

Updates from the 17th World Stroke Congress, 23rd October 2025, in Barcelona, Spain: From Alteplase to Tenecteplase for Acute Ischaemic Stroke: A Catalyst for Stroke Care Improvement

MARTIN JAMES.¹ On behalf of:

CHARLOTTE CORDONNIER,² ROBIN LEMMENS,³ FRANCISCO MONICHE,⁴ AND GISELE SAMPAIO SILVA.⁵

¹Royal Devon and Exeter NHS Foundation Trust, United Kingdom

²Univ Lille, Roger Salengro Hospital, France

³KU Leuven, Flanders Institute for Biotechnology, Belgium

⁴Hospital Universitario Virgen del Rocío, Spain

⁵Federal University of São Paulo, Brazil

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Meeting summary

The symposium, "From Alteplase to Tenecteplase for Acute Ischaemic Stroke: A Catalyst for Stroke Care Improvement," was delivered as a panel discussion followed by an audience Question & Answer, as part of the 17th World Stroke Congress on Thursday 23rd October 2025 in Barcelona, Spain. Acute ischaemic stroke (AIS) is a time-critical neurological emergency where every minute of delay in revascularisation leads to measurable neuronal injury and poorer outcomes. Time to treatment directly correlates with neuronal salvage and functional independence. Historically, alteplase has been the mainstay of intravenous thrombolysis, yet its short half-life, complex dosing, and risk of symptomatic intracerebral haemorrhage (sICH), have limited its use. Tenecteplase (TNK) offers comparable safety and in meta-analysis of randomised controlled trials showed superior functional outcomes, and reduced disability compared to alteplase, while providing significant operational advantages through simplified administration. Switching to TNK acts as a "catalyst" in transforming stroke care delivery, reducing door-to-needle (DTN) times, and improving workflow efficiency. Real-world data from centres that have switched support substantial reductions in DTN time after the TNK transition. Major international and national health authorities have assessed and endorsed TNK for acute ischaemic stroke. TNK represents a clinically-sound paradigm shift toward simplified, faster, and more efficient stroke workflows with the potential to save resources.

KEYWORDS: ALTEPLASE, ACUTE ISCHAEMIC STROKE, DOOR-TO-NEEDLE TIME, DOOR-TO-STROKE-UNIT, INTRAVENOUS THROMBOLYSIS, LARGE VESSEL OCCLUSION, MECHANICAL THROMBECTOMY, PLASMINOGEN ACTIVATOR INHIBITOR-1 (PAI-1), SYMPTOMATIC INTRACEREBRAL HAEMORRHAGE, TENECTEPLASE.

Corresponding author: Martin James - martinjames@nhs.net

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Introduction

Global Burden and Time-Critical Nature of Treatment: Epidemiology of Acute Ischaemic Stroke

Stroke remains one of the leading causes of mortality and disability globally, with AIS accounting for approximately 80% of all acute strokes.¹ The incidence continues to rise in many developed nations, driven by ageing populations and cardiovascular risk factors. In the UK alone, stroke affects over 100,000 individuals annually, with a considerable economic burden on healthcare systems.¹⁻³ A substantial proportion of this disability burden can be avoided through effective prevention strategies targeting modifiable risk factors and optimising acute stroke care.⁴

Time is Brain: The Critical Window

Every minute post-onset of stroke results in cumulative neuronal loss, a concept encapsulated by the phrase "time is brain".⁵ Studies demonstrate that each minute of delay from stroke onset to reperfusion results in the loss of approximately 1.9 million neurons, 14 billion synapses, and 12 km of myelinated fibres.⁶ Rapid revascularisation correlates strongly with markedly better outcomes for patients and healthcare systems. Consequently, median DTN (mDTN) times are not merely process indicators; they directly affect neuronal salvage and functional independence.⁷ The target DTN of less than 30 minutes is evidence-based and internationally endorsed, with recent data suggesting that achieving DTN \leq 30 minutes is associated with 2.35 times the odds of achieving a good functional outcome (modified Rankin Scale 0-2, equivalent to an 'independent' recovery) at 3 months compared to DTN >60 minutes.⁸

Limitations of Alteplase: Pharmacological Constraints

Alteplase, recombinant tissue plasminogen activator (rt-PA), has been the standard thrombolytic agent for AIS since FDA approval in 1996.⁹ However, it possesses several pharmacological limitations. The half-life of alteplase is only 3.5 minutes from the initial bolus, necessitating a continuous post-bolus infusion for 60 minutes.^{9,10} This short half-life limits the pharmacological window and requires careful timing. Additionally, alteplase has relatively low fibrin specificity, 15-fold lower than TNK, and weaker resistance to plasminogen activator inhibitor-1 (PAI-1), reducing efficacy in high-inhibitor environments commonly encountered in acute stroke patients.¹¹⁻¹⁵

