|  |  |
| --- | --- |
| **Committee:** | Northern A Health and Disability Ethics Committee |
| **Meeting date:** | 16 February 2021 |
| **Meeting venue:** | Join Zoom Meeting  <https://mohnz.zoom.us/j/81000135642>  Meeting ID: 810 0013 5642 |

|  |  |
| --- | --- |
| **Time** | **Item of business** |
| 1:00pm | Welcome |
| 1:25pm | Confirmation of minutes of meeting of 15 December 2020 |
| 1:30pm | New applications (see over for details) |
| 1:30-1:55pm  1:55-2:20pm  2:20-2:45pm  2:45-3:10pm  3:10-3:30pm  3:30-3:55pm  3:55-4:20pm  4:20-4:45pm  4:45-5:10pm | 21/NTA/26 Kate O’Connor / Michael Meyer  21/NTA/23 Catherine Garvey / Sotera Catapang  21/NTA/24 Kate O’Connor / Kate Parker  21/NTA/27 Catherine Garvey / Michael Meyer  [break]  21/NTA/30 Kate O’Connor / Sotera Catapang  21/NTA/31 Catherine Garvey / Kate Parker  21/NTA/19 Kate O’Connor / Michael Meyer  21/NTA/21 Catherine Garvey / Sotera Catapang |
| 5:10pm | General business:  Noting section |
| 5.30pm | Meeting ends |

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

## Welcome

The Chair opened the meeting at 1pm and welcomed Committee members, noting that apologies had been received from Karen Bartholomew and Rochelle Style.

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 15 December 2020 were confirmed.

## New applications

|  |  |  |
| --- | --- | --- |
| **1** | **Ethics ref:** | **21/NTA/26** |
|  | Title: | Efgartigimod PH20 SC for the treatment of Primary Immune Thrombocytopenia in Adults. |
|  | Principal Investigator: | Dr Rajeev Rajagopal |
|  | Sponsor: | argenx BV |
|  | Clock Start Date: | 04 February 2021 |

Dr Rajeev Rajagopal, Nicola Jackson and sponsor representative Jen Coetzee 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.

Michael Meyer declared a potential conflict of interest in that he is a colleague of Dr Rajagopal but is not involved in this research. The Committee decided that this was not a conflict of interest.

Summary of Study

1. The main goal of this study is to look at the effect and safety of a drug called efgartigimod in people with primary immune thrombocytopenia (ITP).
2. ITP is an autoimmune disease that affects platelets - a component of the blood that helps with clotting. In ITP, antibodies that our body usually uses to fight and prevent infections are instead produced that attack platelets. These antibodies are referred to as autoantibodies.
3. Efgartigimod is a fragment of a human antibody that has been modified to target the ITP autoantibodies for destruction. It is called a “biological” drug because it is a genetically modified protein produced in animal cells. Efgartigimod may help improve the symptoms of ITP, by reducing the amount of platelet-attacking autoantibodies.
4. In this study, efgartigimod will be combined with PH20 which is thought to improve absorption of efgartigimod into the body.
5. The study screening period is <2 weeks. It is followed by a treatment period of 24 weeks and an End-of-Treatment visit, 1 week later. After the treatment period, participants will enter a treatment-free follow-up period of 8 weeks.
6. After completing the treatment period, participants will be invited to enrol in another trial where everyone receives efgartigimod PH20 (open-label). This trial will be submitted to HDEC for separate review.
7. Participants will receive efgartigimod PH20 subcutaneous (SC) or placebo PH20 SC. Participants have a 2/3 chance of receiving efgartigimod PH20 and a 1/3 chance of receiving placebo.
8. The study is double-blind, neither the participant nor the study staff will know if the participant is receiving efgartigimod PH20 or placebo.
9. Participants will visit the study site weekly to receive study drug for the first 4 weeks. From week 5, participants will continue to have weekly study visits. However, some participants will receive study drug weekly and others fortnightly, depending on their platelet levels. Blood and urine samples will be collected.

