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| **Committee:** | Southern Health and Disability Ethics Committee |
| **Meeting date:** | 09 March 2021 |
| **Meeting venue:** | Join Zoom Meeting  <https://mohnz.zoom.us/j/9738756003>  Meeting ID: 973 875 6003 |

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| **Time** | **Item of business** |
| 10:00am | Welcome |
| 10:25am | Confirmation of minutes of meeting of 9 February 2021. |
| 10:30am | New applications (see over for details) |
| 10:30 – 10:55am  10:55 – 11:20am  11:20 – 11:45am  11:45 – 12:10pm  12:10 – 12:30pm  12:30 – 12:55pm  12:55 – 1:20pm  1:20 – 1:45pm  1:45 – 2:10pm  2:10 – 2:30pm  2:30 – 2:55pm  2:55 – 3:20pm  3:20 – 3:45pm  3:45 – 4:10pm | 21/STH/61 Sarah / Devonie  21/STH/60 Dominic / Mira  21/STH/45 Sarah / Paul  21/STH/43 Dominic / Jean  [break]  21/STH/55 Sarah / Mira  21/STH/50 Dominic / Devonie  21/STH/52 Sarah / Jean  21/STH/53 Dominic / Paul  [break]  21/STH/54 Sarah / Devonie  21/STH/46 Dominic / Mira  21/STH/56 Sarah / Paul  21/STH/59 Dominic / Jean |
| 4:10 – 4:30pm | General business:  Noting section |
| 4:30pm | Meeting ends |

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| **Member Name** | **Member Category** | **Appointed** | **Term Expires** | **Apologies?** |
| Dr Sarah Gunningham | Lay (other) | 05/07/2016 | 05/07/2019 | Present |
| Dr Devonie Waaka | Non-lay (intervention studies) | 18/07/2016 | 18/07/2019 | Present |
| 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 | Present |
| Professor Jean Hay-Smith | Non-lay (health/disability service provision) | 31/10/2018 | 31/10/2021 | Present |
| Mrs Helen Walker | Lay (consumer/community perspectives) | 19/08/2020 | 19/08/2021 | Apologies |
| Mr Dominic Fitchett (Acting Chair) | Lay (the law) | 05/07/2019 | 05/07/2022 | Present |

## Welcome

The Acting Chair opened the meeting at 10am and welcomed Committee members, noting that apologies had been received from Helen Walker.

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 February 2021 were confirmed.

## New applications

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| **1** | **10:30-**  **10:55am** | **Ethics ref:** | **21/STH/61** |
|  |  | Title: | HELIOS-B A study to Evaluate Vutrisiran in Patients with Transthyretin Amyloidosis with Cardiomyopathy |
|  |  | Principal Investigator: | Dr Tim Sutton |
|  |  | Sponsor: | PPD |
|  |  | Date submitted: | 26 February 2021 |
|  |  | Clock Start Date: | 26 February 2021 |

Tim Sutton and Ali Murad 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. ATTR amyloidosis is a rare and serious disease that affects multiple systems of the body including the heart.
2. It is caused by certain differences in the protein called transthyretin (TTR). These differences can be caused by a genetic mutation or by aging.
3. The liver is the main producer of TTR protein, and TTR then circulates in the blood stream. As it circulates, abnormal TTR protein can gradually enter many tissues and organs of the body.
4. This results in collections of proteins called amyloid fibrils. These amyloid fibril collections can often affect the function of important organs such as the heart, the nerves, and the gut. The most common effects of ATTR amyloidosis are when it affects the heart (cardiomyopathy) and the nerves (polyneuropathy).
5. The study drug Vutrisiran consists of a small interfering ribonucleic acid (siRNA) molecule attached to a sugar molecule which helps deliver the siRNA to the liver, where the TTR protein is made.
6. The siRNA in Vutrisiran interferes with the ability of RNA to make TTR proteins in the liver, thereby reducing the body’s TTR protein levels. In turn this may reduce the number of amyloid fibrils in the organs of patients with hereditary ATTR amyloidosis (hATTR).
7. In this study, the study drug received could be either the investigational drug, vutrisiran (at an injection dose of 25 mg), or placebo (a dummy injection that only contains saline, no active drug).
8. Participants will have a 1 in 2 chance of receiving Vutrisiran and a 1 in 2 chance of receiving placebo.
9. The study drug will be given subcutaneously in the abdomen, upper arms or thighs.
10. Neither the participant nor the study doctor will not know what was received (blinded) until the study is complete. The study will last approximately 4 years.
11. Participants will receive study drug (either Vutrisiran or placebo) every 3 months (approximately every 12 weeks) for 30 to 36 months and then be followed up for a year.

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 researcher must inform the HDEC if there is a change in which laboratory the tissue samples are sent to.
2. The Committee noted that question r.3.10 in the application form did not reference the genetic testing and future research noted elsewhere in the application.
3. The Committee noted that question r.3.11 in the application form says that all samples will be destroyed at the end of the study, but that this is inconsistent with information provided in the PIS about optional future research.
4. The researcher clarified that the DNA Sample for TTR genetic testing genotyping is part of standard of care before participants are enrolled in the study.
5. The Committee asked who is “home health services”. The researcher responded that this is someone contracted to see patients off-site (due to COVID-19) to take their blood sample.
6. The Committee noted that in r.1.6 of the application the researcher had mentioned terminating the study for commercial reasons and informed the researcher that in New Zealand you cannot terminate a therapeutic study for commercial reasons.
7. The Committee queried how the researcher would respond to answers in the EQ-5D-5L questionnaire indicating that a participant has depression. The researcher responded that the participants fill out the questionnaire in the presence of a nurse, who will let the CI know of any indications of depression. The CI will then pass this information on to the participant’s GP.
8. The Committee queried why planned Tafamidis is not allowed but unplanned Tafamidis is allowed. The researcher responded that this is to keep the study population as pure as possible, whilst still allowing GPs to treat participating patients with Tafamidis if required.
9. The Committee noted that participants who wish to withdraw from the study must be asked if they also wish to withdraw their optional consent for future research.
10. The Committee noted that the thank you card will be filled in at the discretion of the researchers.

Summary of outstanding ethical issues

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

1. Please inform the Committee of the maximum retention time for tissue samples for people who do not provide consent for optional future research.
2. The Committee requested that during the recruitment process potential participants are given the opportunity to talk with a member of the research team that is not involved in their clinical care. This is in order to mitigate pressure to take part in the study which may be present due to the doctor-patient relationship.
3. Please amend page 6 of the Data Management Plan where you state that “participants will be informed of any breaches of their privacy or confidentiality *at the discretion of the investigator*.” Participants should be informed of any significant privacy or confidentiality breach. This should not be at investigator discretion.
4. Please amend page 7 of the Data Management Plan to reference and adequately address the photos and videos mentioned in the main PIS.
5. The Committee queried what videos need to be stored and why. The researcher thought that maybe this was in reference to ultrasounds but was unsure. The Committee requested the researcher investigate this.
6. Please amend page 9 of the Data Management Plan to state that home health services will receive identified rather than de-identified information.
7. The pregnancy information sheets have not been accepted for review. These should be submitted for review in the event of a participant or partner pregnancy.

