

Thrombolysis with Alteplase for
Acute Stroke in the Safe
Implementation of Thrombolysis
in Stroke Monitoring Study (SITS-
MOST)

Lancet Jan 2007

Background

- Assess Safety and Efficacy of iv Alteplase
- EU safety assessment by comparison with pooled randomised trial data
- Condition for license in EU

Method

- 6483 patients in 285 centres, 14 countries
- 50% little prev experience thrombolysis
- 2002 – 2006
- Prospective, open, monitored, observational
- Comparison of experienced centres (<5 treatments or involvement in studies) and 'new' to thrombolysis centres

Eligibility

- Age 18 – 80
- Presentation within 3 hours of stroke
- Severe strokes excluded (CT evidence extensive infarction)

Primary outcome

- Symptomatic, local or remote type 2 parenchymal haemorrhage + deterioration NIHSS stroke scale >4 , ICH within 24 hours - SITS-MOST definition
- NINDS/Cochrane definition any haemorrhage + deterioration by one point on NIHSS scale
- Mortality at 3 months

Secondary outcome

- Functional outcome at 3 months
- Compared with pooled RCT data

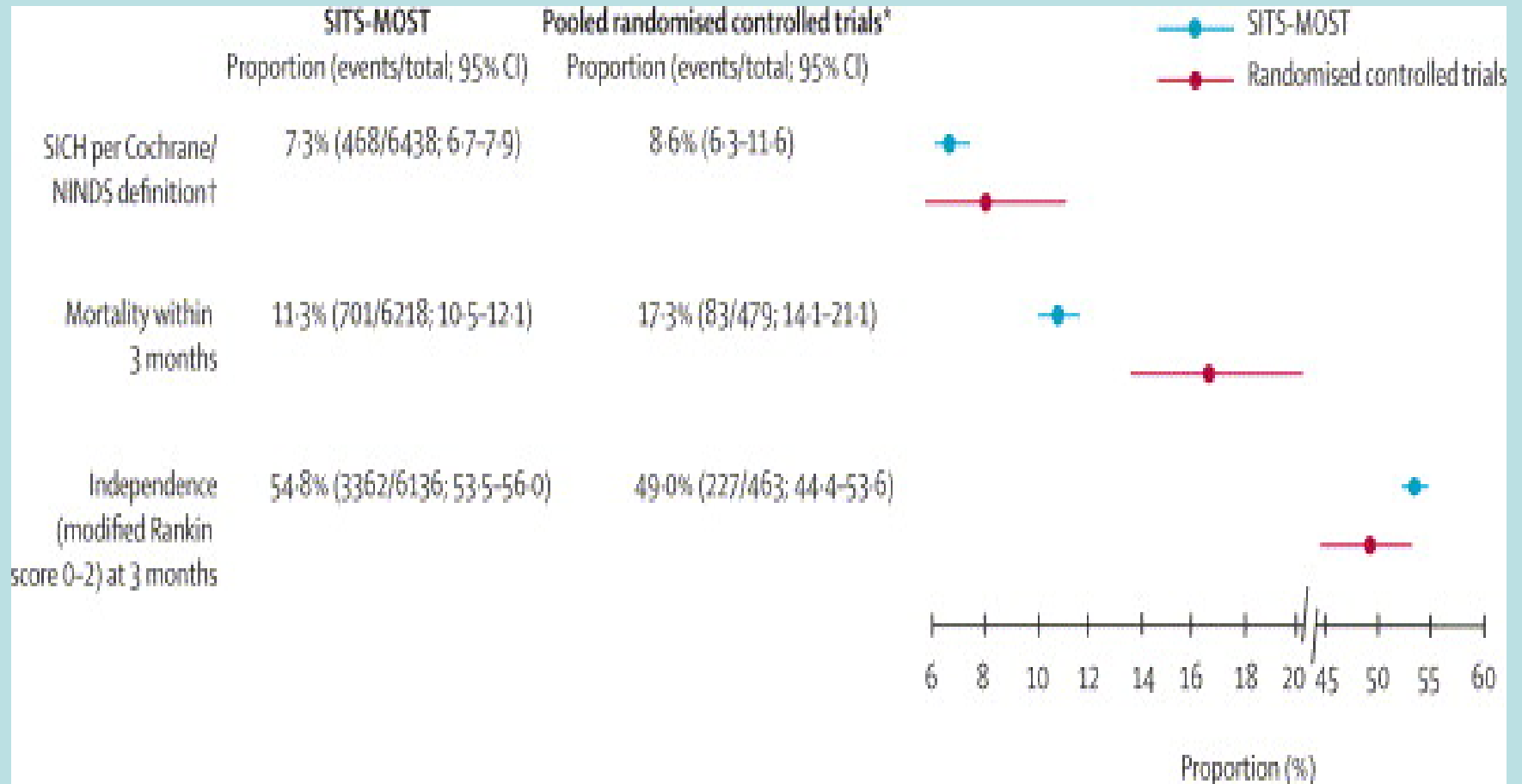
Baseline Characteristics

	SITS-MOST (n=6483)	Pooled randomised controlled trials, ^{1,2} 0-3 h	
		Placebo (n=465)	Alteplase (n=464)
Age (years)	68 (59-75)	67.1 (59.5-74.2)	69.6 (61.3-75.4)
Sex (female)	2581 (39.8%)	187 (40.2%)	186 (40.1%)
Independence (modified Rankin score 0-1) before stroke	5899/6337 (93.1%)	NA	NA
Hypertension	3710/6318 (58.7%)	282 (60.7%)	277 (59.2%)
Diabetes mellitus	1020/6374 (16.0%)	88 (18.9%)	98 (21.1%)
Hyperlipidaemia	1967/5661 (34.8%)	NA	NA
