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# Pharmacology of alteplase VS tenecteplase in acute ischemic stroke

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**ABSTRACT**

Administration of rtPA thrombolysis intravenously (IV) as the management of acute ischemic stroke currently shows satisfactory results in overcoming ischemic stroke attacks which can reduce morbidity and mortality. This study aims to analyze the comparison of alteplase vs tenecteplase therapy in patients with acute ischemic stroke in terms of the benefits, safety and risks of both drugs. Article searches were conducted through Google Scholar and Research Gate using the keywords Pharmacology Tenecteplase and Alteplase in Acute Ischemic Stroke, then a total of 25 articles that met the inclusion criteria were reviewed. The results showed that tenecteplase had a fibrin specificity 14 times greater than alteplase, a longer half-life, slower plasma clearance, and 80-fold greater resistance to type 1 plasminogen activator inhibitor (PAI-1). Its half-life of about 18 minutes allows rapid administration of a single bolus. The efficacy in acute ischemic stroke was shown to be significantly higher than tenecteplase with significant initial neurologic improvement. Regarding the safety assessment, there was no difference related to all levels of symptomatic intracerebral hemorrhage, both tenecteplase and alteplase.



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# INTRODUCTION

Thrombolysis is still the recognized reperfusion therapy in acute stroke. Until now, the use of recombinant tissue plasminogen activator (rt-PA) has been recognized in various parts of the world as a thrombolytic therapy agent in acute stroke with various limitations (Yu et al, 2022; Akbik, 2020) . Alteplase intravenous infusion is the only definitive pharmacological therapy recommended by the latest guidelines (guidelines AHA/ASA, ESO, NICE and PERDOSSI) for thrombolysis in ischemic stroke at a dose of 0.9 mg/kgBW which must be given in less than 4, 5 hours from stroke onset. These recommendations were given after going through various large studies, especially the NINDS TPA II Trial 1995 and ECASS 3 Trial 2008 (Muresanu, Strilciuc, & Stan, 2019; Anderson, 2019) . Alteplase is a human tissue plasminogen activator and is produced by deoxyribonucleic acid (DNA) engineering techniques. Alteplase is an engineered unmodified human tissue plasminogen activator. This drug works more selectively to activate fibrin-binding

plasminogen than free plasminogen in the blood. Thus rt-PA works more selectively against blood clots/fibrin (Bagoly et al, 2019; Nandi, 2020) .

The use of alteplase still has some limitations, namely in the period of administration. In June 2012 a large rt-PA study was published, namely the International Stroke Trial-3 (IST-3) with an extension of administration up to a period of 6 hours after stroke onset, the result was that the incidence of bleeding and death within 7 days was greater in the group given rtPA . Saver et al showed cohort data from 100,000 stroke patients, 400% of whom came to the hospital emergency department for more than 3 hours. Data in Indonesia, Salim et al examined the onset of stroke patients in 5 DKI Jakarta government hospitals which showed above 75% of 110 stroke patients who came to the hospital with conditions more than 3 hours from onset (Ma et al, 2022; Kvistad et al, 2022) . Further research is needed to find a thrombolytic agent to increase efficacy and extend the time period for administration. Tenekteplase seems to be a promising alternative today compared to alteplase. Currently, tenecteplase is approved for the treatment of ST elevation acute myocardial infarction (Putaala, 2021) . Tenekplase is a genetically engineered form of alteplase, is more specific for fibrin, has a longer half-life than alteplase, and is thought to improve vascular reperfusion ability in acute ischemic stroke (Bambari, Panda, & Joseph, 2021; Coutts, 2018) .

Based on the background and several previous studies that have been described by the authors, the authors are interested in studying the Pharmacology of Alteplase VS Tenecteplase in Acute Ischemic Stroke. Several previous studies only explained in detail the pharmacological management of acute ischemic stroke. This study further compares the Pharmacology of alteplase with tenecteplase in acute ischemic stroke. This study aims to compare the pharmacology of alteplase and tenecteplase in acute ischemic stroke. The results of this study are expected to be able to provide insight and additional knowledge to all interested parties regarding the pharmacological comparison of Alteplase and Tenecteplase in Acute Ischemic Stroke.

