National Research Ethics Committee

NREC-CT A Meeting

9th of February 2022

Attendance

Name	Role
Prof. Alistair Nichol	Chairperson, NREC-CT A
Prof. Mary Donnelly	Deputy Chairperson, NREC-CT A
Dr Heike Felzmann	Deputy Chairperson, NREC-CT A
Prof. Tina Hickey	Committee Member, NREC-CT A
Dr Dervla Kelly	Committee Member, NREC-CT A
Dr Jimmy Devins	Committee Member, NREC-CT A
Mr Gerard Daly	Committee Member, NREC-CT A
Prof. Patrick Dillon	Committee Member, NREC-CT A
Ms Ann Twomey	Committee Member, NREC-CT A
Prof. Catherine Hayes	Committee Member, NREC-CT A
Ms Muireann O'Briain	Committee Member, NREC-CT A
Prof. David Brayden	Committee Member, NREC-CT A
Prof. Gene Dempsey	Committee Member, NREC-CT A
Dr Darren Dahly	Committee Member, NREC-CT A
Ms Aileen Sheehy*	Programme Manager, National Office for RECs
Dr Laura Mackey*	Project Officer, National Office for RECs
Dr Marta Pisarska	HRB Postdoctoral Intern, National Office for RECs

*Drafted minutes

Apologies: Dr John O'Loughlin, Prof. John Wells, Dr Geraldine Foley

Quorum for decisions: Yes

Agenda

- Welcome & Apologies
- 22-NREC-CT-014
- 22-NREC-CT-015
- 22-NREC-CT-017
- 22-NREC-CT-018
- 22-NREC-CT-019
- AOB

- The Chair welcomed the NREC-CT A.
  - The minutes from the previous NREC-CT A meeting on 12th of January 2022 were approved.
  - The NREC Business Report was discussed and noted.

Applications

22-NREC-CT-014

- Principal Investigator: Prof. David Keegan

Study title: Phase 3 Randomized, Controlled Study of AAV5-hRKp.RPGR for the Treatment of X-linked Retinitis Pigmentosa Associated with Variants in the RPGR gene

Lead institution: Mater Misericordiae University Hospital

- NREC-CT comments:

- The NREC-CT A noted that this study represents a Phase 3 Randomized, Controlled Study of AAV5-hRKp.RPGR for the Treatment of X-linked Retinitis Pigmentosa Associated with Variants in the RPGR gene.
- The NREC-CT A recognised that this is a much needed and worthwhile study in this disease area.
- The NREC-CT A agreed that additional information was required to inform its deliberations before a final ethics position could be returned.

- NREC-CT Decision:

- Request for Further Information

- Further Information Requested:

- The NREC-CT A queried why studies 22-NREC-CT-014 and 22-NREC-CT-015 were split into two separate trials and requests justification for the rationale.
- The NREC-CT A noted that some of the study questionnaires asks what may be considered invasive questions in relation to the sexual history and preferences of participants and requested justification for the inclusion of these questions or removal from the study.
- The NREC-CT A noted that only 3 female participants will be recruited in Ireland and requested information on the protections in place to protect the identity of this small and potentially identifiable cohort.
- The NREC-CT A was of the view that some of the questions within the questionnaires could lead to negative feelings and requested further information on supports available to participants if they became distressed or upset while completing the questionnaires.
- The NREC-CT A found the clinical justification for 41% efficacy to be limited and requested that further information is provided on this, and also requested that the potential benefits of the study are not overstated in the participant materials.
- The NREC-CT A queried whether this could be the first time participants find out they have the variant on the X chromosome and if so, would genetic counselling be made available to participants?
- The NREC-CT A considered the content in the PIL too complex for a lay audience and requested that it is revised and restructured to ensure the document is accessible to all participants. The Committee also requested that a brief plain English executive summary of the salient points of the study is included at the beginning of the PIL.
- The NREC-CT A requested further information on the location of the maze and the potential distance from the Mater site, and for it to be included in the participant materials.
- The NREC-CT A requested that the participant materials include time estimates for the completion of questionnaires and include an estimate of any school or work time that may be missed.
- The NREC-CT A noted that participants would be interviewed as part of the trial and requested justification for why separate consent would not be sought for the interview process, given that qualitative data is difficult to anonymise.
- The NREC-CT A requested that the Parental Consent form includes reference to the child's own consent being obtained once they come of age.
- The NREC-CT A noted that the Main ICF begins with the instruction to sign and requested that this is amended to state that the PIL should be read and discussed in advance of signing.

