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| **5.2** | **Study Title** | Optimizing the clinical effectiveness of TBS treatment of depression (OPTI-TBS) |
| **PI** | Paul Fitzgerald |
| **Ref** | 2022.ETH.00182 |
| **Reviewer** | Robert Schmidli |
| **What is your recommendation for this item?** |
| [ ] Approve without changes [x] Approve out of session with changes [ ] Not Approve and resubmit*Can sufficient subjects be recruited, given that the protocol is onerous for the subjects, and there is a similar large study to be run concurrently?**PICF needs to be completed. Introduction section on credentials of investigators should be shortened.**Measurement of outcomes uses many questionnaires and scores. Does the statistical analysis allow for sufficient correction for multiple analyses?**Will qualified staff be present in the event of a seizure?* |
| **Review**  |
| * 1. **Research Merit and Integrity (NS1.1):**
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| **Does the research proposal ask a relevant/worthwhile research question?**  | **Yes/~~No~~** |
| Study examines novel form of Transcranial magnetic stimulation (rTMS)– intermittent theta burst stimulation (iTBS). iTBS uses very short bursts at high frequency. Similar efficacy as rTMS, but only takes 3 min, compared to 20-40min for rTMS. Site of stimulation is also considered to be important. Examines optimal dose & schedule and efficacy of dual site stimulation. Proposed mode of action of rTMS/iTBS is not explained in submission. |
| **Has the researcher justified the need for this research?** | **Yes/~~No~~** |
| rTMS established treatment but only 50% patients get substantial responses.  |
| **Will the proposed methodology answer the research question(s)?**  | **Yes/~~No~~** |
| Two studies. No sham treated group – study groups are compared with standard treatment. All subjects receive 35 sessions, 5 days per week:* Standard (3min – has shown best efficacy) vs prolonged (9min) vs repeated (3x3min) iTBS
* As for Standard (above) – L dorsolateral prefrontal cortex vs additional stimulation at more posterior site vs lateral prefrontal cortex

Person administering treatment will be aware of nature of treatment, but assessor will not. Assessment at baseline, 2wk, 4wk, end, 1, 3, 6 months. Subjects must be treatment-resistant with moderate-severe depression.Study involves large number of subjects. Study 2022.ETH.00181 involves similar numbers. Is it feasible to recruit sufficient numbers for the study? Study protocol involves attendance for 5 days a week for six weeks, plus follow-up assessments. This may limit the number of subjects completing the study (although they will receive expensive treatment free of charge). |
| **Is the protocol following good clinical practice?** | **Yes/~~No~~** |
| Investigator’s brochures look more like glossy advertisements than informative document |
| **Are the power calculations, indicating the number of recruits required, accurate?** | **Yes/~~No~~** |
| 80 subjects in each arm. Number of expected recruits from Canberra not stated. Appear to be sufficient |
| **Is the proposed statistical analysis robust and accurate enough to deal with the data generated?** | **Yes/~~No~~** |
| Multiple questionnaires/scales used for assessment. I assume that allowance will be made for multiple analyses. |
| **Are the drug safety issues fully addressed?** | **Yes/~~No~~** |
| Low risk of seizures. Other side effects are uncomfortable or minor. Will qualified staff be present in the event of a seizure? |
| **Are the risks to recruits detailed in the proposal listed fully and completely in the PICF?** | **Yes/~~No~~** |
| Excessive description of credentials of investigators in PICF. Description of iTBS is quite technical, but is adequate, considering the technical nature of the interventions. Many parts of PICF in square brackets need to be completed. Study contact person etc not stated. |
| **Suggested Comments to the Researcher from HREC**  |
| **RMI (NS1.1)** |
| **Do you have comments for the HREC to consider against any of the other NS criteria?** | **Yes/No** |
| **Justice (NS1.4)** |
| **Beneficence (NS1.6)** |
| **Respect (NS1.10)** |
| **General Comments on Risks and Benefits** |