Summary of resolved ethical issues

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

1. The Committee queried whether placebo patients can stay on their usual standard of care. The researcher responded that this is fine so long as it is a stable dose – their ITP medication cannot be increased while participating in the trial.
2. The Committee asked whether platelets can drop very quickly in participants. The researcher confirmed that this can happen and, in this event, would be given rescue medication to increase their platelet count. If patients need multiple rescue treatments, they will be withdrawn from the trial.
3. The Committee asked if the researcher could demonstrate that this research would have a benefit for Māori, for example if there is a known disproportionate burden of ITP in Māori. The researcher responded that they had undertaken a literature review to find data pertaining to Māori and ITP, but that as ITP is a rare condition, there was no data available.
4. The Committee noted that the researchers were planning on using Greenphire for arranging travel for out-of-town patients and making reimbursements. The Committee explained that most sites would prefer to arrange travel and reimbursement on their own. The researcher responded that the use of Greenphire is optional within the consent form, for sites to consider themselves. If sites are not comfortable using Greenphire, then they can arrange travel and reimbursement for their patients on their own.
5. The Committee noted that in the researcher’s COVID-19 Contingency Addendum for home visits and remote monitoring, they had mentioned the contracting of Symphony Clinical Research nurses to perform these site visits. The sponsor noted that this would be optional, and Middlemore have opted out of using them.
6. The Committee queried how many sites would be involved in this research. The researcher responded that the current estimate is three sites, but this could increase or decrease. The Committee asked whether the sites will customise the information sheets according to their own standards of practice. The researcher confirmed this.
7. The Committee asked what the medication does to the normal IGG levels. The researcher responded that the medication drops all IGG. The Committee queried if this would be to a level where infection becomes an issue. The researcher responded that he did not know, but this study would give more information about that.

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 provide a home visit safety protocol and Tikanga protocol for home visits.
2. The Committee requested that the researcher provide a privacy plan if proceeding with the use of third parties such as Symphony Clinical Research or Greenphire.

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

1. On page 8, please reassure the participant that they can still receive the COVID-19 vaccine if they participate in this research.
2. On page 8, please change the wording to clarify that participants are only disqualified from participating in any other *clinical* trials, rather than “any other study” (as they would still be eligible to participate in qualitative research).
3. Please do not say that participants “must not hide information”, as this implies mistrust in the participant. Rather, say something like “participants must tell everything”.
4. Please update your Data Privacy section following the ‘what will happen to my information’ section on the HDEC PIS template, in order to use terminology that we are familiar with in the NZ context (e.g. ‘de-identified’ and ‘coded’ rather than ‘pseudo-anonymised’).
5. On page 18, please change the section about ‘the right to access information at any time’ to use the wording that is used in the [HDEC PIS template.](https://ethics.health.govt.nz/system/files/documents/pages/participant-information-sheet-consent-form-template-sep20.doc)
6. On page 18, please do not say that the HDEC approves the study. Rather, say that the HDEC approves the *ethical aspects* of the study.
7. On the Pregnant Partner Information Sheet, please include an additional consent panel to be signed after the baby is born.

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 Kate O’Connor and Michael Meyer.

|  |  |  |
| --- | --- | --- |
| **2** | **Ethics ref:** | **21/NTA/23** |
|  | Title: | UPLIFT |
|  | Principal Investigator: | Dr Rebecca Slykerman |
|  | Sponsor: |  |
|  | Clock Start Date: | 31 January 2021 |

Dr Rebecca Slykerman and Mrs Naomi Davies 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. Chronic Fatigue Syndrome (CFS) is a debilitating disorder characterised by fatigue that does not improve with rest, physical symptoms of pain, nausea, fatigue, dizziness, headaches and post exertional malaise which is a worsening of CFS symptoms following minimal physical or mental effort.
2. In young people, CFS can disrupt typical adolescent development by impacting a young person’s ability to attend school, socialise with peers, and maintain physical activity. Rates of depression and anxiety are also higher in those with CFS. Currently there is no treatment for CFS and patients are encouraged to manage symptoms.
3. Gut microbiota are the colony of bacteria, fungi and viruses that live in the gastrointestinal tract and play a role in physiological processes in the body. The microbiota-gut-brain-axis refers to multiple bi-directional relationships between the microbes in the gut and the brain. Evidence suggests that disruption to the balance of beneficial versus pathological microbes in the gut (dysbiosis) is present in chronic fatigue, depression and anxiety.
4. Probiotics, defined as live microorganisms that confer a benefit to the host when consumed, are one way in which the healthy balance of microbes can be restored in the gut. Preliminary studies have suggested that supplementation with probiotics can improve psychological well-being in people with CFS. To date there have not been any studies of the effect of probiotics in adolescents with CFS.
5. This study aims to determine whether probiotic supplementation improves the psychological wellbeing of adolescents with CFS using a randomised, double blind placebo controlled intervention that comprises a 10-week supplementation period with a combination of the probiotics Lactobacillus rhamnosus HN001 and Bifidobacterium animalis HN019.

