|  |  |
| --- | --- |
| **Committee:** | Northern B Health and Disability Ethics Committee |
| **Meeting date:** | 19 December 2017 |
| **Meeting venue:** | Novotel Ellerslie, 72-112 Greenlane Road East, Ellerslie, Auckland |

|  |  |
| --- | --- |
| **Time** | **Item of business** |
| 12.00pm | Welcome |
| 12.05pm | Confirmation of minutes of meeting of 7 November 2017. |
| 12.30pm | New applications (see over for details) |
|  | i 17/NTB/230  ii 17/NTB/234  iii 17/NTB/235  iv 17/NTB/236  v 17/NTB/237  vi 17/NTB/238  vii 17/NTB/239  viii 17/NTB/240  ix 17/NTB/241  x 17/NTB/242  xi 17/NTB/243  xii 17/NTB/249 |
| 5.20pm | General business:   * Noting section of agenda |
| 5.30pm | Meeting ends |

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| **Member Name** | **Member Category** | **Appointed** | **Term Expires** | **Apologies?** |
| Mrs Maliaga Erick | Lay (consumer/community perspectives) | 01/07/2015 | 01/07/2018 | Present |
| Mrs Stephanie Pollard | Non-lay (intervention studies) | 01/07/2015 | 01/07/2018 | Present |
| Miss Tangihaere Macfarlane | Lay (consumer/community perspectives) | 20/05/2017 | 20/05/2020 | 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 | Present |
| Mrs Jane Wylie | Non-lay (intervention studies) | 20/05/2017 | 20/05/2020 | Present |

## Welcome

The Chair opened the meeting at 12.00pm and welcomed Committee members.

The Chair noted that the meeting was quorate.

The Committee noted and agreed the agenda for the meeting.

## Confirmation of previous minutes

The minutes of the meeting of 7 November 2017 were confirmed.

## New applications

|  |  |  |
| --- | --- | --- |
| **1** | **Ethics ref:** | **17/NTB/230** |
|  | Title: | POPE-flow |
|  | Principal Investigator: | Dr Nicola Broadbent |
|  | Sponsor: |  |
|  | Clock Start Date: | 07 December 2017 |

Ms Davina Macalister, Dr Nicola Broadbent, Ms Sarah Dandy and Ms Clare Howard 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. The study aims to evaluate operating room efficiency at Auckland City Hospital. An indicator of this is operating theatre utilisation time. The utilisation rate in any theatre will change on a daily basis, depending on numerous factors. Efficiency can be dependent on factors that cause delays such as: transfer delays, consent issues, delayed decision making, missing equipment, communication problems, etc. It is harder to determine theatre efficiency in acute theatres, in comparison to elective ones, because they are technically available for 24 hours, but also often have prolonged periods of inactivity between 10pm and 8 am.
2. This study will investigate the efficiency of acute theatres at Auckland City Hospital by looking at: time between acute cases in theatre, time taken for patients to reach theatre, empty theatre times and possible reasons why delays occurred.
3. The information from this study will be used to assess the quality of the system in place and provide insight into areas that could be improved; ultimately in hopes to lead to improved patient satisfaction.
4. The study will collect four weeks of data (24 hours, 7 days) of all patients entering pre-op. The information collected for each patient is outlined in the CRF attached to this application.
5. The Committee stated that the description of this research fits into the audit and related research criteria. There is use of patient information but this is primarily to collect non-health information within the patient information. Output is service improvement/service delivery which would indicate audit and related activity.

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 the researcher whether they think this is research rather than quality improvement. The Researcher(s) explained that they would be collecting more data than usual, and would potentially lead to change care, but acknowledged that they were not certain that it was either research or quality improvement.
2. The Committee asked about the possible changes that may result from the data collection. The Researcher(s) noted possible changes would be moving surgical preparation to the ward, which could streamline processes. Another aspect was identifying what aspects of care are being delivered prior to patients having adequate engagement with clinical staff. Lastly, there could also be team changes. All of these changes require baseline data to measure against.
3. The Researcher(s) confirmed some clinical personal data is required, but mainly procedural data.
4. The Committee noted publication can occur without the project changing the activity to research.
5. The Researcher(s) explained the consent issues were due to the vulnerability and acute context.
6. Please explain who would be collecting the data from charts. The Researcher(s) stated for the data that is not recorded currently, there will be a general encouragement to record this data from existing staff, driven by the CI and also the quality assurance nurse specialist.
7. The Committee asked the researcher to confirm data collection is retrospective. The Researcher(s) stated all patients will have the new data recorded at the time, and it will be accessed retrospectively for the analyses.
8. The Researcher(s) and The Committee discussed at length the distinctions between QI and research.
9. The Committee noted that quality improvement often involve cycles of interventions that are linked to assessment that have the goal of improving the process, outcome, and efficiency of complex systems of health care. Quality improvement activities can blur the line between research and non-research.
10. Systematic investigation that characterises research may also be an element in other non-research activities. However, a systematic approach using the scientific method is not the same as research intent.
11. The intent of activities is one way to determine whether a project is research or not. Research and audit can be distinguished by examining the justifications (intent) for the different activities. The justification for research is to gain knowledge that can be used to benefit others apart from the participants. While some participants may benefit from the activity, this is not the justification for it. The justification for audit and related activities is to improve health care delivery. If a project started with a non-research intent and resulted in findings or knowledge that extended beyond the scope of the original project, it does not retrospectively change the intent of that project into a research intent.

Decision

The Committee determined that this study was not health research and was not within scope for HDEC review.

|  |  |  |
| --- | --- | --- |
| **2** | **Ethics ref:** | **17/NTB/234** |
|  | Title: | Clostridium Difficile Infection: Prospective ribotype analysis from a rural secondary care centre |
|  | Principal Investigator: | Dr Matthew Johnston |
|  | Sponsor: |  |
|  | Clock Start Date: | 07 December 2017 |

Dr Matthew Johnston 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 aims to provide descriptive data regarding subtypes of clostridium difficile causing infection; clostridium difficile causes a form of infectious diarrhoea and is usually associated but not always associated with antibiotic use.
2. Participants will be prospectively identified by toxin-positive stool specimens submitted for testing for the specific bacteria. Positive stool specimens will be processed further to culture and identify the specific variety of bacteria in the sample. This is considered an extension of routine care in some centres, however is not routine practice in New Zealand. The information generated will not affect patient diagnosis or treatment in any way.
3. Cases will be matched to controls who will be other cases of acute diarrhoea with a negative test for the specific bacteria. Descriptive data will be collected from electronic and physical patient records regarding basic demographic information, as well as comorbidity, laboratory data, prescription and dispensing records and hospital attendance.
4. There will be no direct involvement of cases or controls, and data collection will not affect medical care. Data will be anonymised at the time of collection where possible.
5. Faecal specimens will be processed and handled according to laboratory protocol. Tissue will not be stored after processing/testing.
6. The anticipated benefits include improved understanding of the epidemiology of the disease in New Zealand, and data may be contribute to future surveillance programmes which are being developed. This study would be expected to contribute to our general knowledge of the condition, and hopefully contribute to developments in treatment and testing.

