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| **Committee:** | Central Health and Disability Ethics Committee |
| **Meeting date:** | 22 September 2020 |
| **Meeting venue:** | Via Zoom 871 283 1011 |

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| **Time** | **Item of business** |
| 12:00pm | Welcome |
| 12:25pm | Confirmation of minutes of meeting of 25 August 2020 |
| 12:30pm | New applications (see over for details) |
| 12:30 – 12:55pm  12:55 – 1:20pm  1:20 – 1:45pm  1:45 – 2:10pm  (10 minute break)  2:20 – 2:45pm  2:45 – 3:10pm  3:10 – 3:35pm  3:35 – 4:00pm  (10 minute break)  4:10 – 4:35pm  4:35 – 5:00pm  5:00 – 5:25 | i 20/CEN/210  ii 20/CEN/203  iii 20/CEN/206  iv 20/CEN/207  v 20/CEN/212  vi 20/CEN/201  vii 20/CEN/204  viii 20/CEN/202  ix 20/CEN/209  x 20/CEN/205  xi 20/CEN/211 |
| 5:25pm | General business:  Noting section |
| 5:30pm | Meeting ends |

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| **Member Name** | **Member Category** | **Appointed** | **Term Expires** | **Apologies?** |
| Mrs Helen Walker | Lay (consumer/community perspectives) | 22/05/2018 | 22/05/2020 | Present |
| Mrs Sandy Gill | Lay (consumer/community perspectives) | 22/05/2020 | 22/05/2023 | Present |
| Dr Patries Herst | Non-lay (intervention studies) | 22/05/2020 | 22/05/2023 | Present |
| Dr Cordelia Thomas | Lay (the law) | 20/05/2017 | 20/05/2020 | Present |
| Dr Peter Gallagher | Non-lay (health/disability service provision) | 22/05/2020 | 22/05/2023 | Present |
| Ms Helen Davidson | Lay (ethical/moral reasoning) | 06/12/2018 | 06/12/2021 | Apologies |
| Ms Julie Jones | Non-lay (intervention studies) | 22/05/2020 | 22/05/2022 | Present |
| Dr Jillian Wilkinson | Non-lay (observational studies) | 22/05/2020 | 22/05/2023 | Present |

## Welcome

The Chair opened the meeting at 12:00pm and welcomed Committee members, noting that apologies had been received from Ms Helen Davidson.

The Chair noted that the meeting was quorate.

The Committee noted and agreed the agenda for the meeting.

## Confirmation of previous minutes

The minutes of the meeting of 25 August 2020 were confirmed.

## New applications

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| **1** | **Ethics ref:** | **20/CEN/210** |
|  | Title: | How does peritoneal dialysis affect the removal of oxypurinol in patients with gout |
|  | Principal Investigator: | Professor Robert Walker |
|  | Sponsor: | Health Research South |
|  | Clock Start Date: | 10 September 2020 |

Prof Robert Walker 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. Allopurinol is used to decrease urate production which forms crystals in joints and under the skin, causing gout. For patients on dialysis, the concentration of allopurinol taken out by dialysis is not known. This will be addressed here. 10 patients will be given oxypurinol, a metabolically active metabolite of allopurinol.
2. Observational study: patients already on allopurinol. Peritoneal dialysis. Measure allopurinol, urate etc to determine clearance. Hypothesis is that the current dosing schedule is not enough, urate levels are too high.

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 and confirmed with the researcher that question ‘O’ had been answered incorrectly, and that the study did not involve the administration of a new medication.
2. The Committee noted for future reference that it would be helpful to put evidence of GCP training on the CI’s CV.
3. For future applications, when answering question P.4.2., please explain what cultural issues the research may involve.

Summary of outstanding ethical issues

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

1. The Committee stated that the PIS is quite brief, and several sections are missing. Please refer to the HDEC PIS template to identify missing sections (e.g. a cultural statement).
2. Please remove the yes/no tick boxes from the consent form for all statements that aren’t truly optional, i.e. those where a participant could select ‘no’ and still participate in the study.
3. Please ensure that all information that appears in the consent form is first mentioned in the PIS, e.g. consulting the GP.
4. Please edit for grammar; break up longer sentences; and improve formatting.

Decision

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

*National Ethics Standards* para *7.15*

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.

The Committee noted that while the changes to the PIS could be addressed, it would be logistically easier if the application were re-submitted and reviewed via the expedited pathway.