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

1. Please make it clear that the tissue samples may end up being sent for testing at other laboratories around the world, and whether participants and the approving HDEC will be informed of any changes in testing sites.
2. Please delete the paragraphs and consent clauses about genetic TTR testing, as this is being done as standard of care and is not study-specific.
3. Beyond a brief reference in the main PIS, please keep discussion of optional research confined to the optional PIS.
4. Please refer to people as ‘participants’ rather than ‘subjects’.
5. Please use a short, simple, lay-friendly title for the study.
6. Please ensure that the text does not bleed into the footers as this makes it more difficult to read.
7. Please amend to use more lay language.
8. Please edit for spelling, for example:
   * page 18 should read ‘tafamidis’
   * use UK English e.g. ‘centres’ rather than ‘centers’
   * use macrons on Māori kupu where appropriate e.g. whānau
9. Please ensure consistent formatting e.g. fonts, paragraphing, no orphan headings.
10. On page 3 please provide an estimated number of NZ participants in the study.
11. On page 3, please remove the ‘cultural statement’ heading.
12. Please amend the diagram on page 4 to use lay language.
13. Please remove repetition of information throughout the document.
14. On page 6 please clarify that you are collecting ethnicity data rather than race data.
15. Please amend page 6 to explain that viral hepatitis does need to be reported to the Medical Officer of Health in NZ and that patients will need to be identified.
16. In the table on page 9, please include approximate times for each of the study visits.
17. On page 14, please state how many people have received Vutrisiran to date.
18. On page 15, please remove the section on drug interactions from the reproductive risks section and move it to a more appropriate section.
19. On page 16, please remove the statement about adolescent patients initiating contraception at menarche, as this irrelevant given inclusion criterion age of 18-85 years.
20. Please reconsider statements on sexual abstinence, as the HDEC do not recommend this as an effective means of contraception.
21. Please clarify the reproductive risk for the partners of male participants.
22. Please amend the confidentiality section on page 21 to clearly differentiate between access (and purpose of access) to identifiable versus de-identified data. The Committee suggested the researcher utilises the HDEC PIS template for this.
23. On page 21 please provide clearer information for the use of, storage of and access to videos and images, as these are potentially very identifiable. Explain what videos are being recorded and why.
24. On page 22 please make it clearer that anonymised information will be used for unrelated medical/scientific research.
25. Please update the data section to include the potential risk of a privacy or confidentiality breach.
26. On page 23 it states that “people who wish to withdraw from the study must return for visits until the end of the double-blind period for assessments”. Please make it clear that this is only relevant for participants who wish to withdraw from the study *medication* but remain in the study. Please make it clear that people who wish to withdraw from the entire study can do so at any time.
27. Please amend page 24 to state that notification of withdrawal does not need to be in writing. The participant can withdraw by orally informing the investigator.
28. On page 29 please amend the authorisation of records form to limit access to ‘records relevant to participation in this study’.

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

1. Please refer to Helios-B rather than the study number, which has not been used elsewhere.
2. Please include the risk of privacy and confidentiality breach, particularly with regards to genetic research. Please mention the potential impact of this for blood relatives.
3. Please include the Māori cultural tissue statement.
4. Please replace the compensation statement with the HDEC approved compensation statement.

Decision

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

* Please address all outstanding ethical issues, providing the information requested by the Committee.
* Please update the Participant Information Sheet and Consent Form, taking into account 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 Sarah Gunningham and Devonie Waaka.

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| **2** | **10:55-**  **11:20am** | **Ethics ref:** | **21/STH/60** |
|  |  | Title: | Metabolic Therapy Program in Conjunction with Standard Treatment for Glioblastoma Multiforme |
|  |  | Principal Investigator: | Dr Matthew Phillips |
|  |  | Sponsor: |  |
|  |  | Date submitted: | 02 February 2021 |
|  |  | Clock Start Date: | 18 January 2021 |

Matthew Phillips 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. Glioblastoma multiforme (GBM), a very aggressive brain tumour, is one of the most malignant of all cancers and is associated with a poor prognosis.
2. The majority of GBM cells display damaged mitochondria (the "batteries" of cells), so they rely on an alternate method for producing energy called the Warburg Effect, which relies nearly exclusively on glucose (in contrast, normal cells can use other molecules, such as fatty acids and fat-derived ketones, for energy).
3. Metabolic interventions, such as fasting and ketogenic diets, target cancer cell metabolism by enhancing mitochondria function, decreasing blood glucose levels, and increasing blood ketone levels, creating an advantage for normal cells but a disadvantage for cancer cells.
4. Preliminary experience at Waikato Hospital has shown that metabolic therapy programs utilizing fasting and ketogenic diets are feasible and safe in people with advanced cancer and may provide a therapeutic benefit.
5. This trial aims to determine whether using an MTP concurrently with standard oncological treatment (chemoradiation followed by adjuvant chemotherapy) is feasible and safe, and has treatment outcomes consistent with greater overall treatment efficacy than in published trials, in 20 patients with GBM.

Summary of resolved ethical issues

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

1. The Committee asked if there is previous published research on this topic. The researcher responded that there are six other studies – three randomised trials and three case studies looking at fasting in people with a variety of cancers (most of them stage two, three and four) on chemotherapy. Most have looked at fast durations averaging three to four days. However, only a couple of these studies conducted them through a formal metabolic therapy programme. The difference with the proposed study would be that this fast would be longer and through a more formal programme. The researcher clarified that there were no serious adverse events as a result of any of the previous studies. All of the patients from these previous studies were able to perform the fast from home rather than in a hospital.
2. The Committee noted that, although this is a feasibility study with the primary outcomes being safety and feasibility, the study also aims to collect secondary outcomes relating to efficacy. The researcher clarified that the efficacy outcome will not be measured by comparing outcomes for those who declined to participate. Rather, they will assess efficacy by means of a historical comparison. The researcher clarified that these historical control patients at the Waikato DHB have already given consent for their data to be used in future research.
3. The Committee queried whether the study’s risk mitigation strategy, which entails the researchers texting and emailing the participants who will be fasting from home, is sufficient. The researcher responded that he believes the strategy will be sufficient. For the fast, participants will receive texts/emails every day. For the first few weeks of the keto diet, it will be every three or four days. These texts/emails will instruct the participant to contact the researchers if they are feeling unwell. The researcher also mentioned the possibility of a group Zoom to check in on participants, as well as regular clinical follow ups.
4. The Committee asked about the expense for participants to pay for the ingredients in the keto diet. The researcher explained that this expense will be balanced out by the savings obtained by the participant during the fasting period. The researcher has made sure that all the ingredients are available at PakNSave supermarkets.
5. The Committee noted that they are satisfied with the peer review that has been provided, but requested that the researcher use the peer review template on the HDEC website in the future.
6. The Committee asked whether there is a risk of ketoacidosis in participants with type two diabetes. The researcher responded that there is no risk and his past research has shown that the ketogenic diet has shown to improve type two diabetes.
7. The Committee requested that during the recruitment process potential participants are given the opportunity to talk with a member of the research team that is not involved in their clinical care. This is in order to mitigate pressure to take part in the study which may be present due to the doctor-patient relationship. The researcher asked if it would be appropriate for the oncologist to give potential participants the PIS. The Committee agreed this would be appropriate.

Summary of outstanding ethical issues

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

1. The Committee requested that the researcher upload a Data Management plan using the template from the HDEC website.
2. The Committee noted that in the study protocol and application form, it states that informed consent is being obtained after some of the study specific assessments and questionnaires are completed. The Committee requested that informed consent is obtained before any study specific assessments are done. Please amend the protocol to reflect this.
3. The Committee noted the informed consent process described in the application infers that people get the PIS and give informed consent at the same appointment. The Committee requested that potential participants get the information sheet well in advance of giving informed consent, so they have adequate opportunity to discuss with family and friends. Please amend the protocol to reflect this.
4. The Committee requested that the researcher include information regarding assignment of causality of adverse effects in the study protocol. The Committee noted it is best practice to use ‘probably/possibly/unlikely/unrelated’ causality assignments and to describe how these should be used in the study.
5. The researcher noted that he will provide another study specific adverse effects questionnaire to more thoroughly look at the diet/fasting effects. The Committee requested that if the researcher does this, he should also include in the safety discussion in the protocol a subheading of ‘adverse effects of special interest’ and how they will be followed and managed.
6. The Committee noted that there is a plan to reduce the seven day fast to a five day fast. Please update in the protocol and associated documents.

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

1. Please provide a summary of evidence gathered from past research.
2. Please remove the statement which says “trust your body as it is already an expert at seven day fasts and knows exactly what to do” as this may prevent participants from reporting adverse effects to the researchers.
3. Please undertake a thorough proofread of the PIS as there are multiple editing errors, grammatic errors and missing words.
4. Please amend the PIS and Instruction Booklet so that you are not overpromoting the possible benefits of this intervention. Be clear that this intervention has only been trialled in ten people with cancer in Waikato. You can mention the other studies but be upfront and honest, e.g. that there are no large-scale clinical trials which have established a definite benefit in terms of survival and other outcomes. Make it clear you are just looking at the feasibility. Remain objective and be conservative when making claims about efficacy, as this is not the primary objective of this study.

a) Make the language more objective, for example delete “if we are to turn the tables on this aggressive cancer, this is what we need to do”.

