National Research Ethics Committee

NREC-CT D Meeting

12th June 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
Prof Andrew Green	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
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 Chanel Watson	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
Dr Jeff Moore	Observer

Rachel McDermott	National Office for RECs

Apologies: None

Quorum for decisions: Yes

Agenda

- Welcome & Apologies
- 2024-511363-28-00
- 2022-502215-10-00 SM-8
- 23-NREC-CT-034_Mod-5
- 21-NREC-CT-007_Mod-3
- 22-NREC-CT-167_Mod-2
- AOB

- The Chair welcomed the NREC-CT D.
  - The NREC Business Report was discussed and noted.

Applications

2024-511363-28-00

Institutions: St Vincent's University Hospital

Study title: A phase 3, randomized, double-blind, placebo-controlled, multicenter study to evaluate the efficacy and safety of subcutaneous sonelokimab in adult participants with moderate to severe hidradenitis suppurativa (M1095-HS-302)

Dossiers Submitted: Part I and II

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

- **Additional Information Required RFI**

Part I Considerations (RFI) for addition to CTIS

1. The Sponsor is requested to clarify the power calculation and associated sample size specification and in particular how the estimated effect size was derived.
2. It was noted that Protocol contains a placebo-controlled phase up to 16 weeks, while the EMA advice was to have a longer duration of the placebo-controlled phase up to 24 weeks. Justification is required for not extending the placebo-controlled phase to 24 weeks as recommended by the EMA.

Part II Considerations

1. Compliance with national requirements on data protection

- No NREC considerations raised

2. Compliance with use of biological samples

- No NREC considerations raised

3. Financial arrangements

- The NREC-CT noted that Compensation for trial participants document Q 2 does not provide participants reimbursement for accommodation expenseS. This could exclude participants who do not live within a commutable distance of the study site. The Committee requested that the compensation for trial participants document be updated to include accommodation costs.

4. Proof of insurance

- No NREC considerations raised

5. Recruitment arrangements

- The NREC-CT stated that the wording on the Poster "When you want to be comfortable in your own skin" is overpromising and inappropriate as it suggests that participating in the trial will mean relief for all participants. The Committee requested that the wording be removed or amended.

6. Subject information and informed consent form

- The NREC-CT noted that the section on future research in the SIS and ICF Main (pg 9, 16, 19 and 23) and SIS-ICF Pregnant Partner (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,
    - it should be confined to the disease or drug under study in this trial. 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: 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 Sponsor is requested to submit any participant-facing documentation that requires updates as a result of the Part I Assessment.
- 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 as these documents are composed of images, rather than searchable text, and cannot be optimised for use with assistive software.
- The Committee requested that SIS-ICF Main pg 5 be updated to add a statement to inform participants that the study team are required to report any positive HIV and/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 requested that the SIS-ICF Main pg 21 be updated to include specific statement that the participant confirms that a copy of the signed and dated Informed Consent Form will be provided to them and that a copy will be retained by the study doctor.
- The NREC-CT noted that SIS and ICF Main pg 18 states *"At the end of the storage period, data will be destroyed or anonymised."* The Committee requested that the SIS and ICF Main pg 21 be updated to include a specific 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 requested that the SIS-ICF Main pg 21 be updated to move the optional consent items (use of personal data, informing GP and Greenphire reimbursement process) to the following page with a signature box separate to that for consent to the main study to enable participants to explicitly consent, or not, to these optional components.

- The NREC-CT noted that on pg 19 of the protocol the risks of infection are outlined and include opportunistic infections respiratory infections such as TB, oropharyngeal, oesophageal and systemic Candida infections. The Committee requested that the statement in the SIS-ICF Main pg 12 *"infections in general, including candida (thrush) have been reported in patients etc"* be expanded to list these more serious infections they will have an increased risk of catching while taking the IMP and include a sentence that this is as a direct consequence of how the IMP acts.
- As this cohort is at greater risk of infection, the NREC-CT suggested that the SIS-ICF Main may benefit from a recommendation that participants should avoid large crowds where possible.
- The NREC-CT requested that SIS-ICF Main pg 11 be updated to include the risk of cytopenia / lymphopenia in line with the Investigator Brochure.
- The NREC-CT noted that the study restricts access to treatments that will be made available to participants directly related to the condition under investigation. The Committee requested that the SIS-ICF Main be updated to make it clearer to participants that they will not have access to existing effective treatments, (e.g. antibiotics and pain relief) related to the condition under investigation during the trial, if they were not already taking them prior to enrolment in the trial. The Committee also requested that detail be added around what the risks of not having access to these treatments might be.
- The NREC-CT requested that the SIS-ICF Main pg 12 be updated to make it clearer to participants the risk that their condition may get worse, stay the same or improve while taking the study drug, similar to the wording provided around Placebo risk.

