National Research Ethics Committee

NREC-CT A Meeting

12th January 2022

Attendance

Name	Role
Prof. Mary Donnelly<	Deputy Chairperson, NREC-CT A
Dr Heike Felzmann	Deputy Chairperson, NREC-CT A
Dr John O'Loughlin	Committee Member, 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. John Wells	Committee Member, NREC-CT A
Dr Geraldine Foley	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

<Chaired meeting

*Drafted minutes

Apologies: Prof. Alistair Nichol

Quorum for decisions: Yes

Agenda

- Welcome & Apologies
- 21-NREC-CT-170
- 21-NREC-CT-171
- 21-NREC-CT-172
- 21-NREC-CT-173
- 21-NREC-CT-174
- AOB

- The Chair welcomed the NREC-CT A.
  - The minutes from the previous NREC-CT A meeting on 17th November 2021 were approved.
  - The NREC Business Report was discussed and noted.

Applications

21-NREC-CT-170

- Principal Investigator: Dr Desmond Michael Murphy

Study title: A 52-week, randomised, double-blind, double-dummy, parallel group, multi-centre, non-inferiority study assessing exacerbation rate, additional measures of asthma control and safety in adult and adolescent severe asthmatic participants with an eosinophilic phenotype treated with GSK3511294 compared with mepolizumab or benralizumab

Lead institution: Cork University Hospital

  - NREC-CT comments:

- The NREC-CT A noted that this application represents a 52-week, randomised, double-blind, double-dummy, parallel group, multi-centre, non-inferiority study assessing exacerbation rate, additional measures of asthma control and safety in adult and

adolescent severe asthmatic participants with an eosinophilic phenotype treated with GSK3511294 compared with mepolizumab or benralizumab.

- The NREC-CT A commented that this application was impressive overall.
- While the NREC-CT A noted that while the application was clearly presented, 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 whether the number of 'in person' visits could be reduced in favour of remote or virtual visits outside of the provisions specified for COVID-related planning.
- The NREC-CT A requested a copy of the Data Monitoring Committee Charter.
- The NREC-CT A noted that 245ml of blood will be extracted from participants and requested further information on the volume of blood obtained from participants, in particular minors, at individual study visits.
- The NREC-CT A requested further information whether the OLE study is limited to those on the study drug or whether it will also be open to those on the placebo arm.
- The NREC-CT A noted that an assent form is available for the main PIL / ICF but requested that an assent form is also made available for the separate genetic and biomarker consent forms, and future biomedical research consent form.
- The NREC-CT A requested that all documents are thoroughly proof-read to correct a number of typos and inconsistencies across the participant materials.
- The NREC-CT A requested further information on the supports available for participants in the event they become distressed in completing the quality of life questionnaires. This information and potential risks should also be captured in the participant materials.
- The NREC-CT A requested that further information on expenses is captured in the PIL such as information on how payment will be made and whether the retention of receipts will be required.
- The NREC-CT A requested that the PIL is furnished with further information on the expected time requirements for participants for each of the study visits.
- Under Irish legislation, the age of consent for participation in a clinical trial is 16 years while consent for the processing of personal data for health research purposes is 18. The NREC-CT A noted some discrepancies in the documentation around the age of consent and suggested that consent for participation and consent for data processing are separated in the participant materials to reflect this.

- The NREC-CT A noted that the term anonymisation is used where it should be pseudonymisation in some of the materials and requested that this inaccuracy is corrected.
- The NREC-CT A requested further information on whether out-of-pocket expenses will be covered as part of participation in the study.
- In the PIL, the NREC-CT A requested that the information on what to do if you experience side-effects should be separated from 'What side effects can you expect'.
- The NREC-CT A noted that the main PIL states that study staff may ask for names and contact information of some of your friends, which the Committee considered inappropriate and requested that it is removed from the PIL.
- The NREC-CT A noted that the PIL states on Page 6 '…the study doctor may tell your regular doctor…'. The Committee suggested that this should be amended to '…will tell your regular doctor…'.
- The NREC-CT A noted the possibility that an external recruitment campaign may be undertaken if an adequate number of participants cannot be identified across the trial sites. If this scenario were to arise, the NREC-CT A would require the submission of a substantial amendment with the relevant recruitment materials and information.
- The NREC-CT A noted that the text across the site suitability forms have been copied verbatim and requested confirmation that all the information provided across the different sites is accurate.
- The NREC-CT A requested CVs from the site Principal Investigators.
- 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 will undergo full ethics review. This should also 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 specific reference to GDPR in the participant materials.
- The NREC-CT A requested confirmation that data transferred outside of the EEA will be stored and processed in line with GDPR. This should also be captured in the participant materials.
- The NREC-CT A requested that a precise retention period is added for personal data in the PIL to ensure that the participant is adequately informed.
- The NREC-CT A requested that the PIL updated to include precise information on what happens to the participant data in the event of study withdrawal.
- The NREC-CT A noted that the PIL states that coded data will be shared with 'other companies, organisation as or universities to carry out research separate from GSK'. The

Committee considered this too broad and requested that the specific organisations / institutions are identified in the PIL.