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 use of samples without consent was justified by the researcher.
2. The Committee asked about the increased data use, including de-identification and how results from samples will be managed. The Researcher(s) explained cases may result in positive toxin tests, which will be identifiable, as the laboratories process these. This will involve NHI. For study purposes, it is not important to know identifiable information. The laboratory will notify that a sample is positive, the NHI will be used to extract data from the electronic data base and paper records, but that data is stored in a format that is not identifiable. The Researcher(s) acknowledged that as some would require further linking, the specimen would be given a case number, which enables specimen results being linked from specimen result to demographic data etc. The data stored with researchers will be in a form that is not identifiable. Recurrent cases would be identified as best as possible, but it will not be able to be directly attributable to the first case that happened.
3. The Committee noted that the link would remain so they could link recurrent cases. The Researcher(s) stated they did plan to break the link, as the risks with this study are risks of confidentiality and risks to data. The link will be broken right after data collection.
4. The Committee asked if the laboratory can manage potential repeat cases. The Researcher(s) explained that recurrence during the study period would have already had a positive test. The Researcher(s) confirmed they would check records and take recurrent cases out.
5. The Researcher(s) explained that they are using three different laboratories. Once specimen is given a case number all correspondence would use the case number. Other laboratories will not use any identifiable data. Data is reported electronically via email.
6. Please explain why it is not feasible to consent participants for use of their data. The Researcher(s) explained for the descriptive research study, the process of obtaining informed consent, explaining it and getting direct consent, would be onerous for patients – as this would not impact their life, as well as the logistics for the study may be prohibitive. The Committee noted respecting people is the cornerstone of research, but noted the cases made for not seeking consent.
7. Please explain adverse events being reported to the chief medical officer. The Researcher(s) explained that this is an institutional protocol requirement. This relates to any breaches of confidentiality etc.
8. Please comment on sample size and feasibility. The Researcher(s) explained the rationale, explaining how many cases were reported recently. This data is not solid incidence data, which is not available locally. The Researcher(s) noted assays are changing as well, which could increase or decrease false positives.
9. The Committee noted ethnicity collection questions required updating to be in line with census protocols. The Researcher(s) confirmed that it was.

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 the scientific validity of the case-control study. Please justify choice of acute diarrhoea cases as controls for establishment of primary risk factor (PPI use) as PPI use has also been associated with other forms of infectious diarrhoea. The Committee queried whether there was any other control available.
2. The Committee suggested powering by age or living in rest homes, but the current measure (PPI use) may cause scientific validity problems.
3. The Committee suggested further peer review around case control for the study.
4. Please explain the rate of successful culture of C.difficile from a toxin +ve specimen. The Researcher(s) explained that they were not too sure of the figure. The Committee suggested checking this study factor to ensure power takes into account cases that are lost.

Decision

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

* Please provide evidence of favourable independent peer review of the study protocol, taking into account the case control and power of the study (*Ethical Guidelines for Intervention Studies* Appendix 1).

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

|  |  |  |
| --- | --- | --- |
| **3** | **Ethics ref:** | **17/NTB/235** |
|  | Title: | BE10-1003: Study of the safety of increased doses of Citramel inhalation in healthy volunteers |
|  | Principal Investigator: | Dr Bridget Maher |
|  | Sponsor: |  |
|  | Clock Start Date: | 07 December 2017 |

Dr Bridget Maher 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. Citramel is being developed by Breathe Easy, Ltd. for patients with Cystic Fibrosis (CF). The purpose of this study is to investigate the safety and tolerability of increasing doses of Citramel inhalation in healthy volunteers. Three cohorts each of 5 healthy volunteers will receive the Citramel inhalation twice daily for 28 days. They will be assessed for safety and tolerability at the end of each week and will have a final followup call about 2 weeks after their last inhalation of Citramel.
2. This study will identify the doses to be used in further clinical studies of Citramel in CF patients. Safety will be assessed by vital signs, laboratory tests, spirometry, ECG, adverse events and symptoms. Previous Phase 2 studies in CF patients at a lower dose were safe but ineffective.
3. It is anticipated that Citramel will increase the clearance of sputum and therefore provide an improvement in lung function in people with CF. This may in turn reduce the number of pulmonary infections, providing an enhanced quality of life and leading to lower health costs.

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 Maori consultation will be submitted. The Committee asked for confirmation of this.
2. The Committee noted the stopping rules around haemoptysis: 2 participants have to cough up 50ml of blood in order to stop the trial. A healthy person should not cough up any blood. The Researcher(s) stated this is due to the difficult haemoptysis identification. The Committee noted if one person coughs up 20ml of blood this should be regarded as significant. Under the current rules this would not be considered significant, even if three people coughed up 20ml each.
3. Advertisement says 'a dose of study drug' rather than bd dosing for 28 days. Please amend
4. The Committee noted while a minor point, the MPS certificate for Dr Maher, PI, is at the reduced rate for a registrar/Fellow in training. Please confirm that this is the correct category for her so that Professional Indemnity is valid. The Researcher(s) confirmed that they are updating the indemnity.
5. The Committee suggested that date of birth and initials is not a confidential way to describe participants, people generally used a unique study number which has no trace of any potentially identifiable personal information.
6. Please specify if DSMB is internal or independent, and what is the process for data submission. The Researcher(s) stated they will have to clarify this.

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

1. PICF suggest that initials and DOB may be removed to 'de-identify. The Researcher(s) explained that labplus often use date of birth and initials. The Committee asked if this information goes to the sponsor. The Researcher(s) stated only on-site monitoring, actual results will only have study number and date of birth. The Committee strongly suggest the researchers go with unique number in every circumstance to prevent identification of participants. Data is also going to the sponsor and labtests in this form which is not appropriate. (application pr.2.4.1). The Researcher(s) confirmed for sponsor, no date of birth and no initials. The Committee stated they can confirm age for sponsor, but do not need to give date of birth.
2. The Committee noted there is no place on PICF to indicate wishing to receive summary of results, the line which may provide this doesn’t make sense and doesn't have a tickbox.

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 submit evidence of CI indemnity. (*Ethical Guidelines for Intervention Studies* *para 4.20)*
* Provide details of the Data Safety Monitoring Committee’s composition and monitoring plan *(Ethical Guidelines for Intervention Studies para 6.50).*
* Provide further information on the study design, *in particular the stopping rules* (*Ethical Guidelines for Intervention Studies para* 5.4)

This following information will be reviewed, and a final decision made on the application, by Mrs Leesa Russell and Mrs Tangihaere.

|  |  |  |
| --- | --- | --- |
| **4** | **Ethics ref:** | **17/NTB/236** |
|  | Title: | KCP-330-009: SADAL: Selinexor Against Diffuse Aggressive Lymphoma |
|  | Principal Investigator: | Dr Ruth Spearing |
|  | Sponsor: | Karyopharm Therapeutics Inc. |
|  | Clock Start Date: | 07 December 2017 |

Carolyn Lauren 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. Diffuse Large B-Cell Lymphoma (DLBCL) is an aggressive cancer with a median survival of < 6 months without treatment. With current immuno-chemotherapy, 60-65% of patients are progression-free at 2 years, ~30% are disease-free at 10 years. Remaining patients have a poor prognosis with disease resistant to available agents.
2. Selinexor is a new type of oral drug that works by trapping “tumour suppressing proteins” and other growth modulators within the cell causing the cancer cells to die or stop growing.
3. The aim of this study is to confirm the activity of selinexor, in relapsed and/or refractory (R/R) DLBCL in patients who have no therapeutic options of demonstrated clinical benefit.
4. This multicentre, open-label phase 2b study will include ~130 patients with R/R DLBCL who have ≥2 but ≤5 previous regimens and are not eligible for high-dose chemotherapy with stem cell rescue at the time of study entry.
5. Participants will take 60 mg selinexor orally twice weekly on Days 1 and 3 of Weeks 1 to 4 of each 4-week cycle (total of 8 doses per cycle). Patients should remain on study treatment until the assessment of progressive gisease (PD) from the central imaging laboratory has been obtained (unless medically contraindicated).

