National Research Ethics Committee

NREC-CT Meeting

29th January 2025

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
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
Prof Lina Zgaga	Committee Member, NREC-CT D
Mr Gerry Daly	Committee Member, NREC-CT D
Ms Deirdre McLoughlin	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 Chanel Watson	Committee Member, NREC-CT D
Ms Chita Murray	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
Dr Jane Bryant	Programme Officer, National Office for RECs
Emma Heffernan	Project Officer, National Office for RECs
Dr Emily Vereker	Unit Manager, National Office for RECs

Rachel McDermott	Project Administrator, National Office for RECs
Deirdre Ni Fhloinn	Project Officer, National Office for RECs
Peadar Rooney	Project Officer, National Office for RECs
Ciaran Horan	Administrative Assistant, National Office for RECs

Apologies: Tina Hickey, Jeff Moore, Andrew Green

Quorum for decisions:

Agenda

- Welcome & Apologies
- 2024-512925-95-00
- 2024-519128-26-00
- 2024-517500-11-00 SM-1
- 2023-506361-56-00 SM-8
- 2023-508372-10-00 SM-3
- 2022-502116-36-00 SM-5
- 2024-515469-32-00 SM-2
- 2023-505579-53-00 SM-3
- 2024-510985-17-00 SM-2
- 2022-502110-85-00 SM-5
- AOB

- The Chair welcomed the NREC-CT D.
  - The minutes from the previous NREC-CT D meeting on 18th December 2024 were approved.
  - The NREC Business Report was discussed and noted.

Applications

2024-512925-95-00

Institutions: Mater Misericordiae University Hospital, Cork University Hospital, Mater Private Hospital, St James's Hospital, Beaumont Hospital, St Vincent's University Hospital

Study title: C4391024 - An Interventional, Open-Label, Randomized, Multicenter Phase 3 Study of PF-07220060 Plus Letrozole Compared to CDK4/6 Inhibitor Plus Letrozole in Participants Over 18 Years of Age With Hormone Receptor (HR)-Positive, HER2-Negative Advanced/Metastatic Breast Cancer who Have not Received any Prior Systemic Anticancer Treatment for Advanced/Metastatic Disease (FourLight-3)

Dossiers Submitted: Part I & II

- **NREC-CT Decision:**

- Request for Further Information

- **Additional Information Required RFI**

Part II Considerations

1. Recruitment arrangements

- 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 avoid the participants' condition or participation in the trial being shown publicly.
- The NREC-CT noted that pre consent materials are mentioned on page 2 of K1_Recruitment and informed consent Procedure – videos, brochure, digital ads however these have not been submitted for review. The Committee requested confirmation that these will be submitted for review before use.

2. Subject information and informed consent form

- If applicable, the Sponsor is requested to submit any Part 2 documentation that require updates as a result of the Part 1 Assessment. Please include detail of the Part 1 consideration that triggered the update to the Part 2 documentation
- The National Office requests that all documentation provided in response to RFI is presented in an accessible and searchable format (Word or original PDF). We are unable to accept scanned documents (including documents modified using Optical Character Recognition) as these documents cannot be optimised for use with assistive software.
- The NREC-CT requested that the Main ICD pg 2 be updated to include the 14 digit EU Clinical Trial number for participants.
- The NREC-CT were unclear on the wording in Main ICD pg. 4 *"This consent document is for participants who may or may not have the capacity to consent to their participation"* as this trial is not recruiting any incapacitated adults, minors or those in emergency situations. Please clarify and update the Main ICD as applicable.
- The NREC-CT requested that Main ICD pg. 10 Biological samples be updated to detail which countries the samples may be sent to be analysed.