- The NREC-CT A noted that the assent forms cover ages 6-10 and 12-15 years and requested that minors aged 11 years are captured in one of these forms.
- The NREC-CT A requested clarification on whether out-of-pocket expenses will include loss of earnings and to clarify this in the participant materials.
- The NREC-CT A requested that the participant materials make reference to information related to private insurance and any potential impacts is included.
- The NREC-CT A noted that the PIL includes a statement '*In addition the sponsor will retain your coded data for time periods as allowed per applicable laws for the identified use*'. The Committee requested further information about this statement as the implications are not clear.
- The NREC-CT A requested clarification on whether paediatric participants would be recruited to the trial at Irish sites, where these participants would be recruited from and the process in place for recruitment.
- Due to the low numbers of participants anticipated to be recruited in Ireland, the NREC-CT A requested clarification on whether the adverts shared with the Committee for review would be used in Ireland.
- The NREC-CT A noted that those lacking capacity would be excluded from the study. The Committee supports the principles that capacity should always be presumed until proven otherwise and requested further information on the process in place to assess capacity.
- The NREC-CT A requested further information on whether the results from the previous studies would be made available to potential participants in advance of participating in the trial.
- The NREC-CT A noted that the insurance certificate provided does not cover the full duration of the trial and requested assurances that cover will be in place for the full duration of the trial.
- The NREC-CT A requested further information on the funding available for this study.
- The NREC-CT A noted the consent process for the future use of biological samples and data is not in line with national regulations on 'explicit consent' (the Health Research Regulations 2018) and requested that the applicant provides the participant with specific choices as to how their samples and data will be used for future purposes, such as limiting future use to a specific disease area.
- Further to the above, NREC-CT A requested confirmation that any future research project using samples or data from participants involved in this study would undergo full ethics review and that this would be captured in the participant materials.
- The NREC-CT A requested that consent for future biomedical research is separated out from the main consent form.
- The NREC-CT A requested that reference to the Health Research Regulations is included in the DPIA.
- The NREC-CT A requested further information on the aims and scope of data collection.

- The NREC-CT A requested further information on whether data will be transferred to a third country.
- The NREC-CT A requested an outline as to how personal data will be handled in line with relevant legislation through-out the lifecycle of the study.

22-NREC-CT-015

- Principal Investigator: Prof. David Keegan

Study title: Phase 3 Follow-up Study of AAV5-hRKp.RPGR for the Treatment of X-linked Retinitis Pigmentosa Associated with Variants in the RPGR gene

Lead institution: Mater Misericordiae University Hospitalv

- NREC-CT comments:

- The NREC-CT A noted that this study represents a Phase 3 Follow-up Study of AAV5-hRKp.RPGR for the Treatment of X-linked Retinitis Pigmentosa Associated with Variants in the RPGR gene.
- The NREC-CT A recognised that this is a much needed and worthwhile study in this particular disease area.
- The NREC-CT A agreed that additional information was required to inform its deliberations before a final ethics position could be returned.

- NREC-CT Decision:

- Request for Further Information

- Further Information Requested:

- The NREC-CT A queried why studies 22-NREC-CT-014 and 22-NREC-CT-015 were split into two separate trials and requested justification for the rationale.
- The NREC-CT A noted that some of the study questionnaires asked what may be considered invasive questions in relation to the sexual history and preferences of participants and requested justification for the inclusion of these questions or removal from the study.
- The NREC-CT A noted that only 3 female participants will be recruited in Ireland and requested information on the protections in place to protect the identity of this small and potentially identifiable cohort.
- The NREC-CT A was of the view that some of the questions within the questionnaires could lead to negative feelings and requested further information on supports available to participants if they become distressed or upset while completing the questionnaires.

- The NREC-CT A found the clinical justification for 41% efficacy to be limited and requests that further information is provided on this. The Committee also requested that the potential benefits of the study are not overstated in the participant materials.
- The NREC-CT A queried whether this could be the first time participants find out they have the variant on the X chromosome and if so, would genetic counselling be made available to participants?
- The NREC-CT A noted that no specific sample size estimate was provided for this study and requested that this is submitted.
- The NREC-CT A considered the content in the PIL too complex for a lay audience and requested that it is revised and restructured to ensure the document is accessible to all participants. The Committee also requested that a brief plain English executive summary of the salient points of the study is included at the beginning of the PIL.
- The NREC-CT A requested further information on the location of the maze and the potential distance from the Mater site, and for it to be included in the participant materials.
- The NREC-CT A requested that the participant materials include time estimates for the completion of questionnaires and include an estimate of any school or work time that may be missed.
- The NREC-CT A noted that participants would be interviewed as part of the trial and requested justification for why separate consent would not be sought for the interview process, given that qualitative data is difficult to anonymise.
- The NREC-CT A requested that the Parental Consent form includes reference to the child's own consent being obtained once they come of age.
- The NREC-CT A noted that the Main ICF begins with the instruction to sign and requested that this is amended to state that the PIL should be read and discussed in advance of signing.
- The NREC-CT A noted that the assent forms cover ages 6-10 and 12-15 years and requested that minors aged 11 years are captured in one of these forms.
- The NREC-CT A requested clarification on whether out-of-pocket expenses would include loss of earnings and to clarify this in the participant materials.
- The NREC-CT A requested that the participant materials make reference to information related to private insurance and any potential impacts is included.
- The NREC-CT A noted that the PIL includes a statement '*In addition the sponsor will retain your coded data for time periods as allowed per applicable laws for the identified use*'. The Committee requested further information about this statement as the implications are not clear.
- The NREC-CT A requested clarification on whether paediatric participants would be recruited to the trial at Irish sites, where these participants will be recruited from and the process in place for recruitment.
- Due to the low numbers of participants anticipated to be recruited in Ireland, the NREC-CT A requested clarification on whether the adverts shared with the Committee for review would be used in Ireland.

