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| **Committee:** | Southern Health and Disability Ethics Committee |
| **Meeting date:** | 14 July 2020 |
| **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 09 June 2020 |
| 11:40am | New applications (see over for details) |
| 11:45 – 12:10pm  12:10 – 12:35  12:35 -1:00  1:00 – 1:25  [10 minute Break]  1:35 – 2:00  2:00 – 2:25  2:25 – 2:50  2:50 – 3:15  [10 minute Break]  3:40 – 4:05  4:05 – 4:30  4:30 – 4:55 | i 20/STH/51  ii 20/STH/107  iii 20/STH/114  iv 20/STH/103    v 20/STH/105  vi 20/STH/106  vii 20/STH/111  viii 20/STH/101    ix 20/STH/118  x 20/STH/116  xi 20/STH/98 |
| 4:55pm | General business:  Noting section of agenda |
| 5:00pm | Meeting ends |

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| **Member Name** | **Member Category** | **Appointed** | **Term Expires** | **Apologies?** |
| Dr Sarah Gunningham | Lay (other) | 27/10/2015 | 27/10/2018 | Present |
| Dr Devonie Waaka | Non-lay (intervention studies) | 18/07/2016 | 18/07/2019 | Apologies |
| Assc Prof Mira Harrison-Woolrych | Non-lay (intervention studies) | 28/06/2019 | 28/06/2020 | Present |
| Dr Paul Chin | Non-lay (intervention studies) | 27/10/2018 | 27/10/2021 | Apologies |
| Professor Jean Hay-Smith | Non-lay (health/disability service provision) | 31/10/2018 | 31/10/2021 | Present |
| Mrs Helen Walker | Lay (other) | 19/08/2020 | 19/02/2021 | Present |
| Mr Dominic Fitchett | Lay (the law) | 05/07/2019 | 05/07/2022 | Present |
| Dr Pauline Boyles | Lay (consumer/community perspectives) | 05/07/2019 | 05/07/2022 | Present |
| Dr Patries Herst | Non-lay (intervention studies) | 22/05/2015 | 22/05/2023 | Present |

## Welcome

The Chair opened the meeting at 11:30am and welcomed Committee members, noting that apologies had been received from Dr Devonie Waaka and Dr Paul Chin.

The Acting Chair noted that it would be necessary to co-opt members of other HDECs in accordance with the Standard Operating Procedures. Dr Patries Herst confirmed their eligibility, and were co-opted by the Chair as members of the Committee for the duration of the meeting.

The Acting 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 09 June 2020 were confirmed.

## New applications

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| **1** | **Ethics ref:** | **20/STH/51** |
|  | Title: | NZ DIETS \_ASIA Study |
|  | Principal Investigator: | Prof Sally D Poppitt |
|  | Sponsor: | The University of Auckland |
|  | Clock Start Date: | 26 March 2020 |

Dr Ivana Sequeira and Dr Louise WW Lu 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. Previous studies have found a distinct biomarker fingerprint for Asian-Chinese patients as opposed to Caucasian patients, which is associated with adverse metabolic outcomes.
2. The Researchers now want to assess whether it is diet or biology that is primarily causing the difference between these biomarkers. This new study will control for diet to assess its role in the biomarker, as well as assessing the influence of certain foods typical of a Mediterranean-style diet which are known for their positive influence on metabolic outcomes.
3. 30 pre-diabetic participants (20 Asian Chinese and 10 European Caucasian) between 18-60 years of age, and who are either overweight or obese (BMI 24-40 kg/m2), will be recruited to the 2-week residential diet controlled programme. The two diet arms will adhere to NZ and Chinese national dietary guidelines for good metabolic health, and are:

1) a healthy (‘control’) diet

2) a healthy diet + added nutrients (‘synergy’ diet), with some additional nutrients hypothesised to improve metabolic health.

Both diets are matched for energy content, and tailored so that participants maintain body weight throughout the study. Both intervention arms are expected to have beneficial effects. Participants will reside at the Human Nutrition Unit facility in Mt Eden, Auckland. The study team will cook all their food (and drinks) and only foods from HNU can be consumed. Before the start of study, participants will have body composition (using dual x-ray absorptiometry and magnetic resonance imaging), an oral glucose tolerance test (OGTT) to determine diabetic profile, and clinical markers of diabetes risk (glucose, insulin, and metabolomics) including microbiome measured. Changes in these markers will be assessed at the end of the 2 week study.

Summary of resolved ethical issues

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

1. It was confirmed that the study had been registered in a clinical trials registry.
2. The Committee asked in what situations the Researchers might choose not to inform participants’ GPs of any incidental findings. The Researchers stated that they would typically meet with participants to discuss any incidental findings, and ask them if they would like to report those findings to their GP. The Committee asked for the Researchers to ensure that any serious incidental findings are notified to the GP as well as discussed with the participant. Please amend the PIS and protocol to make clear that notification of serious findings is not optional.
3. It was clarified that a second ethics application would be made for a following study assessing the effect of diet on these biomarkers for individuals in real surroundings.
4. The Committee asked about the Researchers’ relationship with participants’ GPs. The Researchers confirmed that they will be seeking information from GPs, but only if incidental findings are detected and in that case agreement from the participant will then be sought.
5. It was confirmed that health information generated in the study would be kept for 10 years.
6. The Committee asked how the findings of the study might benefit Māori, noting that the study was not including Māori participants. The Committee further noted that ethnicity is a social construct, and that someone might not identify as Māori and yet have Māori tīpuna. The Researchers explained that a separate study within the National Science Challenge (the Healthier Lives Group) will look at nutrition in Māori, and that the same methodologies are used and results will be shared between the studies.
7. The Committee asked if dietary advice may be given at the end of the study, and the Researchers confirmed that they would provide advice and recommend that participants continue to follow the Healthy Diet.
8. The Committee asked whether 2 weeks will be sufficient to achieve a noticeable difference across the biomarkers. The Researchers stated that previous studies have shown an effect on the biomarkers over just 6 hours, and for this study the power calculation shows that the sample size should be sufficient over the two week period. The Researchers expressed confidence that due to the study being in a controlled residential environment, they are confident that few datapoints should be compromised (by participants not following the required diet).

