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| **Committee:** | Northern A Health and Disability Ethics Committee |
| **Meeting date:** | 17 July 2018 |
| **Meeting venue:** | Novotel Ellerslie, 72-112 Greenlane Rd East, Ellerslie, Auckland |

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| **Time** | **Item of business** |
| 1:00pm | Welcome |
|  | Confirmation of minutes of meeting of 19 June 2018 |
| 1:30pm | New applications (see over for details) |
|  | i 18/NTA/99  ii 18/NTA/104  iii 18/NTA/107  iv 18/NTA/108  v 18/NTA/110 |
| 5:00pm | General business:   * Noting section of agenda |
| 5:30pm | Meeting ends |

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| **Member Name** | **Member Category** | **Appointed** | **Term Expires** | **Apologies?** |
| Dr Brian Fergus | Lay (consumer/community perspectives) | 11/11/2015 | 11/11/2018 | Present |
| Dr Karen Bartholomew | Non-lay (intervention studies) | 13/05/2016 | 13/05/2019 | Present |
| Dr Christine Crooks | Non-lay (intervention studies) | 11/11/2015 | 11/11/2018 | Present |
| Dr Kate Parker | Non-lay (observational studies) | 11/11/2015 | 11/11/2018 | Present |
| Dr Catherine Jackson | Non-lay (health/disability service provision) | 11/11/2016 | 11/11/2019 | Present |
| Ms Toni Millar | Lay (consumer/community perspectives) | 11/11/2016 | 11/11/2019 | Present |
| Ms Rochelle Style | Lay (ethical/moral reasoning) | 14/06/2017 | 14/06/2020 | Apologies |

## Welcome

The Chair opened the meeting at 1:00pm and welcomed Committee members, noting that apologies had been received from Mrs Rochelle Style.

The Chair noted that the meeting was quorate.

The Committee noted and agreed the agenda for the meeting.

## Confirmation of previous minutes

The minutes of the meeting of 19 June 2018 were confirmed.

## New applications

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| **1** | **Ethics ref:** | **18/NTA/99** |
|  | Title: | MK3475 - 811 |
|  | Principal Investigator: | Dr Ben Lawrence |
|  | Sponsor: | ANZ MSD |
|  | Clock Start Date: | 05 July 2018 |

Dr Ben Lawrence, Sara Derballa and Lisa Fong 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.

Dr Kate Parker declared a potential conflict of interest, and the Committee decided to have Dr Parker not take part in discussion or decision of this application.

Summary of Study

1. MK3475 -811 is a Phase III, Randomized, Double-blind Trial Comparing Trastuzumab Plus Chemotherapy and Pembrolizumab With Trastuzumab Plus Chemotherapy and Placebo as First-line Treatment in Participants With HER2 Positive Advanced Gastric or Gastroesophageal Junction Adenocarcinoma. Approximately 692 participants will be randomized in the Global Cohort in a 1:1 ratio to receive pembrolizumab or placebo each in combination with chemotherapy plus trastuzumab.
2. The investigator has 2 chemotherapy regimen choices, FP or CAPOX, which must be chosen prior to randomization in the trial. All participants will receive trastuzumab. Participants should continue on the fluoropyrimidine and platinum chosen prior to randomization throughout the study. Exceptions may be permitted after consultation with the Sponsor. Participants will be stratified by geographic region, PD-L1 status, and chemotherapy treatment prior to randomization.

Summary of ethical issues (resolved)

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

1. The Researchers were commended on the readability of the PIS despite its complexity, and the helpful format of the drug side effects.
2. The Committee queried whether Trastuzumab was standard of care in New Zealand.
3. The Researcher(s) stated Trastuzumab is not funded, so is not offered with chemotherapy. If it was funded they would use it in New Zealand, adding in other countries it is standard of care and funded.
4. The Researcher(s) explained that in all study arms the participants would get better treatment than provided standardly in New Zealand, as both arms get Trastuzumab.
5. The Committee asked for an update on continued access. The Researcher(s) explained sponsor is providing funding for 2 years, and not beyond this period. The Researcher(s) explained the survival context for this study population is 6-7 months.
6. The Researcher(s) explained that if the intervention arm does well and survival is longer than 6-7 months, they would run out of funded Transtuzumab. In that situation the Researcher(s) would seek other sources of Transtuzumab.
7. The Researcher(s) explained the funding options available to provide continued access.
8. The Researcher(s) stated they cannot guarantee further funding for continued treatment after 2 years, but would try, and think it is feasible.
9. The Committee asked why one standard of care chemotherapy treatment option over another would be chosen. The Researcher(s) explained that it means no centres are excluded. This reflects local practice standards of care, and enables flexibility in relation to co-morbidities.
10. The Committee noted participants retain the right to access their own health information at any time. They should know if they do so it may result in withdrawal from the study.

