

ESC Heart & Brain Workshop

Debate 4: Thrombolytics have much broader indications than mechanical thrombectomy in stroke- Contra

Jan 18th, 2018

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Boehringer
Ingelheim



Daiichi-Sankyo



Bristol-Myers Squibb

Medtronic
Further Together

Declaration of Interest

Financial Disclosures (grants¹, presentations², consultant³, meetings⁴, other⁵)

French Stroke Foundation¹

French Ministry of Health^{1,5}

Boehringer^{3,4}

Servier³

Astra Zeneca²

Bayer⁴

Medtronic^{2,4}

Acticor³

Amgen²

Club NeuroVasculaire Ile De France⁵

Thrombolytics: tPA

- Efficacy
- Relevance
- Safety



tPA

- Efficacy
- Relevance
- Safety



Mechanical thrombectomy in acute ischemic stroke: Consensus statement by ESO-Karolinska Stroke Update 2014/2015, supported by ESO, ESMINT, ESNR and EAN

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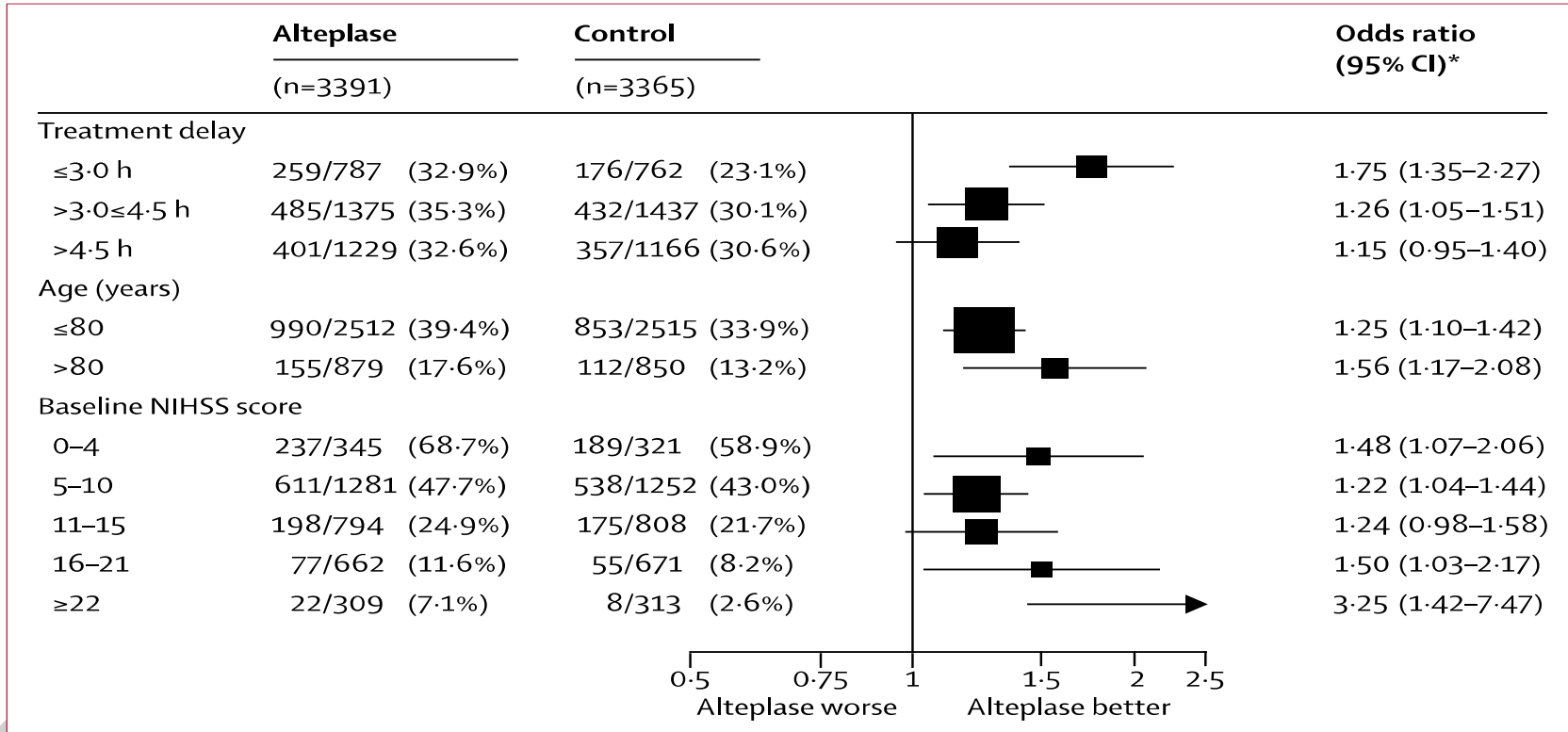
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 SAGE