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| **2** | **Ethics ref:** | **20/CEN/203** |
|  | Title: | ABP-671-201: Study to Assess the Efficacy, Safety, and Pharmacokinetics of ABP-671 in Patients with Gout or high uric acid level in the blood |
|  | Principal Investigator: | Dr Barnaby Montgomery |
|  | Sponsor: | Atom Bioscience Australia Pty. Ltd |
|  | Clock Start Date: | 10 September 2020 |

Ann Madrid, Kasuni Kottachchi and Abdi Elmi 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. ABP-671, a new urate transporter 1 (URAT1) inhibitor, is being developed for the treatment of gout associated with hyperuricaemia. Sustained hyperuricaemia is the most important risk factor for the development of gout. Available uric acid lowering therapies have serious side effects. ABP-671 is expected to have similar or better efficacy with a superior safety profile.
2. This is a Phase 2a, multicenter, randomized, double-blind, placebo-controlled, dose-ranging efficacy, safety, and PK study evaluating 6 different dose regimens of ABP-671 compared with placebo. 60 participants will be enrolled at approx. 11 sites in Australia and New Zealand with hyperuricaemic gout. The study will be conducted in 3 sequential ascending dose groups. Each dose group will undergo the following: screening, Run-in, Dose Evaluation, and Follow-up (plus a Gout Treatment Washout Period prior to Run-in if needed).
3. Previous studies with lower doses have been shown to reduce uric acid levels in the blood of participants. This study seeks to find the best dose for patients with hyperuricaemia and gout. Standard of care will continue to be administered.

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 peer review will be sought from SCOTT.
2. P.4.1 and P.4.2 Application form: the Committee stated that article 1 of the Treaty relates to the sovereignty of the crown, and article 2 relates to rights over land, and stated for future reference that the Treaty should not be used to justify the equal participation rights of Māori. Instead, the issue of tissue (which is a Taonga) being used in the study should have been noted.
3. It was clarified that 60 participants will be involved in Australia and NZ.
4. The Committee requested the information regarding future unspecified research to be moved into a separate PIS. **After the meeting, it was clarified that future research involving anonymous information may be consented to as part of the main study (and be included in the main PIS).** A separate PIS is only needed for future research to be conducted with identifiable information or human tissue.

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 how participants would be identified and recruited. The Researchers explained that in the first instance eligible individuals will be identified at participating sites by screening their health information. Those patients will be initially informed about the study by their GP, and then referred to an investigator if they express interest in the study. There Committee noted some inconsistency in the study documentation regarding whether participants will be first contacted by a GP who is not involved in the study, or if their treating clinician is also an investigator.  
   Further information requested: amend the study documents to ensure it is stated that participants will be first contacted by their GP before a member of the study team.

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

1. Main PIS:
   * Page 2: please change the references to Australia to New Zealand.
   * The information about how to take the medication is repeated in different sections: please amalgamate this into one section.
   * Please amend the PIS to state that the GP will be informed of their participation if they choose. All information in the consent form should first be explained in the PIS.
   * Please state that having experienced acute gout flare in the last 30 days is an exclusion criterion for the study.
   * Please update the information about study costs (or submit as an amendment prior to beginning the study if this is not yet known).
   * Please simplify the introduction to the PIS, and simplify acronyms were possible.
   * Page 21: please remove the reference to future uses of coded information. This should instead be put into a separate Future Unspecified Research PIS.
2. Pregnancy PIS:
   * Please clarify that information collected will be *about the mother*.
   * Please also amend the sentence “you may withdraw your consent after…” to reflect the fact that participants may withdraw their consent at any time.
   * Page 2: please correct the statement “all research is reviewed by an HDEC”.
   * Please change “Northern B” HDEC to “Central”.
   * Please amend the section about Consent signed after baby is born to reflect the fact that this is information about the *baby*, not the mother. It should make clear that the parent is consenting on behalf of their child.
   * Please move the consent that is to be signed for the baby *after* the baby is born to a separate consent form.

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 Dr Cordelia Thomas and Dr Peter Gallagher.

