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| **Committee:** | Southern Health and Disability Ethics Committee |
| **Meeting date:** | 09 August 2022 |
| **Zoom details:** | 965 0758 9841 |

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| **Time** | **Review Reference** | **Project Title** | **Coordinating Investigator** | **Lead Reviewers** |
| 10.30-11.00am | 2022 FULL 13016 | A Randomized, Double-blind, Placebo-Controlled, Dose-Ranging Multicenter Study to Evaluate the Efficacy and Safety of ALN-AGT01 in Patients with Mild-to-Moderate Hypertension | Dr Milan Radojevic | Mr Anthony Fallon & Dr Devonie Waaka |
| 11.00-11.30am | 2022 FULL 12766 | An Open-Label Study for Continued Treatment Access for Participants from the B9991001 Avelumab Study | Dr Peter Fong | Mr Dominic Fitchett & Ms Amy Henry |
| 11.30am-12.00pm | 2022 FULL 12285 | AWESSoM Care Home Project: Oral Health | Dr Moira Smith | Mr Anthony Fallon & Associate Professor Mira Harrison-Woolrych |
| 12.00-12.30pm |  | *Break* |  |  |
| 12.30-1.00pm | 2022 FULL 13130 | Relapsed/Refractory Follicular Lymphoma: Epcoritamab in Combination with Rituximab and Lenalidomide | Dr Samar Issa | Mr Dominic Fitchett & Associate Professor Nicola Swain |
| 1.00-1.30pm | 2022 FULL 13123 | BI 1434-0004: A Study to Test BI 764198 in People with a Type of Kidney Disease Called Focal Segmental Glomerulosclerosis. | Dr Nick Cross | Mr Anthony Fallon & Dr Devonie Waaka |
| 1.30-2.00pm | 2022 FULL 13160 | HB0034-03: A Study to Evaluate Multiple Doses of HB0034 in Healthy Adult Participants | Doctor Christian Schwabe | Mr Dominic Fitchett & Ms Amy Henry |

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| **Member Name** | **Member Category** | **Appointed** | **Term Expires** | **Apologies?** |
| Dr Devonie Waaka | Non-lay (Intervention studies) | 18/07/2016 | 18/07/2019 | Present |
| Assc Prof Mira Harrison-Woolrych | Non-lay Intervention/Observational studies) | 28/06/2019 | 28/06/2020 | Present |
| Mr Anthony Fallon | Lay (Consumer/Community perspectives) (Chair) | 13/08/2021 | 13/08/2024 | Present |
| Mr Dominic Fitchett | Lay (the Law) | 05/07/2019 | 05/07/2022 | Present |
| Ms Amy Henry | Non-lay (Observational studies) | 13/08/2021 | 13/08/2024 | Present |
| Ascc. Prof Nicola Swain | Non-lay Intervention/Observational studies) | 22/12/2021 | 22/12/2024 | Present |
| Ms Dianne Glenn | Lay (Consumer/Community perspectives) | 08/07/2022 | 08/07/2025 | Present |
| Ms Neta Tomokino | Lay (Consumer/Community perspectives) | 08/07/2022 | 08/07/2025 | Present |

## Welcome

The Chair opened the meeting at 10.00am with a karakia and welcomed Committee members.

The Chair noted that the meeting was quorate.

The Committee noted and agreed the agenda for the meeting.

## Confirmation of previous minutes

The minutes of the meeting of 12 July 2022 were confirmed.

## New applications

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| **1** | **Ethics ref:** | **2022 FULL 13016** |
|  | Title: | A Randomized, Double-blind, Placebo-Controlled, Dose-Ranging Multicenter Study to Evaluate the Efficacy and Safety of ALN-AGT01 in Patients with Mild-to-Moderate Hypertension |
|  | Principal Investigator: | Dr Milan Radojevic |
|  | Sponsor: | Alnylam Pharmaceuticals, Inc. |
|  | Clock Start Date: | 28 July 2022 |

Dr Milan Radojevic, Dr Mike Williams, Dr Simon Carson, and Vivienne King 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 resolved ethical issues

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

1. The Committee noted that the withdrawal of rescue anti-hypertensive medication between 5 and 6 months would be to look into the therapeutic effect of the study in a late phase, but only in cases where this would not negatively affect participant safety.
2. The Committee noted that there was no reason that the participant could not be withdrawn or withdraw themselves if the study was affecting the health of the participant negatively.
3. The Researcher noted that the 5-participant expectation of recruitment in New Zealand as stated in the application is incorrect, and the number of participants will likely be more than this.

