|  |  |
| --- | --- |
| **Committee:** | Northern A Health and Disability Ethics Committee |
| **Meeting date:** | 20 April 2021 |
| **Meeting venue:** | via Zoom <https://mohnz.zoom.us/j/96507589841>  Meeting ID: 965 0758 9841 |

|  |  |
| --- | --- |
| **Time** | **Item of business** |
| 1.00pm | Welcome |
| 1.15pm | Confirmation of minutes of meeting of 16 March 2021 |
| 1.30pm | New applications (see over for details) |
| 1.30-1.55pm  1.55-2.20pm  2.20-2.45pm  2.45-2.55pm  2.55-3.20pm  3.20-3.45pm  3.45-4.10pm  4.10-4.15pm  4.15-4.40pm  4.40-5.05pm  5.05-5.30pm | i 21/NTA/58  ii 21/NTA/51  iii 21/NTA/52  *Break (10 minutes)*  iv 21/NTA/54  v 21/NTA/55  vi 21/NTA/57  *Break (5 minutes)*  vii 21/NTA/46  viii 21/NTA/60  ix 21/NTA/61 |
| 5.30pm | Meeting ends |

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| **Member Name** | **Member Category** | **Appointed** | **Term Expires** | **Apologies?** |
| Dr Karen Bartholomew | Non-lay (intervention studies) | 18/07/2016 | 18/07/2019 | Present |
| Mrs Kate O'Connor | Lay (consumer/community perspectives) | 29/01/2020 | 29/01/2021 | Apologies |
| Mrs Helen Walker |  |  |  | Present |
| Dr Kate Parker | Non-lay (observational studies) | 11/02/2020 | 11/02/2023 | Present |
| Ms Rochelle Style | Lay (ethical/moral reasoning) | 14/06/2017 | 14/06/2020 | Present |
| Ms Catherine Garvey | Lay (the law) | 19/03/2019 | 19/03/2022 | Present |
| Dr Sotera Catapang | Non-lay (observational studies) | 11/02/2020 | 11/02/2023 | Present |
| Dr Michael Meyer | Non-lay (health/disability service provision) | 11/02/2020 | 11/02/2023 | Absent |

## Welcome

The Chair opened the meeting at 1.00pm and welcomed Committee members, noting that apologies had been received from Kate O’Connor and Dr Michael Meyer. Helen Walker was co-opted to Chair for this 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 16 March 2021 were confirmed.

## New applications

|  |  |  |
| --- | --- | --- |
| **1** | **Ethics ref:** | **21/NTA/58** |
|  | Title: | Open-label long-term trial of efgartigimod PH20 SC for the treatment of Primary Immune Thrombocytopenia in adults. |
|  | Principal Investigator: | Dr Rajeev Rajagopal |
|  | Sponsor: | argenx BV |
|  | Clock Start Date: | 08 April 2021 |

Rajeev Rajagopal, Nicola Jackson and Jen Coetzee, and 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. This trial is an open-label long-term extension of trial ARGX-113-2004 (HDEC ref: 21/NTA/26) and will be conducted at the same sites that participated in trial ARGX-113-2004. The main goal of this study is to look at the effect and safety of a drug called efgartigimod in people with primary immune thrombocytopenia (ITP). ITP is an autoimmune disease that affects platelets - a component of the blood that helps with clotting.

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 the main study of which this is an extension study, has recently been approved (with non-standard conditions) by the Northern A HDEC.
2. The Committed noted the researcher’s confirmation that the main study and the open label extension study have both been approved by SCOTT.
3. The Committee advised that as the Main and Optional Tissue FUR participant information sheet and consent forms (PIS/CF) have already been approved by HDEC in the main study application, they have not been reviewed as part of this application.
4. The Committee noted that the researchers have provided additional information around data privacy protection around third parties, tikanga protocols, and home visit safety for approval of the main 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 Committed asked if the main study has started. The researcher responded that it has not started in New Zealand or anywhere else in the world and she is anticipating initiation of New Zealand sites to begin in the next few weeks. The Committee stated that this application has come through too early as it is not appropriate for them to make a decision on documentation for an extension study where there is no knowledge of the potential side effects or trial results from the main study yet. The Committee agreed that the best option is to decline the application and for the researcher to resubmit it when the results from the main study are known. The Committee recommended that the researcher resubmit the application to Northern A Committee when ready, taking into account the changes to the study documentation requested by the HDEC today. The researchers were comfortable with this approach.
2. The Committee advised that the insurance certificate must be provided for HDEC review. The researcher confirmed that they have this now and will submit it with the next application.
3. The Committee queried why there is a need for so many third parties (i.e. Greenphire, Symphony Clinical Research, ICON Clinical Research, and a Belgium sponsor) to be involved in the trial when there are only three New Zealand participants. The Committee were concerned that the wider the delegation, the more difficult it is to manage the study appropriately according to the protocol.
4. The researcher responded that Greenphire has been dropped from all New Zealand sites and Symphony may potentially be used at one site, Christchurch, and only as a COVID-19 pandemic back up plan for managing home visits. The researcher advised that Symphony is part of ICON, their Clinical Research Organisation in New Zealand and have an established network in New Zealand.
5. The Committee requested that references to Greenphire are removed from all documentation given they are not involved in the New Zealand study.
6. The Committee stated that the home guide for the study drug is complicated and recommended that it is revised and simplified to ensure it can be understood by participants. The Committee also asked for New Zealand contact phone number(s) to be added to the guide to allow participants to more easily access help if needed.
7. The Committee advised that a data safety charter for the DSMB will need to be provided to HDEC for review.
8. The Committee requested that the sponsor is advised that therapeutic studies where participants are potentially receiving therapeutic benefit must not be terminated simply for reasons of commercial interest in New Zealand *(National Ethical Standards for Health and Disability Research and Quality Improvement, para 11.37).*
9. The Committee stated that the researcher will need to either – provide justification for why it is necessary for the overseas samples to have multiple identifies rather than just the study number – or amend the PIS/CFs.
10. The Committee noted that the application form states that participants can choose home visits or clinic visits. The Committee recommended that consideration is given to participants being able to change their mind during the study given it is long term. Please address this in the PIS/CFs.

