## Proposed tables and figures for main publication of the tenecteplase in wake up ischeamic stroke trial (TWIST)

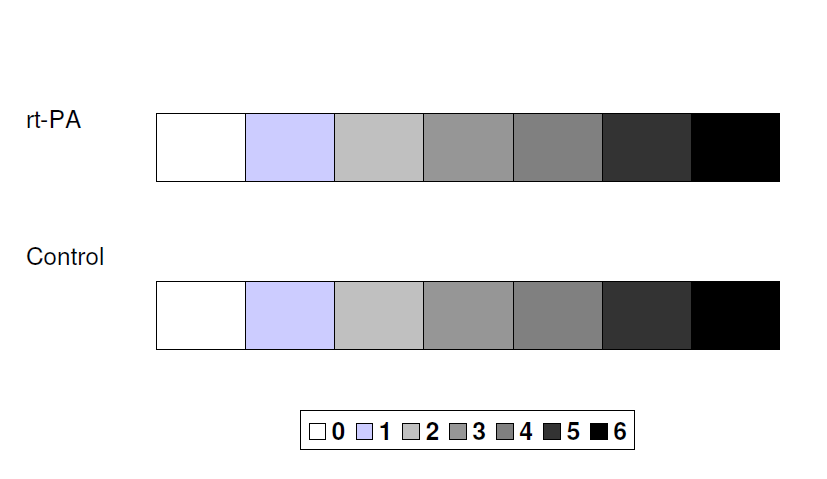
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**Figure 1. Consort 2010 Flow diagram**

|  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- |
| **Table 1. Characteristics of Patients at Baselinea** | | | | | | |
|  |  | |  | **Tenecteplase (n=?)** |  | **Control (n=?)** |
|  | Age-yr | |  |  |  |  |
|  |  | Mean (SD) |  |  |  |  |
|  |  | Median (IQR) |  |  |  |  |
|  | Age groups (years) | |  |  |  |  |
|  |  | <60 |  |  |  |  |
|  |  | 60-79 |  |  |  |  |
|  |  | ≥80 |  |  |  |  |
|  | Sex | |  |  |  |  |
|  |  | Women |  |  |  |  |
|  |  | Men |  |  |  |  |
|  | Country— no. (%) | |  |  |  |  |
|  |  | Norway |  |  |  |  |
|  |  | Sweden |  |  |  |  |
|  |  | Denmark |  |  |  |  |
|  |  | Finland |  |  |  |  |
|  |  | Estonia |  |  |  |  |
|  |  | Latvia |  |  |  |  |
|  |  | Lithuania |  |  |  |  |
|  |  | United Kingdom |  |  |  |  |
|  |  | Switzerland |  |  |  |  |
|  |  | New Zealand |  |  |  |  |
|  | Final diagnosis at discharge — no. (%) | |  |  |  |  |
|  |  | Definite ischemic stroke |  |  |  |  |
|  |  | Probable ischemic stroke |  |  |  |  |
|  |  | Other diagnosis |  |  |  |  |
|  | Stoke risk factors and medical history— no. (%) | |  |  |  |  |
|  |  | Hypertension |  |  |  |  |
|  |  | Diabetes mellitus |  |  |  |  |
|  |  | Atrial fibrillation |  |  |  |  |
|  |  | Active smoker |  |  |  |  |
|  |  | Previous stroke or TIA |  |  |  |  |
|  |  | Coronary artery disease |  |  |  |  |
|  |  | Current use of an anticoagulant agent |  |  |  |  |
|  |  | Current use of an antiplatelet agent |  |  |  |  |
|  | Pre-morbid modified Rankin Scale score | |  |  |  |  |
|  |  | 0 |  |  |  |  |
|  |  | 1 |  |  |  |  |
|  |  | 2 |  |  |  |  |
|  | Median NIHSS score (IQR)b | |  |  |  |  |
|  |  | Mild (0- 7) |  |  |  |  |
|  |  | Moderate (8–14) |  |  |  |  |
|  |  | Severe (≥15) |  |  |  |  |
|  | Endovascular treatment— no. (%) | |  |  |  |  |
|  | Median time from last known to be well to randomisation — (IQR)- min | |  |  |  |  |
|  | Median time from wake-up to randomisation — (IQR) - min | |  |  |  |  |
|  | Median time from wake-up to hospital admission (IQR) - min | |  |  |  |  |
|  | Median time from hospital arrival to initiation of therapy (IQR) - min | |  |  |  |  |

aValues are means ±standard deviations(SD). IQR denotes interquartile range.