- The NREC-CT noted that the following in the Main ICD are not described in line with regulations and best practice as they are not confined to the disease or drug under study
    - pg 32 Privacy statement *"improve the quality, safety, and design of this study and, to the extent permitted by this Privacy Supplement, other research studies."*
    - pg 33 EU Privacy Supplement *"The Sponsor may use and has a legitimate interest in using your Coded Information, biological samples, images and/or audio/video recordings, if collected as part of the study, to support and advance other scientific research projects, including improving the quality, design, and safety of other research studies, research supporting public health aims, and developing medicines, vaccines, diagnostic products, and tools"*
    - pg 35 *"improving the quality, design and safety of this study and, to the extent permitted by this Privacy Supplement, other research studies, including developing diagnostic products and tools."*
    - pg 35 "*You don't have to provide your consent, but you may be unable to take part in this study if you don't."*
    - pg 38 "*Circulating Tumour DNA - Blood samples will be collected to examine the amounts and characteristics of ctDNA and how they change during the study. This will help with understanding cancer and how it responds to the study drugs."*
    - pg 42 Retained Research sample *"Description Detail: A 4 mL sample of your blood will be collected, stored, and used to learn more about the study drug(s) and breast cancer, as well as other diseases. Biological substances in your sample, including your genes, may be studied. This sample may be kept by the Sponsor for as long as the sample is useful for scientific research, which may be for many years (no time limit)"*

  The NREC-CT requested that future use of samples/personal data is sufficiently explained to participants and aligned across all relevant sections of ICD documents 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,

    - it should be made optional
    - it should be confined to a specified disease area or drug under study in this trial (Breast Cancer and/or PF-07220060), and this is clearly stated in the main body of PIS , informed consent sections of the ICF, Privacy Supplement and Appendix A. 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 in the future about other research studies,

  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: NREC guidance on use of biological samples and associated data. https://www.nrecoffice.ie/guidance-on-use-of-biological-samples-and-associated-data
- The NREC-CT noted pg 33 Main ICD states "Furthermore, if your Coded Information, biological samples, images and/or audio/video recordings (if collected

as part of the study) are anonymised such that they can no longer be identified with you, they may be used for other research purposes." The Committee requested that Main ICD informed consent section be updated to have a separate consent statement for the participant to explicitly consent to the processing of their personal data from coded to anonymised data it as per Article 4 (2) and (6) General Data Protection Regulation (GDPR).

- The NREC-CT were unclear from the information provided on CTIS for Ireland (10 participants) and the site suitability forms / Site List (12 participants) in Ireland, how many patients will be enrolled from each of the 6 sites in Ireland. Please update to clarify.
- The NREC-CT requested that the Main ICD pg. 10 paragraph 2, 'Biological samples' which states 'foreign countries', be updated to include detail of the names of the countries the samples may be sent to for processing or storage.
- The NREC-CT noted the some of side effects for Letrozole in the Main ICD pg. 13/14/15 are not clearly explained. The Committee requested the side effects for Letrozole be updated to be described in lay language.
- The NREC-CT noted the Main ICD pg. 24 states that *"in certain circumstances, information that identifies you by name may leave the study……to support the use of digital tools in this study (e.g. electronic consent, mobile apps)"* however there is no description/information on these apps in the Main ICD and there is no reference to electronic consent being used in Ireland in the Recruitment document. Please update the Main ICD and Recruitment document to clarify.

3. Suitability of the investigator

- The NREC-CT requested that the CV for Catherine Margaret Kelly be updated to include more detail in previous clinical trial experience (e.g. the most recent 5 trials) to detail the specific types of trial rather than stating "multiple".

2024-519128-26-00

Institutions: Institute of Eye Surgery, Waterford

Study title: A phase 2, double-masked, randomized, multicenter, parallel group, placebo-controlled study to investigate the efficacy and safety of GAL-101, 2%, ophthalmic solution in patients with non-foveal geographic atrophy secondary to non-neovascular age-related macular degeneration: eDREAM study

Dossiers Submitted: Part I & II

- **NREC-CT Decision:**

- Request for Further Information

- **Additional Information Required RFI**

Part I Considerations (RFI) for addition to CTIS

1. The Sponsor is requested to provide justification for the difference in dosing of IMP at home (2 drops with 5 mins apart) versus in clinic (3 drops).