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 asked about clarification of the requirement for tissue collection, testing and storage. The sponsor is to clarify the tissue storage, biomarker testing and biobanking. Specifics are in point 20.
2. The Researcher(s) confirmed they will send insurance certificates once they update. The Committee asked for assurance that the amount was enough to cover injuries equivalent to ACC.

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

1. Make the comparator clear about its funding status and approval status, in New Zealand.
2. Define ‘cycle’ as 3 weeks.
3. ‘either’ with regards to how long you will be in the study.
4. The Researcher(s) confirmed all patients having chemotherapy will undergo hepatitis testing. This is standard. HIV testing is part of the protocol from the company point of view. This is because it is standard for Transtuzumab. The Committee requested the paragraphs in relation to this need rewording, stating it is a requirement in New Zealand. The Committee also noted both HIV and Hepatitis are notifiable diseases, please explain what this means.
5. The Committee asked whether there would be CT or MRI scans. The Researcher(s) explained MRI if liver predominant, but mostly CT scans. MRI could be removed, it was left in from another study and is unlikely. The Committee asked whether the frequency of CT scan is above standard of care. The Researcher(s) noted it was slightly above standard of care rate of testing.
6. The Committee asked about archival tissue, or fresh tissue. The Researcher(s) stated archival. The Researcher(s) confirmed this was to confirm eligibility. The Researcher(s) stated it is compulsory. Please make this clear, particularly what is mandatory and what is optional. Currently in section 6 of the main PIS it is stated that collection of tissue for biomarker testing is mandatory. The Researcher(s) stated they would check the protocol and ensure the participant information sheet is accurate.
7. The Researcher(s) confirmed only ECHO will be used. The Committee requested remove MUGA from the participant information sheet.
8. Please state drug combination, rather than ‘the drug’.
9. Please view the HDEC website for updated ACC wording.
10. Section 19 and 20 seem to duplicate information, please attempt to reduce this information.
11. Please clarify what withdrawing means in this context too (for side effects)
12. The Committee asked whether year of birth is possible to use. Section 24, page 20 of the participant information sheet. The Researcher(s) explained that this would not be feasible. Please check with the Sponsor.
13. Have clear titles on the PIS written for optional components.
14. Please update Maori contact details to be local services.
15. Add details for where samples are stored (storage facility) (optional participant information sheet).
16. Define FP and CAPOX.
17. Confirm whether the consent form contains the usual elements as per the HDEC template.
18. Clarify the duration of data storage, currently states 50 years.
19. Clarify that in terms of participant access to their results on page 21 in New Zealand participants have the right to view and correct information, although this may have consequences for their ongoing participation in the study.

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 further information on the study design, in particular use of tissue(*Ethical Guidelines for Intervention Studies para* 5.4)
* Please provide information on sponsor insurance. *(Ethical Guidelines for Intervention Studies para 8.4).*

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

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| **2** | **Ethics ref:** | **18/NTA/104** |
|  | Title: | Exploring medication safety with frail older people with multi-morbidity and their families and whānau across care transitions |
|  | Principal Investigator: | Dr Aileen Collier |
|  | Sponsor: | University of Auckland |
|  | Clock Start Date: | 05 July 2018 |

Dr Aileen Collier 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. Older frail people with multiple chronic conditions often see many different healthcare providers and take multiple medications (polypharmacy), therefore are at increased risk of adverse drug events during the frequent care transitions they experience. A care transition can be defined as movement along healthcare professionals, care settings and/or organisations (including primary care, specialist services, hospitals, aged residential care) and as their care needs change.
2. This research will make a unique contribution to the international and national evidence base by exploring how medication safety is enacted and negotiated across care transitions by applying a strengths-based approach and using an innovative research method video-reflexive ethnography to examine care transitions. Video-reflexive ethnography involves negotiated videoing of everyday practices and/or experiences and co-interpretation of the footage to make sense of visual data.
3. This study will draw upon the expertise of older Māori and non-Māori, as well as clinicians and researchers to uncover how medication safety is defined, managed and negotiated across care transitions.