bScores on the National Institutes of Health Stroke Scale (NIHSS) range from 0 (normal) to 42 (death), with higher scores indicating greater deficit.



**Figure II Bar chart showing the distribution of mRS scores in each treatment group**

|  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| **Table 2. Efficacy and safety outcomes (intention to treat population)a** | | | | | | | | | | | | | | |
| **Outcome** | | |  | **Tenecteplase**  **(n=?)** |  | **Control**  **(n=?)** |  | **Unadjusted Effect Sizeh (95% CI)** |  | **P Value** |  | **Adjusted Effect Sizeh (95% CI)** |  | **P Value** |
| **Primary efficacy outcome** | | |  |  |  |  |  |  |  |  |  |  |  |  |
|  | Score on the modified Rankin scale at 3 monthsb | |  |  |  |  |  |  |  |  |  |  |  |  |
|  |  | 0 |  |  |  |  |  |  |  |  |  |  |  |  |
|  |  | 1 |  |  |  |  |  |  |  |  |  |  |  |  |
|  |  | 2 |  |  |  |  |  |  |  |  |  |  |  |  |
|  |  | 3 |  |  |  |  |  |  |  |  |  |  |  |  |
|  |  | 4 |  |  |  |  |  |  |  |  |  |  |  |  |
|  |  | 5 |  |  |  |  |  |  |  |  |  |  |  |  |
|  |  | 6 |  |  |  |  |  |  |  |  |  |  |  |  |
|  | Functional improvementc | |  |  |  |  |  |  |  |  |  |  |  |  |
| **Secondary efficacy outcomes** | | |  |  |  |  |  |  |  |  |  |  |  |  |
|  | Excellent functional outcome at 3 monthsd | |  |  |  |  |  |  |  |  |  |  |  |  |
|  | Good functional outcomee | |  |  |  |  |  |  |  |  |  |  |  |  |
|  | Response to treatmentf | |  |  |  |  |  |  |  |  |  |  |  |  |
| **Safety outcomes** | | |  |  |  |  |  |  |  |  |  |  |  |  |
|  | Death within 3 months after intervention | |  |  |  |  |  |  |  |  |  |  |  |  |
|  | Symptomatic intracranial hemorrhage | |  |  |  |  |  |  |  |  |  |  |  |  |
|  |  | As defined by SITS- MOST |  |  |  |  |  |  |  |  |  |  |  |  |
|  |  | As defined by IST-3 |  |  |  |  |  |  |  |  |  |  |  |  |
|  | Parenchymal hemorrhage type 2 | |  |  |  |  |  |  |  |  |  |  |  |  |
|  | Any intracranial haemorrhage | |  |  |  |  |  |  |  |  |  |  |  |  |
|  | Poor functional outcome or deathg | |  |  |  |  |  |  |  |  |  |  |  |  |

aAdjusted analyses included age, baseline NIHSS score and time since wake-up as covariates.

bScores on the modified Rankin scale range from 0 to 6, with 0 indicating no neurologic deficit, 1 no clinically significant disability (return to all usual activities), 2 slight disability (able to handle own affairs without assistance but unable to carry out all previous activities), 3 moderate disability requiring some help (e.g., with shopping, cleaning, and finances but able to walk unassisted), 4 moderately severe disability (unable to attend to bodily needs without assistance and unable to walk unassisted), 5 severe disability (requiring constant nursing care and attention), and 6 death.

cFunctional improvement was defined as an improvement of at least 1 point on the modified Rankin scale at 3 months and was assessed as a common odds ratio in an ordinal logistic-regression analysis.