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

ALL PIS/CFs

1. The Committee recommended that each information sheet is tailored to the audience it is targeted at and is not just a copy and paste job.
2. Please ensure the forms are New Zealand specific (e.g. refer to the National Ethical Standards for Health and Disability Research and Quality Improvement). For guidance, please refer to the participant information sheet templates on the HDEC website - <https://ethics.health.govt.nz/guides-templates-forms-0/participant-information-sheet-templates>.
3. The role of the HDEC has been overstated, please remove the statements “Their role is to protect your safety, rights, well-being, and dignity” and revise it to more accurately reflect the HDEC’s role to check research meets or exceeds established ethical standards.
4. Please closely review all the information sheets with regards to future research to ensure they comply with *National Ethical Standards for Health and Disability Research and Quality Improvement, para 7.57*. Please ensure there is sufficient information (from the Data Management Plan) on how this will be managed that is tailored to the audience and easy to understand. Refer to the HDEC template referenced above for guidance on what needs to be included.
5. Please closely review all the information sheets with regards to tissue and biobanking to ensure they comply with *National Ethical Standards for Health and Disability Research and Quality Improvement, para 7.58*. Please ensure there is sufficient information (from the Tissue and Data Management Plan) on how this will be managed and ensure it is simple and easy to understand for participants.
6. Please replace the Belgium sponsor’s data protection contact with a New Zealand based contact for data concerns.
7. Please make it explicit in the information sheets that the drug is completely experimental and hasn’t been approved anywhere in the world yet.
8. Please review the information sheets and ensure that the identifiers (ranging from age, year, DoB, gender, etc) mentioned within the document are consistent and note that only one identifier (unique study number) should be used unless justified.

CAREGIVER PIS/CF

1. The Committee were concerned with the insurance statement on page 5 implying that the caregiver may be held liable by the sponsor if something goes wrong. The Committee stated that this is not an acceptable position to take and recommended the insurance is discussed with the sponsor and this section updated. Please including relevant compensation information from HDEC template - <https://ethics.health.govt.nz/guides-templates-forms-0/participant-information-sheet-templates>.
2. The Committee advised that the data section on page 6 is hard to understand and requested it is revised and simplified to reflect the context of the caregiver (i.e. there is not a great deal of personal information being collected from caregivers).
3. Please ensure caregivers are not out of pocket for participants. E.g. by having to pay for text reminders and for visits to their doctor if they suffer an injury performing the role as caregiver. Please ensure the expenses and payments section on page 5 accurately reflects costs.

EXTENSION PIS/CF

1. Please ensure the title clearly states that it is for the extension study.
2. Please ensure participants will not be out of pocket from being involved in the study. E.g. by having to pay for reminder texts (page 8).
3. The HDECs now review pregnancy PIS/CFs only if they occur – please submit via the post approval amendment pathway and amend this section on page 9 accordingly.
4. Please update the data section to ensure all relevant sections of the HDEC data template are included. E.g. about publication which is only mentioned in the consent form.
5. Please ensure all the places that tissue will be banked are listed on page 15. Any additional repositories can be submitted via post approval amendment pathway.
6. Please check compliance of future use of tissue with *National Ethical Standards for Health and Disability Research and Quality Improvement, para 7.58* and provide appropriate information for participants.
7. The consent form states that personal data will be transferred overseas but the privacy and confidentiality section isn’t clear on what exactly this is. Please amend the section to make it clear to the participants what personal information will be sent overseas (i.e. that this is coded data).

COVID 19 PIS/CF

1. Please ensure the PIS and CF are clearly titled “continued participation’.

Decision

This application was *declined* by consensus, as the Committee did not consider that a provisional approval would provide sufficient time for researchers to provide the information requested by the HDEC.

|  |  |  |
| --- | --- | --- |
| **2** | **Ethics ref:** | **21/NTA/51** |
|  | Title: | MAGIC Trial |
|  | Principal Investigator: | DR Benjamin Gladwin |
|  | Sponsor: |  |
|  | Clock Start Date: | 08 April 2021 |

James Moore 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. MAGIC is an investigator-initiated multi-centre, parallel group, single-blind, randomised clinical trial incorporating a nested vanguard pilot phase, which will address the following research question: “Among adults who are invasively mechanically ventilated in the ICU following cardiac surgery with clinically significant vasoplegia does a methylene blue infusion at a rate of 1.5mg/kg/hour for one hour (intervention) compared with an infusion of placebo (1.5ml/kg/hr of 5% dextrose for one hour) (comparator) increase hours alive and free from vasopressors at day 10 post randomisation (primary outcome)”

Summary of resolved ethical issues

1. The Committee asked for clarity on what the usual intervention is for these patients – what is meant by both arms of the study (methylene blue and placebo) being within the range of what currently constitutes the best intervention standard.
2. The researcher advised that methylene blue is an established and recognised intervention standard, however there is little evidence to support the mortality benefits of the treatment. The researcher added that the lack of substantial evidence of the benefits of the treatment results in variability in care where some clinicians choose to use the drug and others do not.
3. The researcher added that the purpose of this trail is to obtain evidence of efficacy of this intervention with the anticipation for it to be accepted as the primary standard of care across the clinical community.
4. The Committee asked if the whole vanguard phase of 60 participants is being carried out in New Zealand or spread across the six international ICUs. The researcher responded that the intention is to commence the vanguard phase and recruit the 60 participants in New Zealand. However, he added that this depends on if other countries start their trials before New Zealand has completed this phase. He added that it is possible that Australia will come on board as part of the vanguard phase as well.
5. The Committee stated that the protocol infers that the vanguard phase is just to determine how accurate the sample size calculation is and not around safety and efficacy and queried if this is correct.
6. The researcher responded that it is a feasibility study to test if there will be any merit to continue to phase 2 trial and to assess recruitment potential for this next phase (sample size). The researcher added that at completion of the vanguard phase, the study will continue if there is evidence of benefit to the participant or stopped if there is no indication of benefit. The researcher added that the purpose is not to assess the safety as there are minimal risks for patients due to it being an established treatment used around the world.
7. The Committee advised that should the researcher decide to enrol participants into research without consent, low recruitment would not be sufficient justification for a best interests argument under Right 7(4) Code of Patients’ Rights and that the researcher would need to justify that alternative consent process would be in the best interests of the participants rather than the researchers.