Summary of outstanding ethical issues

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

1. The Committee asked about the cohort and what was meant by it being a ‘diverse’ group. The Researchers explained that an overweight standard for Chinese individuals is greater than that for Caucasians. The Committee asked if gender was also being considered, and the Researchers confirmed that this variable will be included in the statistical analysis. The Committee asked for this to be made clear in the study protocol.
2. The Committee asked whether participants’ health information should be checked with their GPs, to avoid the risk of incorrect information being reported. The Researchers agreed that they could do this and add it to the PIS, and stated that they typically request participants to bring any list of medications that they are taking. Please update the protocol accordingly.
3. The Committee asked how tissue samples would be stored. The Researchers explained that tissue would be stored with the metabolic health team, but registered in the ‘virtual’ High-Value Nutrition biobank. If samples are requested by researchers through that biobank, permission will first be sought from the participants before they are shared. Only investigators from the study team will have access to any identifying information. The Committee stated that it was not clear what samples were being used in this study and which samples were being kept for biobanking/FUR. Please make sure this information is made clear in the main and biobanking PIS.

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

1. Please provide an example of the extra nutrients designed to improve metabolic activity, to show that they are common whole foods.
2. The Committee asked how full-time residents will be managed and how their diet will be controlled. The Researchers stated that they want to give participants the autonomy to leave the residency for work, studies, and so on. It would be similar to a university hall of residence, but with a set schedule. Participants’ compliance to the set diet will be monitored via urine tests. Please explain this monitoring clearly in the PIS.
3. The Committee suggested that the Researchers make the study data available in a de-identified form for future research. If this were to be done, participants would need to be given the option of consenting for the use of their data in future unspecified research.
4. Please clarify that participants will not be able to meet or socialise with friends who are not participants on the study.
5. Please inform participants that the liver tests may bring up unexpected results, and that you will ask for permission to contact their GPs in that case.
6. The Committee asked for the justification of the hypothesis that the Healthy Diet plus supplements may have benefits for diabetes risk. The Researchers explained that there is strong evidence supporting the Healthy Diet, but it is unknown whether the additional nutrients characteristic of a Mediterranean diet are beneficial. The Committee asked for this equipoise to be explained in the PIS. Please remove the statement that both arms are beneficial, and state instead that both are known to be a healthy diet.
7. Please explain clearly how participants are allocated to each diet arm: that Asian participants will be allocated by chance to either arm, but that Caucasian participants will only be enrolled into the control arm.
8. Please amend the statement “We will ask you to eat all food items from every meal” on page 6, so as to make clear that participants do not need to eat all the food given to them.
9. Please amend the statement under the heading “How will my samples and data be stored?” on page 8 so as not to imply that any samples will be used for research without participants’ consent.
10. Page 1 states that participants will live at the Nutrition Unit. Then on page 5 participants can go out for exercise, page 6 that they can attend university/work. Please clarify for participants exactly what they are able to do.
11. Page 8: "we ask that all the data collected can remain" - please clearly state here that the person can withdraw and that all data collected to that point will remain and be analysed, but that you will collect no more data from that point onwards. Also, if the person has given consent to FUR, you need to check at this point if they wish to withdraw consent for that.
12. Page 10: please clarify that the University of Auckland is sponsoring this study.
13. Page 11: implies that all samples are kept for FUR in a biobank and that it is not a separate consent, please clarify this.
14. Tissue Banking PIS: Please add more details about the tissue bank and where samples will be stored. Please also add a warning statement that if samples are shared with overseas researchers, the legal and ethical protections may not be the same as in NZ.
15. Tissue banking: please remove the first paragraph on the first page. It is confusing as it mixes up storage of samples for main study (which should be part of the main PIS/CF as everyone has to know it) and the information/consent for FUR (and how, where, how long etc. the FUR samples are stored). Please remove the OGTT details or otherwise explain.
16. Advertisement: please make clear whether people can or can't leave the unit, and what for.

Decision

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

* Please amend the information sheet and consent forms, taking into account the suggestions made by the Committee.
* Please amend the study protocol, 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 Dr Pauline Boyles and Professor Jean Hay-Smith.

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| **2** | **Ethics ref:** | **20/STH/107** |
|  | Title: | (duplicate) Interbleed |
|  | Principal Investigator: | Dr Matt Wheeler |
|  | Sponsor: | The Population Health Research Institute |
|  | Clock Start Date: | 17 July 2020 |

Dr Matt Wheeler and John Eikelboom 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. One of the side effects associated with antithrombotic medications for heart conditions is that patients may experience some type of bleeding during the course of their treatment. This study will explore the risk factors for bleeding and what types of outcomes occur after bleeding. The study takes the form of a case-control study, involving the comparison of a person with a GI bleed to a control participant who has not been hospitalised for a bleed within the last year. Both case and control patients will have been diagnosed with a heart condition and are matched according to age. Questionnaires and physical measurements, along with details regarding the clinical presentation will be obtained. Both groups will be reviewed (either physically or over the phone) at 3 months and 12 months for measurement of cardiovascular and functional outcomes, bleeding events and antithrombotic medication use.

Summary of resolved ethical issues

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

1. The Committee clarified that the study is not an audit, but a case-control observational study.
2. The Committee stated that the primary ethical issue is the inclusion of a sub-group of patients who are unable to consent due to being either seriously ill, unconscious or having died due to their condition. It was noted that those who cannot consent at the time of data collection but will recover will be asked to consent for use of their collected data in the study, and the data from those who die could be used, however it would not be legally possible to include data from those patients who do not regain the capacity to consent over the duration of the study (see right 7(4) of the Code of Health and Disability Services Consumers' Rights). The Committee asked whether excluding those patients would bias the results. The Researchers stated that they do not know how many participants will not be able to provide consent by the end of the study, but expect it to be a small number, and therefore not critically bias the results.

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 cases and the controls will all be on anti-thrombotic medication. The Researchers stated that not all patients will be on that medication, so that anti-thrombotic medication may be explored as a correlator of bleeding. The Committee asked for the title to be amended to reflect this.
2. The Committee asked how the control participants will be recruited. The Researchers stated that in the initial phase both cases and controls will be recruited from inpatients at the general medical service at Wellington hospital. The Committee asked for the study protocol to be amended to reflect this and to explain how those control participants will be recruited.
3. The Committee questioned whether recruiting control participants from inpatients would affect the scientific validity of the study, and it was suggested that validity would be maintained if inpatients are used for both the control and case groups. The Researchers explained that the study has had local peer review from Dr Noel Chan, in addition to numerous reviews internationally. The Committee asked to see evidence of that international review
4. Please provide a detailed data management plan, ensuring that it meets the different aspects laid out in para 12.15 of the National Ethics Standards.
5. The Committee asked for evidence that formal Māori consultation is being sought.