dExcellent functional outcome was defined as a score of 0 to 1 on the modified Rankin scale at 3 months.

eGood functional outcome as a score of 0 to 2 on the modified Rankin scale at 3 months.

fResponse to treatmentis defined as mRS 0 for patients with mild deficits at study entry (NIHSS <=7), mRS 0-1 for patients with moderate deficits (NIHSS 8-14), and mRS 0-2 for patients with severe deficits (NIHSS >14).

gPoor functional outcome defined as patients with mRS score of 4-6 at 3 months.

hEffect sizes are assessed as odds ratios, except for death within 3 months assessed as hazard ratios. The 95% confidence intervals for the secondary outcomes were not adjusted for multiple comparisons.

|  |  |  |  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| **Table 3. Efficacy and safety outcomes (intention to treat population) stratified according to thrombectomy treatmenta** | | | | | | | | | | | | |
|  | | |  | **Patients not treated with thrombectomy** | | | |  | **Patients treated with thrombectomy** | | | |
| **Outcome** | | |  | **Tenecteplase**  **(n=?)** | **Control**  **(n=?)** | **Adjusted Effect Sizeh (95% CI)** | **P-Value** |  | **Tenecteplase**  **(n=?)** | **Control**  **(n=?)** | **Adjusted Effect Sizeh (95% CI)** | **P -Value** |
| **Primary efficacy outcome** | | |  |  |  |  |  |  |  |  |  |  |
|  | Score on the modified Rankin scale at 3 monthsb | |  |  |  |  |  |  |  |  |  |  |
|  |  | 0 |  |  |  |  |  |  |  |  |  |  |
|  |  | 1 |  |  |  |  |  |  |  |  |  |  |
|  |  | 2 |  |  |  |  |  |  |  |  |  |  |
|  |  | 3 |  |  |  |  |  |  |  |  |  |  |
|  |  | 4 |  |  |  |  |  |  |  |  |  |  |
|  |  | 5 |  |  |  |  |  |  |  |  |  |  |
|  |  | 6 |  |  |  |  |  |  |  |  |  |  |
|  | Functional improvementc | |  |  |  |  |  |  |  |  |  |  |
| **Secondary efficacy outcomes** | | |  |  |  |  |  |  |  |  |  |  |
|  | Excellent functional outcome at 3 monthsd | |  |  |  |  |  |  |  |  |  |  |
|  | Good functional outcomee | |  |  |  |  |  |  |  |  |  |  |
|  | Response to treatmentf | |  |  |  |  |  |  |  |  |  |  |
| **Safety outcomes** | | |  |  |  |  |  |  |  |  |  |  |
|  | Death within 3 months after intervention | |  |  |  |  |  |  |  |  |  |  |
|  | Symptomatic intracranial hemorrhage | |  |  |  |  |  |  |  |  |  |  |
|  |  | As defined in SITS- MOST |  |  |  |  |  |  |  |  |  |  |
|  |  | As defined in IST-3 |  |  |  |  |  |  |  |  |  |  |
|  | Parenchymal hemorrhage type 2 | |  |  |  |  |  |  |  |  |  |  |
|  | Any intracranial haemorrhage | |  |  |  |  |  |  |  |  |  |  |
|  | Poor functional outcome or deathg | |  |  |  |  |  |  |  |  |  |  |

aAdjusted analyses included age, baseline NIHSS score and time since wake-up as covariates.

bScores on the modified Rankin scale range from 0 to 6, with 0 indicating no neurologic deficit, 1 no clinically significant disability (return to all usual activities), 2 slight disability (able to handle own affairs without assistance but unable to carry out all previous activities), 3 moderate disability requiring some help (e.g., with shopping, cleaning, and finances but able to walk unassisted), 4 moderately severe disability (unable to attend to bodily needs without assistance and unable to walk unassisted), 5 severe disability (requiring constant nursing care and attention), and 6 death.

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**Figure III**

Kaplan Meier survival plot tenecteplase treated patients versus controls.