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 this purpose of the study is not articulated well in the participant information sheet and consent form (PIS/CF) and recommended the researcher ensure it is explained clearly to assist potential participants to make an informed decision on the study.
2. The Committee noted the researcher’s confirmation that they will be seeking prospective consent from New Zealand participants and will not enrol any participants that arrive at ICU without having given advance consent prior to surgery. The Committee recommended the parallel step of seeking views from whānau in ICU for continuation in the study is removed from the consenting process as gaining consent from the participant prior to surgery is sufficient and keeps the consenting process clean.
3. The Committee requested that all documents, including the Protocol and PIS/CFs are revised and amended to appropriately reflect the method by which consent will be obtained as noted above.
4. The Committee noted that a data management plan, DSMB guidelines and charter, or a detailed study monitoring plan haven’t been uploaded and stated that these need to be provided to HDEC for review. Please ensure the plan complies with section 12 of the *National Ethical Standards for Health and Disability Research and Quality Improvement*. For guidance, please refer to the Data Management Plan template on the HDEC website - <https://ethics.health.govt.nz/guides-templates-forms-0> .
5. The Committee requested that the data management plan includes the ANZICS registry.
6. The Committee advised that letters of support from people involved in the study are not acceptable as independent peer review. Please provide a truly independent peer review, using the HDEC template on the website - <https://ethics.health.govt.nz/system/files/documents/pages/hdec-peer-review-template-june-2020.docx>
7. The Committee stated that evidence of the co-ordinating investigators medical indemnity insurance is required by the HDEC.
8. The Committee was concerned that the protocol does not represent the New Zealand context of ICU research, given the substantial number of New Zealand participants (e.g. there are irrelevant references to substitute decision makers, guardianship board, opt-out, etc.) Please ensure the protocol is relevant to the New Zealand context ensuring it complies with the relevant New Zealand ethical standards.

The Committee requested the following changes to the Participant Information Sheet and Consent Form:

1. Please note that a participant can’t withdraw at any time because once consented, they will be randomised while unconscious (page 1). Please amend the statement and check further discussion of this issue throughout the PIS/CF to ensure it makes sense.
2. According to the protocol, there has been more than one trial which shows the benefit of methylene blue. Please ensure this section (on page 2) is amended and improved with more information to allow participants to make a fully informed decision
3. Please explain what the standard of care treatments are for low blood pressure and if there are any alternative treatments to using methylene blue.
4. Please explain the purpose of the study clearly as mentioned above.
5. Please provide more information about the vanguard phase as mentioned above.
6. Please describe how the medication will be given (e.g. that it will be by infusion).
7. Please include more information on the data that will be stored on ANZICS registry and how it will work. Please ensure the content about future research complies with *National Ethical Standards for Health and Disability Research and Quality Improvement, para 7.57*.
8. Please bring the reference to ANZICS registry further to the front of the form.
9. Please state that the coded data will be sent overseas on page 5.
10. Please correct the contradictory statements about information use after withdrawing as one states optional and the other says it is mandatory (page 6).
11. Please remove the word “physically” from sentence about destroying data after 10 years.

Decision

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

* Please address all outstanding ethical issues, providing the information requested by the Committee.
* 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 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 Ms Catherine Garvey and Dr Karen Bartholomew.

|  |  |  |
| --- | --- | --- |
| **3** | **Ethics ref:** | **21/NTA/52** |
|  | Title: | A Phase 3, Open-label Extension Study of Viltolarsen in Ambulant Boys with Duchenne Muscular Dystrophy (DMD) |
|  | Principal Investigator: | Dr Gina O'Grady |
|  | Sponsor: | Clinical and Regulatory Services (CARSL) Consultin |
|  | Clock Start Date: | 08 April 2021 |

Gina O’Grady 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. This study aims to analyse the safety and tolerability of new investigational product "Viltolarsen", which is designed to interact with dystrophin RNA by exon skipping. This study is an open-label extension study in which boys who have already completed 48 weeks of treatment in the HDEC approved NS-065/NCNP-01-301 protocol (placebo or Viltolarsen), will receive Viltolarsen administered IV at weekly doses of 80mg/kg over 96 weeks. All participants will receive Viltolarsen.

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 for clarity on status of the 301 study and why this open label extension study is happening.
2. The researcher responded that there was only one participant recruited in New Zealand in the 301 study who had the specific genetic mutation required for the study. The previous study was a randomised placebo-controlled study and therefore it is unclear if the boy received the placebo or the active drug. This open label study guarantees the participant receives the active drug.
3. The Committee noted that the main study is scheduled to be completed at end of June or beginning of July.
4. The Committee stated that there is not a lot of information in the participant information sheet and consent form (PIS/CF) on the serious side effects of this drug. The Committee asked what information there is on the side effects and if the PIS/CF will be updated when the results of the main study are known.
5. The researchers responded that the participant has not experienced any side effects from his involvement in the main study, but there is a possibility that he is receiving a placebo. The researcher confirmed that the sponsor notifies them about any side effects that develop, including internationally, and these are updated in the PIS/CF.
6. The Committee reminded the researchers that therapeutic studies where participants are potentially receiving therapeutic benefit must not be terminated for reasons of commercial interest in New Zealand *(National Ethical Standards for Health and Disability Research and Quality Improvement, para 11.37).* The researchers confirmed that the study would only be stopped for efficacy or safety reasons.
7. The Committee noted that the researchers are confident that the assent form is appropriate to the single participant’s comprehension level.
8. The Committee noted that there is a mental health question directed at the parent and asked what their safety plan was for managing this if the parent shows signs of depression. The researcher advised that they would refer the information to the parent’s family doctor and that they also have pathways into Starship hospital health practitioners if the issue presented as urgent (with the parent’s consent).
9. The Committee asked for clarity on where and when the infusions and therapy take place. The researchers confirmed that the infusions taking place in Christchurch and the physio assessments were being done in Auckland on a weekly basis. However, now most of the treatments take place in Christchurch with the more infrequent physical and neurological examinations taking place in Auckland.
10. The Committee noted the researcher’s confirmation that they have not used and will not be using any promotional material (such as the Caregiver Handbook The Racer 53-X brochure and the FAQ document) other than the PIS/CF. The Committee clarified that it will not be approving the use of the promotional material as part of this application.

