

Table 2. Incidence of End Point Events by Treatment in Per-Protocol Population

	Antiplatelets (n = 101)	Anticoagulants (n = 96)
Ischemic stroke		
Ipsilateral	3	1
Other	0	0
TIA		
Ipsilateral	1	3
Other	1	0
Major bleeding	0	1
Death	0	0
Stroke, death, or major bleeding	3	2

Data given in No.

TIA, transient ischemic attack.

Reproduced with permission from H Markus, BM Bch.

The power calculation revealed that the sample size for a definitive study would have to be 9752 patients (power set to 0.8 and significance to 0.05). However, Prof Markus mentioned that although it would be very challenging to recruit such a large number of patients, this was a rather wide estimate because of the low number of end points.

In conclusion, Prof Markus highlighted that the recurrent stroke rate in the CADISS trial was much lower than that reported in some observational studies. He also cautioned that the diagnosis of dissection was not confirmed in 20% of cases, suggesting that diagnostic criteria may not always be properly applied in clinical practice.

Endovascular Intervention Beneficial in Pooled Analysis of MR CLEAN and IMS III

Written by Alla Zarifyan

Joseph P. Broderick, MD, University of Cincinnati, Cincinnati, Ohio, USA, reported results of a pooled analysis of patients with a National Institutes of Health Stroke Scale (NIHSS) score ≥ 20 in the MR CLEAN trial [Berkhemer OA et al. *N Engl J Med.* 2015] and IMS III trial [Broderick JP et al. *N Engl J Med.* 2013]. The pooled analysis of the 2 trials examined the efficacy of endovascular therapy in addition to intravenous tissue plasminogen activator (IV tPA) vs IV tPA alone and demonstrated that endovascular therapy after IV tPA improved outcomes in patients presenting with severe stroke.

MR CLEAN was the first study to demonstrate efficacy of intra-arterial treatment received within 6 hours of stroke onset in patients with acute ischemic stroke due to intracranial anterior circulation occlusion. IMS III was terminated due to futility but showed evidence of potential treatment benefit in some patient subgroups, including those with NIHSS ≥ 20 . The pooled analysis included all patients in this subgroup from both trials who were treated with IV tPA within 3 hours of onset. However, NIHSS was defined at the time of randomization in MR CLEAN, which was often several hours after starting IV tPA. Thus, an additional exploratory pooled analysis was performed using only those patients from IMS III who had NIHSS ≥ 20 at 40 minutes after starting IV tPA to better approximate MR CLEAN population.

The primary analysis was a logistic ordinal regression on modified Rankin Scale (mRS) at 90 days. The secondary analysis was logistic regression on dichotomized (0-2 vs 3-6) mRS at 90 days.

The pooled analysis included 342 patients (191 in endovascular group vs 151 receiving IV tPA alone). The ordinal analysis of mRS at 90 days favored endovascular intervention with a consistent shift in mRS in both trials and pooled data (adjusted OR, 1.81; 95% CI, 1.21 to 2.70). The dichotomized analysis revealed that 24.1% of patients in the endovascular group had mRS 0 to 2 vs 13.9% receiving IV tPA alone (adjusted OR, 1.85; 95% CI, 1.03 to 3.33).

The exploratory pooled analysis using those patients in IMS III who had NIHSS ≥ 20 at 40 minutes after starting IV tPA included 290 patients (157 in the endovascular group vs 133 receiving IV tPA alone). The following change in NIHSS score occurred in IMS III from pretreatment to 40 minutes: 16 patients worsened to NIHSS ≥ 20 , and 68 patients improved to NIHSS < 20 .

The ordinal analysis of mRS at 90 days favored endovascular intervention (adjusted OR, 2.07; 95% CI, 1.33 to 3.20). Dr Broderick highlighted that 78% of patients were still not functionally independent even after receiving endovascular therapy in addition to IV tPA. The dichotomized analysis showed that 22.3% of patients had mRS 0 to 2 in the endovascular group vs 10.5% receiving IV tPA alone (adjusted OR, 2.65; 95% CI, 1.31 to 5.34).

Dr Broderick concluded that endovascular therapy after IV tPA improved outcome at 90 days for patients with severe stroke, with no increase in mortality. Also IV tPA treatment was associated with improvement to NIHSS < 20 in approximately a third of patients in the IMS III subgroup of those with NIHSS ≥ 20 . He also called for a thoughtful consideration of triage in regional communities for patients with severe stroke who are candidates for endovascular therapy.