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 noted some biomarker studies on tissue are immediate and integral to the study. However, there is a suggestion of Future Unspecified Use of tissues in a way which is optional. See below from p.12: "Any blood or tissue samples obtained during the study may be retained for future research related to understanding DLBCL and how it responds to selinexor. Samples may be kept for a maximum of 15 years. If there are any remaining samples after that time, they will be destroyed. If at any time you decide to not allow your samples to be used for future research, you can notify your study doctor and your samples will be destroyed". The Committee queried the future genetic component, asking whether it is optional. If yes, then need separate PGX PIS & CF PIS.
2. Please provide incidence figures for Maori.

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

1. Add ‘reasonable’ travel expenses, including taxis, due to the driving restrictions.
2. Stopping for purely commercial interest is not acceptable under New Zealand ethical guidelines. Please remove this statement pg.13.
3. Consider putting study procedures in a table against visits.
4. Consider using word other than "treatment" when referring to study drug
5. Change restriction of "any other study" to any "other clinical trial".
6. Remove 'treatment option' phrase at beginning of p.1
7. Mention ondansetron or similar under 'What will participation involve' so it is clear up front there are 2 meds needed.
8. Local doctor should be changed to either general practitioner or family doctor.
9. Strengthen wording around pregnancy - strongly advise to 'must not get pregnant' complete extra radiation section
10. The Committee queried the need for detailed description of standard of care tests & medications p10-11, and counselling for HepB/C testing p12.
11. They would normally have Hep testing for standard immuno-chemo rx for DLBCL.
12. Remove tests that are not done in New Zealand e.g. PET-MRI.
13. Radiation dose figures to be added on page 11.
14. The Committee queried the headline of the radiation info box.

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 address incidence in Maori (*Ethical Guidelines for Intervention Studies* *para 4.7*).
* Clarify whether the tissue testing is future unspecified or not, and if so – 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*).

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

|  |  |  |
| --- | --- | --- |
| **5** | **Ethics ref:** | **17/NTB/237** |
|  | Title: | Assess Safety and Efficacy of Vilaprisan in Subjects with Uterine Fibroids |
|  | Principal Investigator: | Dr Katrina L. Allen |
|  | Sponsor: | Bayer Australia |
|  | Clock Start Date: | 07 December 2017 |

Nirvana Naidoo, representing the sponsor, 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 is a randomized, double-blind, open-label, placebo-controlled, parallel-group, multicentre Phase III study. Eligible patients will be randomized in a 1:1:1:1 ratio to one of four treatment groups (Group A1, A2, B1 or B2). The primary objective of the study is to show superiority in the treatment of heavy menstrual bleeding (HMB) of vilaprisan compared to placebo in subjects with uterine fibroids.
2. The study will be comprised of a screening period, treatment period and a follow up period. The screening period should be no longer than 120 days, during which eligibility will be determined, including the presence of uterine fibroids and heavy menstrual bleeding.
3. Eligible patients will be randomised into one of the 4 groups at the end of screening:
   * Group A1 will receive 2mg vilaprisan for 2 cycles of 12 weeks with a bleeding event in between.
   * Group A2 will receive 2 cycles of 2mg vilaprisan with no bleeding event (i.e. 24 weeks continuous treatment).
   * Group B1 will have 1 cycle of placebo for 12 weeks and then 2mg vilaprisan for 12 weeks with a bleeding cycle in between.
   * Group B2 will have 2mg vilaprisan for 12 weeks followed by a bleeding cycle then 12 weeks of placebo.
4. After the end of the final treatment period, all subjects will be followed up until day 7 to 15 of the second menstrual cycle after end of treatment visit.
5. In total, subjects will be involved for between 11 and 16 months depending on their menstrual cycle. Assuming a subject completes the study per protocol, they will have 2 cervical smears, 8 ultrasounds and 3 endometrial biopsies. For the entire duration of their participation, subjects will need to document their daily menstrual bleeding and symptoms on an eDiary device as well as additional patient-reported outcome questionnaires during selected site visits. Subjects will need to collect their used sanitary products for analysis of blood loss using the alkaline hematin method throughout the study.

Summary of ethical issues (resolved)

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

1. r.7.1 should have included explanation of risks to unborn children in more detail.

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 have some unease about the lack of critical review or oversight of the project in New Zealand by anyone with specialist expertise in women's health. In particular with the CI not being adequately qualified. The Researcher(s) noted they have experience with woman’s health – but acknowledge the CIs will need to make the case for their skills and experience for this study.
2. The Committee noted there is no formal internal DSMC as would be expected in a Phase 3 study. Monthly overview meetings by the sponsor's medical team does not constitute adequate data monitoring as the team composition does not necessarily include a statistician and there are no formal data monitoring processes laid out. The Researcher(s) noted this was correct, confirming there was biostatistician. The Committee asked to see the terms of reference or a charter.
3. The Committee also expressed some concern that women will be enrolled without informing GP if they chose. An up-to 11 month study is a long period to not inform a primary health carer. The Researcher(s) stated they can make GP notification a requirement. The Committee asked the researchers to check with the CI on whether they felt this was a risk
4. The Committee noted that barrier contraceptives may be as good as hormonal /IUCD treatments if used correctly but they rely on the male partner using them - some women may be at considerable increased risk of pregnant.
5. Please describe where and how you will be getting participants. p.3.1 mentions advertising, but no materials were submitted. The Researcher(s) stated a sub-investigator will recruit their patients, as well as P3 having connections to clinics which will seek referrals. The Researcher(s) noted the gynaecologist was not listed on the application. The Researcher(s) confirmed that gynaecologists will both recruit and also be involved in the study. All study procedures will be treated through their referring gynaecologist.
6. The Committee asked if there is a finder fee for referrals. The Researcher(s) stated no.
7. The Committee asked please clarify GP referrals. The Researcher(s) explained there will be patient brochures and investigator pamphlets which can be provided to GPs and doctors who can give them to potential participants. Patients can contact P3 directly or authorise someone to contact them. The Committee confirmed that they need to see all recruitment materials.
8. The Researcher(s) confirmed referrers will not conduct consent for study participation.
9. The Committee noted conflict of interest between treating and research gynaecologist must be addressed.
10. The Committee noted importance to ensure equal access to the trial and to support those who may be embarrassed or shy.
11. A.1.5 of the application states ‘there are no ethical issues’. The Researcher(s) stated that at the time they did not think there were ethical issues – but acknowledged placebo. The Committee requested that researchers reconsider this question.
12. The Committee noted researchers should offer a summary of results to all not await a request.
13. Used sanitary items collection - how will this be handled so it is not time consuming and distasteful.
14. The Committee noted that the answer to r.5.4.1 managing conflicts of interest is not sufficient
15. The Researcher(s) provided an update on Maori consultation process.

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

1. The Committee asked what happens if a woman doesn't want to take a bleed-inducer if no bleed after 21 days from end of trial. After all they came into the trial to stop the bleeding. Are there risks if they don't induce a bleed? The Researcher(s) stated they would check this matter, but thought it was for scientific validity not for safety reasons. The Committee requested this must be clear what happens if someone said no, and justified or explained why it was required.
2. Explain who the sponsor is, where they are from, in the compensation section.
3. Explain where samples are stored.
4. Pg17 – remove US law.
5. Add a statement on human tissue and Maori.
6. The Committee asked about progesterone-releasing IUCDs as a non-surgical treatment for HMB from fibroids. While this treatment may not work well in all patients, HMB in association with fibroids it is a listed indication on the Medsafe Patient Information sheet for Mirena IUCD. The Committee expected to see it in the PISC as an alternative to participating in the research. Maybe also NSAIDs and tranexamic acid? Please explain these options further.
7. The Researcher(s) explained a gynaecologist could be booked to ensure potential participants understand their treatment options.
8. p.6 PIS. Presume you mean rectum not rectus (which is an abdominal muscle)
9. Provide PIS detail of where overseas the tissue samples will be stored/analysed
10. Please use PICF template from HDEC, ensuring that the Consent Form component is not overloaded with information.
11. Compensation section in the form needs revision as well as the consent section. The information provided in this section needs to be worked through earlier in the form.
12. How will you ensure cultures or people who are embarrassed or shy are provided with equal opportunities to be represented in this trial?
13. Make it clear in PICF where overseas samples are being sent

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).
* Provide further information on the study design, taking into account the HDECs outstanding ethical issues (Ethical Guidelines for Intervention Studies para 5.4)
* Provide assurance that the investigators are suitably qualified or experienced.

