|  |  |
| --- | --- |
| **Committee:** | Northern A Health and Disability Ethics Committee |
| **Meeting date:** | 15 May 2018 |
| **Meeting venue:** | Novotel Ellerslie, 72-112 Greenlane Rd East, Ellerslie, Auckland |

|  |  |
| --- | --- |
| **Time** | **Item of business** |
| 1:00pm | Welcome |
| 1:05pm | Confirmation of minutes of meeting of 17 April 2018. |
| 1:30pm | New applications (see over for details) |
|  | i 18/NTA/60  ii 18/NTA/66  iii 18/NTA/68  iv 18/NTA/69  v 18/NTA/70  vi 18/NTA/71 |
| 4:30pm | General business:   * Noting section of agenda |
| 4:45pm | Meeting ends |

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

## Welcome

The Chair opened the meeting at 1:00pm 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 17 April 2018 were confirmed.

## New applications

|  |  |  |
| --- | --- | --- |
| **1** | **Ethics ref:** | **18/NTA/60** |
|  | Title: | The benefits of participating in a 'dementia-friendly' book group at the public library: A qualitative study. |
|  | Principal Investigator: | Dr Brenda Sally Rimkeit |
|  | Sponsor: |  |
|  | Clock Start Date: | 03 May 2018 |

Dr Brenda Sally Rimkeit was present in person, and Gill Claridge and Dalice Sim 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 qualitative study has the following aims and questions:
   * how people living with dementia experience reading literary fiction in a book group at the public library;
   * whether participation enhances language skills for the people living with dementia; and,
   * whether participation enhances the confidence of the people living with dementia to regain their place in community.
2. The book groups have been designed to be 'dementia-friendly', with use of adapted literary fiction and specialised book group facilitation. Participants will be recruited through posters at the local Alzheimers/Dementia Association and Public Library.
3. All participants will give informed, written consent through a face-to-face interview with a co-investigator.
4. Data will be collected from an audiotaped pre- and post semi-structured interviews with participants and 10 weekly book groups, held at the public library.
5. All book groups will be facilitated by the co-investigators.
6. Data will be de-identified, transcribed and analysed linguistically and thematically. Results will be published in peer reviewed journals.

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 participants who cannot provide their own consent will be involved. The Researcher(s) explained that all participants will have capacity, sometimes the capacity would be lower and would require supported assistance, but individual consent will be determined to be legally possible. The Researcher(s) confirmed that they would ensure all participants can legally consent, as per Convention on the Rights of Persons with Disabilities and in accordance with the Code of patients Rights.
2. The Researcher(s) confirmed they have removed assent processes.
3. The Researcher(s) confirmed this is a different cohort, with different severity of dementia, from previous studies.
4. The Committee asked how capacity will be determined. The Researcher(s) explained it will be through a consenting interview. This interview will also be used to ensure no participants will be recruited who would likely experience harm or frustration from being in the book group, if they are too aphasic, for example.
5. The Researcher(s) confirmed the co-ordinating investigator will conduct all consenting interviews, and noted her professional experience with determining capacity and appropriateness of participation.
6. The Committee asked about how the sessions are run. The Researcher(s) explained that there are three facilitators (co-investigators) and outlined their expertise and referred to the facilitation manual for the study. The Researcher(s) explained that the Librarians will be invited to be involved if they want, though they are very busy. The fidelity of the intervention is not so important, rather the lived experience of these participants, in the library context and doing the book group.
7. The Committee requested that librarians must sign confidentiality agreements.
8. The Researcher(s) confirmed that they would put a training process in place so the facilitators can work with the librarians before they are involved in accordance with the facilitators manual and the Committee requested a copy of that manual be uploaded onto the portal.
9. The Researcher(s) confirmed that in this study they are not accessing health information to recruit. Participants are recruited by responding to posters in key contexts. Diagnosis will not be checked through accessing medical records, only through verbal discussion during consent process. This is a naturalistic process.
10. The Committee noted that participants can leave the study at any time, not at 6 months. If a participant were to withdraw make it clear that the researchers would like to retain the data up until the point of withdrawal.
11. The Researcher(s) confirmed that once transcription occurs the audio will be deleted.

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 that quality of life is mentioned in the poster and participant information sheet. The Researcher(s) stated this related to lived experience, so it is an informal use of the term.
2. The Committee asked whether validated quality of life questionnaires will be used in this study, noting there was a lot of wording around quality of life outcomes but the only questionnaire submitted is very limited in that respect. The Researcher(s) stated that a semi-structured interview would be conducted in this study, which asks about relationships with community. The Researcher(s) noted they could add a quality of life questionnaire component to this study, noting it would take about 10 minutes. The Researcher(s) added that they think this would generate valuable data. The Committee noted this would require HDEC submission.

