ESO Expedited Recommendation on Tenecteplase for Acute Ischaemic Stroke

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Disclosures

Disclosures of the 11 module working group members are provided in Suppl Table of the recommendation

Personal Financial Disclosures:
• Participation in advisory meetings & satellite symposia for Boehringer Ingelheim, Astra-Zeneca, Pfizer, Amgen
• Principal investigator of the Tenecteplase treatment in Ischemic Stroke (TETRIS) registry, which receives financial support from Boehringer Ingelheim
• Principal investigator of ToGiac trial supported by a research grant from Roche-Shugai

Personal Intellectual Disclosures:
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Background – Intravenous thrombolysis (IVT) in acute ischaemic stroke (AIS) patients

**Tenecteplase**

A genetically modified form of alteplase
- Longer half life
- Greater resistance to plasminogen activator inhibitor 1

Advantages in the setting of AIS
- Door to needle time
- Intra and inter-hospital transfers in patients eligible for mechanical thrombectomy (MT)

Single bolus administration

Easier administration

- Phase 2 trials in AIS
- Preliminary efficacy and safety data

Background. Intravenous thrombolysis – ESO Guidelines 2021

Berge E et al, Eur Stroke J 2021; 6: I-LXII

### Recommendation

**AIS <4.5h**

For patients with acute ischaemic stroke of <4.5 h duration and not eligible for thrombectomy, we suggest **intravenous thrombolysis with alteplase over intravenous thrombolysis with tenecteplase**.

Quality of evidence: Low ★★★

Strength of recommendation: Weak ↑?

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**AIS + LVO <4.5h**

For patients with acute ischaemic stroke of <4.5 h duration and with large vessel occlusion who are candidates for mechanical thrombectomy and for whom intravenous thrombolysis is considered before thrombectomy, we suggest **intravenous thrombolysis with tenecteplase 0.25mg/kg over intravenous thrombolysis with alteplase 0.9mg/kg**.

Quality of evidence: Low ★★★

Strength of recommendation: Weak ↑?

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* TNK S2B (0.25-0.40 mg/kg) ATTEST (0.25 mg/kg) NorTest (0.40mg/kg)

* TAAIS (0.25 mg/kg) EXTEND-IA (0.25 mg/kg)

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2022: 4 published RCTs comparing IVT with tenecteplase and alteplase

AcT / TASTE A / NorTest 2A /TRACE ---- TWIST (results presented)
Methodology – GRADE approach...

**PICO**

**Population**

PICO 1. Acute ischaemic stroke patients <4.5 h
PICO 2. Acute ischaemic stroke patients <4.5 h and large vessel occlusion
PICO 3. Wake-up stroke / unknown onset

**Intervention (IVT)**

Tenecteplase 0.25 mg/kg
Tenecteplase 0.40 mg/kg

**Comparator**

Current standard of care
Alteplase 0.9 mg/kg

*Steiner T et al, Eur Stroke J 2021; 6(3): CXXII-CXXXIV*
## Outcomes of interest (rating of the importance - secret ballot voting)

<table>
<thead>
<tr>
<th>Population</th>
<th>Critical outcomes (score 9-7)</th>
<th>Critical outcomes (score 9-7)</th>
<th>Important outcomes (score 6-4 : AIS-AIS+LVO)</th>
<th>Important outcomes (score 6-4)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>AIS</strong></td>
<td>mRS= 0-1 at 90 days Excellent functional outcome (8.7)</td>
<td>Reduced disability at 90 days (7.8)</td>
<td>Major neurological improvement at 24-72 h (6.2)</td>
<td>Recanalization after MT-24 h (mTICI) score ≥2b (6.8)</td>
</tr>
<tr>
<td>14 Outcomes</td>
<td>mRS = 0-2 at 90 days Good functional outcome (7.9)</td>
<td></td>
<td>Reperfusion at 24 h (6.2-6.3)</td>
<td>Recanalization before MT-first angiographic acquisition (mTICI) score ≥2b (6.8)</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Final infarct volume at 24 h (5.9-6.2)</td>
<td>Needle to groin puncture time (5.6)</td>
</tr>
<tr>
<td><strong>AIS + LVO</strong></td>
<td>mRS= 0-2 at 90 days Good functional outcome (8.3)</td>
<td>sICH at 24-48 h (7.7)</td>
<td>Quality of life metrics (5.8-5.9)</td>
<td></td>
</tr>
<tr>
<td>17 Outcomes</td>
<td>mRS= 0-1 at 90 days Excellent functional outcome (8.2)</td>
<td>Mortality at 90 days (7.6)</td>
<td>Ischemic core growth within the first 24 h (5.6-5.7)</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Door-to-needle time (5.4-5.8)</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Any ICH (5.1)</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Onset-to-treatment time (5.0)</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Extracranial bleeding (4.7)</td>
<td></td>
</tr>
</tbody>
</table>
Choice of a pre-defined non-inferiority margin (secret ballot voting)