- The Sponsor is requested to provide clarity on the differences in study durations for participants on the trial. Specifically, as AMD is a slow-growing condition, please provide clarity as to whether there will be sufficient time to see significant difference between IMP and placebo in terms of efficacy. Furthermore, please provide clarity as to whether it is hypothesized that the 2 groups will show enough difference in 55 patients to demonstrate efficacy, particularly those participants that will be on the trial for 12 months.
- The Sponsor is requested to provide justification for the final follow-up being only for 2 weeks post study termination as it would be expected to be longer.
- It was noted that drug formulation has changed from phase 1 to phase 2 with different excipients being used. The Sponsor is requested to confirm that the excipients are still at an acceptable dose level.

Part II Considerations

1. Financial arrangements

- The NREC-CT requested the Compensation for trial participants document be updated to include Q 2. the monetary payment which is detailed in the ICF, and Q3 to list the requirement to provide receipts as detailed in ICF.
- The NREC-CT noted that patients with advanced AMD may need support from a carer/companion to attend hospital visits. The Committee requested that compensation for carers/companions also be provided, and this be updated in both the Compensation for trial participants document and ICF.

2. Recruitment arrangements

- The NREC-CT requested the number of participants to be recruited in Ireland is specified. The site suitability form states 30 participants, whereas the PIL says 20 in Ireland

3. Subject information and informed consent form

- If applicable, the Sponsor is requested to submit any Part 2 documentation that require updates as a result of the Part 1 Assessment.Please include detail of the Part 1 consideration that triggered the update to the Part 2 documentation.
- The National Office requests that all documentation provided in response to RFI is presented in an accessible and searchable format (Word or original PDF). We are unable to accept scanned documents (including documents modified using Optical Character Recognition) as these documents cannot be optimised for use with assistive software.
- The NREC-CT noted that the following statement in the SIS and ICF page 18 *"The Sponsor and its collaborators will have the right to use such samples for studies that may be conducted in the future. These future studies may provide additional information that will be helpful in understanding neurogenerative diseases, or other diseases or conditions, including research to develop investigational tests, treatments, drugs or devices that are not yet approved by any Regulatory Agency, such as the EMA."* does not describe future research in line with regulations and best practice, as it is not confined to the disease or drug under study.
  The NREC-CT requested that future use of samples/personal data is sufficiently explained to participants and aligned across all relevant sections of SIS and ICF

documents 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,

- It should be made optional
- it should be confined to a specified disease area or the drug under study in this trial (AMD and /or GAL-101,), and this is clearly stated in the main body of PIS and informed consent sections of the ICF. 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 in the future about other research studies,

The PISCF should also make it clear to participants that any future research they are consenting to, will also be subject to ethical assessment once clearly defined. For further guidance, please see: NREC guidance on use of biological samples and associated data. https://www.nrecoffice.ie/guidance-on-use-of-biological-samples-and-associated-data

- The NREC-CT noted that the Compensation document lists accommodation and meal expenses as being offered however this is not detailed in the SIS ICF. The Committee requested the SIS-ICF be updated to include this information.
- The NREC-CT noted that there are many exams at each visit, including administration of dilation drops, blood draws etc. The Committee requested that the SIS and ICF be updated to detail approximately how long will a participant can expect to spend at the hospital for these visits.

4. Suitability of the clinical trial sites facilities

- The NREC-CT noted a discrepancy between the information in site suitability form which states 30 participants will take part in Ireland however the SIS-ICF states 20 participants will take part in Ireland. The Committee requested the documents be updated to align.

2023-506361-56-00 SM-8

Institutions: Bon Secours Hospital Cork, St James's Hospital

Study title: A Phase 3 Randomized, Open-label, Active-comparator Controlled Clinical Study of Pembrolizumab versus Platinum Doublet Chemotherapy in Participants With Mismatch Repair Deficient (dMMR) Advanced or Recurrent Endometrial Carcinoma in the First-line Setting (KEYNOTE-C93/GOG-3064/ENGOT-en15)

Dossiers Submitted: Part I & II

- **NREC-CT Decision:**

- Favourable

2023-508372-10-00 SM-3

Institutions: Beaumont Hospital, St Vincent's University Hospital

Study title: A Phase 2 Randomized Double-blind 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)