Recruitment posters:

1. Add in the words: We hope they are enjoyable to read and to share with others.
2. Add in that Pre and post intervention interviews will also be taped and transcribed.
3. Warn that not everyone who is interested may be able to participate (this will cover the situation if the competency of some is such that they are unable to consent)
4. The Committee noted that the poster and advertising implies predetermined study outcomes. Please remove bias, make language more neutral.

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

1. Generally, check for typos – there are a few errors throughout the participant information sheet.
2. Tick boxes should only contain yes if truly optional
3. Explain de-identified (page 6).
4. The researchers cannot claim that the participation ‘will be fun’. (page 4)
5. If the interviews involve making an assessment about a potential participant’s capacity, participants should be told, especially if the researchers make notes about that.
6. The Researcher(s) confirmed they would remove the GP being informed of study participation (participant information sheet). But retain the section which explains that the participant’s GP will be contacted if there are serious concerns about the participant
7. The family member participant information sheet should not seek the views on the relative’s participation in the research. This is not a Right 7(4) situation unless the researchers propose to enrol person living with dementia who have more than moderate dementia.
8. The Committee note the participant information sheet should be reframed to state that participants should only sign the consent form if they understand the study and want to take part in it. It should avoid reference to best interests.
9. Amend participant information sheet for the family to delete references to seeking the family member’s views on the person living with dementia’s participation in the research.
10. Similar amendments needed for the family participant information sheet as for the person living with dementia participant information sheet but, in addition, delete the suggestion that the book club may ‘possibly even [improve] his/her mood, language and memory” (page 5).
11. The participant information sheet for the family member may benefit from a bit more detail about the risk management plan and that the researchers would seek family member’s phone number and to stay within easy reach of the library.
12. Amend definitive statement that the relative can join or continue to participate in a book club after the study is finished (page 6)
13. Family ‘consent/views’ form Requires significant amendment based on previous comments and also delete the page which allows for the family member/carer to write ‘any other views you may have regarding your relative’s participation in the study”.
14. Application a.1.5 and b.2. 2 - Researchers must advise participants that the interviews will be recorded and transcribed as well as the book clubs.
15. Rights of correction need to be mentioned (page 8) on the consent form for person living with dementia

Decision

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

* Please amend the information sheet and consent form, taking into account the suggestions made by the Committee (*Ethical Guidelines for Intervention Studies* *para 6.22).*
* Provide further information on the study design, *in particular use of quality of life questionnaires and the facilitators manual* (*Ethical Guidelines for Intervention Studies para 5.4)*

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

|  |  |  |
| --- | --- | --- |
| **2** | **Ethics ref:** | **18/NTA/66** |
|  | Title: | Renal Function in Elderly Persons Continuing and Ceasing Lithium |
|  | Principal Investigator: | Dr Brian Deavoll |
|  | Sponsor: | Canterbury Distric Health Board |
|  | Clock Start Date: | 03 May 2018 |

Dr Brian Deavoll 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. The study investigates Bipolar Affective Disorder (BPD) is a chronic relapsing condition. Lithium Carbonate is the most effective treatment for Bipolar Affective Disorder. Lithium may cause accelerated deterioration in renal function in some patients. Doctors treating older patients with mood disorders stabilized on Lithium, with deteriorating renal function, have no guidelines in determining whether ceasing Lithium slows, halts or reverses renal function decline.
2. There are very few studies world-wide looking at this issue and none from New Zealand.
3. Aims:

1) To describe the renal function of elderly patients in the CDHB area, for whom data is available, remaining on lithium for at least one year and those who have been on lithium for at least one year and then ceasing it (for any reason) for at least 6 months.

2) To describe the frequency of monitoring of serum Lithium levels and renal function in elderly patients in the CDHB area, for whom data is available.

1. All prescriptions for all types of lithium preparations in persons age 65 and over living in the CDHB area will be obtained from Ministry of Health/ Pharmac records between 1/1/2007 and 31/12/2017. Preliminary enquiries of the Ministry of Health have indicated 90% availability of NHI numbers for these prescriptions.
2. All Lithium estimations and estimated Glomerular Filtration Rates for patients who have been prescribed Lithium for at least 12 months over the study period, will be obtained from CDHB Laboratory data warehouse.
3. Rate of decline in renal function when on and when off lithium will be described.
4. Frequency of monitoring of renal function and lithium estimation for patients taking lithium will be described. Non-zero Lithium estimations will be a proxy check to determine medication compliance.

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 Maori consultation process.
2. The Researcher(s) explained why they were not collecting ethnicity data. The Committee accepted the explanation, due to potential identifiability and stigma.