- Thrombectomy in association with IV tPA within 4.5 h
- LVO of anterior circulation within 6 h
- IV tPA should not delay thrombectomy
- Thrombectomy to be considered as a first-line choice in the setting of tPA contra-indication

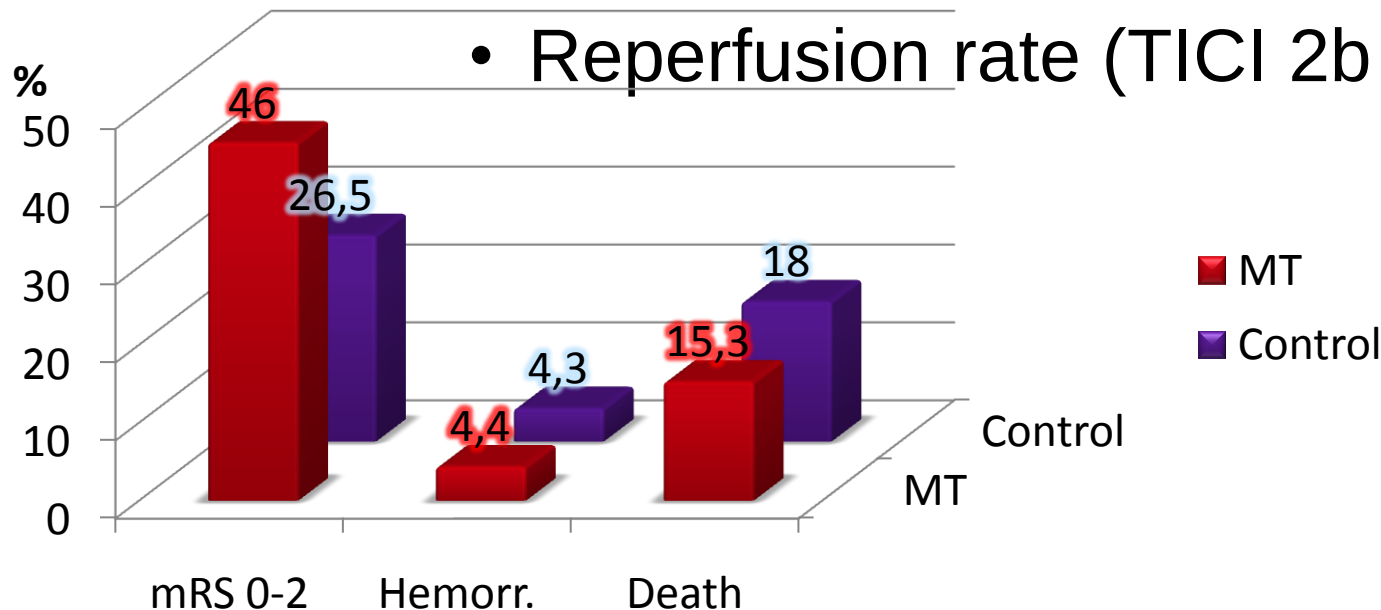
tPA: better than control



THROMBECTOMY better than

- **TPA** disability reduction OR 2.49 (95% CI 1.76–3.53; $p < 0.0001$)
- **NNT: 2.6**

