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| **Committee:** | Northern B Health and Disability Ethics Committee |
| **Meeting date:** | 04 October 2016 |
| **Meeting venue:** | Novotel Ellerslie, 72-112 Greenlane Road East, Ellerslie, Auckland |

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| **Time** | **Item of business** |
| 12.00pm | Welcome |
|  | Confirmation of minutes of meeting of 06 September 2016 |
|  | New applications (see over for details) |
|  | i 16/NTB/168  ii 16/NTB/176  iii 16/NTB/166  iv 16/NTB/167  v 16/NTB/171  vi 16/NTB/172  vii 16/NTB/173  viii 16/NTB/174  ix 16/NTB/177  x 16/NTB/178  xi 16/NTB/179  xii 16/NTB/181 |
| 6.30pm | General business:  Noting section of agenda |
| 6.45pm | Meeting ends |

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| **Member Name** | **Member Category** | **Appointed** | **Term Expires** | **Apologies?** |
| Mrs Maliaga Erick | Lay (consumer/community perspectives) | 01/07/2015 | 01/07/2018 | Apologies |
| Mrs Stephanie Pollard | Non-lay (intervention studies) | 01/07/2015 | 01/07/2018 | Present |
| Miss Tangihaere Macfarlane | Lay (consumer/community perspectives) | 19/05/2014 | 19/05/2017 | Present |
| Mrs Phyllis Huitema | Lay (consumer/community perspectives) | 19/05/2014 | 19/05/2017 | Present |
| Mrs Kate O'Connor | Lay (ethical/moral reasoning) | 14/12/2015 | 14/12/2018 | Present |
| Dr Nora Lynch | Non-lay (health/disability service provision) | 24/07/2015 | 24/07/2018 | Present |
| Mrs Leesa Russell | Non-lay (intervention studies), Non-lay (observational studies) | 14/12/2015 | 14/12/2018 | Present |
| Mr John Hancock | Lay (the law) | 14/12/2015 | 14/12/2018 | Apologies |
| Dr Brian Fergus | Lay (Co opt NTA) | Lay (Co opt NTA) | Lay (Co opt NTA) | Present |

## Welcome

The Chair opened the meeting at 12.05pm and welcomed Committee members, noting that apologies had been received from Mrs Maliga Erick and Mr John Hancock.

The Chair noted that fewer than five appointed members of the Committee were present, and that it would be necessary to co-opt members of other HDECs in accordance with the SOPs. Dr Brian Fergus confirmed his eligibility, and was co-opted by the Chair as a member of the Committee for the duration of the meeting.

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 6 September 2016 were confirmed.

## New applications

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| **1** | **Ethics ref:** | **16/NTB/168** |  |
|  | Title: | A Global Study Characterising the Safety and Tolerability of Anifrolumab in Participants with Active Systemic Lupus Erythematosus |  |
|  | Principal Investigator: | Dr Alan Doube |  |
|  | Sponsor: | Pharmaceutical Research Associates Ltd NZ |  |
|  | Clock Start Date: | 22 September 2016 |  |

Mrs Denise Darlington was present by teleconference for discussion of this application.

Potential conflicts of interest

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

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

Summary of Study

1. This is a Phase 3, multicentre, multinational, randomised, double-blind, placebo-controlled, long-term extension (LTE) study to characterise the long-term safety and tolerability of an intravenous (IV) treatment regimen of anifrolumab (300 mg) versus placebo in adult subjects who completed a Phase 3 study (D3461C00004 or D3461C00005) through the 52-week double-blind treatment period.
2. This LTE will allow subjects to continue with treatment for an extended period of up to 3 years. Subjects who were receiving anifrolumab (150 or 300 mg) in the previous Phase 3 study will receive anifrolumab (300 mg) in the LTE, and subjects who were receiving placebo in the previous Phase 3 study will be re-randomised to receive anifrolumab (300 mg) or placebo in a 1:1 ratio in the LTE study. Therefore, it is expected that the ratio of subjects receiving anifrolumab (300 mg) or placebo in the LTE study will be approximately 4:1.
3. Subjects randomised to placebo in the LTE study serve as a comparator to support interpretability of the data collected for subjects randomised to anifrolumab. Subjects who were receiving anifrolumab 150 mg in the previous Phase 3 study will switch to 300 mg in the LTE to provide long-term safety data on the higher study dose. This study allows for adding new oral immunosuppressant or changing background immunosuppressants, as well as for flexible oral corticosteroids (OCS) use, so that subjects may achieve adequate control of their disease during the study.
4. Although the study will initially be completely double-blind, (ie, blind for subjects, Investigators/site staff, and Sponsor/designated clinical research organisation [CRO]), at the conclusion of the Phase 3 Studies D3461C00004 or D3461C00005 treatment allocation for most subjects may become known to the Sponsor staff and/or designated CRO. The blind will be maintained for the Investigator and investigational site staff, and for the subjects.
5. The Researcher(s) noted the study drug appears to have favourable results so far, adding there is 1 participant in New Zealand with ongoing active recruitment.

Summary of ethical issues (resolved)

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

1. The Committee noted that the one participant is blinded currently and queried if they will remain blinded on the extension. The Researcher(s) confirmed it was possible, noting this is the first time they had seen this type of blinding in an extension study, noting those on placebo will be randomised again 1:1 to be on placebo again or treatment.
2. The Committee queried whether it was justifiable to potentially have a participant on placebo for four years. The Researcher(s) explained the background medication options were flexible and available. The Researcher(s) added if the participant is not doing well they could withdraw.
3. The Committee noted the Co-ordinating Investigator’s CV is very brief and does not reference any research literature. Please submit more extensive CV in future.
4. The Committee noted placebo was not listed on ethical issues section on application. For next time please explain primary ethical issues, like placebo for extended periods of time.
5. The Committee queried why AstraZeneca was not listed as the sponsor in the ethics application. The Researcher(s) stated they did not know.
6. The Committee noted incidence for this data in Maori would be beneficial. The Committee noted the condition is overrepresented in Maori, Asian and Pacific.
7. The Researcher(s) confirmed they are collecting ethnicity and are using current census methods.
8. The Committee queried how fasting is managed. The Researcher(s) explained their methods to ensure safe fasting.
9. The Researcher(s) confirmed the Maori consultation would occur shortly.