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 that they can only approve access to identifiable health information without consent for research in certain circumstances. The Ethical Guidelines for Observational Studies states at Paragraph 6.43:
   1. *Access to identified or potentially identifiable data for research without the consent of the people the data identifies or makes potentially identifiable may be justifiable when:*
      1. *the procedures required to obtain consent are likely to cause unnecessary anxiety for those whose consent would be sought; or the requirement for consent would prejudice the scientific value of the study; or it is impossible in practice to obtain consent due to the quantity or age of the records; and*
      2. *there would be no disadvantage to the participants or their relatives or to any collectives involved; and*
      3. *the public interest in the study outweighs the public interest in privacy.*
2. Different consent considerations apply for audit studies, as they also do for vulnerable populations
3. Another important element that should be considered is evidence of good data governance.
4. The Committee asked the researcher to make a case for the benefit of the study as well as addressing the reasons why consent cannot be sought, noting some of these considerations had been indirectly made in the application made by the researcher.
5. The Researcher(s) explained that many patients on lithium experience `renal function problems. Changing treatment from lithium to other treatments, has in some cases, been disastrous. The Researcher(s) explained the benefit of the study would be that it goes some way towards reducing use of alternative treatments from lithium, as alternative treatment options have side effects that are particularly bad for older people.
6. One of the questions the study aims to answer is what kind of renal functions should result in cessation of lithium.
7. The Researcher(s) explained the lack of guidance on how to make decisions when faced with liver function deterioration verses ceasing lithium and the resulting issues related to mental health.
8. The Researcher(s) explained that lithium and renal function testing is generally poor, with low levels of testing. In order to access this data, Ministry of Health and Pharmac data was required.
9. The Researcher(s) explained that it was also unknown what happens when lithium was stopped with regards to renal function – does it deteriorate following cessation, or does it improve, noting this was an important question as it would impact decision making around stopping treatment due to renal function.
10. The Committee noted some of this study is classified as audit, particularly reviewing testing adherence versus guidelines.
11. The Committee noted that some of the research questions posed in the study were unable to be answered with the current design, highlighting scientific validity issues, noting the numerous confounders. The current design cannot show causality; it is descriptive.
12. The Committee is not clear on the benefit of undertaking the first aim, given the researchers concede that it will not be possible to determine if total lifetime duration of lithium use is associated with renal function decline (refer to the protocol and to the app b.1.3).
13. The Researcher(s) explained that the statistician involved did raise concerns relating to ‘stoppers and starters’ of lithium. However this phenomenon is more common with younger people with bipolar, treated with lithium. As a rule, older people remain on their lithium consistently. The Committee noted that the statistician should be involved in analysis.
14. The Researcher(s) explained the data inclusion criteria addresses some of the confounders.
15. The Committee noted the protocol could be improved by the addition of more details – data sets, management plans, linking plans and statistical analyses.
16. The Committee noted that there are impracticality justifications for use of data without consent, due to size of cohort.
17. The Committee noted that some harms had been identified, in terms of seeking consent.
18. The Researcher(s) also noted some participants would have passed away, so consent was not possible in those cases either.
19. The Committee asked about linking mortality data, which could be done by the Ministry of Health. The Ministry could also link to mortality and to laboratory data. This reduces movement bias. If the researcher proposes to do the linking then additional ethical concerns arise which the researcher must address.
20. The Committee noted excluding people with no blood results causes study validity concerns.
21. The Committee stated that the study could be improved by use of national cohorts, and with the Ministry doing the linking, it reduces risk of data loss and confidentiality.
22. The Committee requested that protocol is amended to revise the study design – it is descriptive only - a naturalistic observational cohort study that is exploratory and hypothesis framing etc. The protocol should also include desired variables, collections access, how the researcher wants data returned (i.e. identifiability).

Decision

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

* Amend protocol taking into account the suggestions from the Ethics Committee. *Ethical Guidelines for Observation Studies* 7
* An investigator who proposes not to seek informed consent for use of identified or potentially identifiable data for research must explain to an ethics committee the reasons for not seeking consent, and how the study would be ethical in the absence of consent. *Ethical Guidelines for Observation Studies* 6.45
* Address scientific validity concerns and seek further advice on datasets available from national collections to reduce risk of disclosure of identifiable records *Ethical Guidelines for Observation Studies* 8.1 and consider the linking guidelines 8.11

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

|  |  |  |
| --- | --- | --- |
| **3** | **Ethics ref:** | **18/NTA/68** |
|  | Title: | A Study to Assess the Safety, Tolerability, Pharmacokinetics, and Pharmacodynamics of ACH-0145548 in Healthy Participants |
|  | Principal Investigator: | Dr Paul Hamilton |
|  | Sponsor: | Clinical Network Services Ltd |
|  | Clock Start Date: | 03 May 2018 |

Dr Paul Hamilton and Ms Shuruthi Balachandran 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. The study is commercially sponsored research and a first in human study.
2. The study involves assessment of a complement factor inhibitor for the treatment of complement alternative pathway (AP)-mediated haematological diseases (eg paroxysmal nocturnal haemoglobinuria and AP-mediated renal diseases).
3. The study is double-blind placebo controlled, ascending dose, 3 sequential cohorts, New Zealand only, with 28 patients (though it could be extended up to 32 additional healthy participants for a total of 60 potential participants).
4. Primary objective to assess safety and tolerability.
5. The study has been submitted to SCOTT.
6. 28 days participation, excluding screening.