1. Please complete areas where you have left things in square brackets.
2. On page 5 and 6 of the PISCF please remove risks of standard of care treatment. Only include study specific risks, though make it clear that the risks of the keto diet may be exacerbated when combined with the risks of standard of care.
3. Please provide specific advice encouraging participants to seek help for adverse effects.
4. On page 14 please take out the yes / no options for informing the GP, as this is a mandatory requirement.
5. On page 14 please add an optional tickbox for the use of data for future unspecified research.

Decision

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

* Please address all outstanding ethical issues, providing the information requested by the Committee.
* Please update the Participant Information Sheet and Consent Form and Participant Instruction Booklet, 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 Dominic Fitchett and Mira Harrison-Woolrych.

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| **3** | **11:20-**  **11:45am** | **Ethics ref:** | **21/STH/45** |
|  |  | Title: | CLEAR STUDY |
|  |  | Principal Investigator: | Professor Peter Gilling |
|  |  | Sponsor: | ProArc Medical Ltd |
|  |  | Date submitted: | 25 February 2021 |
|  |  | Clock Start Date: | 25 February 2021 |

Tami Abeister, Yair Feld, Thijs Wervelman, Audra Wilson, Rachael Hamill and Deborah Bell were present via videoconference for discussion of this application.

Potential conflicts of interest

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

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

Summary of Study

1. The objective of this study is to evaluate the safety and efficacy of the ClearRing system for the treatment of Lower Urinary Tract Symptoms (LUTS) due to Benign Prostatic Hyperplasia (BPH).
2. This is a multi-centre, single arm, open label, non-randomized, prospective study.
3. Patients enrolled in the study will have a procedure, implanting the device into the urethra by positioning supporting C shape implants embedded in the perimeter of the enlarged prostate tissue.
4. All participants will require 1 follow up phone call and 4 follow up visits over the course of 12 months.
5. The evaluations will include medical and surgical history and physical examination.
6. The researchers will perform laboratory testing for Prostate Specific Antigen (a test for prostate cancer) and standard nomenclature, urine dipstick/MSU, Cystoscopy, Trans Rectal Ultrasound and Uroflowmetry.
7. Participants will be given validated questionnaires such as Visual Analogue Scale (VAS), International Prostate Symptom Score (IPSS)/Quality of Life, Sexual Health Inventory for Men (SHIM).
8. A maximum of 5 clinical sites will be used to enrol up to 30 participants across New Zealand, Israel and Europe.

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 they are satisfied that the major issues from the previously declined application has been resolved.
2. The Committee queried whether there would be any implications for future prosthetic surgery after the intervention device had been deployed, for example whether it makes surgical interventions any more difficult. The researcher responded that this would not be an issue.
3. The Committee noted that there is a less than 10% risk of UTI. The Committee queried if this was in the perioperative period or in the longer-term follow up. The researcher responded that this is over the two-year follow up.
4. The Committee noted that in r1.6 of the application form, the researcher had mentioned terminating the study as an administrative decision. The Committee clarified that in New Zealand you cannot terminate a therapeutic study for commercial reasons.

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

1. Please add a lay title.
2. Please clarify what type of testing the current version of the device has had.
3. Please clarify that the risk of UTI is over the two-year follow up period.
4. Please clarify that this is an experimental device and not registered for use in any country.
5. On page 11 under “what happens after the study or if I change my mind”, please repeat that if participants change their mind and want the implant removed, this will be done free during the first two months after which they have to pay.
6. Please provide contact details on page 13.
7. Please proofread the PIS to get rid of odd use of capital letters in places, e.g. ‘skin Burn’ and ‘penile Tip’.
8. Edit for formatting and typographical errors.

Decision

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

* Please update the Participant Information Sheet and Consent Form, taking into account the suggestions made by the Committee.

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| **4** | **11:45-**  **12:10pm** | **Ethics ref:** | **21/STH/43** |
|  |  | Title: | Micronutrient supplementation in metabolic syndrome |
|  |  | Principal Investigator: | Dr Anitra Carr |
|  |  | Sponsor: | University of Otago |
|  |  | Date submitted: | 23 February 2021 |
|  |  | Clock Start Date: | 25 February 2021 |

Anitra Carr 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. Metabolic syndrome (MetS) is a cluster of conditions that, when occurring together, increase the risk of heart disease, stroke and type-2 diabetes.
2. These conditions include hypertension (high blood pressure), insulin resistance (high blood sugar), excess fat around the waist, and elevated cholesterol or triglyceride levels.
3. Inflammation is believed to be a major driver of MetS, and those with the condition often show increased levels of inflammatory markers in their blood, such as C-reactive protein (CRP), which is a known risk factor for cardiovascular diseases.
4. As such, there is a growing interest in using anti-inflammatory agents to potentially slow and/or prevent progression of MetS to the more severe diseases such as type 2 diabetes and cardiovascular disease.
5. Vitamin C is a potent antioxidant with anti-inflammatory properties. Research has shown that people with MetS have lower vitamin C levels than those without, and higher vitamin C levels have been associated with a lower risk of MetS.

1. Vitamin C can also improve markers of metabolic health, such a blood sugar control and lipid profiles, including cholesterol and triglycerides. Humans cannot produce vitamin C endogenously, therefore, we must obtain it through our diet.
2. The aim of this study is to determine whether vitamin C plus micronutrient supplementation of people with metabolic syndrome (MetS) and elevated inflammation results in decreased markers of inflammation.
3. The researchers will undertake a 12-week RCT (1 daily effervescent micronutrient tablet or placebo) in a group of volunteers with MetS.
4. The researchers will measure a number of blood and urine markers of inflammation, changes to anthropomorphic measures, and changes to mood/fatigue at clinic visits at baseline and weeks 6 and 12.

Summary of resolved ethical issues

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

1. The Committee asked about the potential commercial interest of Bayer, the study funder. The researcher clarified that:
   1. Bayer is the funder but not the sponsor of the study.
   2. Bayer have reviewed and approved the protocol.
   3. Bayer will not receive raw data, only aggregated data/report of final data analysis at the end of the study.
   4. Bayer will not be involved in the interpretation of the data.
   5. Bayer will presumably use the results of this study to make health claims about their product.

The researcher clarified that this is an investigator driven study, and the commercial interest is not the primary purpose of this study. This satisfied the Committee that sponsor indemnity/insurance is therefore not required.

Summary of outstanding ethical issues

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

1. The Committee noted that in r.3.11 of the application form that the researcher stated that tissue will be retained by the research team for use in another study for potential measurement of other relevant related biomarkers. The researchers clarified that this tissue would only be used in direct relation to the current study, for example if another biomarker of interest comes up during the research. The Committee requested that the researcher make this clearer in the protocol, including that they won’t be testing any genomic biomarkers.

1. The Committee requested that the researchers provide a Data and Tissue Management Plan (see HDEC template), covering how long the researchers will retain samples for and for what purpose. This can go either in the study protocol or be uploaded as a separate document.

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

1. Please use lay language to describe the study. Simplify the first paragraph in particular.
2. Please proofread.
3. Please include an optional tick box on the main PIS for storage of tissue for future use directly related to this study. If you intend to store tissue for purposes beyond this study, please note this will require a separate PISCF for future unspecified research.
4. Please clarify that future use of tissue will not include testing for genomic biomarkers.
5. Please amend your documentation to take out the yes / no options for informing the GP, as this is a mandatory requirement.
6. Please combine the screening PIS with the main PIS, to eliminate this extra step.
7. Please clarify what is meant by fasting – e.g. for how long, can participants drink water, can they take their usual medications.
8. Please be consistent with grammar throughout – use ‘you’ and ‘your’ rather than ‘the participant’.
9. On page 6, please tell participants that the results will be shared with Bayer.
10. Please explain who Bayer are.
11. Please inform the participant in the body of the info sheet that you will tell their GP about abnormal study results that may require follow up.