- AIS patients: Absolute difference to achieve excellent functional outcome (mRs 0-1)
  - 3.0% (7/9)
  - To conserve at least half of the conservative alteplase effect
  - 1.3% (2/9): secondary analysis

- LVO patients: Absolute difference to achieve good functional outcome (mRs 0-2)
  - 1.3% (9/9)
  - Consistency with ESO Guidelines on Bridging therapy

G Turc, Webinar 2022

PICO 1. AIS patients of <4.5 h duration

PICO 1.1 For patients with acute ischaemic stroke of 4.5h duration, does intravenous thrombolysis with tenecteplase 0.25mg/kg compared with intravenous thrombolysis with alteplase lead to:

a) a non-inferior proportion of patients with excellent functional outcome (mRS 0-1) at 90 days?

b) non-inferior or better results on other efficacy outcomes (mRS shift analysis at 90 days, mRS 0-2 at 90 days…)?

c) a reduction in the risk of adverse events (mortality at 90 days, sICH…) ?

d) a reduction in key time metrics (onset-to-treatment time, door-to-needle time)?

e) an improvement in neuroimaging parameters?
### Quality of evidence

#### Risk of bias domains

- **Randomization process**
- **Deviation from intended intervention**
- **Missing outcome data**
- **Measurement of outcome**
- **Selection of the reported result**

#### Table: Trials

<table>
<thead>
<tr>
<th>Trials</th>
<th>N</th>
<th>Design</th>
</tr>
</thead>
</table>
| Act (2022), Phase 3-Canada      | 1600 | AIS<4.5h  
Non inferiority : -5%       |
| ATTEST (2015) Phase 2b/3-UK     | 104  | AIS <4.5h      |
| TAAIS (2012) Phase 2b- Australia| 75  | AIS<6H  
Vessel occlusion-mismatch CT >20%, 
Tenecteplase 0.10 and 0.25mg/kg, no MT |
| EXTEND-I A (2018) Phase 2-Australia| 202 | AIS with LVO eligible to MT |
| TNK-2S (2010) Phase 2b/3-USA    | 112  | AIS<3h  
Tenecteplase 0.10 vs 0.25 vs 0.40 mg/kg |
| TASTE A (2022) Phase 2-Australia| 104  | AIS<4.5h, MSU |
| TRACE (2021) Phase 2-China      | 236  | AIS<3h  
Tenecteplase 0.10 vs 0.25 VS 0.40 mg/kg |

#### Quality of evidence matrix

<table>
<thead>
<tr>
<th>Study</th>
<th>D1</th>
<th>D2</th>
<th>D3</th>
<th>D4</th>
<th>D5</th>
<th>Overall</th>
</tr>
</thead>
<tbody>
<tr>
<td>AcT 2022</td>
<td>+</td>
<td>-</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>-</td>
</tr>
<tr>
<td>ATTEST 2015</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>-</td>
<td>+</td>
<td>-</td>
</tr>
<tr>
<td>TAAIS 2012</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
</tr>
<tr>
<td>EXTEND-I A TNK 2018</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
</tr>
<tr>
<td>TASTE-A 2022</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
</tr>
<tr>
<td>TNK-S2B 2010</td>
<td>+</td>
<td>-</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
</tr>
<tr>
<td>TRACE 2021</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
</tr>
</tbody>
</table>
Excellent functional outcome (mRS 0-1 at 90 days)

Non inferiority margin = -3% (-1.3%)
Good functional outcome (mRS 0-2 at 90 days)

PICO 1.1 AIS of <4.5 h duration - IV Tenecteplase 0.25mg/kg

Unadj. RD = 8.11 % (95% CI = -1.41% to 17.69%)
PICO 1.1 AIS of <4.5 h duration - IV Tenecteplase 0.25mg/kg

