AuSCR Research Task Group approved projects

Title	**Comparative effectiveness of routine Tenecteplase versus Alteplase in acute ischaemic stroke: an international collaboration using real world data (CERTAIN Collaboration)**
Principle investigator	Professor Dominique Cadilhac/Professor Chris Bladin
Institute	Monash University/Ambulance Victoria
Co-investigators	Dr Joosup Kim, Associate Professor Timothy Kleinig, Dr Jackson Harvey, Associate Professor Bruce Campbell
Submission date	06 December 2021
AuSCR role	Data provision
Approved	01 March 2022
Status	In progress
Summary	Intravenous tenecteplase (0.25mg/kg) in patients with intracranial large vessel occlusion before endovascular thrombectomy is associated with higher rates of early recanalization when compared to standard dose alteplase. In patients with minor stroke symptoms intravenous tenecteplase (0.4mg/kg) appears to be equivalent to alteplase without safety concerns. In a meta-analysis of 5 randomised controlled trials, intravenous tenecteplase at doses from 0.1-0.4mg/kg was at least non-inferior when compared with alteplase in achieving functional independence without signal for increased haemorrhagic risk. Other potential benefits of tenecteplase over alteplase include reduced dosing complexity, potentially shorter door to needle times (as more readily administered as a single bolus in the CT scanner) and reduced inter hospital transfer complexity (which may also hasten transfers). Globally, several hospitals and health services have begun routinely using tenecteplase for stroke thrombolysis, including in Australia. The primary objective of this international collaborative study is to systematically assess differences in functional outcomes, safety and processes of care between treatment with tenecteplase and alteplase. Data from the Victorian Stroke Telemedicine Service will be linked to the Australian Stroke Clinical Registry (AuSCR) in order to obtain information on a tenecteplase, adverse events, outcomes and other routinely collected information on the demographic characteristics, clinical characteristics, and treatment of patients. This linkage is required because data on the thrombolytic agent used is available in the Victorian Stroke Telemedicine Service dataset only and data on outcomes after discharge from hospital are available in the AuSCR dataset only. We have previously demonstrated the feasibility of this linkage using probabilistic and deterministic methods considering matches in hospital, medical record number, date of birth, date of admission and date of discharge. For the period of 1 July 2019 to 30th June 2020, only 5 out of 138 patients (4%) indicated as being administered thrombolysis according to the VST Service were not linked to a patient in the AuSCR. These linked data will be pooled with data from other hospitals and health services Australia, New Zealand and the United State of America that are using tenecteplase either routinely or preferentially for specific patient subgroups such as large vessel occlusion. Multi-level multivariable regression models with level by hospital and region will be used to assess the association between the thrombolytic agent used and: 1) clinical outcomes of interest (logistic regression); and 2) door-to-needle times (linear regression). Age, sex, premorbid modified Rankin Scale and NIHSS will be included in models regardless of significance and/or model fit. All other desired variables will be considered for inclusion into the multivariable model based on statistical significance and/or model fit. The regression analyses will be conducted in two ways: 1) on the entire cohort; and 2) in a propensity score matched cohort. The propensity score matching will be performed 1:1 (tenecteplase : alteplase) to the nearest neighbour with caliper set at 0.2 standard deviations of the logit of propensity score. Variables to be considered in the matching will include age, sex, and premorbid modied Rankin Scale, NIHSS.