|  |  |
| --- | --- |
| **Committee:** | Southern Health and Disability Ethics Committee |
| **Meeting date:** | 10 September 2019 |
| **Meeting venue:** | Sudima Hotel, Christchurch Airport, 550 Memorial Drive, Christchurch |

|  |  |
| --- | --- |
| **Time** | **Item of business** |
| 11:00am | Welcome |
|  | Confirmation of minutes of meeting of 13 August 2019 |
| 11:30 | New applications (see over for details) |
| 11:30-11:55  11:55-12:20  12:20-12:45  12:45-1:10  1:10 – 1:35  1:35 -2:00  2:00 – 2:25  2:25-2:50  2:50-3:15  3:15-3:40  3:40 – 4:05  4:05 – 4:30pm | i 19/STH/163  ii 19/STH/158  iii 19/STH/159  iv 19/STH/160  v 19/STH/161  vi 19/STH/162  vii 19/STH/164  viii 19/STH/165  ix 19/STH/166  x 19/STH/169  xi 19/STH/170  xii 19/STH/171 |
|  | General business:  Noting section of agenda |
| 4:30pm | Meeting ends |

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
| **Member Name** | **Member Category** | **Appointed** | **Term Expires** | **Apologies?** |  |
| Dr Sarah Gunningham | Lay (other) | 05/07/2019 | 05/07/2022 | Present |  |
| Dr Devonie Waaka | Non-lay (intervention studies) | 18/07/2016 | 18/07/2019 | Present |  |
| Assc Prof Mira Harrison-Woolrych | Non-lay (intervention studies) | 27/10/2015 | 27/10/2018 | Present |  |
| Mrs Leesa Russell | Non-lay (intervention studies), Non-lay (observational studies) | 14/12/2015 | 14/12/2018 | Present |  |
| Dr Paul Chin | Non-lay (intervention studies) | 27/10/2018 | 27/10/2021 | Apologies |  |
| Professor Jean Hay-Smith | Non-lay (health/disability service provision) | 31/10/2018 | 31/10/2021 | Apologies |  |
| Mrs Helen Walker | Lay (consumer/community perspectives) | 01/07/2015 | 01/07/2018 | Present |  |
| Mr Dominic Fitchett | Lay (the law) | 05/07/2019 | 05/07/2022 | Present |  |
| Dr Pauline Boyles | Lay (consumer/community perspectives) | 05/07/2019 | 05/07/2022 | Apologies |  |

## Welcome

The Chair opened the meeting at 11:00am and welcomed Committee members, noting that apologies had been received from Dr Pauline Boyles, Prof Jean Hay-Smith, and Dr Paul Chin.

The Chair noted that it would be necessary to co-opt members of other HDECs in accordance with the Standard Operating Procedures. Mrs Leesa Russell and Mrs Helen Walker confirmed their eligibility and were co-opted by the Chair as members of the Committee for the duration of the meeting.

The Chair noted that the meeting was quorate.

The Committee noted and agreed the agenda for the meeting.

## Confirmation of previous minutes

The minutes of the meeting of 13 August 2019 were confirmed.

## New applications

|  |  |  |  |
| --- | --- | --- | --- |
| **1** | **Ethics ref:** | **19/STH/163** |  |
|  | Title: | BETTER SLEEP |  |
|  | Principal Investigator: | Dr Michael Hlavac |  |
|  | Sponsor: | Nyxoah |  |
|  | Clock Start Date: | 29 August 2019 |  |

William Johnston was present in person for discussion of this application. Dr Malina Storer and Mrs Rochelle Walsh attended via teleconference.

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

This study aims to evaluate the safety and performance of the Genio system, a device implanted in the chin area to stimulate the hypoglossal nerve via energy pulses, for the treatment of Obstructive Sleep Apnoea in participants with and without complete concentric collapse of the soft palate. This process can help maintain open airway and normal breath while sleeping.

Summary of resolved ethical issues

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

1. The Committee asked if the device is intended to target extreme cases of sleep apnoea. The Researchers answered that roughly 50 percent of patients with sleep apnoea cannot tolerate standard C-PAP treatment. Patients like these usually remain untreated, with invasive surgery as a “last line” option with long term consequences. The study device is considered an alternative to both no treatment and more invasive interventions in this population.
2. The Committee queried whether the study surgeries will take place at a private hospital. The Researchers confirmed Southern Cross Hospital as the study site. The Committee then asked if therefore only private patients would be eligible to participate. The Researchers responded that potential participants would be approached by a multi-disciplinary sleep team, and likely be high-risk patients in the public system who have not had success with standard treatments. The Committee asked whether the cost of treatment in a private hospital would be covered for eligible patients. The Researchers confirmed that there would be no cost to participants in terms of the procedure or follow-up.
3. The Committee observed that some of the Researchers will also be providing usual care for participants, and asked how this conflict of interest will be managed. The Researchers responded that the multi-disciplinary clinic is made up of several clinicians, of which only Mrs Walsh and Dr Michael Hlavac are involved in the study. There will therefore be a check-point via other clinicians in terms of eligibility, and patients will also have discussions with Dr Storer outside the clinical setting prior to being inducted.
4. The Committee queried what was meant by the statement “The inclusion criteria was selected to increase good responder patients.” The Researchers clarified that in a previous study, patients with a “negative cricomental space” did not have a strong connection between the external and internal parts of their device during the titration process. The Researchers therefore do not want to take patients where the connection between these parts can be guaranteed. Study results will make clear that this is a limitation of the device.
5. The Committee questioned why participants would be withdrawn if they became pregnant, and what the risks might be. The Researchers answered that there was no evidence to suggest there would be harm to a pregnant participant or foetus, but that this was a precautionary measure given that this is only the second generation of the device.

