Extending thrombolysis to 4.5-9 hours and wake-up stroke using perfusion imaging:

A meta-analysis of individual patient data from EXTEND, ECASS4-EXTEND and EPITHET

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Background and Hypothesis

- **Background**: Currently thrombolysis is recommended up to **4.5 hours** after ischemic stroke onset and wake up stroke patients are excluded

- **Perfusion mismatch** identifies patients who benefit from reperfusion therapy (thrombectomy) up to 24 hours after onset.

- **Hypothesis:** Intravenous alteplase improves functional outcome in ischemic stroke patients more than 4.5 hours (up to 9 hours) and wake up stroke who have perfusion mismatch (CT or MRI)

- We performed an individual patient data meta-analysis of **EXTEND, ECASS4-ExTEND** and **EPITHET** to test the hypothesis

[1]Thomalla NEJM 2018

Result and Conclusion

- Alteplase **improves excellent functional outcomes (mRS 0-1)** at 3 months when administered **4.5-9h** or after **wake-up stroke** <9h from midpoint of sleep in patients with perfusion mismatch (adjusted odd ratio 1.86 95% CI 1.15-2.99 p=0.011)

- Alteplase archived higher rate of good functional outcome, reperfusion, recanalization compared to placebo

- **Consistent** effect in age, time, Large vessel strata

- **sICH increased** but did not negate the net benefit in ordinal analysis

- Mortality **not** significantly different

- Both benefit and risk **similar** to 0-4.5h alteplase

- Benefit predominantly seen in the patients with **automated perfusion mismatch**

- **Now it is time to extend the thrombolysis time window to 9 hours and for patients with wake up stroke**