7. Suitability of the clinical trial sites facilities

- No NREC considerations raised

8. Suitability of the investigator

- No NREC considerations raised

2022-502215-10-00 SM-8

Institutions: St James's Hospital

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

Dossiers Submitted: Part I and II

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

- **Additional Information Required RFI**
- None

23-NREC-CT-034_Mod-5

Institutions: Beaumont Hospital

Study title: Phase 2, Multicenter, Randomised, Double-Blind, Placebo-Controlled Study Evaluating Safety and Efficacy of CORT113176 (Dazucorilant) in Patients with Amyotrphic Lateral Sclerosis (DAZALS)

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

- **Additional Information Required RFI**
- It was unclear to the NREC-CT the rationale for the increase in the number of participants. The Committee requested that the cover letter and Substantial Modification form be updated to provide the justification for same. This amended form does not need to be resigned by the Study PI.

21-NREC-CT-007_Mod-3

Institutions: Mater Misericordiae University Hospital

Study title: A phase III, randomized, double-masked, placebo controlled, parallel-group, multicenter study of the safety and efficacy of OT101 (Atropine Sulfate 0.01%) in treating the progression of myopia in pediatric subjects

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

- **Additional Information Required RFI**
- The NREC-CT noted that the consent/assent forms to accompany the information sheets submitted as part of the modification are not included in the submission. The Committee requested that the consent/assent forms for use with these information sheets be updated to show the same date and version as the relevant information sheet and that it be provided for review. The Committee commented that the information sheet and consent form should be one document and not separate to ensure the documents do not have different versions and dates on them.
- The NREC-CT noted the Substantial Modification form Section D Question 5 has been ticked yes, that existing participants will be reconsented; however the process involved in the reconsenting has not been provided. The Committee requested that the Substantial Modification form Section D Q 5 be updated to include the process for reconsenting parents of participants who have not yet reached 16 by the time of the reconsent process following this Substantial Modification, as well as the consenting process for those participants who have reached 16 years of age and can now

consent for themselves. This amended form does not need to be resigned by the Study PI.

Parent Information Sheet

- The NREC-CT noted the use of term “subject” and “patient” interchangeably throughout the Information sheet. The NREC-CT recommended that the information sheet be reviewed, and the terms subject/patient be replaced with participant.
- The NREC-CT noted updated information in the protocol pg 56 & 64 regarding contraception. The Committee requested that on pg 4 of the Parent information sheet, the first paragraph also be updated for clarity to include the amended information that *“For non-sexually active females, abstinence will be considered an acceptable form of birth control.”*
- The NREC-CT noted that some wording on pg 7 section 6 has been updated but the surrounding text has not been updated accordingly in all cases. The Committee requested that this section be reviewed, and wording updated to correct grammar.
- The NREC-CT requested that font size on pg 9 be the same for all side effects. Please review and update.

PIS for Children who turn 16

- The NREC-CT noted that the text on Page 2 of the PIL is not relevant to ongoing participants of the trial reaching age 16. The Committee requested confirmation that this is made clear to ongoing participants as part of the reconsent process.
- The NREC-CT requested that font size on pg 4 be the same for all side effects. Please review and update.

PIS for Children Aged 11-15

- The NREC-CT requested that font size on pg 4 be the same for all side effects. Please review and update.
- Although not part of the amendment presented, the NREC-CT recommended that the assent form Aged 11-15 and PIS for Children who turn 16 be updated to include detail that a urine pregnancy test will be completed at baseline (visit 1) and if the test is positive you will not be able to take part in the study.

22-NREC-CT-167_Mod-2

Institutions: CHI Crumlin

Study title: LOGGIC/FIREFLY-2: A Phase 3, Randomized, International Multicenter Trial of DAY101 Monotherapy Versus Standard of Care Chemotherapy in Patients with Pediatric Low-Grade Glioma Harboring an Activating RAF Alteration Requiring First-Line Systemic Therapy