Summary of outstanding ethical issues

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

1. The Committee asked that Mrs Walsh’s details, as the lead surgeon, be provided.
2. The Committee noted that issues arise from participants retaining the study device post study, and asked that these be addressed. Some outstanding questions include: who will pay for the device being removed post study (for example, if the participant changes their mind and wants it removed or the device stops working), what is the potential on-going cost for participants? Such post-study processes should be made clear.
3. The Committee advised that any new safety information must be conveyed to participants in a timely manner and should ideally be in a face-to-face setting. The information and consent documents need updating, but the participant should not have to wait for this to receive important safety information.
4. The Committee advised that all participants are entitled to receive a lay-summary of study results, and that this should be accommodated.
5. The Committee requested that informing participants’ GPs not be optional, as this is an implantable medical device.
6. The Committee advised that the trial cannot be stopped for commercial reasons.
7. The Committee requested that advertising material be amended: state that the device is experimental, remove the “path to restful nights” tagline, and remove the statement “this prevents sleep events such as apnoeas and hypopneas from occurring, allowing the user to enjoy a restful night” (as this is what the study is investigating). The patient letters should also be amended to reflect this and ‘New Zealand-ised’.

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

1. Please remove the long study title. The short title should also be amended to something less suggestive (non-promotional), such as a lay-version of the long title. This should be the title of the information sheet.
2. Please provide an up-front statement saying that this is the second study of the second generation of this device, and how many people have been exposed to it. This should make clear that it is an investigational device. Please also include how many people have been exposed to previous generations.
3. Please include a diagram of the device where appropriate.
4. Please remove jargon on page 3, such as “cricomental space” and “sub-mental volume.” Technical jargon should be removed in general, for example “paradoxical reaction,” “functionality issues,” and “acceptable aesthetic result.”
5. Please be clear that the surgery implant visit will only take place once the screening tests have been completed and the participant is confirmed to be eligible for the study.
6. Please include serious adverse events in the risks section. Please also use the HDEC reproductive risks template.
7. State clearly how much it will cost participants to continue using the device post study.
8. Please update the compensation statement in line with the HDEC template.
9. Please remove statement about commercial reasons for stopping trial.
10. Please remove reference to the National Statement.
11. Please add routine sections on data use from HDEC template.
12. Please remove statement on the optionality of already collected data being used post the participant’s withdrawal, as this is not an option.
13. On page 8, please improve wording around shaving to make clear this needs to be continuous.
14. Please check the document for typos.
15. Please provide an optional check box in the consent form for participants to request a lay-summary of study results.
16. As above, please remove the statement that informing GPs of participation is optional

Notes

1. For the Researchers’ future reference when completing the application form, the Committee noted that it prefers a summary of each point rather than simply referrals to the protocol. Acronyms should also not be used without being laid out in full first, and jargon should be limited.

Decision

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

* Please provide Mrs Walsh’s details, including a CV (*Standard Operating Procedures for Health and Disability Ethics Committees* para. 42.4.2).
* Please amend the participant information sheet and consent form, taking into account the suggestions made by the Committee (*Ethical Guidelines for Intervention Studies* para. 6.22).
* Please clarify the management plan for the devices post study, ensure that new safety information is communicated to participants in a timely manner, and ensure that GPs are informed of participation. (*Ethical Guidelines for Intervention Studies* para. 5.41).
* Please ensure that participants are given the option of receiving a summary of study results (*Ethical Guidelines for Intervention Studies* para. 7.21).
* Please ensure that the study is not terminated for commercial reasons (*Ethical Guidelines for Intervention Studies* para. 6.65).
* Please amend advertising material and patient letters as requested by the Committee (*Ethical Guidelines for Intervention Studies* para. 6.2).

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

|  |  |  |  |
| --- | --- | --- | --- |
| **2** | **Ethics ref:** | **19/STH/158** |  |
|  | Title: | A Phase 3, open label study comparing Zanubrutinib plus Rituximab vs Bendamustine plus rituximab in Patients with Previously untreated Mantle cell Lymphoma |  |
|  | Principal Investigator: | Dr Marie Hughes |  |
|  | Sponsor: | Beigene |  |
|  | Clock Start Date: | 22 August 2019 |  |

Charlie Stratton and Alison Heard were present via 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

The purpose of this study is to evaluate Zanubrutinib plus Rituximab, followed by Zanubrutunib monotherapy, versus bendamustine plus Rituximab, followed by observation in approximately 500 patients with Mantle Cell Lymphoma who are ineligible for stem cell transplantation due to age or comorbidities.

Summary of resolved ethical issues

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

1. The Committee queried how incidental findings of clinical significance will be managed. The Researchers responded that these will always be dealt with by the primary investigator, and participants will have their notes reviewed both prior to and during clinic visits.

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

1. Please state that bendamustine and rituximab are standard treatment in New Zealand.
2. Please amend page 16 to be clear that consent will be sought for the collection of the infant’s health information.
3. Please clarify the meaning of the paragraph on page 17 which reads “Your pregnant partner will be asked to sign a separate consent form…Any premature termination of the pregnancy will be reported. The study doctor will discuss this with you further should this action be necessary.”
4. Please align the consent form with the HDEC template, as important clauses have been omitted and irrelevant information, such as a reference to MedImmune, added. Point 2 should also refer to *coded* data.
5. Please add an addendum to the pregnancy PISCF to facilitate consent after the child is born.
6. Please include that the results of Hepatitis B and C testing are notifiable in New Zealand.
7. On page 5, please include how long a cycle is for the zanubrutinib and rituximab group.
8. Please add percentages for side-effects.