This following information will be reviewed, and a final decision made on the application, by Mrs Leesa Russell Mrs Mali Erik.

|  |  |  |
| --- | --- | --- |
| **6** | **Ethics ref:** | **17/NTB/238** |
|  | Title: | The effect of antibiotic prophylaxis on human microbiological flora in total knee arthroplasty: Intra-osseous Vancomycin vs. IV Vancomycin vs. IV Cephazolin. |
|  | Principal Investigator: | Dr Mustafa Saffi |
|  | Sponsor: | NZOA Wishbone trust |
|  | Clock Start Date: | 07 December 2017 |

Mustafa Saffi was not 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. Total Knee Arthroplasty has revolutionised the way clinicians manage degenerative joint disease of the knee. However, despite all standard peri-operative precautions the rate of surgical site infections continues to be 0.9- 2.5%. Antibiotic prophylaxis has been shown to reduce the rate of surgical site infections.
2. Studies have shown Intra-Osseous delivery of Antibiotics to produce much higher and more effective tissue concentrations (10-15x) of antibiotics than Intra-venous delivery. Furthermore Vancomycin has been used as a Prophylactic agent in patients with an allergy to Cephazolin and those who are deemed higher risk for a surgical site infection as it is effective against MRSA and CNS.
3. However, the routine use of Vancomycin may be associated with increased VRE (Vancomycin Resistant Enterococci) colonisation. It, is unknown whether the generation of VRE is associated with the method or dose of administration. We would like to investigate the role of IV Cephazolin, IV Vancomycin and Intra-Osseous Vancomycin on patient’s bacterial flora. The Researcher(s) will test for the pre and post-surgical presence of VRE, MRSA, CoNS.

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 noted this is not a device, and that in the application the ethical issues poorly described, IDMC ticked but not going to have one.
2. The Committee noted patients are only made aware of the study on day of surgery.
3. The Committee noted that the peer reviewer in same organisation and same department.
4. Please confirm this is a pilot study. The Committee noted the need to rewrite the protocol with this in fore front of mind, emphasising the goals of assessing feasibility of methods and gleaning some idea of relative drug effects on bacterial flora as a preparatory study to a larger definitive trial.
5. The detail around consenting process, randomisation process, background rates of carriage of CN Staph, nasal Staph aureus, MRSA, vancomycin-resistant enterococcus in the Auckland community population should be researched and inserted into the document.
6. Look at and better define exclusions related to "abnormal cardiac and renal function" – The Committee asked whether the researchers mean liver and renal as per HDEC form. The Committee asked if this means any abnormality even a GGT of 50. Define what 'nephrotoxic drugs' means. Does this include NSAIDS because if so, The Committee noted you may have trouble in this population recruiting sufficient participants.
7. Please consider collecting all side-effects not just Redman syndrome in the pilot study
8. Please explain recruitment and consent timelines.
9. As far as the answers in the HDEC form are concerned – sponsor is WDHB not the Wishbone trust.

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

1. Additional suggestion, replace the word 'modalities' (1st sentence) with 'ways'.
2. Generally the document is both too brief and too complicated. This must describe the study purpose, procedures and risks/benefits etc in plain English. Please explain 'intraosseous antibiotics', NZOA, 'randomly assigned', what the 3 drug regimens are, who will take swabs.
3. Provide information about the nature and expected incidences of potential side effects of intraosseous injection; separate the potential side effects of vancomycin from SOC cephazolin
4. What are the responsibilities to the study that the participant is signing up to in the consent form? Put them in the PIS or remove the clause from the consent form
5. Consider what will happen if a patient converts to MRSA or vancomycin-resistant enterococcus positivity after surgery. How will you explain this, what are the implications for the patient's health or how they would be housed during a future hospitalisation. Although this can happen with standard of care, swabs are not taken routinely so they would generally not be aware. This must be thought through and potentially discussed with infectious disease specialist.
6. Add a lay title and remove tick boxes from non-optional clauses in the consent form.
7. Consent section remove yes or no options for statements that are not truly optional.

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 further information on the study design, in particular that this is a feasibility study (Ethical Guidelines for Intervention Studies para 5.4).
* 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).

|  |  |  |
| --- | --- | --- |
| **7** | **Ethics ref:** | **17/NTB/239** |
|  | Title: | He Tapu Te Whare Tangata - Offer of HPV self-testing to under-screened women |
|  | Principal Investigator: | Professor Beverley Lawton |
|  | Sponsor: | Victoria University of Wellington |
|  | Clock Start Date: | 07 December 2017 |

Dr Fiona Cram in person and Professor Bev Lawton (PI) and Jane MacDonald 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. He Tapu Te Whare Tangata is a randomised controlled community trial that aims to increase the rate of cervical screening by offer of Human Papilloma Virus self-testing to under-screened Māori women.
2. The trial will randomise primary care clinics to intervention clinics (that is, offer of self-test to under-screened women) or control clinic (that is, offer of usual cervical smear standard care to under-screened women). Under-screened women are defined as women between the ages of 25 and 69 years who have not had a cervical smear for 4 or more years and all ethnicities will be included. The study is powered to compare the outcome for under-screened Māori women.
3. The study will work with communities and primary care practices and the intervention will use technology that has been proven effective overseas in screening women for infection with the types of Human Papilloma Virus (HPV) that cause cervical cancer. The study therefore aims to improve the detection of pre-cancerous lesions in Māori women and ultimately reduce the unnecessary inequity in mortality from a preventable cancer that disproportionately affects Maori women.
4. The rationale behind the study is that even though cervical cancer is preventable, our current screening programme is failing some Māori women and Māori women are twice as likely to die from cervical cancer as non-Maori women are. This project will enable what works for Maori women to inform any national rollout of HPV screening and is Māori led and Māori centred.

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 a similar HRC study is being worked in tandem. The Researcher(s) stated their study is complimentary, as we are doing more of a rural community based study, rather than a mail out study. The Researcher(s) are meeting with them reasonably regularly, every three months or so. The results at the end of both studies will be able to analysed together and presented to National Screening Unit.
2. The Committee asked whether the National Screening Unit will receive the study data. The Researcher(s) confirmed they will receive that data.
3. The Committee asked whether participants will be recalled by the register if they self-test in this study. The Researcher(s) explained current plan is not to automatically register the positive results. The primary practitioner will need to follow this up. During the study the register may update but at the moment it is not possible.