- Reperfusion rate (TICI 2b / 3): 71%



Effect of Endovascular Contact Aspiration vs Stent Retriever on Revascularization in Patients With Acute Ischemic Stroke and Large Vessel Occlusion
The ASTER Randomized Clinical Trial

Bertrand Lapergue, MD, PhD; Raphael Blanc, MD, MSc; Benjamin Gory, MD, PhD; Julien Labreuche, BSc; Alain Duhamel, PhD; Gautier Marnat, MD; Suzana Saleme, MD; Vincent Costalat, MD, PhD; Serge Bracad, MD; Hubert Desal, MD, PhD; Mikael Mazighi, MD, PhD; Arturo Consoli, MD; Michel Plotin, MD, PhD; for the ASTER Trial Investigators

JAMA. 2017;318(5):443-452. doi:[10.1001/jama.2017.9644](https://doi.org/10.1001/jama.2017.9644)

THE NEW ENGLAND JOURNAL of MEDICINE

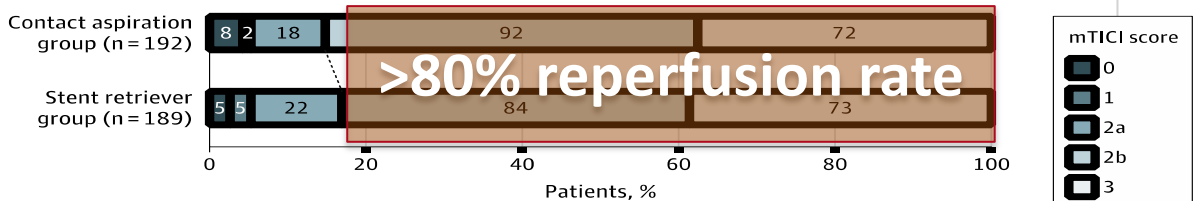
ORIGINAL ARTICLE

Thrombectomy 6 to 24 Hours after Stroke with a Mismatch between Deficit and Infarct

R.G. Nogueira, A.P. Jadhav, D.C. Haussen, A. Bonafe, R.F. Budzik, P. Bhuva, D.R. Yavagal, M. Ribo, C. Cognard, R.A. Hanel, C.A. Sila, A.E. Hassan, M. Millan, E.I. Levy, P. Mitchell, M. Chen, J.D. English, Q.A. Shah, F.L. Silver, V.M. Pereira, B.P. Mehta, B.W. Baxter, M.G. Abraham, P. Cardona, E. Veznedaroglu, F.R. Hellinger, L. Feng, J.F. Kirmani, D.K. Lopes, B.T. Jankowitz, M.R. Frankel, V. Costalat, N.A. Vora, A.J. Yoo, A.M. Malik, A.J. Furlan, M. Rubiera, A. Aghaebrahim, J.-M. Olivot, W.G. Tekle, R. Shields, T. Graves, R.J. Lewis, W.S. Smith, D.S. Liebeskind, J.L. Saver, and T.G. Jovin, for the DAWN Trial Investigators*