Notes

1. The Committee noted that the application form (question a.1.6) indicated there were no ethical issues with this study. This is seldom the case for clinical trials. It could have been stated, for example, that this is an experimental treatment in a potentially vulnerable participant population (and how this will be addressed), rather than simply stating that any issues arising will be dealt with.
2. The Committee observed that cultural issues involved with sending tissue overseas had been noted, but advised that data is also a taonga for Māori. This is expected to be discussed during the study’s formal Māori consultation.

Decision

This application was *approved* by consensus, subject to the following non-standard conditions:

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

|  |  |  |  |
| --- | --- | --- | --- |
| **3** | **Ethics ref:** | **19/STH/159** |  |
|  | Title: | A Phase 2/3 Safety Study of MEDI8897 Against Respiratory Syncytial Virus, in High- risk children. |  |
|  | Principal Investigator: | Mr. Jane Alsweiler |  |
|  | Sponsor: | IQVIA(Quintiles Pty Limited) |  |
|  | Clock Start Date: | 29 August 2019 |  |

Mrs Jane Alsweiler and Sarah Philipsen were present via 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

This study will evaluate the safety and effectiveness of a new RSV antibody called MEDI8897, in a participant population of high-risk infants,

Summary of resolved ethical issues

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

1. The Committee queried whether these high-risk infants would be recruited from outpatient clinics. The Researchers confirmed that this would be the case.

Summary of outstanding ethical issues

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

1. The Committee stated the parents of participants should not be required to pay for medications for side-effects potentially related to study drug or procedures.
2. The Committee asked for clarification on the publication restrictions imposed by the sponsor.
3. The Committee requested that study data be retained for 10 years from when the child participants turn 16.
4. The Committee advised that the first approach to parents should be made by their clinical care team, and that if they are open to recruitment the research team can then become involved.
5. The Committee requested that ethnicity data, in line with New Zealand census categories, be collected alongside international categories of race, to ensure applicability to the New Zealand context.
6. The Committee advised that the parents of participants should have the option of receiving a lay-summary of study results.
7. The Committee asked that the parent brochure be amended, as it currently attests that there is “no risk” involved with the study drug. It could instead read that the intervention is “generally well tolerated.”
8. The Committee observed that the territorial limits of the insurance policy were set within Australia. Evidence of insurance within New Zealand needs to be provided.

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

1. Please remove the statement which reads “No risks have been identified so far,” as this is unlikely and contradicted elsewhere in the document. All risks, not just serious adverse events, need to be included.
2. Please review the formatting of the document, which is dense and not well laid out. For example, bullet points could be used in the risks section, one for anaphylaxis, one for immune reaction, and so on.
3. Please amend the paragraph on the risks of donating blood samples. This is emboldened and capitalised unnecessarily.
4. Please use a simple lay-title. The introductory sentences should be simplified as well.
5. Please review the document for phrases like “your child is being asked,” as assent will not be sought from the infant participants. There are also instances where the reader is addressed as a participant, e.g. “if you decide to withdraw,” and these must be amended to “your child…”
6. Please include a cultural statement for the use of tissue, in line with the HDEC template.
7. Please state how incidental findings will be managed.
8. Please remove that the study may be stopped for commercial reasons, as this is not acceptable under the NEAC Guidelines.
9. Please provide an optional PISCF for the use of tissue in future unspecified research. The HDEC FUR template can be used if required.
10. Please provide a check-box whereby parents can request a lay-summary of the study results.

Decision

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

* Please amend the participant information sheet and consent form, taking into account the suggestions made by the Committee (*Ethical Guidelines for Intervention Studies* para. 6.22).
* Please ensure that parents are compensated for medications required as a result of side-effects of study processes (Ethical Guidelines for Intervention Studies para. 8.4).
* Please clarify any publication restrictions for this study (Ethical Guidelines for Intervention Studies para. 7.15).
* Please ensure that study data is retained for 10 years after the children turn 16 (Ethical Guidelines for Intervention Studies para. 1.10).
* Please ensure that parents of participants are first approach by their clinicians for recruitment into the study (Ethical Guidelines for Intervention Studies para. 6.2).
* Please also collect ethnicity data, using categories from the New Zealand census (Ethical Guidelines for Intervention Studies para. 4.10 & 5.1).
* Please provide parents with a lay-summary of study results, if requested (Ethical Guidelines for Intervention Studies para. 7.21).
* Please amend the parent brochure as requested (Ethical Guidelines for Intervention Studies para. 6.2).
* Please provide evidence of New Zealand-specific insurance (*Standard Operating Procedures for Health and Disability Ethics Committees* para. 42.4.7).

After receipt of the information requested by the Committee, a final decision on the application will be made by Mr Dominic Fitchett and A/Prof Mira Harrison-Woolrych.

|  |  |  |  |
| --- | --- | --- | --- |
| **4** | **Ethics ref:** | **19/STH/160** |  |
|  | Title: | A Phase 3 Efficacy Study of MEDI8897 Against Respiratory Syncytial Virus, in Healthy Late Preterm and Term Infants |  |
|  | Principal Investigator: | Mrs. Jane Alsweiler |  |
|  | Sponsor: | IQVIA (Quintiles Pty Limited) |  |
|  | Clock Start Date: | 29 August 2019 |  |

Mrs Jane Alsweiler and Sarah Philipsen were present via 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

This study will evaluate the effectiveness of a new RSV antibody called MEDI8897 in healthy infants.

