Supplementary Methods

Outcomes assessment

The assessment of National Institutes of Health Stroke Scale (NIHSS) score at admission and follow-up were performed by the same assessor, who was not blinded to the treatment allocation.

Follow-up at 90 days, including assessment of the modified Rankin Scale (mRS) score, was performed in person or by telephone through blinded measurements by trained and certified assessors at each center who were unaware of the treatment allocation or clinical details.

Statistical analysis

For the treatment effect on outcomes, such as the occurrence of early neurological deterioration (END) at 7 days, excellent functional outcome at 90 days, and favorable functional outcome at 90 days, the absolute number of events, and absolute difference (risk difference, RD) with their 95% confidence intervals (CIs) were estimated.

We estimated the odds ratios (OR) with 95% CIs for the treatment effect of the mRS score distribution at 90 days.

We estimated the geometric mean ratio (GMR) with 95% CIs for the treatment effect of the change in NIHSS score between admission and at 14 days.

For other secondary outcomes, such as time to occurrence of a new stroke within 90 days, as well as other vascular events or all-cause death within 90 days, we estimated the absolute number of events and hazard ratio (HR) with their 95% CIs.

As time is a continuous variable, unadjusted analyses, which included antiplatelet treatment and time, were performed as in Model 1. The adjusted analyses that accounted for any imbalance in baseline variables, with *P* value <0.1 between treatment groups were performed as in Model 2. Based on Model 2, the adjusted analyses accounted for the following pre-specified covariates in the ATAMIS trial as in Model 3. Pre-specified covariates included age, sex, history of diabetes, history of hypertension, NIHSS score at randomization, and presumed stroke cause based on the Trial of Org 10172 in Acute Stroke Treatment (TOAST) classification.[1]

For the categorical variable time, unadjusted analyses including antiplatelet treatment were performed as in Model 1 in each time subgroup. Models 4 and 5 are similar to those in the adjusted analysis of continuous time.

To avoid nonconvergence when all covariates were simultaneously introduced into the adjusted analyses, we introduced a propensity score calculated from the logistic regression analysis, including all covariates. Missing covariate data included in the adjusted analyses were imputed through simple imputation.

The associations between the time and effect of antiplatelet treatment on outcomes were assessed using a generalized linear model, or Cox regression analysis with the treatment, time, or time subgroup and their interaction term as independent variables and the *P* value presented for the interaction term. The adjusted interactions were conducted by including imbalanced baseline variables between time subgroups with *P* value <0.1.

Propensity score matching was performed to generate a new cohort with a balanced sample size for each time subgroup. Baseline characteristics, including age, sex, history of diabetes, history of hypertension, NIHSS score at admission, presumed stroke cause, treatments, and imbalanced confounders (*P*<0.1) between time subgroups were matched with a ratio of 1:1, caliper of 0.01, and a nearest-neighbor matching strategy.

Patients were analyzed by grouping with different time from stroke onset to antiplatelet therapy (OTT) cutoff values, such as 12 hours or 18 hours.