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Comparative effectiveness of Tenecteplase and Alteplase for ischemic stroke: real-world data from a stroke center

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Abstract

Background Tenecteplase (TNK) and Alteplase (rt-PA) are intravenous thrombolytics used in acute ischemic stroke (AIS). While Alteplase has long been the standard of care, TNK is now also approved for AIS by both the EMA and FDA. Its single-bolus administration and favorable pharmacokinetics offer practical advantages. Despite growing guideline support, real-world data comparing both agents remain limited. This study aimed to compare clinical characteristics, imaging findings, treatment outcomes, and complication rates of AIS patients treated with TNK versus Alteplase at a single stroke center.

Methods We conducted a retrospective monocentric analysis of 101 AIS patients treated with TNK ($n=39$) or Alteplase ($n=62$). We compared demographics, vascular risk factors, imaging findings, reperfusion therapies, and clinical outcomes using independent samples t-tests, Chi-square, and Mann–Whitney U-tests as appropriate.

Results Baseline characteristics were comparable between groups, including age (TNK: 72.7 ± 14.4 vs. Alteplase: 70.1 ± 14.3), sex, and pre-stroke mRS. Initial NIHSS scores were similar (TNK: 6.0 ± 6.3 vs. Alteplase: 7.2 ± 8.2, $p=0.83$). No significant differences were found in LVO rates (15.4% vs. 27.4%, $p=0.16$), perfusion delay, or infarct demarcation. Functional outcomes at discharge (mRS: 2.3 ± 1.8 vs. 2.0 ± 1.9, $p=0.39$) and rates of symptomatic intracranial hemorrhage (11.1% vs. 10.3%, $p=0.91$) were similar.

Conclusion This real-world study found that TNK and alteplase had similar early clinical and safety outcomes during the initial implementation of TNK. These observational findings generate hypotheses and support the need for larger prospective studies to assess long-term outcomes and reduce confounding factors related to the transition.

Keywords Acute ischemic stroke, Tenecteplase, Alteplase, Intravenous thrombolysis, Door-to-needle time

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Introduction

In acute ischemic stroke (AIS), a leading cause of death and disability worldwide, timely reperfusion therapy remains the cornerstone of effective treatment [1]. Intravenous thrombolysis with alteplase (recombinant tissue plasminogen activator, rt-PA) has long represented the gold standard in acute ischemic stroke treatment, backed by strong clinical evidence and regulatory approval, including from the U.S. Food and Drug Administration (FDA) [2]. However, its use is limited by a narrow therapeutic window and a complex administration regimen involving an initial bolus followed by a continuous infusion period over one hour [3].

Tenecteplase (TNK), a genetically engineered variant of the tissue plasminogen activator originally developed for acute myocardial infarction, is now approved for the treatment of acute ischemic stroke by both the FDA and the European Medicine Agency (EMA). Its single bolus administration, greater fibrin specificity, and higher resistance to plasminogen activator inhibitor-1 are practical and pharmacologic advantages over alteplase. Major stroke organizations also endorse its use: the European Stroke Organization issues a strong recommendation for 0.25 mg/kg TNK as a safe and effective alternative to alteplase within 4.5 h of stroke onset (and prefers TNK for large-vessel-occlusion candidates), while the AHA/ASA recognizes TNK as an alternative in its guidelines [4–8].

Some studies suggest that TNK achieves comparable or even superior reperfusion and functional independence rates compared to alteplase, particularly in patients undergoing endovascular therapy or with large-vessel occlusions [4, 9]. However, the results of these studies are inconsistent, due to differences in dosing regimens, patient selection, and imaging protocols.

Although the evidence base for TNK is growing, head-to-head comparisons with alteplase in routine clinical practice remain sparse. Much of the literature originates from randomized controlled trials and selected stroke networks or high-volume centers, which can limit external validity. More multicenter, real-world studies — spanning diverse hospital types, workflows, and dosing protocols— are needed to confirm TNK effectiveness and safety in broader, unselected populations.