Summary of ethical issues (outstanding)

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

1. The Committee queried if there is a participant alert card. The Researcher(s) confirmed there is. The Committee requested it was submitted with the provisional response.
2. The Committee noted R.1.8 (compensation description) is not ACC equivalent. Please remove the limitations (caveats for limitations in compensation) in Participant Information Sheet, and re-confirm ACC equivalent compensation is available for participants in this study.
3. The Committee the Participant Information Sheet states the study may be terminated for commercial reasons. Please remove this, as the National Ethics Advisory Committee Ethical Guidelines state that studies should not be terminated for purely commercial reasons. Please also provide assurance for the HDEC.

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

1. The Committee queried why there were mandatory pap smears, noting the whakama (potential for shame or embarrassment) associated with them. The Researcher(s) explained that they had a patient who had not had one before in a prior trial, leading to the request for increased screening. The sponsor asked if the researchers could conduct screening that might detect cancer to make sure they are not exposing any participants to any risk. The Researcher(s) confirmed they would not conduct a pap smear if the participant has already had one within an acceptable amount of time. This general rule applies to any similar screening tests. The Committee requested the rationale for screening is made clear to participants.
2. The Committee noted that the protocol refers to local guidelines. Please be specific about the guidelines in the participant in the Participant Information Sheet.
3. The Committee noted receipts are not possible for mileage, which may cause confusion as receipts are currently requested for all reimbursement. The Researcher(s) confirmed they would remove that statement, as IRD calculations are used to pay for mileage.
4. The Committee noted the statement that participants can ‘be withdrawn for any reason by the sponsor’ is concerning. Please modify the statement to limit the general nature of withdrawal. For example, add for reasons of safety.
5. Add to Participant Information Sheet that Covance is overseas (with regards to tissue).
6. The Committee requested summary of inclusion exclusion criteria from application in the Participant Information Sheet.
7. The Committee requested information on risks from ongoing placebo is clearly explained in Participant Information Sheet.
8. Add GP notification of involvement in study to Participant Information Sheet.
9. The Committee queried how incidental findings are managed. The Researcher(s) explained anything that is picked up during testing or analysis that is of significance is reported back to the patient, either by phone or in person. The Researcher(s) confirmed GPs would also be notified after every research visit. The Committee requested the whole process is made clear.
10. Regarding the PAP smears Pg. 5. Rather than talk about following regional guidelines, put in the New Zealand Guidelines (which have just recently changed the entry age from 20 to 25 years). Explain who will conduct them.
11. Remove all reference to Belimumab. It is not available in New Zealand.
12. The Researcher(s) confirmed positive HIV results would go back to GP, however this is discussed with participants before the test is referred to GP. The Committee noted HIV is notifiable. This must be clearly explained to participants.
13. Study Visits Pg. 3: add an approximate duration for these monthly visits. The Committee suggested tabulation if possible, but noted this was not a request for change for this Participant Information Sheet but something to consider for future applications.
14. Change ‘might’ to ‘would’ in terms of right to access participant’s own data in Participant Information Sheet.
15. The Researcher(s) explained that potentially patients are going from placebo to active treatment, so we will check to ensure they stay in clinic when this potentially changes. The Researcher(s) will clarify the extended observation at the beginning, and will add to Participant Information Sheet.
16. The Researcher(s) noted pregnancy confirmation should be on consent form.
17. Add option to receive results from the study.
18. Page 3 – make it clear that a dose increase may occur, from 150 to 300mg.
19. Pg. 14 & 15: Clearly indicate withdrawal process

Decision

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

* Please amend the information sheet and consent form, taking into account the suggestions made by the Committee (*Ethical Guidelines for Intervention Studies* *para 6.22*).
* Please provide criteria for study termination. (*Ethical Guidelines for Intervention Studies* *para 6.64*).
* If cover under the Accident Compensation Act 2001 will be excluded for the intervention study, investigators and study sponsors have responsibilities to ensure alternative compensation cover for study participants to at least ACC-equivalent standard. This may include earnings-related compensation. (*Ethical Guidelines for Intervention Studies* *para 8.4)*

This following information will be reviewed, and a final decision made on the application, by Mrs Stephanie Pollard and Mrs Kate O’Connor.

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| **2** | **Ethics ref:** | **16/NTB/176** |  |
|  | Title: | A Phase 1a/1b study of ABI-H0731 in healthy volunteers and patients with chronic hepatitis B |  |
|  | Principal Investigator: | Prof Ed Gane |  |
|  | Sponsor: | Novotech (New Zealand) Limited |  |
|  | Clock Start Date: | 15 September 2016 |  |

Prof Ed Gane and Ms Rebecca Hu were present by teleconference 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 the first clinical study of a new drug called ABI-H0731 that targets the inhibition of the hepatitis B virus replication.
2. In Part I of this study, different doses of ABI-H0731 will be given to healthy people. We hope to learn whether ABI-H0731 is safe and tolerated when taken at different doses or after repeated doses. If the data from Part I is favourable, ABI-H0731 will be given to subjects with chronic hepatitis B in Part II of the study to see whether it is effective.
3. In total, up to 72 healthy people will participate in Part I of the study and up to 42 subjects with CHB in Part II.

Summary of ethical issues (resolved)

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

1. The Committee noted the low risk of adverse events.
2. The Committee noted the independent data review between phases of study.
3. The Committee queried why the first part of the study is 7 days treatment in healthy participants, then 28 days in patients.
4. The Researcher(s) noted this was not first in class of drugs and that duration is short and high in healthy participants to give safety data for patients, adding they often use this strategy.
5. The Researcher(s) explained why participants can go on standard of care within 48 hours of completion.
6. The Committee commend layout of the first Participant Information Sheet in particular the tabulation and background colouring.

Summary of ethical issues (outstanding)

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

1. Amend storage of health data to 15 not 50 years.

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

Part 1:

1. 1.1- add a sentence make it clear that they are in Part 1 only
2. 2.3 Table 2- explain 'Holter monitor'
3. 4.4.1 Contraception for females. Does "able to become pregnant" include women on effective contraception? Rephrase for clarity.
4. 6.1 Add details of overseas labs, as done in the other PISCs in same study
5. A7-9 2.3 Table 2 It needs something to indicate there is dosing at home on day 5 and 6. As it stands, you could be forgiven for omitting doses on those days.
6. Part 2 Pg1 - typo- it still says “In this part of the study, the drug will be tested in healthy volunteers" This is the Hep B part of the study.
7. Pg. 2 1.1 Para2. States eligibility “because you have not yet started on any treatment for hepatitis B". However, patients in
8. B1-3 are allowed to have had treatment as long as off it for 3 months. Revise this statement.
9. Pg4 Give some idea of the time commitment for study days e.g. half a day, whole day.
10. PISC Optional Sampling Pg 1 Line 3:define "clinical repository" Line 8: define "virologic".