# RESEARCH METHOD

This research is a literature study by seeking and collecting theoretical and methodological references that are relevant to a topic related to the research question about alteplase vs tenecteplase pharmacology in acute ischemic stroke. Literature studies are journals, books, and other documents that describe theory as well as information both past and present organizes the literature into the topics and documents needed (Aspers & Corte, 2019) . The data used and used in this library research are secondary data, namely data obtained from the results of research that has been carried out by previous researchers. Secondary data sources in this literature study are original articles from published research journals related to the pharmacology of alteplase vs tenecteplase in acute ischemic stroke. This literature review uses journals that have been published in the 2012-2022 range which use English, the type of original research article (original article), and is available in full-text (full text) pdf format with the journal theme on alteplase pharmacology vs tenecteplase in acute ischemic stroke.

A total of 1,640 of the journals found according to these keywords were subjected to rapid screening, 1,548 journals were excluded because they did not match the theme based on the research title. An in-depth assessment and feasibility assessment was carried out on 92 full-text available journals. Journals that did not meet the inclusion criteria and were duplicated were carried out in 67 journals, so that 25 full-text journals were obtained which were the most relevant for review. In writing a review using the Systematic Literature Review (SLR) method, any data found during the search will be evaluated based on questions that are in accordance with the Quality Assessment. In-depth analysis of journals or research literature is carried out by reading the abstract and full-text of the journal carefully, then making a summary to be analyzed according to the contents written in the research objectives.

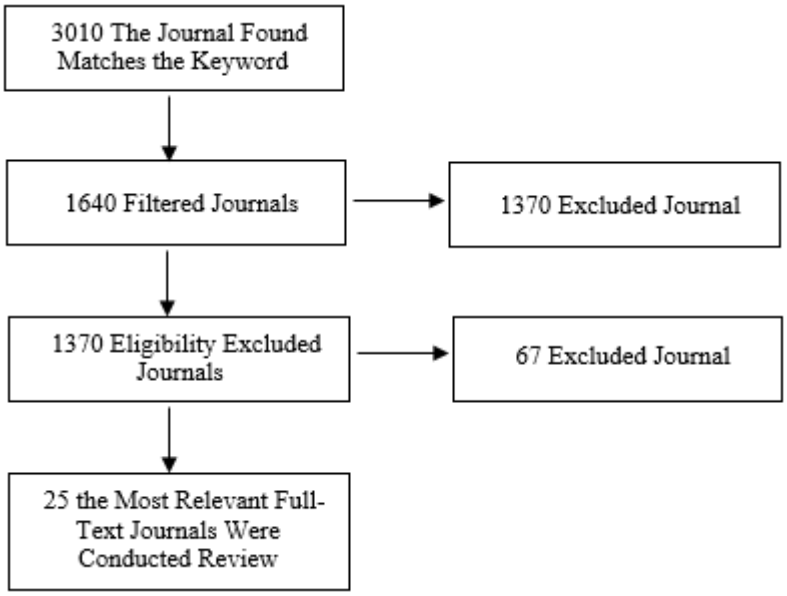


**Figure 1.** Journal Review Flowchart

# RESULTS AND DISCUSSIONS

**Results**

Based on the results of a literature study on the Pharmacology of Alteplase VS Tenekteplase in Acute Ischemic Stroke conducted by the author, the following results were obtained:

**Table 1.** Pharmacokinetic parameters of tenecteplase compared to alteplase (Transwell & Modi, 2002)

| Dosage (mg) and regimen | n | CL(ml/min) | C max (µg/ml) | V1 ( L) | V.s.s. ( L) | Initial t 1/2 (min) | Terminal t 1/2 (min) | Initial AUC (%) |
|---|---|---|---|---|---|---|---|---|
| Tenecteplase bolus, phase I (TIMI 10A) | | | | | | | | |
| 5 | 5 | 216±98 | 0.70 ± 0.39 | 8.4 ± 6.3 | 10±5.3 | 11±5.2 | 41±16 | 31±22 |
| 7.5 | 5 | 168±66 | 1.0 ± 0.07 | 5.8 ± 1.8 | 8.4 ± 2.8 | 16±8.5 | 96±73 | 58±16 |
| 10 | 5 | 185±35 | 1.5 ± 0.30 | 6.4 ± 1.1 | 11±5.5 | 15±8.1 | 121 ± 100 | 57±14 |
| 15 | 6 | 182±76 | 2.7 ± 1.2 | 6.7 ± 3.3 | 9.6 ± 3.7 | 11±7.9 | 54±13 | 42±30 |
| 20 | 7 | 169±63 | 2.8 ± 6.5 | 7.6 ± 2.7 | 15±7.3 | 18±6.8 | 138±84 | 56±25 |
| 30 | 26 | 143±45 | 5.9 ± 3.0 | 6.3 ± 4.0 | 9.9 ± 6.0 | 18±7.7 | 132 ± 140 | 64±20 |
| 40 | 18 | 130±41 | 9.5 ± 3.4 | 4.3 ± 1.9 | 6.3 ± 1.8 | 17±5.6 | 88±45 | 69±15 |
| 50 | 7 | 125±25 | 8.8 ± 1.4 | 5.7 ± 1.4 | 6.7 ± 1.3 | 20±5.5 | 65±25 | 55±29 |
| Tenecteplase bolus, phase II (TIMI 10B) | | | | | | | | |
| 30 | 48 | 98.5 ± 42 | 7.5 ± 5.2 | 4.2 ± 2.6 | 6.3 ± 3.3 | 22±8.2 | 116±63 | 72±22 |
| 40 | 31 | 119±49 | 9.5 ± 8.1 | 5.4 ± 2.7 | 8.0 ± 5.9 | 24±5.5 | 129±87 | 75±16 |
| 50 | 20 | 99.9 ± 32 | 11.6 ± 4.4 | 4.7 ± 2.6 | 6.1 ± 2.4 | 20±10 | 90.4 ± 35 | 66±29 |
| Alteplase infusion over 90 minutes | | | | | | | | |
| 100 (phase II, TIMI 10B [7] ) | 53 | 453 ± 170 | 4.3 ± 3.4 | 7.2 ± 4.1 | 28.9 ± 22 | | 144 ± 100 | |
| 100 (earlier data, TAPS [1] ) | 10 | 572 ± 130 | 4.0 ± 1.0 | 3.4 ± 1.5 | 8.4 ± 5.0 | 3.5 ± 1.4 | 72 ± 68 | 85±15 |

*Source: Transwell & Modi Research Results (2002)*

Initial t1/2 alteplase was not sampled, pharmacokinetic data came from non-compartmental analysis.

AUC = area under the concentration-time curve ; CL = total body clearance ; Cmax = peak plasma concentration ; n = number of patients ; TAPS = rt-PA-APSAC Patency Study ; TIMI = Thrombolysis in Myocardial Infarction ; $t_{1/2}$ = half-life; $V_{ss}$ = volume of distribution at steady state ; $V_1$ = initial volume of distribution.

**Table 2.** Comparison of alteplase and tenecteplase properties research (Behrouz, 2013)

| Agents | Fibrin specificity | Thrombolytic potential | PAI-1 resistance | Fibrinogen depletion | PRT activity | Clearance (mL/kg/min) |
|---|---|---|---|---|---|---|
| Landfill | ++ | + | - | ++ | ++ | 16.1 |
| KNP | +++ | +++ | ++ | + | +++ | 1.9 |

*PAI-1 plasminogen activator inhibitor type 1 , PRT platelet-rich thrombus*

*Source: Behrouz Research Results (2013)*

**Table 3.** Results of research on alteplase with tenekteplase phase 2B research by Haley, Thompson, et al (2015)

| | KNP 0.1mg/kg (N=31) | KNP 0.25mg/kg (N=31) | KNP 0.4mg/kg (N=19) | rtPA 0.9mg/kg N=31) |
|---|---|---|---|---|
| Rankin good, no. (%, 95% CI) | 14 (45.2%, 27.3– 64.0) | 15 (48.4%, 30.2– 66.9) | 7 (36.8%, 16.3– 61.6) | 13 (41.9%, 24.6 – 60.9) |
| Rankin poor, no. (%, 95% CI) | 7 (22.6%, 9.6–41.1) | 11 (35.5%, 19.2–54.6) | 6 (31.6%, 12.6–56.6) | 10 (32.3%, 16.7–51.4) |
| MNI, no. (%, 95% CI) | 7 (22.6%, 9.6–41.1) | 11 (35.5%, 19.2–54.6) | 4 (21.1%, 6.1–45.6) | 5 (16.1%, 5.5–33.7) |