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 more information on the reference in the application to an overseas ethics committee declining the study. The researcher advised that she will investigate this and provide more information.
2. The Committee asked if the risk stated about anaesthesia is relevant. The researcher responded that as the single participant is managing with cannulation and hasn’t required a port to be inserted for anaesthesia, this risk is not relevant and can be removed from the PIS/CF.
3. The Committee asked for confirmation that the blood tests being sent to Singapore will in fact be destroyed after one month as this is unusual. The researcher advised that they will clarify this with the laboratory in question.
4. The Committee asked for more information on the home visits protocol. The researchers responded that the home visits are no longer feasible for this study and will remove it from the protocol and PIS/CF.
5. The Committee asked for clarity around what the videos are for and why they are necessary. The researcher advised that the videos are being used for physio training to ensure the different therapists are performing the assessments consistently. The Committee requested that more information detailing the use of the videos is provided in the information sheet and the data management plan is updated to include how the identifiable data will be managed.
6. The Committee asked for an explanation of the term “buzzy” that is used in the assent form. The researcher advised that it is something used for helping with pain during cannulation but as the participant has not been using it, they will remove reference to.
7. The Committee noted there are different durations for the storage of data and requested that these are amended to the correct duration which is for 10 years after the single participant turns 16. E.g. application mentions 15 years and PIS/CF states 25 years, etc.)
8. The Committee requested that the researchers ensure that the questionnaires have coded data about the participant and nothing identifiable.

The Committee requested the following changes to the Participant Information Sheet and Consent Form:

1. Please ensure the forms are relevant to the New Zealand context and replace the American language around IRBs and benefits, etc.
2. Please review the Māori tissue statement on page 10 as it could be a bit confusing to refer to genetic studies because there is no genetic analysis here.
3. Please include a section about how identifiable data will be used and shared on page 14. For example, there will be a number of people who may see identifiable data who fall outside the research team – home nurse, clinical person doing the strength tests and the physio reviewing any videotape.
4. Please update the content on future data use as per the Data and Tissue Management Plan (DTMP) and ensure it complies with *National Ethical Standards for Health and Disability Research and Quality Improvement, para 7.57*. For example, on page 15 – there is no mention of data FUR but it’s clear from the DTMP there will be – refer section 8.4 and 12.2.1 of the DTMP and amend accordingly.
5. Please reword the cultural statement to avoid confusion as it currently mentions genetic information that is not being conducted in this study.
6. Please remove reference to “buzzy” as mentioned above.
7. Please provide more on the use of the videos as mentioned above.
8. Please remove the “Primary Care Physician / Specialist notification option” section on page 21 of the consent form and add a sentence stating that a study doctor will talk to them about whether or not they want their GP to know.
9. Please remove the risk on anaesthesia and the reference to home visits as per the points above.
10. On page 18, as previously noted with other studies conducted at the site, the diagram requires amendment. For example, who is the ‘medical team’ and how are they different to the ‘study doctor’
11. Please ensure all matters included in the consent forms have been explained in the body of the participant information sheet. E.g. abnormal results going to GP and GP being told about participation in the study.
12. In the form titled “Agreement to allow your child to participate and authorisation for the videotaping of your child “ please check whether New Zealand has “master physiotherapists” and also state whether the video will be sent overseas or who will see it, if anyone, other than the physio.

Decision

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

* Please address all outstanding ethical issues, providing the information requested by the Committee.
* 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 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 Mrs Helen Walker and Dr Karen Bartholomew.

|  |  |  |
| --- | --- | --- |
| **4** | **Ethics ref:** | **21/NTA/54** |
|  | Title: | GS-US-465-4439: A Phase 2a Study to Evaluate the Safety and Efficacy of Selgantolimod-Containing Combination Therapies in Patients with Chronic Hepatitis B |
|  | Principal Investigator: | Prof Edward Gane |
|  | Sponsor: | Gilead Sciences, Australia and New Zealand |
|  | Clock Start Date: | 08 April 2021 |

Professor Edward Gane and Courtney Rowse 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. This is an open-label study to evaluate the safety and efficacy of Selgantolimod (SLGN)-containing combination therapies for the treatment of Chronic Hepatitis B (CHB).

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 the study design is complex with different treatment regimens depending on the cohort the participant is in. The Committee asked how the consent process will work to ensure participants understand what is required in their cohort. The researcher advised that it looks more complex than it is and that there are only two populations involved in the study, one that is already receiving treatment and the other that has received no treatment. He advised that because they will know what treatment the participant is receiving; this will make it simpler when they run through the consent process with them.
2. The Committee noted the researcher’s confirmation that Tenofovir is approved in NZ.
3. The Committee asked why people must be eligible to work in New Zealand to participate in the study. The researcher advised that is likely for the reason that people must have access to publicly funded health care if they are to participate in a trial.
4. The Committee asked if there is a risk of augmented side effects when the two drugs are given simultaneously. The researcher responded that they have combined these drugs in several other Hep B studies and have not seen any additive side effects of administering the two drugs together. He further added that the side effects listed about Nivolumab are from their use in oncology where the dose is 10 times higher than what they use in Hep B studies.
5. The Committee queried if, in the optional PK sub-study for SLGN, there is a risk of hypoglycaemia since participants needs to fast before blood withdrawal. The researcher advised that participants are required to fast for 8 hours pre-dose and 4 hours post-dose. The researchers intend to book visits for blood sample collection early in the morning so participants are fasting overnight. The researcher added that they will not be able to recruit diabetic participants who are insulin dependent.
6. The Committee noted that cohort 3 is to be initiated at the discretion of the sponsor after Cohort 2 completion of enrolment. The Committee asked if this means cohort 3 may not be included in the study. The researcher advised that cohort 3 will be included in the study as it is when participants will take all the drugs together, however it cannot start until after cohort 2 has completed treatment and results have been compared.
7. The Committee asked what volume of blood will be extracted from PK sub-study participants and if there is a chance of hypoglycaemia at all. The researcher advised that the total blood drawn will be 26 millilitres and advised that as this is not a large blood draw the risk of hypoglycaemia is low.
8. The Committee queried why there appears to be inequality in the reimbursement that participants will receive for their involvement in the study. The researcher advised that amounts are calculated in an equitable way that reflects the time and inconvenience of being involved in the study. The researcher added that they use a tried and tested formula based on time spent in the unit as well as the number of the procedures involved. For this study, there are participants who are in the study for a longer duration and will therefore receive a greater reimbursement.

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 the insurance certification is for $5m cover and asked if this was sufficient for the anticipated 20 participants. The researcher advised that they will confirm with the sponsor that the $5m insurance cover is per occurrence rather than aggregate.
2. The Committee questioned the categorical statement (in the Main and Tissue Future Unspecified Research (FUR) participant information sheet/consent forms) on Māori data sovereignty that reads “The following data sovereignty principles make sure that the data generated from the research is protected and can benefit Māori now and into the future”. The Committee recommended that this statement be amended as it may be making promises about benefit to Māori that cannot be kept.