Thrombectomy efficacy still increasing

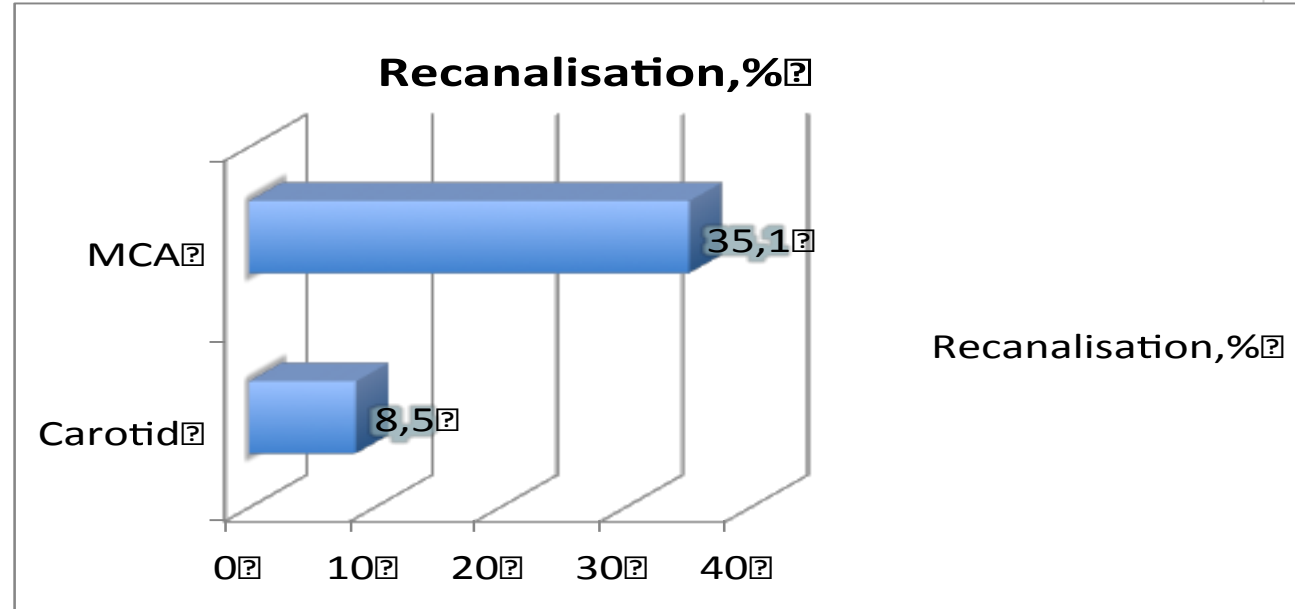
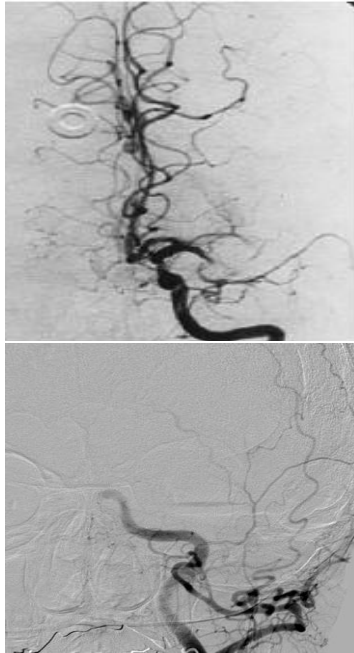
A mTICI score at the end of all endovascular procedures^{a,b}



	Treatment arm N=107
Procedure duration (minutes) (median IQR)	56.0 [33.0-90.0]
Total number of Trevo device passes (median IQR)	2.0 [1.0-3.0]
Core lab adjudicated TICIs	
Post procedure mTICI ≥ 2B	84.0%
Post procedure oTICI ≥ 2B*	
Post procedure TICI 3	10.4%