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 the researcher to confirm the role of Fonterra. The researcher clarified that Fonterra is supplying the probiotics and placebo capsules, but is not acting in the role of a sponsor or funder, would not be using the results of the study to promote the health benefits of their product, and would not be getting access to study data. The researcher stated that Fonterra would have no input into the study design, data collection, or analysis. The researcher stated that Fonterra would have 30 days to read any manuscript the researchers prepare. This is to provide Fonterra the opportunity to lodge a patent based on the results, but Fonterra cannot change or influence what the researchers write or how they report it.
2. The Committee asked whether the researcher is confident in Fonterra’s good manufacturing practice. The researcher confirmed this, stating that this is one of the reasons they had chosen to work with Fonterra. Fonterra puts the products through pharmaceutical grade testing and will provide the researchers with testing certificates.
3. The Committee queried whether the agreement with Fonterra required them to provide Fonterra with the raw research data. The researcher clarified that the agreement did not require this, and that they would not supply Fonterra with the raw research data.
4. The Committee asked how the researcher would recruit for the study. The researcher responded that they would be recruiting through three different sources:
5. General paediatricians at Starship and Waitemata
6. A GP who has a special interest in chronic fatigue
7. An advertisement posted by administrator(s) of support group of people with chronic fatigue

The researchers will contact these three different sources, asking if they will provide interested potential participants with the PIS. Interested potential participants can then choose to contact the researchers to opt-in. The researchers will not be contacting any potential participants directly.

1. The Committee queried how the researchers planned on getting the probiotic/placebo capsules to the participants. The researcher responded that once participants are registered, they will provide a postal address, to which the capsules and instructions will be sent in a non-signed track-and-trace courier. The researchers will then trace the courier and follow up with the participants to check they received the package.
2. The Committee queried what monitoring or follow-up would be enacted once the capsules had been delivered, to ensure compliance that the probiotic/placebo was being taken daily by the participant. The researcher responded that the participants would receive a bulk text at four, six and eight weeks from the researchers (through a secure online website) checking in. The researchers hoped that this would serve as a reminder for participants to keep taking their probiotic. The researchers noted that participants would be able to text back or email the researchers if they had any questions or concerns.
3. The Committee queried how participants will consent via the online consent form. The researcher explained that there is a tick box [yes/no] asking for the participant’s consent.
4. The Committee asked if there was a plan in place for following up on concerning responses to wellbeing questions on the adolescent and parent questionnaires. The researcher responded that although there are questions about mood and feelings, there are no ‘critical questions’ in the questionnaires, such as those pertaining to self-harm etc. Every participant will receive a copy of support services that they can access in their community if they have concerns. They can also contact the researcher with these concerns and the researcher will give the guidance on where they can go for help. The researcher will not pass on this information to the participant’s GP without the participant’s permission.
5. The Committee queried whether the sample size of the study is big enough to get a significant result. The researcher responded that the small sample size is because it is a pilot study to test the feasibility of a larger study.
6. The Committee asked what the outcomes measure of the study are. The researcher responded that the main outcome measure is the mood and feelings questionnaire of the probiotic group, compared with the placebo control group.
7. The Committee asked if there is a specific time for the intervention to be taken, or if it had to be taken before or after meals. The researcher responded that no, the participants can take the probiotic/placebo at any time of the day, with or without food. They clarified that this is because they wanted the study design to reflect what people do in real life.
8. The Committee queried how the study would deal with several missed doses. The researcher responded that this is acceptable, and the possibility of missed doses is built into the study design. Again, this is because it will mirror real-life usage of the intervention. Participants are advised to continue taking the intervention the following day, even if they miss a day.
9. The Committee queried why the questionnaires ask about the stress levels of the parents. The researcher responded that there is anecdotal evidence that there is stress associated with caring for a child with chronic fatigue but there is currently no research to validate this claim. This data will therefore help the researchers figure out if there is a better way to support parents.
10. The Committee queried why the researchers were collecting identifiable health information of the participant (name and address). The researcher responded that this is in order to ensure the probiotic/placebo capsules are successfully delivered to the participant’s address. The name is also collected to ensure that consent has been obtained.

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 put a data management plan into your protocol (can adapt from HDEC template).

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

1. Please see the [HDEC PIS template to](https://ethics.health.govt.nz/system/files/documents/pages/participant-information-sheet-consent-form-template-sep20.doc) be guided on distinguishing between identifiable and de-identified health information of the participant and at which point the analysis happens on de-identified data.
2. Please include information in the PIS and protocol on how the researchers will ensure that the capsules are successfully delivered, and what monitoring and follow up will occur once the capsules have been delivered.
3. Please [refer to the HDEC data privacy template](https://ethics.health.govt.nz/system/files/documents/pages/data-only-management-template-oct2020.docx) and incorporate what is relevant to your study into your PIS for both the parents and the adolescents.
4. The Committee requested that the researcher send a copy of the completed consent form to the participant.
5. Please update your recruitment advertisement to state that the intervention is being tested against a placebo.