- The NREC-CT A noted that those lacking capacity would be excluded from the study. The Committee supports the principles that capacity should always be presumed until proven otherwise and requested further information on the process in place to assess capacity.
- The NREC-CT A requested further information on whether the results from the previous studies would be made available to potential participants in advance of participating in the trial.
- The NREC-CT A noted that the insurance certificate provided does not cover the full duration of the trial and requested assurances that cover will be in place for the full duration of the trial.
- The NREC-CT A requested further information on the funding available for this study.
- The NREC-CT A noted the consent process for the future use of biological samples and data is not in line with national regulations on 'explicit consent' (the Health Research Regulations 2018) and requested that the applicant provides the participant with specific choices as to how their samples and data will be used for future purposes, such as limiting future use to a specific disease area.
- Further to the above, NREC-CT A requested confirmation that any future research project using samples or data from participants involved in this study would undergo full ethics review and that this would be captured in the participant materials.
- The NREC-CT A requested that consent for future biomedical research is separated out from the main consent form.
- The NREC-CT A requested that reference to the Health Research Regulations is included in the DPIA.
- The NREC-CT A requested further information on the aims and scope of data collection.
- The NREC-CT A requested further information on whether data will be transferred to a third country.
- The NREC-CT A requested an outline as to how personal data will be handled in line with relevant legislation through-out the lifecycle of the study.

22-NREC-CT-017

- Principal Investigator: Dr Damian Griffin

Study title: A Phase 3 Study to Evaluate the Efficacy and Safety of ARO-APOC3 in Adults with Familial Chylomicronemia Syndrome

Lead institution: University Hospital Galway

- NREC-CT comments:

- The NREC-CT A noted that this study represents a Phase 3 Study to Evaluate the Efficacy and Safety of ARO-APOC3 in Adults with Familial Chylomicronemia Syndrome.

- The NREC-CT A commented positively on the overall presentation of this application.
- The NREC-CT A agreed that additional minor clarifications were required to inform its deliberations before a final ethics position could be returned.

  - NREC-CT Decision:

- Request for Further Information

  - Further Information Requested:

- The NREC-CT A noted that two sub-studies would be available to participants and while the Committee regarded the pharmacokinetic sub-study as well-communicated, it requested further information related to the second sub-study. This information would need to be further elucidated in the participant materials to ensure participants are fully informed.
- The NREC-CT A considered the information included in the PI CV to be limited and requested that a more comprehensive CV is resubmitted.

22-NREC-CT-018

- Principal Investigator: Dr Dearbhaile Collins

Study title: A Phase 3, Randomized, Double-Blind Study of MK-7684A in Combination with Etoposide and Platinum Followed by MK-7684A vs Atezolizumab in Combination with Etoposide and Platinum Followed by Atezolizumab for the First-Line Treatment of Participants with Extensive-Stage Small Cell Lung Cancer

Lead institution: Cork University Hospital

  - NREC-CT comments:

- The NREC-CT A noted that this study represents a Phase 3, Randomized, Double-Blind Study of MK-7684A in Combination with Etoposide and Platinum Followed by MK-7684A vs Atezolizumab in Combination with Etoposide and Platinum Followed by Atezolizumab for the First-Line Treatment of Participants with Extensive-Stage Small Cell Lung Cancer.
- The NREC-CT A praised the clarity and accessibility of the participant materials in particular.
- While the NREC-CT A noted that while the application well-structured and comprehensive, additional information was required to inform its deliberations before a final ethics position could be returned.