Summary of outstanding ethical issues

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

1. The Committee noted there was no discussion around the ethical justification for the use of placebo in the application. The researcher clarified that the participants would be monitored closely, and risk assessed, and should there be evidence that there is need for standard of care, this would be provided. This needs to be addressed in the participant information sheet (PIS).
2. The Committee noted that monitoring of blood pressure during the wash-out period pre-study enrolment would need to be defined better and would need to be documented in the PIS and the application. This should include a schedule indicating frequency of blood pressure monitoring during this period.
3. The Committee requested that all participants should be offered the choice in the PIS to receive a lay summary of the results.
4. The Committee noted that during the recruitment and informed consent process, there should be a member of the study team independent to the provider give information to the participant.
5. The Committee noted per specific HDEC instructions for C6, Te Tiriti o Waitangi should not be cited as a health benefit. Equal access to participation in clinical research is not a health benefit but rather the default expectation.
6. Please note that C11 does not describe the Pacific consultation process for the study. If no specific consultation has been undertaken, please state this clearly.
7. The Committee noted the application form states participants will not be reimbursed for participation, however the PIS/CF states there will be a per visit and per ABPM payment made, in addition to travel, parking and meal expenses. Please provide the payment amounts to be made, noting that these should be consistent across NZ sites.
8. The Committee noted that the responses to E4-E5.1 do not state how clinically significant abnormal results experienced by a participant will be managed. Please describe how any such findings will be managed / followed-up. Please also confirm that General Practitioner (GP) notification of such results will be a mandatory component of study participation.
9. The Committee noted that in New Zealand, therapeutic trials cannot be terminated due to decisions made in the commercial interests of the Sponsor.
10. The Committee noted the response to E9 is not consistent with the requirement that at least ACC-equivalent compensation is available in case of study-related injury. Please confirm that compensation will potentially be available for all entitlements described in E12.
11. The Committee noted that the study hub documents appear to require use of a personal email address for set-up. Please clarify whether participants will be provided with a study-specific email address for this purpose.
12. The Committee requested the following changes be made to the Data and Tissue Management Plan (DTMP):
    1. Please note that full date of birth is considered identifiable information and should not be included with unidentified tissue or data samples.
    2. Please amend to state that mandatory future research is restricted to data only.

The Committee requested the following changes to the Participant Information Sheet and Consent Forms (PIS/CF):

Main PIS/CF

1. Please provide more information around what would happen should participants experience significant hypotension as a result of the study drug.
2. Please delete repeated explanations of terms (e.g. hypertension).
3. Please state whether reassignment of the placebo group to active treatment arms is randomised.
4. Please delete teaspoon and cup references for blood volumes and replace with millilitre measurements.
5. Participants should not have to pay for care or medication required to 'address side effects or symptoms' related to study participation. Amend the statement on page 14 accordingly.
6. Optional research descriptions should be limited to 1 - 2 sentences in the main PIS/CF. Delete all information under 'Group 2 samples' (page 15) and ensure this is included in the appropriate optional PIS/CF(s); delete optional sample collection from the schedule of assessments (page 11); and combine optional sample collection and delete specific information such as blood volumes from table (page 7).
7. Simplify contraception section, using language likely to be readily understood by a lay person.
8. Please quantify the risks of not taking standard of care anti-hypertensive medication for up to 5 months if blood pressure remains elevated throughout the placebo treatment period. State what happens if BP exceeds eligibility limits after initiation of dosing, during the withholding periods specified per protocol (especially where the protocol states no additional anti-hypertensive therapy should be used). Provide information regarding symptoms of significant hypertension that participants should be mindful of. It is unclear why this risk is placed below minor procedure risks for ECG and venepuncture; please ensure this is given adequate prominence.
9. Please delete 'Decisions made in the commercial interests of the Sponsor' from reasons for study termination (page 21).
10. Please delete the additional text inserted into the HDEC-approved compensation in event of injury statement (page 23).
11. Please note race and ethnicity are not considered sensitive personal information in New Zealand; amend accordingly (page 24).
12. Please move information about access to medical records to the identifiable information section.
13. Please amend consent such that notification of primary health care practitioner is mandatory (consent form).
14. Please consider reducing the size of the footer.