Part 2:

1. B.1 – 4: states healthy volunteers – but this is patients, please remove.
2. Eligibility – ‘not yet started any’…but even people who off treatment for 3 months, are eligible. Change to currently not on treatment.
3. Page 4 – add time commitment on study day.
4. Viologic – terminology revise.

Decision

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

* Please amend the information sheet and consent form, taking into account the suggestions made by the Committee (*Ethical Guidelines for Intervention Studies* *para 6.22*).

This following information will be reviewed, and a final decision made on the application, by Dr Brian Fergus and Dr Nora Lynch.

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| **3** | **Ethics ref:** | **16/NTB/166** |  |
|  | Title: | Denosumab in addition to ULT for Bone Erosions in Gout |  |
|  | Principal Investigator: | Prof Nicola Dalbeth |  |
|  | Sponsor: | PRA Health Sciences |  |
|  | Clock Start Date: | 22 September 2016 |  |

Prof Nicola Dalbeth was not present or 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. Bone erosions are a common manifestation and feature of structural damage in severe/chronic tophaceous gout. Management of this destructive and often debilitating gout complication has focused exclusively on urate-lowering therapy (ULT) to reduce frequency of gout attacks, but little attention has been given to prevention or reversal of gout related bone erosions and other structural damage to bone caused by gout. Since there is no known effective treatment to attenuate or improve structural damage caused by gout, we propose a pilot, controlled, proof-of-concept study in which denosumab, an FDA approved and MEDSAFE approved medication for the treatment of bone loss, will be added to standard ULT in 20 patients with erosive gout.
2. Eligible subjects will be enrolled into the study, which includes a total of 6 study visits -- a screening visit and 5 study visits after enrolment. Details of planned clinical/laboratory assessments for each visit are explained further in this form. In addition at visits 1, 3, and 5 Participants will be asked to complete questionnaires where they will report on their QOL by Health Assessment Questionnaire (HAQ), physical function and mental health by Short Form Health Survey (SF-12), pain by visual analogue scale (VAS), frequency of gout flare occurrence, and medication use. In addition we will measure serum CTX levels ( bone turnover marker) at baseline, visit 4 and visit 5. Bone turnover refers to the total volume of bone that is both resorbed and formed over a period of time, usually expressed as percent/year. Bone turnover can be estimated by measuring relevant bone biomarkers such as CTX.
3. All subjects will continue on ULT standard of care and will need to have a serum urate level of 0.300 mmol/L (≤5 mg/dL) at the time of randomization. Patients will continue prescribed ULT throughout the study. Gout flares will be treated as per practice guidelines.
4. The Chair noted there were insufficient grounds for a closed meeting and rejected the request, noting the study drug was not a new medicine.

Summary of ethical issues (outstanding)

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

1. Provide information on the single independent safety monitor.
2. Please reword the advertisement in lay language.
3. The Committee requested a substantial explanation around sponsor involvement, as this will determine whether ACC is available for participants or whether commercial insurance is required. Please justify the relationships between investigators, the university and sponsor, as it is currently unclear, for example there are many references to sponsor in Participant Information Sheet.
4. Peer review not independent; please provide further independent peer review.
5. The termination of the study cannot be for purely commercial reasons, the National Ethics Advisory Committee Ethics Guidelines state studies should not be terminated for such reasons.

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

1. Under "How long will I be participating.." Add detail of number of visits. The Committee noted withdrawal does not need to be in writing, it can be verbal. Make this clear to participants.
2. The Committee noted participants GP should be informed for this study and consent sought for this.
3. "Concomitant medication" rephrase.
4. Remove Americanisms.
5. Length of visits not clear.
6. Explain where is blood going? Explain what tests occurring on blood.
7. Please refer to ethnicity rather than race.
8. Review complex language Participant Information Sheet eg subcutaneously.
9. The Committee requested a separate Participant Information Sheet for future unspecified research that includes all required information from the Ministry of Health Guidelines for Consent for Future Unspecified Research.

Decision

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

* Please amend the information sheet and consent form, taking into account the suggestions made by the Committee (*Ethical Guidelines for Intervention Studies* *para 6.22*).
* Please clarify sponsored status of study. If this is a commercially sponsored study, please submit evidence of sponsor insurance. *(Ethical Guidelines for Intervention Studies para 8.4).*
* Provide details of the Data Safety Monitoring *(Ethical Guidelines for Intervention Studies para 6.50).*
* Please provide evidence of favourable independent peer review of the study protocol (*Ethical Guidelines for Intervention Studies* Appendix 1).

This following information will be reviewed, and a final decision made on the application, by Mrs Kate O Connor and Mrs Stephanie Pollard.

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| **4** | **Ethics ref:** | **16/NTB/167** |  |
|  | Title: | Increasing retention in an alcohol and other drug therapeutic community |  |
|  | Principal Investigator: | Mrs Jo Willcocks |  |
|  | Sponsor: |  |  |
|  | Clock Start Date: | 22 September 2016 |  |

Jo Willcocks and Dr Sarah Christofferson were present by teleconference 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 purpose of this study is to investigate retention in a residential alcohol and other drug therapeutic community, and test whether Motivational Interviewing (MI) for engagement will improve retention. There will be two parts to the study.
2. Firstly, it is hypothesised that there are specific time points where a client is more likely to discharge prior to completion of the program, either enforced or voluntarily. To test these hypotheses, data from client files admitted to the programme over a 12 month period will be collected and analysed to determine time points or patterns of vulnerability for early discharge.
3. Secondly, it is hypothesised that MI for engagement, during the time point as determined by Study 1, will increase retention and engagement in the programme. MI for engagement sessions will be conducted during the first three weeks of residence, however, if the outcome of Study 1 suggests that MI may be better utilised further into the programme, then MI for engagement will be replaced by MI for continuation of treatment and abstinence. The prediction is that the MI sessions will improve motivation, engagement and retention. Impact on retention and engagement will be evaluated.

Summary of ethical issues (resolved)

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

1. The Committee queried whether these participants are a captive population. The Researcher(s) stated that majority of clients are mandated to attend to finish a sentence, or in lieu of going to jail. A number also self-refer, but these members are minimal.
2. The Committee noted the ethical considerations around researching in captive populations. The Committee noted there was a level of coercion involved due to the conflict of interest between researcher and treatment provider, as well as a perception that it will assist their release. The Researcher(s) explained that participants could finish their sentence at Odyssey house, and continue on in the study.
3. The Committee queried how many people are at the site at any time. The Researcher(s) stated there are 22 people in the house at any one time and around 5-8 will be involved in the study. The average length of stay can vary between 2 weeks to 12-13 months. The Researcher(s) explained they want to pinpoint the times they are more vulnerable to leave, and then target the treatment (motivational interviewing).
4. The Committee queried how support is given for participants and how their participation is kept confidential. The Researcher(s) explained interviewing is not in-group settings.
5. The Researcher(s) explained the sessions for part 2 occur with caseworker, which happens already on regular basis. If one session has interviewing component there is no reason anyone else would be aware of what is going on with session. The Researcher(s) confirmed they could merge it into their everyday care.
6. The Researcher(s) explained the current design offers everyone the same opportunity; it is up to the client to decide if they want to participate.