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| **3** | **Ethics ref:** | **20/CEN/206** |
|  | Title: | FIS 002-2020: A study assessing single and multiple doses of FTX-6058. |
|  | Principal Investigator: | Dr Chris Wynne |
|  | Sponsor: | Fulcrum Therapeutics |
|  | Clock Start Date: | 10 September 2020 |

Dr Chris Wynne 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. FTX-6058 is being developed for the treatment of sickle cell disease. This is the first study of FTX-5058 in humans, and will enrol healthy male and female participants. The study will be conducted in four parts:
   * Part A (6 dose groups) will assess single increasing doses of FTX-6058 or placebo.
   * Part B (4 dose groups) will assess multiple increasing doses of FTX-6058 or placebo.
   * Part C (1 dose group) will assess the effect of food on how FTX-6058 is processed and cleared from the body, by evaluating single fed and fasted doses of FTX-6058.
   * Part D (1 dose group) will assesses the effect of FTX-6058 on a liver drug-processing enzyme called CYP3A, by evaluating single midazolam doses taken before and after a ten-day course of FTX-6058.
2. Blood samples to measure study drug levels and the body's response to the drug will be collected at specific time points during the study, safety will be monitored, and any changes in health will be recorded. The results will be used to inform the further clinical development of FTX-6058.

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 any future unspecified research was intended. The Researcher explained that optional genomic research was planned, but not FUR. The Committee congratulated the Researcher on the cultural wording in the genomic PIS.

Summary of outstanding ethical issues

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

1. Please update the Participant Information sheet, amending the wording regarding the mechanism of the study drug to make this clearer.

Decision

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

* Please address all outstanding ethical issues raised by the Committee.
* Please update the Participant Information Sheet and Consent Form, taking into account the suggestions made by the Committee.

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| **4** | **Ethics ref:** | **20/CEN/207** |
|  | Title: | Pharmacogenetics in General Practice |
|  | Principal Investigator: | Dr Simran Maggo |
|  | Sponsor: |  |
|  | Clock Start Date: | 10 September 2020 |

Dr Simran Maggo and Dr Ben Hudson 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 project seeks to find out if there is a genomic or pharmacogenomic link to why some people start an antidepressant drug and then discontinue or stop it indefinitely. The study will specifically investigate whether there is a genetic basis for how the drug is broken down in the body.
2. Potential participants will be identified from Pegasus, a public health organisation. Eligible patients will then be contacted via their GP’s, and invited to contact the research investigators if they wish to participate.

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 several issues raised in the study’s peer review, the first concerning the study’s exclusion criteria. The Researchers explained that they are not trying to see whether the person’s genetics is associated with depression, but rather whether their genetics is causing a pattern of drug metabolism which is causing them to stop taking treatment.
2. The second issue raised in the peer review concerned the lack of a depression scale. The Researchers clarified that it is a purely PK issue that they want to look at, rather than depression.
3. The Committee asked why the participants had been described as not being vulnerable. The Researchers explained that as over 15% of the adult population in Canterbury experiences depression at some point, this was not thought to characterise them as vulnerable for the purposes of participating in research.
4. The Committee asked how the researchers intended to recruit at least 20% Māori participants. The Researchers explained that it is an aspirational number, but they will be targeting practices that have a high number of Māori participants.

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 if participants will be recruited from the PHO, and whether the methods will be in accordance with the health information privacy code. The Researchers confirmed that potential participants will be identified through a PHO, however they will first be contacted by their GP, and will only be referred to the researchers once the patient has expressed interest in the study. The Committee noted the sensitive nature of the study and the potential vulnerability of the participants.  
   Further information requested: Researchers must choose a method of selecting and approaching participants that avoids unduly influencing potential participants. Please upload the letter which will be sent from the GP to potential participants (*National Ethics Standards* para *11.7*).
2. The Committee stated that stigmatisation from the study is possible for Māori, and that this should be considered in deciding how the study results will be presented.
3. The Committee queried the relevance of the questions contained in the questionnaires for achieving the study outcomes, and suggested that fewer and more direct questions could answer the study questions more effectively. Researchers should only collect that information which is relevant to a study’s outcomes.

(*National Ethics Standards* para 12.23).

The Committee requested the following changes to the Participant Information Sheet and Consent Form (*National Ethics Standards* para *7.15*, *7.16*):

