Multimodal Cerebral AVM Treatment: A 12 Year Cohort and Comparison to Key Outcomes of the ARUBA Trial

Benjamin Pulli¹, Paul H. Chapman², Christopher S. Ogilvy³, Aman B. Patel², Christopher J. Stapleton², Thabele M. Leslie-Mazwi^{2,4}, Joshua A. Hirsch⁵, Bob S. Carter² and James D. Rabinov^{2,5}

¹Department of Radiology, Stanford Medical Center, Stanford University, Stanford, CA, USA
²Department of Neurosurgery, Massachusetts General Hospital, Harvard Medical School, Boston, MA, USA
³Neurosurgical Service, Beth Israel Deaconess Medical Center, Boston, MA, USA
⁴Department of Neurology, Massachusetts General Hospital, Harvard Medical School, Boston, MA, USA
⁵Department of Radiology, Massachusetts General Hospital, Harvard Medical School, Boston, MA, USA

Object: Curative treatment of unruptured brain AVMs remains controversial after the only randomized controlled trial, ARUBA, was halted prematurely because interim analysis revealed superiority of the medical management group. In contrast, meta-analyses of retrospective cohorts suggest that intervention is much safer than found in ARUBA.

Methods: We retrospectively analyzed 318 consecutive adult patients with brain AVMs treated at our institution with embolization, surgery, and/or proton-beam radiosurgery. Analysis was performed on 142 ARUBA eligible patients (baseline mRS 0-1, no history of hemorrhage), and results were compared to primary and secondary outcomes from ARUBA intervention (N=106) and medical cohorts (N=120).

Results: Patients in our AVM cohort were not statistically different from ARUBA Trial cohorts in age, gender, neurologic exam, and Spetzler-Martin category. There were slightly more left hemisphere AVMs in our study compared to ARUBA intervention arm (N=79; 55.6% vs. N=48; 42.1%, p=0.006)). Embolization was used less frequently as a stand alone or combined therapy in our study compared to ARUBA (N=33; 23.2% vs. N=66; 62.3%, p=0.0001). Surgery and Radiosurgery were both used with more frequency but these were not statistically different from ARUBA.

Annualized stroke rate (hemorrhagic or ischemic) in our cohort was 1.8%, 4.9% in the first 12 months, and 0.8% after the first 12 months, lower than natural history studies and the ARUBA medical management arm (p=0.001). The primary ARUBA endpoint (symptomatic stroke or death) was reached in 13 patients (9.2 %), which compares favorably to the ARUBA intervention arm (39.6%, p=0.0001) and is similar to the ARUBA medical management arm (9.2%, P=1.0). The secondary ARUBA endpoint (mRS ≥2 at 5 years follow-up) was reached in 14.3% of patients compare to 40.5% in the ARUBA intervention arm (p=0.002) and 16.7% in the ARUBA medical management arm (p=0.6).

Conclusions: Our multimodal approach to brain AVM patient selection and treatment yields good clinical outcomes with key safety endpoints (stroke, death and mRS 0-1) better than the ARUBA intervention arm and similar to the ARUBA medical arm at 5 years follow-up. This suggests that tertiary care centers with integrated programs, expertise in patient selection and individualized treatment approaches may allow for better clinical outcomes than reported in ARUBA. It supports current registry studies and merits consideration of future randomized controlled trials of brain AVM patients.

Table 1: Key Clinical Outcomes – Compared to ARUBA

	ARUBA eligible (N=142)	ARUBA intervention (N=106) *	P-value [†]	ARUBA medical management (N=120) *	P-value [‡]
Complete AVM obliteration (%)	80 (56.3%)	47 (44.3%)	0.073	n/a	n/a
mRS 0-1 at 5 years (%)	54/62 (87.1%)	25/42 (59.5%)	0.002	45/54 (83.3%)	0.607
Disability (mRS ≥2) at 5 years (%)	5/62 (8.1%)	13/42 (31.0%)	0.004	7/54 (13.0%)	0.54
Symptomatic stroke (ischemic or hemorrhagic) (%)	13 (9.2%)	42 (39.6%)	0.0001	11 (9.2%)	1.000
Death (%)	3 (2.1%)	4 (3.8%)	0.465	2 (1.7%)	1.000

Reference: Mohr JP, Parides MK, Stapf C, Moquete E, Moy CS, Overbey JR, et al: Medical management with or without interventional therapy for unruptured brain arteriovenous malformations (ARUBA): a multicentre, non-blinded, randomised trial. Lancet 383:614-621, 2014