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| **Committee:** | Southern Health and Disability Ethics Committee |
| **Meeting date:** | 09 April 2019 |
| **Meeting venue:** | Sudima Hotel, Christchurch Airport, 550 Memorial Drive, Christchurch |

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| **Time** | **Item of business** |
| 11:30am | Welcome |
| 11:35am | Confirmation of minutes of meeting of 12 March 2019 |
| 11:45am | New applications (see over for details) |
| 11:45-12:10pm  12:10:12-35pm  12:35-1:00pm  1:00-1:25pm  1:25-1:50pm  1:50-2:15pm  2:15-2:40pm  2:40-:305pm  3:05-3:30pm | i 19/STH/67  ii 19/STH/68  iii 19/STH/69  iv 19/STH/70  v 19/STH/71  vi 19/STH/72  vii 19/STH/73  viii 19/STH/74  ix 19/STH/78 |
| 3:30pm | General business:  Noting section of agenda |
| 3:35pm | Meeting ends |

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| **Member Name** | **Member Category** | **Appointed** | **Term Expires** | **Apologies?** |
| Ms Raewyn Idoine | Lay (consumer/community perspectives) | 27/10/2015 | 27/10/2018 | Present |
| Dr Sarah Gunningham | Non-lay (intervention studies) | 27/10/2015 | 27/10/2018 | Present |
| Assc Prof Nicola Swain | Non-lay (observational studies) | 27/10/2015 | 27/10/2018 | Present |
| Dr Devonie Waaka | Non-lay (intervention studies) | 13/05/2016 | 13/05/2019 | Present |
| Mrs Kate O'Connor | Lay (ethical and moral reasoning) | 14/12/2015 | 14/12/2018 | Present |
| Assc Prof Mira Harrison-Woolrych | Non-lay (intervention studies) | 27/10/2015 | 27/10/2018 | Present |
| Dr Cordelia Thomas | Lay (law) | 01/07/2015 | 01/07/2018 | Present |
| Dr Paul Chin | Non-lay (intervention studies) | 27/10/2018 | 27/10/2021 | Present |
| Professor Jean Hay-Smith | Non-lay (health/disability service provision) | 31/10/2018 | 31/10/2021 | Present |

## Welcome

The Chair opened the meeting at 11:30 and welcomed Committee members.

The Chair noted that it would be necessary to co-opt members of other HDECs in accordance with the Standard Operating Procedures. Kate O’Connor and Dr Cordelia Thomas 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 12 March 2019 were confirmed.

## New applications

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| **1** | **Ethics ref:** | **19/STH/67** |  |
|  | Title: | Trial of Exenatide in Acute Ischaemic Stroke (TEXAIS) |  |
|  | Principal Investigator: | Dr Teddy Wu |  |
|  | Sponsor: | Monash University |  |
|  | Clock Start Date: | 28 March 2019 |  |

Dr Teddy Wu was present in person 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 investigates whether the short-term (5 days) use of subcutaneous injections of Exenatide (Byetta®) in patients with acute ischaemic stroke improves stroke outcome when compared to standard stroke unit care alone.
2. TEXAIS is a 3 year Phase 2, multicentre, prospective, randomised, open label, blinded endpoint trial. The length of participation is 90 Days.
3. The primary end point of early neurological improvement at 7 days, and secondary end points of recovery at 90 days.
4. Continuous glucose monitors will track the intraday dynamic variability of glucose in acute stroke in all trial patients (treatment and standard care).

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 the Researcher anticipated recruiting ten awake participants. The Researcher stated this was a very conservative estimate and was confident they could recruit more.
2. The Committee stated the main issue with the research as proposed was with consent. The Committee queried whether the majority of potential participants would be too unwell to provide informed consent. The Researcher stated some would but would have agreement from friends and relatives. The Committee advised that proxy consent was inconsistent with New Zealand law and participants could not be enrolled this way. The Researcher clarified the enrolment would be done by the clinician determining best interests in accordance with Right 7(4**)** of the Code of Health and Disability Services Consumers' Rights.
3. The Committee queried how the Researcher would determine the best interest of an individual. The Researcher stated involvement in the study would provide access to exenatide and would involve additional follow up, more clinician interest and potential benefit for secondary stroke injury. The Committee stated the issue was the Researcher could not guarantee benefit to an individual and it would be difficult to definitively state participation would be in each individual’s best interest.
4. The Researcher stated many stroke patients (e.g. those with aphasia or intracerebral haemorrhage) would be excluded and suggested the study could target patients who present with small strokes in the brain who may have severe symptoms (e.g. balance / coordination issues, nerve pain) but no cognitive problems.
5. The Committee reasoned that if the Researcher can recruit competent participants able to provide consent there would be no need to involve individuals who cannot or to do a best interests determination.
6. The Committee stated it would be able to approve the study if it would only include participants able to provide informed consent. The Researcher agreed to this change.
7. The Committee advised that an individual who is competent but physically impaired (i.e. incapable of writing a signature) can still indicate and provide consent. The Committee explained that someone else can record the consent (or the participant could provide a signature if able) as long as the process was properly documented.
8. The Committee queried whether people who are on insulin would be excluded as this was not mentioned on the protocol. The Researcher stated they had not identified that as a specific exclusion but would be careful as they would not wish to cause hypoglycaemia in participants. The Researcher stated the monitoring machine has an alarm to alert clinicians of a trend toward hypoglycaemia by measuring glucose levels in real-time.
9. The Committee queried whether participants with moderate renal impairment would be included and whether monitoring of the drug would occur. The Researcher stated they would usually look at routine blood tests to check renal function and monitor glucose to check on the effect of the drug but would not measure the levels of the actual drug itself. The Researcher stated the glucose itself will be a surrogate for the anti-diabetic properties of the drug. The Researcher stated if an individual has moderate renal impairment and is on other medications there may be an interaction that could cause increased side effects and this may be reason to exclude those participants. The Committee noted this was not included in the study protocol. The Researcher stated all participants would be enrolled on a case-by-case basis and confirmed this would be considered.

