Supplementary Table 1. Data sources

Center	Unmatched groups			PSM groups		
	TNK	rt-PA	Total	TNK	rt-PA	Total
Keshiketeng Banner Traditional Chinese Medicine Mongolian Medicine Hospitalorem Ipsum	489 (43.94%)	57 (2.42%)	546	489 (43.97%)	51 (4.58%)	540
Yantai Affliated Hospital of Binzhou Medical University	168 (15.09%)	188 (7.97%)	356	168 (15.09%)	77 (6.92%)	245
Nanshi Hospital of Nanyang	96 (8.63%)	479 (20.30%)	575	96 (8.63%)	288 (25.88%)	384
Shenyang Fifth People's Hospital	95 (8.54%)	0 (0%)	95	95 (8.54%)	0 (0%)	95
Fushun General Hospital of Mining Bureau	61 (5.48%)	9 (0.38%)	70	61 (5.48%)	3 (0.27%)	64
The First Affiliated Hospital of Ningbo University	31 (2.79%)	381 (16.14%)	412	31 (2.79%)	196 (17.61%)	227
Jilin Liuhe Hospital	34 (3.05%)	0 (0%)	34	34 (3.05%)	0 (0%)	34
SHANGHAI						
Huashan Hospital, Fudan University	5 (0.45%)	436 (18.47%)	441	5 (0.45%)	168 (15.09%)	173
Shanghai Pudong Gongli Hospital	33 (2.96%)	40 (1.69%)	73	33 (2.96%)	23 (2.07%)	56
Shanghai East Hospital (South Branch)	28 (2.52%)	77 (3.26%)	105	28 (2.52%)	34 (3.05%)	62
Shanghai East Hospital	24 (2.16%)	62 (2.63%)	86	24 (2.16%)	35 (3.05%)	59
Shanghai Putuo Liqun Hospital	18 (1.62%)	31 (1.31%)	49	18 (1.62%)	6 (0.54%)	24
Shanghai Fourth People's Hospital	10 (0.9%)	115 (4.87%)	125	10 (0.9%)	59 (5.3%)	69
Shanghai 10th People's Hospital	9 (0.81%)	456 (19.32%)	465	9 (0.9%)	159 (14.29%)	168
Ruijin Hospital Luwan Branch	9 (0.81%)	0 (0%)	9	9 (0.81%)	0 (0%)	9
Shanghai Ninth People's Hospital Huangpu Branch	2 (0.18%)	17 (0.72%)	19	2 (0.18%)	8 (0.72%)	10
Shanghai Deji Hospital	1 (0.09%)	9 (0.38%)	10	1 (0.09%)	3 (0.27%)	4
Shanghai Tianyou Hospital	0 (0%)	3 (0.13%)	3	0 (0%)	3 (0.27%)	3
Total	1113	2360	3473	1113	1113	2226

Supplementary Table 2. Details of missing values and imputation status

Characteristic	TNK (N=**1113**) Missing values, n (%)	Multiple imputation	rt-PA (N=**2360**) Missing values, n (%)	Multiple imputation
Demographics				
Age	3 (0.27%)	Yes	1 (0.042%)	Yes
Sex	0 (0.00%)	No	0 (0.00%)	No
Risk factors				
smoking	4 (0.36%)	Yes	56 (2.37%)	Yes
Medical history				
History of hypertension	0 (0.00%)	No	0 (0.00%)	No
History of diabetes	0 (0.00%)	No	2 (0.085%)	Yes
History of hyperlipidimia	0 (0.00%)	No	2 (0.085%)	Yes
History of atrial fibrillation	0 (0.00%)	No	5 (0.212%)	Yes
History of coronal heart disease	0 (0.00%)	No	93 (3.94%)	Yes
History of heart failure	0 (0.00%)	No	420 (17.80%)	Yes
History of ischemic stroke/TIA	0 (0.00%)	No	59 (2.5%)	Yes
Concomitant medication				
Antiplatelets	0 (0.00%)	No	3 (0.13%)	Yes
Anticoagulants	0 (0.00%)	No	5 (0.212%)	Yes
Pre-stroke disability				
Pre-mRS	2 (0.18%)	Yes	5 (0.212%)	Yes
Clinical presentation on admission				
NIHSS score on admission	2 (0.18%)	Yes	5 (0.212%)	Yes
ER glucose	138 (12.40%)	Yes	407 (17.25%)	Yes
ER SBP	4 (0.36%)	Yes	22 (0.93%)	Yes
Thrombolysis parameters				
Onset to treatment time, OTT	0 (0.00%)	No	1 (0.042%)	Yes
Door to needle time, DNT	2 (0.18%)	Yes	17 (0.72%)	Yes
TNK/rt-PA dose	5 (0.45%)	Yes	13 (0.55%)	No
Door to puncture time, DTP	7 (0.63%)	Yes	8 (0.34%)	Yes
Outcomes				
24-hours NIHSS	5 (0.45%)	No	36 (1.53%)	No
90-day mRS	19 (1.71%)	No	152 (6.44%)	No
90-day mortality	19 (1.71%)	No	152 (6.44%)	No