Summary of ethical issues (resolved)

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

1. Adaptive features pose a challenge for ethical oversight. This study has identified these issues well, but in future studies, could researchers please flag this in a cover letter. This assists understanding regarding adaptive sections of the study.
2. The Committee asked for information on why this first in human study was being conducted in New Zealand. The Researcher(s) explained that the study site have a good relationship with the sponsor.
3. The Committee asked if this molecule is similar to the other similar studies conducted by ACS. The Researcher(s) explained that it is very similar structurally (third generation compound). This drug tries to address the potency issues from prior generations. This molecule strength is a little higher, so pharmacodynamics effect should be better. It is expected that the half-life is a little longer. The first generation drug is currently used in patients, however it involves dosing 3 times a day. This new compound should address those concerns and make the treatment easier to adhere to.
4. The Committee asked, considering the increased half-life, does it result in need for more cautious phase 1 testing. The Researcher(s) stated the predicted half-life is in region of 8 hours, based on preclinical animal data. The Researcher(s) explained wash out period is well within the follow up period for the study.
5. The Committee asked whether the half-life, if demonstrated to be longer than anticipated, would extend follow up. The Researcher(s) confirmed it would.
6. The Researcher(s) explained the adaptive nature of the protocol, based on safety data and PK data.
7. The Researcher(s) explained the risk mitigation factors that were in place.

Summary of ethical issues (outstanding)

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

1. The application refers to locked archive room but no details are provided for electronic security. Please provide further information.
2. The Committee queried whether there is future unspecified research, noting the participant information sheet states that the samples being analysed for biomarker studies may be stored ‘at a facility selected by the sponsor to enable further analysis of biomarker responses’ The Researcher(s) explained it is non genetic biomarker tests, within this study.
3. The Committee asked whether samples can be destroyed prior to 3 years. Please make it clear in the participant information sheet whether that biomarker research is mandatory or not, and whether samples can be destroyed. Please also address this point in a cover letter to HDEC.
4. The Committee noted that careful monitoring for signs and symptoms of infections will be implemented for all studies. A panel of infectious disease physicians with expertise in complement deficiencies has been assembled to advise on infection risks and management for all clinical trials” page 42. The Committee asked if this panel been convened already, and whether it was in New Zealand. The Researcher(s) explained that this is an international Committee, adding that an Auckland specialist was involved in this Committee for a previous compound. The Committee requested that there is a confirmation that this panel is active for the study.
5. Data management - all participants have a unique study number but the researches also propose to use date of birth (app r.2.4.1) The Committee do not think date of birth should be used in addition to the study number. Please use year of birth instead.
6. Furthermore, the participant’s full name should not be used for onsite files (app r.2.3). Please provide explanation about identifiable records being kept separate from study data. Please explain processes about clearly separating internal ACS files and study data.
7. Clinical Trial Snapshot document must refer to the fact it is first in humans. Total participation time should also be stated (ie, 28 days) similarly with the Spartan print and Digital text.
8. Radio text – The concepts of helping science and being paid should not be conflated. “Do you want to help Science and be paid for your time?” The concepts should be kept separate. Need to mention 28 days and also first in humans. Please make payment and screening clear.
9. Please report to the Committee after the initial 3 cohorts have been undertaken before beginning any further cohorts

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

1. Data management - Achillion Pharmaceuticals, Inc. may use data derived from this trial for the purpose of research and development. – this needs to be explicit in the participant information sheet
2. Data management – the data may be disclosed by Achillion Pharmaceuticals, Inc. to other investigators, the FDA, other government agencies, or foreign drug regulatory authorities, or to the public. This is inappropriate – please explain the wide range of data sharing. The Researcher(s) stated this would be aggregate data, not identifiable, for example in presentations.
3. The Committee asked whether there is a separate participant information sheet for partners who may become pregnant. Please add participant information sheet to the pregnancy data release form. Reference template on HDEC reference.
4. The Committee noted pregnancy outcome is covered by this consent form, but this would not extend to born child data.
5. The participant information sheet does not contain any information about the transfer of data overseas and the level of protection available in the countries it is being sent to.
6. The participant information sheet must avoid repetition.
7. Mention the telephone calls for AEs on days 4 and 5 (page 5);
8. Advise that some of the diseases being screened for are notifiable and there is an obligation to report them to regulatory authorities
9. The paragraphs about where the samples will be sent are confusing – please clarify whether all samples sent to both Australia and to the US. The Researcher(s) stated both.
10. the participant information sheet states samples will be coded and only identified by participant’s study number and initials – this is contradictory to what the protocol says which is that a study number and date of birth will be used (page 9)(and date of birth shouldn’t be used, or initials).
11. Please explain how race information is collected. The Researcher(s) explained the templates that are provided from international sponsors, usually referring to black white Native American Pacific Island etc. The Committee noted these categories do not apply in New Zealand. The Committee noted the Ministry of Health ethnicity collection protocols. The Researcher(s) acknowledged this point and explained their system used that translates the New Zealand ethnicity to the race categories, and that meets the sponsor requirements. This is completed with a note to file.
12. The Committee asked whether the sponsor is happy with this process, as FDA requires self-reporting of race. The Researcher(s) confirmed sponsor was happy with the translation process from ethnicity to race by the research team.
13. Make it clear that there is CCTV, recording of participants and that participants will require staying in the centre for a number of days and nights with restricted movement.
14. The Committee noted while the participant information sheet does contain information about coming in and out of the centre in the table, it does not make it clear that participants cannot leave the site at certain points. Please make this clearer.
15. Please use template wording for pregnancy risks <https://ethics.health.govt.nz/guides-templates-forms-0>
16. Consent form should be in template form with tick boxes for truly optional matters. Also needs to include consent for (i) access to participant’s medical records; (ii) providing any necessary medical information to the participant’s health care provider and where necessary to regulatory authorities; (iii) destruction of samples; (iv) samples going overseas; (v) data going overseas