Dossiers Submitted: Part I & II

- **NREC-CT Decision:**

- Favourable

2022-502116-36-00 SM-5

Institutions: St Vincent's University Hospital

Study title: A Phase 3 Multicenter, Randomized, Double-blinded, Active-controlled, Clinical Study to Evaluate the Safety and Efficacy of Lenvatinib (E7080/MK7902) with Pembrolizumab (MK-3475) in Combination with Transarterial Chemoembolization (TACE) Versus TACE in Participants with Incurable/Nonmetastatic Hepatocellular Carcinoma (LEAP-012)

Dossiers Submitted: Part I & II

- **NREC-CT Decision:**

- Favourable

2024-515469-32-00 SM-2

Institutions: Children's Health Ireland Temple Street

Study title: ApproaCH: A Phase 2b, Multicenter, Double-Blind, Randomized, Placebo-controlled Trial evaluating Efficacy and Safety of Subcutaneous Doses of TransCon CNP Administered Once Weekly for 52 Weeks in Children with Achondroplasia followed by an Open Label Extension period

Dossiers Submitted: Part II

- **NREC-CT Decision:**

- Request for Further Information

- **Additional Information Required RFI**

Part II Considerations

1. Subject information and informed consent form

- The NREC-CT noted that the following are not described in line with regulations and best practice as it is not confined to the disease or drug under study pg.13 Parent PIS-ICF "*Your child's personal data collected in this study may also be*

relevant and significant for future research purposes conducted by Ascendis Pharma. Any such use of your child's personal data for the purpose of future research, which is not described in, related to or compatible with the purposes of this study or which is not necessary according to Ascendis Pharma's legal or regulatory obligations, will be based on your explicit consent if you chose to provide this" and pg. 19 Parent PIS-ICF *"I understand that the storage and processing of my child's personal data and/or blood samples may be used for the purpose of future research, once approved by a relevant research ethics committee. YES, I agree to the use of my child's personal data and/or blood samples for future research purposes NO, I don't agree to the use of my child's personal data and/or blood samples for future re-search purposes*"
The NREC-CT requested that future use of samples/personal data is sufficiently explained to participants and aligned across all relevant sections of SIS and ICF documents 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,

- it should be made optional
- it should be confined to a specified disease area or drug under study in this trial (Achondroplasia and/or TransCon CNP), and this is clearly stated in the main body of Parent PIS pg 13 and informed consent section of the ICF pg 19. 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 in the future about other research studies,

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: NREC guidance on use of biological samples and associated data. https://www.nrecoffice.ie/guidance-on-use-of-biological-samples-and-associated-data

- It was unclear to the NREC-CT whether the data collected as part of ApproaCH study will require to be transferred even if the child isn't participating in the new AttaCH study or if data will only be transferred for those children who will be taking part in the AttaCH study. Please clarify.

2023-505579-53-00 SM-3

Institutions: Mater Misericordiae University Hospital, University Hospital Galway, Bon Secours Hospital Cork

Study title: A Phase 3, Single-Arm, Open-Label, Multicenter Study to Evaluate the Safety and Efficacy of Tafasitamab Plus Lenalidomide in Participants With Relapsed or Refractory Diffuse Large B-Cell Lymphoma.

Dossiers Submitted: Part I & II

- **NREC-CT Decision:**

- Favourable

2024-510985-17-00 SM-2

Institutions: St Vincent's University Hospital

Study title: A Phase 2, Open-Label, Randomized Study to Assess the Efficacy of Zolbetuximab (IMAB362) in combination with Nab-Paclitaxel and Gemcitabine (Nan-P + GEM) as First Line Treatment in Subjects with Claudin (CLDN)18.2-Positive, Metastatic Pancreatic Adenocarcinoma

