



**I**SCHEMIC STROKE IS A DEVASTATING CONDITION with a high burden of neurologic disability and death. As a systemic treatment, intravenous alteplase has been shown to be better than conservative care.<sup>1,2</sup> Among patients with a proximal vessel occlusion in the anterior circulation, 60 to 80% of patients die within 90 days after stroke onset or do not regain functional independence despite alteplase treatment.<sup>3,4</sup> The major reason for the limited efficacy of alteplase is the modest rate of early reperfusion among patients with a large-vessel occlusion.<sup>5,6</sup>

Local treatment of large-vessel occlusion began with intraarterial delivery of thrombolytic drugs.<sup>7</sup> The Prolyse in Acute Cerebral Thromboembolism (PROACT) II study was the first positive trial of endovascular treatment involving patients with angiographically visualized occlusion of the middle cerebral artery.<sup>8</sup> Unfortunately, subsequent trials did not confirm the clinical benefit even with the addition of first-generation thrombectomy devices.<sup>3,9,10</sup> Key lessons learned from these previous trials are the need for proof of proximal vessel occlusion,<sup>11</sup> rapid and effective imaging methods to exclude patients with a large infarct core,<sup>12-14</sup> an efficient workflow to achieve fast recanalization,







group crossed over to receive endovascular treatment. In the intervention group, 14 participants did not receive any interventional therapy. Four participants (1.3%) were lost to follow-up; missing data on outcomes in these participants were not imputed (Fig. S1 in the Supplementary Appendix).

Baseline characteristics were similar in the two treatment groups (Table 1, and Table S1 in the Supplementary Appendix). Imaging protocol violations, identified by personnel who interpreted the images at the core laboratory, occurred in 26 participants (8.3%): 11 of 308 participants in whom the ASPECTS could be evaluated (3.6%) had a score of less than 6 on the ASPECTS scale, 20 of 315 participants (6.3%) had poor collateral circulation, and 14 of 315 participants (4.4%) had inappropriate target-vessel occlusion (some participants had >1 protocol violation). Collateral circulation was assessed with the

United Kingdom (1), a total of 316 participants underwent randomization before the trial was stopped: 165 participants were assigned to the intervention group, 150 participants were assigned to the control group, and 1 participant was excluded owing to improper consent procedures. The trial enrolled 1.44 participants per center per month from February 2013 through October 2014. One participant in the control

**Table 2. Primary and Secondary Efficacy Outcomes.**

Outcome	Intervention (N = 165)	Control (N = 150)	Difference (95% CI)*	Effect Variable	Unadjusted Value (95% CI)	Adjusted Value (95% CI)†
Primary outcome: modified Rankin score at 90 days‡				Common odds ratio	2.6 (1.7–3.8)	3.1 (2.0–4.7)
Modified Rankin score of 0–2 at 90 days — no./total no. (%)§	87/164 (53.0)	43/147 (29.3)	23.8 (13.2–34.4)	Rate ratio	1.8 (1.4–2.4)	1.7 (1.3–2.2)
NIHSS score of 0–2 at 90 days — no./total no. (%)¶	63/165 (38.2)	25/150 (16.7)	21.5 (10.7–32.3)			

serious adverse event and 14 had a nonserious adverse event (Table 3, and Table S2 in the Supplementary Appendix).

secondary outcomes and subgroup analyses  
 Secondary clinical and imaging end points favored the intervention group. The rate of patients with a score on the Barthel Index of 95 to 100 at 90 days was 57.7% in the intervention group versus 33.6% in the control group, the rate of patients with a 90-day NIHSS score of 0 to 2 was 51.6% versus 23.1%, and the median 90-day score on the EuroQoL Group 5-Dimension Self-Report Questionnaire (EQ-5D) visual-analogue scale (range,

0 to 100, with higher scores indicating better quality of life) was 80 versus 65 (Table 2).

There was no evidence of heterogeneity of effect across any of the prespecified subgroups (defined according to age, sex, baseline NIHSS score, baseline ASPECTS, occlusion location, and status with respect to alteplase treatment) or according to the presence or absence of cervical carotid occlusion. All variables showed a direction of effect in favor of the intervention (Fig. 2, and Fig. S6 in the Supplementary Appendix). However, the absolute proportion of good outcomes varied substantially according to subgroup (Fig. 1B, and Fig. S7 in the Supplementary Appendix).





compared with slower reperfusion, was associated with a better clinical outcome.<sup>16,33</sup> The ESCAPE trial achieved shorter interval times than those seen in past trials, with a median time from study noncontrast CT to first reperfusion of 84 minutes. A prespecified efficiency target for the time from noncontrast CT to reperfusion encouraged fast image acquisition and interpretation and fast decision making.<sup>16,34-37</sup> Critical to the achievement of rapid treatment was parallel decision making and action. For example, participants in the intervention group underwent groin puncture while alteplase was being infused, and complete reperfusion was achieved in some participants before the alteplase infusion was fin-

ished. The primary emphasis was on achieving early reperfusion.<sup>15,16,34,35</sup>

Imaging-related selection criteria focused on the population with a small infarct core at bhd24.7(l)7.1(e 8(s)3.7(io)2.4

Endovascular treatment appeared to benefit all ages (the oldest person enrolled in the trial was 93 years of age), both sexes, patients with moderate strokes and those with severe strokes, patients

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