Summary of ethical issues (outstanding)

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

1. The Committee queried how the study question would be answered. The Researcher(s) stated they will compare the individuals who receive MI against phase 1 average length of stay, as well as individuals being their own control (i.e. self reported impact on whether they would have left earlier or not).
2. The Committee queried if consent is sought to access historical information, including case notes. The Researcher(s) stated Odyssey house has provided consent. The Committee noted this is not appropriate and that Odyssey house cannot consent for use of identifiable health records for research. Either researchers seek individual consent, make a justification of use without consent, or lastly – the data could be provided in a de-identified format. The Committee also queried why identifiable information was required for the first phase of the research.
3. The Researcher(s) explained that they thought the data was collected on the condition that it may be used for research or service evaluation. The Researcher(s) noted they only wanted to view retention times, not interviews and case notes. The Committee stated the protocol stated case notes and interviews.
4. The Committee queried why Odyssey house couldn’t provide aggregate data on key time points, i.e. 4 weeks or 7 months.
5. The Researcher(s) explained the most important part for part 1 is date of discharge, what reason and how long they stayed.
6. The Committee noted Odyssey should provide aggregate data, as there is no need for identifying information for phase 1 of the study.
7. The Committee noted the conflict of interest, as the investigator works at Odyssey house had not been addressed.
8. The Researcher(s) confirmed CI would not be at any motivational interviewing. The Researcher(s) (CI) currently works on weekends at the site.
9. The Researcher(s) confirmed CI has no reason to speak to any clients, stating this mitigates conflict of interest. The Committee noted that the participants would recognise the CI name on the information sheet.
10. The Researcher(s) confirmed study 1 is going to now involve de-identified information. Please amend the protocol to outline this change.
11. Mitigate plan for conflict, risk management of staff doing interviewers / researchers.
12. The consent being truly voluntary – explain how to ensure this occurs.
13. Privacy and confidentiality need to be better addressed in the protocol.
14. The Committee expressed concerns about the study design and felt it was not feasible to conduct this research as a Masters. The Committee noted the design did not appear to be able to answer the question, and requested further independent peer review. The researcher could also seek advice from other researchers who have conducted research in captive populations.
15. The Committee felt that the motivational interviewers had a lack of training, which needed to be addressed.
16. The Committee queried whether the workforce is part of the study. Requires more consideration of their role in the project if they are being involved.

Decision

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

* Please provide evidence of favourable independent peer review of the study protocol (*Ethical Guidelines for Intervention Studies* Appendix 1).
* Provide details on what processes are in place to accommodate the highly vulnerable context of recruitment *(Ethical Guidelines for Intervention Studies para 6.2).*
* Explain whether any of the participants will not be able to give informed consent, and elaborate on the vulnerability of the participant group *(Ethical Guidelines for Intervention Studies para 5.28*)
* Explain how the conflict of interest resulting from care provider being the researcher is addressed *(Ethical Guidelines for Intervention Studies para 4.19)*
* Explain what happens to health information (*Ethical Guidelines for Intervention Studies* *para 7.7)*
* Provide further information on the study design, *in particular* how the study will answer the study question, due to the small sample size and variance with individuals(*Ethical Guidelines for Intervention Studies para* 5.4)

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| **5** | **Ethics ref:** | **16/NTB/171** |  |
|  | Title: | MK-3475-365 |  |
|  | Principal Investigator: | Dr Peter Fong |  |
|  | Sponsor: | Merck |  |
|  | Clock Start Date: | 22 September 2016 |  |

Peter Fong and Elizabeth Wardrop were present in person 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 nonrandomized, multicenter, multicohort, open-label, Phase Ib/II trial of pembrolizumab (MK-3475) combination therapy in subjects with metastatic castration-resistant prostate cancer (mCRPC).
2. The primary objectives of this trial are to evaluate the safety and tolerability of pembrolizumab combination therapies and to estimate the prostate specific antigen (PSA) response rate for each combination cohort. After a screening phase subjects will be assigned to 1 of the following 3 cohorts based on prior treatment for mCRPC and other eligibility criteria for each cohort.
3. For Cohorts B and C, the investigator’s choice of standard of care will also be used to allocate subjects due to some overlap in entrance criteria. Cohort A: Pembrolizumab 200 mg intravenous (IV) every 3 weeks (q3w) + olaparib 400 mg by mouth (PO) twice a day (bd).
4. Subjects assigned to this cohort must have previously received docetaxel for mCRPC. Prior treatment with one other chemotherapy for mCRPC is allowed, as well as up to two second-generation hormonal manipulations (e.g., abiraterone acetate and/or enzalutamide). Cohort B: Pembrolizumab 200 mg IV q3w + docetaxel 75 mg/m2 IV q3w + prednisone 5 mg PO bd. Subjects assigned to this cohort must have previously received either abiraterone acetate or enzalutamide (but not both) in the pre-chemotherapy mCRPC state. Cohort C: Pembrolizumab 200 mg IV q3w + enzalutamide 160 mg PO every day (daily). Subjects assigned to this cohort must have previously received abiraterone acetate in the pre-chemotherapy mCRPC state (prior docetaxel for metastatic hormone-sensitive prostate cancer is allowed if ≥4 weeks have elapsed from the last dose of docetaxel).
5. The Researcher(s) explained that chemotherapy is quite standard, adding the study drugs adds some time to treatment, and provides an unfunded source of treatment for these patients. Requirement for a biopsy, for example.
6. One site in New Zealand. 5 participants, potentially more.

Summary of ethical issues (resolved)

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

1. The Committee queried why researchers are paying petrol vouchers but not paying for parking. The Researcher(s) noted this is traditionally what they give patients, explaining the vouchers should cover the parking costs. The vouchers can be used for a variety of purchases.
2. The Committee noted indemnity would be submitted to HDEC once updated.
3. The Researcher(s) confirmed that the first safety review would occur before the 5 New Zealand participants were recruited.
4. The Researcher(s) confirmed Maori consultation had been submitted.
5. The Researcher(s) explained the prevalence in Maori.