Optional PIS/CF

1. Please state what genes and DNA are in lay language (page 2). Explain that participants can agree to Future Unspecified Research (FUR) but can also choose whether this includes genetic research.
2. Please state whether there is any risk of DNA matching across genetic databases (e.g. law enforcement)
3. Please delete repetition regarding optional nature of research and ability to participate in Main Study.
4. Please delete reference to ACS from cultural statement (page 3)
5. Much of the information on page 4 is either repeated or is not relevant to the collection of samples for future research (e.g. reviewing medical files). Please review and amend.
6. Page 2 states that 'the link between you and your blood and urine samples will be removed before your DNA and Biomarkers are analysed'. Page 4 states samples will be labelled with a 'secret code' - which means they can be re-identified if required. Please clarify what is intended and ensure information is consistent.
7. The information sheet states tissue will be retained for up to 10 years; the consent form states retention is 'indefinite'. Please clarify what is intended and amend for consistency.

**Decision**

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

1. Please address all outstanding ethical issues, providing the information requested by the Committee.
2. Please update the participant information sheet and consent form, taking into account feedback provided by the Committee. *(National Ethical Standards for Health and Disability Research and Quality Improvement, para 7.15 – 7.17).*
3. Please update the study protocol, taking into account the feedback provided by the Committee. (National Ethical Standards for Health and Disability Research and Quality Improvement, para 9.7).

After receipt of the information requested by the Committee, a final decision on the application will be made by Dr Devonie Waaka and Mr Anthony Fallon.

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| **2** | **Ethics ref:** | **2022 FULL 12766** |
|  | Title: | B9991046 (Sub-Study B9991001C) AN OPEN-LABEL STUDY FOR CONTINUED TREATMENT ACCESS FOR PARTICIPANTS FROM THE B9991001 AVELUMAB STUDY |
|  | Principal Investigator: | Dr Peter Fong |
|  | Sponsor: | Pfizer Australia Pty Ltd. |
|  | Clock Start Date: | 28 July 2022 |

Dr Peter Fong 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 resolved ethical issues

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

1. The Committee requested clarification as to if there would be restrictions to publication. The researcher confirmed that standard authorship arrangements are in place.
2. The Committee queried whether pregnancy and contraception information is required in the New Zealand participant information sheet (PIS) if all potential participants had been pre-identified and the information is not relevant to them. However, it was noted that this information should be retained if there was a possibility other participants may be enrolled.

Summary of outstanding ethical issues

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

1. The Committee requested the following change to the Data Management Plan (DMP):
   1. Please delete reference to procedures that are standard of care (SOC). Any safety data provided that arises from imaging / bloods would be obtained from the participant's clinical record.

The Committee requested the following changes to the Participant Information Sheet and Consent Form (PIS/CF):

1. The Committee requested simplification of the study title. This could be reduced to a simple lay title.
2. Please remove any SOC procedures other than a brief description of what ‘Standard of Care’ means and a list of procedures that may be undertaken by the site as part of SOC. Risks related to SOC procedures should also be removed as these are not study specific; a sentence stating ‘your health care provider will discuss risks and inconveniences associated with standard of care assessments’ is sufficient.
3. Please state that there will be approximately 2 participants enrolled into the study in New Zealand.
4. Please note that Pfizer is promoted overly on the first page and this could be removed as it seems overly repetitive.
5. Please remove reference to “What will happen to my biological samples” as this is all standard of care (SoC)

**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 feedback provided by the Committee. *(National Ethical Standards for Health and Disability Research and Quality Improvement, para 7.15 – 7.17).*