Atrial fibrillation	1507/6306 (23.9%)	93 (20.0%)	96 (20.7%)
Congestive heart failure	487/6339 (7.5%)	71 (15.3%)	61 (13.2%)
Smoking (current=1474; previous=1169)	2643/6114 (43.2%)	NA	NA
Aspirin at stroke onset	1918/6441 (29.8%)	134 (28.8%)	169 (36.4%)
Anti-hypertensive	2983/6429 (46.4%)	NA	NA
Blood glucose (mmol/L)	6.4 (5.6-7.7)	6.9 (5.9-8.4)	6.6 (5.8-8.8)
Weight (kg)	75 (68-85)	79.4 (66-90.2)	75 (65-84)
Systolic blood pressure (mm Hg)	150 (137-166)	152 (140-170)	156 (140-170)
Diastolic blood pressure (mm Hg)	81 (74-90)	86 (77-95.5)	84 (78-92)
Degree of neurological severity (NIHSS excluding distal motor function)	12 (8-17)	14 (9-19)	13 (8-18)
Mild (NIHSS 1-7)	1494 (23%)	-	-
Moderate (NIHSS 8-14)	2409 (37%)	-	-
Severe (NIHSS ≥15)	2571 (40%)	-	-
Previous stroke	643/6395 (10.1%)	59 (12.7%)	64 (13.8%)
Previous stroke and reduced functional status (modified Rankin score >1)	80/643 (12.4%)	-	-
Cause of stroke			
Large vessel disease with substantial carotid stenosis	844 (13%)	-	-
Large vessel disease other than substantial carotid stenosis	1435 (22.1%)	-	-
Cardiac origin	2270 (35%)	-	-
Lacunar stroke	535 (8.3%)	-	-
Other	1171 (18.1%)	-	-
Unknown	228 (3.5%)	-	-
Signs of current infarction on baseline imaging study	1315/6450 (20.4%)	-	-
Stroke onset to treatment time (min)	140 (115-165)	138 (90-165)	140 (90-168)
Mean delay between stroke onset and treatment (min)	136 (33)	-	-
Treated within 90 min	671 (10.6%)	-	-
Treated within 120-180 min	4276 (66%)	-	-
Dose to needle time (ie, from entering the facility to receiving treatment with alteplase) (min)	68 (30)	-	-