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

1. B.4.5.2 – please name the site that the tissue and samples will be sent to. Currently too vague.
2. The Committee noted adverse events and side effects – keytruda side effects are in different format than other side effects. Please make them comparable and consistent.
3. Page 8-9 – very common side effects, then these are re-iterated in more serious side effects. The Committee notes this probably means in some patients it is more severe in the latter, but it is currently quite confusing. The Researcher(s) noted there is a need for international comparability. The Committee just requested that it is clear that it is a subset in the latter.
4. The Researcher(s) confirmed risks listed are for individual drugs, not in combination (the risks section). The Researcher(s) noted the verbal information that supplements the Participant Information Sheet.
5. The Committee suggested on page 1 and 2: bold ‘purpose of the study’. Bold combinations that will be tested. Bold name of each of the drugs. This enables people to read that section. Consider bolding phrase, open label study etc. This breaks up page.
6. The Committee queried the information about pregnancy. The Researcher(s) noted the information is mandatory during drug development. Even if chances are very low.
7. Emphasis of risks of biopsy in Participant Information Sheet.
8. Page 16 – Participant Information Sheet – The Committee noted phrasing ‘you will be returned to your regular healthcare providers’. Please explain for participants.
9. The Committee noted biomarker testing, stored for 15 years, stored overseas.
10. Please explain participants can withdraw verbally – not only in writing. Clarify.
11. The Committee queried whether this study involves more ionising radiation that is usual for these patients. The Researcher(s) confirmed there are more frequent scans to check disease progression. The Researcher(s) stated knowing how the disease is progressing is more important than a theoretical future risk due to additional scanning. The Committee noted this; please make clear in Participant Information Sheet.
12. Remove references to us law
13. Pg. 17 access to data section, no placebo in this study.
14. Future unspecified research - check statements for relevance – i.e. withdraw for study related injury’.

Decision

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

* Please amend the information sheet and consent form, taking into account the suggestions made by the Committee (*Ethical Guidelines for Intervention Studies* *para 6.22*).

This following information will be reviewed, and a final decision made on the application, by Secretariat.

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| --- | --- | --- | --- |
| **6** | **Ethics ref:** | **16/NTB/172** |  |
|  | Title: | PROMOTE-SAH Study |  |
|  | Principal Investigator: | Ms Lynette Newby |  |
|  | Sponsor: |  |  |
|  | Clock Start Date: | 22 September 2016 |  |

Lynette Newby was present by teleconference 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.

Mrs Stephanie Pollard declared a potential conflict of interest, and the Committee decided to have Mrs Pollard stay in the room but not participate in the discussion or decision of the application.

Summary of Study

1. This is a prospective multi-center observational study of aneurysmal subarachnoid haemorrhage (aSAH) cases admitted to intensive care units in New Zealand and Australia. The aim is to establish baseline practice in this area, with a view to performing future controlled clinical trials. aSAH is a form of stroke and is a devastating neurological condition commonly affecting young people. Many patients die or are left with life altering disability. aSAH occurs when an artery wall in the brain becomes weak, resulting in a small dilatation area (or widening), referred to as a cerebral aneurysm. The aneurysm can rupture, causing blood to leak onto the surface of the brain. This can trigger a severe headache, and/or a loss of consciousness.
2. Given the poor outcomes associated with aSAH, a clinical imperative exists to improve care for these patients.
3. All admissions to site ICU during the study period will be screened for aSAH diagnosis by site staff. Site research staff will obtain data from review of clinical records record the clinical course during ICU. All data collected is de-identified for submission. Participant outcome will be measured with a telephone interview at 6 months, using validated tools, to determine the extent of recovery.
4. The Researcher explained the process for opt out and consent for use of records. Information will be given to relative/whanau as soon as appropriate with an opportunity to opt-out of the data collection or of only the telephone interview. Participant written or verbal opt-out is possible up to hospital discharge, and again at the 6-month telephone interview.

Summary of ethical issues (outstanding)

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

1. The Researcher(s) noticed there is a lot of variability of care for this treatment group. This will identify the actual care given, and the resulting outcomes, at death or at 6 months functional outcomes. This study will inform randomised trials to improve patient outcomes.
2. The Researcher(s) noted that the data collected is all routinely collected standard of care data.
3. The Committee noted the researchers planned to seek consent from family members to use data of ICU patients. The Committee notes that proxy consent is only legally acceptable in cases where the medical experiment would save the person’s life or prevent serious damage to the person’s health. The Committee noted no person can consent for use of another’s health information.. The Researcher(s) noted this.
4. The Researcher(s) explained that consent could not be sought for use of their data as the participants are incapacitated.
5. The Committee noted there are two means of accessing the records, one is through an audit – as this is outcomes analysis data accessed internally, and does not require consent. The other is through 6.4.3 of the ethical guidelines for observational studies – they outline a process to use to access health records retrospectively without consent.
6. The Committee noted that they can approve access to identifiable health information without consent for research in certain circumstances. The Ethical Guidelines for Observational Studies states at Paragraph 6.43:
   1. *Access to identified or potentially identifiable data for research without the consent of the people the data identifies or makes potentially identifiable may be justifiable when:*
      1. *the procedures required to obtain consent are likely to cause unnecessary anxiety for those whose consent would be sought; or the requirement for consent would prejudice the scientific value of the study; or it is impossible in practice to obtain consent due to the quantity or age of the records; and*
      2. *there would be no disadvantage to the participants or their relatives or to any collectives involved; and*
      3. *the public interest in the study outweighs the public interest in privacy.*
7. To approve a study involving access to health information without consent the Committee must be satisfied that these requirements are met by the study concerned.
8. The Committee felt that because seeking consent from a family member was not a legally valid option, and due to this method potentially reducing the sample size and scientific merit of the study, the researchers should retrospectively access the data once collected for standard of care. This can be through an internal audit, or by a waiver provided by the HDEC.
9. Regarding phase 2 of the study – the Committee explained that a Participant Information Sheet is sent out for phase 2 to get the outcomes required for the study. The Researcher(s) noted calling them is effective for reasons relating to accessibility, response rate and translation. The Committee noted that a call was acceptable, but that information should be sent prior to calling, which is in line with current ethical standards. The letter can explain why the person is calling and verbal consent can be sought on the phone.
10. The Researcher(s) confirmed they check to make sure people are alive before calling at 6 months.
11. The Committee noted receiving a follow up call is a benefit over and above standard of care, and that if the individual is unable to complete the questionnaire themselves, the Committee considered whether the data collected was clinically beneficial, and if so then it may be in their best interests to have that data provided for them, through supported completion of the questionnaire.
12. Please remove the proxy consent process for accessing data. Remove any mention of prospective data collection. The data should be accessed retrospectively.

