Cronostoria dei trial sulla trombolisi nello stroke ischemico

- ✓ 1995
  - MAST-Italy, 1995 (n = 622) Lancet 1995; 346: 1509-14Time to treatment: < 6 hoursResults: 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): 1017-25Time to treatment: < 6 hours, Notable inclusion: Moderate - severe hemispheric strokeResults: No difference in disability or deathOverall: No benefit
  - NINDS-1, 1995 (n = 291) New Engl J Med 1995; 333:Time to treatment: < 3 hoursResults: No difference NIHSS improvement by 4 pts or resolution of deficits at 24 hoursOverall: No benefit
  - NINDS-2, 1995 (n = 333) N Engl J Med 1995; 333Time to treatment: < 3 hoursResults: Planned primary outcome was to be improvement in functional and stroke scores (of 20%).This was changed, post-hoc, to dichotomous favorable vs. unfavorableoutcome. Original primaryoutcome result not reported.Overall: Benefit
- ✓ 1996
  - MAST-Europe (n = 310***) N Engl J Med 1996;335:145.Time to treatment: < 6 hours Notable Inclusion: Mod-severe stroke, MCA territory only Outcome: Nodifference combined disability/death at 6 months; increased ICH (21% vs. 3%) and statisticallynonsignificant increased mortality (47%vs.38%)

OverallHarmful***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 andincreased 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: 1245-51Time to treatment: <6h (20% < 3 hours)Outcome: No difference in favorable outcomes (modified Rankin Scale) at 3 monthsOverall: No benefit

✓ 1999/2000

- ATLANTIS-B, tPA 1999 (n = 613*) JAMA 1999; 282: 2019-26Time to treatment: 20% 3-4 h, 70% 4-5Outcome: 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: 811-16Time to treatment: Initially 0-6 hours, stopped enrolling 0-3 based on NINDS resultOutcome: Improvement in NIHSS score (4 pts) at 24h favored lytics (40% vs. 21%, p=0.02) but at 1month favored placebo (75% vs. 60%, p=0.05). Increased ICH with tPA (11% vs. 0%) and increasedmortality 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 forhigh dose desmoteplase group (stopped early for harm, analyzed, restarted) Overall: No benefit
- ✓ ECASS 3 tPA 2008 (n = 821) N Engl J Med 2008; 359: 1317-29Time to treatment: 3-4.5 hOutcome: More favorable outcomes with tPA (OR 1.34, 1.02-1.76), mortality no differenceOverall: 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