8 **Ethics ref:** **20/STH/139**

Title:

Principal Investigator: Dr Nigel Gilchrist

Sponsor: Florey Institute of Neuroscience and Mental Health

Clock Start Date: 27 August 2020

Nigel Gilchrist and Deirdre Thompson were present via videoconference for discussion of this application.

Potential conflicts of interest

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

A potential conflict of interest was raised by Dr Paul Chin, however upon further discussion no significant conflict was present with regards to this ethics application.

Summary of Study

1. The objective of this randomized clinical trial (n=170) is to test the safety and efficacy of administration of 25 mg perispinal Etanercept in improving patient reported outcomes at 28 days after treatment.
2. The Primary Hypothesis is that treatment with 25 mg perispinal Etanercept improves quality of life in stroke survivors.
3. The Secondary Hypothesis is that repeated administration of perispinal Etanercept 25mg leads to improved quality of life compared to a single administration.
4. This randomized clinical trial will include the following patients:
    a) Patients with a history of acute ischemic or haemorrhagic stroke confirmed on imaging
    b) Age ≥18 years-65 years at time of stroke
    c) Moderate-to-severe disability resulting from stroke as defined by a modified Rankin scale of 3-5
    d) Stroke occurred between 1 and 5 years before enrolment.
    e) SF-36 score <95
    f) Patient is able to complete the SF-36 questionnaire independently or availability of a relative or carer who is able to complete the SF-36 questionnaire on behalf of the patient
    g) Consent can be obtained from the participant

Summary of resolved ethical issues

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

5. The Committee queried whether it is possible for a participant to be randomised to placebo twice. The Researcher stated that this is possible.
6. The Committee queried whether, if there is a clear benefit towards the end of the study, the placebo group would be offered the active treatment once the study is completed. The Researcher stated that this will be offered, however it is not yet addressed in study documentation due to insufficient evidence.

7. The Committee queried whether anyone who cannot consent themselves will be included in the study. The Researcher stated that only those who are competent to consent will be included.
8. The Committee queried whether the target age range for the study may be too young. The Researcher stated that, as the study will also recruit individuals up to five years post-stroke with ongoing disability, that participants will be up to 70 years old when the study commences. Additionally, younger participants are preferred as advanced age tends to introduce a greater number of confounding variables.
9. The Committee queried why a subcutaneous injection into the neck is necessary for the administration of the study drug. The Researcher stated that this is a replication of the original study and clarified that there will be no direct injection into cerebral spinal fluid.
10. The Committee queried whether any tissue was being sent overseas. The Researcher confirmed that no tissue would be sent overseas.
11. The Committee queried whether doing nothing as control would be valid for the study versus administering a placebo injection. The Researcher stated that the injection was an important part of determining a placebo effect.
12. The Committee queried whether there was a risk to participants on coagulants. The Researcher stated that if a risk is identified in an individual participant, they will not receive an injection.

Summary of outstanding ethical issues

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

13. Please amend the protocol to remove the statement that consent can come from a responsible person, as proxy consent is not permitted in New Zealand.
14. Please provide information as to what health information will be accessed for the study.
15. Please provide HDEC with the full review that led to the study grant, or use the HDEC peer review template. Please ensure that justification for the use of a saline injection as placebo is included.
16. Please provide an updated insurance certificate that is New Zealand/site specific.

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

17. Please include Hepatitis B and C as possible unexpected findings, as these will be screened for, and that these infections are notifiable diseases.
18. Please amend the PIS to ensure that it is specific to New Zealand participants, please refer to the HDEC PIS template for guidance.
19. Please state whether the study drug is approved in New Zealand for any indication.
20. Please explain what do to if participants become distressed while completing the study questionnaires.
21. Please provide information on the confidentiality of video recordings.
22. Please amend the contraceptive language to reflect the the contraception template found in the HDEC template PIS.
23. Please explain why researchers may contact participants after the study has ended.
24. Please include data management information, as found in the HDEC PIS template.
25. Please ensure the HDEC Consent Form template is used.
26. Please make it clear that withdrawal of consent does not need to be given in writing.

Decision

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

- Please amend the protocol to remove the statement that consent can come from a responsible person, as proxy consent is not permitted in New Zealand.
- Please provide information as to what health information will be accessed for the study.
- Please provide HDEC with the full peer review that led to the study grant, or use the HDEC peer review template. Please ensure that justification for the use of a saline injection as placebo is included.
- Please provide an updated insurance certificate that is New Zealand/site specific.
- Please amend the Participant Information Sheets and Consent Form, taking into account feedback provided by the Committee (above).

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