IV tPA in the setting of Large

Vessel Occlusion

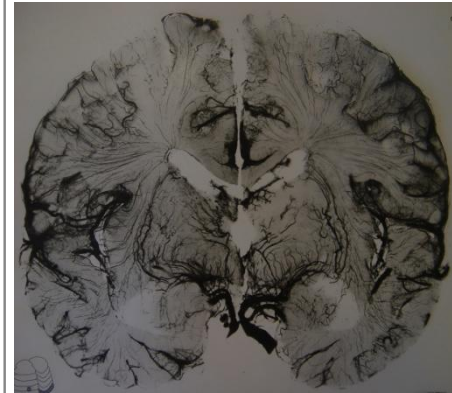
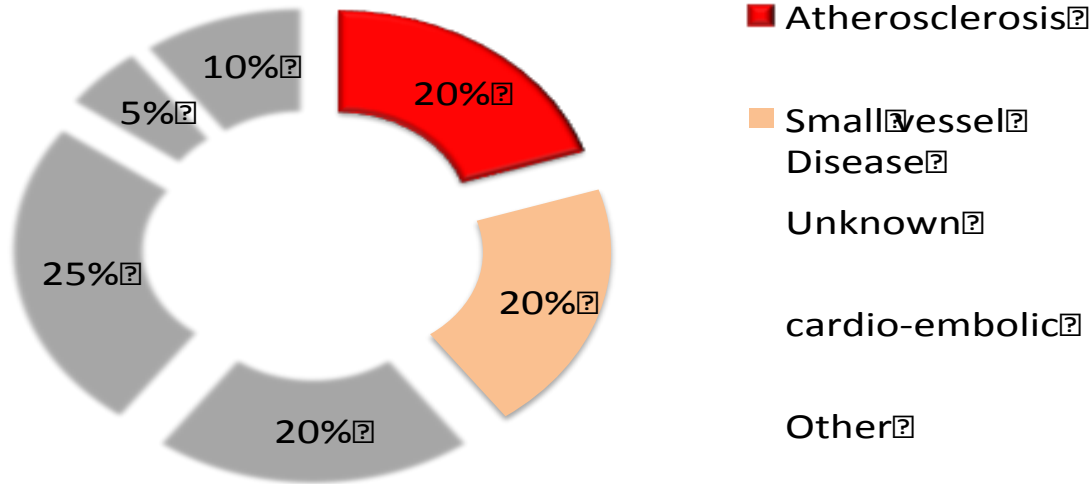