1. Please amend the wording around the purpose of the study, to make clear that the study is seeking to determine the extent to which adverse drug reactions or genes are factors causing individuals to stop taking anti-depressants.
2. Page 2: please correct the statement “if an adverse effect has been confirmed…”
3. Page 2 and consent form: please correct “blood”, replacing with “saliva”.
4. Under the heading “what will my participation in this study involve”, please explain what options there are if they cannot attend the study visit. Please explain how long the visit will be and what will be involved.
5. Please consistently refer to “you” rather than “the participant”.
6. Page 4: please explain that the koha is intended to cover expenses incurred in the study.
7. Page 5, de-identified/coded information: please qualify the language about keeping information confidential to reflect the fact that these measures are not guarantees of confidentiality.
8. Page 5: “future unspecified research will generate as much public good from participant contributions as possible”. Please remove this statement or soften the language.
9. Page 6: please remove the reference to genetic understanding of eating disorders.
10. Page 6, future unspecified genetic analysis methods: please explain ‘mitochondrial DNA’.
11. Please add greater information about what the questionnaires will involve in the PIS (alcohol use, mental health, quality of life).
12. Please add information that samples will be stored in a tissue bank and that samples will be disposed of with a karakia to the PIS.
13. The Committee enquired about the use of cases and controls. The Researchers explained that cases and controls refer to patients who have had to stop their anti-depressants, and patients who have managed to continue their anti-depressants. However, both will undergo the same procedures as part of this study. Please explain this in the PIS.
14. The Committee asked about the process for addressing any results from the questionnaires which may raise concern for a participant’s wellbeing. The Researchers explained that the survey software will automatically alert the Researchers if participants give answers above certain values. The Researchers would then follow up with participants within 24 hours, and advised as appropriate. Please explain this process in the PIS.
15. The Committee asked how the certain questions in the questionnaires (e.g. taking alcohol in the last two months) will help to show why participants stopped taking their medication two months ago. The Committee asked for it to be explained in the PIS how those questionnaires seek to answer the research questions, and for those questionnaires to be adjusted or replaced if necessary.

Decision

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

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| **5** | **Ethics ref:** | **20/CEN/212** |
|  | Title: | Ph1 INBRX-101: Assessment of single and multiple doses of INBRX-101, in adults with alpha-1 antitrypsin deficiency. |
|  | Principal Investigator: | Dr Andrew George Veale |
|  | Sponsor: | Inhibrx |
|  | Clock Start Date: | 10 September 2020 |

Dr Andrew George Veale, Stephanie Pollard, Klaus Wagner, Fay and Jeff Jensen 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. INBRX-101 is being developed for the treatment of alpha-1 antitrypsin deficiency (AATD).

This is the first study of INBRX-101 in humans, and will be conducted in adults with AATD. The trial aims to:

* + Assess how safe and well-tolerated INBRX-101 is.
  + Measure levels of INBRX-101 in the blood over time (pharmacokinetics).
  + Measure the body's response to INBRX-101 (pharmacodynamics).
  + See whether the body makes antibodies to INBRX-101 (immunogenicity)

1. Part 1 of the study will enrol 4 planned dose groups (6 participants per group), with the dose level planned to increase for each successive dose group. Every participant in Part 1 will receive a single dose of INBRX-101, given as an infusion into a vein (IV).
2. Part 2 will enrol 3 dose groups (6 participants per group), with the dose level planned to increase in each successive dose group. Every participant in Part 2 will receive three IV doses of INBRX-101, with a three week gap between each dose.

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 costs of the different participant groups. The Researchers outlined the reimbursement that would be paid for participants at CCST, and stated that while the payment model is different at Waikato DHB, those figures are expected to be slightly lower than at CCST. The Researchers further explained that the study will involve quite a long stay on site, as well as travel costs.
2. A minor issue regarding the deductible on the study insurance was clarified.
3. The Researchers noted three errors in the information provided in the application form: the listed CI should be Dr Andrew Veale; r.1.3 (will your study involve withholding standard treatment from participants?) was answered with ‘yes’, which is incorrect as patients in New Zealand are not receiving the control drug; f.3.1 (will all participants have continued access to the best-proven intervention after the end of your intervention study?) should state that participants will not have access to the best treatment after the intervention, as it is unfunded in New Zealand.

Summary of outstanding ethical issues

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

1. The Committee asked about the likelihood of pregnancy in the study. The Researchers explained that pregnancy is possible, however most participants will be over the age of 50 so a pregnancy is unlikely. Participants are asked to refrain from sex and use two methods of contraception.   
   The Committee asked for it to be stated on the consent form that the participant agrees to inform their partner of the risks.
2. Please amend the statement “your study doctor may wish to contact you to check on your health”, adding “with your consent”.
3. Please remove or correct the clause in the consent form about future unspecified research.
4. Please make it clear to participants that they will be required to go 11 hours without food or water or amend for the correct period of time.
5. Where the form explains that a liquid will be squirted into the lungs, please state what that liquid is.
6. In the PISCF part 2, please correct the missing text on page 2 (No other investigational drugs, IV immunoglobulins, or monoclonal antibody drugs are allowed, for at 30 days before dosing until the end of the study.)
7. The Researchers noted that the duration at day 0 should be described as 4-6 hours rather than 8-10, which will be amended.