Supplemental material

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Supplementary Table 3. Matched baseline characteristics after propensity score matching in TNK and alteplase group

Characteristics	Unmatched groups	After PSM	
	P-value[a]	Standard Mean Difference[b]	*P-value*[a]
Demographics			
Age, years, median (IQR)	0.000	-0.0335	0.214
Male, N, (%)	0.176	0.0281	0.509
Pre-mRS, median (IQR)	0.006	NA	0.595
mRS=0, %		-0.018	
mRS=1, %		0.0076	
mRS=2, %		-0.0161	
mRS=3, %		0.0455	
mRS=4, %		0.0368	
Pre-mRS=0-1, N (%)	0.110	NA	0.66
Risk factors, No. (%)			
Smoking	0.000	0.007	0.869
Hypertension	0.228	NA	0.239
Diabetes mellitus	0.000	-0.0257	0.549
Dyslipidemia	0.000	-0.0693	0.126
Atrial fibrillation	0.000	0.0099	0.814
Previous history, No. (%)			
Coronal heart disease	0.218	NA	0.439
Heart failure	0.015	-0.0609	0.205
Ischemic stroke/TIA	0.000	-0.0282	0.511
Concomitant medication, No. (%)			
Antiplatelet drugs	0.000	0.0184	0.611
Anticoagulant drugs	0.358	NA	0.008
Clinical presentation at emergency			
NIHSS score on admission, median (IQR)	0.334	-0.0308	0.427
Glucose, mmol/L, median (IQR)	0.007	-0.0114	0.423
Systolic blood pressure, median (IQR)	0.023	-0.0355	0.599
Thrombectomy, N (%)	0.008	-0.0519	0.238

[a] Univariate comparison between TNK and alteplase.
[b] A standardized mean difference<0.2 indicated a successful balance between the groups

Supplementary Table 4. Baseline charateristics of the Inner Mongolia center and the rest of the centers in the TNK and alteplase group