In this retrospective, single-center cohort study, we compared patients with acute ischemic stroke who were treated with intravenous thrombolysis (IVT) using either TNK or Alteplase. We assessed differences in baseline characteristics, imaging findings, recanalization metrics, and clinical outcomes, with the aim of informing the comparative effectiveness and safety of these two agents in real-world stroke care.

The study was primarily intended to describe early real-world transition patterns and generate hypotheses for adequately powered prospective studies. Due to the small sample size and low event rates (and the resulting wide uncertainty), the absence of statistically significant differences should not be taken as proof of equivalence or non-inferiority.

Methods

Study design

This retrospective cohort study included consecutive adults (>18 years) with acute ischemic stroke (AIS) who were treated with intravenous thrombolysis (IVT) with either Alteplase (Actilyse) or TNK at the University Hospital of Giessen, Germany between May 1 and October 31, 2024. During the initial phase (May-July 2024), alteplase was the sole thrombolytic agent. Following an institutional protocol change, TNK replaced Alteplase as the default IVT agent on August 1, 2024. Prior to implementation, all personnel involved in acute stroke care—including emergency medicine and neurology physicians and nursing staff—completed structured training on the updated protocol, including dosing, preparation, administration, and documentation. Patients were assigned to Alteplase or TNK group according to the agent administered. We identified all eligible cases from the institutional stroke database and excluded patients who underwent endovascular therapy (EVT) without preceding IVT.

Because TNK was introduced as the default thrombolytic agent during the study period, treatment allocation followed a temporal protocol change rather than random assignment. Accordingly, all comparisons are descriptive and exploratory in nature.

Clinical data were extracted from the institutional stroke registry and electronic medical records. Variables included demographic characteristics, vascular risk factors, imaging findings, stroke severity assessed by the National Institutes of Health Stroke Scale (NIHSS) at admission, treatment times metrics including door-to-needle (DTN), door-to-groin (DTG), and functional outcomes at discharge assessed by the modified Rankin Scale (mRS) and NIHSS after 24 h and at discharge [10, 11]. In patients who underwent additional EVT successful reperfusion was defined as a modified Thrombolysis in Cerebral Infarction (mTICI) score (≥ 2b).

Local stroke treatment

Both thrombolytic agents were administered in accordance with current German stroke treatment guidelines. Alteplase was dosed at 0.9 mg/kg body weight (maximum 90 mg), with 10% of the dose as an initial bolus followed by a 60-minute infusion. TNK was administered as a single intravenous bolus of 0.25 mg/kg (maximum 25 mg); using standardized dosing cards to ensure accurate preparation and administration.

At our center, we routinely perform multimodal CT, including perfusion imaging, in most acute ischemic stroke (AIS) patients, regardless of the time window. For patients presenting within the 4.5-hour of last seen well, treatment decisions were primarily based on non-contrast CT findings. For presentation beyond the 4.5-hours, perfusion imaging or mismatch profiles were used to guide thrombolysis eligibility. Patients receiving oral anticoagulants were assessed individually based on laboratory parameters and guideline recommendations. Intravenous thrombolysis (IVT) was administered in patients on vitamin K antagonists if the international normalized ratio (INR) did not exceed 1.7. For patients receiving direct oral anticoagulants (DOACs), IVT eligibility required drug-specific thresholds: an anti-Xa activity ≤ 100 ng/ml for factor Xa inhibitors, and Dabigatran plasma levels ≤ 100 ng/ml as determined by the Hemoclot assay.

Stroke etiology was classified according to the TOAST criteria as large-artery atherosclerosis (macroangiopathy), small-vessel occlusion (microangiopathy), cardioembolism, other determined etiology, and undetermined etiology (e.g., ESUS: embolic stroke of undetermined source) [12]. Classification was based on an integrated review of the clinical presentation, neuro, and vascular imaging; cardiac diagnostics (e.g., ECG/telemetry, echocardiography), and relevant laboratory tests obtained during the index hospitalization.

