

Supplementary Materials

Dual Antiplatelet vs. Alteplase in Anterior and Posterior Circulation  
Minor Stroke:  
A Secondary Analysis of ARAMIS

Content

Methods.....2

Table S1 Baseline Characteristics Compared Between ACS and PCS. ....3

Table S2 Baseline Characteristics Compared Between Before and After  
Propensity Score Matching. ....4

Table S3 Sensitivity Analysis for Primary Outcome. ....6

Table S4. Sensitivity for Improvement in Early Neurological Function. ....7

## Methods

### Definition of Different Populations in the Sensitivity Analysis.

- (1) Full analysis set (ITT) included all participants with valid informed consent will be included in the full analysis set population according to the treatment to which they are randomized, regardless of whether they prematurely discontinue treatment or are otherwise protocol violators/deviators. Participants lost to follow-up or withdrawn will not be included in the full analysis set population.
- (2) Per-protocol (PP) analysis set will be deemed as a sub-population of the full analysis set population and participants will be excluded from the full analysis set population if they did not adhere to study treatment or switched treatment.
- (3) As-treated population is based on the treatment actually received.

Table S1 Baseline Characteristics Compared Between ACS and PCS.

	ACS (N=566)	PCS (N=153)	P value
Age, y	65 (57-71)	64 (55-70)	0.27
Sex (Female)	174 (30.7)	49 (32.0)	0.76
Current smoker	205 (36.2)	36 (23.5)	0.03*
Current drinker <sup>a</sup>	95 (16.8)	21 (13.7)	0.36
Comorbidities <sup>b</sup>			
Hypertension	289 (51.1)	89 (58.2)	0.12
Diabetes	149 (26.3)	38 (24.8)	0.71
Previous stroke <sup>c</sup>	125 (22.1)	34 (22.2)	0.97
Previous TIA	4 (0.7)	2 (1.3)	0.47
Atrial fibrillation	1 (0.2)	1 (0.7)	0.95
Blood pressure at randomization, mmHg			
Systolic	150 (138-163)	152 (140-166)	0.45
Diastolic	88 (80-95)	89 (81-95)	0.19
FBG at randomization, mmol/L	6.40 (5.39-8.17)	6.21 (5.42-8.19)	0.58
NIHSS score at randomization <sup>d</sup>	2 (1-3)	2 (1-3)	0.18
Estimated premorbid function (mRS score) <sup>e</sup>			
0	413 (73.0)	120 (78.4)	0.17
1	153 (27.0)	33 (26.5)	
OTT, min	182 (133-229)	175 (124-227)	0.36
Duration of hospitalization, d	8 (6-10)	9 (7-12)	0.29
Presumed stroke cause <sup>f</sup>			
Large artery atherosclerosis	76 (13.5)	25 (16.3)	0.37
Cardioembolic	1 (0.2)	1 (0.7)	
Small artery occlusion	125 (22.1)	39 (25.5)	
Other determined cause	5 (0.9)	0 (0.0)	
Undetermined cause	358 (63.4)	88 (57.5)	
Vessel occlusion	154 (22.1)	46 (30.1)	0.13
Large vessel occlusion	29 (5.1)	7 (4.6)	0.16

The data was shown with median (IQR) or number (percentage). Abbreviation: ACS, anterior circulation stroke; DAPT, dual antiplatelet therapy; FBG, fasting blood glucose; mRS, modified Rankin Scale; NIHSS, National Institute of Health Stroke Scale; OTT, time from onset of symptom to intravenous thrombolysis or dual antiplatelet therapy; PCS, posterior circulation stroke; TIA, transient ischemic attack.

<sup>a</sup> Defined as consuming alcohol at least once a week within 1 year prior to the onset of the disease.

<sup>b</sup> The comorbidities were based on the patient or family report.

<sup>c</sup> Previous stroke included ischemic and hemorrhagic stroke.

<sup>d</sup> NIHSS scores range from 0 to 42, with higher scores indicating more severe neurological deficit.

<sup>e</sup> Scores on the mRS of functional disability range from 0 (no symptoms) to 6 (death).

<sup>f</sup> The presumed stroke etiology was classified according to the Trial of Org10172 in Acute Stroke Treatment (TOAST) using clinical findings, brain imaging, and laboratory test results. Other causes included nonatherosclerotic vasculopathies, hypercoagulable states, and hematologic disorder.

Table S2 Baseline Characteristics Compared Between Before and After Propensity Score Matching.