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

1. The Committee considered some of the text required excessive reading for an individual who has recently suffered a stroke and requested the Researcher trim down some of the content to simplify the sheet (e.g. simply state participants will ‘do a questionnaire’ instead of the Rankin scale).
2. The Committee suggested the inclusion of illustrations to aid understanding of the PIS.
3. The Committee noted an ambiguous statement that participants *may* be reimbursed for reasonable travel and queried whether participants would be paid. The Researcher stated they would not but may be offered taxi chits. The Researcher explained they would need to be certain they could offer it before making a conclusive statement regarding reimbursement. The Researcher offered to remove the section.
4. The Committee suggested a revision of the “What is the purpose of the study?” section to remove the sentence on study doctors jumping to conclusions.
5. The Committee requested a revision of the sentence regarding worse clinical outcomes or death as this could potentially be misinterpreted as meaning the study could be giving participants something to make them worse.
6. The Committee suggested not using technical terms when lay terms could be used. Specifically, the Committee requested the removal of all acronyms (e.g. mRS, NIHSS, cFPG, etc) as most of these are unnecessary. The Committee recommended the full names, or lay equivalents (e.g. finger prick test).
7. The Committee requested an explanation of what an anti-emetic is and which one will be used during the study
8. The Committee noted contraception is not discussed in the information sheet but is mentioned on the consent form. Please either remove this from the consent form or add the required information to PIS.

Decision

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

* Please amend the inclusion criteria to only enrol patients capable of providing informed consent.
* Please update the Participant Information Sheet and Consent Form, taking into account suggestions made by the Committee.

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| **2** | **Ethics ref:** | **19/STH/68** |  |
|  | Title: | Micronutrients and traumatic brain injury: case studies |  |
|  | Principal Investigator: | Prof Julia Rucklidge |  |
|  | Sponsor: |  |  |
|  | Clock Start Date: | 28 March 2019 |  |

Prof Julia Rucklidge was present in person 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 investigates whether a micronutrient formula can support a population of children with traumatic brain injury (TBI) to better manage their moods.
2. Previous research conducted by the University of Canterbury and this current study’s PI have found a beneficial effect of micronutrients on emotional dysregulation in children with ADHD. This particular micronutrient formula called DEN (Daily Essential Nutrients) has also been found to support patients with anxiety and depression.
3. In this pilot feasibility study, the researchers are seeking to review a series of individual case studies to investigate the effects of micronutrients on emotional dysregulation in children with TBI recruited through ACC.

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 the design of the study and whether the small number of participants and lack of a control group would be able to show efficacy. The Researcher stated it was not an efficacy trial but rather a feasibility test to determine whether the intervention was acceptable in the study group and if it could have any impact on their symptoms of emotional dysregulation, anxiety and sleep difficulties. The Researcher elaborated that as the participants will have a TBI whether or not they can follow the study requirements is unknown so to launch with a control group would be making an assumption. The Researcher stated with such small numbers of heterogeneous participants even with a control group it would be difficult to establish a causative difference between them. The Researcher stated the overall goal was to establish whether treating a population with TBI with the intervention is viable. The Committee noted that the protocol states the aim of the study is to evaluate the effectiveness and safety of DEN in children with TBI, which is at odds with the researcher’s statement that this could not be assessed in this feasibility study. The Committee noted that it must be clear in the protocol and PIS that this is a hypothesis-generating / feasibility study only.
2. The Committee queried how the Researchers would determine whether the intervention had a beneficial effect. The Researcher stated as the TBI will be at least a year old, participants will have an established baseline of symptoms. The Researcher explained that examining certain symptoms (irritability, dysregulated emotions, mood swings, aggression) over time may allow them to establish a beneficial effect.
3. The Committee noted that the children are a vulnerable population and queried why they were being targeted before further research on adults. The Researcher stated many adults are medicated which is a challenge as the combination of drugs and nutrients adds in a layer of complexity. The Researcher stated they would not wish to change a participant’s medication and children were seen as a fitting group for the research.
4. The Committee queried how the Researchers would attribute any change in symptoms to the intervention versus normal progression. The Researcher stated because the severity of the TBI in each participant will vary along with their own unique background it would be difficult to determine what ‘normal’ progression would be. The Researcher stated that as the injury is at least a year old, symptoms related to it will have been well established.
5. The Committee queried how old participants would be. The Researcher stated between the ages of 6 – 13 years old, having suffered a TBI at least a year ago. The Researcher confirmed no infants would be enrolled.
6. The Committee queried the reason behind the particular micronutrient formula chosen. The Researcher stated it was developed in Canada and was shown to have a benefit to the creator’s family so they made it available for further research. The Committee queried why this particular brand was chosen. The Researcher stated this was mostly due to a lack of alternative products with a similar combination of doses of constituent components on the market developed to target symptoms associated with emotional dysregulation, depression, anxiety etc.
7. The Committee queried whether the study was commercially funded. The Researcher stated it was not but the manufacturer was providing the product for use in the study. The Committee queried whether the participants would continue to receive the product after the trial. The Researcher stated if they chose to continue it would have a cost of about $80 per month but in previous studies the disability allowance has covered the cost.
8. The Committee asked for a clarification to question R.2.2 in the application regarding participants consenting to additional information. The Researcher stated it should read that participants will be asked for consent to access their health information from their GP and agreed to correct the answer.
9. The Committee queried the answer to question R.1.8 which indicated that one of the benefits to the study could be to the participant’s family. The Committee stated research should be undertaken to benefit the participant and not their family. The Researcher stated they were interested in the family relationship and if parental stress is reduced due to the easing of the child’s emotional dysregulation then it could be of benefit to the family in addition to the participant.
10. The Committee queried what would happen to blood samples after testing as the PIS states they will be discarded whereas application form stated they could be returned. The Researcher stated they would be discarded as normal according to lab protocols.
11. The Committee queried whether any of the blood samples would be held for Future Unspecified Research. The Researcher stated they would not be used again.
12. The Committee queried whether data from the study may be used in future research. The Researcher stated it was difficult to know what a future study could involve until you are at that stage but has sometimes been useful in the past to compare blood results from previous trials to report on the overall safety of micronutrients over time. The Researcher confirmed this only involves anonymised data.
13. The Committee queried the involvement of ACC case managers in the study. The Researcher stated the ACC case manager will be going along to home visits. The Committee queried how ACC are screening and referring participants. The Researcher stated ACC would choose appropriate cases. The Committee queried their process. The Researcher stated they would identify children who meet the inclusion criteria and then approach the families to invite them to participate in the research. The Researcher explained it would then be up to the family to choose whether to contact the study team. The Committee advised that any advertising material or flyer promoting the study would require submission and HDEC approval.
14. The Committee advised that as the study may involve Māori participants then formal Māori consultation is required. The Researcher stated this has been undertaken and had just recently received approval. The Committee noted the application form and answered that consultation was not required. The Researcher apologised for the error.

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 whether the study had received independent peer review. The Researcher stated this was in progress. The Committee recommended the Researcher consult and use the HDEC peer review template to ensure all necessary information is captured by the reviewer.

