Title	**A Prospective multicentre, phase 2b randomised controlled double-blind trial, to determine the safety and efficacy of perispinal etanercept on quality of life at 28 days post treatment (PESTO).**
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Institute	The Florey Institute of Neuroscience and Mental Health
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AuSCR role	Recruitment
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Status	In progress
Summary	**Study Hypothesis**: Perispinal etanercept (PSE) improves quality of life after chronic stroke in stroke survivors of working age. **Study Objectives**: To test the safety and efficacy of administration of 25 mg perispinal etanercept in improving patient reported outcomes at 28 days after treatment. **Primary Objectives**: The Primary Hypothesis is that treatment with 25 mg perispinal etanercept improves quality of life in stroke survivors. **Secondary Objectives**: The Secondary Hypothesis is that repeated administration of perispinal etanercept 25mg leads to improved quality of life compared to a single administration. **Design**: Phase 2b, multicentre, prospective, randomised, double blind, placebo-controlled clinical trial **Inclusion Criteria**: 1. Patients with a history of acute ischemic or hemorrhagic stroke confirmed on imaging 2. Age ≥18 years-65 years at time of stroke 3. Moderate-to-severe disability resulting from stroke as defined by a modified Rankin scale of 3-5 4. Stroke occurred between 1 and 15 years before enrolment. 5. SF-36 score 6. 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 7. Consent can be obtained from the participant or person responsible. **Exclusion Criteria**: 1. Contra-indication to etanercept (eg previous hypersensitivity, ongoing infection, use of IL-1 antagonists) 2. History of hepatitis B and C, tuberculosis, HIV, SLE, multiple sclerosis, moderate to severe heart failure 3. History of malignancy 4. Other use of immunosuppressant 5. Clinical diagnosis of dementia 6. mRS 0-2 7. Botulinum toxin injection to limbs in the 4 months prior to Screening Visit 8. Pregnancy (women of childbearing potential must be tested) 9. Breastfeeding 10. Participation in any investigational study in the last 30 days 11. Known terminal illness or planned withdrawal of care or comfort care measures. 12. Any condition that, in the judgment of the investigator could impose hazards to the patient if study therapy is initiated or affect the participation of the patient in the study. 13. Prior exposure to etanercept for stroke **Number of Planned Participants**: 168 **Investigational product**: etanercept (Enbrel) 25 mg **Safety considerations**: Adverse Events and Serious Adverse events will be collected during the course of the trial. **Statistical Methods**: The primary endpoint, an achievement of at least 5 points improvement on the SF-36 score will be tested using a logistic regression model with the treatment arms as an independent variable and baseline value of SF-36, proxy or self-administration of SF-36 as adjustment covariates.