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

1. Please ensure all significant points in the Data and Tissue Management Plan (DTMP) have been included in all of the PIS/CFs – and ensure the information is consistent with the DTMP. For example:
   1. Section 8.4 of the DTMP and especially, but not limited to, the inclusion of de-identified data in larger data sets.
   2. Section 7.3 of the DTMP states that de-identified data will be sent overseas to Singapore, Netherlands, and USA.
   3. The DTMP must cover the biobanking aspects of the optional studies. Similarly, with the submission of any data to international data bases, including any genomic databases.
   4. Please check this statement in the DTMP is correct, “Tissue use is restricted to the mandatory uses specified in the study protocol” given the various sub-studies.

MAIN PISCF

1. Please ensure the most up to date information available on side effects is included in the form.
2. Please add where the sponsor, Gilead, is based (i.e. that it is a US company with global subsidiaries).
3. Please remove the statement on sexual abstinence, as the HDEC do not recommend this as an effective means of contraception.

PK (OPTIONAL) PIS/CF

1. Please complete the statements in blue (e.g. ‘list each objective of the summary in lay terminology’).
2. Please state where the samples will be stored on page 3.
3. Please include a Māori cultural statement for tissue.
4. Please amend the statement that a withdrawal request must be in writing as consent can be verbal in New Zealand (page 4).
5. Please remove the reference to ‘genomic samples’ on page 5 as it is not part of the PK study.
6. Please include more information on venous canula that will be used all day for blood draws.
7. Please review the information that is provided on future research under ‘uses of your information’ section and ensue that it complies with *National Ethical Standards for Health and Disability Research and Quality Improvement, para 7.57*.

GENOMIC SUB-STUDY PIS/CF

1. Please carefully review and revise the content to ensure it is relevant to the genomic sub-study as it appears to be a cut and paste job from other information sheets. For example, there are some sections missing, including whether there will be publication of results and identifiability resulting from that as well as access and correction rights. Some other examples include:
   1. Please state where samples will be stored on page 2.
   2. Please appropriately articulate the risks and benefits for the genomic sub-study as they are different from the main study.
   3. Please revise the ‘What happens if you no longer want to take part in the study’ section on page 3 as it does not make sense for the genomic sub-study.
   4. Please amend statement about withdrawal as it does not have to be in writing on page 3.
   5. Please check, on page 5, that the future research is the same as previously described. I.e. limited to biomarker research about HBV and questions about HBV including causality, prevention, or better treatment and that it will not be used indefinitely because samples will be destroyed after 15 years.
   6. Add a Māori cultural tissue statement.
2. Please ensure the content of this document complies with the *National Ethical Standards for Health and Disability Research and Quality Improvement, para 14.27 – 14.41.*

TISSUE FUR PIS/CF

1. The comments about the other PIS/CFs also relate to this form. Please revise and amend the form accordingly.
2. Please ensure the content of this document complies with the *National Ethical Standards for Health and Disability Research and Quality Improvement, para 7.58.*

Decision

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

* Please address all outstanding ethical issues, providing the information requested by the Committee.
* 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 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 Ms Rochelle Style and Dr Sotera Catapang.

|  |  |  |
| --- | --- | --- |
| **5** | **Ethics ref:** | **21/NTA/55** |
|  | Title: | The SODa-BIC RCT |
|  | Principal Investigator: | Dr Paul Young |
|  | Sponsor: |  |
|  | Clock Start Date: | 08 April 2021 |

No one 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. A multicentre, randomized, double-blind trial to determine if the infusion of sodium bicarbonate in vasopressor-dependent ICU patients with moderate metabolic acidosis increases the number of vasopressor-free hours at day 7.

Summary of resolved ethical issues

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

1. The researchers consider the study could be in an individual’s best-interests under Right 7(4) Code of Patients’ Rights because of the close monitoring of arterial blood gases to monitor acid-base and electrolyte disturbances which goes beyond usual monitoring. They also noted that two clinicians are required to consider whether participation in the study is in an individual’s best interests. After discussion, the Committee was satisfied with this approach.
2. The Committee commended the researcher on making the protocol appropriate to the New Zealand consent context for this 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 stated that Sections 8.5 and 8.6 of the protocol cover some data management issues, but full compliance with National Standards is still required. Statements such as the trial is guided by strict protocols and procedures to protect against privacy but not outlining what these are is insufficient. A standalone data management plan for the New Zealand context or amendment to the protocol is required.
2. The Committee requested confirmation of New Zealand representation on the Management Committee based in Australia which determines access to the data.
3. The specific criteria for access to data is not given – only two general principles are set out which is public health and significance of privacy protection. The Committee requested clarification if New Zealanders have portal access, how they input data and whether this is going into the Australian and New Zealand Intensive Care Society (ANZICS) database.
4. The Committee queried if the researchers will go through the information sheet with the whānau. The current wording in the information sheet suggests not, but the Committee requested clarification.
5. In addition, the Committee queried if a separate information sheet for whānau is possible in the event of continued use of data if the participant dies or never regains capacity. If not, more information about data future use and access to de-identified information by other researchers should be included in the relative/whānau information sheet – refer also to comments below.
6. The protocol sets out 8 scenarios to enrolment (pages 16-17). The Committee noted that there are fewer scenarios in this protocol compared to other ICU enrolment protocols Northern A has reviewed and would like clarification from the researchers about the difference (a missing scenario includes where the person doesn’t recover sufficiently to provide informed consent prior to hospital discharge – some protocols provide for follow-up by phone and conversation noted on file). The Committee noted the following additional matters:
   1. Scenario 6: For participants who don’t recover sufficiently to provide informed consent for continued participation, the protocol states their data will be included because systematically excluding it would undermine the internal validity of the study. However, there is no mention of approaching whānau. Please clarify. This is especially concerning when the ‘flip’ scenario, scenario 8 (participant/whānau want to stop trial specific treatment but agree data can continue to be used), there is a discussion with whānau. Note that Right 7(4) involves a three stage approach – (1) best interests AND (2) steps taken to ascertain participant’s view AND (3) either research is consistent with participant’s view OR take into account views of persons interested who are available to advise
   2. Scenario 7 notes the extreme stress whānau will be under if the participant dies and for that reason, researchers won’t approach them for continued use of data upon the grounds that excluding it would create a bias which would undermine the internal validity of the study. However, the study duration is 2 years – The Committee queried why the researchers cannot approach the whānau after a year.