- The NREC-CT A requested that specific safeguards regarding the transfer of personal information are outlined in the PIL.
- The NREC-CT A requested justification for the retention of blood samples for 15 years. This should also be captured in the PIL.
- The NREC-CT A requested further information on the funding in place for this study and any additional information around financial disclosures.
- The NREC-CT A requested that information regarding the potential impacts on personal health insurance is further elucidated and given more prominence in the PIL. Specifically, the Committee requested a clear statement or where the liability lies in all instances.

21-NREC-CT-171

- Principal Investigator: Dr Desmond Michael Murphy

Study title: A 52-week, randomised, double-blind, placebo-controlled, parallel-group, multi-centre study of the efficacy and safety of GSK3511294 adjunctive therapy in adult and adolescent participants with severe uncontrolled asthma with an eosinophilic phenotype

Lead institution: Cork University Hospital

- NREC-CT comments:

- The NREC-CT A noted that this application represents a 52-week, randomised, double-blind, placebo-controlled, parallel-group, multi-centre study of the efficacy and safety of GSK3511294 adjunctive therapy in adult and adolescent participants with severe uncontrolled asthma with an eosinophilic phenotype.
- The NREC-CT A acknowledged that this application was presented in a clear and comprehensive way
- The NREC-CT A agreed that additional clarification was required in a number of areas to inform its deliberations and was not in a position to return a final ethics opinion.

- NREC-CT Decision:

- Request for Further Information

- Further Information Requested:

- The NREC-CT A NREC-CT A queried whether the number of ‘in person’ visits could be reduced in favour of remote or virtual visits outside of the provisions specified for COVID-related planning.
- The NREC-CT A requested a copy of the Data Monitoring Committee Charter.

- The NREC-CT A noted that 245ml of blood will be extracted from participants and requested further information on the volume of blood obtained from participants, in particular minors, at individual study visits.
- The NREC-CT A requested further information whether the OLE study is limited to those on the study drug or whether it will also be open to those on the placebo arm.
- The NREC-CT A noted that an assent form is available for the main PIL / ICF but requested that an assent form is also made available for the separate genetic and biomarker consent forms, and future biomedical research consent form.
- The NREC-CT A requested that all documents are thoroughly proof-read to correct a number of typos and inconsistencies across the participant materials.
- The NREC-CT A requested further information on the supports available for participants in the event they become distressed in completing the quality of life questionnaires. This information and potential risks should also be captured in the participant materials.
- The NREC-CT A requested that further information on expenses is captured in the PIL such as information on how payment will be made and whether the retention of receipts will be required.
- The NREC-CT A requested that the PIL is furnished with further information on the expected time requirements for participants for each of the study visits.
- Under Irish legislation, the age of consent for participation in a clinical trial is 16 years while consent for the processing of personal data for health research purposes is 18. The NREC-CT A noted some discrepancies in the documentation around the age of consent and suggested that consent for participation and consent for data processing are separated in the participant materials to reflect this.
- The NREC-CT A noted that the term anonymisation is used where it should be pseudonymisation in some of the materials, and requested that this inaccuracy is corrected.
- The NREC-CT A requested further information on whether out-of-pocket expenses will be covered as part of participation in the study.
- In the PIL, the NREC-CT A requested that the information on what to do if you experience side-effects should be separated from ‘What side effects can you expect’.
- The NREC-CT A noted that the main PIL states that study staff may ask for names and contact information of some of your friends, which the Committee considered inappropriate and requested that it is removed from the PIL.
- The NREC-CT A noted that the PIL states on Page 6 ‘…the study doctor may tell your regular doctor…’. The Committee suggests that this should be amended to ‘…will tell your regular doctor…’.
- The NREC-CT A noted the possibility that an external recruitment campaign may be undertaken if an adequate number of participants cannot be identified across the trial sites. If this scenario were to arise, the NREC-CT A would require the submission of a substantial amendment with the relevant recruitment materials and information.

