|  |  |
| --- | --- |
| **Committee:** | Southern Health and Disability Ethics Committee |
| **Meeting date:** | 08 February 2022 |
| **Zoom details:** | <https://mohnz.zoom.us/j/96507589841> |

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| **Time** | **Review Reference** | **Project Title** | **Coordinating Investigator** | **Lead Reviewers** |
| 10:30am-11:00am | 2021 AM 4030 (14/STH/170) | Investigating the high incidence of Maori and Polynesian children with autoimmune neurological disease in New Zealand | Dr Hannah Jones | Mr Dominic Fitchett & Dr Devonie Waaka |
| 11:00am-11:30am | 2021 FULL 11925 | Emergency Department Elderly Head Injury Outcomes Study, ED-EM-HI (re-application) | Dr Devin Faragasso | Ms Kate O'Connor & Ms Amy Henry |
| 11:30am-12:00pm | 2021 FULL 11328 | Study of ATH434 in Participants With Multiple System Atrophy | Prof. Tim Anderson | Ms Catherine Garvey & Associate Professor Mira Harrison-Woolrych |
| 12:00pm-12:30pm | 2021 FULL 11842 | A study of inclisiran to prevent cardiovascular events in participants with established cardiovascular disease | Dr Jocelyne Benatar | Mr Jonathan Darby & Associate Professor Nicola Swain |
| 12:40pm-1:10pm | 2022 FULL 11596 | Rectal tissue concentrations of thioguanine in inflammatory bowel disease | Professor Murray Barclay | Ms Kate O'Connor & Ms Amy Henry |
| 1:10pm-1:40pm | 2022 FULL 10999 | GSN000350: A Phase 2b/3 Trial of Setanaxib with a 52-week Extension Phase in patients with PBC and Elevated Liver Stiffness | Dr Andrew Knox | Mr Jonathan Darby & Associate Professor Nicola Swain |
| 1:40pm-2:10pm | 2022 FULL 11982 | Phase 1 study to assess safety, tolerability, and the immune response KJ103 in healthy adults | Principal Investigator Mark Marshall | Mr Dominic Fitchett & Associate Professor Mira Harrison-Woolrych |
| 2:10pm-2:40pm | 2022 FULL 11228 | Treatment-induced neuroplasticity in children who stutter | Mrs Fathiya Al'Amri | Ms Catherine Garvey & Dr Devonie Waaka |
| 2:50pm-3:20pm | 2022 FULL 11811 | FINER - Phase III Fulvestrant and Ipatasertib for Advanced HER2-, ER+ Breast Cancer | Dr. Sheridan Wilson | Ms Catherine Garvey & Associate Professor Nicola Swain |
| 3:20pm-3:50pm | 2022 EXP 11833 | Genes and exposures in PD | Dr Toni Pitcher | Mr Dominic Fitchett & Ms Amy Henry |
| 3:50pm-4:20pm | 2022 FULL 12095 | Vectorcardiography | Doctor Jessica Wong | Ms Kate O'Connor & Associate Professor Mira Harrison-Woolrych |
| 4:20pm-4:50pm | 2022 FULL 11866 | ETERNAL– A clinical trial comparing thrombolysis to standard care for ischaemic stroke presenting within 24 hours | Dr Teddy Wu | Mr Jonathan Darby & Dr Devonie Waaka |

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| **Member Name** | **Member Category** | **Appointed** | **Term Expires** | **Apologies?** |
| Dr Devonie Waaka | Non-lay (Intervention studies) | 18/07/2016 | 18/07/2019 | Present |
| Assc Prof Mira Harrison-Woolrych | Non-lay Intervention/Observational studies) | 28/06/2019 | 28/06/2020 | Present |
| Mr Anthony Fallon | Lay (Consumer/Community perspectives) | 13/08/2021 | 13/08/2024 | Apologies |
| Mr Dominic Fitchett | Lay (the Law) | 05/07/2019 | 05/07/2022 | Present |
| Ms Amy Henry | Non-lay (Observational studies) | 13/08/2021 | 13/08/2024 | Present |
| Ascc. Prof Nicola Swain | Non-lay Intervention/Observational studies) | 22/12/2021 | 22/12/2024 | Present |
| Mr Jonathan Darby (Co-opted) | Lay (the Law/Ethical and Moral reasoning) | 13/08/2021 | 13/08/2024 | Present |
| Ms Kate O’Connor (Co-opted) | Lay (Ethical/Moral reasoning) | 13/08/2021 | 16/08/2024 | Present |
| Ms Catherine Garvey (Co-opted) | Lay (the Law) | 19/03/2019 | 19/03/2022 | Present |

## Welcome

The Chair opened the meeting at 10.00am and welcomed Committee members, noting that apologies had been received from Mr Anthony Fallon. Ms Kate O’Connor of Northern B was appointed Chair for this Southern meeting.

The Chair noted that it would be necessary to co-opt members of other HDECs in accordance with the Standard Operating Procedures. Ms Kate O’Connor, Ms Catherine Garvey and Mr Jonathan Darby confirmed their eligibility, and were co-opted by the Chair as members of the Committee for the duration of the meeting.

The Chair noted that the meeting was quorate.

The Committee noted and agreed the agenda for the meeting.

## Confirmation of previous minutes

The minutes of the meeting of 14 December 2021 were confirmed.

## New applications

|  |  |  |
| --- | --- | --- |
| **1** | **Ethics ref:** | **(14/STH/170) 2021 AM 4030** |
| ­­­­ | Title: | Investigating the high incidence of Māori and Polynesian children with autoimmune neurological disease in New Zealand (Amendment) |
|  | Principal Investigator: | Dr Hannah Jones |
|  | Sponsor: |  |
|  | Clock Start Date: | 02 December 2021 |

Dr Hannah Jones was present via videoconference for discussion of this amendment.

Potential conflicts of interest

The Chair asked members to declare any potential conflicts of interest related to this application.

No potential conflicts of interest related to this application were declared by any member.

Summary of Study

1. The study aims to investigate autoimmune neurological disease in Australasian children. This involves accessing health information, questionnaires and HLA tissue testing. This discussion relates to the amendment submitted to extend study population from children 18 years and under only to include adults, extend the breadth of diseases studied to include other neuroinflammatory diseases, and add paediatric controls (excluded in the 26.06.2019 amendment).

Summary of resolved ethical issues

The main ethical issues considered by the Committee and addressed by the Researcher are as follows.

1. The Committee noted that this amendment changes the study significantly. They noted that this would be better submitted as a new study. After discussion, it was agreed that the adult portion of the study would be a new study application to the Southern HDEC while a paediatric control can be submitted as an amendment for this study, and approval for this study is maintained.

Summary of outstanding ethical issues

The main ethical issues considered by the Committee and which require addressing by the Researcher are as follows.

