

Cronostoria dei trial sulla trombolisi nello stroke ischemico

✓ 1995

- MAST-Italy, 1995 (n = 622) Lancet 1995; 346: 1509-14
Time to treatment: < 6 hours
Results: Increased early death (OR 2.7), Slight decrease 6 m disability (OR 0.5)
Overall: No benefit
- ECASS, 1995 (n = 620) JAMA 1995; 274(13): 1017-25
Time to treatment: < 6 hours, Notable inclusion: Moderate - severe hemispheric stroke
Results: No difference in disability or death
Overall: No benefit
- NINDS-1, 1995 (n = 291) New Engl J Med 1995; 333: 1501-9
Time to treatment: < 3 hours
Results: No difference NIHSS improvement by 4 pts or resolution of deficits at 24 hours
Overall: No benefit
- NINDS-2, 1995 (n = 333) N Engl J Med 1995; 333: 1155-63
Time to treatment: < 3 hours
Results: Planned primary outcome was to be improvement in functional and stroke scores (of 20%). This was changed, post-hoc, to dichotomous favorable vs. unfavorable outcome. Original primary outcome result not reported.
Overall: Benefit

✓ 1996

- MAST-Europe (n = 310***) N Engl J Med 1996; 335: 145-51
Time to treatment: < 6 hours
Notable Inclusion: Mod-severe stroke, MCA territory only
Outcome: No difference combined disability/death at 6 months; increased ICH (21% vs. 3%) and statistically nonsignificant increased mortality (47% vs. 38%)

Overall Harmful***STOPPED EARLY DUE TO ICH AND MORTALITY, n of 600 planned

- ASK (n = 340**) JAMA 1996; 279: 961. Time to treatment: <4h (small % 4-5h) Outcome: No difference combined disability/death at 3 months; slightly decreased disability and increased mortality at 3 months, OR 1.83 (1.14-2.93) Overall: Harmful***STOPPED EARLY DUE TO MORTALITY, n of 600 planned

✓ 1998

- ECASS-II, tPA 1998 (n = 800) Lancet 1998; 352: 1245-51 Time to treatment: <6h (20% < 3 hours) Outcome: No difference in favorable outcomes (modified Rankin Scale) at 3 months Overall: No benefit

✓ 1999/2000

- ATLANTIS-B, tPA 1999 (n = 613*) JAMA 1999; 282: 2019-26 Time to treatment: 20% 3-4 h, 70% 4-5 Outcome: No difference, favorable outcome at 3 months; increased ICH (7% vs. 1%) and non significant increase in mortality (11% vs. 7%) Overall: Harmful
- ATLANTIS-A, tPA 2000 (n = 142*) Stroke 2000; 31: 811-16 Time to treatment: Initially 0-6 hours, stopped enrolling 0-3 based on NINDS result Outcome: Improvement in NIHSS score (4 pts) at 24h favored lytics (40% vs. 21%, p=0.02) but at 1 month favored placebo (75% vs. 60%, p=0.05). Increased ICH with tPA (11% vs. 0%) and increased mortality at 3 months (23% vs. 7%) Overall: Harmful***STOPPED EARLY FOR HARM - n of 300 planned

✓ 2007

- SITS MOST Sicuro beneficio, stessa mortalità del gruppo di controllo entro le 3 ore

✓ 2008

- ✓ DIAS-2, (n = 193) Time to treatment: 3-9 hours Notable inclusion: reversible ischemic penumbra on MR or CT Outcome: No difference in favorable outcomes; Statistically nonsignificant increase in mortality for high dose desmoteplase group (stopped early for harm, analyzed, restarted) Overall: No benefit

- ✓ ECASS 3 tPA 2008 (n = 821) N Engl J Med 2008; 359: 1317-29 Time to treatment: 3-4.5 h Outcome: More favorable outcomes with tPA (OR 1.34, 1.02-1.76), mortality no difference Overall: Benefit = NNT of 15 for 'favorable' outcome

✓ 2012

- IST 3

Legenda

ECASS: European Cooperative Acute *Stroke* Study

NINDS: National Institute of Neurological Disorders and Stroke

SITS MOST: Safe Implementation of Thrombolysis in Stroke Monitoring Study