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 this was a complex study with a range of different study methods.
2. The Researcher(s) explained that this was a feasibility study, with a view to conduct a larger study.
3. The Researcher noted that she was an experienced practitioner with the study methods and had undertaken these in other care settings.
4. The Researcher was commended by the Committee for the study team supporting the study and the structure of the advisory groups and Māori participation across these elements.
5. The Researcher(s) confirmed that there will be an initial cohort of 20 participants who will be interviewed, and from this a cohort of up to 6 participants for the main ethnography component would be selected. This second part of the study will require a longer term relationship over about 12 months where the initial participant will nominate the health professionals involved in their medication processes, and the researchers will seek their consent to document relevant medication related interactions with the participants. This will include further participant and whanau interviews, and interactions with pharmacists, geriatricians, GPs. nurses, social care workers etc.
6. The Researcher(s) may wish to consider a different information sheet for the initial 20 participants as the main procedure is an interview – this information sheet could mention that a small number may be invited to a longer term interaction and seek consent for further contact about this.
7. This more in depth component is then followed up with participant (and others) viewing of various edited components of the videos, including a second group reflexive session which becomes part of the research itself in this methodology. The Researcher(s) agree that this is a substantial time commitment.
8. The Researcher(s) confirmed that it was only patient related, medication related, interactions, not general procedures.
9. The Researcher(s) confirmed participants are determined to have capacity to consent by clinicians, and researchers will monitor this during the study to ensure they remain competent.
10. The Researcher(s) confirmed videoing is optional, and forms part of the exploratory nature. The Researcher outlined the ongoing iterative process of consent throughout the study, and the importance of this to the research methodology.

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) confirmed that identifying who will conduct/participate in the reflexive viewing part of the study is part of the exploratory aspect of the study, in terms of comfort and consent from the participants. At this stage the roles of participants invited for this aspect is not set in stone. The Committee noted this is a challenge, as health care professionals may not know who will end up observing them. Further information is required both for all participant groups that better covers the nature of the study and its phases/components (eg a diagram or table), who the participants might be at each step, the number and nature of potential interactions and their time commitment, and who might be involved in viewing the various video artefacts at the later stages.
2. The Researcher(s) noted that participants maintain control, and provide express permission. The Committee asked whether this control was for both patient participants and clinician participants. This aspect of the study required further consideration to protect all participants, and consent forms require modification to reflect the various levels of consent (eg the participant nominating the various family, care workers and health professionals they wish to be invited to participate)
3. Please add more information on data management to the protocol and the participant information sheet.
4. Please submit the draft interview prompts.

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

1. Consider adding a picture/diagram or table to better explain the components of the study as above.
2. Pg.2 of participant form, given the nature of this study please record consent in writing. Verbal re-consent during filming is appropriate.
3. Add what the ‘significant risk’ is.
4. The Committee requested that the group of social carers, have their own participant information sheet, tailored to their potential participation requirements
5. The Committee noted the application does not identify any risks. The Committee noted however that there are confidentiality risks, potential risk of highlighting unsafe practices, risks in care. The Researcher(s) are requested to consider and outline in the PIS their duty of care to report if issues identified. There may also be risks to other people’s employment for the social carer group and potentially health professionals. Those risks should be explained and their mitigations outlined.
6. Please make the participant information sheet clear, particularly in relation to the 6 index participants invited to the longer in depth piece. This will require the participant to nominate specific individuals
7. Make the time commitment clear, particularly for different cohorts, and all of the different types of study procedures.
8. Please review all PIS documentation to ensure that the participant rights reflect the study methods eg right to withdraw, correction of information, return of results, to stop recording or take a break if become distressed or tired etc.
9. Please consider revising jargon even for health professionals eg ‘care transitions’.
10. Add ACC wording, review the template participant information sheet from HDEC website.
11. There is some confusion with the term anonymous, however the research required the various components to know the index participant, and the viewing of video footage will require this also. Consider being explicit about this, and discussing the de-identification of materials to be undertake for the purposes of use outside of the agreed participants and study team members.
12. The term ‘comply with the law’ eg participant PIS page 4 is not required.
13. The PIS need Māori cultural contact details and HDEC approval details.
14. Consent form doesn’t require Y/N options unless truly optional, see HDEC website for updated template.