Symptomatic intracranial haemorrhage (study definition)

Safety data

Unadj. OR = 0.98 (95%CI=0.59 to 1.62)

All cause mortality at 3 months

Unadj. OR = 0.88 (95%CI=0.65 to 1.19)
PICO 1.1 AIS of <4.5 h duration - IV Tenecteplase 0.25mg/kg

**Door-to-needle time (mn)**

<table>
<thead>
<tr>
<th>Study</th>
<th>TNK Median</th>
<th>IQR</th>
<th>Total</th>
<th>Alteplase Median</th>
<th>IQR</th>
<th>Total</th>
<th>Difference of Medians IV, Random, 95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>AcT 2022</td>
<td>30</td>
<td>27–49</td>
<td>602</td>
<td>37</td>
<td>29–52</td>
<td>758</td>
<td>-1.0 (-3.1, 1.1)</td>
</tr>
<tr>
<td>TASTE-A 2022</td>
<td>30</td>
<td>25–38</td>
<td>54</td>
<td>37</td>
<td>32–43</td>
<td>49</td>
<td>-7.0 (-11.3, -2.7)</td>
</tr>
</tbody>
</table>

**Total (95% CI)**

100.0%

Heterogeneity: Tau² = 15.93; Chi² = 6.06, df = 1 (P = 0.01); I² = 83%

Test for overall effect: Z = 1.24 (P = 0.22)

**Symptom onset-to-needle time (mn)**

<table>
<thead>
<tr>
<th>Study</th>
<th>TNK Median</th>
<th>IQR</th>
<th>Total</th>
<th>Alteplase Median</th>
<th>IQR</th>
<th>Total</th>
<th>Difference of Medians IV, Random, 95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>AcT 2022</td>
<td>128</td>
<td>93–186</td>
<td>802</td>
<td>131</td>
<td>95–188</td>
<td>765</td>
<td>-3.0 (-11.5, 5.5)</td>
</tr>
<tr>
<td>ATTEST 2015</td>
<td>180</td>
<td>156–215</td>
<td>47</td>
<td>200</td>
<td>160–220</td>
<td>49</td>
<td>-20.0 (-42.1, 2.1)</td>
</tr>
<tr>
<td>EXTEND-IA TNK 2</td>
<td>125</td>
<td>102–156</td>
<td>101</td>
<td>134</td>
<td>104–178</td>
<td>101</td>
<td>-9.0 (-25.2, 7.2)</td>
</tr>
<tr>
<td>TASTE-A 2022</td>
<td>97</td>
<td>68–157</td>
<td>55</td>
<td>92</td>
<td>66–131</td>
<td>49</td>
<td>5.0 (-22.2, 32.2)</td>
</tr>
</tbody>
</table>

**Total (95% CI)**

100.0% -5.2 [-12.1, 1.7]

Heterogeneity: Tau² = 0.00; Chi² = 2.73, df = 3 (P = 0.44); I² = 0%

Test for overall effect: Z = 1.49 (P = 0.14)
Evidence-based Recommendation

PICO1.1 Patients with AIS of <4.5 h duration

For patients with acute ischaemic stroke of <4.5 hrs duration who are eligible for intravenous thrombolysis, tenecteplase 0.25 mg/kg can be used as a safe and effective alternative to alteplase 0.9 mg/kg.

Quality of evidence: **Moderate** ⚫⚫⚫

Strength of recommendation: **Strong** ↑↑
All MWG members suggest favouring tenecteplase 0.25 mg/kg over alteplase 0.9 mg/kg for patients with acute ischaemic stroke of <4.5 hrs duration in light of safety and efficacy data and because tenecteplase can be administered with a single bolus rather than a 1-hr infusion.

