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

Financial Disclosures (grants\(^1\), presentations\(^2\), consultant\(^3\), meetings\(^4\), other\(^5\))

- French Stroke Foundation\(^1\)
- French Ministry of Health\(^1, 5\)
- Boehringer\(^3, 4\)
- Servier\(^3\)
- Astra Zeneca\(^2\)
- Bayer\(^4\)
- Medtronic\(^2, 4\)
- Acticor\(^3\)
- Amgen\(^2\)
- Club NeuroVasculaire Ile De France\(^5\)
Thrombolytics: tPA

- Efficacy
- Relevance
- Safety
• 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

- 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

<table>
<thead>
<tr>
<th></th>
<th>Alteplase (n=3391)</th>
<th>Control (n=3365)</th>
<th>Odds ratio (95% CI)*</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
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<tr>
<td><strong>Treatment delay</strong></td>
<td></td>
<td></td>
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</tr>
<tr>
<td>≤3.0 h</td>
<td>259/787 (32.9%)</td>
<td>176/762 (23.1%)</td>
<td>1.75 (1.35–2.27)</td>
</tr>
<tr>
<td>&gt;3.0≤4.5 h</td>
<td>485/1375 (35.3%)</td>
<td>432/1437 (30.1%)</td>
<td>1.26 (1.05–1.51)</td>
</tr>
<tr>
<td>&gt;4.5 h</td>
<td>401/1229 (32.6%)</td>
<td>357/1166 (30.6%)</td>
<td>1.15 (0.95–1.40)</td>
</tr>
<tr>
<td><strong>Age (years)</strong></td>
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</tr>
<tr>
<td>≤80</td>
<td>990/2512 (39.4%)</td>
<td>853/2515 (33.9%)</td>
<td>1.25 (1.10–1.42)</td>
</tr>
<tr>
<td>&gt;80</td>
<td>155/879 (17.6%)</td>
<td>112/850 (13.2%)</td>
<td>1.56 (1.17–2.08)</td>
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<tr>
<td><strong>Baseline NIHSS score</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>0–4</td>
<td>237/345 (68.7%)</td>
<td>189/321 (58.9%)</td>
<td>1.48 (1.07–2.06)</td>
</tr>
<tr>
<td>5–10</td>
<td>611/1281 (47.7%)</td>
<td>538/1252 (43.0%)</td>
<td>1.22 (1.04–1.44)</td>
</tr>
<tr>
<td>11–15</td>
<td>198/794 (24.9%)</td>
<td>175/808 (21.7%)</td>
<td>1.24 (0.98–1.58)</td>
</tr>
<tr>
<td>16–21</td>
<td>77/662 (11.6%)</td>
<td>55/671 (8.2%)</td>
<td>1.50 (1.03–2.17)</td>
</tr>
<tr>
<td>≥22</td>
<td>22/309 (7.1%)</td>
<td>8/313 (2.6%)</td>
<td>3.25 (1.42–7.47)</td>
</tr>
</tbody>
</table>
• Disability reduction OR 2.49 (95% CI 1.76–3.53; p<0.0001)

• NNT: 2.6

• Reperfusion rate (TICI 2b / 3): 71%
Thrombectomy efficacy still increasing

**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

Bernard Caplan, MD; PhD; Raphael Xiao, MD; MD; Aric Jagiratz; GP; MD; Huijuan Zhang, MD; PhD; Mikaela Bruun, MD; PhD; Cooper Mares, MD; Edna V. Sorensen, MD; Vincent Coutal, MD; PhD; Single Beringer, MD; Albert Chou, MD; PhD; Nitin Mangla, MD; PhD; Alana Conolly, MD; MPH; Fhil Puthy, PhD, for the ASTER Trial Investigators


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


<table>
<thead>
<tr>
<th>Procedure duration (minutes)</th>
<th>(median IQR)</th>
<th>Total number of Trevo device passes (median IQR)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Treatment arm N=107</td>
<td></td>
<td></td>
</tr>
<tr>
<td>56.0 [33.0-90.0]</td>
<td>2.0 [1.0-3.0]</td>
<td></td>
</tr>
</tbody>
</table>

Core lab adjudicated TICI3s

- Post procedure mTICI ≥ 2B
- Post procedure oTICI ≥ 2B
- Post procedure TICI 3

**Treatment arm**

- 84.0%
- 10.4%
IV tPA in the setting of Large Vessel Occlusion

![Image of blood vessels]

- **MCA**: 35.1%
- **Carotid**: 8.5%

Recanalisation, %

Del Zoppo et al Ann Neurol 1992;32:78-86
• Efficacy
• Relevance
• Safety
Stroke heterogeneity

- Atherosclerosis: 20%
- Small vessel Disease: 10%
- Unknown: 25%
- cardio-embolic: 20%
- Other: 20%

Adams et al Stroke 2007
In the setting of Large Vessel Occlusions

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

• Efficacy
• Relevance
• Safety
tPA increases intracranial bleeding risk

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<td>≤3.0 h</td>
<td>22/787 (2.8%)</td>
<td>2/762 (0.3%)</td>
<td>10.86 (2.54-46.41)</td>
</tr>
<tr>
<td>&gt;3.0≤4.5 h</td>
<td>35/1375 (2.5%)</td>
<td>7/1437 (0.5%)</td>
<td>5.63 (2.49-12.76)</td>
</tr>
<tr>
<td>&gt;4.5 h</td>
<td>34/1229 (2.8%)</td>
<td>4/1166 (0.3%)</td>
<td>8.16 (2.88-23.11)</td>
</tr>
<tr>
<td>Age (years)</td>
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<tr>
<td>≤80</td>
<td>59/2512 (2.3%)</td>
<td>9/2515 (0.4%)</td>
<td>6.93 (3.42-14.02)</td>
</tr>
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<td>&gt;80</td>
<td>32/879 (3.6%)</td>
<td>4/850 (0.5%)</td>
<td>7.95 (2.79-22.60)</td>
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<td>Baseline NIHSS score</td>
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<tr>
<td>0–4</td>
<td>3/345 (0.9%)</td>
<td>0/321 (0.0%)</td>
<td>3.90 (1.46-10.44)</td>
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<td>5–10</td>
<td>20/1281 (1.6%)</td>
<td>5/1252 (0.4%)</td>
<td>24.14 (3.25-179.32)</td>
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<td>11–15</td>
<td>23/794 (2.9%)</td>
<td>1/808 (0.1%)</td>
<td>5.00 (1.89-13.20)</td>
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<td>16–21</td>
<td>24/662 (3.6%)</td>
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<td>≥22</td>
<td>21/309 (6.8%)</td>
<td>2/313 (0.6%)</td>
<td>7.14 (3.98-12.79)</td>
</tr>
<tr>
<td>All patients</td>
<td>91/3391 (2.7%)</td>
<td>13/3365 (0.4%)</td>
<td></td>
</tr>
</tbody>
</table>

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

- 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)

Sandercock et al Curr Neurol Neurosci Rep 2017
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 ≥ 100,000 mm$^3$
Blood glucose concentration ≥ 50 mg/dL (2.7 mmol/L)
No seizure with postictal residual neurological impairments
CT does not show a multilobar infarction (hypodensity > 1/3 cerebral hemisphere)
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