<https://ethics.health.govt.nz/system/files/documents/pages/HDEC-Peer-Review-Template.docx>

1. The Committee queried whether review by SCOTT had been undertaken. The Researcher stated they were in contact with the Ministry of Health to determine if it would be required. The Committee requested an update regarding this.
2. The Committee requested an additional PIS for teachers to complete as since they will be answering questionnaires this makes them participants.
3. The Committee noted there was no assent form for older children. The Committee advised that it would be appropriate to provide the older children with contact details of the study team, advocacy contacts etc. The Committee suggested the Researcher consult the following documents on the HDEC website:

* Assent Form Instructions and Checklist: <https://ethics.health.govt.nz/system/files/documents/pages/hdec-assent-form-instructions-and-checklist-may18.doc>
* Model Patient Information Sheet and Assent Form (7 – 11 years old):

<https://ethics.health.govt.nz/system/files/documents/pages/main-assent-7-11-years-clinical-trial.doc>

1. The Committee requested an update to the protocol and PIS to detail the ACC selection process. The Committee expressed concern at the involvement of ACC as participants may feel undue pressure to participate in order to appease ACC. The Researcher stated the intention was for ACC to provide the introduction as the case manager would be familiar to the participants. The Committee requested a disclaimer making it very clear that participation (or not) in the study will have no effect whatsoever on ACC entitlement.

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

1. The Committee noted the Investigator’s Brochure identifies risks that are not mentioned in the PIS. The Committee advised that all potential risks included in the Investigator’s Brochure, must be included in the PIS so individuals can make up their own minds on whether they are happy to accept that risk in a clinical trial. The Committee suggested splitting the risks into different categories (common, uncommon, rare) as applicable
2. The Committee requested it be made clear that the formulation used in the current study was not the same as the formulation used in some of the previous trials that had suggested benefit and safety.
3. The Committee advised that information in the consent form must first be present in the PIS. The Committee requested the section in the consent form stating “If my child has upcoming medical procedures..” is first discussed in the PIS.
4. The Committee noted a consent to be placed in a separate database to be contacted in the future is mentioned for the first time on the consent form and requested information explaining this is included in the PIS.
5. The Committee expressed concern over the study seemingly over promising the benefits of the intervention. The Committee requested the removal of the paragraph in the PIS stating how effective it has been in other trials.
6. The Committee noted the pronouns in the PIS jump switch from referring to parents and children and requested this be corrected (e.g. for the parents it states “How do I take capsules” when it is not the parents who will be taking them).
7. The Committee requested the inclusion of information in the main PIS advising that teachers will fill out questionnaires regarding the emotional mood of participants.
8. The Committee requested the inclusion of a footer and page numbers to the PIS.
9. The Committee requested the addition of a disclaimer advising that blood samples will be tested for haemochromatosis and Wilson’s disease.
10. The Committee requested conservative language regarding benefits and cautioned the Researcher against ‘over-promising’ the intervention’s help with the symptoms of ADHD, anxiety etc.
11. The Committee requested the removal of the word ‘solicit’ from the child assent forms.
12. The Committee noted the formatting of some of the bullet points was inconsistent and requested this be corrected.
13. The Committee requested inclusion of information in the PIS regarding incidental findings and whether the study team will contact the participant’s GP if their blood test results indicate serious concern.

Decision

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

* Please supply an updated protocol. This should address the inability to assess effectiveness using the selected study design (study aims / objectives), and detail ACC’s role in participant selection, recruitment and study visits.
* Please supply an updated participant information sheets and consent forms, taking into account the suggestions made by the Committee.
* Please supply evidence of Māori consultation and independent peer review.
* Please confirm whether the study requires SCOTT approval and provide this if so.

After receipt of the information requested by the Committee, a final decision on the application will be made by the full Southern Health and Disability Ethics Committee at the next available meeting.

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| **3** | **Ethics ref:** | **19/STH/69** |  |
|  | Title: | ENABLE (Engaging Toll-like Receptor Signalling for B-cell Lymphoma Chimeric Antigen Receptor T-cell Therapy) |  |
|  | Principal Investigator: | Dr Robert Weinkove |  |
|  | Sponsor: | Malaghan Institute of Medical Research |  |
|  | Clock Start Date: | 28 March 2019 |  |

Dr Philip George was present in person 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. Chimeric antigen receptor (CAR) T-cell therapy involves genetically modifying patients’ immune cells to redirect them against cancer cells, before returning them as a treatment. CAR T-cells can effectively treat people with certain types of chemotherapy-resistant blood cancers and two ‘second generation’ CAR T-cell therapies are licensed in the U.S. and Europe. Although most patients respond, fewer than half with relapsed lymphoma remain free of disease a year after treatment with current CAR T-cell therapies. One way to address this is through ‘third-generation’ CAR T-cell therapies with improved anti-tumour activity. This is a phase 1 safety dose escalation trial of a new third-generation CAR T-cell therapy, for people with relapsed and refractory B-cell non-Hodgkin lymphoma (B-NHL) without other curative options.
2. Objectives of the study: The primary objective is to assess safety of this therapy (protocol section 10). Secondary objectives include assessing treatment response and feasibility of CAR T-cell manufacture.
3. Methods: After consent, screening and enrolment, patients will undergo a leukapheresis procedure (see protocol section 13.3). Patient T-cells will be genetically modified in a Medsafe-licensed Good Manufacturing Practice (GMP) Laboratory at the Malaghan Institute of Medical Research (IB section 8) to produce CAR T-cells.
4. After cell expansion in the laboratory and when provided the cells meet all testing criteria, patients will receive low-dose chemotherapy before CAR T-cell return. Afterwards they will be monitored closely for symptoms and signs of toxicities.
5. Response Assessment and Follow up: Response to therapy will be assessed by PET-CT scan 3 months post treatment. Trial follow up will take place for 2 years. Participants will be followed up annually in the bone marrow transplant clinic lifelong, with long-term outcomes and events captured by reporting to an international cell therapies registry.

