Voice of Stroke — February 2026

Episode 1: Beyond the window:

What ISC 2026 tells us about treating stroke earlier – or later

Introduction: Welcome to Voice of Stroke – your rapid, reliable update on the science advancing stroke care – brought to you by the European Stroke Organisation.

Body: Despite major advances in acute stroke care, many of the boundaries that guide our decisions, who to treat, when to treat and with what, remain uncertain. At the 2026 International Stroke Conference earlier this month, several key trials revisited these unanswered questions. In this episode of Voice of Stroke, we will highlight three studies presented at the conference that offer new insights into where those boundaries may lie.

We will look at three key questions across three distinct patient populations:

- First: In patients with non–large vessel occlusion acute ischaemic stroke and salvageable brain tissue, does intravenous tenecteplase administered **beyond 4.5 hours** after onset improve outcomes?
- Second: In patients with basilar artery occlusion who presented **up to 24 hours** after symptom onset, does intravenous thrombolysis with tenecteplase improve outcomes?
- And finally: in patients with intracerebral haemorrhage, is recombinant factor VIIa given within 2 hours after symptom onset safe and effective in reducing disability?

Three questions, three trials — and three takeaways for all of us involved in stroke care. Let's get started.

Intravenous thrombolysis is one of the cornerstones of acute ischaemic stroke care, but also an area where key boundaries remain uncertain. In particular, what to do with patients who have non–large vessel occlusion stroke and present beyond the traditional 4.5-hour window.

The OPTION trial, recently published in JAMA, was designed to address this question.

OPTION was a randomised, open-label, blinded end-point clinical trial in China, which recruited 566 patients presenting between 4.5 to 24 hours from last seen well. All patients had non-large vessel occlusion stroke and evidence of potentially salvageable tissue on perfusion imaging. Patients were randomised to receive either intravenous tenecteplase or standard medical treatment with antiplatelet therapy.

The mean age of the study population was 68 years, with a median NIH stroke scale of 7. The median time from last seen well to randomisation was 12 hours. It is also worth noting that around 80% of patients had medium or distal vessel occlusions, predominantly involving the M2-M4 segments of the middle cerebral artery.

So was tenecteplase safe and effective in this late window population?

Overall, treatment with tenecteplase between 4.5 and 24 hours resulted in a higher proportion of patients achieving an excellent functional outcome at 90 days compared with standard medical care with antiplatelet therapy. The number needed to treat for one additional patient to achieve an excellent outcome was 11. However, tenecteplase was also associated with a higher rate of symptomatic intracranial haemorrhage, as well as a numerically higher risk of death at 90 days.

OPTION adds to the growing body of evidence supporting the efficacy of intravenous thrombolysis beyond the traditional 4.5 hour window, an area previously dominated by studies in anterior circulation large vessel occlusion.

Taken together, these findings suggest that in patients with non–large vessel occlusion stroke and salvageable brain tissue, intravenous tenecteplase beyond 4.5 hours may offer clinical benefit. At the same time, the increased bleeding risk highlights the ongoing importance of careful patient selection.

Of course late window isn't only a question in the anterior circulation. For the next study, we will move to the posterior circulation.

A previous study, the EXPECTS trial, showed that the time window for intravenous thrombolysis using alteplase could be extended to 24 hours also in patients with posterior circulation stroke. However, only patients with mild strokes were included in this trial. The question still remains, what about for patients with basilar artery occlusion, which is often associated with more severe deficits and much more devastating outcomes?

The TRACE-5 trial, published in the Lancet, was set out to answer this question. TRACE-5 was a multicentre, open-label, blinded endpoint, randomised trial in China. The trial compared intravenous tenecteplase versus standard medical treatment, given to patients presenting within 24 hours of onset of an acute ischaemic stroke and basilar artery occlusion.

In total, 453 patients with a mean age of 66 years were enrolled. Importantly, two thirds of the population were randomised after 4.5 hours, and 18% had wake-up stroke.

Several aspects of TRACE-5 are worth highlighting.

- The median NIH stroke scale was 12, lower than what we typically see in basilar artery thrombectomy trials.
- About half of the trial population underwent thrombectomy at the discretion of the treating physician, with similar rates in both groups.
- In the standard medical treatment arm, about a third of the patients received intravenous alteplase within 4.5 hours.
- Finally, no advanced imaging was required for patient selection, with most centres relying on non-contrast CT, CTA source images or diffusion weighted imaging to assess baseline ischaemic changes.

What did they find? TRACE-5 met its primary endpoint. Treatment with intravenous tenecteplase led to a higher proportion of patients with no disability at 90 days, with a number needed to treat of 11, without an increase in symptomatic intracranial haemorrhage, severe disability or death. These findings were consistent across multiple subgroups, including age, stroke severity, use of alteplase in the control group, and intention for thrombectomy.

What does this mean for practice? TRACE-5 adds important randomised evidence to support the 2024 European guidelines, which recommended extending the intravenous thrombolysis window up to 24 hours based on expert consensus.

That said, important questions remain - especially for patients intended for thrombectomy. Another trial presented at ISC, the ATTENTION LATE trial, compared bridging with tenecteplase vs. thrombectomy alone in the same population and did not show benefit with the bridging strategy. Ongoing studies, including the POST-ETERNAL trial, as well as a planned individual patient data meta-analysis, should help clarify the role of intravenous tenecteplase in this subgroup.

If OPTION and TRACE-5 ask how far we can extend thrombolysis in ischaemic stroke, the next trial asks a very different question—can ultra-early haemostatic therapy improve outcomes in **intracerebral haemorrhage?**

FASTEST, published in the Lancet, was an international, double-blind, placebo-controlled, adaptive, phase three trial that enrolled patients with spontaneous intracerebral haemorrhage. The investigators set out to ask – does giving recombinant factor VIIa **within 2 hours** of ICH onset improve functional outcome without increasing life-threatening thromboembolic events?

The trial recruited 626 participants with a mean age of 61 years. Unfortunately the trial was stopped early for futility.

There was no difference between treatment groups in the proportion of patients achieving a good functional outcome, despite some signal that recombinant factor VIIa reduced haematoma expansion. On the other hand, while the absolute rate of life-threatening thromboembolic events was below five percent, these events occurred significantly more often in the intervention group.

That said, pre-specified subgroup analyses suggested a potential benefit in patients with a CT spot sign and in those treated within 90 minutes of onset. These hypotheses are now being tested in a more selected population in the ongoing FASTEST-2 trial.

So there we have it. Three highlights from ISC 2026. To summarise:

Together, OPTION and TRACE-5 show that extending intravenous thrombolysis with tenecteplase beyond traditional time windows can benefit carefully selected patients with ischaemic stroke, while FASTEST reminds us that effective acute treatment in intracerebral haemorrhage remains challenging. Across stroke subtypes, these trials reinforce that progress lies not in abandoning boundaries, but in defining them more precisely. There are also other interesting studies presented at ISC that are yet to be published, including the first positive trial for endovascular treatment of medium vessel occlusion, the Chinese ORIENTAL-MeVO trial. Stay tuned!

Ending: That's all for this episode of Voice of Stroke, brought to you by the European Stroke Organisation. You can listen to Voice of Stroke on all your favourite podcast channels, including Spotify and Apple. Visit the European Stroke Organisation E-S-O-dash-stroke-dot-org for more information about our organisation,

mission and our key activities. I’m Linxin Li. Thanks for listening.

Credit: This episode was written by Voice of Stroke Podcast editor-in-chief Linxin Li