Decision

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

* Please address all outstanding ethical issues, providing the information requested by the Committee.
* Please update the Participant Information Sheet and Consent Form, taking into account 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 Dominic Fitchett and Jean Hay-Smith.

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| **5** | **12:30-**  **12:55pm** | **Ethics ref:** | **21/STH/55** |
|  |  | Title: | ABI-H0731-204 - Vebicorvir plus AB-729 plus standard treatment for the treatment of patients with chronic hepatitis B |
|  |  | Principal Investigator: | Prof Edward Gane |
|  |  | Sponsor: | Pharmaceutical Research Associates New Zealand Lim |
|  |  | Date submitted: | 25 February 2021 |
|  |  | Clock Start Date: | 25 February 2021 |

Ed Gane, Courtney Rowse and Chin Kuh were present via videoconference for discussion of this application.

Potential conflicts of interest

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

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

Summary of Study

1. This is an open label multi-cohort study to evaluate the safety and antiviral activity of VBR and AB-729 when added to entecavir or tenofovir in patients with Chronic Hepatitis B Virus Infection.
2. The purpose of this research study is to determine the effect on the health of these patients and how well tolerated when VBR and/or AB-729 are taken with standard of care (SOC) medication in men and women with chronic HBV infection.
3. This study is also being done to test whether adding VBR and/or AB-729 to patients on long-term treatment for HBV is better than taking the current standard treatment alone.
4. There will be approx. 60 patients with 3 treatment groups at a 2:1:1 ratio. Group 1 VBR + AB-729 + SOC (30 patients) Group 2 VBR + SOC (15 patients) Group 3 AB-729 + SOC (15 patients).
5. All patients will receive their assigned treatment for 48 weeks, and then be required to attend 12 follow up visits.
6. Patients will remain on SOC and after the 48-week period will no longer have access to study drug.

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 it is unusual for compounds from different companies to be used in combination and asked if both companies were sponsoring the study. The researcher responded that Assembly are the sponsors, and he is not sure of the relationship with Arbutus, the company that makes the second compound.
2. The Committee noted that the primary risk of this study is that it is an investigational medicine with no guarantee of efficacy. The Committee was satisfied that the researcher has dealt well with this in the application.
3. The Committee noted that in question r.2.1.1 the researcher has answered that he would be sharing de-identified information with the sponsor before the study begins. The Committee noted that while general information about the study can be shared with the sponsor, de-identified data cannot be shared before the patient has consented to partake in the study.
4. The Committee noted that the researcher’s answer to r.2.2 implied the sharing of data for research, which contradicted with an earlier answer (b.4.4) in the application form where they had answered data would not be shared with researchers outside of the study. The researcher clarified that no data will be shared with researchers outside of the study.
5. Please note that remote monitoring is permitted only where no identifiable information is transferred electronically from the site and that screenshots etc. are not permitted.

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 why the researcher had stated in the reproductive risks section that partners of male participants could not use hormonal contraception, and asked for a justification for this. The Committee requested the researcher replace the reproductive and contraceptive statements with the HDEC reproductive risk template.

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

1. Please use a lay title.
2. Please clarify that no data will be shared with researchers outside of the study.
3. Please provide a sponsor address on page 1.
4. Please note that HIV and viral hepatitis are notifiable diseases.
5. Please provide the approximate lengths of time for study visits.
6. Please remove the reference to “legally authorised representative” on page 12, as it is not applicable in New Zealand.
7. Please remove the cultural tissue statement on page 24 as it has already been stated on page 23.
8. The Committee requested the researcher remove information about the pharmacogenetics study from the main PIS, as this has already been covered in a separate information sheet.
9. Please remove repeated information in the data management section.
10. Please replace ‘personal information’ with ‘identifiable information’ or ‘coded / de-identified information’ in the data management section, for clarity.
11. Please provide more information about the use of photos and pictures (mentioned on page 25) – why will they be taken and how will privacy be protected?
12. Please include the risk of privacy breach in the data section (refer to the HDEC template for recommended statement).
13. Please delete repetitive information about withdrawal rights for data on page 25.
14. On page 25, please clarify that remote monitoring is permitted only where no identifiable information is transferred electronically from the site, and that no screenshots or copies may be made of the portal screens.
15. Please remove the standard of care medication risks section. Only include study-specific risks.
16. The information on page 22 about leftover samples can mostly be removed as this has been covered in the optional PIS.
17. The pharmacogenomic information sheet and biomarker information sheet need to include the risks of genomic research with regards to re-identification and potential impacts on blood relatives, and the risks of sending tissue overseas.
18. Please include in the PGx PISCF the risks of genomic research (re-identification, including risk to blood relatives) and risks of sending tissue overseas.
19. The Committee was confused by the PK PISCF in regards to leftover samples. Please review and make edits where appropriate. Include risk of privacy breach and sending tissue overseas. Suggestion: state that samples may be transferred/analysed at other labs subject to HDEC approval.
20. The pregnancy information sheets have not been accepted for review. These are to be submitted for approval in the event of a participant or partner pregnancy.

Decision

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

* Please address all outstanding ethical issues, providing the information requested by the Committee.
* Please update the Participant Information Sheet and Consent Form, taking into account 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 Sarah Gunningham and Mira Harrison-Woolrych.

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| **6** | **12:55-**  **1:20pm** | **Ethics ref:** | **21/STH/50** |
|  |  | Title: | AMO-02-MD-2-003: Tideglusib Versus Placebo for the Treatment of Children and Adolescents with Congenital Myotonic Dystrophy (REACH CDM) |
|  |  | Principal Investigator: | Dr Gina O'Grady |
|  |  | Sponsor: | AMO Pharma Ltd. |
|  |  | Date submitted: | 25 February 2021 |
|  |  | Clock Start Date: | 25 February 2021 |

Gina O’Grady, Emily Fantelli, Margaret Joppa and Joseph Horrigan were present via videoconference for a discussion of this application.

Potential conflicts of interest

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

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

Summary of Study

1. The primary aim of the study is to evaluate the efficacy, from baseline to end of treatment, of weight adjusted 1000 mg tideglusib compared to placebo in children and adolescents with Congenital Type 1 Myotonic Dystrophy (DM1) as measured by the Clinician-Completed Congenital DM1 Rating Scale(CDM1-RS).
2. Approximately 56 participants, aged between 6 and 16 years will take part in this study worldwide. Study participants will be randomized to receive either weight adjusted tideglusib (1000 mg) or placebo.
3. The study will have 5 distinct phases: Screening, Single-blind placebo run-in (Weeks -2 to 0), Double-blind dose titration (Weeks 0 to 4), Double-blind maintenance between Weeks 4-20, Follow-up Period between Weeks 20-22.
4. There are no current approved pharmacological treatments for people with myotonic dystrophy (DM1), a genetic disorder that affects the brain, nervous system, and muscles.
5. There is evidence that the enzyme GSK-3β is very active in patients with Myotonic Dystrophy.
6. Tideglusib is a new compound which research has shown can block the enzyme GSK 3β.
7. It has been shown to penetrate the brain and therefore has the potential to act on both peripheral and central aspects of the disorder e.g. muscle weakness and neuro-cognitive issues.