1. The Committee noted that as this is not a medical experiment (observational study), the potential participant’s power-of-attorney can consent. The Committee stated [Right 7(4) of the Code of Health and Disability Services Consumers’ Rights](https://www.hdc.org.nz/your-rights/about-the-code/code-of-health-and-disability-services-consumers-rights/) can be satisfied too, provided that family members only give their opinion on whether they believe their relative would be ok with participation to support the best-interests argument, but they cannot provide proxy-consent. The Committee requested formal documentation around the justification around how enrolment is legal using the above options, clarifying that family members are not consenting for the participant. *National Ethical Standards for Health and Disability Research and Quality Improvement, para 7.70, 7.71, 7.73, & 7.74)*
2. The Committee noted that the re-consent upon recovery process is not documented in the protocol and requested this is further clarified. *(National Ethical Standards for Health and Disability Research and Quality Improvement, para 9.7).*
3. The Committee stated that the amended questionnaire was not approved as part of the previously declined amendment and was not included in this submission for review. This questionnaire needs to be submitted to be approved.
4. The Committee stated that the statement that participants will not be given an option of receiving serious non-actionable results raises issues with rights to access as these results could impact life decisions and could be actionable in future. This needs to be looked at and addressed in both the amendment and new application.

**Decision**

This amendment was *declined* by consensus, as the Committee did not consider that the study would meet the ethical standards referenced above.

|  |  |  |
| --- | --- | --- |
| **2** | **Ethics ref:** | **2021 FULL 11925** |
|  | Title: | Emergency Department Elderly Head Injury Outcomes Study, ED-EM-HI (re-application) |
|  | Principal Investigator: | Dr Devin Faragasso |
|  | Sponsor: |  |
|  | Clock Start Date: | 27 January 2022 |

No researcher was present via videoconference for discussion of this application.

Potential conflicts of interest

The Chair asked members to declare any potential conflicts of interest related to this application.

No potential conflicts of interest related to this application were declared by any member.

Summary of Study

1. The primary aim of this study is to evaluate the clinical performance of a modified CTHEAD rule for predicting poor clinical outcomes in an undifferentiated cohort of all patients ≥ 65 years-old presenting to the participating EDs after minor head trauma.

Summary of outstanding ethical issues

The main ethical issues considered by the Committee and which require addressing by the Researcher are as follows.

1. The Committee stated that the waiver appears justifiable under National Ethical Standards for Health and Disability Research and Quality Improvement, para 7.46-7.48. The Committee noted however that as a waiver of consent is applicable to this study, the Participant Information Sheet (PIS) should not be used as participants will not be approached regarding study participation. Please amend the documentation to reflect that a consent of waiver has been formally sought and remove all reference to informing participants and use of the PIS. The Committee has found the waiver justifiable and have granted it on the provision the PIS is not to be used.
2. The Committee stated more information in the data management plan (DMP) is required than what is available in the study documentation to satisfy the Committee that privacy and confidentiality is protected and that Standard 12.15a is met. Use of the HDEC template from the [HDEC website](https://ethics.health.govt.nz/guides-templates-and-forms/) is not mandatory but is encouraged to be adapted or used as a guide/starting point to ensure all detail is included.
3. The Committee noted that mortality data sources should be gathered also from discharge summaries and Ministry of Health registries rather than reliance on coronial records.
4. The Committee could not see evidence that the peer review comments were either incorporated as changes or justification for the rebuttal documented. Please provide this, particularly on why people on anticoagulants are excluded as the peer reviewer commented these are a large and important group to follow.
5. The Committee stated that Māori consultation is required and asked that those consulted with be informed that a waiver of consent has been granted.

**Decision**

This application was *provisionally approved* by consensus, subject to the following information being received:

1. Please address all outstanding ethical issues, providing the information requested by the Committee.
2. Please amend the protocol to remove references to approaching patients regarding contribution of their data to the study.
3. Please confirm that the participant information sheet will not be used.
4. Please amend the data management plan to ensure the safety and integrity of participant data. This can be a standalone document or incorporated as part of the protocol *(National Ethical Standards for Health and Disability Research and Quality Improvement, para 12.15).*

After receipt of the information requested by the Committee, a final decision on the application will be made by Ms Kate O’Connor and Ms Amy Henry.

|  |  |  |
| --- | --- | --- |
| **3** | **Ethics ref:** | **2021 FULL 11328** |
|  | Title: | Study of ATH434 in Participants With Multiple System Atrophy |
|  | Principal Investigator: | Professor Tim Anderson |
|  | Sponsor: | Alterity Therapeutics Ltd |
|  | Clock Start Date: | 27 January 2022 |

Professor Tim Anderson and Laura Paermentier were present via videoconference for discussion of this application.

Potential conflicts of interest

The Chair asked members to declare any potential conflicts of interest related to this application.

No potential conflicts of interest related to this application were declared by any member.

Summary of Study

1. MSA is a rare and rapidly progressive neurodegenerative disease. It has a poor prognosis and usually leads to death within 6 to 10 years after diagnosis. Symptomatic therapy has significant limitations and there are no approved therapies that address the underlying pathology of disease. Based on its mechanism of action, the efficacy of ATH434 is expected to be achieved through disease modifying processes. By binding and redistributing excess iron in affected areas of the CNS, it is expected that ATH434 will inhibit α-synuclein aggregation and reduce oxidative stress. The net effect of treatment, if efficacious, would preserve neurons, thus stabilizing or even restoring function. Progression to disability is rapid in MSA, as more than half of patients become wheelchair bound within 5 years of disease onset. Thus, the beneficial effects of ATH434 effects would be expected to improve symptoms and patient quality of life.

Summary of resolved ethical issues

The main ethical issues considered by the Committee and addressed by the Researcher are as follows.

1. The Committee asked how many New Zealand participants are included. The Researchers explained that in Christchurch there will be probably be a maximum of 5, however this may change due to extra interest from other centres.
2. The Committee asked if the participants won’t be in nursing care and will still live at home. The Researchers confirmed this and further explained participants cannot be in care and must have a study companion who lives with them, not a nurse who just sees the participant.
3. The Committee asked how the Researchers plan to introduce the study to potential participants. The Researchers explained they will use the Parkinson’s database, participants who come through the clinic, and those who expressed interest in other studies will be asked if they want to participate in this study with all information provided.
4. The Committee asked about the risks of the studies and how many participants have been exposed in the Phase 1 study in healthy volunteers. The Researcher explained that they have had 88 healthy volunteers with no headaches or seizures.
5. The Committee asked about the reimbursement and how much New Zealand participants will be receiving. The Researcher explained they will receive 100 dollars per visit and travel expenses will also be fully reimbursed.

Summary of outstanding ethical issues

The main ethical issues considered by the Committee and which require addressing by the Researcher are as follows.

1. Pregnancy is a contra-indication to participation in this study and both female and male participants must use effective contraception. There is information about this in the participant information sheet (PIS), but it is not clear. The Committee requested use the [HDEC template](https://ethics.health.govt.nz/guides-templates-and-forms/participant-information-sheet-templates/) for contraceptive advice in the study PIS.
2. The Committee asked that the patient discusses participation with a Researcher not involved in their clinical care at some stage during the informed consent process. This provides the opportunity to decline away from the power imbalance of the doctor-patient relationship.
3. The Committee requested that processes are in place so that if participants withdraw from the main study, they are specifically asked whether they also wish to withdraw consent for future unspecified research (FUR).

The Committee requested the following changes to the Participant Information Sheet and Consent Form (PIS/CF):

All PIS/CFs

1. Please use the simple title provided in the application form as the main header for all PIS/CF documents.
2. Please check for typos throughout.
3. Please specify that this experimental medicine is not approved by Medsafe in New Zealand.
4. Please increase font size for visibility and easy reading.
5. Please check Māori kupu for consistent use of macrons (e.g., whānau).