Summary of resolved ethical issues

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

1. The Committee queried whether participants will be recruited from routine outpatient appointments, as stated in the application form. The Researchers clarified that these healthy infants will be recruited from postnatal wards.

Summary of outstanding ethical issues

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

1. The Committee stated the parents of participants should not be required to pay for medications for side-effects potentially related to study procedures.
2. The Committee asked for clarification on the publication restrictions imposed by the sponsor.
3. The Committee requested that study data be retained for 10 years from when the child participants turn 16.
4. The Committee advised that the first approach to parents should be made by their clinical care team, and that if they are open to recruitment the research team can then become involved.
5. The Committee requested that ethnicity data, in line with New Zealand census categories, be collected alongside international categories of race, to ensure applicability to the New Zealand context.
6. The Committee advised that the parents of participants should have the option of receiving a lay-summary of study results.
7. The Committee asked that the parent brochure be amended, as it currently attests that there is “no risk” involved with the study drug. It could instead read that the intervention is “generally well tolerated.”

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

1. Please remove the statement at the top of page 6 which reads “No risks have been identified so far,” as this is unlikely and contradicted elsewhere in the document. All risks, not just serious adverse events, need to be included.
2. Please review the formatting of the document, which is dense and not well laid out. For example, bullet points could be used in the risks section, one for anaphylaxis, one for immune reaction, and so on.
3. Please amend the paragraph on the risks of donating blood samples. This is emboldened and capitalised unnecessarily.
4. Please use a simple lay-title. The introductory sentences should be simplified as well.
5. Please review the document for phrases like “your child is being asked,” as assent will not be sought from the infant participants. There are also instances where the reader is addressed as a participant, e.g. “if you decide to withdraw,” and these must be amended to “your child…”
6. Please include a cultural statement for the use of tissue, in line with the HDEC template.
7. Please state how incidental findings will be managed.
8. Please remove that the study may be stopped for commercial reasons, as this is not acceptable under the NEAC Guidelines.
9. Please provide an optional PISCF for the use of tissue in future unspecified research. The HDEC FUR template can be used if required.
10. Please provide a check-box whereby parents can request a lay-summary of the study results.

Notes

1. The Committee noted that the application incorrectly identified all participants as providing informed consent, and relevant fields in the application form were therefore not documented. However, the Committee was satisfied that the ethical issues of consent had been managed.

Decision

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

* Please amend the participant information sheet and consent form, taking into account the suggestions made by the Committee (*Ethical Guidelines for Intervention Studies* para. 6.22).
* Please ensure that parents are compensated for medications required as a result of side-effects of study processes (*Ethical Guidelines for Intervention Studies* para. 8.4).
* Please clarify any publication restrictions for this study (*Ethical Guidelines for Intervention Studies* para. 7.15).
* Please ensure that study data is retained for 10 years after the children turn 16 (*Ethical Guidelines for Intervention Studies* para. 1.10).
* Please ensure that parents of participants are first approach by their clinicians for recruitment into the study (*Ethical Guidelines for Intervention Studies* para. 6.2).
* Please also collect ethnicity data, using categories from the New Zealand census (*Ethical Guidelines for Intervention Studies* para. 4.10 & 5.1).
* Please provide parents with a lay-summary of study results, if requested (*Ethical Guidelines for Intervention Studies* para. 7.21).
* Please amend the parent brochure as requested (*Ethical Guidelines for Intervention Studies* para. 6.2).

After receipt of the information requested by the Committee, a final decision on the application will be made by Mr Dominic Fitchett and A/Prof Mira Harrison-Woolrych.

|  |  |  |  |
| --- | --- | --- | --- |
| **5** | **Ethics ref:** | **19/STH/161** |  |
|  | Title: | The ADESTE Study |  |
|  | Principal Investigator: | Professor Richard Troughton |  |
|  | Sponsor: | GLOBAL RESEARCH ON ACUTE CONDITIONS, TEAM ITALY |  |
|  | Clock Start Date: | 29 August 2019 |  |

No Researchers were present via 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

This is a multicentre, prospective, open label, two-arm, phase 2a trial, the primary purpose being to investigate the safety and tolerability of Adrecizumab (AZ) in acute heart failure patient requiring hospitalisation. The drug’s dosing and drug profile will be investigated as a secondary purpose. The study comprises 3 cohorts of participants, each receiving one of 3 escalating doses of AZ.

Summary of outstanding ethical issues

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

1. The Committee noted a number of errors on the application form, such as the statement that there are no ethical issues with the study (there are vulnerable acutely ill participants and a short recruitment phase), an incorrect description of the study (the study is not 2-arm and not an equivalence or bioequivalence study),
2. The Committee observed that study data made available to other researchers will only be partially de-identified. These should ideally be de-identified.
3. The Committee observed that Mark Richards is named as the PI on the insurance certificate, despite not being listed as an investigator.