*Source: Behrouz Research Results (2013)*

**Table 4.** Results of alteplase research with tenekteplase phase 2B Haley, Thompson, et al (2015)

| | KNP 0.1mg/kg (N=31) | KNP 0.25mg/kg (N=31) | KNP 0.4mg/kg (N=19) | rtPA 0.9mg/kg N=31) |
|---|---|---|---|---|
| Symptomatic ICH, no. (%, 95% CI) | 0 (0%, 0 –11.2) | 2* (6.5%, 0.8 –21.4) | 3 (15.8%, 3.4 –39.6) | 1 (3.2%, 0.1–16.7) |
| Asymptomatic ICH, no. (%, 95% CI) | 3 (9.7%, 2.0–25.8) | 2 (6.5%, 0.8–21.4) | 2 (10.5%, 1.3–33.1) | 4 (12.9%, 3.6–29.8) |
| All ICH, no. (%, 95% CI) | (9.7%, 2.0–25.8) | 4 (12.9%, 3.6–29.8) | 5 (26.3%, 9.2–51.2) | 5 (16.1%, 5.5–33.7) |
| Major systemic bleeding, no. (%, 95% CI) | 0 (0%, 0–11.2) | 1 (3.2%, 0.1–16.7) | 0 (0%, 0–17.6) | 0 (0%, 0–11.2) |
| Death within 3 months, all causes, no. (%, 95% CI) | 2 (6.5%, 0.8–21.4) | 7 (22.6%, 9.6–41.1) | 3 (15.8%, 3.4–39.6) | 8 (25.8%, 11.9–44.6) |

*Source: Thompson et al Research Results (2015)*

*NB: None of these 2 ICHs is depicted in the figure as a "0" score because 1 also had an MNI and the second was reassessed from asymptomatic to symptomatic by independent assessment after sequential scores were recorded per protocol.

**Table 5.** Results of alteplase research with tenekteplase phase 2B research by (Thompson et al, 2015) .

| Outcomes | Tenecteplase Group (N=101) | Alteplase Group (N=101) | Effect Size (95% CI) | P Value |
|---|---|---|---|---|
| Primary efficacy outcomes | | | | |
| Substantial reperfusion at initial angiographic assessment — no. (%)* | 22 (22) | 10 (10) | | |
| Difference – percentage points | | | 212 (2-21) | 0.002 |
| Adjusted incidence ratio | | | 2.2 (1.1–4.4) | 0.03 |
| Adjusted odds ratio | | | 2.6 (1.1-5.9) | 0.02 |
| Secondary outcomes | | | | |

| | | | | |
|---|---|---|---|---|
| Score on the modified Rankin scale at 90 days† | | | | |
| Median score (IQR) on ordinal analysis‡ | 2 (0–3) | 3 (1–4) | 1.7 (1.0–2.8) | 0.04 |
| Functionally independent outcome -no. (%)§ | 65 (64) | 52 (51) | | |
| Adjusted incidence ratio | | | 1.2 (1.0–1.5) | 0.06 |
| Adjusted odds ratio | | | 1.8 (1.0-3.4) | 0.06 |
| Excellent outcome — no. (%)§ | 52 (51) | 43 (43) | | |
| Adjusted incidence ratio | | | 1.2 (0.9-1.6) | 0.20 |
| Adjusted odds ratio | | | 1.1 (o.6-2.1) | 0.70 |
| Safety outcomes | | | | |
| Death – no.(%) § | 10 (10) | 18 (18) | | |
| Adjusted risk ratio | | | | |
| Adjusted odds ratio | | | 0.4 (0.2-1.1) | 0.08 |
| Symptomatic intracerebral hemorrhage — no. (%)§ | 1 (1) | 1 (1) | | |
| Risk ratio | | | 1.0 (0.1-15.9) | 0.99 |
| Odds ratio | | | 1.0 (0.1–16.2) | 0.99 |
| Parenchyma hematoma – no. (%)§** | 6 (6) | 5 (5) | | |
| Risk ratio | | | 1.2 (0.4–3.8) | 0.76 |
| Odds ratio | | | 1.2 (0.4–4.1) | 0.76 |

*Source: Thompson et al Research Results (2015)*

The plus–minus value means ±SD. Lesion volume rounded to the nearest milliliter. Two patients did not undergo MRI within 24 hours because of clinical interference (one in the low-dose tenecteplase group and one in the alteplase group) and were not included in the analysis of primary reperfusion outcome (or other imaging-based efficacy outcomes). Five patients died before day 90 and were excluded from the analysis of infarct progression by day 90. Five patients were excluded from the analysis of recanalization results: two patients did not undergo MRI within 24 hours and three patients without initial occlusion.