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 Catherine Garvey and Sotera Catapang.

|  |  |  |
| --- | --- | --- |
| **3** | **Ethics ref:** | **21/NTA/24** |
|  | Title: | BGB-11417 Phase 1b/2 AML and MDS |
|  | Principal Investigator: | Dr Travis Perera |
|  | Sponsor: | BeiGene Aus Pty. Ltd. |
|  | Clock Start Date: | 04 February 2021 |

Dr Travis Perera and Marina Dhezlali 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 be aimed at patients with myeloid malignancies, including acute myeloid leukemia (AML), myelodysplastic syndrome (MDS) or myelodysplastic/myeloproliferative neoplasms (MDS/MPN). MDS/MPN are a group of stem cell malignancies that have a high risk of progression to AML. AML is the abnormal accumulation of leukaemic blast cells in the bone marrow, blood and organs.
2. It most commonly affects the elderly, meaning the majority of patients are deemed unfit to receive standard of care - an intensive chemotherapy regime. For patients ineligible for intensive chemotherapy, treatment options are limited, and provide a marginal survival benefit of 6-10 months.
3. This study will look at the safety and tolerability of the investigational anticancer drug BGB-11417 in combination with azacitidine - a drug already approved for use in AML and MDS. BGB-11417 blocks B-cell lymphoma-2 (Bcl-2), a protein that helps leukaemia cells live and grow. Inhibition of Bcl-2 can slow or stop leukaemia cell growth and allow leukaemia cell death.
4. This study aims to determine the dose of BGB-11417 that can be used safely together with azacitidine.
5. This study consists of 3 parts:

Part 1(dose regimen finding):

* different doses of BGB-11417 and fixed dose of azacitidine will be tested in participants with AML or MDS/MPN.

Part 2(safety expansion):

* an additional 10 participants may be enrolled to each treatment regime that was found safe and tolerable in part 1 to determine whether one regime is better than the others. If a superior treatment is not identified in Part 2 then BGB-11417 at 160mg/day for 10 days plus Azacitidine will be used for part 3.

Part 3(efficacy expansion):

* participants will be enrolled in AML and MDS cohorts (groups of patients that will receive the same treatment) and will receive the best combination treatment from Part 2 to determine the effectiveness of the treatment regime.

Summary of resolved ethical issues

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

1. The Committee clarified with the researcher that the majority of participants will be over 65 years of age.
2. The Committee asked if Azacitidine is the normal treatment for these participants. The researcher confirmed this.
3. The Committee noted that there is a separate data and tissue management plan pending. The researcher noted that this has been received from the sponsor and will be submitted to the HDEC. The Committee clarified with the researcher that this does not say anything contrary to the data and tissue management plan that had been submitted in the PIS.
4. The Committee noted that the researcher’s response to question p.4.1. on the application form, where they cite Article 1 of the Treaty of Waitangi as a health benefit, is best avoided in answer to that question as Article 1 of the Treaty has nothing to do with health.
5. The Committee clarified with the researcher that the UTN number for the trial is pending.
6. The Committee clarified with the researcher that there will be no additional radiation as part of this study.
7. The Committee confirmed that a bone marrow aspirate is compulsory for being in this study. The researcher clarified that this is standard of care anyway. If the participant has already had it, they do not need to have it again.

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 upload the data and tissue management plan received from the sponsor.
2. The Committee queried whether participants in the dose-finding arm of the study will have the option to get the best dosage in the next stage of the study. The researcher believes that those participants will stay on the same dose level throughout but will double-check this. The Committee would like this clarified, as in the application form it says that each participant will receive the best intervention.