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

- **Additional Information Required RFI**

- The NREC-CT noted that Informed Consent Form – Parental Main pg 37 is seeking blanket consent for future use of samples/data for unspecified purposes without further consent. These stored samples can be used for future research purposes by the Study Sponsor. “This may include advances in the diagnosis and understanding of your child’s pLGGO” 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 requested that future research is restricted to research in the area of nervous system diseases and/or the study drug and this is clearly stated in the main body and informed consent sections of the Informed Consent Form – Parental Main pg 42.The Committee also requests that any future use of biological samples is reviewed by an ethics committee and requested that this is captured in the PISCFs.
- The NREC-CT requested that Informed Consent Form Participant Main (16+) pg 3 and Informed Consent Form Parental Main pg 3 be updated to include reference to the Irish regulatory authority rather than just reference to the FDA.
- The NREC-CT noted that the advertising provided for review appears to be aimed at adults. The Committee requested that age-appropriate advertising for children / adolescents also be provided.
- The NREC-CT noted the extensive amendments to Informed Consent Form Parental Main and Informed Consent Form Participant Main (16+) and requested that both the documents be given a full editorial check for typos and grammatical errors. For example, the Committee noted the following on Informed Consent Form Parental Main (please note this is not an exhaustive list):
    - Day101 has not been consistently replaced with Tovorafenib throughout for example, in the Informed Consent Form Parental Main, pg 4 it states: *“If your child receives SoC chemotherapy and your child’s tumour gets worse progresses while receiving SoC chemotherapy your child may have the option to receive DAY101 if the study doctor thinks this is a good option for your child”* and the Frequency of site visits table at end of pg 8 which has the heading DAY101.
    - Pg 6 “What are my child’s responsibilities if my child takes part in this study?” should be updated to read “What are my responsibilities if my child takes part in this study?” as the responsibilities refer to those required from the parent.
    - pg17 Radiation risks be updated to refer to “your child” rather than “you”
    - pg 18 paragraph 3, be updated to refer to “your child’s blood” rather than to “your blood”.
- The NREC-CT requested that in the Informed Consent Form Parental Main pg 4 and the Informed Consent Form Participant Main (16+) pg 4 where it states “you will no

longer receive tovorafenib or SoC chemotherapy provided as part of the study" be updated to provide clarity that SoC treatment would still be available to participants as part of normal clinical care'.

- The NREC-CT noted the Informed Consent Form Parental Main p.7 states: "All attempts will be made to protect your child's identity" and requested that it be replaced with "Every effort will be made to protect your child's identity". The Committee also requested that the Informed Consent Form Parental Main p.7 be updated to specify how data protection will be dealt with e.g. through de-identification.
- The NREC-CT noted the Informed Consent Form Participant Main (16+) p.6 states: "All attempts will be made to protect your identity" and requested that it be replaced with "Every effort will be made to protect your identity". The Committee also requested that the Informed Consent Form Participant (16+) p.6 be updated to specify how data protection be dealt with, e.g. through de-identification.
- The NREC-CT noted the wording on Informed Consent Form Parental Main p.9 *"If your child's scan shows the tumour has grown at Week 12 but your child is not having any symptoms, the study doctor may decide to keep your child on tovorafenib until the next scan at Week 24. The study doctor will decide what is best for your child".* The Committee requested that a sentence "This will be discussed with you and your child at the time" be added to ensure participants/parents are aware that any tumour growth will be discussed with them.
- The NREC-CT noted the wording on Informed Consent Form Participants 16+ p.9 *"If your scan shows the tumour has grown at Week 12 but you are not having any symptoms, the study doctor may decide to keep you on tovorafenib until the next scan at Week 24. The study doctor will decide what is best for you".* The Committee requested that a sentence "This will be discussed with you at the time" be added to ensure participants are aware that any tumour growth will be discussed with them.
- The NREC-CT noted that Informed Consent Form Participant 16+ pg 32 and Informed Consent Form Parental Main p.32 have removed reference to reimbursement of accommodation costs and meals. The Committee requested that this be reinserted as accommodation and meal costs should be reimbursed for both participant and parent/carer.
- The NREC-CT recommended that Informed Consent Form Participant 16+ pg 32 and Informed Consent Form Parental Main p.32 be updated to include detail around how reimbursements will be managed and how often reimbursements will be made.
- The NREC-CT requested that pg 5 Informed Consent Form Assent 13-15 yrs be updated to list the most comment side effects.
- The NREC-CT note the consent for processing of data for 16/17 year olds on pg 42 Informed Consent Form Participant 16+ and Informed Consent Form Parental Main p.43 as previously requested by the NREC. The Committee wish to advise of a recent national policy change informed by discussions at a national level with relevant authorities: participants aged 16yrs+ may consent to both participation in a regulated study and associated data processing. Therefore, the consent for participation in the study and use of personal data for the study, should not be treated separately. As such, there is now no requirement to seek consent from a parent/guardian for data processing for participants aged 16 and17. The National Office is currently finalising guidance on this change. Once finalised, this guidance will be made available on the National Office website.

We acknowledge that this 'decoupled' change to the consent process was initially incorporated by Sponsors at the request of the NRECs. We hope this policy change is viewed as more pragmatic and facilitative for those involved in the recruitment process.

- **AOB:**
  - The EUREC compensation for research participants was discussed.