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| **3** | **Ethics ref:** | **2022 FULL 12285** |
|  | Title: | Ageing Well through Eating, Sleeping, Socialising and Mobility (AWESSoM) Care Home Project: Oral Health |
|  | Principal Investigator: | Dr Moira Smith |
|  | Sponsor: |  |
|  | Clock Start Date: | 28 July 2022 |

Dr Moira Smith and Professor Murray Thomson 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 resolved ethical issues

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

1. The Committee clarified that there would be some overlap between part one and part two of the study.
2. The Committee clarified that the recruitment had been formulated with the managers of the homes and that the research would be introduced by the researchers to workers in order to reduce the feelings of inducement to participate.
3. The Researcher clarified that there was no control group as they viewed this as not being in equipoise.
4. The Committee clarified interpreters would be made available to participants as required.
5. The Committee clarified how potential incidental findings would be resolved.
6. The Committee clarified how potential distress would be mitigated, the researcher noted that the clinicians were well equipped to handle dentally anxious individuals.

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 clarified that this would be a feasibility study and requested this be reflected in all study documentation.
2. The Committee noted that page 17 of the protocol states that 'All staff (including management staff) will be encouraged by the facility management and the research team to attend one or more training sessions on oral health and preventive oral health care'. Please clarify whether attending these sessions equates to study participation, or whether staff may attend the session without participating in the study itself. There are clear ethical issues in relation to 'encouragement' by employers to participate in research. The researcher clarified that training sessions were open to all employees and were not part of study participation. The Committee requested that there be a clear distinction made between study activities and activities open to all employees.
3. The Committee requested that it be made clear that a support person would not be required for residents to participate.
4. The Committee requested a clear outline be provided as to the person(s) identifying capacity to consent, what that assessment would look like, and who would be signing the consent forms.
5. The Committee noted that the best interest test would not need to be employed as Enduring Power of Attorney would be in place for all participants not able to consent as per care home requirements.
6. The Committee requested that a much simpler information sheet be provided for those who have limited capacity to consent.
7. The Committee noted that there was no discussion of culturally sensitive issues such as touching of the head being Tapu. Please address this in future applications.
8. The Committee noted that the study must be registered on a WHO-approved clinical trial registry prior to commencing recruitment activities.
9. The Committee noted that data recording position with organisation will be collected for study staff. Given that n=6 in management roles (per protocol), a combination of role and other demographic data may be sufficient to identify participants. Please clarify the measures in place to mitigate this risk, particularly when data is reported.
10. The Committee noted that D9 states that the researchers will 'utilise existing facility communication channels such as newsletters, and facility Facebook posts to inform residents and staff of the study. Note that participant-facing material of this nature requires review and approval by HDEC prior to use.
11. The Committee noted that evidence of independent scientific peer review must be provided to the HDEC Committee for review.
12. The Committee requested the following changes to the Data Management Plan (DMP):
    1. Please review and amend to ensure it is study-specific (e.g. sources of data) and remove template instructions.
    2. Please note the application form G6 states participants may withdraw from the study up to the time of data analysis. The DMP states collected data will continue to be used regardless of the participant withdrawing. Please clarify what is intended and amend documentation for consistency.

The Committee requested the following changes to the Participant Information Sheet and Consent Forms (PIS/CF):

Resident PIS/CF

1. Please consider a version with pictures or diagrams to assist.
2. Please review for typos and missing words.
3. Please delete 'as part of your usual care' to describe study activities, unless they are standard care to be received by all residents regardless of study participation.
4. Please state approximately how long each study component will take (assessment, questionnaire, interview)
5. Please state whether the interview will be recorded and transcribed, and whether participants can request a copy of the transcript.
6. Please clarify that direct quotes may be used and seek permission for this.
7. If the oral health assessment could result in treatment-related injury, please include the HDEC-approved ACC compensation statement.
8. Please provide information about how data is de-identified, how long it will be retained, and confirm that it will not be used for future research.
9. Please include a statement about risk of privacy breach.
10. Please consider explaining ‘oral health’ early on in each document. For example, “care of mouth, including teeth and gums” or other more lay-friendly explanation.
11. Please explain that personal medical information will be accessed in Part 2 of the study.
12. Please include Māori cultural support details.