The Committee requested the following changes to the Participant Information Sheet and Consent Forms. These refer to all versions unless otherwise specified:

1. Please give each PIS a lay title.
2. The PIS for family/whanau should be re-written to address the family/whanau, and to ensure that it is asking only for their *opinion* as to whether the concerned family/whanau member would have wanted to take part.
3. Please amend the main PIS to reflect the context that participants’ information has already been collected, and you are now seeking consent for the use of that information in research. To do this the form should begin by explaining what has happened already.
4. Please proof-read each PIS for grammar/spelling and test with a lay reader for clarity.
5. Please add greater information on how data will be managed in the study, how it will be stored and in what form, whether it might be shared with other researchers, in what form, and if it might be sent overseas. Refer to the new PIS template for guidance <https://ethics.health.govt.nz/system/files/documents/pages/hdec_pregnancy_follow-up_child_participant_information_sheet_consent_form_template_9_july_2020.docx>
6. “…if there are concerns, we will ask you to see your regular doctor.” If there are serious concerns, it is the Researcher’s responsibility to contact the participant’s GP. Please state that you will do so, or seek the participant’s permission to do so.
7. Please state whether participants/participants families/whanau will have the possibility to receive a lay summary of a results.
8. Please add a new PIS for those participants who are recruited while unconscious, to be invited to consent after they regain the capacity to do so.

Decision

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

* The Standards require that study protocols, among other points, include a clear and ordered plan of study conduct. Significant amendment to the protocol is required to meet this standard, particularly about how participants will be recruited onto the study (*National Ethics Standards* para *9.8*).
* The Standards state that when seeking consent researchers must communicate relevant information in a form, language and manner that enables participants to understand the information provided. For this standard to be met the Committee requires a separate PIS for those participants who are unconscious when they are originally recruited onto the study, as well as the amendments recommended for the other PISCFs to be taken into account. (*National Ethics Standards* para 7.16)
* Researchers and or institutions utilising data must establish proportional, appropriate and robust data governance and data management processes during the life cycle of data (National Ethics Standards para 12.15).

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| **3** | **Ethics ref:** | **20/STH/114** |
|  | Title: | Field Test of ADOC-M/P |
|  | Principal Investigator: | Miss Kato McDonald |
|  | Sponsor: |  |
|  | Clock Start Date: | 02 July 2020 |

Miss Kato McDonald and William Levack 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. Typically, goal-setting is considered one of the cornerstones of the rehabilitation process for clinical patients. There is a lot of evidence internationally that the goal-setting process tends to be dominated by the health professionals, rather than goals which are meaningful for patients. The application ADOC-MP has shown success in Japan in broadening those objectives and tailoring them to patients.
2. This study seeks to assess the usability and efficacy of an adapted version of ADOC-MP for Māori participants. Participants, their whanau and their clinicians will be interviewed after 1-2 months to review their experiences.
3. The app will be used by both the patient and the clinician. The clinician will go through the app with the patient, and pictures of various activities will help to facilitate a conversation between the clinician and patient in order to help them set rehabilitation goals. The app will be used on a DHB iPad, and a print-out of its contents may also be used.
4. The app does not need to interface with hospital software, and will be paid for either by the DHB or the sponsor.

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 Researchers are providing an intervention. The Researchers explained that they are giving the app to clinicians to use as they see fit, and will be conducting an observational study afterwards. No restrictions will be placed on how they use the app.
2. The Committee asked about the amount of time potential participants will have to consider their participation in the study. The Researchers explained that participants will be given the participant information sheet by a health professional, and then if they show interest in the study the Researchers will meet with them for a whakawhanaungata and to explain the project further. They stated that the details of the consenting process are still yet to be determined as part of consultation with iwi in Whanganui.
3. The Committee asked, in relation to the Researchers’ answer to application question R.8.1, what images participants may find demeaning. The Researchers explained that some images acceptable for Japanese patients, such as of a person sitting on a toilet, were found not to be appropriate for Māori.
4. It was clarified that interviews will be 30-90 minutes long. Please ensure this is stated consistently across the study documentation.

Summary of outstanding ethical issues

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

1. The Committee asked for clarification as to whether any participants who lack the capacity to provide informed consent may be recruited onto the study. The Researchers explained that they won’t be recruiting people who are not able to consent for themselves, however they will be recruiting those who may need supported consent for more complicated decisions. The Committee stated that while it is acceptable for an individual to support the participant’s consent, they should not sign on their behalf and this should be removed from the consent form.

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

1. Please add greater detail as to how the app will be used (i.e. on a hospital iPad, together with their health practitioner).
2. Please proofread the whanau PIS for grammar and clarity.
3. All PIS documents: the participant should not be confirming that they meet the criteria, that is the Researcher’s responsibility.
4. Please review the language in the PIS documents to avoid any implication of a hierarchical relationship between researchers and participants. For example, it is preferable to use the term ‘participants’ rather than ‘patients’ where possible.
5. Please make clear in the whanau PIS what information will be collected from them and how (e.g. what kind of questions will be asked). Please state that they may be asked to be part of an interview with the main participant.
6. Please add an ACC statement (as per the HDEC template).
7. Please add contact details for Māori and the independent health and disability advocate (see the HDEC template for details).
8. Please explain in each form whether data may be published or shared with others and whether it will be shared in an identifiable, de-identified or anonymous form. This information should be added to the PIS and also to the protocol.

Decision

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

* Please amend the information sheet and consent forms, 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 Mr Dominic Fitchett and Mrs Helen Walker.

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| **4** | **Ethics ref:** | **20/STH/103** |
|  | Title: | A Media Smart dissemination trial |
|  | Principal Investigator: | Ms Rachel Lawson |
|  | Sponsor: |  |
|  | Clock Start Date: | 02 July 2020 |

Ms Rachel Lawson 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. Media smart is a programme that reduces the risk of eating disorders and has been found to work very well when delivered by psychologists under controlled conditions. Here they want to try that same programme in the intermediate school setting delivered by teachers. 900 students from years 7 and 8 will be recruited in Canterbury and Nelson.
2. A previous pilot showed it could work but suggested a fidelity check, which they have incorporated here by audiotaping the presentations.
3. Students will either attend two lessons per week for four weeks on media smart, or attend class as normal (the control arm). They will fill out questionnaires pre- intervention, post intervention and at 6 and 12 months afterwards.
4. Facilitators of the program will attend training and fill out an adherence checklist. Some of their classes will be audio recorded to assess quality and fidelity of program delivery.
5. The study will also evaluate the effectiveness of the programme for Māori and Pacific ethnicities due to the higher prevalence of eating disorders in those groups.

