Supplemental Tables

Table of Contents:

eTable 1: Baseline Patient Characteristics Stratified by Treatment (Whole Cohort)

	Tenecteplase 0.40 mg/kg (n=150)	Tenecteplase 0.25 mg/kg (n = 251)	Alteplase: 0.9 mg/kg (n=101)	p-value
Age, years; median (IQR)	73 (64-80)	74 (65-82)	75 (67-82)	0.32
Age > 80 years (n, %)	34 (23%)	74 (30%)	29 (29%)	0.31
Female Sex (n,%)	73 (49%)	111 (44%)	49 (49%)	0.62
Cause of Stroke (n, %)				
Cardioembolic occlusion	61 (41%)	117 (47%)	54 (54%)	0.14
Large artery occlusion	24 (16%)	38 (15%)	17 (17%)	0.92
Undetermined/other	65 (43%)	96 (38%)	30 (30%)	0.09
Medical History (n,%)				
Hypertension	94 (63%)	167 (67%)	63 (62%)	0.65
Diabetes	29 (19%)	40 (16%)	18 (18%)	0.68
Dyslipidemia	66 (44%)	92 (37%)	39 (39%)	0.34
Prior Stroke or TIA	17 (11%)	43 (17%)	18 (18%)	0.23
Smoking Status				
Current Smoker	19 (13%)	39 (16%)	11 (11%)	0.23
Ex-Smoker	37 (25%)	50 (20%)	15 (15%)	
Non-Smoker	94 (63%)	161 (64%)	75 (74%)	
Antiplatelet Use	70/148 (47%)	102/248 (41%)	40 (40%)	0.38
Anticoagulant Use	19/148 (13%)	24/248 (10%)	9 (9%)	0.52
Clinical and Laboratory Markers				
Glucose, mmol/L; median (IQR)[a]	6.6 (5.9-8.7)	6.3 (5.7-7.8)	6.4 (5.6-7.8)	0.39
NIHSS; median (IQR)	17 (11-21)	16 (10-21)	17 (13-22)	0.32
Imaging				
Site of Vessel Occlusion (n,%)				
Internal Carotid Artery	37 (25%)	48 (19%)	21 (21%)	0.42
Basilar Artery	7 (5%)	9 (4%)	3 (3%)	0.77
MCA (First Segment)	74 (49%)	139 (55%)	64 (63%)	0.09
MCA (Second Segment)	32 (21%)	55 (22%)	13 (13%)	0.14
Tandem Lesion (n, %)	16 (11%)	40 (16%)	15 (15%)	0.33
Baseline Ischemic Core, mL; median (IQR)[b,d]	13 (0-39)	11 (0-33)	11 (0-24)	0.30
Baseline Perfusion Lesion Volume, mL; median (IQR)[c,e]	116 (67-167)	121 (79-170)	134 (102-169)	0.08
Mismatch Volume, mL; median (IQR)[c]	88 (51-134)	100 (64-143)	112 (85-142)	<0.01
Workflow Processes				
Time from stroke onset to first hospital arrival, min; median (IQR)	79 (51-110)	70 (49-102)	72 (54-108)	0.43
Time from stroke onset to thrombolysis initiation, min; median (IQR)	132 (97-180)	129 (101-165)	134 (104-176)	0.76
Time from stroke onset to arterial puncture, min; median (IQR)	180 (135-258)	175 (144-238)	189 (150-226)	0.95
Interhospital Transfer for Thrombectomy (n,%)	60/149 (40%)	72/250 (29%)	23 (23%)	0.01

[a]Missing 106 patients; [b]Missing 18 patients; [c]Missing 20 patients

[d]Ischemic Core defined as relative cerebral blood volume <30% normal brain

[e]Perfusion lesion volume defined as time to maximum (Tmax) >6s

Abbreviations: IQR=interquartile range; TIA=transient ischemic attack; NIHSS=National Institutes of Health Stroke Scale

eTable 2: Baseline Patient Characteristics Stratified by Age Threshold (> 80 years)