Outcomes

The primary outcome of this study was defined as the treatment metrics (e.g. DTN and DTG). Functional outcomes were assessed using the Modified Rankin Scale (mRS) at hospital discharge. The mRS is a widely used, validated ordinal scale to evaluate global disability after stroke and has been described extensively in the stroke literature [13]. A 90-day mRS was not available due to the retrospective design and lack of standardized follow-up in this early implementation period. In patients undergoing endovascular therapy, reperfusion success was evaluated using the modified Thrombolysis in Cerebral Infarction (mTICI) score, a standardized angiographic grading system to quantify the degree of tissue reperfusion [14]. Successful reperfusion was defined as mTICI ≥ 2b, following widely adopted consensus grading criteria.

Safety outcomes included: (i) radiologically confirmed intracranial hemorrhages by imaging at any follow-up; (ii) classification of hemorrhage subtypes according to the Heidelberg Bleeding Classification (e.g., PH1, PH2, SAH); (iii) presence and extent of infarct demarcation and cerebral edema; (iv) in-hospital mortality; and (v) angioedema.

Statistical analysis

Statistical analysis was performed using JASP version 0.19.3. Categorical variables were expressed as absolute and relative frequencies and compared using the chi-square test or Fisher's exact test. Continuous variables were assessed using the student's t-test or Mann–Whitney U test, depending on normality of distribution. A p-value < 0.05 was considered statistically significant. Subgroup analyses were conducted for patients treated within and beyond 4.5 h of stroke onset, as well as by stroke severity at baseline.

Due to the smallsample size and low event rates, we did not perform multivariable adjustment or propensity score methods, as these models would likely be unstable and prone to overfitting. Therefore, the results are presented as exploratory and descriptive.

Workflow metrics

To investigate potential operational barriers during the transition to TNK, we qualitatively assessed workflow challenges based on chart review and clinical team feedback. Common issues included increased cognitive load during the switch in protocols, unfamiliarity with TNK preparation procedures, dual-agent availability during the transition period, additional verification steps (e.g., dosing cards), and the need to adjust electronic order sets.

Results

Patient inclusion and baseline characteristics

Between May 1 and October 31, 2024, 101 patients with acute ischemic stroke received intravenous thrombolysis at the University Hospital of Giessen. Of these, 39 were treated with TNK and 62 with Alteplase. Patients treated exclusively with endovascular therapy (EVT) without prior thrombolysis were excluded ($n = 72$) (shown in Fig. 1).

Demographic and vascular risk factors were largely balanced between groups (Table 1). Mean age was 72.7 ± 14.4 years in the TNK group and 70.1 ± 14.3 years in the Alteplase group, and approximately half of patients were female in both groups. Common vascular risk factors, including hypertension and hypercholesterolemia, were similarly distributed. A trend toward a higher prevalence of diabetes was observed with TNK (28.2% vs. 12.9%; $p = 0.05$).

Premorbid functional status, assessed by the modified Rankin Scale (mRS), did not differ significantly (TNK: 1.09 ± 1.38 vs. Alteplase: 0.74 ± 1.28; $p = 0.20$). Prior use of antiplatelet or anticoagulant agents was comparable between groups (Table 1).