Main PIS/CF

1. Please provide number of New Zealand participants.
2. Please state how the drug will be administered (i.e., injected under skin, into a vein, etc.)
3. Please use the HDEC template for contraception and reproductive risks (please do not include contraception methods which are unavailable in New Zealand). Ensure lay language in used rather than medical terms (e.g., 'inhibition of ovulation')
4. Please remove unnecessary detail on page 10.
5. Please simplify to state that all the different types of data are going to 'the USA' on page 14.

Partner PIS/CF

1. Please remove statements and sections not applicable to the partner (i.e., that apply only to the participant).
2. Please delete duplicative statements regarding confidentiality risk.
3. Please clarify that the reimbursement can be claimed by only one of the participants in the partner pair.

**Decision**

This application was *approved* by consensus, subject to the following non-standard conditions:

* please address all outstanding ethical issues raised by the Committee
* please update the Participant Information Sheet and Consent Form, taking into account the feedback provided by the Committee. *(National Ethical Standards for Health and Disability Research and Quality Improvement, para 7.15 – 7.17).*

|  |  |  |
| --- | --- | --- |
| **4** | **Ethics ref:** | **2021 FULL 11842** |
|  | Title: | A study of inclisiran to prevent cardiovascular events in participants with established cardiovascular disease |
|  | Principal Investigator: | Dr Jocelyne Benatar |
|  | Sponsor: | Novartis |
|  | Clock Start Date: | 27 January 2022 |

Dr Jocelyne Benatar and Cathrine Patten was present via videoconference for discussion of this application.

Potential conflicts of interest

The Chair asked members to declare any potential conflicts of interest related to this application.

No potential conflicts of interest related to this application were declared by any member.

Summary of Study

1. The primary objective of this study is to demonstrate the superiority of inclisiran compared to placebo in reducing the risk of 3P-MACE (composite of CV death, non-fatal MI and non-fatal ischaemic stroke) in participants with established ASCVD and an LDL-C > or = 1.8 mmol/L (70 mg/dl). Secondary objectives include superiority of inclisiran compared to placebo in reducing risk of CV death, reducing the risk of 4-point MACE (includes urgent revascularization in addition to 3P-MACE), and to evaluate inclisiran compared to placebo in reducing the risk of all-cause death.

Summary of resolved ethical issues

The main ethical issues considered by the Committee and addressed by the Researcher are as follows.

1. The Committee asked about the process and reasoning behind withholding the LDL results for a period of 6 years. The Researchers explained that participants have to be on maximal therapy before being accepted into the study. Monitoring LDL is unique because people can’t change the results through lifestyle changes except minimally.
2. The Committee asked the committee members and the Researchers how they feel about knowing information about a patient that could not be told to the patient. After discussion, the Researcher explained that the patient will consent to not knowing their LDL results.
3. The Committee asked about who is initially approaching the potential participants. The Researchers explained it will be rare for potential participants to be the Researcher’s patients however those patients may have seen the research do talks or had talks with them. The potential participants will be recruited from patients who have been discharged and will be sent the Participant Information Sheet/Consent Form (PIS/CF).
4. The Committee asked about the letter being sent to the potential participants and asked who the letter is from. The Researcher explained that they are a part of the clinical department and that the letter is from the research coordinator after the potential participant shows interest.
5. The Committee noted previous studies vs placebo regarding the injection site reactions and asked whether any other drug-related side effects have arisen. The Researcher explained that the FDA has approved the medicine and that injection site reactions are the only known side effect of this drug.
6. The Committee asked about if any other medication needs to be stopped before prior to commencing the study. The Researcher explained that no other medicine needs to be stopped.
7. The Committee noted that tissue donation for research purposes and the sending of tissue overseas are significant cultural issues.

Summary of outstanding ethical issues

The main ethical issues considered by the Committee and which require addressing by the Researcher are as follows.

1. Regarding recruitment, please ensure patients are initially approached by a member of their standard care team to see if they may be interested in a research study. Should the patient agree, the Researcher may then approach to discuss the study. Where the initial approach is by phone, please ensure a letter is first sent from the patient's clinical department informing the patient they will be contacted about a study, with a phone number, email address provided so the patient can make it known if they do not wish to be called.
2. Please confirm whether there is a cap on expenses, confirm the monetary amount and whether this is consistent across all New Zealand sites.
3. Please provide an updated insurance certificate. The certificate has expired as of December 2021.
4. Please provide updated evidence of CI indemnity. The certificate has expired as of 31 January 2022.
5. The Committee requested the following changes to the Data and Tissue Management Plan (DTMP)
   1. Please amend the error messages visible throughout the document.
   2. Please amend section 11 to specify that lipid results cannot be returned to the participant.
   3. Please further amend section 12, which still contains placeholders to describe use of data and tissue on participant withdrawal.

The Committee requested the following changes to the Participant Information Sheet and Consent Form (PIS/CF):

1. Please use a lay title to head the document.
2. Please review document for repetition and typos.
3. On page 1 please remove the line regarding treating the PIS as confidential and emphasise the right of potential participants to discuss study with others to assist with decision.
4. On page 2, clarify how long participants are expected to stay in the study.
5. Please clarify that there is no additional risk to the participant in not knowing their blood lipid level for up to 6 years (page 3).
6. Please state that fasting does not include avoidance of usual morning medicine and that tea, coffee must be black on page 3.
7. It is stated that ongoing information can continue to be collected from health care records even after study withdrawal on page 5. Please confirm that this will occur only if the withdrawing participant consents.
8. Page 6: states samples will be destroyed; the following paragraph states unused samples may be kept for 15 years. Please clarify.
9. Please remove the word ‘their’ on page 6 from the sentence “many Māori consider their blood to be tapu”, to reduce the emphasis on the individual's blood as tapu.
10. On page 7, please state that confirmed positive results for HIV, HBV and HCV must be reported to the Medical Officer of Health.
11. Please list acceptable contraception on page 8.
12. On page 15 please remove the term ‘biohazard waste’ when referring to biological samples. This is currently inconsistent with the cultural statement in the participant information sheet.
13. Please amend the footers as they are too close to the main body of text.

**Decision**

This application was *provisionally approved* by consensus, subject to the following information being received:

1. Please address all outstanding ethical issues, providing the information requested by the Committee.
2. Please update the participant information sheet and consent form, taking into account feedback provided by the Committee. *(National Ethical Standards for Health and Disability Research and Quality Improvement, para 7.15 – 7.17).*
3. Please update the study protocol, taking into account the feedback provided by the Committee. (National Ethical Standards for Health and Disability Research and Quality Improvement, para 9.7).
4. Please update the data and tissue management plan to ensure the safety and integrity of participant data and tissue *(National Ethical Standards for Health and Disability Research and Quality Improvement, para 12.15, 14.16&14.17).*
5. Please supply updated evidence of ACC-equivalent compensation available to all participants in the event of injury during the study. *(National Ethical Standards for Health and Disability Research and Quality Improvement, para 17.1).*

After receipt of the information requested by the Committee, a final decision on the application will be made by Associate Professor Nicola Swain and Mr Jonathan Darby.

|  |  |  |
| --- | --- | --- |
| **5** | **Ethics ref:** | **2022 FULL 11596** |
|  | Title: | Rectal tissue concentrations of thioguanine in inflammatory bowel disease |
|  | Principal Investigator: | Professor Murray Barclay |
|  | Sponsor: |  |
|  | Clock Start Date: | 27 January 2022 |

No researcher was present via videoconference for discussion of this application.