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

1. The Committee noted that the PIS is very long, repetitive and difficult to digest. The Committee requested the researchers cut it down and think about user-friendly presentation.
2. The Committee requested that the researcher put in a table of visits and what each visit will entail.
3. The Committee asked the researcher to make clear in the PIS how long the study would last.
4. The Committee requested that the researcher change the wording on page 11 of the PIS from ‘survival follow up’ to something less blunt, e.g. ‘we will follow you until you stop responding’.
5. The Committee requested that the researcher make it clearer in the PIS that this intervention is very experimental (only six people have had it).
6. In the pregnancy comment on page 19 of the PIS, please change the wording from “the sponsor *will* collect information about pregnancy and birth” to “the sponsor *would like to* collect information about pregnancy and birth”.
7. Please clarify in s.13 that the decision to discontinue the study can only be for safety/efficacy reasons – it cannot be a commercial decision.
8. Please clarify in s.14 that the company will continue to provide the drug to the participant so long as they are responding.
9. In s.15 please offer the results summary to the participants – this could be opted into in tick-box format in the consent form.
10. Please remove the ‘yes / no’ option for notifying a participant’s GP as this should be mandatory.
11. Please edit page two of the PIS for the optional blood sample as this is still in draft form.
12. Please clarify whether the optional blood sample is for future unspecified research or for related research.
13. Please update the PIS for optional tissue sample to include sections on participants changing their mind, requesting a sample be destroyed, the benefits of being included and privacy. Make sure these sections are included in every PIS.
14. Please clarify in the PIS for the optional biopsy that there will be no benefit to the participant.
15. Please provide a summary clarifying which of the various PIS forms are optional and what each will entail if they provide consent.
16. Please ensure the sponsor details are included on each of the PIS forms.
17. In the optional tumour biopsy PIS, please change the wording about gaining extra information to evaluate “your” disease, as this is overstated.

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 Kate O’Connor and Kate Parker.

|  |  |  |
| --- | --- | --- |
| **4** | **Ethics ref:** | **21/NTA/27** |
|  | Title: | A clinical trial to assess the safety and efficacy of seladelpar in patients with primary biliary cholangitis (PBC) and an inadequate response to or intolerance to ursodeoxycholic acid (UDCA) (2021 re |
|  | Principal Investigator: | Dr Jing Hieng (Jeffrey) Ngu |
|  | Sponsor: | PPD |
|  | Clock Start Date: | 04 February 2021 |

Dr Jing Hieng (Jeffrey) Ngu was not 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 evaluate safety and efficacy of seladelpar when administered to patients with primary biliary cholangitis (PBC) and an inadequate response to or intolerance to ursodeoxycholic acid (UDCA, the first line treatment for PBC).
2. Volunteers’ eligibility to take part in the study will be determined during screening and run-in periods, when a number of assessments will be performed, including medical history review, full physical examination and blood tests.
3. On Day 1, subjects will be randomized into 1 of 2 treatment arms (seladelpar 10 mg or placebo) in a 2:1 ratio.
4. The treatment will be taken orally once a day, at approximately the same time each day over a 52 week period. Participants who are not intolerant to UDCA will be on a recommended dose of UDCA during the study.
5. Participants’ safety (in particular liver, pancreas, muscle safety and certain blood parameters) will be continuously monitored over the course of the treatment and during the post-treatment follow up period, via blood tests, assessments, and collection of adverse events.
6. Participants who complete the entire treatment period will be offered to take part in a long-term safety study. Those who consent to participate will begin the long-term study straight after the completion of the current study, at their Month 12 visit, and will remain on the same dose of seladelpar (the participants who were receiving placebo will initiate seladelpar). The participants who chose not to participate in long-term study will proceed to their follow-up visit.

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 documentation appears to be pertaining to overseas sites.

Please adapt the documentation to reflect the NZ context.

* 1. State NZ providers of third-party services and provide local contact details.
  2. Provide NZ contact details on your website and in your advertising.
  3. Clarify whether payment for participants to continue on UDCA for those who are tolerating it is relevant and funded within a NZ context.

1. Please clarify the extensive role of third parties for home visits, travel reimbursements and the courier service.
2. Please confirm that SCOTT approval has been obtained.
3. Please clarify the meaning of “discontinue for administrative reasons” in s.17 of the study protocol.

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

1. Please clarify what is available in NZ in terms of third-party services such as home visits and reimbursement using Scout Clinical research. Provide local contact details. If not applicable to a NZ context, please remove from the PIS forms.
2. Please tailor the home visit aspect of the COVID-19 addendum to a NZ context.
3. Please provide NZ sponsor details.
4. Please make appropriate for NZ context when discussing “racial origin”.
5. Please clarify what is meant by “you should remain on your current diet and lifestyle, including drinking habits, specifically alcoholic beverages, throughout participation.” Consider rewording to instead state what dietary/alcohol consumption behaviour is not allowable while study participant is taking medication.
6. Please clarify the reference to accessing medical records once consent to participate has been withdrawn. If consent has been withdrawn, there should not be any access to personal or clinical records.
7. Please amend the compensation statement in the optional PIS for blood samples and liver biopsy to:
   1. Include the correct compensation statement for a commercially sponsored study
   2. Provide the correct advocacy details
   3. Clarify which third party companies are used in NZ
   4. Use the proper HDEC application and committee reference rather than a generic reference to HDEC approval.