The mean percentage of reperfusion remained significant (P = 0.003) after adjustment for status for the baseline variables related to diabetes and smoking, blood glucose levels, and time of treatment.

‡ The change in mean NIHSS score at 24 hours remained significant (P = 0.001) after adjusting for initial status variables related to diabetes and smoking, blood glucose levels, and time of treatment.

§ This outcome was defined as a large parenchymal hematoma and clinical deterioration (increase in NIHSS score of 4 points or more).

¶ Recovery was assessed on a modified Rankin scale, ranging from 0 to 6, with higher scores indicating greater disability. Very good recovery is given a score of 0 or 1, very good or good recovery is given a score of 0 to 2, and a poor outcome is given a score of 5 or 6.

‖ Understandably inconsistent is defined as volume inconsistent on initial computed tomographic perfusion imaging that does not progress to infarction.

**Table 6.** Results of alteplase research with tenekteplase phase III research (Logallo, Assmus et al, 2017) .

| | Tenecteplase | Alteplase | Odds ratio (95% CI) | p-value |
|---|---|---|---|---|
| Intention-to-treat analysis | | | | |
| Primary outcome mRS score 0–1 at 3 months | 354/549 (64%) | 345/551 (63%) | 1·08 (0·84–1·38) | 0·52 |
| Secondary outcomes | | | | |
| Any ICH at 24–48 h* | 47/549 (9%) | 50/551 (9%) | 0·94 (0·60–1·45) | 0·82† |
| Symptomatic ICH at 24–48 h‡ | 15/549 (3%) | 13/551 (2%) | 1·16 (0·51–2·68) | 0·70† |
| Major clinical | 229/549 (42%) | 214/551 (39%) | 1·12 (0·89–1·43) | 0·97 |

| | | | | |
|---|---|---|---|---|
| improvement at 24 h§ | | | | |
| Ordinal shift analysis of mRS at 3 months | NA/549 | NA/551 | 1·12 (0·91–1·39) | 0·28 |
| Death within 3 months | 29/549 (5%) | 26/551 (5%) | 1·12 (0·63–2·02) | 0·68† |
| Per-protocol analysis | | | | |
| mRS score 0–1 at 3 months | 244/382 (64%) | 250/391 (64%) | 0·99 (0·74–1·33) | 0·98 |
| Secondary outcomes | | | | |
| Any ICH at 24–48 h* | 40/389 (10%) | 39/400 (10%) | 1·06 (0·67–1·67) | 0·81† |
| Symptomatic ICH 24–48 h‡ | 11/389 (3%) | 8/400 (2%) | 1·42 (0·57– 3·58) | 0·49† |
| Major clinical improvement at 24 h§ | 140/381 (37%) | 140/392 (36%) | 1·04 (0·78–1·40) | 0·76 |
| Ordinal shift analysis of mRS at 3 months | NA/382 | NA/391 | 1·05 (0·82–1·36) | 0·66 |
| Death within 3 months | 20/382 (5%) | 16/391 (4%) | 1·29 (0·66–2·54) | 0·49† |

*Source: Logallo, Assmus et al Research Results (2017)*

Data n/N (%). ECASS = *European Cooperative Acute Stroke Study*. ICH = *intracranial haemorrhagic*. mRS = *modified Rankin Scale*. NA = not applicable. NIHSS = *National Institutes of Health Stroke Scale*. NIHSS = *National Institutes of Health Stroke Scale*. *Any intracranial hemorrhage was defined as hemorrhagic transformation or parenchymal hematoma based on ECASS I criteria. Fisher's exact test. # Symptomatic intracranial hemorrhage defined according to ECASS III criteria. SNIHSS score of 0 or an increase of at least 4 points compared to the baseline.