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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| **6** | **Ethics ref:** | **20/CEN/201** |
|  | Title: | Testing the Brain Injury Screening Tool (BIST) |
|  | Principal Investigator: | Prof Alice Theadom |
|  | Sponsor: | AUT |
|  | Clock Start Date: | 10 September 2020 |

Prof Alice Theadom 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 Brain Injury Screening Tool (BIST) tool aims to standardise how mild brain injuries are assessed across professions and services and to provide advice on suitable care pathways based on international and national clinical guidelines. This study aims to explore the feasibility and clinical utility of the BIST in clinical contexts such as in the trauma department, GP surgery and physiotherapy practices as well as to understand the patient experience and influence on service outcomes and recovery trajectories to ensure any refinements are made before national roll out.

Summary of resolved ethical issues

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

1. The Committee asked for clarification about the functioning of the screening tool. The Researcher explained that the options which the screening tool presents to clinicians are presented in footnotes in the document, which suggest the appropriate course of action to the clinician. In using the tool, the participants’ answers are automatically scored for the clinician.
2. The Committee asked what the participants will see when using the tool. The Researcher explained that the first section is for the clinician, in order to identify if the participant might need hospital-level care. Participants will see the following section and their screening score, which will appear on the ‘manage my health’ app.
3. The Committee asked if participant’s answers to the questionnaires will be reviewed for potential signs of distress. The Researcher explained that the results of the tool will be available to the participants’ GP, and additionally the tool will automatically produce a pop-up if the answers indicate distress, recommending that the participant visit their GP.
4. It was clarified that the PIS documents will be online, and assent will be given electronically.
5. The Committee asked if the research had been reviewed by a measurement expert. The Researcher explained that one of the investigators is a measurement expert and will be leading the measurement study.
6. For future applications, in answering question P.6.2 it is important to differentiate de-identified data from anonymous data.
7. The Committee asked what kinds of questions the clinicians will be asked in the interview. The Researcher explained that the questions will cover their experience using the machine, what they liked and what could be improved etc.

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 about how the BIST is scored.  
   Further information requested: please upload a cover letter or other document explaining how the BIST is scored.
2. P.4.1 the committee noted for future applications that it would be better to state statistics relating to the condition. The Committee also stated that cultural issues in the study are whakama for participants, and that the head is tapu for Māori.

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

1. Please amend thee wording in each PIS to make it appropriate for its target audience, and add a heading to clearly distinguish each form.
2. The Committee asked how younger children will be aided in using the BIST. The Researcher explained that they will encourage participants to seek help in completing the tool if they need it. Please state in each assent form that you may complete it on your own or have someone else complete it with you.
3. Parent PIS: “what if something goes wrong” – please remove the statement asking participants to talk to the researcher, and add a statement about ACC coverage (see the HDEC template for guidance).
4. Each PIS: under “what are my rights”, please add the right to access/correct information.
5. PIS for children:
   * Please state that the parents will also need to give consent.
   * Please state that data will be retained for 10 years after the last participant turns 16.
6. Please proofread the clinician patient information sheet for accuracy.
7. Parent and clinician PIS: under “who is paying for the study”, please state that it is an independent study.

Decision

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

* Please address all outstanding ethical issues, providing the information requested by the Committee.
* Please update the Participant Information Sheet and Consent Form, taking into account 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 Ms Julie Jones.

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| **7** | **Ethics ref:** | **20/CEN/204** |
|  | Title: | The BONANZA trial |
|  | Principal Investigator: | Dr Paul Young |
|  | Sponsor: | Monash University. |
|  | Clock Start Date: | 10 September 2020 |

Dr Paul Young and Andrew Udy 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.

Julie Jones declared a potential conflict of interest and the Committee decided that it was not substantial and that she could participate in the discussion of the application.

Summary of Study

1. The study aims to establish whether monitoring and optimising brain tissue oxygen levels improves outcomes for patients with severe traumatic brain injury (TBI).
2. To be eligible for this study, participants will be required to have a clinical indication for intracranial pressure monitoring (monitoring of the pressure in the brain). At the time intracranial pressure monitoring is established, a brain tissue oxygen monitor will be placed. This brain tissue oxygen monitor would not be inserted as part of standard care. However, based on existing literature no risk of physical harm to participants from this additional monitoring is foreseen (see section 13.5.1 of the protocol) because both monitoring devices will be inserted via a single "burr hole" in the skull.
3. All trial participants are believed to benefit from protocolised management of elevated pressure in the brain. Although interventions that are instituted in response to low oxygen levels in the brain would be expected to reduce the risk of brain damage developing, these interventions also have potential side effects. These risks are outlined in section 13.5.2 but all risks identified are commonly encountered and managed in major trauma victims who are cared for in the ICU.

