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.
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**