Decision

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

* Revise study protocol to involve retrospective access to health records. Justify the use of the records, noting their clinical relevance for this project and taking into account advice provided by the Committee. Revise the method of consent and recruitment for phase 2 of the study. (*Ethical Guidelines for Observation Studies* *para 5.5*).

This following information will be reviewed, and a final decision made on the application, by Dr Nora Lynch and Mrs Phyllis Hutiema.

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| **7** | **Ethics ref:** | **16/NTB/173** |  |
|  | Title: | Work-related risk factors for CVD |  |
|  | Principal Investigator: | Prof Jeroen Douwes |  |
|  | Sponsor: | Massey University |  |
|  | Clock Start Date: | 22 September 2016 |  |

Prof Jeroen Douwes, Amanda eng and Andras Mullacher was present by teleconference 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. Cardiovascular disease (CVD) is the leading cause of death in New Zealand (NZ). There is evidence that occupational risk factors play a role in CVD; however, there are many knowledge gaps in part due to the relative lack of research in this area. Researchers will use our previous NZ Workforce Survey (NZWS) and Māori NZWS as the basis for a prospective cohort study, by following up participants for new CVD outcomes through linkage with health records.
2. The study will assess associations between occupational exposures (including night shift, chemicals, noise, stress, strenuous/sedentary work) and ischaemic heart disease, diabetes, high blood pressure, and high cholesterol. Researchers will also investigate potential intermediate and modifying factors (such as obesity and sleep problems) on CVD risk. This novel study will evaluate whether common and currently relevant workplace exposures increase the risk of CVD and identify specific modifiable occupational risk factors that will contribute to improved prevention.

Summary of ethical issues (resolved)

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

1. The Committee noted data is provided in a de-identified form.
2. Data is linked with IDI data.
3. The Committee noted the favourable peer review.
4. The Committee noted the benefit of research and the scale of the project.

Decision

This application was *approved* by consensus.

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| --- | --- | --- | --- |
| **8** | **Ethics ref:** | **16/NTB/174** |  |
|  | Title: | Developing HABITs |  |
|  | Principal Investigator: | Professor Sally N. Merry |  |
|  | Sponsor: | The University of Auckland |  |
|  | Clock Start Date: | 22 September 2016 |  |

Dr Karolina Stasiak was present in person, and Professor Sally Merry and Dr Terry Fleming were present by teleconference 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 Researcher explained their research team has received funding from the Ministry of Business, Innovation and Employment to partner with Māori and Pacific young people, family/whanau, communities and health/education professionals to co-design and test a digital platform of e-health interventions for common mental health concerns.
2. This application covers the youth and community engagement processes designed to provide input and co-design to make, shape and refine the platform. Co-design methodology offers a way forward by involving community stakeholders in the design of research, promoting their understanding and encouraging uptake of findings.

Summary of ethical issues (resolved)

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

1. The Committee asked for clarification about the age groups of participants. The Researcher(s) stated 12-19, but noted it was a bit unclear at the moment.
2. The Committee discussed the consent assent requirements for the study and the opt out process with parents of children. The Researcher(s) explained prior research projects (SPARX) involved child consent, due to the type of the research (explorative, low risk, focus groups).
3. The Committee noted consent at 16 is legal age for consent to research, but can consent earlier if competent.
4. The Researchers explained recruitment process: they will contact schools, allow researcher to approach young people via teachers or guidance counsellors and school assemblies. The Researcher(s) clarified participants are ordinary normal kids, not those who report mental health issues. The participants will be anyone who has a view on the app / project, but particularly Maori and Pacifica.
5. The Researcher(s) confirmed no targeting of participants, we will advertise and seek people to approach us generally.
6. 42 consultation groups across the project. This includes young people as well as experts and mixed youth groups.
7. The Committee queried what would occur if get 100 interested participants but can only enrol 12. The Researcher(s) stated first come first basis.
8. The Researcher(s) explained why opt out consent was important for this study (need large representation, not just organised children or parents). The Researcher(s) explain children are given information to take home, as well as school publicising the research to parents.
9. The Researcher(s) explained the other important support mechanisms for participants, noting the groups are well-controlled environments.
10. The Researcher(s) confirmed that age separation for the groups was possible. The Committee noted it would be good to keep similar age groups together, or to avoid substantial differences in age.
11. The Committee queried if parents can come to the focus groups. The Researcher(s) stated this has never occurred.
12. The Researcher(s) explained that the groups that work with young people in (addiction etc context) – grant will lead these and the approach will be different. These children would have graduated from a group programme. The Researcher(s) stated they will give children a paper based information form to bring home.
13. The Committee asked about Maori only focus groups, and queried the current consultation process. The Researcher(s) noted this project involves consultation and engagement with Maori and Pacific people, supported through the national science challenges. The Researchers have complex governance structure, involving kaumatua and 3 key science advisors.

Summary of ethical issues (outstanding)

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

1. The Committee request assent form for those under 16 who do need parental consent. The Committee noted that most participants will be able to provide consent, but there will be some who cannot, who will need parental consent and provide assent. In other cases the participants can consent for themselves.

Decision

This application was *approved* by consensus with non-standard condition.

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| **9** | **Ethics ref:** | **16/NTB/177** |  |
|  | Title: | Filgotinib in Combination With Methotrexate in Adults With Moderately to Severely Active Rheumatoid Arthritis Who Have an Inadequate Response to Methotrexate. |  |
|  | Principal Investigator: | Dr Daniel Ching |  |
|  | Sponsor: | Gilead Sciences, Australia & New Zealand |  |
|  | Clock Start Date: | 22 September 2016 |  |

Dr Daniel Ching was present by teleconference 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. Approximately 1650 participants will be randomized in a 3:3:2:3 ratio to filgotinib 200 mg, filgotinib 100 mg, active comparator (adalimumab), or placebo to match (PTM) administered for up to 52 weeks, all in the context of a weekly stable dose of MTX.
2. At Week 14, participants who have not achieved at least 20% improvement from Day 1 in both swollen joint count (SJC) and tender joint count (TJC) will discontinue IP dosing but will continue with study visits and assessments per protocol.
3. At Week 24, all subjects assigned to placebo + MTX will be reassigned 1:1 to either filgotinib 100 mg q.d. or 200 mg q.d. in addition to MTX in a blinded fashion and will continue in the study per protocol up to Week 52.
4. All subjects who continue on study drug will be evaluated for loss of therapeutic response from Week 30 through Week 52. Subjects failing to maintain at least a 20% improvement in SJC & TJC will discontinue from
5. IP but will continue with study visits and assessments per protocol.
6. All subjects meeting this criterion who discontinue from investigational study drug dosing are to receive standard of care treatment for their RA as determined by the investigator.
7. At completion of the 52-week dosing period, subjects who have not discontinued assigned study drug dosing, will be provided the option to enroll into a separate Long Term Extension (LTE) study.