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

Main PIS for continued participation:

1. Please review for tense as some information is presented in the future tense when participation in the study intervention has already happened.
2. For the same reason, on page 3, please revise the following statement as it does not make sense as it is currently worded: “During this study the research team, and other intensive care staff will record information about you and your study participation. You cannot take part in this study if you do not consent to the collection of this information.”
3. Please provide greater transparency on page 4 about Australian and American investigators will have access to participants de-identified data and also that there is industry access.
4. The data future unspecified research on page 4 does not comply with National Standard 7.57. Please refer to the PIS/CF template statement on page 7 (<https://ethics.health.govt.nz/guides-templates-forms-0/participant-information-sheet-templates>)
5. On page 5, please replace ‘patients’ with ‘participants’
6. Please consider whether these research findings could really be ‘used inappropriately to support negative stereotypes, stigmatise, or discriminate against members of the same groups as you.’
7. Please consider, on page 5, statements about access rights when the study is double blinded – it may also need to include advice that access might mean continued use of data is withdrawn.
8. Please ensure that everything in the consent form has already been raised in the body of the PIS first – e.g.: “I agree to my contact information being sent overseas and so that researchers from the Australian and New Zealand Intensive Care Research Centre can contact me for the purposes of conducting study follow up phone calls.”
9. The two declarations at the end need to be for continued participation in the study

PIS for prospective participation

1. Check, where relevant, comments above relating to the main PIS for continued participation and apply changes as necessary.

PIS for persons interested (relative/whānau)

1. Check, where relevant, comments above relating to the main continued participation PISCF and apply changes as necessary.
2. Please review for tense as some information is presented in the future tense - there may be circumstances when the person has already participated. Please ensure both options are covered (ie, prospective participation or participation has already taken place) or split these scenarios into two different PISs
3. Please ensure information around risks is provided.

Decision

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

* Please address all outstanding ethical issues, providing the information requested by the Committee.
* 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*).

After receipt of the information requested by the Committee, a final decision on the application will be made by Full Committee (online)

|  |  |  |
| --- | --- | --- |
| **6** | **Ethics ref:** | **21/NTA/57** |
|  | Title: | The Bone Zone Trial |
|  | Principal Investigator: | Dr Paul Young |
|  | Sponsor: |  |
|  | Clock Start Date: | 08 April 2021 |

No one 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 purpose of this study is to assess whether early use of anti-resorptive drugs has an effect on Bone Mineral Density up to one year after a critical illness.

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 only people who have the capacity to consent will be included in the New Zealand (NZ) trial.

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 evidence of the CI's indemnity needs to be uploaded.
2. The Peer Review made some suggestions raised in relation to exclusion criteria (re: recent haemorrhage, low Hb,history of GI haemorrhage) and inclusion criteria (query over sufficient length of time in ICU to establish a link between critical illness and BMD measurements). The Committee noted it was not apparent that these comments have been responded to or reflected in the Protocol.
3. The Committee noted that, in New Zealand, the Medical Treatment Decision Maker (MTDM) cannot make the decision for the person to enter into the research study
4. Once the results of the first bone-scan are available, three options will be given to participants (page 36, protocol), including standard care for high risk participants (who may have been on placebo). Rather than being a scripted conversation, the Committee stated that options should be written in a separate participant information sheet. Participants should be entitled to consider each option carefully and also the information sheet should include the usual sections, i.e., what happens to the data etc AND what the risks and benefits are for each option (for example, for the women on placebo, if they break the blind early, they will get one of the study drugs free of charge for the duration of the study whereas if they wait until the end of the study period they will not).
5. The Committee queried who pays for the ongoing treatment of denosumab or repeat BMD at 2-years.
6. There is insufficient information in the documentation about the cost-effectiveness study, which data sets will be used and expressly seeking participant consent for it. While the participant information sheet has some information about this, it is unlikely participants will understand that length of hospital stay (said to be routine collection in clinical research) is for the cost-effectiveness study. Please amend all relevant documentation.
7. The Committee noted that the protocol has some information about data management (pages 42- 44), but not enough to comply with the National Standards (Chapter 12). The Committee requested that this is amended, especially regarding submission to ANCICS Registry (de-identified only in the study database) and who data will be shared with.
8. The Committee queried what the pilot study HDEC reference was, as this is referenced in the protocol, but the application form says this is unrelated to a previous ethics application.
9. The Committee requested a plan for findings of depression from the EQ5D-5L.
10. Please clarify the statement in the synopsis – “if eligible, the patient or surrogate decision-maker or MTDM will be approached for consent” which is contrary to Section 13.2 of the protocol to include ONLY patients who have recovered sufficiently to provide written informed consent prior to enrolment. All documentation should be revised for the NZ context where only consenting people will be included in the study.
11. The Committee noted that women 50 years and above are not all post-menopausal and discussed the risk of selection-bias. The Committee requested a clarification of the inclusion criteria.
12. The Committee queried why there is no reimbursement of expenses incurred during follow up visits.

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

1. Please include detail about blood storage and destruction. The protocol notes that hospital and local labs will be used (12.8) but the PIS does not contain any information.
2. The Nested bone turnover marker sub-study is not being undertaken in NZ (page 34, protocol) – please review the PIS to delete reference to markers (there are at least 2 references on pages 3 and 4)
3. The data Future Unspecified Research (FUR) section on page 8 is incomplete – for example, there’s no actual description of the FUR, nor does it say whether some of the research will be undertaken overseas (which, in this case, it likely will be because it will be on the ANZICS registries).
4. The Committee recommended to refer to the HDEC template (<https://ethics.health.govt.nz/guides-templates-forms-0/participant-information-sheet-templates>). The Committee noted there’s no description of the FUR, nor does it say whether some of the research will be undertaken overseas (which, in this case, it likely will be because it will be on the ANZICS registries) Given this, other researchers should also be listed regarding who may access and use de-identified data
5. Please replace all references to “patient” to “participant”
6. On page 8, please note right to access and correct might result in withdrawal from study because of blinding if access and correction sought prior to study end.
7. Please include the total amount of blood extracted for the whole duration of study.
8. Please summarize study procedures and schedule of events during the course of the study in tabular form for better understanding of the participants
9. Add into the GP section of the CF that the GP will get a treatment plan at the conclusion of the study
10. The section regarding contact information being sent overseas so that Australian and New Zealand intensive care researchers can contact participants is not outlined in the information sheet. The Committee noted that the reason for sending data overseas is also because the study database is overseas and for data FUR. It might be for future contact but, if it is, that’s not been covered before this clause appears. Follow-up and contact details should be a separate section.
11. Add in section for thecost-effectiveness study