  - NREC-CT Decision:

- Request for Further Information

- Further Information Requested:

- The NREC-CT A considered that the way some of the information in the PIL is presented could be misleading for participants e.g. 'If the drugs works and if your cancer gets better, you may receive a health benefit'. The Committee requested that the language is amended to reflect the reality that if the drug is effective, it may slow the progression of the cancer.
- The NREC-CT A could not find the Pregnant Partner form in the documentation submitted and requested that this is submitted as part of the response to the request for further information.
- The NREC-CT A was complementary on the approach taken to reimbursement of expenses and requested that the PIL is furnished with a contact point or a brief summary of the claims process around expenses.
- The NREC-CT A requested further information related to the purpose of the Delegation of Authority documentation submitted and would like further clarification as to which organisation holds responsibility in the event of harm or injury arising as part of participation in the trial. This should also be clarified in the participant materials.
- The NREC-CT A requested confirmation that any future research project using samples or data from participants involved in this study will undergo full ethics review, and that this also be captured in the participant materials.
- The NREC-CT A noted that the FBR would be based on leftover samples, however the FBR PIL refers to injury and harm as a result of participation in the FBR. The Committee requested clarification related to this point or a correction if it is an error.
- The NREC-CT A noted that the FBR PIL states that there is a potential risk that people other than the Sponsor may have access to the participant's data. The Committee viewed this as a major breach to the privacy of participants and requested further clarification around this point.
- The NREC-CT A noted that the specifics of the budget were under negotiation at site level and requested confirmation that funding for this study had been secured in advance of submission and for how much.

22-NREC-CT-019

- Principal Investigator: Dr Beatrice Nolan

Study title: A multicenter, open-label phase IV study to evaluate overall health, physical activity, and joint outcomes, in participants aged ≥ 13 and < 70 years with severe or moderate hemophilia a without Fviii inhibitors on Emicizumab prophylaxis

Lead institution: Children's Health Ireland (CHI) at Crumlin

- NREC-CT comments:

- The NREC-CT A noted that this study represents a multicenter, open-label phase IV study to evaluate overall health, physical activity, and joint outcomes, in participants aged ≥ 13 and < 70 years with severe or moderate hemophilia a without Fviii inhibitors on Emicizumab prophylaxis.
- The NREC-CT A commented that this application was well-presented overall, and was an important and pragmatic study.
- While the NREC-CT A agreed that additional clarifications were required before a final ethics position could be returned.

- NREC-CT Decision:

- Request for Further Information

- Further Information Requested:

- Noting several discrepancies in the duration of the trial across the documentation provided the NREC-CT A requested clarity around this point and requested that the relevant documents are amended to ensure consistency.
- The NREC-CT A requested clarity in relation to a statement where it described this submission as not being related to a similar application previously submitted, yet the cover letter described the study as a 'resubmission'.
- The NREC-CT A noted that the age of recruited participants would be >12 years and requested clarity on whether recruitment will begin from the age of 12 or 13 years.
- The NREC-CT A noted that the GCP certificate on the CV is out of date and requested confirmation that the Investigator has updated their training.
- The NREC-CT A requested that a brief plain English executive summary of the salient points of the study is included at the beginning of the PIL, outlining the aim of the study.
- the the NREC-CT requested that the time potential participants were afforded to consider their participation in the trial before consenting is included in the PIL.
- The NREC-CT A noted that some of the information in the PIL related to sites in the US and requested that this information is removed from the PIL.
- The NREC-CT A noted a large volume of questionnaires that must be completed by minors and requested further information around the supports available for these young people to complete these questionnaires in an accurate manner.
- In Irish legislation, consent for trial participation is aged 16 while consent for use of data for health research purposes is 18 years of age. To ensure that these participants are fully involved in the decision-making process, for 16- to 18-year-olds, the NREC-CT A suggested that consent for data protection is separated from consent for participation.

- The NREC-CT A requested that the '*in the event of injury'* section in the PIL is further elucidated to include clear information to participants on the processes in place in the event of injury.
- The NREC-CT A noted that the study drug would be made available to participants after the trial and requested clarification around the general availability of the treatment in Ireland.
- The NREC-CT A noted that in the event of pregnancy, '*your parent or guardian might find out'.* Due to the potential impact this might have on the young person, the NREC-CT A requested that the language is changed to use definitive language whether a participant's parent or guardian will or won't find out.

- AOB:

  The Chair provided an update to the Committee regarding substantial amendments, and the large number of submissions being received by the National Office at present. The Chair described ongoing communications with the Dept. of Health, highlighting the significant workload associated with reviewing a substantial amendment submission, and the finite resources of the NRECs. The Chair noted that a number of solutions have been presented to the Dept. of Health and the National Office is awaiting response before any changes to existing processes are implemented.

- The Chair closed the meeting.