Voting: 9/9 members
PICO 1 AIS patients of <4.5h duration

PICO 1.2 For patients with acute ischaemic stroke of <4.5hr duration, does intravenous thrombolysis with tenecteplase 0.40 mg/kg compared with intravenous thrombolysis with alteplase 0.90 mg/kg lead to:

a) a non-inferior proportion of patients with excellent functional outcome (mRS 0-1) at 90 days?

b) non-inferior or better results on other efficacy outcomes (mRS shift analysis at 90 days, mRS 0-2 at 90 days…)?

c) a reduction in the risk of adverse events (mortality at 90 days, sICH…)?

d) a reduction in key time metrics (onset-to-treatment time, door-to-needle time)?

e) an improvement in neuroimaging parameters?
Excellent functional outcome (mRS 0-1 at 90 days)

### PICO 1.2 AIS of <4.5 h duration- IV Tenecteplase 0.40mg/kg

<table>
<thead>
<tr>
<th>Study</th>
<th>Events</th>
<th>Total</th>
<th>Events</th>
<th>Total</th>
<th>Weight</th>
<th>RD% [95% CI]</th>
</tr>
</thead>
<tbody>
<tr>
<td>NOR-TEST 2017</td>
<td>354</td>
<td>549</td>
<td>345</td>
<td>551</td>
<td>44.0%</td>
<td>1.87 [-3.82, 7.55]</td>
</tr>
<tr>
<td>NOR-TEST 2A 2022</td>
<td>29</td>
<td>96</td>
<td>51</td>
<td>101</td>
<td>35.7%</td>
<td>-20.29 [-33.68, -6.89]</td>
</tr>
<tr>
<td>TNK-S2B 2010</td>
<td>7</td>
<td>19</td>
<td>13</td>
<td>31</td>
<td>20.3%</td>
<td>-5.09 [-32.88, 22.69]</td>
</tr>
<tr>
<td><strong>Total (95% CI)</strong></td>
<td><strong>664</strong></td>
<td><strong>100.0%</strong></td>
<td><strong>683</strong></td>
<td><strong>100.0%</strong></td>
<td><strong>-7.45 [-24.13, 9.22]</strong></td>
<td></td>
</tr>
</tbody>
</table>

Heterogeneity: $\tau^2 = 0.016$; $\text{Chi}^2 = 6.96$, df = 2 ($P = 0.01$); $I^2 = 76$

Test for overall effect: $Z = -0.88$ ($P = 0.38$)

Unadj. RD -7.45 % (95%CI= -24.13% to 9.22%)
PICO 1.2 AIS of <4.5 h duration- IV Tenecteplase 0.40mg/kg

Symptomatic intracranial haemorrhage (study definition)

Unadj. OR = 2.38 (95%CI= 0.69 to 8.23)
For patients with acute ischaemic stroke of <4.5 hrs duration who are eligible for intravenous thrombolysis, we recommend against using tenecteplase at a dose of 0.40 mg/kg.

Quality of evidence: Low ⬤ ⬤

Strength of recommendation: Strong against intervention ↓↓
PICO 1.3 In patients with acute ischaemic stroke of <4.5hr duration with prehospital management with a mobile stroke unit does intravenous thrombolysis with tenecteplase 0.25 mg/kg compared with intravenous thrombolysis with alteplase 0.90 mg/kg lead to:

a) a non-inferior proportion of patients with excellent functional outcome (mRS 0-1) at 90 days?
b) non-inferior or better results on other efficacy outcomes (mRS 0-2 at 90 days…)?
c) a reduction in the risk of adverse events (mortality at 90 days, sICH…)?
d) a reduction in key time metrics (onset-to-treatment time, door-to-needle time)?
e) an improvement in neuroimaging parameters?

<table>
<thead>
<tr>
<th>TASTE A (2022) Phase 2- Australia</th>
<th>N= 104</th>
<th>AIS &lt;4.5h MSU</th>
<th>Tenecteplase VS Alteplase</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td>Reduction of the volume of the post treatment perfusion lesion</td>
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<tr>
<td></td>
<td></td>
<td></td>
<td>Greater ultra-early clinical recovery</td>
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<tr>
<td></td>
<td></td>
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<td>Faster initiation</td>
</tr>
</tbody>
</table>
Evidence-based Recommendation

PICO 1.3 AIS of <4.5 h duration with Mobile Stroke Unit

For patients with acute ischaemic stroke of <4.5 hr duration with prehospital management with a mobile stroke unit who are eligible for intravenous thrombolysis, we suggest tenecteplase 0.25 mg/kg over alteplase 0.90 mg/kg to increase the rate of early reperfusion and to shorten the time from imaging to treatment initiation.