Decision

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

* Please address all outstanding ethical issues, providing the information requested by the Committee.
* 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 protocol, taking into account the feedback provided by the Committee. *(National Ethical Standards for Health and Disability Research and Quality Improvement, para 9.7 & 12.5).*

After receipt of the information requested by the Committee, a final decision on the application will be made Full Committee (online)

|  |  |  |
| --- | --- | --- |
| **7** | **Ethics ref:** | **21/NTA/46** |
|  | Title: | A pilot study of traditional acupuncture as an adjunct treatment for IBS-diarrhoea |
|  | Principal Investigator: | Dr Li Feng |
|  | Sponsor: | New Zealand College of Chinese Medicine |
|  | Clock Start Date: | 31 March 2021 |

Li Feng, Derek Luo, Linda Zhang, Willem Fourie and Stephen Xu 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. A pilot study to investigate the adjunct effect of Chinese acupuncture for treating diarrhoea predominant Irritable Bowel Syndrome (IBS-D). 40 participants with IBS-D will be recruited and randomised into two intervention groups: standard of care vs standard of care plus traditional Chinese acupuncture, for an effectiveness comparison.

Summary of resolved ethical issues

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

1. The Committee commended the researchers for the much-improved study application since it reviewed and declined the initial study, noting the researchers had made significant amendments to it as suggested by the Committee.
2. The Committee asked for clarification around the recruitment process. After discussion, the Committee was satisfied that exclusion criteria would be known as part of standard of care before the potential participant is referred on for the screening process performed by the researchers, and medical notes are not being passed on.

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 queried if any insurance is required for this study covering research specifically. After discussion, the Committee were satisfied this is investigator-led and falls within the scope of the ACC scheme (although a claim may not be accepted for compensation). References to insurance held by the New Zealand College of Chinese Medicine in the information sheet should be removed.
2. Please provide MPS certificate for Dr Derek Luo and certificates for the relevant acupuncturists showing their professional accreditation.
3. The Committee noted that the 10 free sessions for participating in the trial without receiving acupuncture could be a potential inducement to participate in the study. The value of the 10 sessions is significant (approximately $1,000). The Committee requested that the offer for free acupuncture sessions be removed.
4. The Committee queried if potential benefit from the acupuncture could be seen after 12 weeks that differs from the standard of care and suggested that the researchers look into the timeframe and asking participants to keep a daily diary is not outlined and may be burdensome.
5. The Committee noted to ensure the standard of care participants are also reimbursed for their travel costs (petrol or taxi vouchers, etc)
6. The Committee noted that the public email address for Dr Luo should be changed to a private one (not a DHB address)

The Committee requested the following changes to the Participant Information Sheet and Consent Form:

1. Please consider revising for lay-language and amending typos and repeated statements.
2. On page 4, please amend the following statement: “The direct benefit for you from this study is that it is likely that your IBS symptoms are 14 improved after the treatment you receive. The benefit of the pilot study is that it may prove the concept of the adjunct effect of acupuncture for treating IBS-D.” The Committee noted there may be no benefit and the pilot study is too small to make the second claim.
3. On page 7 and the consent form, the intention for use of data for future unspecified researcher (FUR) is inconsistent as to whether it is mandatory or optional. Please review these statements for consistency, bearing in mind Standard 7.57. Please also check and revise the appropriateness of the following statement which, in any event, is inconsistent with previous advice about who will receive coded data: “You will not be told when future research is undertaken using your information. Your coded information may be shared with other researchers. You will not get reports or additional information about research that is done using your data.”
4. Please remove “Appendix 2” from the main title of the participant information sheet.
5. Remove the statement that standard of care treatment is a potential benefit because participants would already be receiving that.

Decision

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

* Please address all outstanding ethical issues, providing the information requested by the Committee.
* 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).*

After receipt of the information requested by the Committee, a final decision on the application will be made by Ms Rochelle Style and Dr Kate Parker.

|  |  |  |
| --- | --- | --- |
| **8** | **Ethics ref:** | **21/NTA/60** |
|  | Title: | GDM and school age outcomes (GiST) |
|  | Principal Investigator: | Dr Jane Alsweiler |
|  | Sponsor: | University of Auckland |
|  | Clock Start Date: | 08 April 2021 |

Chris McKinlay 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 the study is to compare school age outcomes for children of mothers with Gestational diabetes mellitus (GDM) who were part of a randomized trial (preHpod - 13/NTA/8) with children whose mothers did not have GDM.

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 with the researcher that the Clinical Data Research Hub (CDRH), based at the Liggins Institute, University of Auckland is not a general data repository – the Hub will be used in this study to provide data management and it will be accessible by the research team only.

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 queried how the researchers are getting information for the purposes of recruitment. The researcher responded that the women with outcomes needed for participation are recorded in an Auckland City Hospital database and controls would be selected and an invitation sent. After discussion, the Committee requested the researchers apply to HDEC for a formal waiver of consent and justify why it should be granted, having regard to the significant maternal information that would need to be accessed for the cohort matching. *(National Ethical Standards for Health and Disability Research and Quality Improvement, para 7.46-7.48)*.
2. The Committee stated that all future data-linking performed must be more clearly outlined in the protocol/data management plan and all other study documentation, including outlining these risks these participants. Please refer to the National Standards for Health and Disability Research and Quality Improvement, Standards 12.31-12.39. The Committee acknowledged the researchers advice that no current data linking is planned and that any data linking will be submitted by way of amendment in future. The Committee specifically noted that data-linking is not approved as part of the current application. The Committee further noted that the participant information sheets (PIS) currently seek blanket consent for data linking (which is not approved) and the information sheets should be amended accordingly.
3. Please ensure all information is kept for 10 years after each participant turns 16 *(National Ethical Standards for Health and Disability Research and Quality Improvement, para 12.13)*.
4. The Committee requested to see the letter sent to schools that outlines this research and what is required of them which appears to be reasonably significant.
5. The Committee also requested a PIS/CF be submitted for the teachers who are being asked to complete an assessment. While teachers might, in the normal course, complete such assessments, these assessments are for the purpose of research and different requirements therefore apply.
6. The Data and Tissue Management Plan is inadequate and requires more details – eg, De-identified / anonymised data may be sent overseas if requested by other researches (see 8.5). Section 8.6 says: If participants provide optional additional consent de-identified data will be made available to other researchers on request for future research as specified above and / or will be added to data from other sources to form larger datasets – this is inconsistent with the statement there will be no data Future Unspecified Research (FUR).
7. Please upload the Standing operating procedures (SOPs) for key study activities and processes (Appendix 5.6)