Operational and Administrative Challenges

The alteplase infusion regimen (10% as a bolus over 1 minute, followed by 90% infusion over 60 minutes)¹⁶ is complex, increasing the risk of medication errors. Studies have documented that bolus-to-infusion delays of >8 minutes occur in nearly half of cases, with a 5-minute delay from bolus to infusion halving plasma alteplase concentration.^{17,18} This delay has an effect on drug efficacy, and while not statistically significant, trended toward poorer outcomes for patients.¹⁷

The relatively complex infusion regimen for alteplase can hinder patient care, and the drug cannot be easily administered in full in imaging suites, ambulances, or mobile stroke units. The inability to rapidly transfer patients receiving alteplase to thrombectomy-capable centres while the infusion continues creates delays and operational bottlenecks.^{19,20}

Rationale for Tenecteplase: Enhanced Pharmacology

TNK is a rationally designed bioengineered derivative of alteplase with amino acid substitutions that preserve therapeutic efficacy while conferring distinct pharmacological and, therefore, operational advantages.²¹ These modifications result in:

1. **Extended half-life:** ~22 minutes (6-fold increase compared with alteplase), allowing single-bolus administration.^{21,22}
2. **Superior fibrin specificity:** 15-fold higher compared with alteplase, improving targeted clot dissolution.^{21,22}
3. **Enhanced PAI-1 resistance:** 80-fold greater resistance to PAI-1, the primary physiological inhibitor of plasminogen activators.^{21,22}
4. **Improved fibrinogen conservation:** 10-fold better preservation, potentially reducing systemic fibrinolytic effects.^{21,22}

Weight-tiered bolus dosing (0.25 mg/kg, maximum 25 mg) simplifies dosing calculations, and the improved pharmacology avoids the need for an ongoing infusion.¹⁶

Operational Advantages

TNK eliminates the need for infusion pumps and the full dose

can be administered rapidly in the imaging suite, and in mobile stroke units, supporting prehospital thrombolysis models and ambulance-based care.²³ The simplified administration reduces medication errors caused by bolus-infusion timing delays and enables a simpler supply chain with a single vial size, reduced wastage and, in some cases, lower acquisition costs.^{21,23} The reduced complexity and time required for TNK can also save specialist nurse time, further reducing costs and time.¹⁹

Clinical Administration Profile

Weight-based Dosing Regimen

Alteplase dosing requires multiple sequential calculations; clinicians must first determine a patient's weight, calculate the total dose (0.9 mg/kg, maximum 90 mg) and subdivide into a 10% bolus (0.09 mg/kg) plus 90% infusion (0.81 mg/kg), finally programming the infusion pump rate for 60 minutes of continuous administration.^{8,9} This multi-step preparation necessitates two separate drug preparations of a bolus syringe and an infusion, creating vulnerability to bolus-to-infusion related delays.¹²

In contrast, TNK requires a single calculation (0.25 mg/kg with a 25 mg cap), a single preparation (one vial drawn into one syringe), and no infusion pump, eliminating the bolus-to-infusion related delays and reducing drug preparation time from several minutes to seconds. This operational simplicity translates into faster medication delivery (6–7-minute reduction

Table 1. Pharmacokinetics Comparison

Parameter	Alteplase	Tenecteplase
Half-life	3.5 minutes	~22 minutes
Dose	0.9 mg/kg (0.09 mg/kg bolus + 0.81 mg/kg infusion)	0.25 mg/kg (bolus only)
Administration	Bolus + infusion (60 minutes)	5–10 seconds bolus
Fibrin specificity	Baseline	15-fold increase
PAI-1 resistance	Baseline	80-fold increase
Fibrinogen conservation	Baseline	10-fold increase

Table 2. Tiered dosage of TNK by patient's weight

Patient's body weight category (kg)	Tenecteplase (units)	Tenecteplase (mg)	Corresponding volume of reconstituted solution (mL)
50-60	3000	15.0	3.0
≥ 60 to < 70	3500	17.5	3.5
≥ 70 to < 80	4000	20.0	4.0
≥ 80 to < 90	4500	22.5	4.5
≥ 90	5000	25.0	5.0

in CT-to-needle times), lower error risk, and immediate post-thrombolysis mobilisation while TNK's extended half-life (~22 minutes) ensures sustained circulating levels adequate for efficacy parity with alteplase's bolus-infusion regimen.^{15,17,24}

During the conference it was noted that the tiered structure of dosage increments for TNK widely used, increasing in steps of 2.5 mg to a maximum of 25 mg for a patient 90 kg or above, represents a useful simplification of the dosage calculation and reduces the potential for error (Table 2). For administration of TNK, medical team members can estimate a patient's weight allowing for more rapid treatment than alteplase which requires more accurate weight measurement (2 kg rather than 10 kg weight tiers).