Dossiers Submitted: Part I & II

- **NREC-CT Decision:**

- Request for Further Information

- **Additional Information Required RFI**

Part II Considerations

1. Subject information and informed consent form

- The NREC-CT noted that the following are not described in line with regulations and best practice as it is not confined to the disease or drug under study ie.
    - SIS-ICF_Opt PGx – pg. 1 *""Information may also help in the development of new drugs and diagnostic tests and in the improvement of existing drugs."*
    - Main SIS-ICF – pg. 24 *"Astellas may also use and share data from your Study Record for future medical research that may lead to treatments for patients or a better understanding of diseases."*
    - Main SIS-ICF - pg.28 *"When samples have been analyzed for their designated purpose, any remaining sample may be used for other assays, for example, for additional biomarker analysis"*
    - Main SIS-ICF – pg. 30 *"My health information may be added to research databases and used in the future by Astellas and its affiliated companies to study treatments for patients or to develop a better understanding of diseases."*
    - Pregnant Partner SIS-ICF – pg. 5 *" The information collected from you/your baby may also be:… used in research, now or in the future."*
    - PostProg SIS-ICF - pg. 1 *"The purpose of testing your tissue sample is to have additional information to better understand the study drug and how affects people like you with CLDN18.2".*
    - PostProf SIS-ICF - pg 4 is not limited *"I AGREE to allow a tumour biopsy to obtain a post progression tissue sample for future research"*
    - Partial Screening SIS-ICF - pg. 5 *"Astellas may also use and share data from your Study Record for future medical research that may lead to treatments for patients or a better understanding of diseases. In such cases, your identity will not be revealed."*
    - Partial Screening SIS-ICF - pg 9 *"My health information may be added to research databases and used in the future by Astellas and its affiliated*

companies to study treatments for patients or to develop a better understanding of diseases."

The NREC-CT requested that future use of samples/personal data is sufficiently explained to participants in the SIS and ICF documents 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,

- it should be made optional
- it should be confined to a specified disease area or drug under study in this trial (Pancreatic cancer and/or zolbetuximab) and this is clearly stated in the main body of SIS-ICF_Opt PGx –pg.1, Main SIS-ICF pg. 24 , Pregnant Partner SIS-ICF pg. 5, PostProg SIS-ICF pg. 1, Partial Screening SIS-ICF pg. 5 and informed consent section of the ICF Main SIS-ICF pg. 30, ICF Main SIS-ICF pg. 28, PostProf SIS-ICF pg 4, Partial Screening SIS-ICF pg 9. 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 in the future about other research studies,

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: NREC guidance on use of biological samples and associated data. https://www.nrecoffice.ie/guidance-on-use-of-biological-samples-and-associated-data

- The NREC-CT note the SIS-ICF Pregnant Partner pg 2 states *"This information release form may contain words that you do not understand. Please ask the research study doctor or the study staff to explain any words or information that you do not clearly understand"* which is not in any of the other ICF's and implies potential genitive issue for pregnant women. The Committee requested that SIS-ICF Pregnant Partner be updated to replace this sentence with *"If you have any questions about the content of this document please ask the study doctor"*
- The NREC-CT were unclear what is the logic that supports the potential discontinuation of monitoring participant's weight, vital signs and performance status at Study Treatment Discontinuation Visit and 30-day Safety Follow-up Visit. The Committee requested the SIS-ICF Addendum be updated to clarify.
- The NREC-CT were unclear if new participants would sign both SIS-ICF Main and SIS -ICF Addendum. Please clarify. If new participants will not sign the SIS-ICF addendum the Committee requested that the SIS-ICF Main should be updated to include the information contained in the SIS-ICF Addendum.
- The NREC-CT requested the SIS-ICF Main pg. 27 "Which ethics bord reviewed this study" be updated to reference NREC-CT.

2022-502110-85-00 SM-5

Institutions: Children's Health Ireland Blanchardstown, Children's Health Ireland Crumlin, Cork University Hospital

Study title: A Phase 3, Double-blind, Placebo-controlled, Randomized Study to Assess the Efficacy and Safety of Epicutaneous Immunotherapy with DBV712 250 µg in 4-7-year-old Children with Peanut Allergy (VITESSE)

Dossiers Submitted: Part II

- NREC-CT Decision:

Favourable

- Additional Information Required / Favourable with Conditions
- None

- AOB:
  - None