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 facilitators will be teachers or health professionals. The Researchers explained that the facilitators would be either health professionals or teachers working in conjunction with health professionals, depending on the availability in the region. Teachers will all receive at least four hours training before conducting this programme.
2. The Committee queried whether the facilitators are participants in the study. The Researchers confirmed that they will ask the facilitators questions to evaluate their experience of the programme. The Committee asked for them to be consented for that participation with their own PISCF.
3. The Committee asked how children may be supported to ensure that they are comfortable in the programme, and noted the risk of stigmatisation for participants. The Researchers explained that the purpose of the programme itself was largely focused on helping children to manage any stigmatisation or distress due to their eating, and in addition prior experience in Australia has shown that the programme has not caused distress in participants.
4. The Committee asked what will happen if an eating disorder is identified in the programme. The Researcher stated that this is a possibility from the answers to the screening questionnaires, which may cause either immediate distress or identify incidental findings. To mitigate this, after completing those questionnaires participants will be given a de-brief sheet with contact details in case they feel the need to talk to someone. The screening will however not provide a clinical diagnosis.
5. The Committee queried whether an opt-out consenting process will be used. The Researcher stated that once the study information is sent to the parents, if the Researchers do not hear back, they would then contact the parents. However, if the parents do not provide consent then their children will not be involved in the study. The Committee asked for the study protocol to be amended accordingly.
6. The Committee asked if some children may be deemed competent to provide informed consent, and not require the parents’ consent. The Researcher stated that they would seek the parents’ consent in all cases, and if the child wished to consent but the parent did not, then they would talk with those individuals and with the school.
7. The Committee asked about the questionnaire, and if there was any consideration for children who may be stigmatised for being underweight. The Researcher stated that the programme will look at how to handle stigmatisation at school due to their weight/eating, and this will apply regardless of whether they are over or under-weight. Consequently, it should benefit all children.
8. The Committee asked if the programme may be focusing too much on the impact of media, rather than other factors that influence eating patterns such as family dynamics. The Researcher agreed on the importance of those other factors, but stated that those factors can be hard to influence; this programme focuses specifically those aspects that they can work with and for which there is evidence backing the interventions.

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

1. A new PISCF is needed for the facilitators of the programme.
2. To all forms, please add a footer stating clearly which form it is (who it is addressing), the version number, date and page numbers.
3. Please add contact information to all forms: Māori, HDEC, and a contact for an independent advocate. Refer to the HDEC template for guidance (<https://ethics.health.govt.nz/system/files/documents/pages/participant_information_sheet_consent_form_template_july_2020.doc>).
4. Please refer to ‘parents and guardians’ rather than ‘parents and caregivers’.
5. Please make it clear to children that the parents’ consent will also be sought, and that they may only participate if both parties provide consent/assent.
6. To each form, please add more information about what will happen in each class (such as what is included in the Program Overview document).
7. Final page: please remove the statement “we hope you will accept our invitation to be involved”.
8. Please state that data will be kept for 10 years after the youngest participant turns 16.
9. Please explain how the audio recordings will be managed: how they will be stored, whether they will be de-identified, how they will be transcribed and how they will be kept secure and confidential, etc.

Decision

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

* Please amend the information sheet and consent forms, 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 Mrs Helen Walker and Dr Patries Herst.

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| **5** | **Ethics ref:** | **20/STH/105** |
|  | Title: | CST2032-CLIN-007: A study assessing single and multiple doses of the investigational drug CST-2032. |
|  | Principal Investigator: | Dr Chris Wynne |
|  | Sponsor: | CuraSen Therapeutics Inc |
|  | Clock Start Date: | 02 July 2020 |

Dr Chris Wynne and Dr Alex Cole 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 phase 1 first in human open-label ascending single-dose, placebo controlled RCT and ascending multiple-dose study to evaluate the safety, tolerability, pharmacokinetics, and pharmacodynamics of a new medicine (CST-2032) in healthy volunteers and subjects with mild cognitive impairment or Parkinson’s Disease.
2. The study will be conducted in four parts:   
   - Part A (up to 5 dose groups): single increasing doses of CST-2032, in healthy participants.   
   - Food effect (1 dose group): single fasted and fed doses of CST-2032, in healthy participants.   
   - Part B (Up to 4 dose groups): multiple increasing doses of CST-2032 or matching placebo, in healthy participants.   
   - Part C (1 dose group): single dose of CST-2032, in adults with mild cognitive impairment or Parkinson’s disease.
3. The study will be conducted in 2 countries with 70 participants (32 in NZ). Depending on the results of the first dose groups, participants may also receive a low dose of nadolol with each dose of CST-2032. Nadolol blocks heart rate increases seen with medicines similar to CST-2032 (beta agonists, e.g. salbutamol) and will be used if heart rate increases are observed with CST-2032 in this study.

Summary of resolved ethical issues

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

1. It was confirmed that a pregnant partner PIS would be developed in the event of a pregnancy.

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

1. Adverse effects: please re-word “effects on the cells of the heart” for clarity.
2. Please simplify the study title.
3. Consent form for part B: please clarify whether there are 3 or 4 MRI scans.
4. Consent form for part C: please correct the table of assessments to indicate that participants will be dosed from day 2.

Decision

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

* Please amend the information sheet and consent forms, taking into account the suggestions made by the Committee.

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| **6** | **Ethics ref:** | **20/STH/106** |
|  | Title: | A Study of Nivolumab or Placebo in Combination with Docetaxel in Men with MetastaticCastration-resistant Prostate Cancer |
|  | Principal Investigator: | Dr Navin Wewala |
|  | Sponsor: | Bristol-Myers Squibb |
|  | Clock Start Date: | 02 July 2020 |

No member of the research team 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 is a re-submission of an application previously declined by the Southern HDEC (reference: 20/STH/38).
2. This study is a phase 3 trial of an approved medicine (Nivolumab, in combination with Docetaxel), being used in a new indication in Men with Metastatic Castration-resistant Prostate Cancer.
3. The medicine’s clinical benefit, long-term safety, and survival of participants will be assessed. A: Nivolumab, docetaxel, prednisone (up to 10 cycles of 3 weeks each), then continuation with IV nivolumab (max 2 years, in 4 weekly cycles at 4 hours per visit) B: Docetaxel, prednisone, placebo (up to 10 cycles of 3 weeks each), then continuation with IV placebo (max 2 years, in 4 weekly cycles at 4 hours per visit) De-identified data made available for future research. And FUR (consent for FUR of samples collected in the main part of the research). Tissue sent overseas.