Decision

The Committee was disappointed that this research application had not been translated to a NZ context and that the researcher was not present to clarify these issues. However, 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 Catherine Garvey and Michael Meyer.

|  |  |  |
| --- | --- | --- |
| **5** | **Ethics ref:** | **21/NTA/30** |
|  | Title: | Novel intraoral application of knotless sutures in third-molar surgery |
|  | Principal Investigator: | Mr Nigel Tan |
|  | Sponsor: |  |
|  | Clock Start Date: | 04 February 2021 |

Mr Nigel Tan 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. Knotless sutures have been used in gynaecological, plastic, orthopaedic, abdominal and vascular surgery.
2. These surgical specialities have benefitted from the associated reduction in surgical time and cost.
3. The use of knotless sutures in the mouth has been reported but not yet investigated in relation to third molar surgery. Given that surgical third molar (wisdom teeth) removal is one of the most common procedures undertaken in oral surgery, the researchers intend to investigate the feasibility of using knotless sutures for this specific procedure.
4. A randomised split-mouth study design, should allow the researchers to compare the performance and efficacy of knotless sutures against conventional sutures in third molar surgical wound closure.

Summary of resolved ethical issues

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

1. The Committee queried whether the manufacturer of the knotless sutures was providing them to the study. The Researcher stated the study has funding to purchase them and the manufacturer is not sponsoring or involved with the study.
2. The Committee queried how the Researcher would manage dry socket or severe facial swelling. The Researcher stated they would treat them as per standard care and afterhours services are available.

Summary of outstanding ethical issues

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

1. The Committee advised that keeping a study database on excel is not best practice and requested the Researcher explore whether they can use something like REDCap.
2. The Committee recommended adding a question of which side the participant believes the knotless suture is on as this may influence their reporting of pain and study blinding.
3. The Committee stated it does not normally approve research that participants have to pay to be part of and queried whether patients usually have to pay for wisdom tooth extraction. The Researcher stated in the lower South Island it is a partially funded service and while it receives funding from the DHB it does necessitate a co-payment. The Committee stated as a co-payment is required as part of standard treatment outside of the study it can allow it but expects the Researcher to make some sort of koha (e.g. a petrol or grocery voucher) available to participants.
4. Please list any analgesics to be taken and at what time points in the protocol and PIS.
5. The Committee noted an outcome measure in the protocol is irritation versus pain. Please make it clear in the PIS how participants are to differentiate between the two.

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

1. The Committee requested the Researcher adapt [the data management template](https://ethics.health.govt.nz/system/files/documents/pages/data-only-management-template-oct2020.docx) available on the HDEC website.
2. Please insert a statement advising that although the knotless suture has been used previously in other surgeries this is the first time it will be trialled for wisdom tooth removal
3. The Committee recommended a lay friendly title that does not include the term ‘split mouth’ as this may come across as more aggressive to potential participants than intended.
4. Please include all inclusion and exclusion criteria in the PIS (e.g. the swelling measurements are not part of standard of care so participants must be willing to shave their face).
5. Please clearly explain what is standard of care and what is the research so participants understand the difference.
6. Please adapt the data section from the [PIS template available on the HDEC website.](https://ethics.health.govt.nz/system/files/documents/pages/participant-information-sheet-consent-form-template-sep20.doc)
7. Please remove the ‘yes / no’ option for notifying the participant’s GP from the consent form as this should be mandatory.

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 Kate O’Connor and Dr Sotera Catapang.

|  |  |  |
| --- | --- | --- |
| **6** | **Ethics ref:** | **21/NTA/31** |
|  | Title: | The PASSIVATE Study |
|  | Principal Investigator: | Dr Phil Adamson |
|  | Sponsor: | University of Otago |
|  | Clock Start Date: | 04 February 2021 |

Dr Phil Adamson, Prof Mark Richards and Dr Lorraine Skelton were present via videoconference for discussion of this application.

Potential conflicts of interest

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

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

Summary of Study

1. This is a multi-centre study conducted at 14 sites in 4 countries (Singapore, New Zealand and United Kingdom). Approximately 120 patients from each country with Acute Myocardial Infarction (AMI) will be randomised in a ratio 1:1 to receive placebo or AZD5718 125mg. Treatment duration will be for 12 months, once daily in the morning, to be taken with approximately 250ml of water and no restrictions on food intake.
2. PASSIVATE is a mechanistic randomised, double-blind, placebo-controlled Phase IIa trial that investigates how 12 months of treatment with AZD5718 modifies coronary plaque volume. Patients with recent AMI will receive an additional oral dose of AZD5718 (or placebo) once daily to standard clinical care for 12 months. The primary hypothesis being tested in PASSIVATE is that 12 months of treatment with AZD5718, an inhibitor with anti-inflammatory properties, attenuates progression of non-calcified plaque (NCP) volume on serial computed tomography coronary angiography (CTCA) studies.
3. Study medication will be given in addition to standard care.