**Discussions**

The study by Haley et al in this phase 2B/III trial, randomized, compared tenecteplase 0.1, 0.25, and 0.4 mg/kg with alteplase 0.9 mg/kg as standard in patients with acute symptom-onset stroke. 3 hours showed that tenecteplase had the best effectiveness compared to alteplase. Then the study was continued for up to 100 pairs of doses of tenecteplase compared with alteplase for up to 3 months using a modified Rankin Scale Analysis, performed on 112 patients. The tenecteplase dose of 0.4 mg/kg was excluded due to the initial release from the "inferior" tenecteplase dose. Randomization was continued to tenecteplase 0.1 mg/kg tenecteplase, 0.25 mg/kg tenecteplase, and 0.9 mg/kg alteplase. The 0.1 mg/kg tenecteplast group had the lowest proportion output (7 of 31 [22.6%]), while the alteplase group had the second lowest output of 10 of 31 (32.3%). In terms of good outcome, the 0.25 mg/kg tenecteplase group had the highest proportion (15 out of 31 [48.4%]), however the 0.1 mg/kg tenecteplase group also gave the same results (14 out of 31 [45, 2] There were 6 total intracranial bleeding symptoms: 3 of 19 (15.8%) in the 0.4-mg/kg tenecteplase group, 2 of 31 (6.5%) in the 0.25-mg/kg tenecteplase group, and none (0 of 31) in the 0.1 mg/kg tenecteplase group.In comparison, there was 1 of 31 (3.2%) symptomatic intracranial hemorrhage in the alteplase group.In addition, there were 11 asymptomatic intracranial hemorrhages among the 4 groups. There was 1 serious systemic hemorrhage in the 0.25-mg/kg tenecteplase group (retroperitoneal hemorrhage) resulting in life-threatening hypotension that worsened neurological (Haley et al, 2015; Yamamoto, Hattammaru, & Uezono, 2020; Moncharmont, Barday, & Benamara, 2020) .

Research by (Ratziu et al, 2021) in this phase 2B trial, was conducted randomly on 75 patients who received alteplase (0.9 mg per kilogram of body weight) or tenecteplase (0.1 mg per kilogram or 0.25 mg per kilogram of body weight) to ischemic stroke onset less than 6 hours, using the eligibility criteria of a perfusion lesion at least 20% larger than the infarct core on baseline perfusion tomography (CT) imaging and associated vessel occlusion on CT angiography; The best efficacy was tenecteplase (Table 6), with greater reperfusion (P = 0.004) and greater clinical improvement (P < 0.001) within 24 hours in the tenecteplase group than in the alteplase group.

There were no significant differences between groups for intracranial bleeding or more serious side effects.

Research by (Haley et al, 2015) in a phase IIb/III clinical trial related to tenecteplase therapy in treating acute ischemic stroke stated that the highest dose of tenecteplase (0.25 mg per kilogram) was superior to its lower dose and for alteplase for all efficacy outcomes, including the absence of serious disability within 90 days (in 72% of patients, compared to 40% with alteplase; P = 0.02).

Research by (Berge et al, 2021) tested venous blood samples from subgroups of participants in the Alteplase–Tenecteplase Trial Evaluation for Stroke Thrombolysis (ATTEST) study obtained pre, 3 to 12 hours, and 24 ± 3 hours post-intravenous thrombolysis for analysis of plasminogen, inhibitor activator plasminogen-1, d-dimer, factor V, fibrinogen, and fibrin (ogen) degradation products, in addition to routine coagulation tests. In 30 patients included (alteplase = 14 and tenecteplase = 16) with similar basic demographics, alteplase caused significant hypofibrinogenemia (P = 0.002), prothrombin time prolongation (P = 0.011), hypoplasminogenaemia (P = 0.001), and higher factor V. was low (P = 0.002) within 3 to 12 hours after administration with persistent hypofibrinogenaemia within 24 hours (P = 0.011), whereas the tenecteplase group had only mild hypoplasminogenaemia (P = 0.029). Tenecteplase consumed less plasminogen (P < 0.001) and fibrinogen (P = 0.002) than alteplase. In patients with acute ischemic stroke, alteplase 0.9 mg/kg caused significant disturbance of the fibrinolytic system, whereas tenecteplase 0.25 mg/kg did not, and the occurrence of intracerebral hemorrhage was lower with tenecteplase in the ATTEST study (Berge et al, 2021; Olindo, 2022) .