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

1. Please use the HDEC template, as the current PISCF is poorly written/formatted and the compensation, confidentiality, and contraception sections need re-writing. The syntax of the document in general made it difficult to read.
2. Please provide a separate information and consent document for any future unspecified research. Please also consider that current information indicates that samples are going to a non-HDEC-approved tissue bank.
3. Please remove the termination for *any* reason clause.
4. Please provide information on tissue being sent overseas.
5. Please provide clearer information on the procedures participants will undergo.
6. Please indicate the number of participants who have been exposed to the study drug in the past. The seriousness of adverse events should be described in proportion to this population.
7. Please state that this is the first time the study drug will be given to people with heart failure.
8. Please use a lay-title.

Notes

1. The Committee wished to note that if a Researcher had been in attendance many of these outstanding issues could likely have been addressed.
2. The Committee also noted that many of the issues and errors in the PIS raised by the Central HDEC in their review of the study had not been addressed by the research team.
3. The Committee asked that statistics be included in future applications to validate claims such as those pointing to the high incidence of cardiovascular disease in Māori.

Decision

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

* Please amend the participant information sheet and consent form, taking into account the suggestions made by the Committee (*Ethical Guidelines for Intervention Studies* para. 6.22).
* Please ensure the de-identification of study data (*Ethical Guidelines for Intervention Studies* para. 7.2).
* Please take into account the Committee’s comments when completing the application form (*Standard Operating Procedures for Health and Disability Ethics Committees* para. 42.3).
* Please address the concerns of the Committee over the insurance certificate (*Standard Operating Procedures for Health and Disability Ethics Committees* para. 42.4.7).
* Please ensure a phone call to participants at 60 days (*Ethical Guidelines for Intervention Studies* para. 5.41).

|  |  |  |  |
| --- | --- | --- | --- |
| **6** | **Ethics ref:** | **19/STH/162** |  |
|  | Title: | Working Memory Training in Adult TBI |  |
|  | Principal Investigator: | Dr Kristin Gozdzikowska |  |
|  | Sponsor: | N/A |  |
|  | Clock Start Date: | 29 August 2019 |  |

No Researchers were 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

This is a pilot study of a computer-based working memory training system, CogMed, in individuals recovering from traumatic brain injury.

Summary of resolved ethical issues

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

1. The Committee was satisfied with the confidentiality of data, though wished the Researchers to note that these data will be ‘de-identified’ rather than ‘anonymised.’

Summary of outstanding ethical issues

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

1. The Committee noted that Māori consultation *is* required for this study and should be sought.
2. The Committee advised that health information generated in this study must be retained for 10 years. The Researchers should consult with relevant guidelines as to what study data this applies to.

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

1. Please state what will happen to participants’ data (previously collected) when they withdraw from the study. For example, whether they have the option of withdrawing their data.
2. Please proof read the document for typos.

Decision

This application was *approved* by consensus, subject to the following non-standard conditions:

* Please amend the participant information sheet and consent form, taking into account the suggestions made by the Committee (*Ethical Guidelines for Intervention Studies* para. 6.22).
* Please ensure that formal Māori consultation is undertaken (*Ethical Guidelines for Intervention Studies* para. 4.9).
* Please ensure that health information is retained for 10 years (*Ethical Guidelines for Intervention Studies* para. 1.10).

|  |  |  |  |
| --- | --- | --- | --- |
| **7** | **Ethics ref:** | **19/STH/164** |  |
|  | Title: | Pembrolizumab or Placebo Plus Gemcitabine/Cisplatin for First-Line Advancedand/or Unresectable Biliary Tract Carcinoma (KEYNOTE-966) |  |
|  | Principal Investigator: | Dr Rita Sasidharan |  |
|  | Sponsor: | Merck Sharp & Dohme (New Zealand) Limited |  |
|  | Clock Start Date: | 29 August 2019 |  |

Pallavi Wyawahare, April Jacobson, and Ginny Larson were present via 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

This is a phase 3 randomized, double-blind, superiority study of pembrolizumab plus gemcitabine/cisplatin versus placebo plus gemcitabine/cisplatin as first-line therapy in participants with Advanced and/or Unresectable Biliary Tract Carcinoma.

Summary of resolved ethical issues

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

1. The Committee queried whether formal Māori consultation was being undertaken, as this was stated not to be necessary in the application form. The Researchers responded that this was an error, and that consultation would be undertaken as part of DHB locality approval.

Summary of outstanding ethical issues

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

1. The Committee asked that any potential conflict of interest be taken into consideration. If the appropriate separation of clinician and researcher roles cannot be guaranteed during recruitment, a research nurse can be employed. An explanation of how unavoidable conflicts of interest will be managed/minimised should be provided.
2. The Committee noted that genetic testing involving whole genome sequencing was a mandatory aspect of the study. As this is not a primary study primary objective, this testing is usually designated as optional in the protocol for New Zealand sites, due to relevant Māori cultural issues. The Committee requested exploratory genetic testing be made optional, in order to allow fair and representative Māori participation.
3. The Committee advised that participants’ GPs should be informed of their exposure to an investigational drug.

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

1. On the optional future unspecified research document, please identify the location of the tissue bank. This should at least name the city.
2. Please provide the location of the storage facility where stool samples will be held. Additionally, please recognise Māori cultural issues when asking to collect stool samples. There is likely to be whakamā and storing samples in the refrigerator will raise further issues.
3. Please remove any optional study elements from the main PISCF.
4. Please remove from the consent form the option of the participants’ GP not being informed.
5. Please add information on the collection of urine samples.
6. Please include a statement that the effects of the combination of pembrolizumab, gemcitabine, and cisplatin are unknown, and could cause an increase in side-effect rates.