Summary of ethical issues (outstanding)

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

1. Intervention (self-swab) participants with ALL hi risk HPV (not just 16 and 18) are being advised to have colposcopy and are not being offered a smear (cytology screen) first. Colposcopy is more invasive than a smear. Standard of care is to do a smear for some subtypes of high risk HPV and only colposcopy those with abnormalities. The pathway has been devised on the basis of "personal communication from Anna Adcock" and with agreement of local gynaecologist. However, The Committee stated participants with high risk HPV need to be informed of the usual pathway and offered the chance to have a smear first where this is standard care rather than be told they should have colposcopy. The Researcher(s) explained their experience of patients wanting to go straight to colposcopy. The Committee noted it should be disclosed that this would be a deviation of standard of care. The Researcher(s) explained their research looking towards colposcopy, and that going directly to colposcopy would be better as they are rural and may not have another accessible screening chance.
2. The Committee noted that woman can make that choice.
3. p.4.3 Neither tissue sampling nor whakama indicated as cultural issues.
4. Appropriateness of working with a kaumatua (male) versus a whaea (female).
5. Concern for hygiene using community wharepaku. The Researcher(s) explained that they have had further discussions around how this works in practice, most likely to occur in the home or clinic, rather than in public.
6. Koha for the participants.
7. Please include a PISC for medical practices to sign prior to randomisation. The Committee asked if the researchers have agreement from 8 practices in Kaikohe. The Researcher(s) explained that they plan to create these.
8. Please upload the communication which will be sent to the control participants.
9. The Committee asked about NSU MOU. The Researcher(s) explained that NSU supplied a letter of support. Please provide this.
10. The Committee noted that the controls (standard of care smear) won't know their practice is in a randomised cluster trial as no consent to be sought from them. Researchers will only get their anonymised aggregated data on ethnicity, dep.index, age.
11. The Committee noted a reasonable argument offered as to why no consent being sought. However, means a lot of work for the clinician/health centre gathering your data together for you on controls. The Committee asked how researchers will know it is accurate and complete.
12. The database must be stripped of all identifiers once the secondary outcome data of histology/colposcopy reports has come in and been linked to the other research data. It is not necessary to have a fully identified database in existence for 10 years. The risk is not mitigated just by giving the researchers de-identified data to analyse. The Researcher(s) stated they would like to approach the HDEC at 4-5 years to request guidance on taking off the identifiers.
13. The Committee stated that the role between clinician and researcher is being blurred here. The Committee noted they will have a primary healthcare physician who has that data. Keeping the NHI on the database presents unacceptable risk – but keeping a code allows it to be re-identified.
14. The Researcher(s) confirmed that they have hired some researchers that are local.
15. Remove pregnancy clause form the consent
16. PICF Non-consenting participants (in control cohort). The Researcher(s) confirmed are not collecting information at individual level, only aggregated level, so not high risk or particularly personal information. The Researcher(s) clarified that no identifying data will be given to researchers.
17. The Committee asked how laboratories are sending copies of histology/colposcopy results to researchers. These are identifiable and should be transferred safely. The Committee stated this must be encrypted.
18. r.2.1.1 states no identifiable information will be given to researchers, then you say that identifiable information will be given in order to track patients. Storing data in identifiable format is not best practice and has issues for confidentiality. The Researcher(s) confirmed this is with consent, with the intervention cohort. Please make this clearer.
19. Self-HPV swabbing is 9-15% less sensitive for detecting CIN2 or worse, compared with clinician HPV swabbing (according to Ref13 of your protocol). You need to tell participants this in the PISC under "benefits" section.

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

1. The Committee noted the PICF is quite unclear about study design - is this a RCT or do people just have the option of self sampling at some places? Application form says RCT but this is not well communicated in PICF.
2. co-design aspect of study not clear in PICF either
3. Also clarify relationship to primary care i.e. we are working with your GP to identify... Consent form - what risk are associated with pregnancy and why is this not mentioned earlier in the form? Also requests consent to contact GP, you need to say earlier in the form what the purpose of this contact is and that you are requesting it.
4. PICF does not make it clear that you are targeting Maori women and/or that this trial can be of benefit to Maori (not clear enough)
5. PICF does not make clear that their normal GP may also be a study doctor, just that they will give them the swab. This needs to be dealt with in the PICF.
6. The PIS p.2 suggests the intervention group can ask for the health care worker to do the HPV swab. This is not in the protocol and will in fact invalidate the trial because the comparison is between self-swab and SOC smear. Remove this from the PIS (See statement in PIS below: “If you agree to be a participant in this study you will be offered a self- taken vaginal swab. This will be offered by your normal doctor, nurse or a community health worker. This person will explain how you take this swab and you can take your own swab in your own bathroom or bathroom facility on a marae or community centre or you can choose to have your nurse or doctor take the swab in the clinic"). The Researcher(s) explained that the project is to increase rate of testing by the offer of a self test. If a woman has a test in the intervention group by clinician or self-referral, it will count. The Committee and The Researcher(s) discussed this and its impact on scientific validity and analyses.
7. HPV self-swab Intervention Group will be consented to study and release of subsequent swab and colposcopy data direct to researcher. Will Dr Lawton use encrypted email to receive these results in the same way that health practices are required to do?
8. pg. 2: Suggest review following statement as does not make sense in current form. 'This study will have enrol primary care clinics in your area'
9. Amend HDEC statement to indicate Northern B
10. Ensure inclusion of Maori Health Support contact details.
11. First sentence under purpose should be 2 sentences.
12. Para 2 under enrolment - you explain control clinics but not what the other clinics doing the self-sampling are, suggest that you make these 'active study' or similar to distinguish that they differ.
13. Reword first sentence in the after the study paragraph to make it clear HPV swab not available to study participants after the study
14. Make it clear study results will take one year to amass, but the individual clinical results are available much sooner.

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)*

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

|  |  |  |
| --- | --- | --- |
| **8** | **Ethics ref:** | **17/NTB/240** |
|  | Title: | A Study To Evaluate Fasinumab In Patients With Pain Due To Osteoarthritis Of The Knee Or Hip (R475-OA-1688) |
|  | Principal Investigator: | Dr Nigel Gilchrist |
|  | Sponsor: | Regeneron Phrmaceuticals Inc |
|  | Clock Start Date: | 07 December 2017 |

Dr Nigel Gilchrist (CI) and Larissa Roberts 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 study is a randomized, double-blind, placebo- and NSAID-controlled study designed to evaluate the efficacy and safety of fasinumab in patients with osteoarthritis (OA) of the knee or hip who have a history of inadequate pain relief with paracetamol and a history of intolerance to or inadequate pain relief with opioids (or are unwilling to take opioids or have lack of access to opioids).
2. The study consists of a screening period of up to 30 days, a 7-day pre randomization/washout period, a 24-week treatment period, a 20-week follow-up period, and a final phone call approximately 52 weeks after the last dose of study drug.
3. Prior to randomization, patients will undergo screening procedures, including X-ray of the shoulders, hips, and knees, and magnetic resonance imaging (MRI) of the index and contralateral joints to be assessed by the central reading laboratory. During the screening period, all patients will continue to take their current treatment regimen for OA pain, which must include use of an NSAID on a regular basis.
4. Patients eligible for the study will complete a pre-randomization period including a pre-randomization visit 7 days before randomization. During this visit patients will discontinue and/or undergo a washout of their standard of care pain medications for OA. All pain medication, except for the study-provided rescue medication (paracetamol), will be discontinued.
5. Patients will be randomized on day 1 in a 2:2:2:1:1:1 ratio to receive 1 of 6 treatment groups as follows: Fasinumab 1 mg subcutaneous injection every 4 weeks, Fasinumab 3 mg subcutaneous injection every 4 weeks, Fasinumab 6 mg subcutaneous injection every 8 weeks, Diclofenac 75 mg orally twice daily, Celecoxib 200 mg orally once daily or Placebo. To protect the blinding process oral and subcutaneous placebo doses will be administered alongside active treatment. The study-provided rescue medication, Paracetamol, will be available for breakthrough pain.