Staff PIS/CF

1. Please review for typos and missing words.
2. Please state clearly which activities described are open to all staff regardless of study participation, and which activities are study-specific.
3. Please state approximately how long each study component will take (assessment, questionnaire, interview).
4. Please state whether the interview will be recorded and transcribed, and whether participants can request a copy of the transcript.
5. Please clarify that direct quotes may be used and seek permission for this.
6. If the oral health assessment could result in treatment-related injury, please include the HDEC-approved ACC compensation statement.
7. Please provide information about how data is de-identified, how long it will be retained, and confirm that it will not be used for future research.
8. Please include a statement about risk of privacy breach.
9. Please consider explaining ‘oral health’ early on in each document. For example, “care of mouth, including teeth and gums” or other more lay-friendly explanation.
10. Please consider a koha for staff as this likely will take a considerable amount of time with no benefit to the staff participating.
11. Please explain that personal medical information will be accessed in Part 2 of the study.
12. Please make it clear what the staff are consenting to, and why they would be doing so as there is no clear benefit.
13. Please include a statement that none of the staff data will be shared with the employer.

**Decision**

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

1. Please address all outstanding ethical issues, providing the information requested by the Committee.
2. Please update the participant information sheet and consent form, taking into account feedback provided by the Committee. *(National Ethical Standards for Health and Disability Research and Quality Improvement, para 7.15 – 7.17).*
3. Please update the study protocol, taking into account the feedback provided by the Committee. (National Ethical Standards for Health and Disability Research and Quality Improvement, para 9.7).

After receipt of the information requested by the Committee, a final decision on the application will be made by Dr Mira Harrison-Woolrych and Mr Anthony Fallon.

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| **4** | **Ethics ref:** | **2022 FULL 13130** |
|  | Title: | A Phase 3, Open-Label Study to Evaluate Safety and Efficacy of Epcoritamab in Combination with Rituximab and Lenalidomide (R2) compared to R2 in Subjects with Relapsed or Refractory Follicular Lymphoma (EPCORE™ FL-1) |
|  | Principal Investigator: | Dr Samar Issa |
|  | Sponsor: | AbbVie Pty Ltd. |
|  | Clock Start Date: | 28 July 2022 |

Dr Samar Issa, Minh Dinh, Rebekah Conlon, Raquel Llorente, Stephen Samson and Sharon Cheung 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 resolved ethical issues

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

1. The Committee noted that the Participant Information Sheet and Data and Tissue Management Plan stated karakia was available if requested, while the application form indicated this was not possible due to sending samples overseas. It was clarified that the optional donation of tissue would be sent overseas, but with the New Zealand cohort no fresh tissue will be obtained and therefore sent for this purpose. All tissue will be kept in New Zealand and only pathology slides will be sent overseas.
2. The Committee noted that a pregnant participant/partner participant information sheet/consent form should only be submitted as an amendment in the event that a pregnancy occurs so it can be fit-for-purpose. The submitted document has not been reviewed or approved at this time.

Summary of outstanding ethical issues

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

1. Page 18 of the protocol states that a legally authorized representative can consent on behalf of a potential participant. The Committee noted this is not allowed in New Zealand, as this study is a medical experiment. Please have the Sponsor provide a Protocol Clarification Letter or Note-To-File stating that proxy consent is not permissible in New Zealand.
2. The Committee requested the following changes to the Data and Tissue Management Plan (DTMP):
   1. The Committee noted some brackets have been left in.
   2. On page 5, a participant should always be informed of a breach, even if it isn’t notifiable to the privacy commissioner.
3. Please ensure participants’ accommodation and other requirements are reimbursed if a participant is required to stay within 30 minutes of the hospital post-treatment.