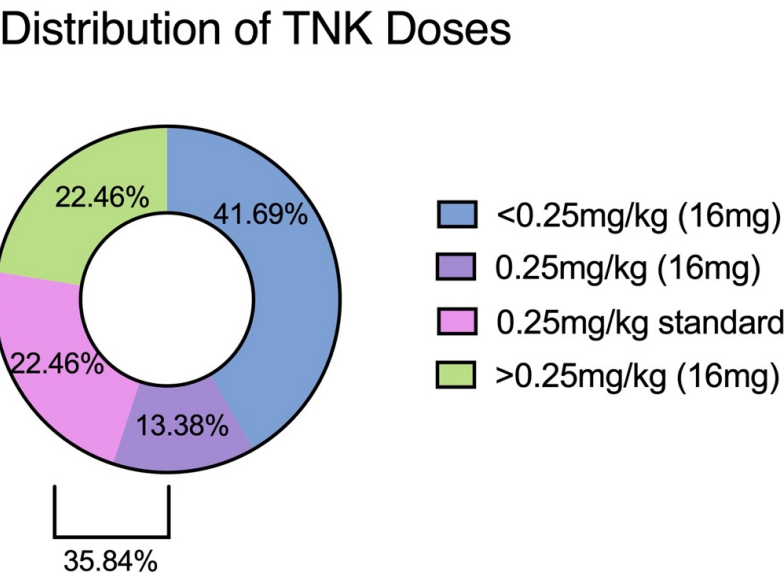| Characteristic	Inner Mongolia	Other centers excluded inner Mongolia	*P-value*[a]	Inner Mongolia	Other centers excluded inner Mongolia	*P-value*[a]
	TNK, N=489	TNK, N=624		Alteplase, N=57	Alteplase, N=2303	
Age, yr, median (IQR)	64 (58, 70.5)	67 (59, 75)	0.0002	68 (61, 73)	68 (60, 76)	0.581
Male, N (%)	306 (62.58%)	407 (65.22%)	0.361	38 (66.67%)	1529 (66.39%)	0.965
Pre_mRS, median (IQR)	0 (0, 0)	0 (0, 0)	0.000	0 (0, 0)	0 (0, 0)	0.026
Pre-mRS=0-1, n/N (%)	489 (100.00%)	579 (92.79%)	0.000	57 (100%)	2178 (94.57%)	0.071
Smoking, N (%)	6 (1.23%)	198 (31.73%)	0.000	2 (3.51%)	808 (35.08%)	0.000
Hypertension, N (%)	309 (63.19%)	393 (62.98%)	0.943	44 (77.19%)	1494 (64.87%)	0.054
Diabetes mellitus, N (%)	40 (8.18%)	161 (25.80%)	0.000	4 (7.02%)	679 (29.48%)	0.000
Dyslipidemia, N (%)	0 (0.00%)	57 (9.13%)	0.000	0 (0.00%)	378 (16.41%)	0.001
Atrial fibrillation, N (%)	9 (1.84%)	81 (12.98%)	0.000	1 (1.75%)	341 (14.81%)	0.006
Coronal heart disease, N (%)	43 (8.79%)	75 (12.02%)	0.083	6 (10.53%)	278 (12.07%)	0.723
Heart failure, N(%)	1 (0.20%)	11 (1.76%)	0.012	1 (1.75%)	53 (2.3%)	0.785
Ischemic stroke/TIA, N (%)	0 (0.00%)	159 (25.48%)	0.000	3 (5.26%)	459 (19.93%)	0.006
Antiplatelet drugs, N (%)	5 (1.02%)	101 (16.19%)	0.000	0 (0.00%)	427 (18.54%)	0.000
Anticoagulant drugs, N (%)	2 (0.41%)	37 (5.93%)	0.000	0 (0.00%)	69 (3%)	0.185
NIHSS score on admission, median (IQR)	5 (4, 6)	5 (3, 12)	0.0968	6 (3.5, 8)	5 (3, 10)	0.43
Thrombectomy, N (%)	0 (0.00%)	93 (14.90%)	0.000	0 (0.00%)	266 (11.55%)	0.006
Baseline glucose, mmol/L, median (IQR)	6.2 (5.4, 7.59)	6.8 (5.8, 8.77)	0.000	5.9 (5.1, 8.6)	6.82 (5.6, 8.8)	0.047
Systolic BP, median (IQR)	140 (130, 155)	150 (133.25, 162)	0.000	150 (136, 153.5)	146 (133, 162)	0.323
Door to needle time, min, median (IQR)	25 (20, 30)	35 (24, 50)	0.000	38 (30, 63)	38 (27, 55)	0.201
Onset to treatment time, min, median (IQR)	192 (143, 236.5)	155 (110, 218)	0.000	194 (135, 223.5)	140 (101, 181)	0.000

[a] Univariate comparison between TNK and alteplase.

BP=blood pressure; IQR=interquartile range; mRS=modified Rankin Scale; NIHSS=National Institutes of Health Stroke Scale; TNK=tenecteplase.