tPA

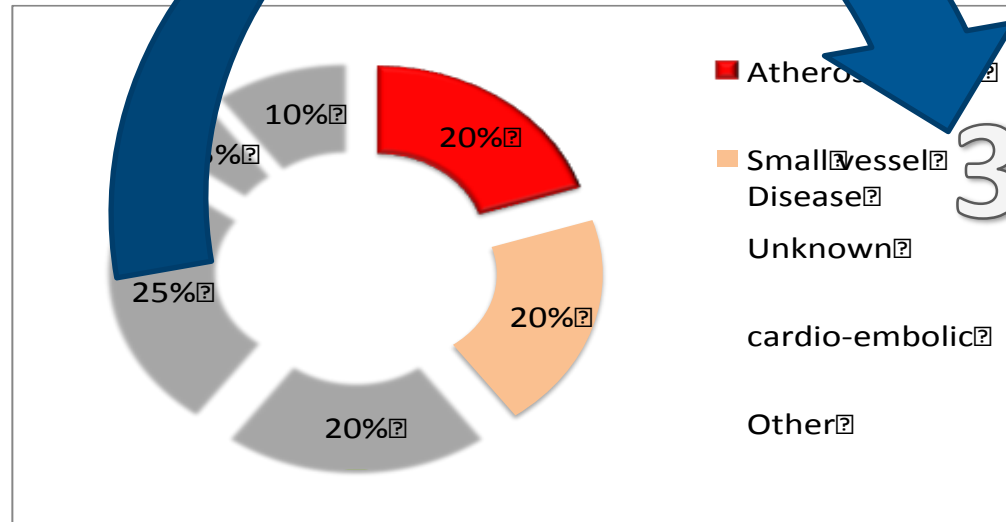
- Efficacy
- Relevance
- Safety



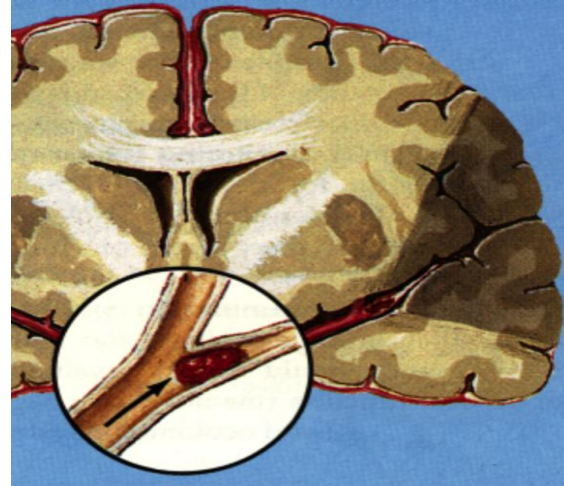
Stroke heterogeneity



In the setting of Large Vessel Occlusions



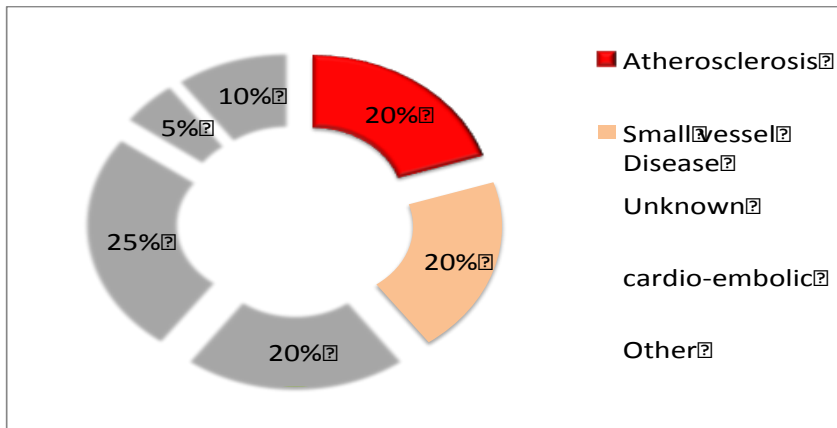
30-50%



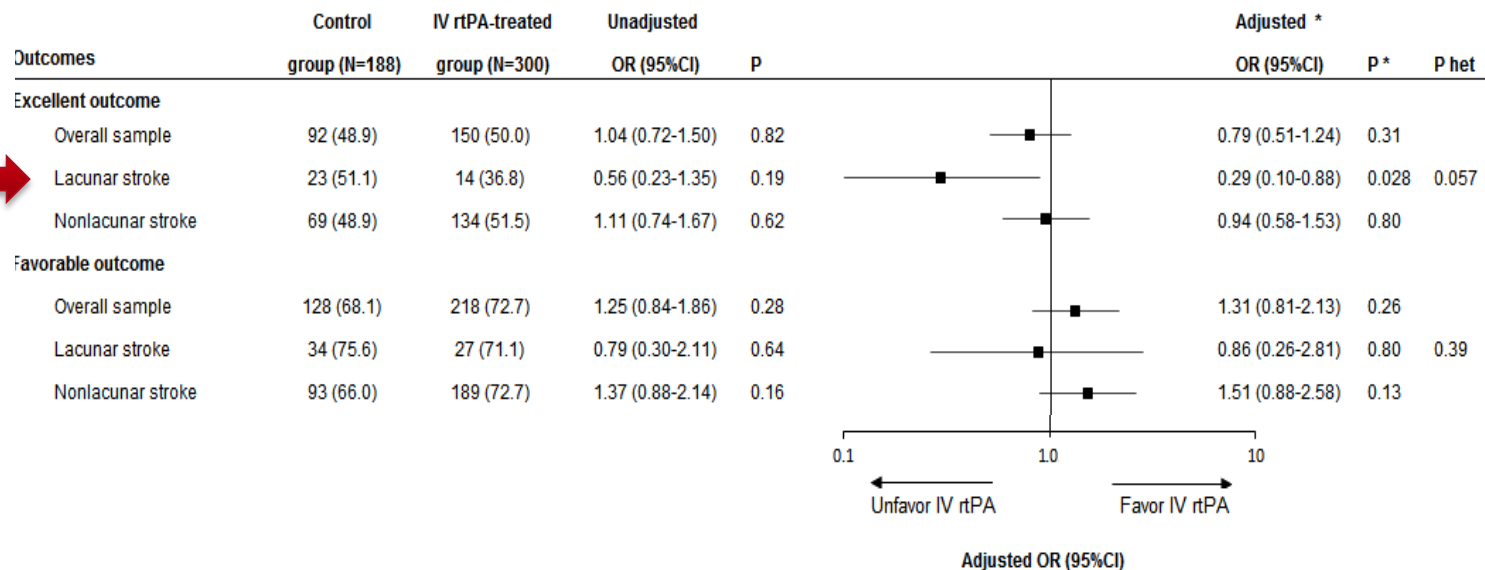
Goyal et al Lancet 2016
Blanc et al Stroke 2017