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 expressed concern at the use of a placebo for up to 2 years. They noted the favourable scientific peer review as well as scientific review through SCOTT, however please explain, if the study question is whether nivolumab with docetaxel is better than docetaxel alone for long term survival, why arm A is continuing with nivolumab and arm B is continuing with placebo (neither of which is combined with docetaxel)? Please further provide a justification for allowing the IV placebo arm, to continue for 2 years - why can't the question be addressed with the up to 10 cycles of drug combination in arms A and B? Please also ensure that this explanation is communicated to participants in the PIS.
2. Please clarify what ‘other’ reasons for terminating the study are, and note that a therapeutic study may not be terminated for commercial reasons.
3. It is not clear that the large number of people who have access to data has been more narrowly defined since the previous decline. Please clarify and justify why those parties should have access to the data.
4. It was not clear, based on the answer to question R.3.12, whether tissue taken during the course of the study can or cannot be re-identified. The sponsor should not strip all identifiers from the sample such that a sample cannot be traced (internally) while the study is in progress. Please clarify whether a participant who withdraws can have their samples returned, and ensure this is stated clearly in the PIS. Please make sure the participants know that if samples are shared for FUR they will not be able to be returned.
5. In response to the answers given to questions r.5.4.1 and p.2.1, the Committee asked how the Researchers would distinguish between introducing the study, providing information and answering questions about the study, and seeking consent from potential participants. The Committee noted the potential for a conflict of interest if it was the same individual doing each part of the consenting process.
6. The Committee stated that question P.1.1 was not answered appropriately, and it was not clear how many visits would be required, of what duration and over how long, and what 'extra' procedures are involved. Please also explain how they differ from standard of care.
7. Please provide evidence that formal Māori consultation is being sought.
8. Please clarify that participants will have access to SOC after the study ends or otherwise explain.
9. Please clarify whether Greenphire need to keep participant information for 7 years (as the PIS states that study information will be deleted at the end of the study), and if so explain why this is necessary.
10. Questionnaires:
    * two of these include questions about mental well-being. Please explain how any results of concern will be detected and what safety protocol there is in place for responding to this.
    * The questionnaires should not be identifiable. Please use the study ID only.
11. For future applications, please note that a reference to the protocol alone is not appropriate, especially as that is rarely written in language for the lay person to easily understand. Please do not attach documents that are not required for the ethical review (e.g. Dear Investigator letter, PSP PAI signed, DIL legal approved, how to take a stool sample, etc). They will not be covered by the review and cannot be approved.

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

1. Please amend the study titles to be suitable for a lay audience.
2. There are various references to numbered sections, yet section headings rather than numbered sections are now being used. Please amend accordingly
3. Please remove or otherwise clarify the statement that HIV testing is required by law.
4. Please make clear that a summary of the study results will be posted on the study website.
5. Please replace any reference to the FDA with whether these drugs are licensed for use in NZ.
6. The PIS currently states that study data will be kept for 15 years as required by law. Please note that health information must be kept in New Zealand for a minimum of 10 years. Please delete the text “as required by law”.
7. Page 21: the section on data management needs to be reviewed, ensuring that it is made clear what information is identifiable, de-identifiable or anonymous, how it is being stored and who has access to each type.
8. Please make clear that participants have the right to request information about them in the trial at any stage, but that if they request information about their treatment, they may have to leave the trial to protect the study’s scientific validity.
9. Consent form:   
   Please correct the statement “I understand that there may be risks in the event of my partner or myself becoming pregnant.”   
   Please remove the yes/no option to be sent a summary of the study results.
10. The Committee notes that the HDEC template used for commercial wording, however it is only acceptable that compensation is not given due to injury caused by the comparator drug (i.e. the drug used in SOC). Please remove the reference to the study drugs.
11. Treatment beyond progression: please add information about continuing expectations of visits and follow up and tests etc. If it all remains the same as the main study please say so. Please also clarify whether reimbursement and compensation arrangements will remain the same.
12. Page 21: please clarify whether the hard copy of participants’ information is being kept with unique study ID and separately a list linking ID and name/DOB/NHI etc.
13. Please proofread each PIS and amend to reduce jargon.
14. Please clarify how long the follow-up period may last for.
15. Page 5: please move the statement about karakia to page 5, when you first mention the collection of tissue.
16. Page 10: it is implied that participants will need to provide follow-up data if their treatment has stopped and if they have withdrawn, please clarify.
17. Page 15: use prednisone rather than corticosteroids, or at least make it clear that prednisone is a corticosteroid.
18. Page 20: please clarify the statement “your personal health information will be kept confidential and, unless required by law, will not be made publicly available" (how required by law?).
19. Page 21: "you agree to the transfer of your personal health information to such countries, including the United States of America and India" – please state if this health information is identifiable, de-identified or anonymous.

Decision

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

* The Standards state that, in general, researchers should design studies to generate accurate scientific information without delaying established effective interventions for, or withholding them from, participants. Greater justification for keeping participants on placebo for the duration of this trial is needed to ensure that this standard is met. (*National Ethics Standards* para *10.21*).
* Studies involving health data should seek to minimise risks and maximise benefits. To minimise risks, the Committee requires that the people with whom identifiable health data will be shared is narrowed. Furthermore, external organisations such as Greenfire who require access to health information should only access that information for as long as is strictly necessary (*National Ethics Standards* para *12.7.a*).
* Where identifiers on human tissue are necessary (for instance, where researchers test tissue samples provided in clinical trials and report on them for a purpose that is fed back to the clinical team and in some way determines or directs the treatment of participants), researchers should include this fact in the information they give to participants as part of the process of obtaining their informed consent (*National Ethics Standards* para *14.20*).
* When patients are recruited as prospective participants, the people directly involved in their care should make the first approach, rather than researchers the patients do not know. In limited circumstances, it may be justifiable for both the researcher and the health care provider to make the first approach (e.g. in a joint letter), or for the researcher to do so with reference to the health care provider. Greater information about the recruitment methods is needed to be sure that this standard is met (*National Ethics Standards* para *11.7.c*).
* Participants must receive the information that a reasonable consumer, in that consumer’s circumstances, would need to make an informed choice or give informed consent prior to their decision to participate in research. Greater detail in the PIS, especially with regards to the length of the study, is required to meet this standard (*National Ethics Standards* para *7.15*).
* For international clinical trials, the Standards state that researchers should make every effort to adapt the protocol, and that engagement with Māori should be achievable at the New Zealand investigator and clinical trial site level. Please provide evidence of Māori consultation to demonstrate that engagement (*National Ethics Standards* para *3.7.a*).
* Before conducting research, researchers must develop and record a plan for how they will handle incidental findings. Given the sensitivity of some questions contained within the questionnaires, a safety plan is required in case these questions produce any incidental findings (*National Ethics Standards* para 11.48).
* Protocols must include all information that is relevant for the type of study