	Before Propensity Score Matching				After Propensity Score Matching			
	Total (N=719)	ACS (N=566)	PCS (N=153)	P Value	Total (N=286)	ACS (N=143)	PCS (N=143)	P Value
Age, y	64 (57-71)	65 (57-71)	64 (55-70)	0.27	65 (56-71)	65 (57-71)	64 (56-70)	0.91
Sex (Female)	223 (31.0)	174 (30.7)	49 (32.0)	0.76	88 (30.8)	43 (30.1)	45 (31.5)	0.80
Current smoker	241 (33.5)	205 (36.2)	36 (23.5)	0.03*	78 (27.3)	42 (29.4)	36 (25.2)	0.48
Current drinker <sup>a</sup>	116 (16.1)	95 (16.8)	21 (13.7)	0.36	44 (15.4)	24 (16.8)	20 (14.0)	0.40
Comorbidities <sup>b</sup>								
Hypertension	378 (52.6)	289 (51.1)	89 (58.2)	0.12	162 (56.6)	80 (55.9)	82 (57.3)	0.81
Diabetes	187 (26.0)	149 (26.3)	38 (24.8)	0.71	64 (22.4)	29 (20.3)	35 (24.5)	0.40
Previous stroke <sup>c</sup>	159 (22.1)	125 (22.1)	34 (22.2)	0.97	60 (21.0)	29 (20.3)	31 (21.7)	0.77
Previous TIA	6 (0.8)	4 (0.7)	2 (1.3)	0.47	2 (0.7)	0 (0.0)	2 (1.4)	0.16
Atrial fibrillation	2 (0.3)	1 (0.2)	1 (0.7)	0.13	0 (0.0)	0 (0.0)	0 (0.0)	0.99
Blood pressure at randomization, mmHg								
Systolic	150 (138-164)	150 (138-163)	152 (140-166)	0.45	153 (140-167)	155 (140-167)	152 (140-166)	0.19
Diastolic	88 (80-95)	88 (80-95)	89 (81-95)	0.19	89 (81-95)	90 (81-95)	90 (81-94)	0.91
FBG at randomization, mmol/L	6.33 (5.40-8.17)	6.40 (5.39-8.17)	6.21 (5.42-8.19)	0.58	6.41 (5.57-9.44)	6.40 (5.57-9.00)	6.51 (5.60-10.60)	0.99
NIHSS score at randomization <sup>d</sup>	2 (1-3)	2 (1-3)	2 (1-3)	0.18	2 (1-3)	2 (1-3)	2 (1-3)	0.99
Estimated premorbid function (mRS score) <sup>e</sup>								
0	533 (74.1)	413 (73.0)	120 (78.4)	0.17	219 (76.6)	108 (75.5)	111 (77.6)	0.68
1	186 (25.9)	153 (27.0)	33 (26.5)		67 (23.4)	35 (24.5)	32 (22.4)	
OTT, min	180 (130-228)	182 (133-229)	175 (124-227)	0.36	176 (125-225)	170 (129-222)	180 (124-228)	0.64
Duration of hospitalization, d	8 (6-10)	8 (6-10)	9 (7-12)	0.29	8 (7-11)	8 (6-11)	8 (7-11)	0.91

Presumed stroke cause <sup>f</sup>								
Large artery atherosclerosis	101 (14.1)	76 (13.5)	25 (16.3)	0.37	43 (15.0)	12 (17.6)	13 (15.3)	0.87
Cardioembolic	2 (0.3)	1 (0.2)	1 (0.7)		0 (0.0)	0 (0.0)	0 (0.0)	
Small artery occlusion	164 (22.8)	125 (22.1)	39 (25.5)		70 (24.5)	34 (23.8)	36 (25.2)	
Other determined cause	5 (0.7)	5 (0.9)	0 (0.0)		0 (0.0)	0 (0.0)	0 (0.0)	
Undetermined cause	446 (62.1)	358 (63.4)	88 (57.5)		173 (60.5)	86 (60.1)	87 (60.8)	

The data was shown with median (IQR) or number (percentage). Abbreviation: ACS, anterior circulation stroke; DAPT, dual antiplatelet therapy; FBG, fasting blood glucose; mRS, modified Rankin Scale; NIHSS, National Institute of Health Stroke Scale; OTT, time from onset of symptom to intravenous thrombolysis or dual antiplatelet therapy; PCS, posterior circulation stroke; TIA, transient ischemic attack.

a Defined as consuming alcohol at least once a week within 1 year prior to the onset of the disease.

b The comorbidities were based on the patient or family report.

c Previous stroke included ischemic and hemorrhagic stroke.

d NIHSS scores range from 0 to 42, with higher scores indicating more severe neurological deficit.

e Scores on the mRS of functional disability range from 0 (no symptoms) to 6 (death).

f The presumed stroke etiology was classified according to the Trial of Org10172 in Acute Stroke Treatment (TOAST) using clinical findings, brain imaging, and laboratory test results. Other causes included nonatherosclerotic vasculopathies, hypercoagulable states, and hematologic disorder.