Potential conflicts of interest

The Chair asked members to declare any potential conflicts of interest related to this application.

No potential conflicts of interest related to this application were declared by any member.

Summary of Study

1. The aim of this study is to determine rectal tissue concentrations of thioguanine following rectal administration of thioguanine by enema. This is in order to validate the sampling, storage and assay methodology with expected high drug concentrations before moving on to measuring concentrations that would be expected to be much lower following oral administration of modified release thioguanine.

Summary of outstanding ethical issues

The main ethical issues considered by the Committee and which require addressing by the Researcher are as follows.

1. Please clarify anticipated study duration. Current end date is 16 April 2021.
2. Please clarify whether the investigational drug or approved thioguanine tablets are to be used and update study documentation accordingly *(National Ethical Standards for Health and Disability Research and Quality Improvement, para 9.7).*
3. Please upload Medsafe datasheets for the Pentasa and Fleet enemas to be administered during the study.
4. Please thoroughly review the entire Investigator’s Brochure document and ensure all information pertains to R178. The IB describes an investigational ketamine product rather than R178 in Section 4.3 (formulation). Section 4.4 (excipient safety) references 60 mg tablets and is likely also describing the ketamine product. Section 4.6 switches between R178 and R107 and stability result tables are absent.
5. Please ensure that once the investigator has introduced the study, the potential participant speaks further with a member of the research team not involved in their direct clinical care regarding the decision to participate. *(National Ethical Standards for Health and Disability Research and Quality Improvement, para 7.14 & 9.7, 11.23, & 11.24).*
6. Please provide a current indemnity certificate for the CI. The MPS Certificate for the CI has expired.
7. Separate consent for future unspecified tissue research (FUR) must be provided. Please also provide clarity what information could be used and clearly state if tissue samples could be used for FUR.
8. The Committee requested the use of the word “subjects” be changed to “participants” throughout participant-facing material.
9. Although E10 of the application form states the study is investigator-initiated, the entire aim of the study is to provide data to inform a trial to advance development of Douglas Pharmaceutical's slow release thioginanine tablets. Participant information also clearly references this ('Information from this study may lead to discoveries and inventions or the development of a commercial product. The rights to these will belong to Douglas Pharmaceuticals'). Given this information, the Committee considered that the balance of benefit in this study lies with the manufacturer, and that this will impact any injured participant’s ability to apply for ACC compensation. Evidence of ACC-equivalent injury compensation insurance must be provided to HDECs.

The Committee requested the following changes to the Participant Information Sheet and Consent Form (PIS/CF) *(National Ethical Standards for Health and Disability Research and Quality Improvement, para 7.15 – 7.17)*:

1. Please state that the lab scientist will be present in the room during the endoscopy on page 3.
2. On page 5, please clarify what medications will be reimbursed; any study-related medication should be provided directly by the research team.
3. Please amend ACC compensation statement on page 5 to commercial insurance statement.
4. Please delete statement on page 6 about screening and safety tests; none are performed as part of the study protocol.
5. Please delete optional YES/NO tick box regarding GP notification of abnormal results as this is mandatory for participation.
6. Please include a statement on disposal of tissue and availability of karakia.
7. Please amend page numbers into correct order on page 1.
8. Please delete repetition of re-consenting process on page 3.
9. Please address the reader as "you" not as the 'participant'
10. Please amend the following sentence "you have been chosen to participate", to "you are receiving this invitation to participate because..."

**Decision**

This application was *declined* by consensus, as the Committee did not consider that the study would meet the ethical standards referenced above.

|  |  |  |
| --- | --- | --- |
| **6** | **Ethics ref:** | **2022 FULL 10999** |
|  | Title: | GSN000350: A Phase 2b/3 Trial of Setanaxib with a 52-week Extension Phase in patients with PBC and Elevated Liver Stiffness |
|  | Principal Investigator: | Dr Andrew Knox |
|  | Sponsor: | Genkyotex Suisse SA |
|  | Clock Start Date: | 27 January 2022 |

Dr Andrew Knox and Sarah Middleton were present via videoconference for discussion of this application.

Potential conflicts of interest

The Chair asked members to declare any potential conflicts of interest related to this application.

No potential conflicts of interest related to this application were declared by any member.

Summary of Study

1. The purpose of this Phase 2b/3 study is to evaluate the effect of setanaxib on biochemical response at Week 52 in patients with primary biliary cholangitis (PBC) and with elevated liver stiffness and intolerance or inadequate response to ursodeoxycholic acid (UDCA).

Summary of resolved ethical issues

The main ethical issues considered by the Committee and addressed by the Researcher are as follows.

1. The Committee asked about the distribution of burden of the disease for participants especially Māori. The Researchers explained that there are very few Māori with primary biliary cholangitis (PBC), and those with PBC in non-Māori are usually already medicated, so not anticipating recruitment numbers to be high.
2. The Committee queried about the withdrawal of consent of tissue and the processes to check if they are also withdrawing from optional parts of the study. The Researcher clarified that they would explain to the participant in detail about the withdrawal process thoroughly.

Summary of outstanding ethical issues

The main ethical issues considered by the Committee and which require addressing by the Researcher are as follows.

1. Please remove C.4: "Clinical trials make available to all study participants drugs that are too costly to access in Aotearoa New Zealand or are not yet available to the general public".
2. Where a relationship exists between the Investigator and patient, please ensure the patient discusses participation with a Researcher not involved in their clinical care at some stage during the informed consent process. This provides the opportunity to decline away from the power imbalance of the doctor and patient relationship.
3. Please ensure that, should it become apparent that the numbers of New Zealand participants screened or enrolled into the study will exceed those listed in the Insurance Certificate, the Certificate will be amended to ensure all participants are covered.
4. The MPS Certificate provided for the CI has expired. Please provide an updated certificate as an amendment submission.
5. Please ensure that processes are in place for all New Zealand participants who withdraw from the main study to be specifically asked whether continued consent is given for optional uses of tissue

The Committee requested the following changes to the Participant Information Sheet and Consent Form (PIS/CF):

Main PIS/CF

1. Please amend sections that are very wordy and technical, ensuring lay language is used.
2. Review and simplify where possible, using lay language such as the following:
   1. 'Setanaxib possesses broad anti-inflammatory and antifibrotic effects'.
   2. 'achieved further reductions in markers of cholestatic injury, improves markers of liver fibrosis '...' on page 1.
   3. 'interim analyses’ on page 3.
   4. ‘urinalyses’ on page 10.
   5. ‘concomitant medications' and adverse event terms on page 17.
   6. Once a word or procedure has been explained, use the simplest way to describe it (e.g. Fibroscan).
3. Please remove repeated information.
4. Please either use words or numbers, not both (e.g. ‘two (2)’).
5. Please remove repeated references to optional tests on page 7 and 12. It is sufficient to say that the participant will be invited to take part in several optional parts of the study, they will be given separate information about it, and they can still take part in the main study if they decline the optional components.
6. Please remove liver biopsy risks.
7. Please provide and include approximate number of New Zealand participants on page 2.
8. Please explain the reasoning for taking one tablet from each bottle with each dose on page 8.
9. Please remove optional study components from table of assessments.
10. Please remove visit window column from table of assessments.
11. Please amend table of assessments as Day 2 column not visible.