Supplementary Table 5. Mediation analysis of DNT for the associations between intravenous thrombolysis drug and sICH
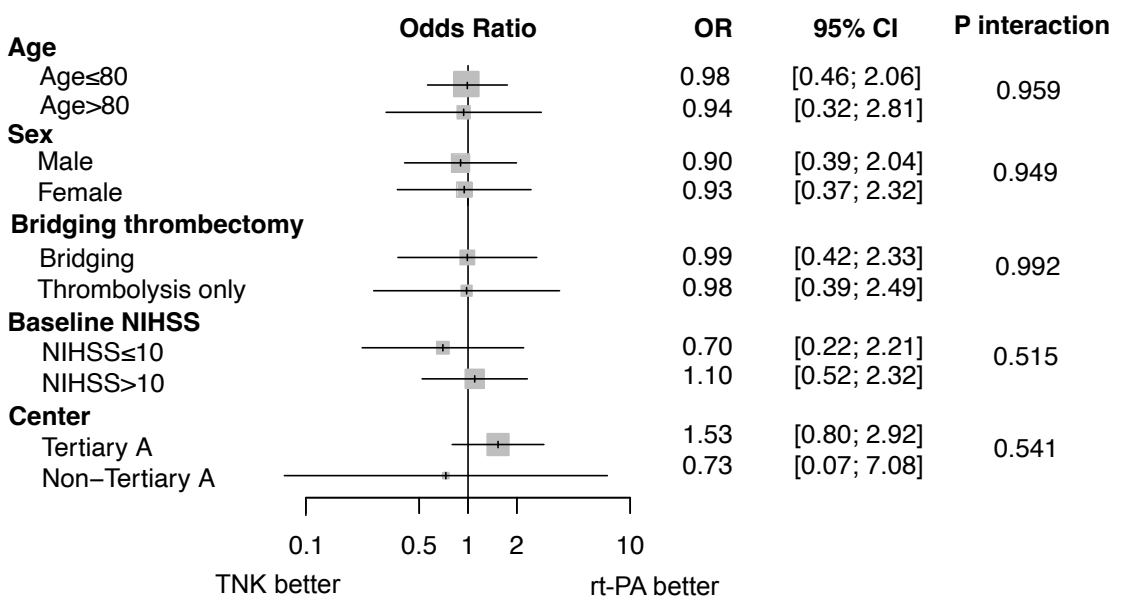
Mediators	Direct effect		Indirect effect		Proportion mediatied
	Effect size (95% CIs)	*p*	Effect size (95% CIs)	*p*	
DNT	-0.001659 (-0.009, 0.01)	0.74	-0.001 (-0.002, 0)	0.64	0.35

Supplementary Figure 1. Distribution of TNK Doses Administered During the Study Period

Distribution of TNK Doses

The figure presents the distribution of TNK doses administered to patients during the study period. A majority of centers used a fixed 16 mg vial (863 patients, 77.54%). Of these, the largest portion (41.69%) received less than 0.25mg/kg of TNK at the fixed 16mg dose. Additionally, 13.38% of patients received exactly 0.25mg/kg at 16mg while another 22.46% received 0.25mg/kg following the standard dosing method. The remaining 22.46% received more than 0.25mg/kg with the 16mg dose.

Supplemental material

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Supplementary Figure 2. Subgroup analyses of intravenous tenecteplase compared to intravenous alteplase **for the sICH (primary outcome)** in the propensity score matched cohort

	Odds Ratio	OR	95% CI	P interaction
Age				
Age≤80		0.98	[0.46; 2.06]	0.959
Age>80		0.94	[0.32; 2.81]	
Sex				
Male		0.90	[0.39; 2.04]	0.949
Female		0.93	[0.37; 2.32]	
Bridging thrombectomy				
Bridging		0.99	[0.42; 2.33]	0.992
Thrombolysis only		0.98	[0.39; 2.49]	
Baseline NIHSS				
NIHSS≤10		0.70	[0.22; 2.21]	0.515
NIHSS>10		1.10	[0.52; 2.32]	
Center				
Tertiary A		1.53	[0.80; 2.92]	0.541
Non–Tertiary A		0.73	[0.07; 7.08]	

0.1　　0.5　1　2　　　10

TNK better　　　　　rt-PA better

CI=confidence interval; OR=odds ratio; mRS=modified Rankin Scale