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*).
* Explain what happens to health information (*Ethical Guidelines for Intervention Studies* *para 7.7)*
* Submit questionnaires(*Ethical Guidelines for Intervention Studies para* 5.4)

This following information will be reviewed, and a final decision made on the application, by Dr Karen Bartholomew and Mrs Toni Millar.

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| **3** | **Ethics ref:** | **18/NTA/107** |
|  | Title: | Lateral Ankle Ligament Augmentation Trial (LALA) |
|  | Principal Investigator: | Dr Shea Timoko-Barnes |
|  | Sponsor: |  |
|  | Clock Start Date: | 05 July 2018 |

Dr Shea Timoko-Barnes was not present for discussion of this application.

Potential conflicts of interest

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

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

Summary of Study

1. This is a multi centred prospective RCT will be conducted by participating surgeons across New Zealand in patients aged older than 18 with ankle instability or pain following grade 2-3 ankle sprain and having completed a minimum of 3 months non-operative treatment.
2. The study compares augmentation of lateral ankle ligament repair with the Internal Brace versus lateral ankle ligament repair alone, with the goal of improved functional outcomes at 3 month.
3. For future reference, application forms should be stand alone and questions should not be answered with.

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 asked what ‘self-funded surgery’ means.
2. Please explain what monitoring of safety data occurs, particularly for adverse events.
3. The Committee noted the economic analyses do not appear robust, and the Researcher may wish to undertake further advice or reconsider this aspect.
4. The Committee noted that although the Protocol was well prepared, the literature review appeared light. For example the Committee queried whether the available publication ‘clinical results of an arthroscopic modified Brostrom operation with and without an internal brace’ impacts the knowledge gap J Orthop Traumatol. 2016 Dec;17(4):353-360. Epub 2016 Apr 23. An RCT is unethical if the knowledge is already known.
5. The Committee noted the statistical advice undertaken, however was not clear what the primary endpoint was and the change anticipated in order to arrive at the sample size. This may have been undertaken but was not clear in the protocol.
6. Explain what process occurs if incidental findings, such as depression identified in the questionnaires, are identified.
7. Please explain whether this study is for an educational qualification.
8. The Committee noted the peer review comment on whether the different post operative rehab course would impact on the study outcomes, and seeks clarification from the Researcher(s).

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

1. Please clarify the two methods eg what is usual care and what is the intervention. The Committee noted that this would be enhanced with the addition of a picture.
2. Please clarify risks, both for the usual care and the intervention, including their frequency/likelihood where known. Add frequency of follow up and time commitments for participants.
3. Review the HDEC template for informed consent on the HDEC website and include all relevant information, particularly on privacy and confidentiality.
4. Please explain whether the brace is permanent, and if so whether it is removed if there is a problem.
5. Participants have the right to a summary of results. Please explain what will happen.
6. Explain the differences in post-op rehab for the two methods.
7. Please revise for lay language and consider a more invitational beginning of the PIS.
8. Explain whether there is a disclosure of what arm the participants was in, at the end of the study.
9. Remove ‘unlikely’ from ACC wording.
10. Clarify duration participant involvement. It appears to be longer in the participant information sheet (36 months). This may refer to the study enrolment period; if so please revise.
11. Remove Y/N from the consent form unless truly options, see updated HDEC template on the website.

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*).
* Every study question should be based on a thorough review of the relevant literature. Please address whether this study question is already answered. (*Ethical Guidelines for Intervention Studies* *para* 5.3).
* The intended number of participants in an intervention study should be sufficient to generate reliable study findings, and the consequent recruitment targets should be realistic. Statistical issues relating to trial design, sample size and analysis can be complex, and usually require expert advice. Please justify number of participants. (*Ethical Guidelines for Intervention Studies* *para* 5.6).

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

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| **4** | **Ethics ref:** | **18/NTA/108** |
|  | Title: | Objective measures and gender differences of sports-related mTBI |
|  | Principal Investigator: | Josh McGeown |
|  | Sponsor: |  |
|  | Clock Start Date: | 05 July 2018 |

Josh McGeown was present in person for discussion of this application. There was no supervisor present.