What about strokes without Large Vessel Occlusion?

- 30% of AIS patients treated with tPA have no occlusion at admission
 - Spontaneous recanalisation
 - Lacunar infarction up to 30%



No clear effect of tPA in patients without Large Vessel Occlusion

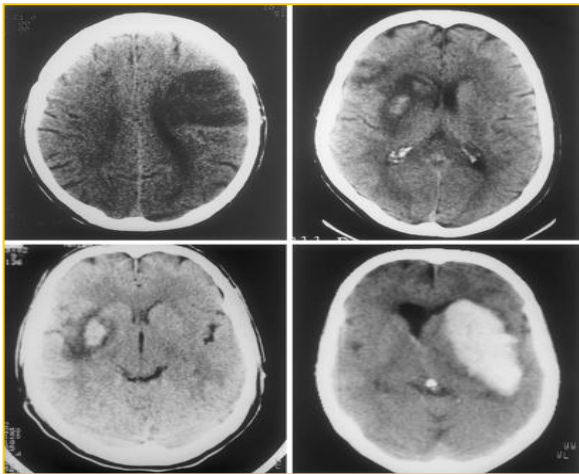


tPA

- Efficacy
- Relevance
- Safety



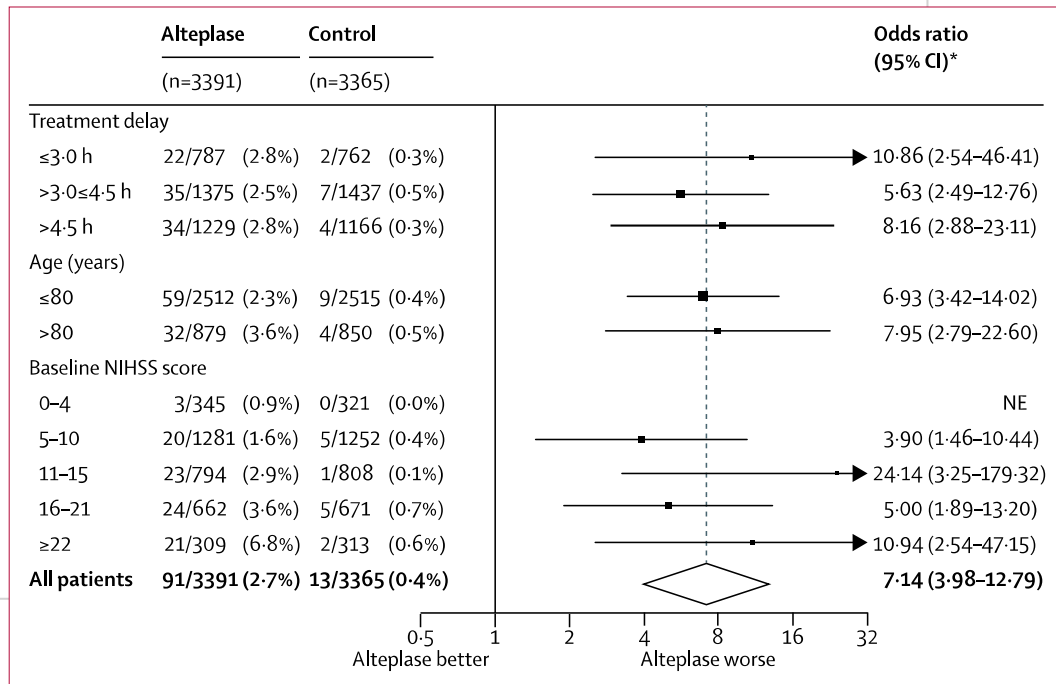
tPA increases intracranial bleeding risk