The Committee requested the following changes to the Participant Information Sheet and Consent Form (PIS/CF):

PIS/CF (main)

1. Please include a lay-friendly title of the study.
2. Please amend blood and urine sample information on page 4 to specifically reflect New Zealand requirements.
3. Remove square brackets from heading (page 6)
4. Please give a lay explanation of what biomarkers are (page 7). State what genes and DNA are in lay language and clarify whether the participant's entire genetic code may be sequenced. State whether there is any risk of matching genetic data across databases (e.g. law enforcement).
5. Remove square brackets at end of page 8.
6. Provide indication of frequency (not just “less common”) of the serious side effects of epcoritamab (page 9) and lenalidomide (page 10)
7. Provide information about the side effects of all rituximab
8. Explain “tumor lysis syndrome” (page 11)
9. Rituximab and Lenalidomide are protocol-specified medications. Please delete the following statement: “The Sponsor may not accept the compensation claim if…the injury was caused by Rituximab and Lenalidomide”
10. Note therapeutic studies cannot be terminated solely for commercial reasons in NZ (page 18)
11. Insert “Southern HDEC” and remove instruction text “add if applicable” (page 20)
12. Ensure researcher and Māori cultural support contact details are provided (page 20)
13. Remove yes/no tick boxes re: informing GP as this isn’t optional (page 22)
14. Remove reference to “Legally Authorised Representative” (page 22)
15. The Committee referred the researcher to [the HDEC reproductive risks template](https://ethics.health.govt.nz/assets/Uploads/HDEC/templates/participant-information-sheet-consent-form-template-reproductive-risks-v.3.0-july2022.docx).
16. Please review and clarify the information provided about Personal Data; in places the term is used instead of Coded Data, when this is what should be referred to (e.g. Sponsor sharing of safety data; the study site sharing Personal Data with 'regulatory authorities and ethics committees worldwide'). For each new description please state whether the data being referenced is identifiable or coded.
17. Please address the risk of privacy breach.
18. The PIS/CF currently states, 'If you are withdrawn because you become pregnant, the study doctor and staff will also collect information about your pregnancy'. Please clarify that additional consent will be obtained in order to obtain pregnancy follow-up information, including information about any new-born.

PIS/CF (optional)

1. Insert “Southern HDEC” (page 5)
2. Ensure researcher and Maori cultural support contact details are provided (page 6)
3. Ensure consent form issues noted for main PISCF are actioned for optional PIS/CFs also.

**Decision**

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

1. Please address all outstanding ethical issues, providing the information requested by the Committee.
2. Please update the participant information sheet and consent form, taking into account feedback provided by the Committee. *(National Ethical Standards for Health and Disability Research and Quality Improvement, para 7.15 – 7.17).*
3. Please update the study protocol, taking into account the feedback provided by the Committee. (National Ethical Standards for Health and Disability Research and Quality Improvement, para 9.7).

After receipt of the information requested by the Committee, a final decision on the application will be made by Mr Dominic Fitchett and Associate Professor Nicola Swain.

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| **5** | **Ethics ref:** | **2022 FULL 13123** |
|  | Title: | A multicenter, randomized, double-blind, parallel group, placebo-controlled study to assess safety, tolerability, pharmacokinetics and pharmacodynamics of BI 764198 administered orally once daily for 12 weeks in patients with focal segmental glomerulosclerosis. |
|  | Principal Investigator: | Dr Nick Cross |
|  | Sponsor: | Boehringer Ingelheim Pty Ltd. |
|  | Clock Start Date: | 28 July 2022 |

Dr Nick Cross, Tania Roulston, Holly Thirlwall, and Julia O’Sullivan 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.

Dr Devonie Waaka declared a potential conflict of interest. It was deemed minor and Dr Waaka was permitted to remain as a reviewer.

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 Researchers that participation in this trial should not prevent entry into future similar trials as far as they were aware.
2. The researcher clarified that initially the New Zealand site would recruit only participants with historical genetic testing confirming. Should additional participants be required, an amendment will be provided to HDEC including this genetic test as a pre-screening activity.
3. The Committee noted that the Eye examination worksheet was out of scope and not reviewed.

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 ensure participants are provided with the full participant information sheet/consent form (PIS/CF) at the same time as the pre-screening PIS/CF. Currently the pre-screening PISCF states that 'If you meet the criteria on the laboratory tests with your 24-hour urine samples, you will be given full information about the main clinical trial', which does not provide patients with enough information to make a decision regarding pre-screening.
2. The Committee requested the following changes to the Data and Tissue Management Plan (DTMP)*:*
   1. Please amend Section 8.4 to clarify that future tissue research will be undertaken only in those participants who provide additional optional consent.

