INBRX-109 in Unresectable or Metastatic Conventional Chondrosarcoma

EudraCT:

- **NREC-CT Decision:**
- Request for more information
- **Additional Information Required RFI**
- The NREC-CT noted the updated Patient Safety Leaflet with information on the potential increase in the risk of liver damage for participants in IXBRX-109 clinical trials. The Committee requested that the Main ICF for the trial be updated to detail more information regarding the increased risk of liver damage, and that participants be reconsented with this updated ICF. The Committee stressed the importance of participants being provided with all risk information in the ICF so they can give

informed explicit consent to take part in the trial. The NREC-CT requests that all ongoing participants are reconsented using the updated Main ICF to ensure that they fully understand the updates to the safety information.'

- The Committee noted that they were unclear regarding the number of current participants in Ireland on this trial and reiterated that it is imperative that this risk information is shared with participants immediately, and the updated ICF be signed by them at the next study visit.

2023-503209-13-00 SM-3

Principal Investigators: Prof Afif EL-Khuffash

Study title: Co-administration of Acetaminophen with Ibuprofen to Improve Duct-Related Outcomes in Extremely Premature Infants – The ACEDUCT Trial

EudraCT: 2023-503209-13-00

- **NREC-CT Decision:**
- Favourable

- **Additional Information**
- None

2023-505023-31-00 SM-2

Principal Investigators: Prof Sean McDermott, Prof Adrian Murphy, Prof Sean McDermott, Prof Richard Banbury

Study title: Multicenter, Double-blind, Randomized Phase 3 Study to Compare the Efficacy and Safety of Belzutifan (MK-6482) Plus Pembrolizumab (MK3475) Versus Placebo Plus Pembrolizumab, in the Adjuvant Treatment of Clear Cell Renal Cell Carcinoma (ccRCC) Post Nephrectomy (MK-6482-022)

EudraCT: 2023-505023-31-00

- **NREC-CT Decision:**
- Favourable

- **Additional Information**
- None

2022-502425-18-00 SM-6

Principal Investigators: Prof Sean Raymond McDermott, Prof Sean Raymond McDermott, Dr Emmet Jordan, Dr Nemer Osman, Dr John McCaffery, Dr John McCaffery

Study title: A double-blind randomised phase III trial evaluating the efficacy of ADT +/- darolutamide in de novo metastatic prostate cancer patients with vulnerable functional ability and not elected for docetaxel or androgen receptor targeted agents

EudraCT: 2022-502425-18-00

- **NREC-CT Decision:**

- Favourable

- **Additional Information Required RFI**

- None

- **AOB:**

- None