	Age > 80 Years (n=137)	Age ≤ 80 years (n=365)	P-value
Age, years; median (IQR)	86 (84 – 90)	69 (61 – 75)	<0.01
Female Sex (n,%)	76 (56%)	157 (43%)	0.01
Cause of Stroke (n, %)			
Cardioembolic occlusion	80 (58%)	152 (42%)	<0.01
Large artery occlusion	18 (13%)	61 (17%)	0.33
Undetermined/other	39 (29%)	152 (42%)	<0.01
Medical History (n,%)			
Hypertension	109 (80%)	215 (59%)	<0.01
Diabetes	21 (15%)	66 (18%)	0.47
Dyslipidemia	63 (46%)	134 (37%)	0.06
Prior Stroke or TIA	29 (21%)	49 (13%)	0.03
Smoking Status*			
Current Smoker	5 (4%)	64 (18%)	<0.01
Ex-Smoker	26 (19%)	76 (21%)	
Non-Smoker	106 (77%)	224 (62%)	
Antiplatelet Use	64 (13%)	148 (41%)	0.22
Anticoagulant Use	21 (15%)	31 (9%)	0.03
Clinical and Laboratory Markers			
Glucose, mmol/L; median (IQR)[a]	6.9 (5.9 – 8.3)	6.3 (5.6 – 7.8)	0.04
NIHSS; median (IQR)	18 (13 – 22)	16 (11 – 21)	0.98
Imaging			
Site of Vessel Occlusion (n,%)			
Internal Carotid Artery	25 (18%)	81 (22%)	0.33
Basilar Artery	8 (6%)	11 (3%)	0.14
MCA (First Segment)	76 (56%)	201 (55%)	0.94
MCA (Second Segment)	28 (20%)	72 (20%)	0.86
Tandem Lesion (n, %)	14 (10%)	57 (16%)	0.12
Baseline Ischemic Core, mL; median (IQR) [b,d]	5 (0 – 26)	13 (0 – 35)	<0.01
Baseline Perfusion Lesion Volume, mL; median (IQR) [c,e]	112 (79 – 160)	126 (82 – 171)	0.11
Mismatch Volume, mL; median (IQR)[c]	97 (64-137)	100 (65-141)	0.57
Workflow Processes			
Time from stroke onset to first hospital arrival, min; median (IQR)	79 (57 – 109)	71 (48 – 104)	0.08
Time from stroke onset to thrombolysis initiation, min; median (IQR)	139 (110 – 170)	128 (99 – 169)	0.03
Time from stroke onset to arterial puncture, min; median (IQR)	190 (151 – 262)	175 (137 – 235)	0.02
Interhospital Transfer for Thrombectomy (n,%)	40 (29%)	115 (32%)	0.59

[a]Missing 106 patients; [b]Missing 18 patients; [c]Missing 20 patients

[d]Ischemic Core defined as relative cerebral blood volume <30% normal brain

[e]Perfusion lesion volume defined as time to maximum (Tmax) >6s

Abbreviations: IQR=interquartile range; TIA=transient ischemic attack; NIHSS=National Institutes of Health Stroke Scale

eTable 3: Multivariable Models of modified Rankin Scales at 90 days (ordinal)

Age > 80 Years	**Model 1**	**Model 2**	**Model 3**
TNK 0.25 mg/kg vs. 0.40 mg/kg	2.70 (1.23-5.94)	2.62 (1.14-6.00)	2.11 (0.91-4.91)
TNK 0.25 mg/kg vs. tPA 0.90 mg/kg	2.28 (1.03-5.06)	2.46 (1.11-5.44)	2.25 (1.01-5.01)
tPA 0.90 mg/kg vs. TNK 0.40 mg/kg	1.18 (0.47-2.95)	1.07 (0.41-2.77)	0.94 (0.36-2.48)
Age (per 1 year)	0.90 (0.83-0.98)	0.90 (0.83-0.98)	0.91 (0.84-0.99)
Symptom Onset to Arterial Puncture (per minute)	1.00 (0.99-1.00)	1.00 (0.99-1.00)	0.99 (0.99-1.00)
Baseline NIHSS (per 1 point)	0.93 (0.89-0.98)	-	0.92 (0.87-0.97)
Baseline Mismatch (per 1 mL)	-	1.00 (0.99-1.00)	1.00 (0.99-1.01)
Age ≤ 80 Years	**Model 1**	**Model 2**	**Model 3**
TNK 0.25 mg/kg vs. 0.40 mg/kg	0.80 (0.52-1.23)	0.93 (0.61-1.43)	0.86 (0.55-1.32)
TNK 0.25 mg/kg vs. tPA 0.90 mg/kg	1.25 (0.76-2.06)	1.33 (0.81-2.19)	1.23 (0.74-2.05)
tPA 0.90 mg/kg vs. TNK 0.40 mg/kg	0.64 (0.38-1.09)	0.70 (0.41-1.19)	0.69 (0.40-1.19)
Age (per 1 year)	0.98 (0.96-0.99)	0.97 (0.96-0.99)	0.98 (0.96-0.99)
Symptom Onset to Arterial Puncture (per minute)	0.99 (0.99-0.99)	0.99 (0.99-0.99)	0.99 (0.99-0.99)
Baseline NIHSS (per 1 point)	0.89 (0.87-0.92)	-	0.90 (0.87-0.93)
Baseline Mismatch (per 1 mL)	-	0.99 (0.99-0.99)	0.99 (0.99-0.99)