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 what the standard of care for the participants is. The Researcher explained that patients receive intra-cranial monitoring and neuro-intensive care (optimising the pressure on the brain). Patients enter the hospital being initiated on life support in a pre-hospital setting, and are taken to the emergency department and have a CT scan. They are then transferred to either the operating theatre if they need emergency surgery, or transferred to the intensive care unit. If they have severe trauma of the brain, of the trauma is assessed with a scan of the brain. It is then decided if the patient can be woken up and assessed neurologically, or if a period of stabilisation and ongoing sedation is required. In that latter scenario, a hole is drilled into the skull and a monitor is inserted into the frontal lobe of the brain. This is to reduce the chance of secondary brain injury due to swelling of the brain causing dangerously high pressure. This can occur over a period of 7-10 days.
2. The Researchers explained that neuro-intensive care is complicated, and this study will provide clinicians with additional protocols for making decisions about the participants’ care and monitoring staff, resulting in a higher standard of care for all participants.

The Committee discussed whether these study inclusion benefits are sufficient to be considered in the patients’ best interests, and noted that some participants would be included in the study without prior consultation with their family/whanau.

1. The Committee asked if there is any risk associated with the addition of a second monitor in the brain. The Researchers explained that the data available suggests that this second monitor will not pose any additional risks, as a hole will already be made for the first monitor.
2. Application question P.4.1: for future applications, please provide statistics of the incidence of this condition in Māori.
3. The Committee noted that there is a risk of whakama in this study depending on the nature of the injury, which should be taken into account.
4. The Committee asked if the comparison of oxygen monitoring alone vs with pressure could be conducted as a retrospective observational study. The Researcher explained that randomization is needed to allow a causal inference to be made.

Summary of outstanding ethical issues

1. Please upload an patient-facing questionnaires for review.

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

1. Relative/Whānau/Friend Information and Consultation Form:
   * The Committee asked if, by telling the family which group the participant is in, it is likely to lead to any requests for withdrawal. The Researchers noted the potential for this to bias the study results, and agreed to remove this such that the family will be blinded.
   * Page 3: telephone follow-up appointments will be conducted 6 months and 12 months after injury. Please make clear that it is the patient who will be contacted.
   * Please proof-read for inappropriate use of “you” or “your” (see ‘rights to access study information and results’, and information about accessing study info).
   * Consent form: please proofread for appropriate use of pronouns, and amend such that they are expressing an *opinion* of the best interests of the concerned individual, rather than providing consent.
2. Main PIS:
   * Participant should not be kept indefinitely. Please clarify how *study* records will be kept.
   * Please use only one of the terms ‘GP’, ‘Local doctor’ and ‘Provider’.
   * Please make clear that study data will be stored in Australia.
   * Please change ‘northern A’ to ‘Central’ on both sheets.
   * Please proofread pages 2 and 3 for accuracy.

Decision

This application was *provisionally approved* following a vote, with five votes in favour and two votes against, 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 Mrs Sandy Gill and Ms Julie Jones.

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| **8** | **Ethics ref:** | **20/CEN/202** |
|  | Title: | Comparing standard blood oxygen measures to a new device in humans in changing oxygen states |
|  | Principal Investigator: | A/Prof M Berry |
|  | Sponsor: | University of Otago Wellington |
|  | Clock Start Date: | 10 September 2020 |

Ms Freya Harrison 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.

Dr Patries Herst declared a potential conflict of interest and the Committee decided that it was not substantial, and that she could remain for the discussion of the application.

Summary of Study

1. The purpose of this study is to test the validity and reproducibility of a novel magnetic resonance based device for the detection of human brain oxygenation. This will be done by comparing the device readings to accepted measurements, like peripheral blood gas analysis, respiratory gas analysis, and infrared oxygen saturation (SpO2).
2. This is a single arm study that will involve cyclical rebreathing phases, followed by a phase of hyperoxygenation.
3. This involves a rebreathing protocol, in which a participant will rebreathe their previously expired air in a mixed 13L bag. Because we breathe out less O2 than we breathe in, this will cause hypoxia (low O2) that will continuously fall for the duration of rebreathing. This will be measured over the course of 7 minutes, and a return to baseline with atmospheric breathing will also be recorded. This will repeat a further 2 times, and then be followed by a period of pure oxygen breathing (7 minutes) and a washout.