Baseline characteristics new and experienced centres

	Experienced (n=4980)	New (n=1503)
Age (years)	68.5 (59-75)	68 (59-74)
Sex (female)	1988 (39.9%)	593 (39.5%)
Independence (modified Rankin score 0-1) before stroke	4556/4861 (93.7%)	1343/1476 (91.0%)
Hypertension	2916/4856 (60.1%)	794/1462 (54.3%)
Diabetes mellitus	820/4892 (16.8%)	200/1482 (13.5%)
Atrial fibrillation	1161/4838 (24.0%)	346/1468 (23.6%)
Congestive heart failure	381/4861 (7.8%)	95/1478 (6.4%)
Previous stroke	507/4904 (10.3%)	136/1491 (9.1%)
Aspirin at stroke onset	1515/4904 (30.6%)	403/1496 (26.9%)
Blood glucose (mmol/L)	6.4 (5.6-7.8)	6.4 (5.6-7.7)
NIHSS score excluding distal motor function	12 (8-17)	13 (8-18)
Systolic blood pressure (mm Hg)	150 (138-166)	150 (135-165)
Diastolic blood pressure (mm Hg)	82 (75-90)	80 (74-90)
Stroke onset to treatment time (min)	140 (110-165)	145 (120-165)
Alteplase dose (mg)	68 (60-77)	68 (60-76)