Table S3 Sensitivity Analysis for Primary Outcome.

Group	No. of events (%)		Unadjusted <sup>a</sup>		Adjusted model <sup>b</sup>		<i>P</i> <sub>int</sub> <sup>d</sup> value
	DAPT	Alteplase	RD (95% CI) <sup>c</sup>	<i>P</i> value	RD (95% CI) <sup>c</sup>	<i>P</i> value	
Propensity score matching analysis set <sup>e</sup>							
ACS	59/62 (95.2)	72/81 (88.9)	6.3 (-2.4 to 15.0)	0.16	6.4 (0.0 to 12.8)	0.05	0.35
PCS	61/66 (92.4)	71/77 (92.2)	0.2 (-8.5 to 9.0)	0.96	0.2 (-8.5 to 9.0)	0.96	
Full analysis set							
ACS	266/283 (94.0)	256/279 (91.8)	2.2 (-2.0 to 6.5)	0.27	2.2 (-2.0 to 6.4)	0.31	0.99
PCS	77/83 (92.8)	63/70 (90.0)	2.8 (-6.2 to 11.7)	0.90	2.8 (-6.2 to 11.7)	0.90	
Per-protocol analysis set							
ACS	205/219 (93.6)	205/226 (90.7)	2.9 (-2.1 to 7.9)	0.25	2.4 (-1.2 to 5.9)	0.19	0.70
PCS	56/62 (90.3)	57/64 (89.1)	1.3 (-9.4 to 11.9)	0.82	1.3 (-9.4 to 11.9)	0.82	
Secondary adjusted model <sup>f</sup> of the as-treated analysis set							
ACS	256/272 (94.1)	266/290 (91.7)	2.4 (-1.8 to 6.6)	0.27	1.6 (-1.5 to 4.7)	0.32	0.53
PCS	62/68 (91.2)	78/85 (91.8)	-0.6 (-9.5 to 8.3)	0.90	-0.8 (-6.9 to 5.3)	0.80	
IPTW adjusted method <sup>g</sup> for the as-treated analysis set							
ACS	256/272 (94.1)	266/290 (91.7)	2.4 (-1.8 to 6.6)	0.27	2.0 (-2.2 to 6.3)	0.35	0.55
PCS	62/68 (91.2)	78/85 (91.8)	-0.6 (-9.5 to 8.3)	0.90	-0.3 (-8.6 to 8.0)	0.95	

Abbreviations: ACS, anterior circulation stroke; CI, confidence interval; DAPT, dual antiplatelet therapy; IPTW, inverse probability of treatment weighting; PCS, posterior circulation stroke; RD, risk difference. \* *P* value <0.05.

<sup>a</sup> Crude analysis in the model.

<sup>b</sup> Adjusted for covariates compared between DAPT and alteplase with *P* value <0.1 in the ACS subgroup. Covariates compared between DAPT and alteplase were balanced in the PCS subgroup.

<sup>c</sup> Calculated using the generalized liner model.

<sup>d</sup> *P* value for interaction was calculated by adjusting covariates compared between ACS and PCS group with *P* value < 0.1 in the analysis set.

<sup>e</sup> Propensity score matching analysis set included patients matched with prespecified covariates in the ARAMIS trial and baseline patient characteristics with *P* value <0.1 between ACS and PCS subgroups in Table 1, under the ratio 1:1, the caliper of 0.01, and a nearest-neighbor matching strategy.

<sup>f</sup> Adjusted for covariates compared between DAPT and alteplase with *P* value <0.1 in each subgroup and prespecified covariates in the ARAMIS trial.

<sup>g</sup> Adjusted for covariates compared between DAPT and alteplase with *P* value <0.1 in each subgroup.

Table S4. Sensitivity for Improvement in Early Neurological Function.

Outcomes	Groups	No.(%) of Patients		Unadjusted		Adjusted <sup>a</sup>	
		DAPT	Alteplase	Treatment difference (95% CI)	P value	Treatment difference (95% CI)	P value
END defined with ≥4-point increase in NIHSS score within 24 h	ACS	8/274 (2.9)	18/292 (6.2)	-3.2 (-6.6 to 0.2)	0.06	-1.9 (-5.3 to -0.5)	0.02*
	PCS	0/68 (0.0)	3/85 (3.5)	-3.5 (NA to NA)	0.12	-3.1 (NA to NA)	0.07
NIHSS scoring 0 at 24 h	ACS	70/274 (25.5)	82/292 (28.1)	-2.5 (-9.8 to 4.8)	0.50	-6.8 (-11.9 to -1.7)	0.009*
	PCS	14/68 (20.6)	18/85 (21.2)	-0.6 (-13.5 to 12.4)	0.93	-3.5 (-12.5 to 5.6)	0.46