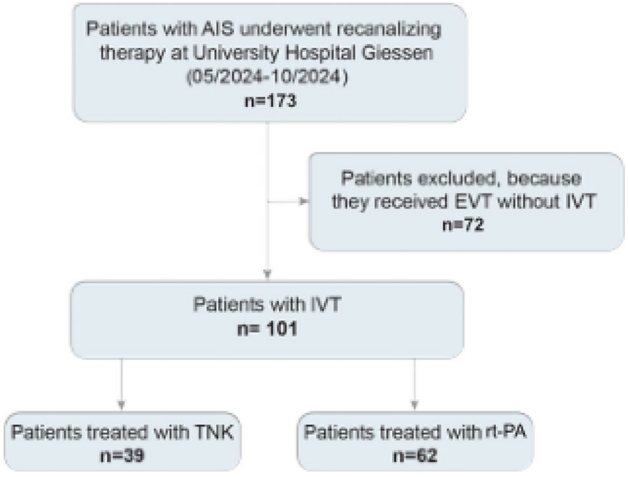


Fig. 1 Flowchart of patient selection for inclusion in the study. A total of $n=173$ patients receiving Intravenous Thrombolysis (IVT) were screened. After application of exclusion criteria, $n=72$ patients were eligible and included in the final analysis, divided into the Tenecteplase (TNK) and Alteplase (rt-PA) treatment groups

Stroke characteristics

Clinical profiles and baseline stroke severity were similar between the TNK and Alteplase groups (Table 2).

The distribution of stroke subtypes according to the TOAST classification was comparable between groups (Table 2). Microangiopathic stroke was present in 28.9% of TNK-treated patients and 25.4% of those receiving Alteplase ($p=0.70$). Macroangiopathy was observed in 23.7% and 33.9% of patients, respectively ($p=0.28$). Cardioembolic strokes occurred in 21.1% of the TNK group versus 23.7% in the Alteplase group ($p=0.76$), while ESUS accounted for 13.2% and 13.6% ($p=0.95$), respectively. Other determined etiologies were slightly more frequent in the TNK group (13.2%) compared to the Alteplase group (3.4%), but without reaching statistical significance ($p=0.07$).

Imaging and treatment characteristics

Most patients underwent initial imaging with perfusion-CT (CTP) (TNK: 97.4%, Alteplase: 98.4%; Table 3). Large vessel occlusion (LVO) was detected in 15.4% of the TNK group and 27.4% of the Alteplase group ($p=0.16$). EVT was performed in 23.1% vs. 36.7%, respectively ($p=0.15$). The choice between CT and MRI was mainly determined by clinical availability, time of presentation, and patient stability, with CT being the preferred first-line modality in acute settings, while MRI was used in selected cases when contraindications for CT existed or when patients presented outside the typical therapeutic window.

Primary outcomes

Regarding primary outcomes Door-to-needle time (DTN) was slightly longer for TNK (42.8 ± 27.1 min) compared to Alteplase (37.5 ± 20.9 min; $p=0.62$), without reaching statistical significance (Table 2).

Door-to-groin time (DTG) was also longer in the TNK group (87.6 ± 48.8 min, $n=9$) compared to the Alteplase group (64.6 ± 73.7 min, $n=22$), although this difference did not reach statistical significance ($p=0.39$).

Table 1 Baseline demographics and vascular risk factors

Baseline Demographics	TNK ($n=39$)	rt-PA ($n=62$)	*P*-value
Age [a]	72.7 ± 14.4	70.1 ± 14.3	0.35
Weight [a]	78.9 ± 13.3	80.6 ± 18.2	0.84
BMI [a]	27.7 ± 4.1	27.2 ± 4.9	0.72
Male [b]	21 (53.8)	32 (51.6)	0.96
Female [b]	18 (46.2)	29 (46.8)	0.96
Risk Factors			
Hypertension [b]	30/39 (76.9)	48/62 (77.4)	0.95
Diabetes mellitus [b]	11/39 (28.2)	8/62 (12.9)	0.05
Hypercholesterolemia [b]	18/39 (46.2)	31/62 (50.0)	0.71
Kidney failure [b]	1/39 (2.6)	2/62 (3.2)	0.85
Atrial fibrillation [b]	6/39 (15.4)	8/62 (12.9)	0.81
Atrial fibrillation ED [b]	2/6 (33.3)	6/8 (75.0)	0.24
Premorbid mRS [a]	1.09 ± 1.38 ($n=35$)	0.74 ± 1.28 ($n=61$)	0.20
Premedication			
ASS [b]	12 (30.8)	22 (35.5)	0.63
Clopidogrel [b]	2 (5.1)	2 (3.2)	0.63
OAC [b]	1 (2.6)	1 (1.6)	0.74
DOAC [b]	1 (2.6)	5 (8.2)	0.25

