

**Supplemental material****Supplemental Table 1 Comparison of study characteristics between 4S and TIMS-CHINA**

	<b>4S</b>	<b>TIMS-CHINA</b>	<b>P</b>
	<b>N=2370</b>	<b>N=1109</b>	
Median Age, yr	65	64.5	0.0077
Sex: Male	66.9%	60.6%	0.0003
Median NIHSS at baseline, points	7	11	0.0000
Median Onset to needle, hours	2.83	2.83	0.0566
% of lower dose	10.1	16.8	0.0000
Median dosage/ per kg	0.9	0.9	0.1779
%History of Hypertension	60.6	59.2	0.4272
%History of Diabetes	22.2	17.5	0.0015
%History of Previous Stroke	9.8	18.6	0.0000
%History of smoking	38.7	40.0	0.4717
%History of atrial fibrillation	16.8	18.2	0.3241
% of sICH in 36h	4.3	4.3	0.9953

*NIHSS=National Institution of Health Stroke Scale; sICH=symptomatic intracranial hemorrhage*

**Supplemental Table 2. Dynamic dosage on the efficacy and safety outcome in acute ischemic stroke**

<b>Group<sup>&amp;</sup></b>	<b>dosage</b>	<b>sICH</b>			<b>Favorable outcome<sup>#</sup></b>		
		<b>mg/kg</b>	<b>HR</b>	<b>95%CI</b>	<b>HR</b>	<b>95%CI</b>	
<i>Mild stroke</i>	tpa 0.9	0.017	0.009	0.029	0.669	0.634	0.703
	tpa 0.8	0.016	0.000	0.087	0.633	0.499	0.754
	tpa 0.7	0.083	0.010	0.269	0.625	0.406	0.812
	tpa 0.6	NA	NA	0.195	0.688	0.413	0.890
	tpa 0.5	0.25	0.006	0.805	0.333	0.008	0.906
<i>Moderate Stroke</i>	tpa 0.9	0.036	0.028	0.047	0.593	0.568	0.618
	tpa 0.8	0.008	0.000	0.046	0.624	0.530	0.712
	tpa 0.7	0.015	0.000	0.083	0.508	0.381	0.634
	tpa 0.6	NA	NA	0.161	0.524	0.298	0.743
	tpa 0.5	NA	NA	0.410	0.714	0.290	0.963
<i>Severe stroke</i>	tpa 0.9	0.081	0.062	0.104	0.661	0.623	0.698
	tpa 0.8	0.130	0.054	0.249	0.696	0.542	0.823
	tpa 0.7	0.143	0.040	0.327	0.640	0.425	0.820
	tpa 0.6	0.167	0.021	0.484	0.500	0.187	0.813
	tpa 0.5	0.091	0.002	0.413	0.600	0.262	0.878

<sup>&</sup>Group: Mild= NIHSS 0-4, Moderate=NIHSS 5-14, Severe=NIHSS  $\geq 15$

<sup>#</sup>Favorable outcome: 7days after onset, the NIHSS of patient has improved to 0 or 1, or decrease 4 points compared to baseline NIHSS score.

NA: Not available due to limited data.

**Supplemental Table 3 Comparison demographics and outcome between mild-moderate stroke and severe stroke subgroups**

	Mild-Moderate stroke N=2649	Severe stroke N=807	P
Number of lower dosage(%)	318(12.00)	105(13.01)	0.4823
Age			<0.0001
<45yr, n	134	17	
45-64yr, n	1267	269	
≥65yr, n	1229	515	
Gender: Male, n(%)	1776(67.04)	463(57.37)	<0.0001
Median Onset to needle, hours	2.833	2.667	<0.0001
History and Risk Factors			
Hypertension, n(%)	1577(59.53)	503(62.33)	0.1675
Diabetes, n(%)	569(21.25)	156(19.33)	0.2592
Previous Stroke, n(%)	302(11.4)	132(16.36)	0.0003
TIA, n(%)	88(3.32)	37(4.58)	0.1154
Atrial Fibrillation, n(%)	325(12.27)	273(33.83)	<0.0001
Outcome			
sICH, n(%)	76(2.87)	71(8.80)	<0.0001
Clinical Improvement, n(%)	1582(59.72)	475(58.86)	0.0350

Group: Mild-Moderate=NIHSS 0-14, Severe=NIHSS ≥15

TIA=transient ischemic attack, sICH=symptomatic intracranial hemorrhage

**Supplemental Figure 1. Histogram of alteplase dosage**