- The NREC-CT A noted that the text across the site suitability forms have been copied verbatim and requested confirmation that all the information provided across the different sites is accurate.
- The NREC-CT A requested CVs from the site Principal Investigators.
- 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 will undergo full ethics review. This should also 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 specific reference to GDPR in the participant materials.
- The NREC-CT A requested confirmation that data transferred outside of the EEA will be stored and processed in line with GDPR. This should also be captured in the participant materials.
- The NREC-CT A requested that a precise retention period is added for personal data is included in the PIL to ensure that the participant is adequately informed.
- The NREC-CT A requested that the PIL updated to include precise information on what happens to the participant data in the event of study withdrawal.
- The NREC-CT A noted that the PIL states that coded data will be shared with 'other companies, organisation as or universities to carry out research separate from GSK'. The Committee considered this too broad and requested that the specific organisations / institutions are identified in the PIL.
- The NREC-CT A requested that specific safeguards regarding the transfer of personal information are outlined in the PIL.
- The NREC-CT A requested justification for the retention of blood samples for 15 years. This should also be captured in the PIL.
- The NREC-CT A requested further information on the funding in place for this study and any additional information around financial disclosures.
- The NREC-CT A requested that information regarding the potential impacts on personal health insurance is further elucidated and given more prominence in the PIL. Specifically, the Committee requested a clear statement or where the liability lies in all instances.

21-NREC-CT-172

Principal Investigator: Professor Janice Walshe

Study title: EPIK-B5: A Phase III, randomized, double-blind, placebocontrolled study of alpelisib (BYL719) in combination with fulvestrant for men and postmenopausal women with HRpositive, HER2-negative advanced breast cancer with a PIK3CA mutation, who progressed on or after aromatase inhibitor and a CDK4/6 inhibitor

Lead institution: St Vincent's University Hospital

- NREC-CT comments:

- The NREC-CT A noted that this application represents a Phase III, randomized, double-blind, placebocontrolled study of alpelisib (BYL719) in combination with fulvestrant for men and postmenopausal women with HRpositive, HER2-negative advanced breast cancer with a PIK3CA mutation, who progressed on or after aromatase inhibitor and a CDK4/6 inhibitor.
- The NREC-CT A spoke positively about the application despite additional documentation requirements.
- The NREC-CT A agreed that additional information was required to inform its deliberations, before a final ethics decision could be returned.

- NREC-CT Decision:

- Request for Further Information

- Further Information Requested:

- 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 NREC-CT A requested that the GP letter is updated to reflect the 6 participants across 3 sites in Ireland.
- The NREC-CT A requested further information on the trial experience of the site PIs at the sites other than the chief PI.
- The NREC-CT A noted the possibility that an external recruitment campaign may be undertaken if an adequate number of participants cannot be identified across the trial sites. If this scenario were to arise, the NREC-CT A would require the submission of a substantial amendment with the relevant recruitment materials and information.
- The NREC-CT A requested assurances that the vulnerability of this very seriously ill participant cohort is taken into account, and that participation in the trial is not 'oversold' to potential participants by the investigators during the recruitment phase, while recognising the individual's choice in how they wish to manage their therapy.
- The NREC-CT A noted that a recruitment brochure was included with the application and requested further confirmation that recruitment will not be through advertising.
- Although the applicant provided a letter related to data protection, the NREC-CT A considered this unacceptable for its purposes and required a completed DPIA with

evidence of DPO input as per NREC requirements. The NREC-CT A is not in a position to issue a final decision until this has been provided for review.

- The NREC-CT A requested further information on who will have access to identifiable participant information as part of this study.
- The NREC-CT A noted that samples will be held for 15 years and requested further justification for this retention period. Rationale for this sample retention period should also be included in the PIL.
- The NREC-CT A requested further information on the funding in place for this study and any additional information around financial disclosures.

21-NREC-CT-173

Principal Investigator: Dr Valerie Byrnes

Study title: A phase IIb, double-blind, randomised, placebo-controlled trial to evaluate the efficacy and tolerability of ZED1227 in celiac disease subjects experiencing symptoms despite gluten-free diet

Lead institution: University Hospital Galway

- NREC-CT comments:

- The NREC-CT A noted that this application represents A phase IIb, double-blind, randomised, placebo-controlled trial to evaluate the efficacy and tolerability of ZED1227 in celiac disease subjects experiencing symptoms despite gluten-free diet.
- The NREC-CT A spoke positively about a number of aspects of this study.
- The NREC-CT A agreed that additional information was required to inform its deliberations, before a final ethics decision could be returned.