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 participants ranged from six to 16 years old. The Committee noted that within this age range some individuals may be able to provide independent informed consent, but that this may not be the case in this study due to intellectual disability. The researcher responded that due to a mild degree of intellectual disability, participants would be providing assent rather than consent. The Committee queried whether there would be any participants who had a degree of intellectual disability such that they could provide consent instead of assent. The researcher responded that this would typically only be the case for the younger participants who would be too young to consent, regardless of disability.
2. The Committee asked that the researchers do not submit items such as syringes, cooler bag etc. for HDEC review. These are not sponsor-branded and are required for the study – they are not in scope for review. None of the following items have been reviewed:
   1. Caregiver binder contents
   2. Sample PPVT manual
   3. Bottle brush image
   4. Cold pack image
   5. Beaker image
   6. Syringe image
   7. Scissors image
3. The Committee asked out of the 500 previous participants who have previously received this medicine, how many were children. The researcher responded that it is only 50 children who have received this medicine.
4. The Committee noted that in the tissue management section, there is reference to optional RNA and protein biomarker research. The Committee queried whether this is restricted to the current study or was for broader research. The researcher noted that this is in reference to the needle biopsy for muscle tissue, which will not be occurring in NZ.
5. The Committee queried what the process would be if participants responded with ‘sometimes/often’ in critical item questions (regarding harming themselves or others) in the questionnaires. The researcher responded that he did not think the questionnaire would include critical item questions but if a concern regarding suicidality or harming others did arise during the study, the clinical team would use the usual customary practices to seek appropriate follow-up for this.
6. The Committee queried whether analyses could produce clinically significant results that are not actionable. If so, there needs to be a process for participants and their whānau getting these results. The researcher responded that they would be doing a pharmacogenomic test on each participant, looking for biological reasons for certain side effects and that this could have clinically significant results. The Committee noted that as this sample would be used for study-specific testing, it is acceptable for parents to consent their children to this (as opposed to if the sample were to be used for future unspecified research).
7. The Committee inquired about the extension study mentioned on page 20 of the parent/caregiver PIS. The researcher responded that this is a 52-weeek open label study which will be offered to participants who were randomised to the placebo group in this study.

Summary of outstanding ethical issues

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

1. The Committee queried whether the various adolescent PIS forms would be understood by study participants and whether it is appropriate to give to them. The researcher responded that it would be the parents who would be reading it to the children. The Committee responded that they preferred PIS forms that the children can look at themselves. Please update the PISCFs according to the advice below.
2. The Committee noted that the insurance is not study specific. The Committee requested that the researcher attains study-specific insurance. The Committee requested that the limit to the indemnity is increased to NZD $10 million, rather than the NZD $5 million currently stated.
3. The Committee noted that the investigator’s indemnity has expired. The Committee requested to see an updated one.
4. For the electronic device, please provide participants with a study-specific email and participant ID to use rather than their identifiable personal email addresses.
5. Please ensure participants receive the PISCF prior to the screening visit. These should be signed at the screening visit.
6. The Committee requested that during the recruitment process potential participants are given the opportunity to talk with a member of the research team that is not involved in their clinical care. This is in order to mitigate pressure to take part in the study which may be present due to the doctor-patient relationship.

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

1. Please proofread each PISCF.
2. Please use a lay title in each PISCF.
3. Please replace the term ‘subject’ with the word ‘participant’ throughout.
4. Please use an abbreviation for CMD after the first use.
5. In the tissue management section, please delete the reference to the optional RNA and protein biomarker research.
6. Please use the 6-year-old PIS for participants judged able to comprehend the document.
7. Please use a very simple one-page PIS with big fonts and pictures for those participants with less cognitive ability. Keep the study doctor name but remove the site, investigator and formal title. Say what the drink tastes like. Simplify the study procedures to a couple of lines. Remove all the contact details. Remove all the consent clauses except “has someone explained the study” and “are you happy to take part?”
8. Please use the 14-16-year-old form for any children that may be able to consent themselves.
9. Please create a separate, optional PISCF for pharmacogenomic testing, due to the cultural issues in NZ around the collection of genetic tissue. Please make it clear that the test may indicate results that could impact on the child’s response to the medication, or on the child’s dosing levels to other medicines they may take. Please inform the participants that in this case, they would be told and so would their GP. Make it clear this information would go on their medical record.
10. Please make it clear that it is mandatory that the GP is informed of any clinically significant findings.
11. Please make it clear that only 50 child participants have previously received this medicine, so that it is apparent how early in its development this medicine is.
12. Please reword/simplify page 2 of the parent PIS, as there are some redundant sentences.
13. Please clarify on page 1-3 of the parent PIS that it is ultimately the child’s decision whether they participate, regardless of the parent or guardian’s decision.
14. Please clarify in the parent PIS that they are also consenting not only for their child’s participation in the study but also for their own.
15. Please change the wording on page 3 of the parent PIS where it states that all participants will receive the placebo at some point in the study. For example: “depending on the group your child is in, they will receive the placebo for two weeks at some point during the trial, or for the whole treatment period”.
16. Delete tablespoon/teaspoon references for blood volumes.
17. On page 2 of the parent PIS please state that Tideglusib is not approved *anywhere*, rather than just NZ.
18. On page 6 of the parent PIS please edit the food intake pre- and post-dosing paragraph as there are some redundancies. Please simplify.
19. Please use the reproductive risk template from the HDEC website.
20. Please remove repeated information in the parent PIS regarding voluntariness and right of withdrawal (p1), placebo definition (p2) and ownership rights (p19+20).
21. Please provide an estimate for time required to complete the questionnaires.
22. Please include important information about the app, e.g.
    1. Can data collected be used or shared by the third-party vendor and in what form?
23. Please state if you would prefer it to be the same parent who fills out the scales each time. E.g. “where possible, it would be appreciated…”
24. Please amend the headers in to use more neutral language.
    1. “What do I have to do” implies they have already consented.
    2. “How will my family benefit” implies that there is a definite benefit.
25. In the caregiver rater video script, please consider amending the wording regarding placebos and reporting of side-effects so as to not give the participants clues about which group they are in based on which side effects they may or may not be experiencing.
26. Please delete mention of 1000 milligrams as this will not be the case in all participants.
27. On page 12 of the parent PIS, please note that Hepatitis A is also notifiable in NZ.
28. Please include incidence numbers on the section about adverse side effects.
29. Please expand on what caregiver participation in the optional sub-study (referred to on page 6) entails.
30. On page 9 of the 14 to 16-year-old assent form, please amend the wording of “we would like to keep the information we have already collected about you” to say “we will keep the information we have already collected about you”.
31. Please amend page 2 of the 7 to 13-year-old assent form to state that if they can run, they should do so rather than walk (e.g. move as fast as you can, as per the protocol)

Decision

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

* Please address all outstanding ethical issues, providing the information requested by the Committee.
* Please update the Participant Information Sheet and Consent Form, taking into account 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 Dominic Fitchett and Devonie Waaka.

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| **7** | **1:20-**  **1:45pm** | **Ethics ref:** | **21/STH/52 (CLOSED)** |
|  |  | Title: | Administrative follow-up of family violence fatalities |
|  |  | Principal Investigator: | Dr Pauline Gulliver |
|  |  | Sponsor: |  |
|  |  | Date submitted: | 25 February 2021 |
|  |  | Clock Start Date: | 25 February 2021 |

Pauline Gulliver and Fiona Cram were present via videoconference for a 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.

**CLOSED SESSION**

Decision

This application was *declined* by consensus, as the Committee did not consider that the study would meet NEAC Standards 7.47 and 7.48.

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| **8** | **1:45-**  **2:10pm** | **Ethics ref:** | **21/STH/53** |
|  |  | Title: | (duplicate) Non-invasive lung imaging system |
|  |  | Principal Investigator: | Dr Kelly Burrowes |
|  |  | Sponsor: | University of Auckland |
|  |  | Date submitted: | 25 February 2021 |
|  |  | Clock Start Date: | 25 February 2021 |

Kelly Burrowes 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. Most critically ill COVID-19 patients will require invasive mechanical ventilation. Management of these patients is challenging.
2. This research will provide a low-cost imaging system for continuous patient monitoring to improve clinical decision making.
3. The researchers will use Electrical Impedance Tomography (EIT), a well-established technology that non-invasively measures changes in lung impedance as it fills with, and empties, of air. EIT is capable of assessing lung recruitment/derecuitment and alveolar overdistension.
4. Despite the availability of several commercial EIT systems and numerous publications supporting its effectiveness for bedside monitoring of lung aeration, it has not had widespread uptake due to technical limitations and difficulty in its clinical interpretation.
5. The researchers are developing an EIT prototype that addresses the most important limitations of EIT: its low imaging accuracy, lack of clinical/patient context, and cost. This will enable its deployment as an accepted and affordable imaging system in NZ to support rapid clinical decision making for management of COVID-19 patients.
6. This project will be testing a custom made EIT system to confirm safety, accuracy, repeatability, fit of the EIT device within the clinical workflow.
7. This study will test the EIT device on ventilated patients in the ICU at Northshore Hospital.
8. Chest X-ray (CXR) will be incorporated into this phase of the testing using a CXR obtained via the standard clinical pathway.
9. The researchers aim to consent patients prior to the procedures if possible, however if patients are unable to consent themselves, they will:
   * gain an opinion from a relative/friend that they believe the patient would want to participate,
   * agreement from the clinician that it is in the patient's best interest and
   * obtain post-procedure consent from the patient after recovery.