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| **7** | **Ethics ref:** | **20/STH/111** |
|  | Title: | nGVS older adults |
|  | Principal Investigator: | Professor Denise Taylor |
|  | Sponsor: | Auckland University of Technology |
|  | Clock Start Date: | 02 July 2020 |

Professor Denise Taylor 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. Falling is a problem amongst older adults, and exercise programmes commonly provided as standard of care only reduce that risk by about one third. Non-invasive noisy galvanic vestibular stimulation (nGVS) may help to make those exercise programmes more effective by enhancing balance and gait. This is a feasibility trial for a future definitive RCT to test the effectiveness of nGVS alongside a balance rehabilitation programme to determine efficacy in improving balance in older adults with moderate to high risk of falls.
2. The study involves a mixed methods RCT design in 72 older adults in the community with moderate to high risk of falling. There are 3 groups:
   * balance rehabilitation plus nGVS,
   * balance rehabilitation plus sham nGVS,
   * or no intervention.

There will also be semi structured interviews with participants and therapists to qualify their views of the intervention.

1. The intervention involves electrodes applied over the mastoid processes using a commercially available nGVS device as per previous research.
2. The exercise involves a 45 minute balance rehabilitation programme delivered by a physiotherapist to groups of 4-6 participants twice a week for 8 weeks.
3. Participants will be assessed using standardised clinical tests for balance and gait.

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 why a no-intervention control group is being included. The Researcher explained that this group is being included to evaluate whether the intervention is having an effect. The Committee queried whether participants’ baseline could be used as their control, but it was agreed that a control arm would make for a more robust trial. The Committee asked for those on the control arm to be offered the standard of care balance treatment after the study, which the Researcher agreed to.
2. The Committee asked how patients at a high risk of falling will be identified. The Researcher explained that three questions from the study falls risk assessment are being used as a first screen for those wishing to participate in the study, and will be assessed by a physiotherapist.
3. The Committee stated that the peer review was lacking in detail, however acknowledged that the study has been favourably reviewed as part of the HRC application process.
4. The Committee asked if this is a trial of a new device. The Researcher stated that the device has approval for use in research (through the FDA), and is quite low-risk.
5. The Committee asked if the Researchers would use a different age cut-off for Māori and Pacific participants, which the Researchers confirmed.

Summary of outstanding ethical issues

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

1. Please provide a detailed data management plan, ensuring that it meets the different aspects laid out in para 12.15 of the National Ethics Standards.

The Committee requested the following changes to the Participant Information Sheet and Consent Form. These refer to all forms unless otherwise specified:

1. Please add a footer to each PIS indicating who the PIS is for, version number, date and the page number.
2. Please update the ACC statement (for guidance, see the wording under the “what if something goes wrong?” section of the HDEC template <https://ethics.health.govt.nz/system/files/documents/pages/participant_information_sheet_consent_form_template_july_2020.doc>)
3. Please explain what will happen to participants’ data, and in particular for the audio-recorded data. Explain whether and how data will be stored, in identifiable, de-identified or anonymous form and for how long.
4. Please add a section on “what are my rights” (refer to HDEC template for guidance).
5. Please add a Māori health contact.
6. PIS for therapists: therapists are participants from the time they start to deliver the treatment, not just the interview. Please clarify this in the PIS and explain:
   * What will happen to the recordings following transcription  
     Will participants have the right to read and correct the transcript  
     Will the transcript be stripped of identifying features?
7. PIS for participants
   * page 1: please correct “gains of design”.
   * page 2: please explain randomisation more clearly, and that participants in the control group will be offered balance therapy after the study.
   * please add information about the semi-structured interviews.
   * please add information about the assessments at 3 and 6 months, and what they will involve.
   * please increase the font size and simplify the technical language, in particular please explain ‘brain stimulation’.
   * Please state that the device has been approved for use in research, that you should not expect to feel the effect and that there are no known adverse effects.
   * Please state how long participants will use the device for.
   * Please explain the 3-step instructions.
   * Risks and benefits: please state that the no-treatment group will have no benefit whatsoever, and that the intervention group has a risk of falling.
   * Please state whether you will notify GPs of their participation, to check their health information or to inform them of the risk of injury.
   * Please add a statement about any cultural concerns participants may have with regards to touching the head.
   * Please clarify that the no-treatment group will not complete the questionnaire.

Decision

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

* Please provide a data management plan that complies with para 12.15 of the National Ethics Standards.
* Please amend the information sheet and consent forms, 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 Dr Sarah Gunningham and Dr Patries Herst.

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| **8** | **Ethics ref:** | **20/STH/101** |
|  | Title: | Younger onset dementia diagnosis |
|  | Principal Investigator: | Dr Brigid Ryan |
|  | Sponsor: | University of Auckland |
|  | Clock Start Date: | 02 July 2020 |

No member of the research team 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 is an observational study of people living with which aims to understand the factors associated with a delayed diagnosis in people under 65 years who have younger onset dementia. People with dementia will be recruited (either by seeking consent for access to their medical records, or if they are deceased then consent will be sought from the executor of the patient’s estate), as well as carers, and health professionals. Data will be collected with questionnaires and by accessing medical records. Data will be sought from 100 individuals with younger onset dementia.

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 there may be a conflict of interest for the CI, who is very involved in the patient community and will be recruiting participants into the study. The Committee asked for clarification about how the roles of clinician, advocate and researcher will be separated in this study so as to reduce any risk that participants may feel pressured to participate.
2. The Committee noted that the Researcher had taken on board the previous committee’s advice that the screening should be done face to face, however stated that in this participant population screening via video calling might also be difficult.
3. The Committee noted that the previous decision to decline had been, in part, due to the difficulty in ascertaining the capacity of the individual with dementia to provide informed consent. However, the Committee expressed concern at the idea of the support person answering on behalf of the participant. They stated that the person with dementia should consent to participate and be encouraged to answer where they can, and that the support person should only be there to support. In this way their consent and participation should be assisted.