The Committee requested the following changes to the Participant Information Sheet and Consent Form (PIS/CF):

1. Please check the layout of the documents once printed and reduce the size of the footers as they can get close to the rest of the text in places.

Main PIS/CF

1. Please simplify the eligibility criteria.
2. Explain in lay language what genes are (please use explanation in the Future Unspecified Research (FUR) PIS/CF). Clarify whether the participant's entire genetic code will be analysed / recorded. State whether the results may have clinical implications for the participant and/or blood relatives (e.g. CYP gain or loss of function mutations). Provide information about return of results and any options for this.
3. Please move the risks of cataracts higher in the list of potential risks.

Screening PIS/CF

1. State clearly whether patients can elect not to undergo pre-screening, or whether this is mandatory.
2. Review and limit only to information relevant to the pre-screening test(s) being performed, including consent clauses.
3. State what happens to information collected during pre-screening if the participant is not eligible for the study and/or does not sign the main PIS/CF.

FUR PIS/CF

1. State whether there is any risk of full / partial genetic data matching across genetic databases (e.g. law enforcement).
2. Delete repeated information in 'WHAT COULD HAPPEN TO ME BY GIVING THESE BIOLOGICAL SAMPLES?' and data risks.

**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 feedback provided by the Committee. *(National Ethical Standards for Health and Disability Research and Quality Improvement, para 7.15 – 7.17).*

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| **6** | **Ethics ref:** | **2022 FULL 13160** |
|  | Title: | A Phase Ic, Randomized, Double-blind, Placebo-controlled, Multiple Dose-Escalation Study to Evaluate the Safety, Tolerability and Pharmacokinetics of HB0034 in Adult Healthy Subjects. |
|  | Principal Investigator: | Dr Christian Schwabe |
|  | Sponsor: | Shanghai Huaota Biopharmaceutical Co., Ltd |
|  | Clock Start Date: | 28 July 2022 |

Dr Christian Schwabe, Julia O’Sullivan, and Holly Thirlwall 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 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 following about the application form:
   1. Please confirm the following statement is correct (in which case this will need to be made clear in the PIS): “Should a participant withdraw consent from the main study, samples provided for the study will continue to be processed and analysed, to protect the integrity of the study” (F8)
   2. It is stated that karakia will not be available at time of tissue destruction (F7), which accords with the PIS, but the DTMP states on page 9 “Options for karakia will be discussed with participants during the informed consent process” - please reconcile conflict
2. The Committee requested the following changes to the Data and Tissue Management Plan (DTMP)*:*
   1. Reconcile conflict regarding availability of karakia at time of tissue destruction as above
   2. Remove references to future research using tissue (pages 6, 11)

The Committee requested the following changes to the Participant Information Sheet and Consent Form (PIS/CF):

1. Provide separation between body of text and footers (throughout document)
2. Remove instruction text “Briefly explain why the participant has been chosen to participate” (page 6)
3. Delete the statement “Smoke more than 5 cigarettes (or equivalent i.e., nicotine containing products including vapes) a day within the 3 months prior to screening”, which is redundant given the following exclusion criteria “Have used any nicotine or nicotine containing products (including vaping products) within 6 months prior to screening” (page 7)
4. Provide brief information about the status of the current Phase Ia study, with regards to the number of people exposed to study drug, the maximum dose used in the study, and the adverse effect profile seen this far.
5. Clarify with the Sponsor whether infection more generally is a potential safety issue and should be noted in the PIS/CF given the mechanism of action of the drug, particularly with more prolonged exposure. It is noted that there are exclusion criteria for infection, and that screening involves tuberculosis (TB) testing.

**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 feedback provided by the Committee. *(National Ethical Standards for Health and Disability Research and Quality Improvement, para 7.15 – 7.17).*

## General business

1. The Chair reminded the Committee of the date and time of its next scheduled meeting:

|  |  |
| --- | --- |
| **Meeting date:** | 13 September 2022 |
| **Zoom details:** | To be determined |

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**
2. **Other business**
3. **Other business for information**
4. **Any other business**

The meeting closed at 2.00pm