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 those participating in the study will be Otago University staff members, as this is a proof of concept study.
2. The Committee asked how safety will be ensured. The Researcher explained that a medical doctor will be on call at all times, and clinical staff at the centre will also be aware of what is going on. The Researchers also have experience running altitude studies with the same limitations and cut-off/cessation points.
3. The Committee asked how the Researchers will ensure that participants (who are employees) do not feel coerced. The Researcher explained that the PIS had been worded so as to reassure the reader that participation will not affect their study or employment status, and they will be referred to contacts who they can discuss their participation with (Māori, Otago ethics contacts).   
   The Committee asked for consent to be sought from someone outside of the core study team
4. It was queried whether Māori consultation is needed for this study, but it was agreed that as previous consultation had been sought on the use of the study device, and as this is a proof of concept study, the issues for Māori had been adequately considered. New consultation may be appropriate for subsequent phases of research on this device.

Summary of outstanding ethical issues

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

1. Please state upfront that this is a first in human study.
2. In the cultural section, please note that participants may consider the head as tapu.
3. Please remove the yes/no tick boxes from the consent form for all statements that aren’t truly optional, i.e. those where a participant could select ‘no’ and still participate in the study.
4. Please add a photo or image of the study device.

Decision

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

* 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 Mrs Sandy Gill Dr Peter Gallagher.

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| **9** | **Ethics ref:** | **20/CEN/209** |
|  | Title: | BO42592: Atezolizumab plus chemotherapy with or without tiragolumab in 1L NSCLC |
|  | Principal Investigator: | Dr Jonathan Davis |
|  | Sponsor: | Roche Products (New Zealand) Limited |
|  | Clock Start Date: | 10 September 2020 |

Dr Jonathan Davis 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 randomized, Phase II, global, multicenter, double-blind study designed to evaluate the efficacy and safety of tiragolumab in combination with atezolizumab plus pemetrexed and carboplatin/cisplatin (the international standard of care) compared with placebo in combination with pembrolizumab plus pemetrexed and carboplatin/cisplatin in patients with previously untreated, locally advanced unresectable or metastatic non-squamous NSCLC. The selection of carboplatin or cisplatin is per investigator’s choice.
2. Patients will be randomized 1:1 between the two treatment arms, and treatment will be administered on a 21-day cycle for 4 cycles.
3. Following the induction phase, patients on both arms will continue maintenance therapy.
4. Serum and tissue tissue will be collected to monitor pharmacokinetics, anti-drug antibodies and for exploratory biomarker assessments.

Summary of resolved ethical issues

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

1. It was clarified that 10 participants are intended to be recruited in New Zealand. Those participants will be relatively healthy.

Summary of outstanding ethical issues

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

1. Main PIS:
   * Page 3: please amend to state that these drugs have not been approved by MedSafe.
   * Please add a table of procedures and visits.
   * Consent form: the potential use of the data is very broad. Please make any non-optional sharing of information more specific, and add an optional clause for sharing of information beyond the purposes of this study.
2. Optional biopsy PIS: please add a cultural statement about sending samples overseas.
3. Stool samples PIS: please clarify whether only one or a number of stool samples will be needed, and how often.
4. Pregnancy follow-up PIS:
   * page 2: please amend, for clarity, the first section under the heading “what does this research involve?”
   * Please remove the references to mother (or replace with ‘parents’) on the consent form.

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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| **10** | **Ethics ref:** | **20/CEN/205** |
|  | Title: | Progesterone loading as a strategy for treating Post-Partum Depression. |
|  | Principal Investigator: | Health Research South Yoram Barak |
|  | Sponsor: | Otago University School of Medicine |
|  | Clock Start Date: | 11 September 2020 |

A/Pro Yoram Barak and Dr Paul Glue 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 study will assess whether orally dosed progesterone will increase concentrations of allopregnanolone in the central nervous system, which should relieve symptoms of Postpartum depression (PPD).
2. The study design is a multiple rising dose study to measure plasma allopregnanolone concentrations after multiple doses of extended release progesterone tablets. 24 healthy volunteers will be recruited and will receive the intervention over two days.
3. The study objectives are 1) To measure plasma allopregnanolone concentrations after 3 days dosing with ascending doses of extended release progesterone tablets. 2) To assess the safety and tolerability of extended release progesterone tablets in healthy volunteers.