Summary of resolved ethical issues

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

1. The Committee was satisfied that the researchers had adequately addressed the issues from the previous decline.
2. The Committee noted that whether this study is in the best interest of the participant is a clinician decision. The clinician will be provided with the standard PIS and the protocol in order to assist in making an informed decision about whether involvement in the study is in the best interest of the participant.
3. The researcher asked if this resubmission altered their Māori approval and locality approval. The Committee answered no – the researcher does not need to re-seek these approvals.

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

1. Please add a lay title.
2. Please remove the best interest statement from the black box.

1. Please remove mention of under 16-year-olds from the breach of privacy section in the data management plan, as this is not relevant.
2. Please proofread the PIS to check for typos and grammatical errors, e.g.
   * Box on page 1: apostrophe in patients
   * “There *are* minor risks of having a device related injury” rather than “there *were* minor risks…”
   * ‘From’ instead of ‘form’, ‘will’ instead of ‘while’.
   * Orphan headings
3. Please update the HDEC study number on all the forms.

Decision

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

* Please update the Participant Information Sheet and Consent Form, taking into account the suggestions made by the Committee.

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| **9** | **2:30-**  **2:55pm** | **Ethics ref:** | **21/STH/54** |
|  |  | Title: | Microfracture and ABEC in Osteochondral Lesions of the Talus (MALT) |
|  |  | Principal Investigator: | Mr NJ Willis |
|  |  | Sponsor: |  |
|  |  | Date submitted: | 25 February 2021 |
|  |  | Clock Start Date: | 25 February 2021 |

Aaron Chester 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. An osteochondral lesion (OCL) is a defect in the cartilage of a joint, which is commonly caused by trauma. It may result in joint pain, locking, stiffness and swelling. These symptoms may limit the ability to walk and perform many of the normal activities of daily living.
2. An OCL can be managed without surgery (e.g. rest and immobilisation), however, this is unsuccessful with 55% of symptomatic OCL.
3. The gold standard among surgical options to treat OCL of less than 15mm in diameter is an operation called micro-fracture, the aim of which is to regenerate cartilage. It involves perforating the bone adjacent to the OCL to allow bleeding and the formation of a blood clot containing stem cells. Over time, this clot provides the basis for new cartilage to form.
4. Autologous bio-scaffold enhanced chondrogenesis (ABEC) is a procedure where, following microfracture, a ‘scaffold' is applied to the OCL. The scaffold is intended to stabilise the blood clot formed through microfracture and increase the rate of successful cartilage formation.
5. There are different ABEC techniques and preparations available; Joint Rep™ (Oligo Medic Inc., Laval Quebec Canada) is an injectable preparation.
6. A single study has reviewed the use of ABEC in OCLs of the talus (a bone involved in the ankle joint). This study did not detect a significant difference in outcomes between patients who received micro-fracture alone and those who received micro-fracture with ABEC; further studies are needed to better answer whether ABEC should be used.
7. This study aims to address this by randomly assigning participants (patients) with symptomatic OCL of the talus to receive micro-fracture alone or microfracture with a brand of ABEC called Joint Rep™.
8. The outcomes (e.g. pain and functioning) of both groups will be compared 1 year after surgery. This information will help to guide orthopaedic surgeons in providing the most appropriate treatment to their patient.

Summary of resolved ethical issues

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

1. The Committee asked if the study is a single-centre trial or if it might be extended overseas. The researcher responded that he is reasonably confident that they will be able to recruit enough participants in NZ, but they are leaving the option open to expand the study into Australia or other countries. The Committee noted that they are approving the application as a single-centre study only at this time.
2. The Committee clarified that there is no sponsor for the trial and asked who had overall responsibility for the study design and conduct. The researcher responded that this is currently Mr Nigel Willis, although they are planning to approach the Orthopaedic Association and apply for funding through the Wishbone Trust.
3. The Committee clarified that due to the double-blind nature of the study, GPs will not be informed of the whether their patient was treated with the MALT technique or was part of the control group. The researcher informed the Committee that nondisclosure of the MALT technique would not put the participant at any risk. If the implant was shown to pose a risk, the researchers would have a record of who received it and would be able to contact the GP.
4. The Committee noted that the researcher must convert the data (including NHI) into de-identified form before it is analysed. The Coordinating Investigator can keep the linking key but must work with the de-identified set.
5. The Committee sought clarification on the researchers’ relationship with Joint Rep™. The researcher clarified that there is no relationship with Joint Rep™ and that they will not be approaching Joint Rep™ for funding. The researcher noted that the compound is patented by Joint Rep™.
6. The Committee sought clarification of how long the researchers will be following up with the patients, as they had found various answers in various places. The researcher responded that they will be following up for 12 months.
7. The Committee sought clarification on what exactly what the Joint Rep™ product is. The researcher responded that it is similar to a compound found in crustaceans, injected over small holes in the cartilage which stabilises the clot which forms, encouraging cartilage formation. The Committee asked if the microfracture technique is the process of making the small holes in the cartilage. The researcher confirmed this.

Summary of outstanding ethical issues

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

1. Please remove all mentions of a sponsor from your documents and replace with the correct person or group of people who have overall responsibility for study design and conduct.
2. The Committee noted that the researcher had responded in question r.2.1 of the application that there would be no review of any health information prior to enrolling people in the study. The Committee inquired as to how they would be enrolling people in the study if this is the case. The researcher responded that they will be identifying patients in the clinic based on what they present with. The Committee requested that the researcher updates the documentation to make it clear that the researchers will be looking at potential participants’ health data prior to gaining consent.
3. The Committee sought confirmation that none of the investigators will be the usual health care providers for the patient, as was stated in the application form. The researcher clarified that the investigators will also be the orthopaedic surgeon doing the operations on the patient. The Committee requested that at some point during the recruitment and informed consent procedure, the researchers give the participants a chance to talk to someone in the research team who isn’t involved in their clinical care, to ensure there is no pressure on the individual to partake due to the doctor-patient relationship.
4. The Committee asked about the potential risk to participants who have a crustacean allergy. The researcher responded that there is no known risk of this product with allergic reactions. The Committee asked why allergy to crustaceans is an exclusion criterion if allergic reaction is not a risk. The researcher was unsure and responded that he will investigate this and confirm.
5. The Committee asked how many patients worldwide have received the Joint Rep™ product, and if any adverse reactions had been reported in any of these patients. The Researcher responded that he will investigate this and confirm. The Committee recommended the researcher looks at the product insert to see if there are adverse reactions listed.
6. The Committee asked if a scientific peer review had been done. The researcher responded that they have requested one from Victoria University of Wellington. The Committee noted that they will need to see this.
7. The Committee requested that the researcher provide a data management plan. Please see the HDEC template for assistance.
8. The Committee noted that there is a very similar study underway overseas which is a blinded pragmatic RCT of 1650 patients comparing microfracture and Joint Rep™ versus microfracture alone in osteochondral lesions of the talus. The Committee queried whether this might undermine the scientific imperative of carrying out this study in NZ. The Committee requested that this is clarified in the peer review.
9. The Committee requested that the researchers ensure no identifiable information is used to complete the surveys – participants should use their participant number instead.

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

1. Please state any important exclusion criteria (e.g. crustacean allergy).
2. Please explain the Joint Rep™ product and microfracture technique clearly on the first page of the PIS, using lay language.
3. Please provide more info about how widely this product has been used in other populations.
4. Please provide more information regarding risks of participating and adverse effects, including frequencies, and what the participant should do if they experience any of these.
5. On page 2, please clarify the statement about identifiable data being sent back to a server housed in the USA.

