MRI-guided thrombolysis with alteplase at 0.6mg/kg for stroke with unknown time of onset: THAWS randomized controlled trial

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Purpose

- To test whether alteplase at 0.6mg/kg is effective and safe in patients with wake-up stroke or stroke with unknown onset time who had DWI-FLAIR mismatch

Trial design

- Investigator-initiated, Phase III, multicenter, randomized, open label, blinded endpoint trial
- Standard indication for intravenous thrombolysis otherwise time window more than 4.5 hours since last-known-well (e.g., wake-up stroke)
- DWI-FLAIR mismatch: acute ischemic lesion on DWI and no remarkable corresponding hyperintensity on FLAIR
- Randomly assigned (1:1) to receive **alteplase at 0.6mg/kg** (rt-PA group) or standard medical treatment (control group)
- Sample size=300 (assumption of positive results of WAKE-UP trial)

Following the early termination and positive results of the WAKE-UP trial, steering committee decided to stop recruitment with 131 patients on 10th July 2018

Primary and Safety Outcomes

	rt-PA Group	Control Group	Relative risk (95% CI)	P Value
Primary outcome				
mRS 0-1 at 90 days, no./total no. (%)	32/68 (47)	28/58 (48)	0.97 (0.68, 1.41)	0.892
Safety outcomes				
Symptomatic ICH at 36 hours†, no./total no. (%)	1/71 (1.4)	0/60 (0)	Infinity (0.06, infinity)	1.0
Major extracranial bleeding‡, no./total no. (%)	0/71 (0)	0/60 (0)	N.A.	N.A.
Death at 90 days, no./total no. (%)	2/71 (2.8)	2/60 (3.3)	0.85 (0.06, 12.58)	1.0

†symptomatic ICH: SITS-MOST criteria (a type 2 parenchymal hemorrhage with deterioration in NIHSS score of ≥4 points)
‡major extracranial bleeding: ISTH major bleeding definition

Conclusions

- There was no difference in favorable outcome (mRS 0-1 at 90 days) between the rt-PA and control groups in ischemic stroke patients with unknown time of onset from our relatively small data set.

- The safety of alteplase at 0.6mg/kg was comparable to that of standard treatment.

- Early study termination precludes any definitive conclusions, and additional research may be warranted.