Summary of ethical issues (resolved)

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

1. The Committee commended the data safety monitoring committee.
2. The Researcher(s) stated it was appropriate to continue methotrexate even if the response was inadequate, explaining they can add more medication to help, but don’t take them off, unless there is a real clinical reason to.
3. The Researcher(s) explained other treatments are based on special authority funding criteria by PHARMAC.
4. The Committee queried why patients would go onto an experimental study when options available are effective. The Researcher(s) stated older drugs are not quite as targeted treatments for arthritis and in his opinion were not as effective, though there is no head to head study to determine this.
5. The Researcher(s) confirmed patients know their treatment options.
6. The Committee queried the risks involved if participants had 12 week of methotrexate then 14 week on placebo. This could be 26 week of inadequate treatment. The Researcher(s) stated if the disease worsens then participants would be randomised again (at 14 weeks). The Researcher(s) confirmed that some could have been on 12 weeks and then another 14 who would then have 26 weeks of subpar treatment. The Researcher(s) explained investigator and patient discuss rescue therapies often. Some can be severe and some are not. Most with more severe disease don’t go into the trial, usually middle range group who enrol.
7. The Committee query what blinded results are not available. The Researcher(s) stated CRP. The Committee asked if CRP is clinically relevant. The Researcher(s) stated it does not affect way we treat the patients. Sometimes if the monitor noted the CRP was really high they unblind and let us know.
8. The Researcher(s) confirmed no individual participant will be approached for all 4 sub studies.

Summary of ethical issues (outstanding)

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

1. The Committee queried if New Zealand is participating in MRI and PK substudy. The Researcher(s) stated not my site but Wellington is. The Committee requested more information about how sites manage consenting for multiple studies, in particular MRI substudy, noting that participants needed to not be overwhelmed with information and studies at any given time.

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

1. Remove flip a coin analogy - due to 4 arms in this study.
2. Sexual active – in line with usual lifestyle (abstinence). This is nonsensical. Please reword.
3. Access to health data – The Committee noted participants can access their own at any time, and do not give up that right, but if they do it during the trial they would be withdrawn. Make this clear.
4. The Committee noted that verbal withdrawal is acceptable, please remove the need to withdraw in writing.
5. Remove US law references.
6. Remove legally authorised statements.
7. Explain acronyms.
8. Incidental findings process – outline for participants.
9. Add information on local guidelines relating to the consumption of alcohol while on MTX
10. Privacy and confidentiality section is unnecessarily long. Please revise and reduce length.
11. The Committee requested a separate Participant Information Sheet for future unspecified research that includes all required information from the Ministry of Health Guidelines for Consent for Future Unspecified Research. Ensure that information is moved from main PIS/CF to the separate one.

Decision

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

* Please provide a separate Participant Information Sheet and Consent Form for the use of tissue for future unspecified research (*Guidelines for the Use of Human Tissue for Future Unspecified Research Purposes, para 2*).
* Please amend the information sheet and consent form, taking into account the suggestions made by the Committee (*Ethical Guidelines for Intervention Studies* *para 6.22*).

This following information will be reviewed, and a final decision made on the application, by Mrs Stephanie Pollard and Mrs Tangihaere MacFarlane.

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| **10** | **Ethics ref:** | **16/NTB/178** |  |
|  | Title: | MK-3862-041: Study of Efficacy and Safety of MK-3682 + MK-8408 in Subjects with Chronic HCV |  |
|  | Principal Investigator: | Prof Edward Gane |  |
|  | Sponsor: | Merck Sharp & Dohme (Australia) Pty Limited |  |
|  | Clock Start Date: | 22 September 2016 |  |

Prof Edward Gane and Ms Kelly Armstrong were present by teleconference 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 study of approximately 250 patients who will receive a new combination of 2 oral antiviral drugs (MK-3682 and MK-8408) which block 2 different steps of virus replication (RNA replication and virus assembly). The study will test the safety and effectiveness of this treatment across many different patient populations including those with all types of HCV, all stages of liver disease (except decompensated cirrhosis) and with HIV. Patients can have failed previous interferon based therapy. Patients will receive this treatment for 12 weeks and be followed in this study for another 24 weeks.
2. The Researcher(s) explained that there is no current treatment for this genotype.

Summary of ethical issues (outstanding)

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

1. Please provide clarification on the data safety monitoring. The Researcher(s) stated it is external but will provide further information.
2. Please remove sending DOB and initials to sponsor – only need to send study number to sponsor.

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

1. Page 9 – what are photos for? The Researcher(s) stated skin rash adverse event, most likely, however the researchers will check and remove if not relevant for this drug.
2. Rights of access – placebo – remove from sub studies.
3. Consent form – 10 bullet point – GP informed. Add into in the information sheet and be clear what abnormal results to go GP without express consent.

Decision

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

* Please amend the information sheet and consent form, taking into account the suggestions made by the Committee (*Ethical Guidelines for Intervention Studies* *para 6.22*).
* Provide details of the Data Safety Monitoring Committee’s composition and monitoring plan *(Ethical Guidelines for Intervention Studies para 6.50).*
* Clarify use of health information (reduce identifiers for sponsor) (*Ethical Guidelines for Intervention Studies* *para 7.7)*

This following information will be reviewed, and a final decision made on the application, by Dr Nora Lynch and Dr Brian Fergus.

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| **11** | **Ethics ref:** | **16/NTB/179** |  |
|  | Title: | Filgotinib + MTX vs Filgotinib alone vs MTX alone |  |
|  | Principal Investigator: | Dr Daniel Ching |  |
|  | Sponsor: | Gilead Sciences Pty Limited |  |
|  | Clock Start Date: | 22 September 2016 |  |

Dr Daniel Ching was present by teleconference 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, double-blind, placebo- and active-controlled, Phase 3 study in adult male and female subjects with moderately to severely active RA who have limited or no prior exposure to MTX therapy.
2. Subjects will be randomized in a 2:1:1:2 ratio to filgotinib 200 mg plus MTX, filgotinib 100 mg plus MTX, filgotinib 200 mg alone, or MTX alone for up to 52 weeks in a double-blind fashion.
3. At Week 24, subjects who have not achieved a 20% improvement from Day 1 in both SJC and TJC will discontinue investigational therapy but will continue with study visits and assessments per protocol. All subjects who discontinue from investigational therapy are to receive standard of care treatment for their RA as determined by the investigator.
4. Responders at Week 24 will continue on the treatment regimens to which they were randomized through Week 52.
5. At completion of the 52-week treatment period, subjects (who did not discontinue assigned study drug or have not met criteria for loss of therapeutic response) will be provided the option to enter a Long Term Extension (LTE) study (GS-US-417-0304).