Summary of resolved ethical issues

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

1. The Committee queried sponsorship of the study. The Researchers stated it was investigator initiated and coordinated by the University of Singapore who are the sponsor. The Researcher explained AstraZeneca were providing funds and the drug and would receive information about efficacy in return. The Researcher stated this would be used for AstraZeneca’s phase 3 trial but the current trial was a phase 2 trial by academic centres. The Researcher stated public funding from Singapore’s equivalent to the Health Research Council was also being used. The Researcher confirmed AstraZeneca would only receive aggregate data and has no rights over publication. The Committee noted the protocol stated AstraZeneca would receive patient level un-blinded SAE reports. The Researcher stated this was a safety requirement.

Summary of outstanding ethical issues

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

1. The Committee stated in this case it can be reassured that the study is not principally for the benefit of the manufacturer but to ensure ACC equivalence is available to participants requested details of the University of Otago’s insurance be added to the compensation section of the PIS as a “back-up” in case ACC declined cover to an injured participant.
2. The Committee noted the data management plan was generic and requested it be tailored specifically to this study.

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

1. Please make it clear in the PIS that the study is *in addition* to standard of care.
2. Please include a statement advising that this is a phase 2 trial of a drug that is not currently approved for use in any country. Please include relevant details of previous testing in humans (e.g. side effects).
3. Please make it clear where samples/data are being stored (e.g. University of Singapore or University of Otago etc.)
4. Please remove the ‘yes / no’ option for notifying a participant’s GP as this should be mandatory.
5. Please put a time limit on the FUR samples (e.g. 10 – 15 years).
6. Please revise the option for withdrawing on the FUR form to explain that this is impossible once samples have been used.
7. Please update the advocacy email on the FUR form.
8. The Committee advised that the study may continue to use a participant’s data after they withdraw if this was originally consented to and recommended adding a clause that ‘If you withdraw from the study then data collected up until the point of withdrawal may continue to be used’ to the consent form.
9. The Committee noted the pregnant participant form did not have a signature to authorise data collection after the baby’s birth but as this is extremely unlikely in this study this can be submitted as an amendment if it occurs.

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 Ms Catherine Garvey and Dr Kate Parker.

|  |  |  |
| --- | --- | --- |
| **7** | **Ethics ref:** | **21/NTA/19** |
|  | Title: | 73763989PAHPB2006: The PENGUIN Study to Assess Efficacy, Safety, Tolerability, and PK of JNJ-73763989, JNJ-56136379, NUCs, and PegIFN Alpha-2a in CHB patients |
|  | Principal Investigator: | Professor Edward Gane |
|  | Sponsor: | Janssen-Cilag Pty Ltd |
|  | Clock Start Date: | 04 February 2021 |

Professor Edward Gane, Ms Chin Kuh, and sponsor representatives Mr Christopher Zizzamia and Dr Nonko Pehlivanov 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 Phase 2 study aims to find out if combination of study drug, JNJ-73763989, JNJ-56136379, Nucleos(t)ide Analogs (NA), and PegIFN-α2a are safe and effective in treating CHB patients.
2. 20 participants with CHB will be enrolled in this open-label study:

* First 12 weeks: Combination treatment with JNJ-73763989 every 4 weeks + JNJ-56136379 daily + NA
* Second 12 weeks: Addition of PegIFN-α2a every 4 weeks on top of the earlier combination treatment regimen
* 48-week follow up period: Participants continue with standard of care NA and stop other study drugs

1. Total duration will be up to 1.5 years.
2. This study is also part of a larger Platform study (Master Protocol PLATFORMPAHPB2001).
3. The Master protocol describes the common design elements, including overall study design, common objectives and endpoints, general study population, as well as the planned analyses that are common to all ISAs.
4. The Intervention-specific Appendix (ISA) describes the specific combination of treatments, referred to as study intervention(s), and includes specific study information, e.g. study procedures, summary of available pre-clinical and clinical data, primary objective and endpoint, etc.
5. A 1-step consent process will be conducted in a participant-centric manner by site staff, to obtain both Platform Master consent and ISA consent at the same time. Once a participant has signed both Participant Information Sheet and Consent Forms (PIS/CFs), screening activities will commence.

Summary of resolved ethical issues

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

1. The Committee accepted the dual-consent process.
2. The Committee queried whether participants would be expected to pay for a dermatology visit if they developed a rash. The Researcher confirmed they would not.