[a] Mean ± SD

[b] *n* (%)

Table 2 Clinical characteristics and TOAST-classification

Clinical Characteristics	TNK (*n* = 39)	rt-PA (*n* = 62)	*P*-value
NIHSS at admission [a]	6.0 ± 6.3 (*n* = 34)	7.2 ± 8.2 (*n* = 61)	0.83
NIHSS after 24 h [a]	10.5 ± 13.5 (*n* = 34)	9.7 ± 13.2 (*n* = 58)	0.74
DTN [a]	42.8 ± 27.1 (*n* = 30)	37.5 ± 20.9 (*n* = 49)	0.62
DTG (door-to-groin time) [a]	87.6 ± 48.8 (*n* = 9)	64.6 ± 73.7 (*n* = 22)	0.39
TOAST-classification			
Microangiopathy [b]	11/38 (28.9)	15/59 (25.4)	0.70
Macroangiopathy [b]	9/38 (23.7)	20/59 (33.9)	0.28
Cardioembolic [b]	8/38 (21.1)	14/59 (23.7)	0.76
ESUS [b]	5/38 (13.2)	8/59 (13.6)	0.95
Other [b]	5/38 (13.2)	2/59 (3.4)	0.07

[a] Mean ± SD

[b] *n* (%)

Table 3 Imaging findings and outcomes

Imaging	TNK (*n* = 39)	rt-PA (*n* = 62)	*P*-value
PCT [b]	38/39 (97.4)	61/62 (98.4)	0.07
MRI [b]	3/39 (7.7)	3/62 (4.8)	0.55
Infarct demarcation [b]	2/39 (5.1)	3/61 (4.9)	0.96
Perfusion delay/DWI [b]	21/38 (55.3)	36/53 (67.9)	0.22
Large vessel occlusion [b]	6/39 (15.4)	17/62 (27.4)	0.16
Distal VO [b]	7/39 (17.9)	9/62 (14.5)	0.65
EVT [b]	9 (23.1)	22 (36.7)	0.15
Successful recanalization [b]	9/9 (100)	21/22 (95.5)	0.52
Stent placement [b]	1/38 (2.6)	7/59 (11.9)	0.11
Intra-arterial thrombolysis [b]	3/9 (33.3)	9/22 (40.9)	0.69
Hemorrhage [b]	4/36 (11.1)	6/58 (10.3)	0.91
Heidelberg Bleeding Classification			
HI1 [b]	0 (0.0)	3 (4.8)	0.830
HI2 [b]	1 (2.6)	0 (0.0)	
PH1 [b]	3 (7.7)	2 (3.2)	
PH2 [b]	0 (0.0)	1 (1.6)	
IVH [b]	2 (5.1)	1 (1.6)	0.316
SAH [b]	1 (2.6)	6 (9.7)	0.174
Outcome			
NIHSS at discharge [a]	3.8 ± 7.8 (*n* = 33)	2.2 ± 4.5 (*n* = 54)	0.17
mRS at discharge [a]	2.3 ± 1.8 (*n* = 34)	2.0 ± 1.9 (*n* = 54)	0.39
PEG placement [b]	0/38 (0)	2/59 (3.4)	0.25
Death [b]	3/39 (7.7)	4/63 (6.3)	0.86

Successful recanalization is defined as TICI 2b-3

[a] Mean ± SD

[b] *n* (%)