Potential conflicts of interest

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

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

Summary of Study

1. The aim of this prospective cohort study is to investigate the clinical utility of an objective assessment battery to measure bodily (physiological) and brain functions in individuals with suspected sports-related mild traumatic brain injury (mTBI) who have been referred to the Axis Sports Medicine mTBI clinic. Specifically, this objective battery includes measuring variability of heart rate, saliva samples to detect proteins linked to brain health, postural stability, and brain connectivity. Currently, Axis Sports Medicine conducts a comprehensive medical examination along with evaluating mTBI using the Sport Concussion Assessment Tool version 5 (SCAT-5), subjective symptom scoring, and a validated treadmill stress test.
2. This objective battery will be integrated within current Axis Sports Medicine clinical practice in order to determine if current clinical measures combined with this objective battery accounts for more variance in days to recovery following sports-related mTBI than current clinical measures alone. The objective battery will include non-invasive collection of a 2 mL saliva sample, completion of a Brain Gauge assessment, designed to measure how the brain responds to external stimulus, and a measuring postural stability as well as variability in heart rate during the treadmill stress test using a device called a BioHarness.
3. This data will provide insight regarding if changes in heart rate variability, proteins within saliva, brain cell connectivity, or postural stability aid in gaining a better understanding of mTBI symptoms and recovery. The results of this study will provide a greater understanding of which objective measures of may be clinically useful in objectively identifying abnormalities in other individuals recovering from sports-related mTBI. To date, little is known about the underlying mechanisms responsible for mTBI symptoms, the data from this prospective cohort study would help guide future investigations.

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 Researcher(s) for their comprehensive approach to this study, and thorough preparation.
2. The Researcher(s) and The Committee discussed the peer review.
3. The Researcher(s) confirmed all adults will consent for themselves, and assent for young children.
4. The Researcher(s) explained the importance of the study, in reducing harm from injury.
5. The Researcher(s) explained the plan if incidental finding of depression is raised during screening. Clinical referral pathways are in place. The Researcher(s) confirmed that this is standard of care.
6. The Researcher(s) explained that results from the study will not be clinically relevant. In terms of their rehab, the clinicians will be managing this. A summary of the study will be released to participants.
7. The Committee asked about recruitment. The Committee noted clinicians are required to screen information for eligibility criteria. The Researcher(s) explained the recruitment processes.

Summary of ethical issues (outstanding)

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

1. Add that this study is being conducted for a PhD.
2. The Committee requested that all participant information sheet and assent forms are uploaded.
3. The Researcher(s) noted age range could be between 8-71 years old. The Committee also queried whether it was necessary to include younger participants in this study. I think we were satisfied with the researcher response that there is an unmet need and lack of knowledge in this area and were satisfied to allow the inclusion of minors in the study. The Researcher(s) noted mild TBI is very relevant for children. The Committee noted the adult participant information sheet would be different from the parent.
4. The Committee noted children’s data should be stored for 10 years following those turning 16.
5. The Committee noted samples can be destroyed following testing but the data can be stored and a duration was required.
6. The Researcher(s) stated study results will not be added to clinical notes, at this stage, due to lack of clinical relevance. Add this detail in the participant information sheet, and explain why the results are not planned to be returned. It was noted that participants have the right to request their rights should they wish, and that requires consideration for those results only collected for the study.
7. The Committee noted if results are asked for, they will need to be provided.
8. The Committee noted that there is another PhD being conducted on gender differences, which will feed into this study. The Committee noted if it is for this study, please add it as a study procedure.
9. Consider how any incidental findings from the hormone testing will be dealt with.

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

1. The Researcher(s) noted this is a proof of concept or feasibility study for an RCT. The Committee requested that this is explained in the participant information sheet.
2. Clarify that the research is seeking to access health information collected as part of usual care for the study, as well as conducting study-specific additional components. Access to health information is a procedure. Consider use of the HDEC template, please see updated template on the HDEC website.
3. The Researcher(s) explained the mobile phone app. It is a concussion tool. Data is not shared outside of clinicians, stored on password protected servers. Explain this in the participant information sheet, and that the study is seeking consent to access this information.
4. Add an introduction participant information sheet, how the participant was identified etc.
5. Consider the phrase ‘why some people feel differently after brain injury’ which may be confusing to participants.
6. Consider downplaying the individual benefit, note benefit for others, adding to scientific knowledge etc.
7. Add the additional study-specific components to the treadmill test, as well as the additional to usual care study components of the saliva sample each visit and questionnaires (eg re hormone status/menstrual cycle information), and add how long the visits are.
8. Add standard ACC wording from the participant information sheet template found on the HDEC website.
9. Add more options on the consent form for the adult participant information sheet.
10. Make it clear that it is ‘observing clinical practice, with some additional tests’ as ‘what the study is’. It is clear in the advertisement.
11. Ensure time estimate is included, including duration of follow up.
12. Please add funding in the participant information sheet.