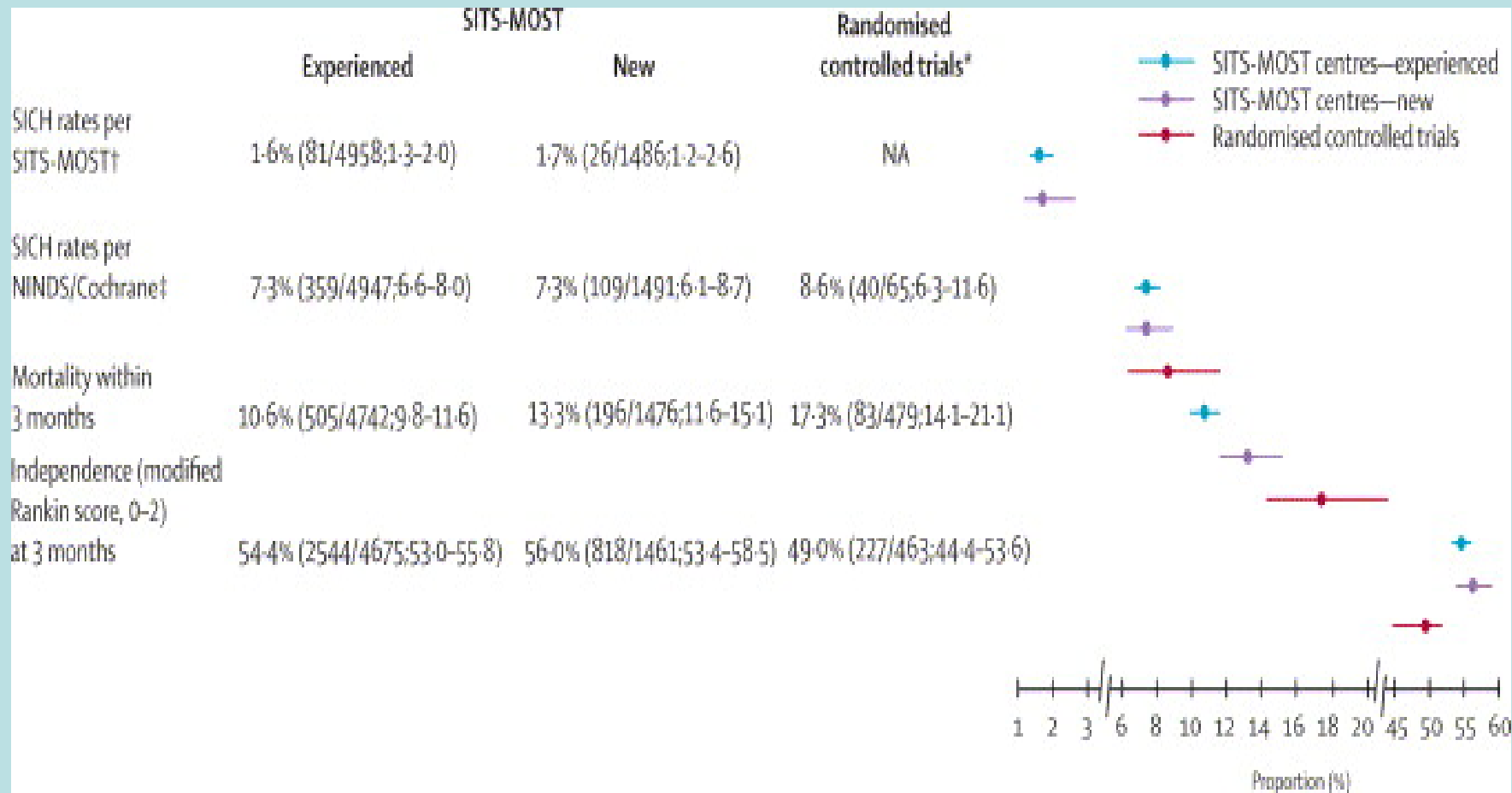
Proportion patients with SICH



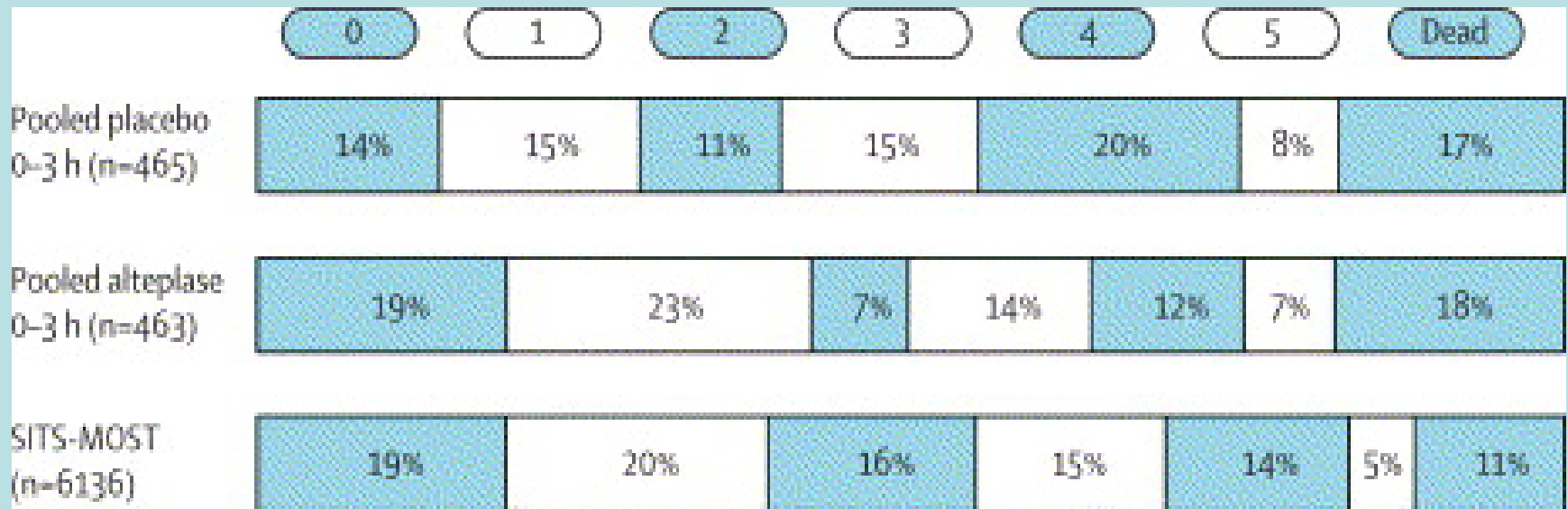
ICH detected by CT 22-36 hrs after and any post-treatment scans

	Haemorrhages at 22-36 h imaging scans	Haemorrhages on any post- treatment imaging scans
Local haemorrhages	n=6283	n=6352
None	5369 (85.5%)	5267 (82.9%)
Haemorrhagic infarct type 1	338 (5.4%)	402 (6.3%)
Haemorrhagic infarct type 2	250 (4.0%)	297 (4.7%)
Primary intracerebral haemorrhage type 1	166 (2.6%)	202 (3.2%)
Primary intracerebral haemorrhage type 2	160 (2.5%)	184 (2.9%)
Known remote haemorrhages	n=6282	n=6350
No remote haemorrhage	6111 (97.3%)	6155 (96.9%)
Remote primary intracerebral haemorrhage type 1	105 (1.7%)	113 (1.8%)
Remote primary intracerebral haemorrhage type 2	66 (1.1%)	82 (1.3%)

Symptomatic SICH and mortality experienced and new centres



Rankin Scores at 3 months



Findings

- Baseline characteristics
- 1.7% SICH at 24 hours v 8.6% pooled trial data
- Mortality 11.3% v 17.3% pooled trial data

- tPa safe if given within 3 hours of onset of stroke
- Even if inexperienced centre
- Similar rates of ICH
- Mortality higher in less experienced centres but not because of ICH and still less than RCT data