Notes

1. The Committee noted that a number of unnecessary documents had been uploaded with the application, such as translation certificates and pictures of the computers. The following do not need HDEC approval and therefore have not been approved:
   * MK-3475-966\_QuickSpecs\_HP Pro x2 612 G2\_Americas\_c05373376 Dated 21Sep2017.pdf
   * MK-3475-966\_Translation Cert Dated 05Jun2019\_Screen Report NZ (English) v1 05Jun2019.pdf
   * MK-3475-966\_Translation Cert Dated Mar2012\_Certified Translation\_EQ-5D-5L English version for NZ.pdf
   * MK-3475-966\_OM-AC1 Toilet Accessory\_User Instructions\_PD-PR-00684 Issue 1\_May2017\_English.pdf
   * MK-3475-966\_OMNIgene-GUT\_Collection Device\_User Instructions\_PD-PR-00442 Issue 5\_Apr2018\_English.pdf

Decision

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

* Please amend the participant information sheet and consent form, taking into account the suggestions made by the Committee (*Ethical Guidelines for Intervention Studies* para. 6.22).
* Please address the Committee’s concerns around the compulsory nature of broad genetic testing (*Ethical Guidelines for Intervention Studies* para. 4.5).
* Please inform GPs of participation (*Ethical Guidelines for Intervention Studies* para. 6.5).
* Please comment on any existing conflict of interest, and how this will be managed (*Ethical Guidelines for Intervention Studies* para. 4.21)

After receipt of the information requested by the Committee, a final decision on the application will be made by Dr Sarah Gunningham and Mrs Leesa Russell.

|  |  |  |  |
| --- | --- | --- | --- |
| **8** | **Ethics ref:** | **19/STH/165** |  |
|  | Title: | Biomarker-guided Management Post-Acute Coronary Syndromes |  |
|  | Principal Investigator: | Professor Rob Doughty |  |
|  | Sponsor: | N/A |  |
|  | Clock Start Date: | 29 August 2019 |  |

Prof Rob Doughty was present via 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

This is a randomised, controlled, two-arm study to assess whether use of a blood test to measure biomarkers of heart stress can be incorporated into current standard care. One arm of the study will receive usual care, and the other the biomarker intervention.

Summary of resolved ethical issues

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

1. The Committee asked for confirmation that potential participants will first be approached by a member of their clinical care team, and not recruited by a “cold call” from the Researchers. This was confirmed by the Researcher, unless the patient is already involved in another study. Even in this circumstance however, it was noted that the GP will likely first be contacted.
2. The Committee noted that the protocol references a qualitative sub-study involving Māori participants, but could not find information about this in other study documents. The Researchers answered that the process for this sub-study is still being developed, and this will be submitted as an amendment once finalised.
3. The Committee queried whether blood samples were being taken for future unspecified research. The Researcher responded that samples were being retained for specific research on heart biomarkers only and would not go into a generic tissue bank.

Summary of outstanding ethical issues

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

1. The Committee requested that the monitoring/oversight process be outlined clearly in the protocol. For example, the study will be monitored internally, but the relationship between the site nurse specialists, nurse study co-ordinator, and primary care providers, and the process by which the titration process is monitored, needs to be defined. The role of the research module, to be completed by GPs, also needs explaining. Overall, there needs to be a very clear methodology.
2. The Committee advised that new information which may impact participants’ decision to remain in the study should be communicated to them directly, rather than via their GP.

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

1. Please provide a lay-title.
2. Please provide a ‘Consent Form’ heading for the consent form.
3. Please add page numbers.
4. Please be clear about the breadth of information being obtained from various sources, in addition to the participant’s medical records.
5. Please include that participants’ GPs will be completing research modules which are visible to the research team.
6. Please add a sentence following the statement on the biomarker group. This should explain that participants in the usual care group will not have their results made available to their GP or added to medical records, but a heart specialist will review results and take action if clinically significant abnormalities are detected.

Decision

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

* Please amend the participant information sheet and consent form, taking into account the suggestions made by the Committee (*Ethical Guidelines for Intervention Studies* para. 6.22).
* Please clearly protocolise the monitoring/oversight of the titration process, taking into account the Committee’s comments (*Ethical Guidelines for Intervention Studies* para. 5.41).
* Please ensure that new safety information is communicated to participants directly (*Ethical Guidelines for Intervention Studies* para. 6.11).

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

|  |  |  |  |
| --- | --- | --- | --- |
| **9** | **Ethics ref:** | **19/STH/166** |  |
|  | Title: | RURAL: Rural vs. Urban Risks of Appendicitis CompLications |  |
|  | Principal Investigator: | Dr Michael Roberts |  |
|  | Sponsor: | Northland District Health Board |  |
|  | Clock Start Date: | 29 August 2019 |  |

No Researchers were 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

This is an observational cohort study which aims to define the effect of rural patient status on the outcomes of paediatric appendicitis, as compared with urban paediatric patients.

Summary of outstanding ethical issues

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

1. The Committee queried how localities will be managed and how it will be ensured that correct study processes are followed. It needs to be made clear how the Researchers will communicate with other hospitals, how training will be provided to lead investigators at each site, and how patients will be consented/recruited from emergency departments and how related ethical issues will be managed. The Committee expressed practical concern over the study design, oversight, and timeframe, and felt at present that there is a lack of information on the mechanics of the study. The Committee needs to be assured of the study’s capacity to answer the research question before it can grant ethics approval.
2. The Committee advised that the analysis of urban versus rural data may stigmatise the latter group, which may have restricted access to hospitals. The potential for stigmatisation and shame/whakamā should therefore be considered during the analysis and reporting of this study.