Summary of resolved ethical issues

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

1. The Committee thanked the Researcher for attending in person and complimented them on a well prepared application.
2. The Committee commended the Researcher on the Māori consultation process and the benefit to participants it will bring.
3. The Committee queried whether any future unspecified research is planned. The Researcher said the plan was to consent participants onto the Malaghan immune tissue bank that can store their samples for future research. The Researcher agreed to supply the information sheet and consent form to the Committee for review.
4. The Committee queried whether participants will be added to a registry. The Researcher stated patients undergoing stem cell treatment are routinely enrolled on a bone marrow registry to capture long term toxicities and that worldwide there are now large cell therapy registries. The Researcher stated they would strongly encourage participants to enrol on a cell therapy registry for similar long term follow up. The Researcher stated Professor Morrison was in discussion with the HDEC Secretariat regarding mandating enrolment on a register as part of entry into the trial.
5. The Committee stated it did not have concerns about registry enrolment being mandatory as long as it is explicated stated on the main participant information sheet, so the participant is properly informed and consenting to it. The Committee advised that this may deter some people from joining the study and may harm recruitment numbers. As an alternative the Committee suggested making an optional “yes / no” box on the consent form for participants to opt-in to.

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 the study would involve questions on participants’ mental health and wellbeing and queried how anyone indicating severe distress would be managed. The Researcher stated this had not been discussed in great detail but they had spoken with the palliative care team who mentioned getting psychiatrist liaison support for the study.
2. The Committee stated the Researchers would need a safety management plan as many studies are including mental health questions, with no plan to manage the answers, which was not acceptable. The Committee explained that this was a potentially unhappy group of people and if the Researchers discovered suicidal ideation in a participant this would need to be managed. The Researcher agreed to consult with the palliative care team.

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

1. The Committee noted the Participant Information Sheet (PIS) stated participant names would not be recorded. The Committee queried how participants would be identified and whether the study would involve unique study ID codes. The Researcher confirmed it would. The Researcher explained the one exception would be the full identifiers would need to be attached to the T-Cells sent to the lab to ensure the right CAR-T treatment is provided to the right participant.
2. The Committee noted the PIS was not using the standard ACC statement. The Committee queried whether the study had any commercial involvement. The Researcher stated a New Zealand-Chinese company owned the rights to the product but had no input on trial management or design. The Committee requested the Researcher use the ACC statement from the HDEC-approved PIS template.

https://ethics.health.govt.nz/system/files/documents/pages/piscf-template-february-2019-v2.doc

1. The Committee queried the instructions on the PIS to contact the study team in an emergency. The Researcher stated these participants would be in a unique situation and would ideally contact the study team rather than the emergency department. The Committee raised concern that if someone had an emergency (e.g. chest pain) they may think they should not call an ambulance. The Committee requested the section be clarified to ensure participant safety.
2. The Committee requested the inclusion of a statement advising participants that their data supplied to the registry will be held overseas.
3. The Committee requested the inclusion of a statement advising participants that this was a ‘first in humans’ trial and the first time this will be trialled in New Zealand.
4. The Committee requested the removal of ‘yes / no’ boxes from the consent form unless it refers to something truly optional (i.e. the participant can answer NO and still participate in the trial).
5. The Committee requested the inclusion of chemotherapy risks along with the frequency with which they occur.
6. The Committee requested the third paragraph on page 5 include the numbers of people previously treated with the 3rd generation CAR-T cell therapy.

Decision

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

* Please supply an updated protocol detailing the safety plan for managing participant distress.
* Please supply an updated Participant Information Sheet and Consent Form, taking into account suggestions made by the Committee.

After receipt of the information requested by the Committee, a final decision on the application will be made by Professor Jean Hay-Smith and Dr Paul Chin.

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| **4** | **Ethics ref:** | **19/STH/70** |  |
|  | Title: | PRO2TECT - CORRECTION |  |
|  | Principal Investigator: | Dr Rabindranath Kannaiyan |  |
|  | Sponsor: | IQVIA RDS Pty. Limited |  |
|  | Clock Start Date: | 28 March 2019 |  |

Dr Rabindranath Kannaiyan was not present 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 main purpose of the study is to test if new study drug vadadustat, also called AKB-6548 can treat anaemia (low red blood cell count) in participants with chronic (long-term) kidney disease. Vadadustat is believed to work by raising the number of red blood cells that are made by the bones. It does this by helping the body produce erythropoietin (or EPO).
2. Study population consists of participants ≥18 years of age with Non-Dialysis-Dependent Chronic Kidney Disease (NDD-CKD). Study consists of a screening period, Treatment Period 1, Treatment Period 2, and the Follow-up Period. Following screening period of up to 8 weeks (56 days), approximately 1850 eligible participants will be randomized 1:1 to vadadustat (150mg tablet) or darbepoetin alfa. Blood and urine samples will be collected for current study and future exploratory analyses (optional).
3. The study will be considered completed when approximately 631 major adverse cardiovascular(involving the heart or blood vessels) events (MACE) have accrued over the 2 NDD-CKD studies (Studies AKB-6548-CI-0014 and AKB-6548-CI-0015) and all enrolled participants have had the opportunity to have their Visit 13 (+/- 5 days).
4. Executive Steering Committee (ESC) blinded to the randomization will oversee the study and provide expert input to assure high scientific standard. Independent Data Monitoring Committee(IDMC) will review and discuss the available study safety data and will meet approximately twice per year throughout the study. IDMC will be unblinded and will include, at a minimum, a nephrologist, a cardiologist, and a biostatistician. An independent safety endpoint adjudication committee (EAC) blinded throughout the course of the study will adjudicate the primary safety endpoints (all-cause mortality, non-fatal myocardial infarction, and non-fatal stroke). Thromboembolic events and hospitalization for heart failure(HF) will also be adjudicated by the EAC.