Quality of evidence: Low ⊕⊕
Strength of recommendation: Weak ↑
PICO 2 For large vessel occlusion acute ischaemic stroke patients of <4.5hr duration does intravenous thrombolysis with tenecteplase 0.25 mg/kg compared with intravenous thrombolysis with alteplase 0.90 mg/kg lead to:

a) a non-inferior proportion of patients with good functional outcome (mRS scores of 0-2) at 90 days?
b) non-inferior or better results on other efficacy outcomes (mRS shift analysis at 90 days, mRS 0-1 at 90 days…)?
c) a reduction in the risk of adverse events (mortality at 90 days, sICH..)?
d) a reduction in key time metrics (onset-to-treatment time, door-to-needle time)?
e) an improvement in neuroimaging parameters (recanalization at 24h or at the end of mechanical thrombectomy, recanalization before mechanical thrombectomy at first angiographic acquisition or averted mechanical thrombectomy…)?
PICO 2  AIS of <4.5 h duration +LVO- IV Tenecteplase 0.25mg/kg

Good functional outcome (mRS 0-2 at 90 days)

Non inferiority margin = -1.3%

Unadj. RD 16.15 % (95%CI= 1.21 to 31.09%)
Excellent functional outcome (mRS 0-1 at 90 days)

### PICO 2
AIS of <4.5 h duration + LVO - IV Tenecteplase 0.25mg/kg

<table>
<thead>
<tr>
<th>Study</th>
<th>TNK Events</th>
<th>Total</th>
<th>Alteplase Events</th>
<th>Total</th>
<th>Weight</th>
<th>Odds Ratio IV, Random, 95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>AcT 2022</td>
<td>32</td>
<td>196</td>
<td>19</td>
<td>193</td>
<td>39.5%</td>
<td>1.79 [0.97, 3.28]</td>
</tr>
<tr>
<td>ATTEST 2015 &amp; TAAIS 2012</td>
<td>18</td>
<td>37</td>
<td>8</td>
<td>32</td>
<td>13.7%</td>
<td>2.84 [1.02, 7.94]</td>
</tr>
<tr>
<td>EXTEND-IA TNK 2018</td>
<td>49</td>
<td>101</td>
<td>41</td>
<td>101</td>
<td>46.8%</td>
<td>1.38 [0.79, 2.41]</td>
</tr>
<tr>
<td><strong>Total (95% CI)</strong></td>
<td><strong>334</strong></td>
<td><strong>326</strong></td>
<td><strong>100.0%</strong></td>
<td><strong>1.69 [1.15, 2.47]</strong></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Heterogeneity: $\tau^2 = 0$; $\chi^2 = 1.53$, df = 2 ($P = 0.47$); $I^2 = 0$

Test for overall effect: $Z = 2.69$ ($P < 0.01$)

Unadj. OR = 1.69 (95%CI=1.15 to 2.47)
PICO 2  AIS of <4.5 h duration + LVO - IV Tenecteplase 0.25mg/kg

Symptomatic intracranial haemorrhage

Safety data

Unadj. OR = 0.50 (95%CI= 0.085 to 2.99)

All cause mortality at 3 months

Unadj. OR = 0.75 (95%CI= 0.49 to 1.13)
PICO 2 AIS of <4.5 h duration + LVO - IV Tenecteplase 0.25mg/kg

Recanalisation (mTICI≥2b) before Mechanical thrombectomy

Unadj. OR = 1.49
(95%CI= 0.58 to 3.85)

Recanalisation (mTICI≥2b) at the end of MT or within 24h

Unadj. OR = 2.07
(95%CI= 0.87 to 4.96)
Evidence-based Recommendation

PICO 2. AIS of <4.5 h duration -LVO

For patients with large vessel occlusion acute ischaemic stroke of <4.5 hr duration who are eligible for intravenous thrombolysis, we recommend tenecteplase 0.25 mg/kg over alteplase 0.9 mg/kg. Intravenous thrombolysis should not delay mechanical thrombectomy.

Quality of evidence: Moderate ⊕⊕⊕
Strength of recommendation: Strong ↑↑
Expert Consensus Statement

PICO 2. AIS of <4.5 h duration - LVO

For patients with large vessel occlusion acute ischaemic stroke of <4.5 hr duration who are eligible for intravenous thrombolysis and are directly admitted to a thrombectomy-capable center, all MWG members suggest IVT with tenecteplase 0.25 mg/kg over skipping IVT. For patients with large vessel occlusion acute ischaemic stroke of <4.5 hr duration who are eligible for intravenous thrombolysis and are admitted to a center without mechanical thrombectomy capability, all MWG members suggest IVT with tenecteplase 0.25mg/kg followed by rapid transfer to a thrombectomy-capable center.