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

1. Please provide age-appropriate assent forms for the child participants. The HDEC templates offer guidance on this. Parent consent forms are also necessary.
2. The existing documents require review for sufficiency and accuracy of information. For example, it is stated that no identifiable data is being collected yet geodata location is being used.

Notes

1. The Committee did not believe that the outstanding ethical issues could be adequately addressed in a response to a provisional approval, and regretted that no member of the Research team could be in attendance to address these in discussion. The Committee encouraged reapplication.

Decision

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

* Please amend the participant information sheet and consent form, taking into account the suggestions made by the Committee (*Ethical Guidelines for Observational Studies* para. 6.10).
* Please acknowledge and take into consideration the potential for stigmatisation in the reporting of this study (*Ethical Guidelines for Observational Studies* para. 10.8).
* Please provide more information on the study design, particularly with reference to the Committee’s comments (*Ethical Guidelines for Observational Studies* para. 5.11).

|  |  |  |  |
| --- | --- | --- | --- |
| **10** | **Ethics ref:** | **19/STH/169** |  |
|  | Title: | Study Designed to Assess the Safety, Tolerability and PK of PTI-808 in Adults with Cystic Fibrosis |  |
|  | Principal Investigator: | Dr Mark O'Carroll |  |
|  | Sponsor: | Covance New Zealand Limited |  |
|  | Clock Start Date: | 29 August 2019 |  |

Dr Mark O’Carroll and Margaret Joppa were present via 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

This is a phase 1/2 double-blind, placebo-controlled, first-in-human study to evaluate the safety, tolerability, and pharmacokinetics of the study drug PTI-808. The New Zealand sites will only involve adults with cystic fibrosis (part 4). The phase 1 dose-finding parts of this study will be conducted overseas (parts 1-3).

Summary of resolved ethical issues

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

1. The Committee noted that dose level recommendations from the data safety monitoring board of part 1 of this study had been provided for part 4, and this was not at first confirmed by the Researchers. This was later said to be an oversight, and the DSMB recommendation was confirmed.
2. The Committee questioned whether tissue samples being retained for future unspecified research would be stored in a tissue bank. The Researcher clarified that these would go to the ‘EPI’ which is the storage site for this study.
3. The Committee acknowledged that amendments would be forthcoming in the event of new safety information arising.

Summary of outstanding ethical issues

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

1. The Committee asked that it be clarified in what form study data will be provided to other researchers. For example, whether these will have identifiers removed non-identifiable) or study code retained (re-identifiable), or be aggregated.
2. The Committee advised that new safety information which becomes available must be communicated to participants in a timely manner. This should be done face to face, and not delayed until the provision of new information and consent documents. The Committee also noted that an incorrect answer has been provided by ACS to question p.2.7 on numerous occasions and asked that the template response be updated to reflect the above.
3. The Committee noted that identifiers on blood samples should be limited to year of birth.

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

1. The document must be very clear on the front page, within a text box, about the process of this study. It is okay to state that this study as a whole is first-in-human, but it must also be stated that the drug and these doses have been tested in the antecedent parts of the study. It should also be emphasised that this is the first time this combination has been used in patients with cystic fibrosis. Please also amend the definition of ‘experimental,’ which should be that the study drug is not available in *any* market. Additionally, please outline this part’s relation to the other parts of the study.
2. Please remove the long study title and replace with a simple lay-title. This should not contain technical language.
3. Please re-write in lay-language, particularly at the bottom of page 1. Spacing should be re-considered as well.
4. Please simplify footers.
5. Please review the information provided regarding the likelihood of receiving the ‘new’ study drug, as this is not 80 percent in all cohorts.
6. Please review terms for understandability, such as ‘serum follicle-stimulating hormone test’ and ‘nasal sampling procedure’.
7. Please add reproductive risks in line with the HDEC template.
8. Please summarise study procedures and processes in a table, using lay terms.
9. Please add bullet-points to ‘Expectations.’
10. Please move content on allergic reactions to the study drug risk section, which is currently in the procedural risks section.
11. Please simplify the animal data, as this is currently too dense.
12. Please remove the statement that study drugs will be given as a finite course because they will be of no further benefit. This may be inaccurate. State instead that they will not be available due to its investigational nature.
13. On the optional PISCF for future unspecified research, please explain the terms ‘pharmacogenomics’ and ‘biomarker samples,’ and ‘individually re-identifiable specimens.’ Please also review the cultural content, which states that samples will be taken from *some* participants.
14. On the ‘Greenphire’ optional form please state clearly what this is, as the document is currently confusing. It should be reduced to one page with a new explanatory title.

Notes

1. The Committee observed that this study is comprised of 4 parts, the first three of which are being conducted overseas. Part 4 was said by the Researchers to function essentially as a phase 2 study within a greater phase 1/2 study. The Committee believed the study was well protocolised and part 4 could be reviewed. The Researchers also confirmed that part 4 would not go ahead prior to information from parts 1-3 being released. The early parts of the study are underway.

Decision

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

* Please amend the participant information sheet and consent form, taking into account the suggestions made by the Committee (*Ethical Guidelines for Intervention Studies* para. 6.22).
* Please clarify how identifiable study data will be when these are shared with other researchers. Please also limit identifiers on blood samples to year of birth. (*Ethical Guidelines for Intervention Studies* para. 7.2).
* Please ensure that participants are informed in a timely manner of updated safety information (*Ethical Guidelines for Intervention Studies* para. 5.41).