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 was disappointed to see an application and participant information sheet not suitable for a New Zealand context.
2. The Committee advised that terminating a study for commercial reasons was not a valid reason in New Zealand and requested a revision on page 17 of the main PIS to remove this.
3. The Committee advised that the onus to inform the participant’s GP of any medically serious findings is the responsibility of the research team and not the participant and requested an amendment on page 9 of the main PIS.
4. The Committee advised that in New Zealand verbal withdrawal is permitted at any time and for any reason and requested an amendment on page 9 of the main PIS to reflect this.
5. The Committee advised that any pregnant participants or their partners would require a separate consenting process to allow the Researchers to gather information on the pregnancy.
6. The Committee advised that some participants ‘lost to follow-up’ aren’t ‘lost’ but rather no longer wish to participate or have contact and that chasing them down with a 3rd party is excessive. The Committee noted the locator company has extensive search rights and this should be optional. The Committee advised that participants should have the right to withdraw consent for such companies to be used. The Committee requested a revision of page 17 to address this.
7. The Committee requested the addition of a statement on page 17 advising that significant identifiable information may be provided to participant locator companies.
8. The Committee requested a revision to the risk of serious heart problems with darbepoetin on page 13 to elaborate and clarify.
9. The Committee queried whether the active comparator was available in New Zealand, whether it was subsidised and whether it was standard of care. The Committee requested this information be included on the main PIS.
10. The Committee queried whether the exploratory testing on page 8 of the main PIS was optional. The Committee queried whether genetic testing will potentially be performed. The Committee advised that if this is optional it needs to be removed from the main body of the PIS and have a separate consent process.
11. The Committee requested clarification regarding medication to address side effects and how participants may need to pay for this on page 9. The Committee advised that the costs of medications required to treat potentially study-related adverse events should be reimbursed by the study centre. The Committee requested this be amended, or the Researchers provide a justification on why participants should incur the cost.
12. The Committee advised that any planned future unspecified research would require a separate consent form for participants to agree to.
13. The Committee queried whether the research would involve pharmacokinetic analysis and requested detail regarding this if so.
14. The Committee queried what tests the research would involve and requested a clarification on what is meant by some tests now and some in the future.
15. The screening text discusses an optional sub-study and consent form on stress hormones. The Committee requested the removal of this if it is not relevant to New Zealand, otherwise please provide information regarding this.

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

1. The Committee requested a revision of the tone of language to be less authoritative (e.g. reword statements of “you must”) and simplify the technical language.
2. The Committee noted the PIS reads as if participants cannot withdraw consent for follow-ups and implies they must stay until the very end. The Committee advised that participants have the right to withdraw at any time for any reason and requested a revision to amend this.
3. The Committee noted information regarding insurance claims on the pregnant participant information sheet irrelevant to New Zealand and requested its removal.
4. The Committee noted contraceptive options on page 15 of the main PIS were out of date or unavailable in New Zealand (e.g. the contraceptive sponge). The Committee requested this be amended to reflect options accessible in New Zealand.
5. The Committee requested a clarification to whether stated risks apply to the study drug or rescue medication.
6. The Committee noted a statement advising to please see information under the “What are my rights?” heading but the information is not present. The Committee requested this be corrected.
7. The Committee requested the removal of any references to a ‘legally authorised representative’ in the pregnancy form. The Committee advised that proxy consent was inconsistent with New Zealand law and participants could not be enrolled this way
8. The Committee requested the inclusion of a cultural statement regarding the storage and distribution of blood samples (please see the HDEC website for guidance: <https://ethics.health.govt.nz/guides-templates-forms-0/cultural-questions-%E2%80%93-guidance>).

Decision

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

* Please supply an updated protocol addressing the concerns raised by the Committee.
* Please supply an updated participant information sheet and consent form, taking into account suggestions made by the Committee.

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

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| **5** | **Ethics ref:** | **19/STH/71** |  |
|  | Title: | PRO2TECT - CONVERSION |  |
|  | Principal Investigator: | Dr Rabindranath Kannaiyan |  |
|  | Sponsor: | Akebia Therapeutics, Inc. |  |
|  | Clock Start Date: | 28 March 2019 |  |

Dr Rabindranath Kannaiyan was not present 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 the study is to evaluate whether vadadustat is safe and effective in treating anaemia and has fewer side effects than a currently used prescription medication (darbepoetin alfa). Serious heart problems (e.g, stroke, heart attack, etc.) are known to be a serious side effect of darbepoetin alfa in the treatment of anaemia. This study is also being done to further understand these side effects of vadadustat compared to darbepoetin alfa. This potential new drug is being tested to treat anaemia (low red blood cell count) in patients with chronic (long-term) kidney disease.
2. The vadadustat is believed to work by raising the number of red blood cells that are made by the bones. It does this by helping the body produce erythropoietin (or EPO). The study drug comes as a tablet. Darbepoetin alfa is an ESA prescription medication that has been approved to treat anaemia by regulatory authorities. It is used to treat anaemia by increasing the amount of red blood cells in the blood. Darbepoetin alfa is given as an injection just under the skin.
3. This research project is made up of the following parts: Screening Period, Treatment Period 1, Treatment Period 2 and Follow-Up Period. Approximately 1850 participants will be randomised to either receive vadadustat 300 mg per day or Darbepoetin alfa subcutaneous injection. The study will last for up to 4 years and may involve up to 34 visits to the study centre. The study doctor will also check the haemoglobin monthly in Years 2, 3 and 4 of the study.
4. An IDMC will be established to review and discuss the available study safety data as participants are enrolled and followed. An independent safety EAC, blinded to treatment group, will be formed prior to study commencement to adjudicate the components of the primary safety endpoints. Thromboembolic events and hospitalization for HF will also be adjudicated by the EAC.

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 was disappointed to see an application and participant information sheet not suitable for a New Zealand context.
2. The Committee noted reference to bone marrow samples in the application but not the PIS. The Committee requested clarification on whether bone marrow was involved in the study.
3. The Committee advised that terminating a study for commercial reasons was not a valid reason in New Zealand and requested a revision on page 17 of the main PIS to remove this.
4. The Committee advised that the onus to inform the participant’s GP of any medically serious findings is the responsibility of the research team and not the participant and requested an amendment on page 9 of the main PIS.
5. The Committee advised that in New Zealand verbal withdrawal is permitted at any time and for any reason and requested an amendment on page 9 of the main PIS to reflect this.
6. The Committee advised that any pregnant participants or their partners would require a separate consenting process to allow the Researchers to gather information on the pregnancy.
7. The Committee advised that some participants ‘lost to follow-up’ aren’t ‘lost’ but rather no longer wish to participate or have contact and that chasing them down with a 3rd party is excessive. The Committee noted the locator company has extensive search rights and this should be optional. The Committee advised that participants should have the right to withdraw consent for such companies to be used. The Committee requested a revision of page 17 to address this.
8. The Committee requested the addition of a statement on page 17 advising that significant identifiable information may be provided to participant locator companies.
9. The Committee requested a revision to the risk of serious heart problems with darbepoetin on page 13 to elaborate and clarify.
10. The Committee queried whether the active comparator was available in New Zealand, whether it was subsidised and whether it was standard of care. The Committee requested this information be included on the main PIS.
11. The Committee queried whether the exploratory testing on page 8 of the main PIS was optional. The Committee queried whether genetic testing will potentially be performed. The Committee advised that if this is optional it needs to be removed from the main body of the PIS and have a separate consent process.
12. The Committee requested clarification regarding medication to address side effects and how participants may need to pay for this on page 9. The Committee advised that the costs of medications required to treat potentially study-related adverse events should be reimbursed by the study centre. The Committee requested this be amended, or the Researchers provide a justification on why participants should incur the cost.
13. The Committee advised that any planned future unspecified research would require a separate consent form for participants to agree to.
14. The Committee queried whether the research would involve pharmacokinetic analysis and requested detail regarding this if so.
15. The Committee queried what tests the research would involve and requested a clarification on what is meant by some tests now and some in the future.
16. The screening text discusses an optional sub-study and consent form on stress hormones. The Committee requested the removal of this if it is not relevant to New Zealand, otherwise please provide information regarding this.