Pharmacological Rationale for Clinical Advantage

Improved Fibrin Targeting

Higher fibrin specificity ensures drug concentration localises to the thrombus rather than causing systemic fibrinolysis. Off-target proteolysis and the risk of systemic bleeding are potentially reduced, with alteplase (0.9 mg/kg) causing significant disruption of the fibrinolytic system, whereas TNK 0.25 mg/kg did not, preserving circulating fibrinogen and other clotting factors.^{11,25,26}

PAI-1 Resistance

PAI-1 is the primary physiological inhibitor of plasminogen activators. Elevated PAI-1 levels are common in acute stroke and associated with poorer outcomes for patients.¹³⁻¹⁵ TNK's 80-fold greater resistance enables sustained thrombolytic activity despite high PAI-1 levels, whereas alteplase is rapidly inhibited in high-PAI-1 environments, limiting efficacy.^{27,28}

Extended Half-Life Benefit

The longer circulation time allows single bolus administration with steady drug levels without peak-trough fluctuations from infusion. This reduces cumulative medication errors from timing delays and provides more predictable pharmacokinetics.^{21,29}

Implementation Strategies and Best Practices

Guidelines and Regulatory Endorsement

Often the stimulus for implementation is a change in guidelines. International clinical guidelines have endorsed the switch to TNK for AIS. The European Stroke Organisation (ESO) published expedited recommendations in February 2023 with unanimous expert consensus (9/9 working group members) favouring TNK 0.25 mg/kg over alteplase 0.9 mg/kg for patients within 4.5 hours of symptom onset, citing comparable safety and efficacy with superior ease of administration.³⁰ The ESO recommendations extend beyond the conventional therapeutic window, indicating that TNK is reasonable for wake-up and unknown-onset stroke after advanced imaging confirmation of salvageable tissue, typically identified with CT perfusion techniques. ESO also recommends TNK over alteplase for large vessel occlusion candidates proceeding to mechanical thrombectomy, with intravenous thrombolysis preferable to omitting thrombolysis entirely even in direct admission scenarios.

Additionally, product availability and label indication should be considered. In the UK regulatory approval and health technology assessment rapidly followed EMA approval. The Medicines and Healthcare products Regulatory Agency (MHRA) granted full acute stroke licensing for TNK 25 mg on 26 April 2024. NICE Technology Appraisal TA990 (July

Table 3. Efficacy and Safety of Tenecteplase versus Alteplase: Summary of Nine Randomised Controlled Trials (2010-2024) and Pooled Meta-Analysis Results

Study	Year	Type	Country	TNK (n)	Alteplase (n)	mRS 0-1 (RR)	sICH (RR)
TNK-S2B	2010	Phase II	United States	31	31	1.15	2
TAAIS	2012	Phase II	Australia	25	25	1.8	0.33
ATTEST	2015	Phase II	United Kingdom	53	51	1.36	0.49
EXTEND-IA TNK	2018	Phase II	Australia	101	101	1.2	1
TASTE-A	2022	Phase II	Australia	55	49	1.02	Not reported
AcT	2022	Phase III	Canada	802	765	1.06	1.07
ATTEST-2	2024	Phase III	United Kingdom	885	892	1.05	1.34
TASTE	2024	Phase III	Multiple/International	339	341	1.03	1.51
ORIGINAL	2024	Phase III	China	732	733	1.03	1.01
PALAIODIMOU META-ANALYSIS	2024	9 RCTs	Multiple	2,669	2,987	1.05 (1.00-1.10)	1.14 (0.81-1.60)

2024) recommended TNK based on clinical effectiveness, cost-effectiveness, and operational benefits including simplified administration, elimination of pump infrastructure, single-vial streamlining, and no requirement for medical escort during ambulance transfer.³¹

Local stroke association recommendations should also be considered. The British and Irish Association of Stroke Physicians (BIASP) published consensus guidance in October 2024 recommending TNK as Standard-of-Care for AIS.³² Critically, BIASP recommended complete national transition from alteplase to TNK across both conventional and extended time windows to simplify treatment pathways and eliminate potential dosing errors from parallel availability of both agents.