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 justify how it is ethical to withdraw NSAID pain relief in a patient who has failed paracetamol as analgesia, then put on placebo +/- paracetamol for 24+ 16 weeks, without the option of trial intervention at any point. The Researcher(s) explained that placebo group can have paracetamol. The Researcher(s) will see the participants on a regular basis. If pain gets out of control they will be exited from the study. The Committee noted that paracetamol has already failed with this group.
2. The Committee discussed comparing active treatments opposed to placebo. The Committee requested that the researchers consider active vs active competitor study. Please justify ethically and scientifically why this cannot be run as an active vs active study.
3. The Committee noted participants can aim to please their clinicians and may not inform clinicians about their real pain levels. This must be considered when interacting with participants.
4. The Committee noted it is 24 + 16 weeks for placebo arm and 16 weeks for NSAID arms with effectively no pain relief. The Researcher(s) noted the possibility of getting surgery faster through participation, as the pain was not manageable. The Committee asked how participation in the study would have any impact on access to surgery.
5. Please explain the logic in pooling results from 2 NSAIDs which are being used differently: diclofenac at medium dose and celecoxib at low dose.
6. The Committee noted that according to inclusion/exclusion criteria, it would be possible to enrol a person who had a myocardial infarct 18 months previously and was taking naproxyn 250mg for OA pain. Such a person could be randomised to diclofenac 150mg /day which many cardiologists would have significant reservations about. Justify this in terms of non-maleficence (reducing harm).
7. According to the protocol and PIS, the sponsor plans to keep remaining samples for research into other disease than OA. This is Future Unspecified Research for which separate consent must be obtained. Please provide a separate PIS/CF for the future unspecified research. (From protocol: "8.2.5.2. Future Biomedical Research Unused research samples, as well as unused PK and ADA samples, will be stored for up to 15 years after the final date of the database lock. The unused samples may be utilized for future biomedical research of OA and other diseases. No additional samples will be collected for future biomedical research. After 15 years, any remaining samples will be destroyed"
8. The Committee is concerned about the exclusion of liability statement at pgs 17 and 18 of the PIS form - what is the basis for this. Does this reflect the limits of the researcher’s indemnity insurance cover? The Committee is yet to see a PIS form with exclusionary statements to this extent. The Committee is particularly concerned that it states that Regeneron (to whom the insurance certificate submitted to NTB is issued) will not compensate participants for loss suffered as a result of negligence by the institution and its staff carrying out the study. The Committee is therefore not satisfied, by the documents submitted, that there is an adequate level of protection for participants.
9. The Committee note it is hard to see how the interests of participants are being protected based on the general information on this study in terms of 1) high risk of medication side effects 2) potential for significant pain in participants, even prior to study start, 3) wide ranging future unspecified research 4) significant concerns raised by the Committee.

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

1. Use New Zealand brand names, not American ones, for NSAIDs and paracetamol Withdrawal does not have to be in writing.
2. Remove references to US and European law.
3. Change americanisms- "throwing up & "needle stick"
4. Confidentiality - make it clear that no identifiable patient information or samples will leave the research sites.
5. Patient information will be coded by a study number that can only be linked by the Investigator at the research sites.
6. The Confidentiality Info on pp18 & 19 makes it appear as if the Sponsor has access to identifiable personal information. Clarify in PISCF that health information will not be identifiable to the "researchers", its collaborators or contractors (except as required by on-site audit).
7. Any health information released by Regerneron (bottom p.18) will be ANONYMOUS to protect privacy.
8. Genomics sub-study similar privacy issues with the Genomics Sub-study PISCF page 4. and page 8 and 10 #4.
9. NO records with personal identifiers should be available to Sponsor or its scientists even if re-linkable only by key code. (p.4 currently states "data will be kept in a separate file from records containing your name & personal information")
10. Remove requirement for witness in both CF's.
11. Please view the HDEC template for informed consent and use the template wording for ACC compensation <https://ethics.health.govt.nz/>

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)*
* Justify use of Placebo *(Ethical Guidelines for Intervention Studies para 5.22)*
* Provide further information on the study design, *in particular in relation to outstanding ethical issues* (*Ethical Guidelines for Intervention Studies para* 5.4)
* 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*).

This following information will be reviewed, and a final decision made on the application, by Mrs Jane Wylie and Mr John Hancock.

|  |  |  |
| --- | --- | --- |
| **9** | **Ethics ref:** | **17/NTB/241** |
|  | Title: | Evaluation of infection control advice and infection-related change in treatment plan. |
|  | Principal Investigator: | Dr Scott Macfarlane |
|  | Sponsor: |  |
|  | Clock Start Date: | 07 December 2017 |

Dr Scott Macfarlane was 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.

Dr Nora Lynch declared a potential conflict of interest, and the Committee decided to allow her to be involved in the discussion of the application.

Summary of Study

1. Children undergoing acute lymphoblastic leukemia (ALL) treatment are at increased risk of developing infections, which can lead to delays or changes in treatment. Families are usually given advice from staff at their child's treatment centre about how to approach situations where their child is more likely to be exposed to infection. However, there is no existing body of research that determines an optimal approach with regards to when children undergoing treatment for cancer should return to education and other social activities. There currently appears to be a difference in the standard advice provided by the two specialist paediatric oncology treatment centres (located in Auckland and Christchurch) regarding when children should return to school/ECE following a leukaemia diagnosis. This study will verify that the advice being given is different and then consider how this, alongside advice received from other parties, impacts on parental perceptions and practice regarding educational facility attendance, infection and ultimately the optimal delivery of treatment.
2. This mixed-methods study of current practice for patients with Acute Lymphoblastic Leukaemia (ALL) will include qualitative interviews with patient families, an online questionnaire of health professionals and NGO support workers who provide advice to families, and quantitative data analysis of patients' education attendance records and infection-related treatment changes
3. The study participants are a cohort of children diagnosed with ALL between 1/1/2014 and 31/12/2016. ALL is the most common childhood cancer. The long, typically 2-3 years, of immunosuppressive chemotherapy treatment means that there is an increased risk of infection-related complications.
4. The study will inform the development of a national evidence-based approach to infection control advice provided to families in order to ensure optimal social, educational and health outcomes for child cancer patients.

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) explained Auckland and Canterbury will be conducted face to face, with the remainder as skype or phone. The Researcher(s) confirmed no home visits.

Summary of ethical issues (outstanding)

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

1. Researcher contact letter should offer option of participation of just accessing records if they don't want an interview.
2. Emotional risk to researcher, of doing 30 interviews with ALL families. Suggest setting up automatic debriefing sessions along the way for her with an appropriate person to allow any off loading and a check on her wellbeing. The Researcher(s) acknowledged this risk, citing the experience of the researcher. The Researcher(s) explained that the researchers have a personal process in place for managing stress and accessing counselling. The Committee discussed debriefs formally, but is directed by the researcher. This should not be the research team.
3. Ensure interviews are done in a private space. A public library, which is one of the suggested options, would not be an appropriate place.
4. Provide participants with individual copies of the to-be-published results rather than direct them to a public website to view them.
5. Consider whether a follow-up phone call should be made to interviewees after the interview to check on their wellbeing.
6. The Committee asked if they will provide parking /petrol money to any interviewee who travels to an interview venue. The Researcher(s) stated they will have taxi vouchers.

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

1. Audio recording should be clearly outlined in the PIS.
2. Simplify the 7-12 assent form if possible.
3. Consent form – talks in language ‘I’ and add ‘or my child’ where appropriate.

Decision

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

|  |  |  |
| --- | --- | --- |
| **10** | **Ethics ref:** | **17/NTB/242** |
|  | Title: | SHARP-C |
|  | Principal Investigator: | Prof Ed Gane |
|  | Sponsor: | Kirby Institute |
|  | Clock Start Date: | 07 December 2017 |

Prof Ed Gane, Sarah Middleton, Sarah Kate and Tom X 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. SHARP-C is an observational cohort study investigating the effect of direct-acting antiviral (DAA) therapy and reinfection in people with chronic HCV and recent injecting drug use. A prospective, observational cohort design will be used to enrol patients attending tertiary drug and alcohol and primary health care services.
2. Participants will be prescribed a direct-acting HCV medication as per the standard of care. The on treatment phase will vary dependent on the type of a direct-acting antiviral prescribed as per standard of care. Once patients have completed their treatment course they will be followed up every 3 months for up to 3 years following the end of treatment phase.
3. If the participant becomes re-infected during the follow up phase, further tests will be undertaken as per protocol to look what happens during the early stages of re-infection.
4. The study will aim to evaluate the incidence of HCV reinfection following successful DAA treatment over the three years of follow up. The study will also evaluate the proportion of patients with undetectable HCV RNA at 12 weeks post end of treatment (SVR12) with direct-acting HCV therapy.