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 Safety Monitoring Committee’s operation *(Ethical Guidelines for Intervention Studies para 6.50).*
* Explain what happens to health information (confidentiality and privacy) (*Ethical Guidelines for Intervention Studies* *para 7.7)*

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

|  |  |  |
| --- | --- | --- |
| **4** | **Ethics ref:** | **18/NTA/69** |
|  | Title: | Effect of HM30181A on the Pharmacokinetics of Dabigatran |
|  | Principal Investigator: | Dr Christopher Jackson |
|  | Sponsor: | Athenex Pharmaceuticals |
|  | Clock Start Date: | 03 May 2018 |

Michelle Lockhart 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.

Dr Kate Parker declared a potential conflict of interest, and the Committee decided it was not a conflict of interest.

Summary of Study

1. The primary objective of this study is to determine the effect of multiple once-daily doses of HM30181A on the single-dose pharmacokinetics of dabigatran. In addition, the study will estimate the duration of the effect on P-gp inhibition by HM30181A on dabigatran exposure by determining the PK of dabigatran at 2 and 4 weeks after the administration of HM30181A.
2. Eligible participants will receive a single dose of dabigatran and will provide blood samples for analysis for 48 hours post-dosing (Treatment Period 1). After at least a 7 day washout, Treatment Period 2 will start. Participants will receive daily doses of HM30181A for 3 days. One hour after the third dose they will receive another dose of dabigatran. Blood samples will be collected for Days 1-8. On Day 17, they will have another dose of dabigatran with blood samples collected for 5 days post-dose. On Day 31 they will have a final dose of dabigatran with blood samples collected for 48 hours post-dose.
3. There will be a followup phone call about 2 weeks after the last blood sample is collected.
4. Safety will be monitored regularly with laboratory tests, aPPT, recording of AEs, ECGs and vital signs.
5. Participants will be resident at the Zenith Clinical Site for dosing and days when multiple blood samples are required.

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 Zentech involvement. The Researcher(s) explained the role of the Co-ordinating Investigator and Zentech, noting that Zentech were assisting with conduct of the study.
2. The Researcher(s) explained history of other drugs and studies related to this study drug.
3. The Researcher(s) explained that the Co-ordinating Investigator understands the HM tablet well due to their oncology trial involvement.
4. The Researcher(s) confirmed no advertising was planned at this stage.

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 suggested that researchers provide independent peer review using HDEC template, as it is helpful for researchers and the Committee and is typically part of Zenith Technology applications.
2. The Committee asked why an investigator brochure was not submitted for the HM tablet. The Researcher(s) stated there is some information on the HM tablet alone, but it is usually used in conjunction with other pharmaceuticals. The Committee requested the investigators brochure for the HM tablet.
3. The Committee noted there is no data sheet uploaded for Dabigatran. The Researcher(s) confirmed it will be a form of New Zealand commercial stock. Please submit copies once supplier identified.
4. The Committee requested more information about the insurance for the study, noting that the Insurance certificate was broad cover and unrelated to specific studies.
5. The Committee requested that date of birth should not be collected as a study identifier, in order to protect confidentiality.
6. Please use Statistics New Zealand's ethnicity classifications when collecting ethnicity data to ensure the options available are suitable for New Zealand participants. These classifications are: New Zealand European, Maori, Samoan, Cook Islands Maori, Tongan, Niuean, Chinese, Indian, Other (such as Dutch, Japanese, Tokelauan).
7. Add detail in protocol or on cover letter about privacy and confidentiality of study data. The Committee request that the study data plan is uploaded.