Decision

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

* Please address all outstanding ethical issues, providing the information requested by the Committee.
* Please update the Participant Information Sheet and Consent Form, taking into account 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 Sarah Gunningham and Devonie Waaka.

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| **10** | **2:55-**  **3:20pm** | **Ethics ref:** | **21/STH/46** |
|  |  | Title: | An Open-label Study to Evaluate the Long-term Safety and Efficacy of CSL312(Garadacimab) in the Prophylactic Treatment of Hereditary Angioedema |
|  |  | Principal Investigator: | Dr Hilary Longhurst |
|  |  | Sponsor: | Syneos Health New Zealand Limited, a Syneos Health |
|  |  | Date submitted: | 25 February 2021 |
|  |  | Clock Start Date: | 25 February 2021 |

Hilary Longhurst was present via videoconference for discussion of this application.

Potential conflicts of interest

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

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

Summary of Study

1. The primary objective of the study is to evaluate the long-term safety of subcutaneous administration of CSL312 (also known as garadacimab) in the prophylactic treatment of participants with Hereditary Angioedema.
2. The secondary objectives of this study are to evaluate the long-term efficacy, safety and patient reported assessment of response to therapy.
3. This phase 3b study will evaluate long-term safety and efficacy of CSL312 (also known as garadacimab) when administered subcutaneously (SC) once monthly for at least 12 months.
4. The study will consist of screening, run-in (for CSL312-naïve participants), open label treatment, and follow-up periods.
5. For participants naïve to CSL312, there will be up to 1-month Screening Period followed by a Run-In Period, which may last at least 1 month and up to 2 months.
6. Participants entering CSL312\_3002 will be from 3 sources:
   * Participants who participated in Study CSL312\_2001
   * Participants who participated in Study CSL312\_3001
   * CSL312-naïve HAE Participants who have not participated in either of the above studies.
7. CSL312-naïve participants who meet all eligibility criteria during the Run-In Period will then enter the at least 12- month Treatment Period.
8. Participants rolling over from Studies CSL312\_2001 or CSL312\_3001 will enter directly into the Treatment 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 clarified with the researcher that all participants in this study will be garadacimab naïve.
2. The researcher clarified that they are looking to recruit approximately five participants in NZ.
3. The Committee noted that when referring to vulnerability and when using adolescent assent forms, age 16 is deemed to be the age of competency in NZ, although this is flexible (as some under 16s can be competent). The Committee queried who would make the competency assessment. The researcher responded that this would normally be a discussion between the physician, the parent or guardian, and the young person themselves. The Committee stated that the person or people making the competency assessment need to know the adolescent and be qualified to make that decision. The Committee noted that the researcher must ensure adolescents have the option to say no to participating in the study, regardless of whether their parent consented.
4. The researcher clarified that adolescents in this study will not be involved in future unspecified research. The only additional study is an optional pharmacokinetic 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 researcher clarified that they will be saving samples for optional future research. The Committee requested that the researcher clarify what this research might entail. If it is future research specifically related to the current study, the Committee will accept an optional tick box for consent. If it is for broader future research, the Committee requires a separate optional PISCF form for the use of this tissue. The Committee stated that the use of tissue for future unspecified research should not be an option for participants not able to provide independent informed consent
2. The Committee noted that in NZ, studies cannot be terminated for commercial reasons. Please make this clear in the protocol and PIS.
3. Please use the HDEC reproductive risks template.
4. Please provide a clinical trial registration number.
5. Please provide a data management plan. See the HDEC template.
6. Please ensure that participants do not use personal email addresses/names to register on the electronic devices. Please give them a study specific email address to log in with.

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

1. Please use lay title and language.
2. Please undertake a thorough edit
   * Remove orphan headings
   * P. 4 Change ‘clotting’ to ‘clot’
   * Remove duplicated information e.g. information about withdrawal is in twice – remove second reference on page 17.
3. Please provide expected number of NZ participants.
4. Please state how many participants have taken the drug to date.
5. Please add contact details on page 18.
6. Make it clear that it is ultimately the child’s choice to participate, regardless of whether the parent has consented. If the child says no, you cannot recruit them.
7. Please clarify the length of time that tissue samples will be saved for, depending on whether they consent to optional future research.
8. Please amend to state that the parent, not the child, should call 111 in the case of an allergic reaction.
9. Please remove the section on parents/guardians consenting to collecting information should their child become pregnant. This would be required as a separate PISCF created at the time of pregnancy. HDEC does not review or approve pregnancy sheets unless a pregnancy has occurred. This would be submitted as an amendment. Please note that parents cannot consent to collecting information from their child’s partner.
10. Please clarify the use of blood samples in the biomarker and optional future research sections. Please clarify what a biomarker is. Please clarify what is optional and what is not. Please clarify if there will be any genetic component to optional future research.
11. Please clarify that informing the GP is mandatory – remove the optional tick box from the consent form.
12. Please provide approximate times for study visits.
13. Please add incidence numbers of adverse effects in the risks section.
14. Please state whether the data collected on the device will be uploaded to a cloud or third-party vendor.
15. Please replace the term ‘subject’ with ‘participant’ throughout.

Decision

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

* Please address all outstanding ethical issues, providing the information requested by the Committee.
* Please update the Participant Information Sheet and Consent Form, taking into account 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 Dominic Fitchett and Mira Harrison-Woolrych.

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| **11** | **3:20-**  **3:45pm** | **Ethics ref:** | **21/STH/56** |
|  |  | Title: | Proof-of-concept study of BAY 1817080 in OAB patients |
|  |  | Principal Investigator: | Dr Sharon English |
|  |  | Sponsor: | Bayer New Zealand Ltd |
|  |  | Date submitted: | 25 February 2021 |
|  |  | Clock Start Date: | 25 February 2021 |

Sharon English and Barbara Gordon were present via videoconference for discussion of this application.

Potential conflicts of interest

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

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

Summary of Study

1. The aim of the study is to determine, for the first time, whether the P2X3 receptor antagonist BAY 1817080 has therapeutic benefit in OAB patients with urgency urinary incontinence (UUI), as well as determination of safety and tolerability in this patient population.
2. The study will test the hypothesis that treatment with BAY 1817080 will result in improvement versus placebo in average change from baseline over Week 4, 8 and 12 in the primary endpoint of urgency urinary incontinence frequency.
3. Following screening phase, participants will be enrolled into a single-blind, 2-week placebo run-in period, after which participants who are still eligible, are to be randomized to 12 weeks of double-blind treatment with BAY 1817080 or placebo.
4. Participants will take a 125 mg dose of BAY1817080 or Placebo twice daily orally for 12 weeks. During this phase there will be 6 study visits. Subsequently, a follow-up visit will be performed 4 weeks after last administration of study intervention.

Summary of resolved ethical issues

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

1. The Committee clarified with the researcher that there will be an independent data management authority.
2. The Committee clarified with the researcher that participants will not be asked to stop taking concurrent medications whilst on the trial except for those related to overactive bladder.
3. The Committee noted that the researcher had incorrectly answered question 3.1.x of the application form, which stated that the medicine would be available to participants after the study had ended. This answer should state ‘no’.

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 the study reimburses the participants for time and inconvenience, as this is a placebo-controlled proof of concept study only. The Committee was not satisfied that the current $200 reimbursement given for travel and parking costs was enough to cover time and inconvenience.
2. The Committee requested that during the recruitment process potential participants are given the opportunity to talk with a member of the research team that is not involved in their clinical care. This is in order to mitigate pressure to take part in the study which may be present due to the doctor-patient relationship.
3. The Committee noted that page 11 of the PIS noted that “some of your biomarker samples and pharmacogenetic samples… will be stored to be used in the future”. The Committee queried if these samples would be used for future research. The researcher was unsure but would find out. The Committee noted that if these samples are being used for future research, HDEC would need to know the breadth of this research, and it may necessitate an optional future research PISCF.

