

## Specific treatment: thrombolysis

### Recommendations

- Intravenous rtPA (0.9 mg/kg body weight, maximum 90 mg), with 10% of the dose given as a bolus followed by a 60-minute infusion, is recommended within 4.5 hours of onset of ischaemic stroke (**Class I, Level A**), although treatment between 3 and 4.5 h is currently not included in the European labelling.
- Second bullet point removed
- Further bullet points unchanged
- The use of multimodal imaging criteria may be useful for patient selection for thrombolysis but is not recommended for routine clinical practice (Class III, Level C)
- It is recommended that blood pressures of 185/110 mmHg or higher is lowered before thrombolysis (Class IV, GCP)
- It is recommended that intravenous rtPA may be used in patients with seizures at stroke onset, if the neurological deficit is related to acute cerebral ischaemia (Class IV, GCP)
- It is recommended that intravenous rtPA may also be administered in selected patients under 18 years and over 80 years of age, although this is outside the current European labelling (Class III, Level C)
- Intra-arterial treatment of acute MCA occlusion within a 6-hour time window is recommended as an option (Class II, Level B)
- Intra-arterial thrombolysis is recommended for acute basilar occlusion in selected patients (Class III, Level B). Intravenous thrombolysis for basilar occlusion is an acceptable alternative even after 3 hours (Class III, Level B)
- It is recommended that aspirin (160–325 mg loading dose) be given within 48 hours after ischaemic stroke (Class I, Level A)
- It is recommended that if thrombolytic therapy is planned or given, aspirin or other antithrombotic therapy should not be initiated within 24 hours (Class IV, GCP)
- The use of other antiplatelet agents (single or combined) is not recommended in the setting of acute ischaemic stroke (Class III, Level C)
- The administration of glycoprotein-IIb-IIIa inhibitors is not recommended (Class I, Level A)
- Early administration of unfractionated heparin, low molecular weight heparin or heparinoids is not recommended for the treatment of patients with acute ischaemic stroke (Class I, Level A)
- Currently, there is no recommendation to treat ischaemic stroke patients with neuroprotective substances (Class I, Level A)

## **Addition to text:**

### **Thrombolytic therapy**

The recently published trial European Cooperative Acute Stroke Study III (ECASS III) has shown that intravenous alteplase administered between 3 and 4.5 hours (median 3 h 59 min) after the onset of symptoms significantly improves clinical outcomes in patients with acute ischemic stroke compared to placebo [Hacke 2008]; the absolute improvement was 7.2% and the adjusted OR of favorable outcome (mRS 0-1) was 1.42, 1.02-1.98. Mortality did not differ significantly (7.7% versus 8.4%), but alteplase increased the risk of SICH (2.4% vs 0.2%). Treatment benefit is time-dependent. The number needed to treat to get one more favourable outcome drops from two during the first 90 minutes through seven within 3 hours and towards 14 between 3 and 4.5 hours [387; Hacke et al 2008].

The SITS investigators compared 664 patients with ischaemic stroke treated between 3 and 4.5 hours otherwise compliant with the European summary of the product characteristics criteria with 11 865 patients treated within 3 hours [Wahlgren 2008a].

In the 3-4.5-hour cohort, treatment was started on average 55 minutes later after symptom onset. There were no significant differences between the 3-4.5-hour cohort and the 3-hour cohort for any outcome measures, confirming that alteplase remains safe when given between 3 and 4.5 hours after the onset of symptoms in ischaemic stroke patients who otherwise fulfil the European summary of product characteristics criteria [Wahlgren 2008a].

### **The Latest References:**

Hacke W, Kaste M, Bluhmki E, Brozman M, Dávalos A, Guidetti D, Larrue V, Lees KR, Medeghri Z, Machnig T, Schneider D, von Kummer R, Wahlgren N, Toni D, for the ECASS Investigators. Thrombolysis with Alteplase 3 to 4.5 Hours after Acute Ischemic Stroke. *New Engl J Med* 2008; 359: 1317-1329.

Wahlgren N, Ahmed N, Dávalos A, Hacke W, Millán M, Muir K, Roine RO, Toni D, Lees KR. Thrombolysis with alteplase 3-4.5 h after acute ischaemic stroke (SITS-ISTR): an observational study. *Lancet* 2008; 372: 1303-1309.

Wahlgren N, Ahmed A, Eriksson N, Aichner F, Bluhmki E, Dávalos A, Erilä T, Ford GA, Grond M, Hacke W, Hennerici M, Kaste M, Köhrmann M, Larrue V, Lees KR, Machnig T, Roine RO, Toni D, Vanhooren G, for the SITS-MOST investigators. Multivariable analysis of outcome predictors and adjustment of main outcome results to baseline data profile in randomized controlled trials; Safe Implementation of Thrombolysis in Stroke Monitoring Study (SITS-MOST). *Stroke* 2008; 39: 3316-3322.

Changes implemented 29<sup>th</sup> January 2009