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

1. The Committee generally noted that the HDEC template and Zenith template would assist researchers in adding missing information and with formatting. Please review those templates and make changes to the current participant information sheet.
2. Page 3 – please add more information on exclusion criteria.
3. Hepatitis B and HIV are notifiable diseases – please explain what happens if positive result i.e. that it is mandatory to report results to regulatory authorities.
4. Change ‘your identity won’t be disclosed in such presentations” (bottom page 7) to “will not be published in a form that could reasonably be expected to identify you “- similarly with the same statement made on page 8 (about half way down the page).
5. The Committee asked about unexpected findings. The Researcher(s) stated that the tests they will conduct should not identify any incidental findings. Add more potential information from the investigator brochure to the participant information sheet about any potential incidental or unexpected results.
6. Add where data is stored, for how long and if going overseas etc. \ The participant information sheet does not contain any information about the transfer of data overseas and the level of protection available in the countries it is being sent to.
7. Explain what a ‘wash out period’ is.
8. See <https://ethics.health.govt.nz/guides-templates-forms-0> for information on reproductive risks
9. Add information from Zenith template about freezing samples.
10. Please clarify how long data will be stored for, and in what form of identifiability. Please make this clear in the participant information sheet.
11. The Committee suggested a graphic or table could be used to explain different study arms, bloods taken and other relevant study procedures.
12. The Committee noted that the participant information sheet was full of jargon - e.g. PK, chemotherapeutics. Please use lay language.
13. The Committee noted that New Zealand ethical guidelines do not allow stopping a study for commercial reasons.
14. Please justify, in a cover letter, why women are excluded from this study.
15. Pg.8 – ‘satisfaction of knowing’ – change to ‘may have satisfaction of knowing’.
16. Add clarity about participants being photographed, videoed and must stay in confines of building and that Zenith also allows sponsor to ‘watch’ participant when the treatment is being administered. This is through an online video system. Zenith have this in their participant information sheet and it should be included in both 69 and 70
17. The Committee noted that there should be more side effects listed, particularly any rare but serious side effects.
18. The participant information sheet should advise participants that their plasma will be frozen (bottom page 5).

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 sponsor insurance. *(Ethical Guidelines for Intervention Studies para 8.4).*
* Submit outstanding documentation and cover letters addressing ethical issues.

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

|  |  |  |
| --- | --- | --- |
| **5** | **Ethics ref:** | **18/NTA/70** |
|  | Title: | Effect of HM30181A on the Pharmacokinetics of Digoxin |
|  | Principal Investigator: | Dr Christopher Jackson |
|  | Sponsor: | Athenex Pharmaceuticals |
|  | Clock Start Date: | 03 May 2018 |

Michelle Lockhart 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.

Dr Kate Parker declared a potential conflict of interest, and the Committee decided it was not a conflict of interest.

Summary of study

1. The primary objective of this study is to determine the effect of multiple once-daily doses of HM30181A on the single-dose PK of digoxin.
2. Eligible participants will receive a single dose of digoxin and will provide blood samples for analysis for 6 days post-dosing (Treatment Period 1). After at least a 10 day washout, Treatment Period 2 will start.
3. Participants will receive daily dosed on HM30181A for 3 days. One hour after the third dose they will received another dose of digoxin. Blood samples will be collected for days 1-8, and at Day 17.
4. Safety will be monitored regularly with laboratory tests, recording of AEs, ECGs and vital signs.
5. Participants will be resident at the Zenith Clinical Site for dosing and days when multiple blood samples are required.

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 Zentech involvement. The Researcher(s) explained the role of the Co-ordinating Investigator and Zentech, noting that Zentech were assisting with conduct of the study.
2. The Researcher(s) explained history of other drugs and studies related to this study drug.
3. The Researcher(s) explained that the Co-ordinating Investigator understands the HM tablet well due to their oncology trial involvement.
4. The Researcher(s) confirmed no advertising was planned at this stage.

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 suggested that researchers provide independent peer review using HDEC template, as it is helpful for researchers and the Committee and is typically part of Zenith Technology applications.
2. The Committee asked why an investigator brochure was not submitted for the HM tablet. The Researcher(s) stated there is some information on the HM tablet alone, but it is usually used in conjunction with other pharmaceuticals.
3. The Committee noted there is no data sheet uploaded for Dabigatran. The Researcher(s) confirmed it will be a form of New Zealand commercial stock. Please submit copies once supplier identified.
4. The Committee requested more information about the insurance for the study, noting that the Insurance certificate was broad cover and unrelated to specific studies.
5. The Committee requested that date of birth is not collected as a study identifier, in order to protect confidentiality.
6. Please use Statistics New Zealand's ethnicity classifications when collecting ethnicity data to ensure the options available are suitable for New Zealand participants. These classifications are: New Zealand European, Maori, Samoan, Cook Islands Maori, Tongan, Niuean, Chinese, Indian, Other (such as Dutch, Japanese, Tokelauan).
7. Add detail in protocol or on cover letter about privacy and confidentiality of study data. The Committee request that the study data plan is uploaded.