Genetic Testing PIS/CF

1. Please review for lay language and simplify (e.g., genotype, genome, metabolite...)
2. Please delete information about PBC (1st 2 paras of Section 2) as it is present in the Main PIS/CF.

Exploratory PIS/CF

1. Please explain genetic research, genes, genome etc. in lay language.

**Decision**

This application was *approved* by consensus, subject to the following non-standard conditions:

* please address all outstanding ethical issues raised by the Committee
* please update the Participant Information Sheet and Consent Form, taking into account the feedback provided by the Committee. *(National Ethical Standards for Health and Disability Research and Quality Improvement, para 7.15 – 7.17).*

|  |  |  |
| --- | --- | --- |
| **7** | **Ethics ref:** | **2022 FULL 11982** |
|  | Title: | Phase 1 study to assess safety, tolerability, and the immune response KJ103 in healthy adults |
|  | Principal Investigator: | Dr Mark Marshall |
|  | Sponsor: | Shanghai Bao Pharmaceuticals Co.,Ltd. |
|  | Clock Start Date: | 27 January 2022 |

Sharmin Bala and Dr Mark Marshall was present via videoconference for discussion of this application.

Potential conflicts of interest

The Chair asked members to declare any potential conflicts of interest related to this application.

No potential conflicts of interest related to this application were declared by any member.

Summary of Study

1. The study aims to evaluate how safe and well tolerated KJ103 is in healthy volunteers through measuring levels of kJ103 in the blood over time, following a single dose. Observations of the body’s response to a single dose of KJ103 and assessment of the body’s immune response to KJ103 will also be undertaken.

Summary of resolved ethical issues

The main ethical issues considered by the Committee and addressed by the Researcher are as follows.

1. The Committee clarified that the study would only be conducted at the Auckland site.

Summary of outstanding ethical issues

The main ethical issues considered by the Committee and which require addressing by the Researcher are as follows.

1. The Committee requested that in response to question C4 please do not cite the benefit of the research to Māori as being access to otherwise costly treatments. This is patronising and irrelevant to the question asked which is inquiring to the incidence or statistics of disease or condition in the Māori population.
2. The Committee requested that the inclusion criteria of vaccination against COVID-19 be removed from the Information Sheet. Even if it may be site policy for health and safety, this can be explained to participants and is not appropriate as study inclusion criteria.
3. The Committee noted that whilst there was a statement in the application form declaring commercial sponsor authorisation was not required, this is not the case and HDECs require this approval to be noted for the application to be approved.
4. The Committee required the study to be registered with an approved clinical trials registry prior to recruitment in New Zealand.
5. The Committee required a new certificate of CI indemnity as the current one provided is expired.
6. The Committee noted that the statement concerning Māori consultation being conducted for the Christchurch site. Please amend, as it has been confirmed that this is an Auckland-only study.
7. The Committee noted the following changes for the Data Management Plan (DMP):
   1. Please amend 7.4 to include future use of data as well as the future use of tissue.
   2. Please correct the incomplete sentence “commercial use of data and tissue”.
   3. Please amend plan and refer to the standard template to correct the wording concerning the notification of breaches of privacy.

The Committee requested the following changes to the Participant Information Sheet and Consent Form (PIS/CF):

1. Please review for lay-language and clarity, particularly for Pharmacokinetic, PK, Pharmacodynamic, PD, and Immunology blood samples that are on page 12.
2. Please simplify the information for contraception in male participants given the explanation given on pages 8 and 9 are repeated from the section for female participants.
3. Please review for spelling and typo errors.
4. Please include the drug name in titles where necessary.
5. Please include the name of the laboratory and include the location.
6. Please amend on page 2 to remove repeated descriptions of mode of action for the drug.
7. Please simplify the explanation of auto-immune diseases.
8. Please address future uses of data generated in the study. See the HDEC template for guidance
9. Please address duplication of information of ownership rights.

**Decision**

This application was *provisionally approved* by consensus, subject to the following information being received:

1. Please address all outstanding ethical issues, providing the information requested by the Committee.
2. Please update the participant information sheet and consent form, taking into account feedback provided by the Committee. *(National Ethical Standards for Health and Disability Research and Quality Improvement, para 7.15 – 7.17).*
3. Please update the study protocol, taking into account the feedback provided by the Committee. (National Ethical Standards for Health and Disability Research and Quality Improvement, para 9.7).
4. Please update the data management plan to ensure the safety and integrity of participant data. *(National Ethical Standards for Health and Disability Research and Quality Improvement, para 12.15).*

After receipt of the information requested by the Committee, a final decision on the application will be made by Mr Dominic Fitchett and Associate Professor Mira Harrison-Woolrych.

|  |  |  |
| --- | --- | --- |
| **8** | **Ethics ref:** | **2022 FULL 11228** |
|  | Title: | Treatment-induced neuroplasticity in children who stutter |
|  | Principal Investigator: | Mrs Fathiya Al'Amri |
|  | Sponsor: | Canterbury Medical Research Foundation |
|  | Clock Start Date: | 27 January 2022 |

Mrs Fathiya Al'Amri and Catherine Theys were present via videoconference for discussion of this application.

Potential conflicts of interest

The Chair asked members to declare any potential conflicts of interest related to this application.

No potential conflicts of interest related to this application were declared by any member.

Summary of Study

1. The study will investigate how stuttering therapy changes brain function in children who stutter (CWS) and if therapy normalise brain activity. The researchers hypothesise that a positive association will be shown between normalisation of brain functioning and behavioural stuttering treatment outcomes.

Summary of outstanding ethical issues

The main ethical issues considered by the Committee and which require addressing by the Researcher are as follows.

1. The Committee required the study be registered with an approved clinical trial registry prior to commencing recruitment.
2. The Committee noted that locality authorisation must be in place prior to commencing the study at each locality. Note that St George's Radiology must also authorise locality.
3. The Committee recommend creating a separate consent form for future unspecified research (FUR) and clearly stating if the information for FUR will be identifiable.
4. The Committee queried whether there would be issues for the participants recruited through clinics and if their treatment would be disrupted and potential effects of this.
5. The Committee requested that information about recording of daily severity and stutter ratings, in terms of advice to parents, and information about how this is documented.
6. The Committee requested more information be included in the study documentation to the previous findings of Magnetic Resonance Imaging (MRI) neural mechanisms of CWS.
7. The Committee requested rationale be provided for the inclusion of a control cohort as baseline imaging and pre-treatment MRI serve as their own controls, as well as the rationale for the selected treatment duration and confirmation this is long enough for MRI-visible change to be evident.
8. The Committee requested rationale for including children up to age 10 should initial target recruitment not be met, as duration of stutter is not controlled for in the current protocol. As the study intention is to report neuroimaging pre and post treatment in 'children close to the onset of developmental stuttering', a definition of 'close' in months or years should be provided.
9. The Committee requested the inclusion of processes for management of incidental findings, of potential clinical significance, including newly diagnosed behavioural / speech / developmental issues and imaging abnormalities, for both cohorts.
10. The Committee queried whether dropouts will be replaced, or whether the sample size has been adjusted to allow for withdrawals (e.g., inability to comply with MRI protocol).
11. The Committee noted that the submission of videos to FluencyBank would not be considered best practice, particularly where involving minors. The Committee suggested this option be removed from the study. The Committee requested that the FluencyBank information and consenting should be a separate document and an audio-only option should be considered.
12. Please clearly state who will be viewing the MRI images and what international or national guidance is followed in terms of conclusions drawn.
13. The Committee suggested un-bolding the statements of “Free Speech Therapy” and similar in recruitment material and noted that these statements should not carry exclamation marks.
14. The Committee requested the following changes for the Data Management Plan (DMP):
    1. Please add mention of St George’s Radiology as an important locality to section 3. Please ensure it is clear their policies will apply.
    2. Please amend section 8.1 to state that MRI’s will become part of the clinical record.
    3. Please clarify whether video will be retained in identified form or be de-identified.
    4. Please amend section 8 which states that 'With consent, the deidentified videos and their transcripts will also be uploaded to FluencyBank.'. As this is not consistent with the protocol, which states identified video will be uploaded if the parent selects this. Also clarify how the video footage will be de-identified (i.e., how the participant's identifying facial features will be sufficiently obscured).
    5. It is stated that identified data will be shared with Deryk Beal, based in Canada. The Committee requested that it is clearly defined which identifiable data is being provided, and processes in place to minimise privacy breach.
    6. The Committee noted that some health information must be retained until 10 years after the participant turns 16 (Sections 9.1 and 9.2).