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

1. The Committee requested a revision of the tone of language to be less authoritative (e.g. reword statements of “you must”) and simplify the technical language.
2. The Committee noted the PIS reads as if participants cannot withdraw consent for follow-ups and implies they must stay until the very end. The Committee advised that participants have the right to withdraw at any time for any reason and requested a revision to amend this.
3. The Committee noted information regarding insurance claims on the pregnant participant information sheet irrelevant to New Zealand and requested its removal.
4. The Committee noted contraceptive options on page 15 of the main PIS were out of date or unavailable in New Zealand (e.g. the contraceptive sponge). The Committee requested this be amended to reflect options accessible in New Zealand.
5. The Committee requested a clarification to whether stated risks apply to the study drug or rescue medication.
6. The Committee noted a statement advising to please see information under the “What are my rights?” heading but the information is not present. The Committee requested this be corrected.
7. The Committee requested the removal of any references to a ‘legally authorised representative’ in the pregnancy form. The Committee advised that proxy consent was inconsistent with New Zealand law and participants could not be enrolled this way
8. The Committee requested the inclusion of a cultural statement regarding the storage and distribution of blood samples (please see the HDEC website for guidance: <https://ethics.health.govt.nz/guides-templates-forms-0/cultural-questions-%E2%80%93-guidance>).

Decision

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

* Please supply an updated protocol addressing the concerns raised by the Committee.
* Please supply an updated participant information sheet and consent form, taking into account suggestions made by the Committee.

After receipt of the information requested by the Committee, a final decision on the application will be made by Dr Sarah Gunningham and Dr Paul Chin.

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| **6** | **Ethics ref:** | **19/STH/72** |  |
|  | Title: | MK-7339-010: Phase 3 Study of Pembrolizumab Plus Olaparib Versus Abiraterone Acetate or Enzalutamide in mCRPC |  |
|  | Principal Investigator: | Dr Peter Fong |  |
|  | Sponsor: | Merck Sharp & Dohme (New Zealand) Pty Limited |  |
|  | Clock Start Date: | 28 March 2019 |  |

Dr Peter Fong was not present 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. Mk7339-010 is a phase 3, randomised, open-label study treating participants with mCRPC, who are unselected for HRR and whose disease has progressed on NHA and chemotherapy.
2. Approximately 780 participants will be randomly assigned in a 2:1 ratio to Group A or Group B respectively. Participants randomised to 'Group A' will receive pembrolizumab plus olaparib and participants randomised to 'Group B' will receive abiraterone acetate plus prednisone/ prednisolone (if they previously received enzalutamide) OR enzalutamide (if they previously received abiraterone acetate).
3. Participants randomised to Group 'A' will receive Pembrolizumab on D1 of each 3-week dosing cycle and will continue until discontinuation criteria is met, or until the participant has received 35 administrations (approximately 2 years) of treatment. If they are eligible for second course treatment, participants may receive up to 17 more administrations of pembrolizumab. Oral dosing with olaparib will begin on pembrolizumab Cycle 1 Day 1 and continue on a daily dosing schedule. If one drug is stopped due to toxicity the participant may continue to receive the other drug. Participants randomised to Group 'B' abiraterone acetate plus prednisone/ prednisolone OR enzalutamide will begin dosing on D1 and continue on a daily dosing schedule until discontinuation criteria is met. Patients who have discontinued treatment will be followed up 12 weekly
4. Quality of Life reported outcomes will also be collected throughout 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 requested an updated insurance certificate specific to the study.

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

1. The Committee advised that follow-ups should be optional and requested this be amended.
2. The Committee requested the inclusion of a “Yes / No” box on the consent form by the last bullet point indicating permission for the study doctor to contact the participant’s GP.
3. The Committee requested the removal of any mention of ‘authorised representatives’ as proxy consent is inconsistent with New Zealand law.
4. The Committee requested section 7 (biomarkers) be re-written in lay language as it is currently too technical.
5. The Committee noted the title of section 8 (“What do I do on my own?”) is potentially ambiguous and requested a clarification that these are responsibilities of the participant during the trial.
6. The Committee requested a revision of section 14 (sending tissue overseas) to simply list the countries the tissue will be sent to.

Decision

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

* Please amend the Participant Information Sheet, taking into account suggestions made by the Committee.
* Please supply a protocol-specific insurance certificate.

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| **7** | **Ethics ref:** | **19/STH/73** |  |
|  | Title: | CA209-8FC: A Study to Compare Nivolumab Drug Product Process D to Nivolumab Drug Product Process C in Participants with Stage IIIa/b/c/d or Stage IV Melanoma after Complete Resection |  |
|  | Principal Investigator: | Dr Sanjeev Deva |  |
|  | Sponsor: | Bristol-Myers Squibb |  |
|  | Clock Start Date: | 28 March 2019 |  |

Dr Sanjeev Deva was present by teleconference 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 Phase I, multi-centre, randomized, double-blind study to Compare Nivolumab Drug Product Process D to Nivolumab Drug Product Process C in Participants with Melanoma skin cancer after Complete Resection.
2. Participants will be randomized (1:1) to one of the following 2 treatment arms:

Arm A - Nivolumab Process C

Arm B - Nivolumab Process D

1. Participants are assessed at different time points to see whether they have responded to treatment and have blood tests (PK, chemistry, haematology) to measure the activity of Nivolumab Process C and D in the body. Archival tissue blocks will be collected for the biomarker analysis. Efficacy assessment in a form of periodic CT/MRI imaging will be performed. Safety assessments will be performed every cycle and reviewed by the investigators on the site level and by the Independent Data Safety Monitoring committee on the Sponsor level.
2. Study duration is approximately 6 years with a 1 year treatment period and 5 years of the follow-up period.