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

1. The Committee stated further information around data privacy and right to access/correct information is required and recommended the researcher refer to the HDEC template for guidance (<https://ethics.health.govt.nz/guides-templates-forms-0/participant-information-sheet-templates>)
2. Please remove any Yes/No tick box from the consent form that are not optional for participation.
3. Please include a section in the consent form for a parent to consent for the child’s teacher to complete the assessment.
4. Please include risks of incidental findings which could be upsetting and what can be done about that.
5. The Consent Form needs to include consent for the parent to receive a copy of the child’s results, currently it only refers to the results of the study

Decision

This application was *declined* by consensus, as the Committee did not consider that the study would meet the ethical standards referenced above. The Committee recommended the applicant resubmit to Northern A.

|  |  |  |
| --- | --- | --- |
| **9** | **Ethics ref:** | **21/NTA/61** |
|  | Title: | The CRITICAL-ACS Study |
|  | Principal Investigator: | Dr Philip Adamson |
|  | Sponsor: | University of Otago |
|  | Clock Start Date: | 08 April 2021 |

Philip Adamson and Lorraine Skelton 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. This is a prospective, open-label, pragmatic randomised controlled trial that will compare the strategy of Computed Tomography Coronary Angiography (CTCA) first with standard care with InTerventIonal Coronary Angiography (ICA) first amongst patients with Acute Coronary Syndrome (ACS) across New Zealand (NZ). The researchers intend to recruit 700 patients from 9 hospitals comprising a diverse demographic mix including 50% from hospitals without on-site access to ICA.

Summary of resolved ethical issues

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

1. After discussion, the Committee was assured that coronary disease that will need an angiogram will be detected via CT.
2. The Committee stated that the animation should not replace the participant information sheet but an abbreviated consent process (with an information sheet) can be used if required. The researcher confirmed the animation will never be used in place of an information sheet and noted that no potential participant is in need of critical care that abbreviated consent 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 requested confirmation that having a CT scan in the second arm of the study isn’t going to delay an angiogram in that cohort. The researcher confirmed that those who would need an angiogram within 24 hours are excluded from the study, but there is a small risk of delay. The Committee requested this is outlined in the participant information sheet.
2. The Committee, after confirming that the leftover blood biomarker component of the study is optional, requested that the researcher takes all information out of the main participant information sheet and create a new information sheet for this optional component. The main information sheet should outline what biomarkers are tested as part of the main study and then note there is a separate optional study in a separate participant information sheet/consent form (PIS/CF).
3. The Committee requested more information in the data and tissue management plan around ANZACS-QI such as who has access to this data, how the registry works in terms of data sharing and who has oversight in addition to the research module information. Similarly, with the Vascular Informatics using Epidemiology and the Web (VIEW)
4. The Committee noted the commercialisation of IP statement for optional research and queried if this was likely in the future. The researcher responded that it is plausible but unlikely. The Committee stated that the University of Otago should be named as sponsor in regard to this.
5. The Committee noted that information on the Christchurch Heart Institute (CHI) biobank to be provided – please refer to Chapter 15 of the National Ethical Standards.
6. The Committee noted that samples (Optional) may go overseas to a large number of companies AND the researchers may work in conjunction with Roche, Abbott Laboratories, Beckman-Coulter and Siemens. No details are provided in any of the documentation about this potential collaboration and no details are given of overseas biorepositories. Please amend the documentation accordingly. In that regard, the Committee also noted the protocol refers to requiring prior written agreement from the sponsor or its designee for the disclosure of any confidential information to other parties (page 22) – it is unclear who is the sponsor and what are the rules/guidelines for determining access. This is important given the potential collaboration with multinational pharma.
7. The Committee noted that the Data and Tissue Management Plant (DTMP) is headed as being the CHI’s and relates to Covid 19 ANTibody and T-cell Assays. The Committee was not sure this DTMP applied to this study, and requested a study-specific DTMP. *(National Ethical Standards for Health and Disability Research and Quality Improvement, para 12.15 & 14.17).*
8. Following publication of the primary paper, a de-identified individual participant data set will be submitted to a data archive for sharing purposes. Access to the de-identified dataset will be under a controlled access model (page 23, protocol). The Committee noted this hasn’t been mentioned in the DTMP or in the information sheets. Please amend. The other additional comments were raised about the DTMP
   1. Section 7.1 does not mention all the NHI identifiable data – this is a large omission and must be rectified please
   2. Section 8.2 has no mention of the multi-national drug companies de-identified data may be included in.
   3. Section 8.7 contains insufficient information to comply with the Linking Standards, nor does it have sufficient information about clinical trial registries and data banks and where de-identified tissue may be included in biobanks. *(National Ethical Standards for Health and Disability Research and Quality Improvement, para 12.31-12.39).*
9. Please upload the Trial Steering Committee charter (page 21, protocol) and the charter for the independent data safety monitoring committee together with the charter for the Māori oversight group. *(National Ethical Standards for Health and Disability Research and Quality Improvement, para 11.25).*

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

Main PIS/CF

1. Requires information about the risks of linking and more linking details including the role of NIHI. – refer to Standards 12.31 – 12.39.
2. Please outline in more detail the purpose of the ANZACS-QI registry, who has access to their data and what form their data is stored in addition to information about participant data being submitted to VIEW and its use for predictive analytics.
3. If safety and screening tests for notifiable diseases are not being undertaken, please remove references to this in the main PIS.
4. Please remove the discussion in several places about saliva.
5. Please clearly outline in the main PIS that participants would be consenting to four different components that include use of their hospital data, the intervention itself, use of other registry data (and what sorts of data that is), then linking for future health use.

Optional Tissue FUR PIS/CF

1. Refer to comments above – there are sections missing here and there’s more detail in the main PISCF which should be in this PISCF. This PIS needs considerable amendment – refer also to Standards 7.57 and 7.58.

Decision

This application was *declined* by consensus, as the Committee did not consider that the study would meet the ethical standards referenced above. The Committee recommended the applicant resubmit to Northern A.

## General business

1. The Committee noted the content of the “noting section” of the agenda.
2. Members raised that more work or information should be done to assist researchers in completing data management plans and meeting the National Standards. Similar was raised regarding using the other HDEC templates.
3. The Chair reminded the Committee of the date and time of its next scheduled meeting, namely:

|  |  |
| --- | --- |
| **Meeting date:** | 18 May 2021, 01:00 PM |
| **Meeting venue:** | ONLINE via Zoom |

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.

The meeting closed at 5.30pm