Data represented as adjusted common odds ratio

Abbreviations: TNK=tenecteplase; tPA=alteplase; NIHSS=National Institutes of Health Stroke Scale

eTable 4: Sensitivity Analysis - Multivariable Models of Secondary Clinical Outcomes

Freedom From Disability (mRS 0-1 or no change from baseline)			
Age > 80 Years	Model 1[a]	Model 2[b]	Model 3[c]
TNK 0.25 mg/kg vs. 0.40 mg/kg	2.97 (0.92-9.60)	3.50 (1.21-10.11)	2.92 (0.87-9.89)
TNK 0.25 mg/kg vs. tPA 0.90 mg/kg	8.54 (1.83-39.79)	4.12 (1.37-12.39)	5.25 (0.87-31.80)
tPA 0.90 mg/kg vs. TNK 0.40 mg/kg	0.35 (0.05-2.50)	0.85 (0.22-3.32)	0.56 (0.05-5.88)
Age ≤ 80 Years			
TNK 0.25 mg/kg vs. 0.40 mg/kg	0.74 (0.45-1.23)	0.90 (0.54-1.48)	0.74 (0.44-1.25)
TNK 0.25 mg/kg vs. tPA 0.90 mg/kg	0.94 (0.52-1.72)	1.01 (0.57-1.80)	1.08 (0.59-1.97)
tPA 0.90 mg/kg vs. TNK 0.40 mg/kg	0.79 (0.42-1.50)	0.89 (0.47-1.66)	0.69 (0.36-1.32)
Functional Independence (mRS 0-2 or no change from baseline)			
Age > 80 Years	Model 1[a]	Model 2[b]	Model 3[c]
TNK 0.25 mg/kg vs. 0.40 mg/kg	1.99 (0.67-5.88)	2.23 (0.73-6.83)	1.91 (0.63-5.81)
TNK 0.25 mg/kg vs. tPA 0.90 mg/kg	4.11 (1.06-15.90)	2.53 (0.51-12.51)	2.71 (0.64-11.50)
tPA 0.90 mg/kg vs. TNK 0.40 mg/kg	0.49 (0.08-2.87)	0.88 (0.10-7.68)	0.71 (0.10-4.95)
Age ≤ 80 Years			
TNK 0.25 mg/kg vs. 0.40 mg/kg	0.82 (0.47-1.43)	0.94 (0.55-1.59)	0.80 (0.45-.41)
TNK 0.25 mg/kg vs. tPA 0.90 mg/kg	1.21 (0.64-2.31)	1.28 (0.70-2.34)	1.44 (0.76-2.72)
tPA 0.90 mg/kg vs. TNK 0.40 mg/kg	0.68 (0.34-1.34)	0.73 (0.38-1.40)	0.55 (0.28-1.11)
Mortality			
Age > 80 Years	Model 1[a]	Model 2[b]	Model 3[c]
TNK 0.25 mg/kg vs. 0.40 mg/kg	0.34 (0.13-0.91)	0.39 (0.14-1.07)	0.40 (0.14-1.14)
TNK 0.25 mg/kg vs. tPA 0.90 mg/kg	0.50 (0.18-1.37)	0.45 (0.17-1.23)	0.52 (0.19-1.45)
tPA 0.90 mg/kg vs. TNK 0.40 mg/kg	0.69 (0.23-2.09)	0.86 (0.27-2.75)	0.76 (0.23-2.47)
Age ≤ 80 Years			
TNK 0.25 mg/kg vs. 0.40 mg/kg	0.99 (0.31-3.22)	0.75 (0.32-1.75)	0.85 (0.31-2.27)
TNK 0.25 mg/kg vs. tPA 0.90 mg/kg	0.71 (0.13-3.81)	0.84 (0.32-2.22)	0.69 (0.23-2.06)
tPA 0.90 mg/kg vs. TNK 0.40 mg/kg	1.41 (0.13-15.84)	0.89 (0.32-2.48)	1.23 (0.38-3.98)