The Committee requested the following changes to the Participant Information Sheet and Consent Form (PIS/CF):

Case PIS/CF

1. Please amend to include page numbers and version numbers to footers.
2. Please explain in lay language, the possibility of finding abnormalities in MRI scans or other assessments not something expected in the study, and state that any significant findings will be reported to a General Practitioner (GP).
3. Please provide a description of why the MRI is needed and what the Researchers are specifically looking for.
4. Please clearly state who will be viewing the MRI images and what international or national guidance is followed in terms of conclusions drawn.
5. Please review for lay terms ('psychosocial', 'monolingual' etc.) and explain what is meant by 'brain changes'.
6. Please state the number of assessments and time they will take rather than naming the assessment tools.
7. Please state where and when video recordings may be used and whom they will be accessible by.
8. Please provide contact detail for Māori cultural support.
9. Please provide an optional YES/NO tick box for consent to video recordings used for teaching that is clearly distinct from other consent clauses.
10. Please remove the tick box option for reporting findings to a General Practitioner (GP).

Control PIS/CF

1. Please amend as with the Case PISCF.
2. Please limit the information provided as relevant to the control group.

**Decision**

This application was *provisionally approved* by consensus, subject to the following information being received:

1. Please address all outstanding ethical issues, providing the information requested by the Committee.
2. Please update the participant information sheet and consent form, taking into account feedback provided by the Committee. *(National Ethical Standards for Health and Disability Research and Quality Improvement, para 7.15 – 7.17).*
3. Please update the study protocol, taking into account the feedback provided by the Committee. (National Ethical Standards for Health and Disability Research and Quality Improvement, para 9.7).
4. Please amend the data management plan to ensure the safety and integrity of participant data *(National Ethical Standards for Health and Disability Research and Quality Improvement, para 12.15).*

After receipt of the information requested by the Committee, a final decision on the application will be made by Ms Catherine Garvey and Dr Devonie Waaka.

|  |  |  |
| --- | --- | --- |
| **9** | **Ethics ref:** | **2022 FULL 11811** |
|  | Title: | FINER - Phase III Fulvestrant and Ipatasertib for Advanced HER2-, ER+ Breast Cancer |
|  | Principal Investigator: | Dr Sheridan Wilson |
|  | Sponsor: | Canadian Cancer Trials Group (CCTG) |
|  | Clock Start Date: | 27 January 2022 |

Dr Sheridan Wilson and Vivian Sun were present via videoconference for discussion of this application.

Potential conflicts of interest

The Chair asked members to declare any potential conflicts of interest related to this application.

No potential conflicts of interest related to this application were declared by any member.

Summary of Study

1. The primary objective of the FINER study is to compare investigator assessed progression free survival (PFS) using RECIST 1.1 in patients with ER+/HER2- advanced (metastatic or loco-regionally recurrent not amenable to curative therapy) breast cancer treated with ipatasertib and fulvestrant versus placebo and fulvestrant after progression on first line CDK 4/6 inhibitor plus AI treatment.

Summary of resolved ethical issues

The main ethical issues considered by the Committee and addressed by the Researcher are as follows.

1. The Committee asked if fulvestrant is a standard of care drug in New Zealand. The Researcher outlined that it has been fully funded in New Zealand for the past 18 months.
2. The Committee asked for clarification on recruitment. The Researcher explained that all participants are already involved with the clinics as they are receiving first-line treatment.
3. The Committee asked whether there would be someone involved in the study (who is an investigator or research nurse, not the participant’s clinician) who will sit down with the participant and go through the study and make sure they have informed consent prior to agreeing to take part in the study. The Researchers explained the process will follow Good Clinic Practice (GCP) guidelines. Participants will be provided with written information which will be discussed with a research nurse who is unrelated to their direct clinical care.
4. The Committee asked about the scope of Hoffman-La Roche Ltd’s (Roche) role in the study. The Researcher explained that all study drugs, Ipatasertib, matched placebo and Fulvestrant will be provided free of charge by Roche. Roche will also have access to the safety data but will have no other access to data produced during the study. They will not have any influence over the publication of the study.

Summary of outstanding ethical issues

The main ethical issues considered by the Committee and which require addressing by the Researcher are as follows.

1. The Committee asked for the section on stopping the study for commercial reasons to be removed.
2. The Committee requested that Māori consultation is undertaken at all localities, not only the lead site.
3. The Committee stated more information around data management is required than what is available in the study documentation satisfy the Committee that privacy and confidentiality is protected and that Standard 12.15a is met. Use of the HDEC template from the [HDEC website](https://ethics.health.govt.nz/guides-templates-and-forms/) is not mandatory but is encouraged to be adapted or used as a guide/starting point.

The Committee requested the following changes to the Participant Information Sheet and Consent Form (PIS/CF):

1. Please clarify that ipatasertib is not currently approved for use in New Zealand.
2. Please include further information on who will pay for medications that will mitigate any side effects experienced because of the trial.
3. Please explain Roche’s role in the study and their access to data.
4. Please clarify the reference to data linking and what this will mean regarding the participant’s data, identifiable information and how long this data will be held for.
5. Please reconsider the phrase ‘registration blood sample’ and explain what it is for. This could be rephrased as ‘screening blood sample’.
6. Please change the section on effective contraception. There is a ‘Reproductive risks’ template available on the [HDEC website](https://ethics.health.govt.nz/guides-templates-and-forms/participant-information-sheet-templates/). Please simplify this section by removing information for males, as they will likely not be included in the study.
7. Please remove the duplicate Māori tissue statement.
8. Please remove the repetition between page 3 of the PIS and pages 3 and 5 of the Future Unspecified Research (FUR) PIS.
9. Please reconsider whether the diagrams add anything to informing the participant about the study
10. Please make note that karakia will not be available during tissue destruction
11. Please include a statement on the withdrawal of tissue or images
12. Please add information on whether whole genome research will be conducted in the FUR PIS.