Planning Phase

Governance and Procurement

With regulatory approval, guideline endorsement, and national recommendations established, successful implementation requires coordinated institutional action. Departments making the transition to TNK will need to secure institutional approval for a revised reperfusion protocol, engage pharmacy to obtain TNK supply and remove alteplase from routine stroke protocols. This is while still maintaining a small reserve for other indications (such as exceptional AIS cases determined locally, and non-stroke uses such as pulmonary embolism), and comprehensively revise institutional policies, electronic order sets, and documentation. Protocol development should update stroke indications and maintain identical inclusion/

exclusion criteria, replace alteplase dosing schedules with TNK weight-based dosing charts and pre-calculated reference cards for common weights, and modify emergency stroke response procedures.

Multidisciplinary engagement is essential, encompassing emergency department physicians and nurses, stroke team neurologists, pharmacy staff, radiology/imaging personnel, and hospital administration. Comprehensive staff training must include clinical sessions explaining TNK pharmacology and administration, simulation-based acute scenario training, bedside reference materials with pre-calculated dosing, and video tutorials for those unable to attend live sessions.¹⁹ A single go-live date on a scheduled weekday maximises impact; all alteplase is removed from stroke protocols on that date (maintaining a separate, clearly labelled small stock for non-stroke indications), with advance staff notification and on-unit support during the first week. Post-implementation success requires daily DTN monitoring for one month then weekly, continuous tracking of door-in-door-out (DIDO) times, thrombolysis rate assessment, and outcome surveillance (NIHSS, modified Rankin Scale (mRS), sICH, mortality). Regular team debriefs over the transition period can identify barriers and solutions, celebrate successes, and share results with leadership and frontline staff.

Practical Tips from Early Adopters

Experience from early adopter centres provides practical guidance for successful implementation. Hospital Virgen del Rocío identified a key challenge – sterile water for TNK

reconstitution may not be readily available in computed tomography suites. The solution, taping sterile water vials to each TNK vial as part of pre-assembled intravenous thrombolysis kits containing water, saline, syringes, needles, and dosing guides, ensures immediate availability and eliminates delays.

Overcoming organisational resistance requires understanding facilitators and barriers to adoption. Early experience demonstrates that team buy-in, physician, nursing, and pharmacy engagement are critical. Previously cited barriers have been substantially mitigated: guideline gaps addressed by ESO, NICE, and BIASP; insufficient evidence overcome by robust randomised controlled trials and meta-analyses, and administrative concerns alleviated by cost-effectiveness data. Success ultimately depends on ensuring local clinical teams are convinced of the evidence, completing comprehensive staff training, and securing hospital administration engagement.

Monitoring

Monitoring and challenging one another are key to improving stroke care. In the UK TNK's pharmacological advantages have been seen to translate reliably into measurable operational improvements across diverse healthcare settings. Royal Berkshire Hospital demonstrated substantial gains in post-thrombolysis workflow efficiency following transition to TNK. During the pre-transition alteplase era (September–November 2024), median door-to-stroke-unit time was 122 minutes, decreasing to 76 minutes post-transition (December 2024–February 2025), a 46-minute reduction representing 38% improvement in throughput to stroke unit care.³³ Thrombolysis rates remained stable at 23.9%, confirming operational gains without reducing patient access to acute reperfusion therapy.

Forth Valley Royal Hospital achieved sustained improvements in DTN performance while maintaining a thrombolysis rate of 13%. Forth Valley's in-hours mDTN time improved from 29 minutes to 21 minutes, and out-of-hours performance improved from 48 minutes to 42 minutes. In the alteplase era, 50% of patients were treated with a DTN within 30 minutes, which increased to 100% within 30 minutes in-hours after the transition to TNK, along with an out-of-hours DTN improvement from 51.5% to 87.5% of patients treated within 60 minutes.³³ Qualitative feedback highlighted easier protocol adherence, reduced complexity for junior doctors, and marked reduction in infusion equipment-related errors. Hospital

Virgen del Rocío (Spain) demonstrated mDTN time reduction from 50 minutes (pre-2018) to 32.5 minutes (2022, $p < 0.001$), with DTN <30-minute compliance increasing from 35% to 65% – credited to a shift to providing TNK in the imaging suite. Real-world transition experience from a German tertiary care centre demonstrated significantly shorter door-to-groin times ($p = 0.002$) for patients undergoing endovascular thrombectomy after TNK treatment compared to alteplase.³⁴

Potentially the shift to TNK could allow for increased thrombolysis rates. National SSNAP data demonstrate that as TNK adoption increased from 23% to 75% of intravenous thrombolysis (Q4 2024 to Q2 2025), overall intravenous thrombolysis rates increased from 11.8% to 14.0%.