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 only participants over the age of 60 are being included. The Researchers explained that post-menopausal women are being recruited so as to avoid fluctuations in progesterone and or allopregnanolone levels.
2. The Committee asked about the purpose of the form FDA3005B. The Researchers explained that this form is for reporting adverse events or side effects. However, for the purpose of the study a regular case record form would be used.
3. P.4.2: the Committee noted that whakama as well as taking blood samples are cultural issues for Māori in this study.
4. It was clarified that Māori consultation is being sought as part of locality review.
5. The Committee asked if compensation will be provided for participants’ time or travel issues. The researchers explained that no compensation is being provided.
6. The Committee asked how participants will be recruited onto the study. The Researchers stated that public meetings on postpartum depression will be held, in which the study will be mentioned and people interested in the study could then get in touch for further information. In addition advertisements may be made, which would be submitted as an amendment.
7. With reference to question P.4.1. of the application form, the Committee queried whether being Māori increases the likelihood of experiencing post-partum depression. The Researchers clarified that the data from studies in the USA shows evidence of greater rates of post-partum depression for those of low socioeconomic status and ethnic minorities.
8. The Committee asked how the study results would be published so as to avoid any risk of stigmatisation for Māori. The Researchers stated that if a relationship is found between ethnicity and outcomes, this would not be assumed to be caused by ethnicity itself, but may be due to (for example) socioeconomic outcomes.

Summary of outstanding ethical issues

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

1. Please add greater detail under the heading “what will my participation involve” (where will they go, what time, will they get food etc).
2. Under ‘benefits’, please state first that there are no benefits for the participant in this study.
3. Please update the ACC clause, using the HDEC template for guidance.
4. Under ‘what are my rights’, please add the right to access and correct participant data.
   * Please clarify the statement that participants will be informed of the study results – refer to the HDEC template for standard wording.
   * Please move the sentence about informing participants of the study outcomes to a later section in the PIS.
5. Please add a paragraph about cultural issues that may arise in the study, especially for Māori. Refer to the HDEC template for guidance.
6. Page 2: please convert to simple language the information about perinatal hormones etc.

Decision

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

* 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 Mrs Sandy Gill and Dr Patries Herst.

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| **11** | **Ethics ref:** | **20/CEN/211** |
|  | Title: | Comparison of two iron polymaltose tablets. |
|  | Principal Investigator: | Dr Noelyn Hung |
|  | Sponsor: | Neo Health (OTC) Pty Ltd |
|  | Clock Start Date: | 10 September 2020 |

Dr Noelyn Hung and Linda Holland 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 study will compare the rate and extent of absorption of the study drug when taken orally in a fasted state. Males only are used in this study due to iron level fluctuations in women particularly around menstruation.
2. The duration of the study is approximately 5 weeks, including up to 3 weeks for screening and 10 days on study (two periods of 2-day dosing/sampling and a 1-week washout period).
3. For a period of 4 days prior to and until 36 hours after dosing in each study period, subject’s food intake will be controlled with a diet low in iron and fat.
4. All meals will be reviewed for nutritional balance (using appropriate levels of protein, fat and carbohydrate) and will be provided to subjects to consume at home and at the Clinical Site during the confinement periods. Because we are measuring iron in serum after an iron tablet is taken, diet control is required to stabilise levels before dosing.
5. Subjects will be housed at the Zenith Clinical Site for 12 hours prior to dosing until 24 hours after dosing in each study period. The blood sample at 36 hours will be collected by venepuncture at Zenith Technology.
6. Following an overnight fast of at least 10 hours, each subject will receive a single dose of either formulation. Subjects will receive one formulation in one period and the other formulation in one period. There will be at least 1 week washout (7 days) between each dosing period.
7. Blood samples will be collected at baseline (prior to dosing at -2.0,-0.5 and 0 hours) and at specified times up to 36 hours after dosing. Serum will be assayed for total iron by using a Colorimetric method. The single-dose safety and tolerability of the formulations will also be assessed.
8. To assure the good health of subjects, pre-study physical examinations, ECG and clinical laboratory tests will be performed. Post-study laboratory tests, vital signs and safety assessments will also be carried out and subjects will be monitored for AE’s throughout the study.

The Committee congratulated the researchers on a well put-together application.

Decision

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

* Please update the Participant Information Sheet and Consent Form, correcting the spelling of ‘necessary’.

## 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:** | 22 September 2020 |
| **Meeting venue:** | Videoconference |

1. **Review of Last Minutes**

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

The meeting closed at 5:30pm.