Data represented as adjusted odds ratio

[a]Adjusted for age, time symptom onset to arterial puncture, baseline NIHSS

[b]Adjusted for age, time symptom onset to arterial puncture, baseline mismatch

[c]Adjusted for age, time symptom onset to arterial puncture, baseline ischemic core

Abbreviations: TNK=tenecteplase; tPA=alteplase; NIHSS=National Institutes of Health Stroke Scale

eTable 5: Comparisons of Outcomes Stratified by Age Threshold

	Age > 80 (n=137)	Age ≤ 80 (n=365)	P-Value
Freedom from Disability[a]	42 (31%)	201 (55%)	<0.01
Functional Independence[b]	49 (36%)	240 (66%)	<0.01
Mortality	41 (30%)	35 (10%)	<0.01
Symptomatic Intracranial Hemorrhage[c]	5 (4%)	6 (2%)	0.17
Substantial Reperfusion at initial angiogram[d]	33 (24%)	57 (16%)	0.03
Follow-up Ischemic Core, mL; median (IQR)[e]	17.6 (3.7 – 61.3)	16.9 (4.2 – 63.2)	0.92

[a]Defined as modified Rankin scale (mRS) score of 0-1 or no change from baseline
[b]Defined as mRS score of 0-2 or no change from baseline
[c]Symptomatic intracranial hemorrhage defined as intracerebral hemorrhage (large parenchymal hematoma - blood clot occupying >30% of infarct volume with mass effect; and ≥4 point increase in NIHSS) or symptomatic subarachnoid hemorrhage
[d]Substantial reperfusion was defined as restoration of blood flow to >50% of the involved territory or no retrievable intracranial thrombus at the initial angiogram.
[e]Ischemic Core defined as relative cerebral blood volume <30% normal brain

eTable 6: Sensitivity Analysis – Exclusion of Patients with Parenchymal Hematoma or Symptomatic Subarachnoid Hemorrhage

Age > 80 Years						
	TNK 0.40 mg/kg (n=30)	TNK 0.25 mg/kg (n=72)	tPA 0.90 mg/kg (n=26)	Effect Size TNK 0.25 mg/kg vs. TNK 0.40 mg/kg	Effect Size tPA 0.90 mg/kg vs. TNK 0.40 mg/kg	Effect Size TNK 0.25 mg/kg vs. tPA 0.90 mg/kg
Freedom from Disability[a,c]	6 (20%)	31 (43%)	3 (12%)	2.57 (0.79 – 8.37)	0.19 (0.02 – 1.58)	13.42 (2.42 – 74.22)
Functional Independence[b,c]	8 (27%)	32 (44%)	7 (27%)	1.75 (0.58 – 5.27)	0.34 (0.06 – 2.14)	5.10 (1.24 – 20.87)
Mortality[c]	10 (33%)	15 (21%)	9 (35%)	0.39 (0.13 – 1.17)	0.86 (0.25 – 2.88)	0.46 (0.16 – 1.33)
Age ≤ 80 Years						
	TNK 0.40 mg/kg (n=113)	TNK 0.25 mg/kg (n=167)	tPA 0.90 mg/kg (n=70)	Effect Size TNK 0.25 mg/kg vs. TNK 0.40 mg/kg	Effect Size tPA 0.90 mg/kg vs. TNK 0.40 mg/kg	Effect Size TNK 0.25 mg/kg vs. tPA 0.90 mg/kg
Freedom from Disability[a,c]	68 (60%)	94 (56%)	38 (54%)	0.78 (0.47 – 1.31)	0.76 (0.39 – 1.45)	1.03 (0.55 – 1.90)
Functional Independence[b,c]	80 (71%)	112 (67%)	43 (61%)	0.78 (0.44 – 1.38)	0.64 (0.32 – 1.28)	1.24 (0.64 – 2.37)
Mortality[c]	11 (10%)	12 (7%)	6 (9%)	0.72 (0.30 – 1.75)	0.77 (0.26 – 2.29)	0.94 (0.32 – 2.72)

[a]Defined as modified Rankin scale (mRS) score of 0-1 or no change from baseline
[b]Defined as mRS score of 0-2 or no change from baseline
[c]Adjusted for baseline NIHSS score, age, and time from symptom onset to arterial puncture

Supplemental Figures

Table of Contents:

eFigure 1: Boxplot Distribution of Patient Age Stratified by Treatment