

STROKE THROMBOLYSIS TRIALS

NINDS.

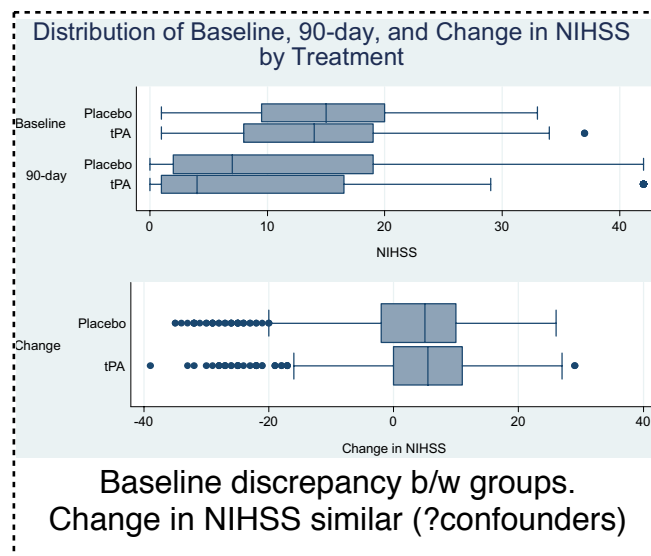
- Randomised, double-blinded.
- t-PA vs placebo
 - 0-180 mins.
- 624 patients.

Findings.

- No difference detected at 24 hrs [ie. complete symptom resolution *or* ↓ NIHSS by ≥ 4]
- t-PA = better NIHSS at 3 months.
 - OR 1.7 [1.2-2.6] p = 0.008.
- No difference in mortality (17 vs 21%, p=0.30)
- 10-fold increased in ICH.
 - Associated with worse NIHSS at baseline

Issues.

- Industry funded. Genentech.
- 50% of patients treated w/in 90mins ?generalisability
- Baseline imbalance in stroke severity between groups
 - Identical Δ -NIHSS.
- Reported '*benefits*' occurred in post-hoc comparisons.



ECASS III.

- Randomised, double-blinded.
- t-PA vs placebo
 - 3 - 4.5 hours.
 - Dichotomised modified Rankin scale [0-1 vs 2-6].
- 821 patients.

Findings.

- t-PA had higher rates of 'favourable neurological outcome'
 - 52.4% vs 45.2%, OR 1.34, (95%CI 1.02-1.76)
- No difference in mortality.
- Higher rates of ICH with t-PA [27 vs 17.6%]

Issues.

- Industry funded. Boehringer Ingelheim.
- Excluded big strokes [NIHSS > 24]
- Endpoint of mRS (0-1) is inappropriate. ?mRS of 2 is good !!
 - mRS of 2 = *Slight disability*. Can look after own affairs without assistance, but unable to carry out *all* previous activities.
 - Benefit of t-PA disappears when reclassified mRS 0-2 vs 3-6 !!
- Baseline imbalance in stroke severity between groups, plus *Hx of stroke*.
 - Favours the t-PA group

IST-3.

- Randomised, open-treatment trial !!
- t-PA vs NO placebo
 - 0 - 6 hours.
 - Oxford Handicap Score (OHS) at 6 months [0-2 vs ≥ 3]. Similar to mRS.
- 3035 patients.

Findings.

- No difference in primary outcome [OHS 0-2 @ 6 months]
 - 37% vs 35% [OR 1.13, 95%CI 0.95-1.35, p=0.181]
- Higher rates of "Fatal / Non-fatal ICH" in t-PA group.
 - 7% vs 1%. [OR 6.94, 95%CI 4.07-11.8]
- Higher rates of "death within 7 days" in t-PA group.
 - 11% vs 7% [OR 1.60, 95%CI 1.22-2.08, p=0.001]
 - By 6 months, this had equalised [27% in each group].

Time to randomisation (h)	132/431 (30.6%)	95/418 (22.7%)		
0-3				1.64 (1.03-2.62)
3-4.5				0.73 (0.50-1.07)
>4.5				1.31 (0.89-1.93)

- This goes against the 'time is brain' theory for thrombolysis.

Issues.

- Benefits only discovered w/ 'secondary exploration' of data.
 - Ordinal analysis
- Open-label trials generally favour the treatment group.
 - ?is there actually concealed harm.