Frequent+++



Motto C, et al. Stroke. 1999
Emberson et al Lancet Neurol 2014



tPA increases intracranial bleeding risk



Early administration of aspirin in patients treated with alteplase for acute ischaemic stroke: a randomised controlled trial

ASPIRIN 300 mg within 90 min following IV ALTEPLASE

	Aspirin (n=148)	Standard treatment (n=137)	Relative risk (95% CI)	p value*	Absolute difference (95% CI)
Initial ischaemic stroke (including progressive stroke)	99 (66.9%)	102 (74.5%)	0.90 (0.77 to 1.04)	0.16	-7.6% (-18.1 to 3.0)
Recurrent ischaemic stroke	10 (6.8%)	3 (2.2%)	3.09 (0.87 to 10.89)	0.09	4.6% (-0.2 to 9.3)
Symptomatic intracranial haemorrhage	11 (7.4%)	1 (0.7%)	10.18 (1.33 to 77.83)	0.006	6.7% (2.2 to 11.2)
Other cerebral pathology	2 (1.4%)	4 (2.9%)	0.46 (0.09 to 2.49)	0.43	-1.6% (-5.0 to 1.8)
Systemic ischaemic disease (including myocardial infarction)	0	0	..	..	..
Systemic haemorrhage	1 (0.7%)	1 (0.7%)	0.93 (0.06 to 14.66)	1.00	-0.1% (-2.0 to 1.89)
Other systemic pathology	8 (5.4%)	5 (3.6%)	1.48 (0.50 to 4.42)	0.48	1.8% (-3.1 to 6.6)
Pre-existing poor functional status	17 (11.5%)	21 (15.3%)	0.75 (0.41 to 1.36)	0.34	-3.9% (-11.8 to 4.1)



Published Online
June 28, 2012
[http://dx.doi.org/10.1016/S0140-6736\(12\)60949-0](http://dx.doi.org/10.1016/S0140-6736(12)60949-0)

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- Thrombectomy in association with IV tPA within 4.5 h
- LVO of anterior circulation within 6 h
- Thrombectomy to be considered as a first-line choice in the setting of tPA contra-indication
 - Anticoagulation (1/6-1/3 of the patients with a Fib)

The neurological signs should not be clearing spontaneously
The neurological signs should not be minor and isolated
Caution should be exercised in treating a patient with major deficits
The symptoms of stroke should not be suggestive of subarachnoid hemorrhage

Onset of symptoms <3 hours before beginning treatment

No head trauma or prior stroke in previous 3 months

No myocardial infarction in the previous 3 months

No gastrointestinal or urinary tract hemorrhage in previous 21 days

No major surgery in the previous 14 days

No arterial puncture at a noncompressible site in the previous 7 days

No history of previous intracranial hemorrhage

Blood pressure not elevated (systolic <185 mm Hg and diastolic <110 mm Hg)

No evidence of active bleeding or acute trauma (fracture) on examination

Not taking an oral anticoagulant or if anticoagulant being taken, INR ≤ 1.5

If receiving heparin in previous 48 hours, aPTT must be in normal range

Platelet count $\geq 100\,000\text{ mm}^3$

Blood glucose concentration $\geq 50\text{ mg/dL}$ (2.7 mmol/L)

No seizure with postictal residual neurological impairments

CT does not show a multilobar infarction (hypodensity $> \frac{1}{3}$ cerebral hemisphere)

tPA contra-indications.

Take home messages

- tPA is inferior to Thrombectomy in the setting of Large Vessel Occlusion
- tPA efficacy in absence of LVO is debated
- tPA is associated with significant increased bleeding risk
- Several tPA contra-indications
- tPA useful when thrombectomy not accessible