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 Catherine Jackson and Mrs Toni Millar.

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| **5** | **Ethics ref:** | **18/NTA/110** |
|  | Title: | B-FAST: BLOOD-FIRST ASSAY SCREENING TRIALB-FAST: BLOOD-FIRST ASSAY SCREENING TRIAL |
|  | Principal Investigator: | Dr Laird Cameron |
|  | Sponsor: | Roche Products (New Zealand) Limited |
|  | Clock Start Date: | 05 July 2018 |

Dr Gillian Vernon, Dr Laird Cameron 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 study involves performing blood tests that will determine if a potential participant's blood contains indicators of certain circulating tumour DNA markers from their Non Small Cell Lung Cancer (NSCLC), which would qualify them for specific treatments in the second part of the study. Depending on the results of the blood tests, a prospective participant may qualify to receive a study treatment matched to the genetic signature of their NSCLC.
2. The overarching structure of the B-FAST study is an umbrella screening and interventional study, which will screen patient blood samples for the presence of potentially oncogenic somatic mutations (an experimental procedure, currently only done on tumour tissue) and biomarker positivity by the blood tumour mutational burden (bTMB) assay in NSCLC via blood-based assays, and will treat patients with a drug or drug regimen tailored to their results. Initially, three cohorts testing the efficacy and safety of therapy directed at specific mutations or biomarkers (ALK, RET, and biomarker positive by the bTMB assay) will be implemented.
3. Additional cohorts may be added to address various identified somatic mutations or other biomarkers via future protocol amendments. Each cohort may have separate endpoints, screening, and treatment requirements and will be instigated via protocol amendments should the need arise.
4. The Committee noted that a cover sheet should explain the complex umbrella protocol with a diagram, with what is standard of care, etc. This is a note for future applications.

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 the method of doing the test is experimental.
2. The Researcher(s) explained there has been an amendment. Arm B is closed. Arm A and C are open.
3. The Researcher(s) confirmed that participants will receive different drugs depending on the results of the blood tests.
4. The Researcher(s) explained the standard of care testing in New Zealand. The Committee asked how this study interacts with standard of care testing. The Researcher(s) confirmed they are not looking at patients who are EGFR positive. If we know this already, we will not enrol them into this study, as there is a target treatment already. If an EGFR mutation is identified as part of the screening test for this study, the patient will revert to standard of care, publically funded.
5. The Researcher(s) confirmed the study is being submitted to SCOTT.
6. R.1.6 – termination of the study. The Committee asked what would happen for participants already enrolled, if study is terminated due to low enrolment. The Researcher(s) stated all participants already enrolled will continue with study treatment.
7. The Researcher(s) confirmed that study scans mirror what is reflected in standard of care.
8. The Committee asked whether there are support processes in place for incidental findings such as depression. The Researcher(s) stated there are referral pathways in place.

Summary of ethical issues (outstanding)

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

1. R.3.7 – tissue stored for a minimum of 15 years. Please put a maximum period. The Researcher(s) stated they think it is 25 years. Please confirm with the Sponsor.
2. The Committee asked about the tissue repository (RBR) referred to in questionB.4.5.2 and in each participant information sheet. The Researcher(s) confirmed it is Roche owned. The Committee asked that more detail is provided on where this facility is based (this information must also be added to each participant information sheet).
3. In the application form (r.5.4) it states that the PI for the study will not be the oncologist for any patients enrolled into the study. Please confirm this is the case, or if not, outline how the PI will avoid any risk of patients feeling coerced to participate.