Special Considerations and Clinical Scenarios

Low Body Weight Patients

Current Approach

The marketing authorisation and clinical trials used weight-based dosing at 0.25 mg/kg up to a maximum of 25 mg in 10 kg, by 10 kg weight tiers. This approach was designed for speed and simplicity and has been successfully used in STEMI for over 20 years.³⁵

Population vs Individual Risk

The AcT trial and other major RCTs did not specifically restrict enrollment by weight, and safety outcomes were comparable across weight ranges.³⁶ During the discussion, it was noted that outside of the UK anecdotal data of patients who were <50 kg at the time of admission, were treated successfully with TNK using the standard dosage of 0.25 mg/kg. However, the panel noted specifically in the UK and Ireland the BIASP consensus suggests considering alteplase for patients <50 kg as a precautionary measure, though evidence for differential risk is limited.

Onset of Intracerebral Haemorrhage

A theoretical concern regarding TNK's single bolus administration is the inability to stop the medication if clinical features of developing sICH occur. However, clinical evidence does not support this concern. sICH occurs within the first 24 hours post-treatment, with haemorrhagic events during active drug infusion very rarely reported. In a large US real-world series of 511 patients receiving alteplase, only

one patient experienced deterioration due to intracranial haemorrhage within one hour of bolus administration. In a second registry of 933 patients, there were no documented cases of sICH during alteplase infusion. These data demonstrate that once haemorrhagic transformation begins, stopping the infusion provides minimal additional clinical benefit, rendering the theoretical advantage of stopping alteplase infusion clinically insignificant. Consequently, the inability to discontinue TNK does not represent a meaningful clinical disadvantage compared to alteplase.

Haemostasis Disruption

Alteplase causes prolonged derangement of haemostasis (decreased fibrinogen, decreased plasminogen) up to 24 hours post-administration. Stopping an alteplase infusion is therefore unlikely to significantly modify either systemic or intracranial bleeding complications once the bolus has been administered.

Bolus-to-Infusion Delays

A 5-minute delay from bolus to infusion halves plasma concentration of alteplase.¹⁸ Infusion delays exceeding two alteplase half-lives (>8 minutes) occurred in almost half of patients in one registry of 276 treated patients. Importantly, 3-month mRS outcomes were poorer (though not significantly different) in patients with delays >8 minutes compared with 0–8 minutes.^{14,15}

Conclusions

TNK for AIS represents not merely a pharmaceutical substitution, but a system-level innovation that optimises acute stroke workflows, reduces operational delays, and measurably improves stroke service performance. The transition from alteplase to TNK is supported by robust clinical trial evidence demonstrating non-inferiority and emerging signals of superiority, particularly in large vessel occlusion stroke.^{37,38}

The pharmacological advantages of TNK, with a longer half-life, greater fibrin specificity, and enhanced resistance to PAI-1 translate directly into operational benefits: single 5–10 second bolus administration, elimination of infusion pumps and associated equipment, simpler and faster patient transfer for thrombectomy, and support for prehospital delivery.³⁵ Real-world NHS experience demonstrates how

implementation can deliver immediate and sustained improvements in DTN and DIDO times.²⁹

National and international guidelines unequivocally support TNK as the preferred agent for thrombolysis in AIS. Economic analyses demonstrate cost savings through elimination of infusion infrastructure, reduced wastage, decreased nursing time (approximately 50 minutes per patient). At the patient level, achieving DTN times ≤ 30 minutes is associated with 2.35 times higher odds of excellent functional outcome, and 22.7% reduction in total hospitalization, underscore the principle that "time is brain" and the urgency of streamlined acute stroke care.^{7,8}

Recommendations for Implementation

Stroke centres not yet using TNK should transition as soon as feasible, focusing on:

- 1. Robust governance** approval and multidisciplinary protocol development
- 2. Comprehensive staff education** including simulation-based training
- 3. Single go-live date** with pre-calculated dosing charts and bedside reference materials
- 4. Monitor performance** monitoring DTN, DIDO, thrombolysis rates, and clinical outcomes
- 5. Quality improvement mindset** with iterative refinement based on local experience.

The evidence is clear, the guidelines are aligned, and the operational benefits are proven. The transition from alteplase to TNK is no longer a question of "if" but "how quickly" healthcare systems can implement this transformative change to improve outcomes for stroke patients.

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