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

1. The Committee generally noted that the HDEC template and Zenith template would assist researchers in adding missing information and with formatting. Please review those templates and make changes to the current participant information sheet.
2. Page 3 – please add more information on exclusion criteria.
3. Hepatitis B and HIV are notifiable diseases – please explain what happens if positive result.
4. Change ‘your identity won’t be disclosed in such presentations” (bottom page 7) to “will not be published in a form that could reasonably be expected to identify you “- similarly with the same statement made on page 8 (about half way down the page).
5. The Committee asked about unexpected findings. The Researcher(s) stated that the tests they will conduct should not identify any incidental findings. Add more potential information from the investigator brochure to the participant information sheet about any potential incidental or unexpected results.
6. Add where data is stored, for how long and if going overseas etc. The Committee noted the offshore transfer of data – the Privacy Bill contains provisions which impose additional obligations on agencies disclosing personal information to overseas persons. Disclosure will now generally only be permissible if the individual consents, the overseas person is required to protect the information in a way comparable to New Zealand legislation, or the overseas person is in a country with comparable privacy legislation to New Zealand legislation. The participant information sheet does not contain any information about the transfer of data overseas and the level of protection available in the countries it is being sent to.
7. Explain what a ‘wash out period’ is.
8. See <https://ethics.health.govt.nz/guides-templates-forms-0> for information on reproductive risks
9. Add information from Zenith template about freezing samples.
10. Please clarify how long data will be stored for, and in what form of identifiability. Please include in a cover letter for the Committee and make this clear in the participant information sheet.
11. The Committee suggested a graphic or table could be used to explain different study arms, bloods taken and other relevant study procedures.
12. The Committee noted that the participant information sheet was full of jargon - e.g. PK, chemotherapeutics. Please use lay language.
13. The Committee noted that New Zealand ethical guidelines do not allow stopping a study for commercial reasons.
14. Page 8 – ‘satisfaction of knowing’ – change to ‘may have satisfaction of knowing’.
15. Add clarity about participants being photographed, videoed and must stay in confines of building etc.
16. The Committee note that there should be more side effects listed, particularly any rear but serious side effects.
17. The participant information sheet should advise participants that their plasma will be frozen (bottom page 5).

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 sponsor insurance. *(Ethical Guidelines for Intervention Studies para 8.4).*
* Submit outstanding documentation and cover letters addressing ethical issues.

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

|  |  |  |
| --- | --- | --- |
| **6** | **Ethics ref:** | **18/NTA/71** |
|  | Title: | BO39633 - Atezolizumab Oncology Extension Study (IMBRELLA) |
|  | Principal Investigator: | Dr Richard Sullivan |
|  | Sponsor: | Roche Products (NZ) Ltd |
|  | Clock Start Date: | 03 May 2018 |

Arthi Sunkari 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.

Dr Karen Bartholomew declared a potential conflict of interest, and the Committee determined it was not a conflict of interest.

Summary of Study

1. The purpose of this study is to provide continued atezolizumab-based treatment and/or treatment with comparator agent(s) to cancer patients who were previously enrolled and treated in a Genentech or Roche-sponsored atezolizumab study (parent study).
2. Participants will be allowed to continue the same treatment regimen received in their parent study, which will be one of the following:

-atezolizumab alone or

-atezolizumab in combination with other agent(s) or

-comparator agent(s)

1. At present, one Roche parent study in New Zealand (OAK - HDEC ref: 13/NTA/221) is nearing conclusion and participant(s) will be eligible to participate in BO39633 study if they wish. The OAK study is concluding June 2018, and OAK participants will have the option of either discontinuing treatment or participating in BO39633 study to continue receiving treatment.
2. The study aims to evaluate the safety and overall survival of atezolizumab alone and in combination with other agent(s). Study treatment will continue until disease progression or beyond if deemed clinically beneficial to the patient by the investigator; death or withdrawal from study.
3. Atezolizumab is an antibody (a protein produced by the body's immune system) that affects the immune system. By blocking the PD-L1 pathway, atezolizumab may help the immune system stop or reverse the growth of tumours.

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 this study is an extension study, used to enable continued drug access. In this application it is for one patient. However the plan is that this study is available for other studies to have their participant’s transition over in order to continue treatment access. The Committee noted amendments would need to be submitted if the study changes.
2. The participant information sheet states that the study may be stopped for administrative reasons – please note this cannot be for commercial reasons.
3. The Committee asked about indefinite follow up and access to medical records. The Researcher(s) explained that generally indefinite follow up will not be for very long for these participants, due to their age.
4. The Committee noted that the application as written was confusing. The Researcher(s) and the Committee discussed the different types of participation (treatment, follow up, no treatment etc).
5. The Researcher(s) explained the survival rates for these drugs, and how it differs in different patient groups.
6. The Committee asked about the request for participants to stop other therapies. The Researcher(s) confirmed for this group of people there are no other effective treatments available – they have run out of treatment options, and this is a second line therapy.
7. The Researcher(s) stated there are no additional scans.
8. The Committee noted the long list of side effects. The Researcher(s) noted all patients I in this study have been on the parent trial – nothing in the participant information sheet is new to the participants.