Summary of ethical issues (resolved)

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

1. The Researcher justified the 24 week treatment window.

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

1. Add the location of tissue stored overseas.
2. The Committee noted that verbal withdrawal is acceptable, please remove the need to withdraw in writing.
3. Remove US law references.
4. Remove legally authorised statements.
5. Explain acronyms.
6. Incidental findings process – outline for participants.
7. Add information on local guidelines relating to the consumption of alcohol while on MTX
8. Privacy and confidentiality section is unnecessarily long. Please revise and reduce length.
9. The Committee requested a separate Participant Information Sheet for future unspecified research that includes all required information from the Ministry of Health Guidelines for Consent for Future Unspecified Research. Ensure that information is moved from main PIS/CF to the separate one.

Decision

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

* Please provide a separate Participant Information Sheet and Consent Form for the use of tissue for future unspecified research (*Guidelines for the Use of Human Tissue for Future Unspecified Research Purposes, para 2*).
* Please amend the information sheet and consent form, taking into account the suggestions made by the Committee (*Ethical Guidelines for Intervention Studies* *para 6.22*).

This following information will be reviewed, and a final decision made on the application, by Dr Nora Lynch and Dr Brian Fergus.

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| **12** | **Ethics ref:** | **16/NTB/181** |  |
|  | Title: | CO39262: Vemurafenib, cobimetinib & atezolizumab triplet combination in advanced melanoma |  |
|  | Principal Investigator: | Dr Richard North |  |
|  | Sponsor: | Roche Products (New Zealand) Limited |  |
|  | Clock Start Date: | 22 September 2016 |  |

Ms Taina Von Blaramberg and Ms Lesley Goodman were present by teleconference for discussion of this application.

Potential conflicts of interest

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

Mrs Stephanie Pollard declared a potential conflict of interest, and the Committee decided to have Mrs Pollard stay in the room but not participate in the discussion or decision of the application.

Summary of Study

1. This is a phase 3, double-blinded, placebo-controlled, randomised multicentre study designed to evaluate the efficacy, safety and pharmacokinetics of Atezolizumab + Cobimetinib + Vemurafenib (Arm A) compared with Placebo + Cobimetinib + Vemurafenib (Arm B)in patients with BRAF+ unresectable/metastatic melanoma. The primary endpoint of the study is progression-free survival.
2. Subjects will be randomised 1:1 to Arm A or Arm B. There will be an initial run-in phase of 28 days in which all subjects will receive Cobimetinib + Vemurafenib, after which subjects will receive assigned Arm A or Arm B Treatment. Treatment will continue until confirmed disease progression (as per Response Evaluation Criteria in Solid Tumours [RECIST]), unacceptable toxicity, pregnancy, or withdrawal of consent. After treatment discontinuation, subjects will be followed for disease progression if applicable, and followed for survival until death, withdrawal of consent, or loss to follow up.
3. Subjects in the control arm are not eligible for crossover to the treatment arm at disease progression.
4. Visits will occur every 2 weeks for study drug administration. Imaging to monitor tumour response will be every 8-12 weeks.
5. This appears to be more targeted than existing care. Combination therapy.

Summary of ethical issues (resolved)

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

1. The Researcher(s) confirmed SCOTT pending.

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

1. The Committee noted FUR seems like fishing exercise – not clear about what it will be used. Requires separate Participant Information Sheet / CF for this tissue. Main study mandatory study tests can be in the main Participant Information Sheet but optional should be separate.
2. Add risks of biopsy.
3. Placebo against 1 drug not 2 (on participant card).
4. Obligations page 3 – can’t participate in any other research study. Be more specific, just clinical trials.
5. Pap smear, can check screening register as to avoid unnecessary pap smear? The Researcher(s) noted it is unclear. Please clarify.
6. Add tissue offshore
7. Page 11 – stopping reasons – note National Ethics Advisory Committee ethical guidelines state studies should not be terminated for purely commercial reasons.
8. Remove legal representative for incapacitated patients. The Researcher(s) confirmed no non-consensual research.
9. Should GP be optional? Make mandatory for safety and transparency (due to clinical follow up).
10. Remove withdrawal by writing requirement. Verbal consent is acceptable.
11. Please ensure samples destroyed when withdraw occurs, not a 2 step process – however investigators can ask to keep them.
12. R.1.6 no commercial
13. Maori – disproportionate disease? Less than European The Researcher(s) stated.
14. P 28-29 – ‘use disclose health information, identifiers you’. The Committee noted no identifiable health information should be shared. Transferred data should be de-identified.

Decision

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

* Please amend the information sheet and consent form, taking into account the suggestions made by the Committee (*Ethical Guidelines for Intervention Studies* *para 6.22*).

This following information will be reviewed, and a final decision made on the application, by Ms Kate O’Connor and Mrs Leesa Russell.

## General business

1. The Committee noted the content of the “noting section” of the agenda.

* Dr Angela Ballantyne from the University of Otago introduced herself to the Committee. She is conducting research on the ethical issues considered by HDECs when they assess applications for access to clinical data or tissue for secondary use without patient consent. This is a Marsden fast Start grant project. As an introduction she will be attending one of our committee meetings as an observer. She will then return later in the year to conduct a focus group, scheduled as part of a regulate meeting. Committee members may choose whether to participate in the focus group, and each participating member will be giving their own consent Individual members will also have the opportunity to participate in personal interviews if they have more to say on the topic.
* The observation session is to allow Dr Ballantyne to get a feel for how the meetings run as each committee has its own approach. The observation session will serve as a background to the research itself (focus groups and interviews) and allows the committee to get to know her prior to the formal research. Dr Ballantyne is interested in group processes not individuals or specific applications. Her aim is to describe the sorts of issues raised in relation to applications for secondary use of clinical material, not to critique specifics decisions.

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

|  |  |
| --- | --- |
| **Meeting date:** | 08 November 2016, 12:00 PM |
| **Meeting venue:** | Novotel Ellerslie, 72-112 Greenlane Road East, Ellerslie, Auckland |

1. **Problem with 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 5.40pm