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

1. In the initial screening PIS (first part of the study) please make clear that the diagnostic screen using circulating tumour DNA is also experimental. Please reconsider the term ‘qualify’ for the study and consider invite or similar.
2. The Committee asked about incidental findings. The Researcher(s) explained that there may be other genes that drive cancer that do not correlate to treatment cohort. Participants need to be aware of this, and that the test may identify rare mutations where either New Zealand does not have targeted treatment funded or where there is no current treatment availableThe Committee noted this is not clear. The Researcher(s) confirmed they are running a panel, not just three genes. The Researcher(s) stated foundation report is given to Dr in order to then go to participants. The Committee requested information on incidental findings and return of results needs to be very clear in the participant information sheet, including stating that participants can request to see their results if they wish.
3. The Committee asked whether the participants’ family will be provided summary of results in event of participant passing away. The Committee requested that it is checked whether the participant is alive before sending, to reduce the risk of harm to family.
4. The Committee asked about ethnicity data collection. The Researcher(s) acknowledged the global study will not use New Zealand ethnicity, but local collection will follow census. Please localise terminology eg remove ‘race’ from page 3 of the participant information sheet, and remove IRB.
5. Please explain the diary in the participant information sheet as a study procedure, and provide an estimate of the time required to complete this.
6. Please add information on all study visits required, including an estimate of the time required. Participants need to be aware of the time commitment of being involved in the study.
7. The Committee asked about exploratory biomarker studies. The Researcher(s) agreed that it was ambiguous, and would clarify with Roche. The Committee noted it reads like it is future unspecified research. The PIS should explain clearly what tests are to be done if this is a mandatory part of the study. If it is future unspecified research it will need to be optional, ideally removing this from the main PIS and adding it to the optional participant information sheet.
8. The Committee asked about the privacy wording, asking whether ‘research samples’ will really go ‘all over the world’. The Researcher(s) stated this was in relation to de-identified data, and noted this was not clear. Please confirm with the Sponsor that research samples will not be sent to anywhere in the world.
9. Page 6 of screening participant information sheet. The Committee asked what side effects of blood tests were expected.
10. Please explain what ‘performance status’ means on page 3 of the screening participant information sheet. Please remove jargon, generally.
11. Participant information sheet for cohort A on page 1, future unspecified research, please outline what tests might be, currently it is too ambiguous. Please remove the reference to “any additional samples your doctor decides to collect during the study” all samples collected should be as per the protocol and outlined in the PIS
12. Pregnant partner participant information sheet – cohorts A. The Committee noted the participant information sheet reads like a consent form. This should be re-written as a participant information sheet. This should be signed by the pregnant partner, not the participant. Please also confirm no health information on the child would be collected.
13. Also, add detail on what data is to be collected from the pregnant partner, privacy information etc.
14. Please also add a consent form for a potential pregnant participant (rather than a pregnant partner), as this is also a possibility.
15. Please review all tissue use and provide an overview of what is and is not optional.
16. Please specify what additional research, and where samples are going.
17. Tumour tissue information needs to outline risks of biopsy. The Researcher(s) noted it will primarily be archival samples. The Committee noted this could be made a lot clearer for participants. If no fresh biopsies are to be taken, then this section should be removed from the PIS.
18. Spell out standard of care in the participant information sheet, including options for participants once they stop the study due to disease progression or adverse events.
19. The consent forms are very brief, please view the HDEC template for guidance, on the HDEC website.
20. For cohort C, please add that HIV is notifiable earlier than it currently is stated.
21. Revise for grammar, layout, taking into account the HDEC template.
22. Add approval status of the drug(s) in New Zealand.
23. Please change compensation to new ACC wording from the HDEC template.
24. On the pregnancy form, please note there is no requirement to withdraw in writing in New Zealand. The Committee suggested building the participant information sheet for potential when participants may get pregnant.

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 further information on the study design, in particular use of tissue(*Ethical Guidelines for Intervention Studies para* 5.4)

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

## General business

1. The Committee noted the content of the “noting section” of the agenda.
2. The Committee discussed a complaint made to the Committee about the review of application 18/NTA/85.
3. The Chair reminded the Committee of the date and time of its next scheduled meeting, namely:

|  |  |
| --- | --- |
| **Meeting date:** | 21 August 2018, 01:00 PM |
| **Meeting venue:** | Novotel Ellerslie, 72-112 Greenlane Rd East, Ellerslie, Auckland |

The following members tendered apologies for this meeting.

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 4:00pm