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

1. The Committee stated that the PIS/CF should be for the individuals with dementia (who are the ‘main’ participants), and should not merely address the support person. If information is being collected from the support person, then they should be given and have to sign a separate PIS/CF.
2. Family/whanau PIS page 2: please remove “you need to be the executor or administrator of their estate”. It is appropriate to seek the consent from a family member, regardless of whether they are the executor or administrator of the person’s estate. Please also remove this from the advertisement.
3. Please amend the language throughout all documents to reflect the fact that the person with dementia is the main participant from whom information will be collected (e.g. in the carer PIS/CF consent form, it should not refer to “my health information”. This language is appropriate if the carers are being asked questions about themselves, however this is not clear).
4. Questionnaire: from question 55, the wording changes to “you” and it is not clear whether this refers to the person with dementia or the carer. Please amend accordingly.

Decision

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

* Researchers must identify real, potential and perceived conflicts of interest, and then manage, reduce or eliminate them. They must assess conflicts of interest in terms of both their likelihood and their consequences. The Committee required greater assurance of a separation between the CI’s role as researcher, advocate and health professional to be confident that any conflict of interest would be managed, particularly in the recruitment process (*National Ethics Standards* para *11.23*)
* Where a consumer has diminished competence, that consumer retains the right to make informed choices and give informed consent, to the extent appropriate to his or her level of competence (*Code of Health and Disability Service Consumers Rights* right *7(3)*).

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| **9** | **Ethics ref:** | **20/STH/118** |
|  | Title: | BGB-3111-LTE1 |
|  | Principal Investigator: | Dr Henry Chan |
|  | Sponsor: | BeiGene Aus Pty. Ltd. |
|  | Clock Start Date: | 02 July 2020 |

Dr Henry Chan was present via videoconference for discussion of this application.

Potential conflicts of interest

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

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

Summary of Study

1. The study allows participants both from the parent study (who were on EP547) and those who were on the comparator drug to receive EP547.
2. The study is a phase III open-label, long-term extension study to evaluate the long-term safety and efficacy of zanubrutinib, as monotherapy or in combination, in patients with B-cell malignancies, who are or were previously enrolled in the parent study, and who are still benefiting or may benefit from treatment with zanubrutinib, or who are willing to have long-term survival follow-up.
3. There are 500 participants worldwide and 27 in NZ. Ethics approval has been granted in Australia and the USA.

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 decisions being made on who should participate in this follow-up study were based on clinical benefit, and should not pose any substantial risk to participants.
2. The Committee noted the issue of tissue being sent overseas, but was satisfied that participants will be informed of this in the main PIS. It was confirmed that, for participants receiving the survival PIS, no tissue would be sent overseas.
3. The Committee queried why data will be kept for 15 years. The Researchers stated that storing data for 15 years is a requirement of the sponsor.
4. The Committee asked how long the study will last for, and the Researchers explained that the treatment will continue for as long as it is shown to be beneficial.
5. Pregnant partner PIS: noted that a follow-up PIS would need to be submitted as an amendment after the baby is born.

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 SCOTT approval would be needed for this study. It was confirmed that SCOTT approval was obtained for the parent study, and the Committee asked for approval to be sought from SCOTT for the use of the medicine in this extension study.
2. The Committee asked which patients are eligible for the study… please make this clear in the PIS.
3. The Committee asked how serious adverse events would be monitored. The Researchers confirmed that there are both internal and external safety monitoring bodies.
4. The Committee asked for a detailed data management plan, ensuring that it meets the different aspects laid out in para 12.15 of the National Ethics Standards.

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

1. Please amend the PIS title, removing “survival” to avoid causing any alarm, and make it meaningful for lay readers.
2. Please update the pregnancy risks section, and refer to the HDEC template for guidance (<https://ethics.health.govt.nz/system/files/documents/pages/participant-information-sheet-consent-form-template-reproductive-risks-17apr20.docx>).
3. Please state that treatment will continue for as long as it is beneficial.
4. Please proofread both the main and survival PIS and simplify any technical language, and check formatting for readability. The main PIS needs a shorter title and some information is duplicated in the document.
5. Please ensure that the consent form is referred to consistently throughout the documents.
6. Please clarify the statement that participants will have to pay for any medication needed to treat the side effects of the study drug.
7. Please clarify in the data management section which data is identifiable and which is de-identified, and who will have access to each type.
8. Please remove the statement “however, [Name of institution] may charge study doctors a fee to recover some of the costs of storing and administering the blood samples”.

Decision

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

* Please provide a detailed data management plan, ensuring that it meets the different aspects laid out in para 12.15 of the National Ethics Standards.
* Please amend the information sheet and consent forms, 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 Mr Dominic Fitchett and Dr Mira Harrison-Woolrych.

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| **10** | **Ethics ref:** | **20/STH/116** |
|  | Title: | Study of EP547 in Adult Healthy Volunteers as well as in Patients with or without itch due to Liver or Kidney disease |
|  | Principal Investigator: | Professor Edward Gane |
|  | Sponsor: | Novotech (New Zealand) Limited |
|  | Clock Start Date: | 02 July 2020 |

Professor Edward Gane 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. It has been determined that bile acids and heme metabolites activate a sensory receptor in the skin that is responsible for mediating itch called Mas-related G protein-coupled receptor x4 (MRGPRX4). This study will evaluate a new medication (EP547) that has been designed to turn off this sensory receptor and stop the unrelenting sensation of itch in these patients. This first in human study will initially evaluate the safety of single doses of EP547 in multiple groups of healthy volunteers, first by assessing a low dose level followed by gradually increasing dose levels. Following confirmation of safety with a range of single doses, further safety evaluation of these doses will be conducted by assessing the safety of daily treatment over 7 days also in multiple groups of healthy volunteers at increasing dose levels. Following confirmation of safety and characterization of the pharmacokinetics (PK) of EP547 in healthy volunteers, the medication will be evaluated in patients with liver disease and kidney disease for safety, PK of EP547 and the ability to decrease itching. An important safety assessment step is included in the study design which compares the PK of a single low dose of EP547 in patients with liver disease or kidney disease to that of healthy volunteers before proceeding with multidose evaluations in these target populations.