Voting: 9/9 members
**PICO Question**

**PICO 3. Wake-up stroke/unknown onset**

**PICO 3.1** For patients with acute ischaemic stroke on awakening from sleep or acute ischemic stroke of unknown onset and who are eligible for intravenous thrombolysis, does intravenous thrombolysis with tenecteplase 0.25 mg/kg **compared with no intravenous thrombolysis** lead to:

a) a non-inferior proportion of patients with **excellent functional outcome (mRS scores of 0-1)** at 90 days?

b) non-inferior or better results on other efficacy outcomes (mRS 0-2 at 90 days…)?

c) a reduction in the risk of adverse events (mortality at 90 days, sICH…)?

d) a reduction in key time metrics (onset-to-treatment time, door-to-needle time)?

e) an improvement in neuroimaging parameters?

<table>
<thead>
<tr>
<th>TWIST (2022-23)</th>
<th>N= 578</th>
<th>Within 4.5h from awakening</th>
<th>Tenecteplase VS No thrombolysis : no difference</th>
</tr>
</thead>
<tbody>
<tr>
<td>Phase 3-</td>
<td></td>
<td>Patient selection : Non contrast CT</td>
<td>Shift analysis of mRS : Primary endpoint</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Mortality</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>sICH</td>
</tr>
</tbody>
</table>
Evidence-based Recommendation

PICO 3 Wake –up/unkown onset

For patients with acute ischaemic stroke on awakening from sleep or acute ischaemic stroke of unknown onset who are selected with no brain imaging other than plain CT, we recommend against intravenous thrombolysis with tenecteplase 0.25 mg/kg outside the context of a clinical trial.

Quality of evidence: Low ⊕⊕

Strength of recommendation: Strong against intervention ↓↓
PICO Question

PICO 3. Wake-up stroke/unknown onset

PICO 3.2 For patients with acute ischaemic stroke on awakening from sleep or acute ischemic stroke of unknown onset and who are eligible for intravenous thrombolysis, does intravenous thrombolysis with tenecteplase 0.25 mg/kg or 0.40 mg/kg compared with intravenous thrombolysis with alteplase 0.90 mg/kg lead to:

a) a non-inferior proportion of patients with excellent functional outcome (mRS scores of 0-1) at 90 days?

b) non-inferior or better results on other efficacy outcomes (mRS 0-2 at 90 days…)?

c) a reduction in the risk of adverse events (mortality at 90 days, sICH…)?

d) a reduction in key time metrics (onset-to-treatment time, door-to-needle time)?

e) an improvement in neuroimaging parameters?
Evidence-based Recommendation

For patients with acute ischaemic stroke on awakening from sleep or acute ischemic stroke of unknown onset and who are eligible for intravenous thrombolysis, there is continued uncertainty over the potential benefits and harms of tenecteplase compared with alteplase.

Quality of evidence: Very low ⊕
Strength of recommendation: -

Expert Consensus Statement

All MWG members suggest that tenecteplase 0.25 mg/kg could be a reasonable alternative to alteplase 0.9 mg/kg for patients with acute ischaemic stroke on awakening from sleep or acute ischemic stroke of unknown onset and who are eligible for intravenous thrombolysis after selection with advanced imaging (FLAIR-DWI mismatch or perfusion mismatch as outlined in the 2021 ESO Guidelines on IVT).

Voting: 9/9 members

Berge E et al, Eur Stroke J 2021; 6: I-LXII
Conclusion

- **Take Home Message**
  
  Patients with AIS of < 4.5 h duration who are eligible for IVT

  - Tenecteplase 0.25mg/kg can be used as safe and effective alternative to alteplase:
    moderate evidence, strong recommendation

  - Expert consensus statement: WGM suggest tenecteplase over alteplase

  Patient with AIS of < 4.5h duration and LVO who are eligible for IVT

  - Tenecteplase 0.25mg/kg is recommended over alteplase

  - ESO-2021 recommendation on IVT upgraded
    
    Evidence: Low=> Moderate // Strength of recommendation: Weak=> Strong

- **Tenecteplase shortage in Europe – Appropriate packaging**

- **European Medicines Agency approval?**

- **Perspectives**: the next frontiers for tenecteplase in stroke