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 the study would be offering participants a different drug to what is ‘tried and true’ and requested the Researcher justify the potential benefits compared to the potential risks.
2. The Researcher stated the trial drug has the same genealogy and protein sequence as the approved drug but undergoes a less expensive manufacturing process. The Researcher stated the study would allow participants an opportunity to receive a chance to receive a drug they may otherwise be ineligible for. The Researcher explained the drug was not currently funded before stage IV on a pharmacoeconomic basis. The Researcher stated it was available through self-funding but at a cost of approximately $100,000 a year so very few people were able to afford it.
3. The Committee queried whether the trial involved a randomisation process with PK analysis to assess whether people randomised to arm B are getting equivalent concentrations of the investigational product compared to the approved product. The Researcher confirmed this would happen.
4. The Committee queried the incidence of melanoma in Māori. The Researcher stated it would be less than the general population as it is predominantly a fair skin disease but noted that when Māori do present with melanoma it tends to be thicker and more severe. The Committee advised that this information would have been helpful when answering question P.4.1 and requested the Researcher keep this in mind for any future applications.

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 on whether the study required approval from SCOTT.
2. The Committee queried the duration of the trial. The Committee noted it was described as a bioequivalence study but considered a one year treatment period would be longer than necessary to establish bioequivalence. The Researcher stated the initial pharmacokinetics sampling would be much shorter but the therapy duration is based on the results of a previous trial in which the participants received the treatment for one year. The Researcher explained PK data would be harvested at the beginning and then the participants would continue to receive the treatment for the remainder of the year.
3. The Committee advised that if it were determined early on that the drugs were not bioequivalent it would be unethical to continue with the trial for the entire year duration. The Researcher stated there would be data monitoring safety committees during the study but was not sure when would be triggered. The Researcher agreed to clarify the arrangements with the Sponsor and provide an update.

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

1. The Committee suggested an overall revision of the PIS to simplify some of the content as it may be difficult for a layperson to understand.
2. The Committee requested the statement “both processes share the same genealogy, meaning it has been derived from the same origination” be re-written and discussed in laypersons’ terms.
3. The Committee requested a short lay title for the study
4. The Committee requested the inclusion of a statement advising that this was a ‘first in humans’ trial. The Committee advised this should explain that as this was the first time one of the drugs was to be used in humans participants may not receive any benefit and as it has not been tested there was an unknown risk of harm.
5. The Committee queried what circumstances may arise where it would not be possible for a unique study ID to be attached to a participants information. The Committee requested an explanation of what these circumstances would be included in the PIS. If this is not applicable to a New Zealand context the Committee requested its removal.
6. The Committee noted the Māori tissue statement was under the wrong heading and requested it be moved to the appropriate section.
7. The Committee advised that the statement on the consent form regarding whether interpreters is available is an instruction from the template meant for researchers.
8. The Committee requested an explanation in laypersons terms for what an ‘infusion’ is when mentioned on page 4.
9. The Committee requested the inclusion of discussion regarding the normal treatment course with nivolumab (treatment frequency, dose and duration) and whether it is the same as proposed in the study.
10. The Committee noted the bullet point formatting was off in the compensation statement and requested its correction.

Decision

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

* Please confirm whether the study requires SCOTT approval. If so please supply evidence of this.
* Please clarify the DMSC arrangements.
* Please supply an updated Participant Information Sheet and Consent Form, taking into account the suggestions made by the Committee.

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

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| **8** | **Ethics ref:** | **19/STH/74** |  |
|  | Title: | Survivors of medically serious suicide attempts |  |
|  | Principal Investigator: | Dr Sarah Fortune |  |
|  | Sponsor: |  |  |
|  | Clock Start Date: | 28 March 2019 |  |

Dr Sarah Fortune was present by teleconference 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 investigates reasons why suicide via hanging is a commonly chosen method in New Zealand.
2. The prevalence of hanging as a method of suicide in Aotearoa/New Zealand is unusually high, particularly among Māori, men and consumers of mental health services but we do not know why.
3. This mixed-methods observational study of n = 30 patients, presenting to hospital following a medically serious suicide attempt, aims to explore factors which influenced their decision to use, or contemplate using, highly lethal methods of suicide.
4. Participants will be interviewed by an experienced, culturally appropriate clinician/researcher using an interview guide and responses analysed using thematic analysis.
5. Participants will also complete a brief, standard measure of suicidal behaviours (Beck Scale for Suicide Ideation).
6. All participants will be in the clinical care of the Psychiatric Consult Liaison Team at Middlemore.
7. Study findings will inform strategies to reduce the salience or appeal of hanging as a high case-fatality method of suicide.

Summary of resolved ethical issues

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

1. The Committee requested a brief overview of the research. The Researcher explained they were a clinical psychologist and over the years have unfortunately interviewed a number of people very soon after they’ve made a medically significant suicide attempt. The Researcher stated they have become increasingly curious over time about the high frequency with which people have used hanging as a method. The Researcher stated academic research has revealed that New Zealanders seem to be much more likely to choose hanging as a method of suicide compared to other comparable countries. Furthermore Māori and Pacific communities are disproportionately affected, accounting for upwards of 90% of hanging deaths. The Researcher stated despite various national strategies the suicide rate in New Zealand has remained high and is increasing in the Māori population. The Researcher stated it was important to understand why people make a range of choices about suicide method (in particular why hanging is so common) in order to help guide prevention strategies.
2. The Committee queried whether the study was focusing on hanging exclusively or whether other methods would be studied. The Researcher stated hanging was the primary method but the research would involve a mixture of all medically serious methods. The Researcher explained they were interested in emerging trends in other types of potentially lethal methods (e.g. overdosing on diabetes treatment medications) and would also evaluate the similarities and differences between people who choose hanging and other serious methods.
3. The Committee noted a research assistant would be doing most of the interviews. The Committee queried who this would be and whether they had the appropriate expertise. The Researcher explained they were a registered psychiatric nurse with at least 15 years’ experience. The Researcher stated they were a clinical nurse specialist with an expert level of clinical practice and their daily routine involves interviewing patients.
4. The Committee queried who the second interviewer would be if the first was unavailable. The Researcher stated the backup interviewer has up until recently been the suicide prevention coordinator at CMDHB, is an occupational therapist with a current practicing certificate and a clinical lead in child and adolescent mental health services. The Researcher stated they were currently undertaking a PhD but confirmed this study was not related.
5. The Committee noted the interviews would be transcribed by a professional service and queried whether they had signed confidentiality agreements. The Researcher confirmed this and explained it was the same transcription service used by the psychiatric team in Christchurch.
6. The Committee noted this was not explained on the Participant Information Sheet, only that the interview would be recorded. The Committee requested the inclusion of a statement advising that it would be transcribed and reassuring the participant that confidentiality would be maintained. The Committee advised that it would be up to the Researcher whether to allow participants to review the transcript as this may have the potential to cause distress.
7. The Committee queried the study title and what ‘medically serious’ suicide attempt means. The Researcher stated they have had different discussions about it and the research is interested in near-fatal suicide attempts as opposed to those that are not physically significant (e.g. swallowing several paracetamol tablets). The Researcher explained that focusing on potentially lethal attempts would be the ‘best proxy’ to fatal incidents.
8. The Committee advised the Researcher that the supplied peer review contained sufficient information was using an outdated template. The Committee requested the Researcher use the latest HDEC template for future applications:

<https://ethics.health.govt.nz/system/files/documents/pages/HDEC-Peer-Review-Template.docx>

1. The Committee queried whether there was an element of deception involved, as if the primary focus of the research was on hanging it did not come across this way from reading the Participant Information Sheet (PIS). The Researcher stated the nature of suicide often involves elaborate plans which are then abandoned in a moment of distress and replaced by another method (e.g. a planned drug overdose switched to dangerous driving or hanging). The Researcher stated they have interviewed a number of people where this seems to be the case and the decision-making process needs to be understood. The Researcher stated many of the potential participants will likely have harmed themselves in other ways during the same attempt (e.g. be intoxicated and cut themselves and then attempted hanging). The Researcher stated the focus on hanging reflected the clinical reality rather than trying to deceive participants and it was pertinent to the flow of the decision-making process of suicidal people. The Committee accepted the Researchers explanation.
2. The Committee queried the identifiability of data and considered that digital recordings would have participant voices speaking and could include identifiable names, locations, family members etc. The Researcher agreed this would be challenging and stated they had no desire to include names but certain contextual details of their story may be difficult to remove without losing the context of the narrative.
3. The Committee noted the application mentions data will be de-identified but did not believe an audio recording could be de-identified, as even if given a coded title the voice itself would still be identifiable. The Committee queried whether these recordings would be kept or destroyed after transcription. The Researcher stated the plan would be to destroy them.
4. The Committee queried whether the transcripts would be stripped of identifiable features. The Researcher agreed this would be possible. The Committee suggested the removal of proper nouns so confidentiality is maintained and context is preserved.
5. The Committee queried whether any recordings or transcripts of a participant’s would be destroyed if they withdrew consent from the study. The Researcher confirmed they would.

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 Researcher would manage participants who indicate severe distress or suicidal ideation. The Researcher stated the interview would be halted. The Committee queried what would happen if the participant experienced distress after the interview. The Committee explained that the Researcher would need a safety plan in the protocol to properly manage this. The Researcher agreed to formulate a safety management plan and include it in the protocol.

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

1. The Committee requested a general revision for consistency as some information ‘jumps around’ the sections.
2. The Committee requested the inclusion of a table detailing the appointment schedule and how much time participation would involve.
3. The Committee requested the inclusion of the data management plan in the PIS.
4. The Committee noted an optional consent clause on including participant details in national mortality collections. The Committee requested information explaining what this is be added to the PIS.
5. The Committee noted an optional consent clause on contacting the participant’s GP regarding study participation and/or abnormal results in the consent form. The Committee requested information explaining this is added to the PIS.
6. The Committee reasoned that the inclusion of the word ‘medically’ in the title may be potentially confronting to participants and suggested its removal.
7. The Committee advised that by using HDEC template the Researchers have picked up italic font and formatting dashes that are meant for designing the template and suggested a revision.
8. The Committee advised that the italic text on the consent form stating to only include yes / no if optional was a template instruction and could be removed.
9. The Committee suggested the inclusion of an email contact box for participants to fill in if they wish to receive results from the study.

Decision

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

* Please supply an updated Participant Information Sheet and Consent Form, taking into account suggestions made by the Committee.
* Please supply an updated protocol detailing the safety management plan for the event of participants indicating severe distress.

After receipt of the information requested by the Committee, a final decision on the application will be made Dr Paul Chin and Dr Sarah Gunningham.

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| **9** | **Ethics ref:** | **19/STH/78** |  |
|  | Title: | CBP-201AU002: Study of the Safety and Effect of CBP-201 in Adults with Atopic Dermatitis |  |
|  | Principal Investigator: | Assoc. Prof Marius Rademaker |  |
|  | Sponsor: | Connect Biopharma |  |
|  | Clock Start Date: | 28 March 2019 |  |

Assoc. Prof Marius Rademaker was not present 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. CBP-201, a human monoclonal antibody (mAb), is being developed for the treatment of adults with moderate to severe atopic dermatitis (AD) and other inflammatory conditions.
2. The proposed double-blind, randomized, placebo-controlled, multi-centre, multi-national, multiple ascending dose (MAD) study is being undertaken in male and female adults diagnosed with AD, and otherwise good health. The study is intended to evaluate the safety, tolerability, pharmacokinetics (PKs) and efficacy trends of escalating multiple ascending doses (MAD) of CBP-201. Participants will receive four doses, one week apart, of CBP-201 or matching placebo administered by subcutaneous (SC) injection at planned dose levels of 75 mg, 150 mg or 300 mg.
3. Safety will be evaluated by occurrence of adverse events (AEs), physical examinations, concomitant medications, safety laboratory assessments (chemistry, haematology and urinalysis) and review of 12-lead ECGs. Injection sites will be specifically examined over time to detect reactions.
4. Efficacy trends as well as the PK and pharmacodynamic (PD) profile will be evaluated to aid dose selection in later studies in AD and other indications.
5. A Safety Monitoring Committee (SMC) will be included to minimize risks to participants. The SMC will review blinded interim Cohort safety data prior to dose escalation in the subsequent Cohort.

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 advised that collecting information on a participant partner’s pregnancy will require a separate Participant Information Sheet and Consent Form, as well as an additional consent process to collect any information on the baby after birth.

Decision

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

* Please supply an additional PISC for the event of a participant or their partner becoming pregnant.
* Please clarify which of the documents supplied to HDEC with the application is the revised PISC.

## General business

1. The Committee noted the content of the “ noting section” of the agenda.
2. The Chair reminded the Committee of the date and time of its next scheduled meeting, namely:

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| **Meeting date:** | 14 May 2019 |
| **Meeting venue:** | Sudima Hotel, Christchurch Airport, 550 Memorial Drive, Christchurch |

The following members tendered apologies for this meeting.

* Raewyn Idoine
* Sarah Gunningham
* Mira Harrison-Woolrych

1. **Problem with 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 3:35 pm.