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 stated the use of initials and DOB on clinical record forms and tissue samples makes them identifiable. With a New Zealand sample of< 40, it would be easy to pick who the data came from. Please remove, add a second unique code if you are concerned about mix ups
2. Section 12.2 of the protocol reads: 12.2 Linkage of data Participant data will be linked with routinely collected data from a range of population databases and registers. The collection of participant names, date of birth, sex, and post code in SHARP-C is essential for accurate data linkage. Participant data will be linked to a variety of health variables including information on hepatitis C notifications, HIV/AIDS notifications, use of hepatitis services, opioid substitution treatment, incarceration, hospitalizations, emergency department use, cancer, and mortality through the New South Wales Centre for Health Record Linkage (www.cherel.org.au) and the Australian Institute of Health and Welfare (www.aihw.gov.au). Linkage will be both retrospective and prospective, with the time period covered dependent on the properties of the specific data set. Approval from the NSW Population Health Ethics Committee and all other required Human Research Ethics Committees will be sought prior to any data linkage being performed. The Committee asked whether researchers intended to seek permission to obtain this sort of personal data and link it to results of this study.
3. Please submit questionnaires for final review.

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

1. Remove tick boxes of statements in consent form that are not truly optional.
2. Study cannot be terminated for commercial reasons.
3. Provide cards for the participants with contact numbers in case of emergency,
4. State how long treatment phase is likely to be.
5. Correct typos and grammar and add commas to improve readability. e.g. p.3 Baseline visit 1st sentence- participate, not participant. Add comma after "social factors such as housing", after each stated mL of blood sample- add 'of" or comma. Under p6 "What are the alternatives....?"
6. Clarify that participants have the option to be treated with DAA the same as used in this study without having to participate in the study (if this s the case).
7. Page 7, "Who pays for the study?" - appears to be several clauses repeating or giving similar information. Simplify.
8. Top of p8. & also p3 in Optional Future Research PISCF: clarify wording "data protection law New Zealand’s privacy regime." should remove "data protection law" and state "under NZ privacy law..."
9. Consent: remove Yes/No's unless truly optional.
10. Optional Future research PISCF should state that the ethical approval of future studies in other countries may not take into account the same cultural factors as New Zealand.
11. Page 2 – ‘re-identifiable sample’ – for the FUR. The Researcher(s) will clarify.
12. Page 2 –accessing drugs through PHARMAC. Participants may not understand this, please explain, i.e. provided by your doctor funded in New Zealand etc.
13. Page 2 – ‘no treatment provided in this study’ – reword to ‘treatment is provided outside of this study’.
14. Remove commercial interest stopping criteria.

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

This following information will be reviewed, and a final decision made on the application, by Jane Wylie and Mrs Mali Erik.

|  |  |  |
| --- | --- | --- |
| **11** | **Ethics ref:** | **17/NTB/243** |
|  | Title: | Metronidazole After Haemorrhoidectomy |
|  | Principal Investigator: | Professor Andrew Hill |
|  | Sponsor: | The University of Auckland |
|  | Clock Start Date: | 07 December 2017 |

Dr Weisi (Wes) Xia was 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. Haemorrhoids, also known as piles, are a common adult disorder affecting over a third of the adult population. Although conservative treatment involving office-based interventions, as well as lifestyle and dietary changes, are adequate for the majority of patients, surgical intervention is indicated in those with symptomatic advanced grades. Excisional haemorrhoidectomy is the accepted gold standard for the treatment of symptomatic, higher grade haemorrhoids. While an effective treatment at preventing recurrence, it is associated with significant pain resulting in a decreased quality of life and prolonged return to normal activity.
2. Given the prevalence nature of the disease, the population group affected (working age adults) and the significant recovery time required following surgery, there remains considerable interest in the development of safe, affordable, simple and effective pain management strategies. Metronidazole has been traditionally been used in surgical prophylaxis and treating certain types of infections. It has been postulated to decrease pain following haemorrhoidectomy.
3. This will be a prospective multicentered, double-blinded, randomised placebo-controlled trial comparing metronidazole in its oral versus its topical route of administration. Adult patients undergoing elective excisional haemorrhoidectomy in the three public hospitals in Auckland region, as well as private Ormiston Hospital, will be invited to participate. The primary outcome will be self-recorded pain scores on a daily Visual Analogue Scale for seven days after the operation. Secondary outcomes will be total analgesia consumed, complications, adverse reactions, wound healing, return to normal activity, the cost of intervention for each use and patient satisfaction scores.
4. Select patients will be approached to perform self-swabs of the affected surgical region after the operation to determine the type and number of bacteria growing.

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 sample size is based on a difference between arms of '0.5'. Does this mean 0.5cm o a 10cm VAS? If so, this may be statistically significant but it is not clinically significant - it's the same as saying that if treatment A has a mean pain score of 6/10 and treatment B has a mean pain score of 6.5/10, treatment A is better. Have you consulted a biostatistician yet? The Researcher(s) noted this.
2. The Committee asked why exclusions don't include pregnant women.
3. Blinding will be difficult to maintain because oral metroniadzole commonly gives a metallic taste. This is unfortunate because the primary outcome is subjective. While you can't easily mitigate this, suggest you include a question at end of study asking participants (and researchers) to guess their treatment allocation, to assess the efficacy of blinding. The Researcher(s) noted this. Add detail to protocol.
4. The Committee noted that recruiting every patient at all 3 DHBs and Ormiston presents something of a logistical issue. How will this be managed? (180 pats) Is this only patients from one surgeon? If so, how will researchers account for bias? The Researcher(s) explained further funding is coming to support the study. The Researcher(s) also stated that they have since learnt that Middlemore has 80, Auckland has a similar amount. The Researcher(s) stated they could just conduct the study at two sites. Please revise protocol.
5. Protocol is unclear about rolling out plan, just 'starting at CMH'. This should be better structured.
6. The Committee noted it seems that consent will be from an operating surgeon and non-member of the study team, how will you ensure this is consistent and appropriate? Day of operation does not give participants much time to consider the information and consult with their whanau. Inferior pain management (in one arm) noted to be an ethical issue by researcher - there is no plan to monitor this in the protocol and I think they would benefit from a mitigation of this issue. Should be excluding patients allergic to this antibiotic also. The Committee asked whether the PIS could go out with the appointment sheet. The Researcher(s) stated they would do this.
7. Having no plan for DSMC for a trial of analgesia running over a year doesn't seem right. What if there was a clear benefit separation part way through with an inverse side-effect separation? Suggest interim BLINDED look at data is required.
8. The Researcher(s) stated if someone is in pain they will go to standard of care. The Committee noted keeping participants in is ideal for the study validity, so try to not withdraw and just treat the pain.
9. The Researcher(s) stated they have no incidence data for Maori – but are working on it.
10. The Committee requested option for GP knowing they are in the trial participants.