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

1. Pg.4 add detail on testing for HIV and that it is notifiable.
2. Remove Americanisms
3. Remove jargon – i.e. lVEF
4. Remove incapacitated adult section. The Researcher(s) confirmed no participants would not be able to provide their own informed consent.
5. Note that wording implies identifiable records may be shared. This must be amended.
6. Page 14 – who is IQVIA? The Researcher(s) stated this is the CRO. Please make this clearer.
7. The consent form (page 17 of the PIS) needs to be in template form <https://ethics.health.govt.nz/guides-templates-forms-0> and should also include consent to: (i) transfer of data overseas; (iii) future specified research; (iv) notification of some results to regulatory authorities where mandated; (v) whether participants want study results.
8. Regarding the participant information sheet for the observational study - change title so it refers only to the observational study and not to the extension part of the study.
9. To avoid confusion, the introduction section of the participant information sheet should explain that this is a participant information sheet for the observation study only. Can participants stay in the extension study if they decline to participate in the observational study
10. Page 2 – delete the word ‘experiences’ in the first line and replace with something like “In an observational study, health information from routine treatments is collected”. The participant information sheet for the observation study should include more detail about the kind of health information that will be accessed.
11. Page 3 – it is potentially confusing to refer to ‘screening assessments’ because all participants consenting to the observation study will be included. For similar reasons it is also confusing to refer to assessments during the study as if there are separate study assessments when the reality is that any assessments are only for the purpose of usual medical care. Similarly with including possible side effects (page 4) and the information about what will happen if I am injured in this study – all should be deleted
12. Participants in the extension study should not have to refer back to documentation pertinent to the parent study – for example, to obtain a list of the medications not allowed in the parent study (page 6, PIS) or for the side effects of atezolizumab in combination with other agents (page 11).
13. Use contraceptive risk template <https://ethics.health.govt.nz/guides-templates-forms-0> in place of wording on page 11 and 12.
14. Pages 14-15 – the way in which participants’ data will be disclosed to others is made very clear, including that it may be given to other researchers who are not participating in the study. It also outlines future specified research and refers to the fact that the data will be sent overseas. Note going forward, offshore transfer of data – Privacy Bill contains provisions which impose additional obligations on agencies disclosing personal information to overseas persons. Disclosure will now generally only be permissible if the individual consents, the overseas person is required to protect the information in a way comparable to New Zealand legislation, or the overseas person is in a country with comparable privacy legislation to New Zealand legislation. The participant information sheet does not contain any information about the transfer of data overseas and the level of protection available in the countries it is being sent to.
15. Under the heading “Study Treatment” (page 5) the issue of dose is confusing – on the one hand it says you will take the same dose and in the next paragraph it says that if you were on a weight-based dose that will change to a fixed dose. The Researcher(s) explained this related to the study being able to be joined by other studies. This drug has fixed dose, but other old studies was on kg/ml. If an old study was ml per kg, would move to fixed dose – which is standard of care. The Committee requested this is made clearer.
16. The Researcher(s) confirmed at this stage it is not possible to be on different schedules. The Researcher(s) conceded it could be possible in future due to have other study designs ‘dropping into’ the study. The Committee confirmed this would require an amendment if it were to occur.
17. Page 6 – how long in study – and you continue to derive clinical benefit and also when your disease progresses – these seem in conflict. The Researcher(s) explained that drug can remain beneficial even if disease progresses. Please make this clearer to apply to different possible patient types.
18. In future please use format of HDEC template, particularly for consent form.
19. On observational study participant information sheet – this is just follow up, not clinical research. The Committee suggested the following wording ‘because you have been on a clinical trial’.
20. The Committee noted it is not experiences collected as stated, rather it is health information (observational follow up participant information sheet).

The Pregnancy health Information participant information sheet

1. The Committee noted that regarding information about the child – this consent must occur once the child is born. Split the consent for the female’s health information to be used from the child’s health information.
2. The Committee noted that this is very broad and seeks family medical history
3. Note unlimited consent including for child’s health data – this is not appropriate. Please remove this and limit the access to what is necessary.
4. Consent form needs amendment to reflect above comments and should be in template form, as appropriate. Including data transfer overseas.

Decision

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

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

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

## 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:** | 19 June 2018, 08:00 AM |
| **Meeting venue:** | Novotel Ellerslie, 72-112 Greenlane Rd East, Ellerslie, Auckland |

1. **Problem with Last Minutes**

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

The meeting closed at 5.00pm