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 need to include a placebo arm. The Researcher explained that a placebo arm was needed so that measures of safety could be compared for the single dose trial. The Committee asked for this to be made clearer in the PISCF.
2. It was confirmed that SCOTT approval is being sought for this study.
3. The Committee asked if the low-moderate metabolic clearance detected in the animal studies may be a risk worth noting for participants in the present study who have liver or kidney failure. The Researcher explained that patients with kidney disease should not be affected, but that it may have some impact for those with advanced liver disease. The itch test is only a 5 minute exposure to a small area of the arm and thus very transient.
4. It was clarified that the answer given to question F.2.1 of the application form, stating that the study drug is to be used in people with no clinically significant disease, was incorrect.

Summary of outstanding ethical issues

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

1. All PIS’s are quite long and contain some duplication. Please proof read the documents and shorten them if possible.
2. PISCF for healthy participants, page 4 paragraph 2: please remove the sentence that refers to other treatment options.
3. Main study PIS: please add more information about the genetic testing on kidney and liver patients.
4. Please add a cultural statement about the use of tissue for research and genetic research. The Committee suggested using the cultural paragraph from study “ABI-H0731-205 Phase 2a Combination of core inhibitor with standard of care NrtIs for CHB” (HDEC ref: 20/STH/98).
5. Please explain if there are any risks for healthy participants, and how long the effect of the itch stimulus lasts.
6. Main PISCF page 6: where it is explained that samples will be sent overseas, please acknowledge that the same cultural values may not be held by overseas researchers.
7. The Committee asked about how the study can be expected to improve outcomes for Māori and Pacific peoples. The Researcher explained that the study may have benefit for Māori or Pacific people with renal failure, as renal failure is far more prevalent in Māori and Pacific people. However, it would not have any greater benefit for those with liver disease. Please add a brief statement to the PIS clarifying this.
8. Form for healthy volunteers on SAD: please take out the form for determining whether the study drug is effective.
9. MAD CO UP PIS:
   * Please state at the start why the reader is being invited onto the study.
   * Please check for consistency whether participants will need to stop taking their standard medication.
   * Where it states that you will take a “3mm biopsy the size of this circle”, please add the circle.
   * Before the table, please clarify where the 8 day confinement is mentioned that participants may go home and come back.
   * At day 6 and day 7, please define “UP and CP”.
   * Reimbursement: please state that the difference in reimbursement relates to the number of tests or time taken.
   * Please add contact details for the PI to the end of the form.

Decision

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

* Please amend the information sheet and consent forms, taking into account the suggestions made by the Committee.

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| **11** | **Ethics ref:** | **20/STH/98** |
|  | Title: | ABI-H0731-205 Phase 2a Combination of core inhibitor with standard of care NrtIs for CHB |
|  | Principal Investigator: | Professor Edward Gane |
|  | Sponsor: | Pharmaceutical Research Associates Ltd (NZ) |
|  | Clock Start Date: | 25 June 2020 |

Professor Edward Gane and Ms Debbie Cao 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 is a phase 2a, randomized, placebo-controlled study evaluating the safety, antiviral activity, and PK of ABI-H0731 administered in addition to standard of care (Nucleotide RT inhibitors) in subjects with Chronic Hep B who have not achieved adequate virologic suppression of HBV DNA. The study will be carried out in 4 countries, with 40 participants and 8 in NZ.
2. Participants will be randomized in a 1:1 ratio to the treatment groups: group 1 will receive ABI-H0731+NrtI for 96 weeks and Group 2 will receive Placebo+NrtI for 48 weeks; then ABI-H0731+NrtI for 48 weeks until Week 96. All subjects will continue to receive NrtI alone during the 24-week follow-up period from week 96 through week 120. Safety, antiviral activity, and PK will be assessed during treatment and the 24-week follow-up period.
3. Many patients with liver disease or kidney disease have intense itching which significantly impacts their quality of life disrupting sleep and entire lifestyles. One theory for the association of itch with these conditions is that the disease states result in components of bile, such as bile acids and heme metabolites, accumulating in the skin and causing itch. There are no approved effective medications for treating cholestatic pruritus (liver disease-related itch) or uremic pruritus (kidney disease-related itch) and in some situations only liver or kidney transplantation will cure this itching sensation.

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 main ethical issue, aside from exposure to the new medication, is the possibility of interaction between the new treatment and standard of care (SOC) treatment. The Researchers stated that although the previous trials of this treatment in hepatitis patients were not in combination with SOC, combination studies have been run with healthy volunteers showing no interaction effects. The Committee asked for this to be explained in the PIS, and for it to be acknowledged that an interaction effect is still a possibility.
2. The Committee noted the high burden on participants in the control arm of the study, who will be receiving placebo for 48 weeks, and asked if participants on placebo may be offered the active treatment if it is shown to be effective. The Researcher stated that there is no plan switch participants over to active treatment within the study, but that in previous studies where the treatment had been shown to be effective the sponsor had offered it to all participants afterwards.

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

1. Main PIS:
   * Please add additional methods of effective contraception to the section on reproductive risks, and refer to the new HDEC template for reproductive risks (<https://ethics.health.govt.nz/system/files/documents/pages/participant-information-sheet-consent-form-template-reproductive-risks-17apr20.docx>).
   * Please remove the sub-headings 1.1 and 1.2.
   * Please refer to “the study drug” instead of the drug code.
   * Please proofread for readability, removing jargon and unnecessary sub-headings. In particular, amend the headings on page 2 under “why are we doing the study”.
   * Please amend the wording describing the study drug, ensuring that the possible benefits are not over-stated.
   * Page 10 list of side effects: please state the dose going to be used in this study so that the reader may compare it.
   * Please check the references to animal studies, and if there is new information from the human studies that have been conducted since, please update them accordingly.
   * Page 17 Under 7.3 right to access information: please state that if participants want to know which arm they are in they will have to leave the study.
2. If participants withdraw from the main study, please confirm whether the participant wishes to withdraw their samples from the sub-study.
3. On all forms, please check the formatting for readability, e.g. footers, orphan headings, keeping summary statements together with tables, remove the protocol number. Please keep line spacing at 1.5.

Decision

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

* Please amend the information sheet and consent forms, taking into account the suggestions made by the Committee.

## 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:

|  |  |
| --- | --- |
| **Meeting date:** | 11 August 2020 |
| **Meeting venue:** | 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.

1. **Other business**

The Committee asked whether the position for the role of chair on the Committee will be advertised. It has since been confirmed that the chair will be appointed by the Minister of Health from the lay members on the Committee.

The meeting closed at 5:00pm.