Summary of outstanding ethical issues

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

1. The Committee noted the MPS certificate has expired and requested an updated certificate.

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

1. The Committee noted the optional PIS/CFs follow the HDEC templates and there is material there that may not be necessary e.g. broad access to hospital and GP records for the optional components; the interchanging use of study and sub-study means reimbursement is not clear; the PK form refers to genetic research. Please undertake a general revision of these forms.

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.

|  |  |  |
| --- | --- | --- |
| **8** | **Ethics ref:** | **21/NTA/21** |
|  | Title: | A study to test efficacy of different doses of BI 456906 in people with non-alcoholic steatohepatitis (NASH) and liver fibrosis. |
|  | Principal Investigator: | Prof Ed Gane |
|  | Sponsor: | Boehringer Ingelheim Pty Ltd |
|  | Clock Start Date: | 04 February 2021 |

Professor Edward Gane and Miss Emily Griffiths 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. There is no treatment approved for patients with NASH and fibrosis, leaving a huge unmet medical need to develop treatments. At present, treatment of NASH relies on treatment of the metabolic syndrome such as obesity and diabetes.
2. BI 456906 is being developed for the treatment of non-alcoholic steatohepatitis (NASH).
3. The study will be conducted in approximately 264 adults. The trial aims to:

• Assess how different doses of BI 456906 affect liver scarring and NASH progression.

• See how well BI 456906 works compared to placebo.

• Assess how safe and well tolerated BI 456906 is.

• See whether BI 456906 improves participants' quality of life.

1. Participants will be randomized to one of 4 planned dose groups:

• Group 1 will receive BI 456906. The dose will gradually increase from 0.3 mg to 2.4 mg, then stay at 2.4 mg per week from Visit 16.

• Group 2 will receive BI 456906. The dose will gradually increase from 0.3 mg to 4.8 mg, then stay at 4.8 mg per week from Visit 20.

• Group 3 will receive BI 456906. The dose will gradually increase from 0.3 mg to 6.0 mg, then stay at 6.0 mg per week from Visit 24.

• Group 4 will receive placebo during the entire treatment period (Day 1 to Week 48).

1. BI 456906/placebo will be administered once every week, for 48 weeks. Each dose will be given as 2 injections under the skin.
2. Blood and urine samples will be collected during the study, safety will be monitored, and any changes in health will be recorded. Participants will also complete questionnaires at regular intervals. Liver biopsy, MRI liver scan, and FibroScan will be performed at specified time points.
3. The results will be used to inform the further clinical development of BI 456906 as a treatment for NASH.

Summary of resolved ethical issues

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

1. The Committee queried whether the offer of assistance with administering the study drug would be manageable. The Researcher confirmed this can be done by videoconferencing otherwise a participant could designate someone to accompany their visit to learn how. The Researcher confirmed that study staff are equipped to allow a participant who requires assistance at the study site to attend for study drug administration in the event this is necessary.

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 a disparity in reimbursement for participants depending on whether they are recruited at Middlemore or ACS. Please address this inequity.
2. The Committee queried whether the Researcher had used the Science 37 app previously. The Researcher stated they had not. The Committee requested a copy of the Science 37 phone app’s privacy policy and asked the Researcher to ensure that they are familiar with this also, to understand what is being utilised by participants and to explain it as needed.

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

1. Please add COVID-19 to the list of notifiable diseases.
2. Please add a local sponsor to the PIS.
3. Please insert a statement into the PIS advising that if the mental health questionnaires indicate distress the Researchers will manage this appropriately (e.g. if X is found the study team will do what is specified in the protocol).
4. The Fibroscan PIS is procedure specific rather than study related so states participants are free to decline. Please clarify this for study participants, and what will happen if they do (e.g. can they participate in the research and how their care will be managed).
5. Please specify what the drug and dosage is for the “two injections every day” and add this information to the protocol and PIS.
6. Please use lay friendly language to explain scientific terms and concepts like NASH / non-alcoholic steatohepatitis, fibrosis, the study drug mode of action etc.
7. Please check the possible typo of Bl 730357 in the last paragraph of “Why are we doing the 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 Ms Catherine Garvey and Dr Sotera Catapang.

## General business

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

|  |  |
| --- | --- |
| **Meeting date:** | 16th March 2021 |
| **Meeting venue:** | Zoom, link TBC |

1. **Review of Last Minutes**

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

1. **Matters Arising**

* The Committee requested that the HDEC Secretariat update the PIS template to say “contact the HDEC that approved *the ethical aspects* of this study” (rather than the HDEC that approved the study).

The meeting closed at 5:30pm.