After receipt of the information requested by the Committee, a final decision on the application will be made by Dr Sarah Gunningham and A/Prof Mira Harrison-Woolrych.

|  |  |  |  |
| --- | --- | --- | --- |
| **11** | **Ethics ref:** | **19/STH/170** |  |
|  | Title: | Bronchodilator speed of onset. |  |
|  | Principal Investigator: | Professor Richard Beasley |  |
|  | Sponsor: | The Medical research Institute of New Zealand |  |
|  | Clock Start Date: | 29 August 2019 |  |

Matthew Williams and Dr Nethmi Kearns were present via 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

The study involves administering salbutamol and budesonide/formoterol to participants with stable asthma who have airflow limitation that are not exacerbating. The participants will be a model of those presenting to emergency departments whose airflow limitation is severe enough for medication to have an effect but are not sufficiently unwell to warrant emergency treatment. The aim is to establish the non-inferiority of Symbicort to salbutamol following a single dose of rescue medication in adult asthmatics, to improve lung function and respiratory symptoms.

Summary of resolved ethical issues

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

1. The Committee queried whether spirometry being undertaken at 1, 2 ,3, and 5-minute intervals would be a strain on participants. The Researcher answered that participants will blow for only a 3-second duration, and that asthmatics find spirometry easier as they are used to respiratory discomfort. These intervals were said to be acceptable if completed carefully. The Committee asked whether there was a safety protocol in place. The Researcher confirmed that a crash kart and resuscitation kit would at hand. Participants would also be seated and advised not to blow too hard.
2. The Committee questioned the study contingencies for withholding medication. The Researcher replied that participants will be advised to treat their asthma as a priority over study compliance. They will therefore take Ventolin as needed and can book study visits for another date.
3. The Committee checked on the status of Māori consultation. The Researchers responded that this was being conducted, but still forthcoming.

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

1. Please amend the consent form so that it is not optional for participants to be informed of clinically relevant incidental findings.
2. Please proof read the document for typos.

Notes

1. The Committee commended the use of lay-language in the PISCF.
2. The Committee noted that the co-ordinating investigator and sponsor are both Professor Richard Beasley, and there will therefore be a financial relationship between these two parties.

Decision

This application was *approved* by consensus, subject to the following non-standard conditions:

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

|  |  |  |  |
| --- | --- | --- | --- |
| **12** | **Ethics ref:** | **19/STH/171** |  |
|  | Title: | Check Mate 9DW: CHECKpoint pathway and nivoluMAb clinical Trial Evaluation 9DW |  |
|  | Principal Investigator: | Professor Edward Gane |  |
|  | Sponsor: | Bristol-Myers Squibb |  |
|  | Clock Start Date: | 29 August 2019 |  |

No Researchers were 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

The purpose of this study is to evaluate the safety and efficacy of nivolumab plus ipilimumab as first line therapy for participants with advanced Hepatocellular carcinoma (HCC). This is a Phase 3, open-label, randomised controlled study where participants will be randomised to one of two arms: Nivolumab and Ipilimumab, or Lenvatinib (a new oral treatment similar to sorafenib which has been approved in some countries for first line treatment of HCC).

Summary of outstanding ethical issues

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

1. The Committee observed that study data will only be partially de-identified and shared with other researchers. It was asked that it be explained how identifiable study data will be (for example, whether this implies a study code being retained) and how these will be stored. There must also be confirmation that data stored for secondary or future use will be de-identified only. Additionally, no data must be shared with the sponsor prior to recruitment.
2. The Committee required clarification on whether this study will exhaust all archival tissue of the participants, or whether some residual samples will remain. The preference is that there is leftover tissue or tissue returning to the archive, in case of future studies. If new biopsies will be taken this should be clearly stated.

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

1. Listing common and very common side-effects alongside each other is confusing and makes reading difficult. Please list side-effects linearly.
2. Please use the HDEC contraception standard wording on page 19 with regard to condom use and sperm donation. Abstinence also should not be listed as a contraceptive method.
3. On the pregnant partner document, please clearly define what information is being collected after the child’s birth and for how long. Also note that the sentence “data will help doctors to monitor the potential risks…” is repeated in the following paragraph.
4. Please complete the radiation risks section.
5. Please remove that advanced liver cancer is a “highly deadly cancer,” as this is unnecessary.
6. In the optional future unspecified research form, please remove the compensation statement as this does not apply.
7. Please add a lay-title, without acronyms.
8. On page 10, please amend the sentence “XXXX is approved in New Zealand. If you receive XXXX, benefits may be expected.” Given the information provided this may over-promising. Additionally, if this refers to Lenvatinib note that it is not approved.

Decision

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

* Please amend the participant information sheet and consent form, taking into account the suggestions made by the Committee (*Ethical Guidelines for Intervention Studies* para. 6.22).
* Please clarify the identifiability of and security arrangements for study data (*Ethical Guidelines for Intervention Studies* para. 7.2).
* Please clarify whether participants will have residual tissue samples remaining at the conclusion of the study (*Ethical Guidelines for Intervention Studies* para. 5.5).

After receipt of the information requested by the Committee, a final decision on the application will be made by Mrs Helen Walker and Mrs Leesa Russell.

## 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:** | 8 October 2019 |
| **Meeting venue:** | Sudima Hotel, Christchurch Airport, 550 Memorial Drive, Christchurch |

The following members tendered apologies for this meeting:

* Dr Devonie Waaka

1. **Problem with Last Minutes**

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

The meeting closed at 4pm.