Secondary and safety outcomes

Secondary and safety outcomes were broadly similar between groups (Table 3). NIHSS at 24 h did not differ (TNK 10.5 ± 13.5 vs. Alteplase 9.7 ± 13.2; $p = 0.74$), and mean NIHSS at discharge was 3.8 ± 7.8 vs. 2.2 ± 4.5 ($p = 0.17$). Discharge mRS distributions were comparable (shown in Fig. 2): favorable outcome (mRS 0–2) in 59% (20/34) with TNK and 64% (38/59) with Alteplase; excellent outcome (mRS 0–1) in 38% (13/34) vs. 48% (28/59); and severe disability or death (mRS 5–6) in 18% (6/34) vs. 14% (8/59).

Safety endpoints showed no meaningful differences. Any intracranial hemorrhage occurred in 11.1% vs. 10.3% ($p = 0.91$), and infarct demarcation on follow-up imaging in 44.7% vs. 42.9% ($p = 0.862$). Regarding hemorrhagic complications assessed by the Heidelberg Bleeding Classification, relevant bleeding subtypes occurred in both groups, albeit at low frequency and the distribution of haemorrhagic complications did not differ significantly between the two groups. Haemorrhagic infarction type 1 (HI1) occurred in no patients (0.0%) in group A (TNK) and in 3 patients (4.8%) in group B (rt-PA) ($p = 0.830$).

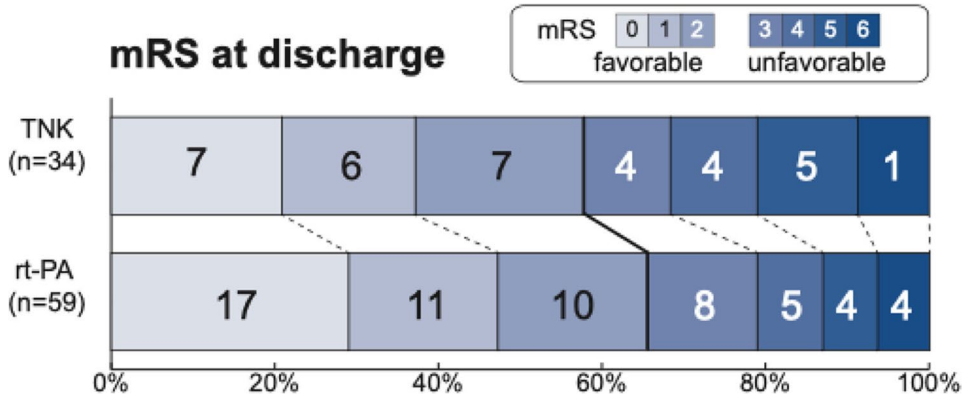


Fig. 2 Distribution of modified Rankin Scale (mRS) scores at discharge in patients treated with Tenecteplase (TNK) versus Alteplase (rt-PA). Stacked bar charts display the proportion of patients across the full mRS range (0–6) at hospital discharge. Favorable outcome was defined as mRS 0–2, unfavorable outcome as mRS 3–6. Numbers within the bars indicate absolute patient counts for each mRS category. TNK group: $n = 34$; rt-PA group: $n = 59$

Haemorrhagic infarction type 2 (HI2) was observed in 1 patient (2.6%) in the TNK group and in none of the patients in the alteplase group. Parenchymal hematoma type 1 (PH1) was documented in 3 patients (7.7%) in the TNK group and 2 patients (3.2%) in the Alteplase group, whereas parenchymal hematoma type 2 (PH2) occurred in none of the patients in the TNK group and in 1 patient (1.6%) in the Alteplase group. Intraventricular haemorrhage (IVH) was seen in 2 patients (5.1%) treated with TNK and in 1 patient (1.6%) treated with Alteplase ($p = 0.316$). Subarachnoid haemorrhage (SAH) was observed in 1 patient (2.6%) in the TNK group compared with 6 patients (9.7%) in the Alteplase group ($p = 0.174$). Overall, there was no statistically significant difference between groups in the occurrence of bleeding patterns, indicating a comparable hemorrhagic risk profile. Among patients who underwent EVT, successful reperfusion (mTICI ≥ 2b) was achieved in 100% with TNK and 95.5% with Alteplase ($p = 0.52$). In-hospital mortality was 7.7% (3 patients) vs. 6.3% (4 patients) ($p = 0.86$). Rates of PEG placement and other complications were low in both groups.

