Letter by Scheitz et al Regarding Article, "Randomized Controlled Trial of Early Versus Delayed Statin Therapy in Patients With Acute Ischemic Stroke: ASSORT Trial (Administration of Statin on Acute Ischemic Stroke Patient)"

To the Editor:

Based on the evidence from the SPARCL trial (Stroke Prevention by Aggressive Reduction in Cholesterol Levels), statins are generally recommended to reduce stroke and cardiovascular events among patients with recent atherothrombotic stroke or transient ischemic attack.1 Because of rapid cholesterol-independent vasoprotective effects of statins shown in experimental settings,2 there is an ongoing discussion whether it might be beneficial to start statin treatment as early as possible.

Adding to this discussion, we read with interest the results from the randomized, controlled ASSORT (Administration of Statin on Acute Ischemic Stroke Patient) trial.3 Although the trial missed the primary endpoint on improvement of modified Rankin Scale at 3 months, there were no safety concerns attributable to early statin administration. This is in line with the STARS trial (Stroke Treatment With Acute Reperfusion and Simvastatin) published last year.4 Unfortunately, the STARS trial had to stop early for slow enrolment and was underpowered to detect statistically robust effects. In ASSORT, the assumed effect size of statin treatment was probably not realistic, and the inclusion of mildly affected patients with small infarctions led to beneficial outcomes in the vast majority of patients although analysis of outcome by considering the full range of the modified Rankin Scale mitigates case-mix limitations. We would like to draw the attention to a recently published analysis from the Virtual International Stroke trials Archive (vistacollaboration.org).5 Patients with early statin use within 3 days after stroke onset (n=626) were compared with patients with later or no statin use. Matching for age, sex, severity measures, and use of other oral medications was performed to attenuate the inherent drawbacks of the nonrandomized design. We found that initiation of statin treatment within 3 days after ischemic stroke was associated with lower mortality (hazard ratio, 0.67; 95% CI, 0.46–0.97) and a signal toward a (slightly) improved distribution of modified Rankin Scale at 90 days (hazard ratio, 1.21; 95% CI, 0.98–1.50). There was no increased risk of acute or postacute intracerebral hemorrhage among statin users. In contrast to the ASSORT population, we confined our analysis to statin-naive patients and were able to analyze more severely affected patients, with median National Institutes of Health Stroke Scale 11.

We agree that further trials are desirable to test the effect of early statin administration, especially in combination with revascularization therapies. However, it is challenging to conduct such a randomized controlled trial with reasonable efforts and costs for several reasons. First, it is common practice in many stroke centers to start statin treatment already during (increasingly short) hospitalization. Moreover, the high prevalence of premorbid statin use and the lack of an intravenous statin formulation to treat severely affected patients reduce the chance to enroll a suitable target population to prove a beneficial effect of statins on stroke recovery.

To conclude, we would like to point out that, currently, there seems to be no reasonable argument to delay statin treatment given the preclinical and observational data and the reassuring safety results from ASSORT and STARS. Moreover, we would like to highlight that open clinical trial registries like Virtual International Stroke trials Archive offer the unique opportunity to perform or confirm estimation of effect sizes of a given intervention before the start of an extensive randomized controlled trial.

Disclosures

None.

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