**Decision**

This application was *provisionally approved* by consensus, subject to the following information being received:

1. Please address all outstanding ethical issues, providing the information requested by the Committee.
2. Please update the participant information sheet and consent form, taking into account feedback provided by the Committee. *(National Ethical Standards for Health and Disability Research and Quality Improvement, para 7.15 – 7.17).*Please update the study data and tissue management plan, taking into account the feedback provided by the Committee. (National Ethical Standards for Health and Disability Research and Quality Improvement, para 12.15, 14.16&14.17*).*

After receipt of the information requested by the Committee, a final decision on the application will be made by Ms Catherine Garvey and Associate Professor Nicola Swain.

|  |  |  |
| --- | --- | --- |
| **10** | **Ethics ref:** | **2022 EXP 11833** |
|  | Title: | Genes and exposures in PD |
|  | Principal Investigator: | Dr Toni Pitcher |
|  | Sponsor: |  |
|  | Clock Start Date: | 27 January 2022 |

Dr Toni Pitcher was present via videoconference for discussion of this application.

Potential conflicts of interest

The Chair asked members to declare any potential conflicts of interest related to this application.

No potential conflicts of interest related to this application were declared by any member.

Summary of Study

1. The study aims to obtain high-quality Parkinson’s-specific genetic risk data, occupational and environmental exposures data, and other risk factor data. This will allow them for the first time to determine the occupational and environmental exposures and lifestyle factors specifically associated with Parkinson’s in New Zealand. This is particularly relevant because of the country’s unique ethnic mix and potentially specific risks due to being a country with extensive agricultural and horticultural industries.

Summary of resolved ethical issues

The main ethical issues considered by the Committee and addressed by the Researcher are as follows.

1. The Committee wished to clarify that the control group would be notified as to where the study came across their data. The Researcher explained that this is included in the participant information sheet (PIS).
2. The Committee asked for assurance that referral to a local genetics counsellor will be available to all participants across New Zealand. The Researcher explained that in the event of a participant not having access to a genetics counsellor or neurologist that they could help provide these services.

Summary of outstanding ethical issues

The main ethical issues considered by the Committee and which require addressing by the Researcher are as follows.

1. The Committee asked for clarification on the consent process, such as whether it is signed or verbal consent being gathered from the participants, and the management of a control group. The Researcher explained that verbal consent would be collected over the phone and that this would be the same process for the control group.
   1. The Committee requested the script that will identify the questions asked to gain informed consent. The Researcher explained that these questions are included in the database, and any information from this database will be deidentified.
   2. The Committee asked whether the optional portions of the surveys will be discussed verbally with the participant and made clear that these sections are optional. The Committee suggested the use of an electronic consent form to simplify this process.
   3. The Committee suggested including the Future Unspecified Research (FUR consent process to the electronic consent form. The Researcher explained that this form would be sent as a hard copy as part of the saliva collection which was being delivered via mail.

The Committee requested the following changes to the Participant Information Sheet and Consent Form (PIS/CF):

1. Please explain what a ‘control participant’ is in lay language
2. Please provide a definition of ataxia and dystonia in lay language
3. Please remove the tick-box on GP being informed of the test results if clinically significant or actionable. Please be sure that this is reflected across documents.
4. Please provide participants with a separate information sheet about the additional New Zealand study they are being asked to contribute NHI numbers to. State clearly what data from the current study will be shared.
5. Please correct any grammar or spelling mistakes

**Decision**

This application was *provisionally approved* by consensus, subject to the following information being received:

1. Please address all outstanding ethical issues, providing the information requested by the Committee.
2. Please update the participant information sheet and consent form, taking into account feedback provided by the Committee. *(National Ethical Standards for Health and Disability Research and Quality Improvement, para 7.15 – 7.17).*
3. Please update the study protocol, taking into account the feedback provided by the Committee. (National Ethical Standards for Health and Disability Research and Quality Improvement, para 9.7).

After receipt of the information requested by the Committee, a final decision on the application will be made by Mr Dominic Fitchett and Ms Amy Henry.

|  |  |  |
| --- | --- | --- |
| **11** | **Ethics ref:** | **2022 FULL 12095** |
|  | Title: | Vectorcardiography |
|  | Principal Investigator: | Dr Jessica Wong |
|  | Sponsor: |  |
|  | Clock Start Date: | 27 January 2022 |

No researcher was present via videoconference for discussion of this application.

Potential conflicts of interest

The Chair asked members to declare any potential conflicts of interest related to this application.

No potential conflicts of interest related to this application were declared by any member.

Summary of Study

1. The study aims to determine if there is a difference in QRS-T angle in youth with type 1 diabetes compared with controls and whether there is an association with poor glycaemic control and, if possible, comparing those with and without cardiovascular autonomic neuropathy. However, this may not be possible if the study reveals low numbers of patients with cardiovascular autonomic neuropathy.

Summary of resolved ethical issues

The main ethical issues considered by the Committee and addressed by the Researcher are as follows.

1. The Committee queried whether this study was out of scope and should be reviewed under accreditation from their institutional ethics committees. They determined that as the study is recruiting children, it qualifies for HDEC review due to the potential vulnerability of these participants.
2. The Committee noted that this study appears to be too much work for a Master’s study, and that if the Researcher limited participants to over the age of 16, they would not need HDEC approval, although review by the institutional committee would be required

Summary of outstanding ethical issues

The main ethical issues considered by the Committee and which require addressing by the Researcher are as follows.

1. The Committee stated that it was unclear whether over-16s would be consenting for themselves. The Committee also noted that there is no process whereby a competent participant under the age of 16 could consent for themselves nor an assessment of how such a child could do so. The Committee noted that the adult Participant Information Sheet/Consent Form (PIS/CF) and 13+ PIS/CF were very similar. This suggests that participants over 13 are consenting themselves, yet the 13+ PIS/CF has a space for both child and parent to sign. Some children would be able to provide consent without their parent’s signature. Please provide clarification around whether these children will provide consent and how this will be assessed. Additionally, please also provide further explanation on the role of the parent and protocol for if a child provides consent and the parent refuses. *(National Ethical Standards for Health and Disability Research and Quality Improvement, para 6.22, & 7.15-7.17).*
2. Please provide the puberty questionnaire and explain how the Researcher will manage potential embarrassment from participants.
3. The Committee queried whether the Researchers would be reimbursing travel costs. They determined that participants would be refunded through future appointments at the diabetes clinic, however there is no clear recruitment strategy or reimbursement for the controls who are not a part of the clinic.
4. Please state how many children will be included in the study in study documentation.
5. The Committee stated that if the only difference between control participants and patient participants is the blood test, then each group does not need their own PIS.
6. The Committee stated more information around data management is required than what is available in the study documentation satisfy the Committee that privacy and confidentiality is protected and that Standard 12.15a is met. Use of the HDEC template from the [HDEC website](https://ethics.health.govt.nz/guides-templates-and-forms/data-and-tissue-management-plan-templates/) is not mandatory but is encouraged to be adapted or used as a guide/starting point.