- NREC-CT Decision:

- Request for Further Information

- Further Information Requested:

- The NREC-CT A considered that the information available on allocation concealment is limited and requested a more detailed description of the process in place, in particular how concealment will be ensured, including the packaging of the IMP and placebo.
- The NREC-CT A requested further information on this exclusion criterion at the end of an extensive screening period, specifically to understand the likely frequency at which a participant would surpass a VH/CrD ratio greater than 2 and the rationale behind it.
- The NREC-CT A noted that three conditions will be examined as part of the interim analysis. The NREC-CT A considered that the first condition is well explained, but the two others lacked detail. The Committee requested further information on these

conditions and their potential impact on the operating characteristics of the trial in terms of error-control.

- The NREC-CT A queried why the EQ5D is administered through paper form rather than electronic form?
- The NREC-CT A requested further information on the planned exclusion of those lacking decision-making capacity from the study.
- The NREC-CT A noted that many sections within the application form were not adequately completed e.g., Sections D2 and D7 and requested that the application form is adequately completed and resubmitted as part of the response to the Request for further information.
- 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 NREC-CT A noted that the participant diary is quite long and queried whether it could be reduced without impacting the trial aim?
- The NREC-CT A requested further information on the following points in relation to financial arrangements at hospital sites;
    - How the 'per patient fee' will be broken down,
    - Compensation for hospital resources such as endoscopes,
    - Specific details on resources available for specific procedures related to the trial,
    - Confirmation that the hospitals involved have agreed on the appropriate compensation.

21-NREC-CT-174

Principal Investigator: Dr Michelle Marie O'Shaughnessy

Study title: A Phase 3, Randomized, Double-blind, Placebo-controlled Study of Atrasentan in Patients with IgA Nephropathy at Risk of Progressive Loss of Renal Function (The ALIGN Study)

Lead Institution: Cork University Hospital

- NREC-CT comments:

- The NREC-CT A noted that this application represents a Phase 3, Randomized, Double-blind, Placebo-controlled Study of Atrasentan in Patients with IgA Nephropathy at Risk of Progressive Loss of Renal Function (The ALIGN Study).
- The NREC-CT A commented that this was a well-written application and in particular, spoke positively about the approach to participant reimbursement.
- The NREC-CT A agreed that it was not in a position to return a final ethics opinion and that further information was required to inform its deliberations.

- NREC-CT Decision:

- Request for Further Information

- Further Information Requested:

- The NREC-CT A requested that a definition of ‘independent’ is provided in relation to the ‘Independent Data Monitoring Committee’.
- The NREC-CT A requested further details on the Data Monitoring Committee (DMC). In particular will recommendations made from this committee be mandatory or advisory; to whom will it report and who has final decision-making authority if a dispute between the research team and the committee should arise?
- The NREC-CT A requested specifics as to the frequency of the DMC meetings
- The NREC-CT A sought clarification on why women of child-bearing age were not selected as a potential participant cohort in the application form.
- The NREC-CT A requested clarity on the intended number of participants in Ireland that will be recruited to the study.
- The NREC-CT A requested further information on how the recruitment brochure included in the application will be used.
- 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 and right not to participate.
- The NREC-CT A noted a number of typos and inconsistencies across the PIL and requested that all documents are thoroughly proof-read for accuracy.
- The NREC-CT A requested that the PIL includes the potential for currently unknown side-effects that may arise over the duration of the trial.
- The NREC-CT A requested that the PIL is adapted to specify that participants can to speak to their GP about any medical problem that may be related to trial participation, as the current PIL seems to encourage participants to only talk to clinicians involved in the trial in the first instance when a medical issue arises.
- The NREC-CT A requested further information on the procedures in place if the participant cannot reach the investigator or a member of the research team by phone in the event of injury or harm.
- To improve readability, the NREC-CT A suggested that the frequency of side-effects is given as frequency (1 in xx) as well as percentages.
- The NREC-CT A requested confirmation that data transferred outside of the EEA will be stored and processed in line with GDPR. This confirmation should be included in the PIL with a list of jurisdictions where the data will be transferred to.
- The NREC-CT A requested that the data controller is clearly identified in the participant materials.

- The NREC-CT A requested further justification for a sample retention period of 25 years. Rationale for this sample retention should also be included in the PIL.
- The NREC-CT A noted discrepancies in the documentation on where the samples will be stored. The Committee requested confirmation as to where samples will be stored.
- The NREC-CT A requested that any potential impact on personal insurance is established by the research team in advance of the prospective participant agreeing to participate in the trial.
- In the event of injury or harm, the NREC-CT A noted that compensation may not be given to a participant depending on the competence of the participant to adhere the protocol. The Committee considered that this is an onerous burden to place on participants and requested further clarity around this caveat and an overview of how participant adherence will be assessed.

- AOB:
  - None

- The Chair closed the meeting.