Supplementary Table 1. Multivariable model for clinical primary outcome: variables prior to randomization

Variable	RR	95% CI	*P*	P_{int}
Nerinetide treatment	1.17	1.01–1.36	0.0396	-
Age (per year older)	0.98	0.98–0.99	<0.0001	0.4276
NIHSS (per point increase)	0.98	0.97–0.99	0.0056	0.7892
Glucose (per mmol/L increase)	0.95	0.91–0.98	0.0060	0.8803
ECG showing AFIB at baseline	0.80	0.65–0.98	0.0322	0.8923
Imaging factors (core lab)				
ASPECTS 0–4	1.00	Reference		
ASPECTS 5–7	1.64	0.92–2.92	0.0933	*
ASPECTS 8–10	1.80	1.02–3.18	0.0408	0.0141
Occlusion location (core lab)				
ICA	1.00	Reference		
M1-MCA	1.40	1.13–1.74	0.0025	0.3617
M2-MCA or distal	1.11	0.64–1.91	0.7089	0.2151
Procedural sedation				
General anesthesia	1.00	Reference		
Conscious sedation	1.49	1.15–1.93	0.0027	0.5963
None	1.72	1.29–2.28	0.0002	0.8968
Onset to randomization time (per 60 min)	0.96	0.94–0.98	0.0002	0.4957

The table summarizes a parsimonious multivariable regression model including main effects only of variables known prior to or at randomization, associated with primary outcome with $P<0.05$. The right-hand column describes the test statistic for separate models that assessed for a treatment by covariable interaction. ASPECTS scores show suspected evidence of an interaction with nerinetide treatment. The direction of effect was that nerinetide treatment compared to saline control, was associated with a larger effect size and better outcome for ASPECTS 8–10 compared to ASPECTS 5–7 (Figure 2).
NIHSS, National Institutes of Health Stroke Scale; ECG, electrocardiogram; AFIB, atrial fibrillation; ASPECTS, Alberta Stroke Program Early CT Score; ICA, internal carotid artery; MCA, middle cerebral artery; RR, risk ratio; CI, confidence interval; P_{int}, *P*-value for interaction term.
*In the ASPECTS 0–4 subgroup, zero patients in the control group had a favorable outcome leading to an incalculable interaction term. ASPECTS 0–4 was a technical exclusion criterion for the trial; patients with unfavorable scans were included in the trial unintentionally.

Supplementary Table 2. Multivariable model for clinical primary outcome: variables at the end of the EVT procedure

Variable	RR	95% CI	*P*	P_{int}
Nerinetide treatment	1.15	0.99–1.35	0.0726	-
Age (per year older)	0.98	0.97–0.99	<0.0001	0.2262
eTICI 2b-3	2.01	1.38–2.93	0.0003	0.9357
Onset-to-randomization (per 60 min)	0.96	0.94–0.98	0.0004	0.7129
Procedural sedation				
General anesthesia	1.00	Reference		
Conscious sedation	1.53	1.17–2.00	0.0020	0.7921
None	1.71	1.28–2.29	0.0003	0.3691

The table summarizes a parsimonious multivariable regression model including main effects only of variables known at the end of the EVT procedure, associated with primary outcome with $P<0.05$. The right-hand column describes the test statistic for separate models that assessed for a treatment by covariable interaction. There were no variables that showed effect modification.
EVT, endovascular treatment; eTICI, expanded Thrombolysis In Cerebral Infarction; RR, risk ratio; CI, confidence interval; P_{int}, *P*-value for interaction term.