Given the limited sample size and event rates, the absence of statistically significant differences should be interpreted with caution and does not imply equivalence or non-inferiority between TNK and Alteplase.

Discussion

This single-center retrospective analysis provides exploratory real-world insights into the early implementation phase of TNK for acute ischemic stroke. While clinical and radiological outcomes appeared broadly comparable between TNK and Alteplase, the study was not powered to detect small-to-moderate differences, and the absence of statistically significant findings should not be interpreted as evidence of equivalence or non-inferiority.

In our TOAST-based aetiological classification, the distribution of major stroke subtypes was similar in the TNK and rt-PA groups in this cohort. However, given the small sample size and exploratory nature of this retrospective analysis, these comparisons are underpowered and should not be interpreted as evidence of equivalence between the two groups. Overall, we did not identify a strong indication that differences in aetiological composition alone could explain the observed clinical or radiological patterns, but residual confounding factors and misclassification remain possible. Taken together, our findings suggest that TNK was used to treat a variety of ischaemic stroke etiologies in routine care, which is consistent with previous reports evaluating TNK in diverse stroke patient groups [15, 16].

No statistically significant differences were observed between TNK and alteplase in terms of angiographic reperfusion (mTICI among EVT patients), early neurological improvement (24-hour NIHSS) or functional status at discharge (mRS). In this exploratory real-world analysis, therefore, outcome patterns and point estimates were broadly similar between groups. This provides descriptive data on TNK use at contemporary dosing in routine practice, contextualising our findings within the existing randomised and observational literature [17, 18]. Hemorrhagic complications were uncommon in both treatment groups and were within the range reported in prior randomised trials and real-world cohorts [19, 20].

Importantly, treatment allocation coincided with a mid-study protocol change, which introduced potential confounding factors related to calendar time as well as workflow. Early implementation phases are typically characterized by learning curve dynamics, staff adaptation and, in some settings, the temporary parallel use of legacy and newly introduced agents. In this context, observed differences (or the absence of differences) may reflect system-level factors as well as pharmacological properties .

In our cohort, the door-to-needle time (DTN) was longer for the TNK group than for the alteplase group (42.8

± 27.1 vs. 37.5 ± 20.9 min), though this difference was not statistically significant (p = 0.62). Given the pre/post nature of treatment allocation and the early implementation phase at our centre, this pattern may reflect workflow-related factors during the transition. These factors may be more responsible for the difference in DTN than an inherent disadvantage of TNK. Several prior studies have reported shorter DTN with TNK, attributing this to bolus administration and the elimination of infusion-related steps. Our findings emphasise that such potential operational advantages may not be realized immediately during the early implementation phase [21].

Several operational barriers may have contributed to the observed patterns, particularly during the initial implementation period. These include an increased cognitive load during the transition to the new protocol, initial unfamiliarity with TNK preparation and dose verification, the need for additional safety steps (e.g. dosing aids and double-check processes) and the fact that alteplase and TNK workflows were available in parallel. Furthermore, the lack of a unified, fully integrated electronic order set at the beginning of the transition may have reduced the potential operational benefits of TNK.

To facilitate smoother transitions, several practical measures can be considered. These include structured multidisciplinary training prior to protocol change, standardized dosing aids, unified electronic order sets, simulation-based workflow rehearsals, and regular interdisciplinary feedback meetings during the early transition period. Such measures are generally low-cost, scalable, and potentially applicable across different healthcare systems.