The Committee requested the following changes to the Participant Information Sheet and Consent Form (PIS/CF) *(National Ethical Standards for Health and Disability Research and Quality Improvement, para 7.15 – 7.17)*:

1. The Committee suggested the use of the [PIS/CF template found on the HDEC website](https://ethics.health.govt.nz/guides-templates-and-forms/participant-information-sheet-templates/).
2. Please include further explanation surrounding the process of the electrocardiograph (ECG), including how participants may maintain their dignity and privacy, particularly with young girls, and whether they will be provided with a hospital gown. Especially as it could be medical students undertaking the ECG.
3. Please explain what Vectorcardiography is in lay terms.

**Decision**

This application was *declined* by consensus, as the Committee did not consider that the study would meet the ethical standards referenced above.

|  |  |  |
| --- | --- | --- |
| **12** | **Ethics ref:** | **2022 FULL 11866** |
|  | Title: | ETERNAL– A clinical trial comparing thrombolysis to standard care for ischaemic stroke presenting within 24 hours |
|  | Principal Investigator: | Dr Teddy Wu |
|  | Sponsor: | University of Melbourne |
|  | Clock Start Date: | 27 January 2022 |

Mrs Kathleen Bremner and Dr Teddy Wu were present via videoconference for discussion of this application.

Potential conflicts of interest

The Chair asked members to declare any potential conflicts of interest related to this application.

No potential conflicts of interest related to this application were declared by any member.

Summary of Study

1. The study seeks to test the hypothesis that tenecteplase administered within 24 hours of symptom onset is superior to current best practice alteplase in achieving excellent functional outcome or return to baseline following a stroke with large vessel occlusion

Summary of resolved ethical issues

The main ethical issues considered by the Committee and addressed by the Researcher are as follows.

1. The Committee complimented the Researcher in how they have dealt with the necessity to achieve a best interest standard for participants, especially as they will be in a position where they are unable to give consent.
2. The Committee noted the in the application form under B7.1 it states that withdrawing current treatment is justified as "The experimental treatment is expected to have equivalent or better outcomes than current best practice", yet in B9 it says, "It is not proven if tenecteplase is superior or equivalent to current best practice". The Researchers responded that there is evidence that shows that tenecteplase is better than alteplase, however, there have only been two trials with a total of 600 participants that show this, both of which the Researcher has been involved with. Additionally, the American guidelines which are followed internationally are yet to be updated following the second trial. There is also no evidence for the effectiveness of tenecteplase past 4.5 hours. The Committee accepted this clarification.

Summary of outstanding ethical issues

The main ethical issues considered by the Committee and which require addressing by the Researcher are as follows.

1. The Committee asked about the standard care for using alteplase at Christchurch hospital. The Researcher stated that the window for receiving this medication after a stroke is usually 4.5 hours, but there is evidence that this could be extended up to 9 hours, or 4.5 hours if the patient has woken up with a stroke. The overseas guidelines have made a moderate recommendation to consider extending this period, however, New Zealand standard care follows that these patients would usually have their clot removed past 4.5 hours with a 5% risk of bleeding. The Researcher stated that most studies concerning this have been done before clot-retrieval was standard practice.  
   Patients which are sent to the Researcher’s practice that have exceeded 4.5 hours are sent straight to clot retrieval, however, the Researcher stated they would still recommend that select patients travelling to their centre to take this medication beforehand as there is a 10-20% chance that their clot would be gone before they arrive. The Researcher stated that evidence for the effectiveness of tenecteplase exists but is not substantial enough to make this standard in New Zealand. The Committee requested that standard care practices be clarified in the Participant Information Sheet (PIS), particularly whether participants arriving after a certain period and allocated to the alteplase arm will receive alteplase.
2. The Committee queried whether there will be participants that could consent. The Researcher stated that it would be about half. Those that have retained their language capacity would be able to consent; patients with a dominant left-side of the brain or patients with severe cases would not be able to provide consent. The Researcher stated that it would be difficult to ascertain participants’ capabilities to provide consent with certainty as they would be having a stroke, although they stated that roughly 60-70% of patients recall discussions had during their stroke the following day.   
   The Committee requested Researchers simplify sections of the PIS for those participants who are able to provide informed consent (e.g., using diagrams and bullet points to break up dense paragraphs or reduce information where possible).
3. The Committee asked if the Researcher were sending identifiable information to Melbourne because they would be conducting the interviews. The Researcher confirmed this and stated that they would need to clarify this process. The Committee requested they do so and added that this process should be stated in the Data Management Plan (DMP). Additionally, please state how much of this data is identifiable.
4. The Committee noted that as the interviewers are based in Melbourne, the application form states that participants will be referred to their General Practitioner (GP) if the interviewer is alerted to significant depression or anxiety from their responses. However, the PIS states that participants will be asked to get in touch with their GP to discuss how they’re feeling. The Committee noted that older participants may be reluctant to do this without referral. The Committee asked what processes were in place to make sure the right people were notified, particularly as the interviews will be conducted from Australia. The Researcher stated that they would follow up with the participants personally themselves to tie up any loose ends including acknowledging these responses.
5. The Committee requested that the Researcher explicitly state what processes are in place to respond to participants who show signs of significant anxiety or depression through these questionnaires or interview. The Researcher stated that they would discuss with Melbourne over conducting the follow-ups locally. The Committee supported this idea and asked how many participants would be interviewed in the New Zealand arm of the study and whether it would be feasible for the interviewers to conduct these. The Researcher stated they could feasibly conduct the interviews and that the New Zealand arm would study 1-2 participants a month for however long the study runs.
6. The Committee noted that the informed consent paragraphs on page 23 and in section 15.4 of the protocol don’t reflect New Zealand’s standards of practice. Please produce a New Zealand-specific addendum that covers how informed consent will be obtained in New Zealand. The Committee added that should the Researchers change the arrangements for participant follow-ups, this change could be included in the addendum.

The Committee requested the following changes to the Participant Information Sheet and Consent Form (PIS/CF):

1. The Committee noted that it states in the Best Interests form that this for is to be used for participants who are able to understand and consent to the study but cannot commit this consent to writing. If this is the case, these people do not need to be covered by this Best Interests section. Instead, please provide a mechanism to document their verbal consent.
2. Please update the Committee that has reviewed the ethical aspects of this study to be Southern HDEC.
3. The Committee noted that the frequency data for tenecteplase allergies is based on the data for alteplase allergies despite frequency data existing for tenecteplase. Please use this data instead.

**Decision**

This application was *provisionally approved* by consensus, subject to the following information being received:

1. Please address all outstanding ethical issues, providing the information requested by the Committee.
2. Please update the participant information sheet and consent form, taking into account feedback provided by the Committee. *(National Ethical Standards for Health and Disability Research and Quality Improvement, para 7.15 – 7.17).*
3. Please update the study protocol, taking into account the feedback provided by the Committee. (National Ethical Standards for Health and Disability Research and Quality Improvement, para 9.7).

After receipt of the information requested by the Committee, a final decision on the application will be made by Dr Devonie Waaka and Mr Jonathan Darby.

## General business

1. The Chair reminded the Committee of the date and time of its next scheduled meeting:

|  |  |
| --- | --- |
| **Meeting date:** | 08 March 2022 |
| **Zoom details:** | To be determined |

1. **Review of Last Minutes**

The minutes of the previous meeting were agreed and signed by the Chair and Co-ordinator as a true record.

1. **Matters Arising**
2. **Other business**
3. **Other business for information**
4. **Any other business**

The meeting closed at 4.50pm