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

1. Add that this is for a PhD
2. Explain randomisation
3. Explain the purpose of matching IV /topical placebo
4. Make the warning against alcohol much more emphatic
5. Explain that swabs are taken externally
6. Explain what the participant should do with the swabs collected until the day 7 appointment ( and please don't say 'put it in the fridge')
7. ACC compensation clause – please view the HDEC template for informed consent at <https://ethics.health.govt.nz/>
8. Digitise files and destroy paper.
9. Be clear around withdrawing from the study, what happens to care, data etc.
10. Offer costs of transport to clinic at day 7 unless this is a routine time of follow up. The Researcher(s) confirmed it was not. The Committee requested reimbursement.
11. Add what the standard of care at each of the institutions is with respect to metroniadazole use post-haemorrhoidectomy. i.e. clearer explanation of how participation will differ from standard of care.
12. PICF needs work. Overall it needs an improvement in readability and clarity. The template PIS should help with this.
13. PICF what will happen in the study needs to be rewritten "your group will not affect the operation" is clumsy p2. Rewrite the compensation paragraph in line with our standard one.
14. Withdrawal paragraph poorly worded and confusing, also, split up the ideas a bit please p3 summary of results on consent page doesn't have a place to indicate choice of results or not.
15. Note number of participants on PICF.

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 on what processes are in place for recruitment *(Ethical Guidelines for Intervention Studies para 6.2).*
* Provide details of the Data Safety Monitoring Committee’s composition and monitoring plan *(Ethical Guidelines for Intervention Studies para 6.50).*

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

|  |  |  |
| --- | --- | --- |
| **12** | **Ethics ref:** | **17/NTB/249** |
|  | Title: | Mana Tū: a mana whanau approach to improving diabetes outcomes |
|  | Principal Investigator: | Dr Matire Harwood |
|  | Sponsor: | NHC |
|  | Clock Start Date: | 07 December 2017 |

Dr Matire Harwood was 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.

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

Summary of Study

1. Diabetes is a long term condition with significant ethnic and social disparities in prevalence and outcomes. There is huge scope to reduce diabetes inequalities however the complex nature of the condition means a comprehensive and sustained approach that tackles the wider determinants for causes, management and complications is required. We propose to evaluate Mana Tū, a programme that was co-designed with experts in long-term-conditions including clinicians, policy-makers, academics and importantly whānau living with diabetes. Mana Tū aims to improve the impact of clinical and lifestyle interventions for people with poorly controlled diabetes; and their whānau who are living with prediabetes. Mana Tū deploys skilled and supported Kaimanaaki-whānau (KM) in primary care practices. The KM are similar to Case Managers but instead they use a mana whānau approach and work with General Practice teams while being operationally supported by a central hub. The hub coordinates broader community and social service support systems for whānau, and provides training and quality improvement support, within a rich data environment.
2. There are four parts to the evaluation:
   * 1. Mana Tū for Clients – will measure clinical (including changes in HBA1c, hospital admission numbers) and other (satisfaction, goal attainment) outcomes in 200 people in five general practice clinics who receive Mana Tū, over 12 months. Data will be compared to a ‘control group’ of 200 from five different practices who wait 12 months until they too receive Mana Tū.
     2. Mana Tū the Service – will investigate the impact of Mana Tū on hospital and primary care services including cost effectiveness
     3. Implementing Mana Tū – will explore barriers and facilitators to the implementation and uptake of Mana Tū
     4. Integrating Mana Tū – will integrate the findings from the three other parts to understand the relationship between process and outcomes. The findings will provide valuable information for future purpose.

Summary of ethical issues (resolved)

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

1. The Committee was also interested that the initial assessment form has a whole section (section 3) on socio-economic issues with questions regarding financial status, employment and housing. section 8 (health literacy and cultural safety) also included questions on experiences of discrimination/verbal attacks due to ethnicity; and unfair treatment by health professionals/in employment/in respect of housing - this information is likely to be useful in ascertaining the extent of barriers to accessing services/systemic discrimination; however is data on housing and employment too tangential (and potentially uncomfortable for participants) given the purpose of the research. The Researcher(s) explained that stakeholder surveys confirmed that racism did impact on treatment and care for diabetes – which supports the recording of information around social and perceptions. The Committee accepted that the questions were relevant to the study aims.

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 noted the project currently only sought to involve the services and use a cluster design without individual consent. The Committee noted individual participants have the right to know at the time of referral offer from primary practice, that they have a 50% chance of immediate start and a 50% chance of waiting 12 months to join the programme. This could be by way of an information sheet which states that start time will be by randomisation and notes that by agreeing to have their willingness to hear more about the programme passed back to Mana Tu, they are aware they may have to wait. The Committee explained that without this, harm could come from feeling let down by a service which they anticipated starting soon. The Researcher(s) acknowledged this and discussed other instances of cluster controlled trials.
2. The Committee noted that individual consent was possible given all of the opportunities to interact with research / health staff, where other interventions involved in cluster randomisation do not engage with patients.
3. The Committee noted that the practices should also formally document their involvement. This should be formalised with written information provided to the service. The Committee asked for some more formal process around the GPs in the same practice being consented for their practice to be enrolled.
4. The Committee noted that the baseline questionnaire the Mental Health (2.1) and Anxiety (2.3) questionnaires have identical questions 8 and 9. Please review the questionnaires.
5. The Committee noted that the education questionnaire (3.1) contained language that may not be applicable to a New Zealand audience, for example 'graduate high school'. The Committee asked if this an American questionnaire. The Researcher(s) was not sure what the origin of the questionnaire was, but would make sure it was amended to reflect language that was familiar for New Zealanders.
6. Please explain the reference to 'audio recordings' in the PIS p. 3 and 'workshops and interviews with stakeholders' in the HDEC form b.2.1. There is no reference to focus groups/interviews in the protocol or PIS. The Researcher(s) stated this was an error.
7. The Committee note the HRC's comments in their grant approval letter: how have these been addressed since? The Researcher(s) will respond to these and provide the full peer review documentation.
8. The Committee noted there was no evidence of a safety plan for KM-W support workers included - what processes / protocols do the researchers have in place to ensure safety during home visits. The Researcher(s) explained the process and training that was in place and stated they would provide the basic details of the protocol to the Committee.
9. The Committee asked the researcher to also address cultural safety protocols in relation to interviewing and home visits.
10. The Committee asked if there was a conflict of interest with relation to the funding of the study and the research team. The Researcher(s) explained the relationship between Chief Executive of HRC also being involved in the research. The Researcher(s) explained the history of involvement and the mitigation of conflict of interests, for example they were not involved in peer review or funding decisions, and was involved early in the project which spanned over a number of years.
11. The Committee requested further evidence of peer review.
12. The Committee noted that this is not an observational audit but an interventional trial.
13. The Committee suggested combining consent to the programme and consent into research. Explain randomise, either 12 months or coming soon.

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

1. Add Maori Health Support contact details.
2. P.2 inform that participants that (mental health and income) questions will be asked but they are free to answer only what they are comfortable with. Participants may also refuse to answer any question.
3. P.2 inform that hospital as well as medical records will be checked as some people think only GP records are meant by 'medical records' Indicate the approximate time commitment for each monthly appointment consent form: remove tick boxes from anything which is non-optional.
4. It is recommended that passing information to GP is non-optional as otherwise, community workers who uncover thoughts of self-harm in baseline questionnaire or other medically concerning information at monthly meetings may be conflicted about how to proceed.
5. The Researcher(s) explained the consultation groups involved for Pacifica and Maori.
6. Be clear about goal setting being separate from the main focus of the study (diabetes). The Committee suggests reconsidering the examples given to meet this condition.

Decision

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

* Individual recruitment and consent process must be outlined and justified (Ethical Guidelines for Intervention Studies para 6.2).
* Please provide evidence of HRC favourable independent peer review of the study protocol (Ethical Guidelines for Intervention Studies Appendix 1).
* 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*).
* Address outstanding ethical issues in a coverletter.

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

## General business

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

|  |  |
| --- | --- |
| **Meeting date:** | 08 February 2018, 12PM |
| **Meeting venue:** | Novotel Ellerslie, 72-112 Greenlane Road 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 5.40pm