Research by (Logallo et al, 2017) in a phase III trial conducted in 13 stroke units in Norway, with the inclusion criteria of adult patients suspected of acute ischemic stroke who are eligible for thrombolysis with an onset of symptoms 4.5 hours or within 4.5 hours of symptom onset, or who are eligible for bridging therapy before thrombectomy. Patients were randomized (1:1) to receive intravenous tenecteplase 0.4 mg/kg (up to a maximum of 40 mg) or alteplase 0.9 mg/kg (up to a maximum of 90 mg. The main outcome was excellent functional outcome based on a modified Rankin Scale (mRS) score 0–1 at 3 months.There were 1107 patients who met the inclusion criteria and seven patients were excluded because informed consent was withdrawn or consideration of the appropriateness of thrombolytic use.1100 patients were randomly assigned to the tenecteplase group (n = 549) and alteplase (n = 551).The participants' mean age was 77 years (IQR 64–79) and the National Institutes of Health Stroke Scale score was 4 points (IQR 2–8).A final diagnosis other than ischemic stroke or transient ischemic attack was found in 99 (18%) patients in the tenecteplase group and 91 (17%) patients in the alteplase group Primary outcome was achieved by the tenecteplase group 354 (64%) patients and 345 (63%) patients in the alteplase group (odds ratio 1.08, 95) % CI 0.84-1.38; p = 0.52 ). Within 3 months, 29 (5%) patients died in the tenecteplast group compared to 26 (5%) patients in the alteplase group. The frequency of serious adverse events was the same between each group (145 [26%] in the tenecteplase group, and 141 [26%] in the alteplase group; p = 0.74). In this phase III trial, tenecteplase was not superior to alteplase and showed the same safety profile. Most of the patients enrolled in this study had mild strokes (Logallo et al, 2017; Amarenco et al, 2018; Khatri et al, 2018) .

A meta-analysis by (Thelengana et al, 2018) comparing efficacy and safety in patients with acute ischemic stroke, the efficacy outcome assessment was based on parameters: immediate major neurological improvement, excellent functional outcome in 90 days, and good functional outcome in 90 days ; showed that the tenecteplase group had major favorable immediate neurologic improvement (RR = 1.56, 95% CI [1.00, 2.43], p = 0.05).

A meta-analysis by Na Xu et al, of a randomized controlled trial of tenecteplase versus alteplase as a thrombolytic in acute obstructive stroke, showed that there was initial neurologic improvement at 24 hours and functional outcome at 3 months on tenecteplase. Administration of tenecteplase showed significant (P = 0.035) initial neurological improvement compared to alteplase. In addition, tenecteplase showed neutral effect (P = 0.309), good functional outcome (P =

0.275), and tissue reperfusion (P = 0.3). There is no significant difference in the safety of using the two drugs. In subgroup analyses, tenecteplase dose of 0.25 mg/kg showed significant improvement in initial neurologic improvement (P < 0.001). These results are similar to the meta-analysis conducted by (Thelengana et al, 2018; Xu, et al 2018; Klok et al, 2023; Psychogios, 2021) .

# CONCLUSION

Based on the results and discussion of the Pharmacology of Alteplase VS Tenecteplase in Acute Ischemic Stroke which has been described by the authors above, the authors can draw the following conclusions, namely 1) Research from several studies shows tenecteplase has a specificity of fibrin 14 times greater than alteplase, has a longer half-life, plasma clearance is slower, and resistance is 80-fold greater to plasminogen activator inhibitor type 1 (PAI-1). Its half-life of approximately 18 minutes allows rapid single bolus administration, 2) From several studies, comparing the efficacy in acute ischemic stroke between tenecteplase and alteplase it appears that tenecteplase is more significant in terms of significant early neurological improvement, and 3) In terms of safety assessment, tenecteplase compared to alteplase shows there was no difference with regard to all grades of symptomatic intracerebral hemorrhage. In addition, based on the conclusions regarding the Pharmacology of Alteplase VS Tenecteplase in Acute Ischemic Stroke that has been described by the authors above, the authors' recommendation is that further data is needed, especially in the elderly with acute ischemic stroke to better understand the relationship between pharmacokinetic and pharmacodynamic effects related to the use of alteplase vs tenecteplase . The future research that can be done is "Comparison of the Effectiveness and Safety of Alteplase and Tenecteplase in the Treatment of Acute Ischemic Stroke: A Prospective, Randomized, Control Study".

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