Imbalances in baseline characteristics such as a higher prevalence of diabetes in the TNK group (reflecting differences in comorbidity burden/ vascular risk profile), and higher LVO rates in the Alteplase group (reflecting differences in stroke severity), may have contributed to the observed patterns of outcomes. These differences further emphasise the exploratory nature of our findings and restrict the scope for causal interpretation.

From an operational perspective, our experience of transitions suggests that implantation measures can be feasible in different settings. However, broader generalisability should be interpreted cautiously.

Finally, the nearly universal use of multimodal CT with perfusion imaging at our center reflects local workflow and resource availability. While this approach enables comprehensive tissue-based decision-making, it may limit generalizability to centers employing more selective imaging strategies.

This study has several limitations. First, the retrospective and single-center design limits causal inference and generalizability. Second, the sample size was relatively small, resulting in limited statistical power and wide confidence intervals for several outcomes. Third, functional outcome was assessed at hospital discharge only; standardized 90-day modified Rankin Scale data were not available due to the lack of routine long-term follow-up in this retrospective cohort, limiting comparability with randomized controlled trials. Fourth, treatment allocation coincided with a protocol change, introducing potential temporal and workflow-related confounding. Furthermore, the potential effect of modifying the analysis according to LVO status and treatment window could not be formally evaluated due to the small size of the subgroups and the low number of events, which would have made the stratified estimates and interaction models statistically unstable. Finally, the high rate of baseline perfusion imaging may limit generalizability to centers using more selective imaging strategies, as differences in imaging triage can influence patient selection and workflow times.

Despite these limitations, our real-world data support the continued evaluation of TNK as a viable alternative to Alteplase in acute ischemic stroke management. Further large-scale, prospective studies are needed to confirm these findings and define patient subgroups who may particularly benefit from TNK.

Conclusions

In this exploratory real-world cohort, TNK and Alteplase showed broadly comparable clinical and safety profiles during the early implementation phase of TNK introduction. Given the limited sample size and observational design, these findings should be interpreted as hypothesis-generating. Our results highlight the importance of structured implementation strategies and underscore the need for larger, prospective studies to evaluate long-term outcomes and minimize transition-related confounding.

Abbreviations

AIS	Acute ischemic stroke
CT	Computed tomography
DOAC	Direct oral anticoagulants
DTN	Door-to-needle time
DTG	Door-to-groin time
EVT	Endovascular treatment
ICH	Intracranial hemorrhage
INR	International normalized ratio
IQR	Interquartile range
IVT	Intravenous thrombolysis
LVO	Large vessel occlusion
MRI	Magnetic resonance imaging
mRS	Modified Rankin Scale
NIHSS	National Institutes of Health Stroke Scale
rt-PA	recombinant tissue plasminogen activator or Alteplase
TICI	Thrombolysis in Cerebral Infarction
TNK	Tenecteplase

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Authors' contributions
OAO conceived the research idea, analyzed the data, prepared and reviewed the first draft and final version of manuscript. TM and FC collected and analyzed the data as well as prepared, edited and reviewed the first draft. MS, PB, SH, SG, TB, MV, MJ und HK provided equally data, reviewed results, and provided guidance on data analysis and approved the final version of the manuscript.

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Data availability
The datasets used and/or analysis during the current study are available from the corresponding author on reasonable request.

Declarations

Ethics approval and consent to participate
The study was conducted in accordance with the Declaration of Helsinki and approved by the local institutional review board of the Department of Medicine at Justus Liebig University in Giessen, Germany (approval number: AZ220/21; clinicaltrials.gov: NCT05295862). Ethic approval date 22 January 2025. Patient consent was waived by the local institutional review board of the Department of Medicine at Justus Liebig University in Giessen, Germany.

Consent for publication
Not applicable.

Competing interests
The authors declare no competing interests.

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