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

1. Please put the lay title first at the top.
2. Check for formatting errors, e.g. spacing between paragraphs etc.
3. Please ensure the use of macrons for Māori kupu.
4. Please make it clearer (e.g. page 2 rather than page 8) that participants will have to stop taking overactive bladder medications that they are already on.
5. Please make it clear earlier on in the PIS that this intervention is an investigational study, that it has not been used in an overactive bladder study before and that it is not approved anywhere in the world. Move the statement from page 7 rather than repeating it.
6. Please state that this medication will not be available after the study has concluded.
7. Please include the approximate length of time that hospital visits will take.
8. Please provide a summary table of visits / assessments, in lay language.
9. Please clarify that measuring the amount of urine in the bladder will be done by way of ultrasound.
10. On page 5, please explain what is meant by “physical treatments”.
11. Please amend the statement that notes that the placebo might not work as well as the participants’ former treatment, to also note that the trial drug might also not work as well as the former treatment.
12. If safety samples include Hepatitis and HIV, please inform the participant that these are notifiable diseases.
13. On page 9 please use the HDEC template for contraception.
14. Please delete split blood volumes on page 11, just provide total blood volume for study.
15. Information on optional studies on page 12 should not be included in the main PIS, as this is covered in the optional PIS.
16. Please use the HDEC reproductive risks template.
17. Please include a Māori tissue statement and information about opportunities for karakia.
18. Please amend page 12 section 9 to make it clear that patients have the option to withdraw from the study and *not* have further information collected about them.
19. Please amend page 12 where it explains that female participants will have data collected regarding pregnancy and outcomes to make it clear that this would require additional consent from the participant.
20. Please include the risk of privacy and confidentiality breach in the ‘what happens to my information section’ – see template paragraph in HDEC PIS.
21. Please use the HDEC approved compensation statement.

Pharmacogenetic testing PIS:

1. Please state in lay terms whether genomic testing may include whole genome analysis.
2. Include Māori cultural statement and information about opportunities for karakia.
3. Include risk of confidentiality privacy breach and risk of re-identification.
4. Please explain the link between genes and family inheritance.

Pregnancy PIS

1. Pregnancy information sheets have not been reviewed or approved – these will only be reviewed if there is a pregnancy during the study. Please submit as an amendment in this case.

Decision

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

* Please address all outstanding ethical issues, providing the information requested by the Committee.
* Please update the Participant Information Sheet and Consent Form, taking into account 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 Sarah Gunningham and Paul Chin.

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| **12** | **3:45-**  **4.10pm** | **Ethics ref:** | **21/STH/59** |
|  |  | Title: | A Phase II double blind study of Clenbuterol and Nadolol on cognitive performance in Neurodegenerative Disorders |
|  |  | Principal Investigator: | Prof Tim Anderson |
|  |  | Sponsor: | InClin Clinical Research Organization |
|  |  | Date submitted: | 25 February 2021 |
|  |  | Clock Start Date: | 25 February 2021 |

NZBRI representatives 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 II, randomized, placebo-controlled, double-blind, crossover study on the central nervous system (CNS) and pharmacodynamics effects of CST-103 (clenbuterol) co-administered with CST-107 (nadolol) in four subject populations with Neurodegenerative Disorders:
   1. Parkinson’s Disease (PD) with rapid eye movement (REM) Sleep Behaviour Disorder (RBD) and Depressive Symptoms
   2. Mild Cognitive Impairment (MCI) with Depressive Symptoms
   3. Dementia with Lewy Bodies (DLB) with Cognitive Fluctuations
   4. Parkinson’s Disease Dementia (PDD) with Cognitive Fluctuations
2. The primary objective of this study is to identify a CNS signal in one of the planned pharmacodynamic measurements after multiple oral doses of CST-103 in the presence of CST-107.
3. After completion of the screening visit, participants who meet all the eligibility criteria will attend a “lead in” visit up to two weeks before being randomised into their treatment group.
4. This is a cross over study, which means that participants will have different treatments in turn (Treatment Period 1 and Treatment Period 2, each lasting 14 days).
5. Between the treatment periods, there will be a minimum period of 14 days of study medication washout to ensure that the study medication is cleared from the body before starting the second treatment period.
6. Participants will take their study medication once a day during each treatment period.
7. Study visits are described in the protocol (from page 44).
8. Study assessments include neurological examinations, health and mood questionnaires, cognitive testing (some on a device), blood and urine specimen collections, Pupil light reflex, Electro encephalograms, Electrocardiograms, wearable device.

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 researchers are using GDS and HADs questionnaires which measure depression. The Committee asked if this is just for screening, or if they were likely to find depression in people who have not been previously diagnosed for it. The researchers answered it is for screening, as they are looking for participants with a mild level of depression, but that there is the potential that this might not have been diagnosed in some potential participants. The Committee clarified that the researchers have a process for dealing with these individuals.
2. The Committee clarified in regards to question r.2.1.1. that identifiable health information will not be provided to the sponsor prior to obtaining informed consent

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 PIS has a very low readability score. The researcher explained that this is because of a lot of medical language such as medication and names of symptoms. Please shorten and simplify.
2. The Committee noted that there is significant burden for the participants in this non-therapeutic study with no reimbursement offered for time and inconvenience. Please discuss with the sponsor if reimbursements could be arranged. The researchers noted that the length of the appointments is not uncommon for patients with Parkinson’s.
3. The Committee requested that during the recruitment process potential participants are given the opportunity to talk with a member of the research team that is not involved in their clinical care. This is in order to mitigate pressure to take part in the study which may be present due to the doctor-patient relationship.
4. The Committee noted that the researchers have said that this is a therapeutic study, but due to the length of the study this cannot be described as a therapeutic study for the participants involved. Please do not present it as such – make it clear in all documentation that this is not a therapeutic study.

Data management plan:

1. Please customise to the current study.
   * Use NZBRI data and tissue SOPs rather than CDHB SOPs.
2. Please include addresses for CRO and overseas laboratories.
3. Delete under 16yo breach of confidentiality section.
4. Make sure your responses in s7.1 match your responses in application form regarding labelling samples with identifiers.
5. Ensure biostamp and EEG data etc. are referenced in the appropriate sections e.g. 7.2
6. Make sure your responses in section 8.1 match your response in application form regarding local lab staff and identifiable tissue.

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

1. Please make lay title more lay.
2. Please make PIS more user friendly, especially regarding age group and target populations. Review for lay terms e.g. “physiological functions”, “respiratory systems”, etc. – can simplify.
3. Make sentences short and simple.
4. Remove repeated information – each piece of information should only be in there once.
5. Increase font sizes for tables as these are too hard to read, especially for risk section.
6. Please do a rigorous proofread for spelling, grammar and formatting errors.
7. Please make your ‘biostamp terms of use’ and ‘subject instructions for use’ documents more lay friendly. Important information about data sharing, risks and precautions around it need to be included in PIS.
8. Please ensure that if people are taking hormonal contraception, it has been commenced in sufficient time to ensure it is effective from study Day 1.
9. Please provide city level information for overseas labs.

1. Please provide retention times for PD samples.
2. Please remove the optional tick box for the GP notification consent clause as it is a mandatory requirement to inform the GP. Make it clear in the PIS that the GP will be notified.
3. Please clarify the role of the caregiver and that if the caregiver withdraws from the study, the participant would also be withdrawn.
4. No participant will be under the age of 16 – please amend accordingly.
5. Please amend the statement on page 2 of main PIS which states that nadolol is a treatment for respiratory disease, as this is not true.
6. Page 15: please revise the section on nadolol, as there are data on nadolol in pregnancy, and beta-blockers are expected to cause intrauterine growth restriction. While there appears to be less data on clenbuterol, there are data on other beta-agonists in pregnancy, which could be mentioned.
7. Add statement about access to medicine after the study.

Mild cognitive impairment PIS

1. Please clarify how long data will be stored for.
2. Please simplify and make more readable for people with cognitive impairments.

Decision

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

* Please address all outstanding ethical issues, providing the information requested by the Committee.
* Please update the Participant Information Sheet and Consent Form, taking into account 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 Dominic Fitchett and Jean Hay-Smith.

## 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:** | 13 April 2021, 10:00 AM |
| **Meeting venue:** | ONLINE - Zoom Meeting |

The following members tendered apologies for this meeting.

* Jean Hay-Smith
* Paul Chin
* Dominic Fitchett

1. **Review of Last Minutes**

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

The meeting closed at 4.30pm.