tPA in patients with ischemic stroke. The final results of ARTSS were presented by Andrew D. Barreto, MD, and James C. Grotta, MD, University of Texas-Houston, Houston, Texas, on behalf of the ARTSS investigators.

The primary (safety) outcome for ARTSS was the incidence of significant (ie, symptomatic or PH-2) intracerebral hemorrhage (ICH). Secondary (signal of efficacy) outcomes included rates of recanalization, measured at 2 and 24 hours by transcranial Doppler (TCD) ultrasonography or CT-angiogram, and modified Rankin Scale score at discharge. There was also a preplanned historical control comparison with the control data (IV-rtPA alone) from the CLOTBUST study [Alexandrov AV et al. *NEJM* 2004].

Eligibility included patients from 18 to 85 years of age who were admitted between 0 and 4.5 hours of stroke onset and met the criteria for intravenous tPA therapy. Subjects were also required to be within the NIH stroke scale (NIHSS) limits of 5–20 on the left hemisphere and 5–15 on the right hemisphere, have a proximal intracranial arterial occlusion that was measured by TCD or CT-angiogram, an INR ≤1.5, and no known hepatic disease. Subjects received full-dose IV-tPA (0.9 mg/kg) plus argatroban, given as a 100-mcg/kg bolus that was started during the tPA infusion and then as a 1-mcg/kg infusion over 48 hours. Argatroban was titrated to a target partial thromboplastin time (PTT)=1.75 by the patient's baseline.

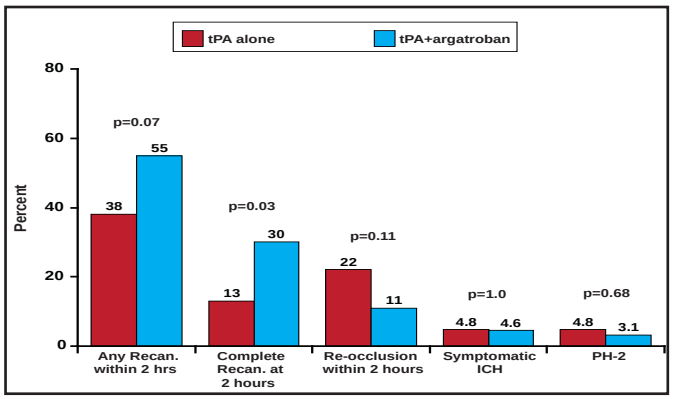
Subjects (n=65) had a mean age of 63 years, and 45% were men. The median subject NIHSS score was 13. Ninety percent of patients had middle cerebral artery occlusions, and the majority of patients were enrolled using TCD (n=47). The median time from the symptom onset to tPA bolus was 128 minutes (interquartile range 94 to 170 minutes). There was a median time of 17 minutes of overlap for the tPA and argatroban.

Target PTT (±10%) was achieved. Significant ICH occurred in 4 subjects (6.2%); three of them were symptomatic hemorrhage (4.6%) and 2 were parenchymal hemorrhage type 2 (PH-2; 3.1%). One patient was symptomatic and had a PH-2. There were 185 adverse events; 28 were considered serious, 3 were likely related to the treatment, and none was considered definitely related to treatment. There were 7 deaths (10.8%) by discharge or Day 7.

Of the 47 subjects who received TCD, 55% recanalized (complete recanalization in 30% and partial recanalization in 26%) at 2 hours. Five subjects (11%) recanalized before 2 hours but reoccluded at 2 hours. Of the 60 subjects with 24-hour data, 60% had complete recanalization and 18% had partial recanalization.

When compared with the controls from the CLOTBUST study, significantly (p=0.03) more patients in ARTSS achieved complete recanalization at 2 hours (Figure 1). There was also a trend toward reduced reocclusion. No difference in symptomatic ICH was found. A randomized, controlled Phase IIb study is planned to confirm and extend these findings.

Figure 1. Comparison to CLOTBUST Controls.



Reproduced with permission from A. Barreto, MD.

Results From the SENTIS Trial

The Safety and Efficacy of NeuroFlo™ (CoAxia) Technology in Ischemic Stroke (SENTIS; NCT00119717) study is a multinational, randomized trial that evaluated partial abdominal aortic occlusion using the NeuroFlo™ catheter as a treatment for acute ischemic stroke. Results were presented by Ashfaq Shuaib, MD, University of Alberta, Edmonton, Canada, and William P. Dillon, MD, University of California, San Francisco, California.

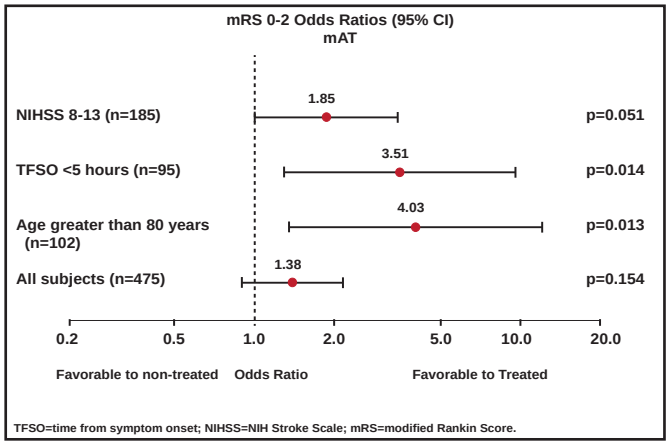
Treatment with NeuroFlo™ involves femoral access and placement of the catheter in the descending aorta, followed by sequential inflation of two independently controlled balloons in the infra- and suprarenal positions, each to 70% luminal occlusion, for 45 minutes. Preclinical studies in swine have demonstrated a 35% to 50% increase in cerebral blood flow with this technique [Hammer M et al. *Cerebrovasc Dis* 2009], and studies in small animals have shown a reduction in infarct size [Noor R et al. *J Neuroimaging* 2009]. Safety and indications of clinical benefit have been shown in human feasibility trials in ischemic stroke [Liebeskind D. *Curr Cardiol Rep* 2008]. The hypothesis is that partial occlusion of the abdominal aorta will augment cerebral blood flow via collateral perfusion, thus limiting stroke progression and improving outcomes.

The SENTIS trial included subjects (n=515) with a clinical diagnosis of stroke, a time from symptom onset of 0 to 14 hours, and a baseline NIH Stroke Scale (NIHSS)

score of 5–18 and those who were ineligible for IV-tPA or thrombectomy. All subjects had baseline CT or MRI imaging to exclude hemorrhage and 24-hour scans postenrollment, when possible. Eligible subjects were randomly assigned to standard medical management or to NeuroFlo™ treatment plus the same medical management.

There was no significant difference in the overall population between the treatments in either the primary global efficacy score (OR, 1.17; p=0.407) or secondary endpoint of improvement in dichotomized modified Rankin Score (mRS) 0–2 (OR, 1.34; p=0.202), as measured in the predefined modified intent-to-treat population. Findings were similar when measured in the as-treated population, with a mRS 0–2 (OR, 1.38; p=0.154; Figure 1). Within the Rankin distribution, use of the NeuroFlo™ was associated with a 9% increase in subjects with a mRS score of 0–2 and a 30% decrease in those with a score of 5–6. A post hoc analysis revealed that subjects with NIHSS scores of 8–13 were more likely to benefit from NeuroFlo™ treatment (OR, 1.85; p=0.051) and that there was a significant (p=0.014) benefit associated with early treatment (<5 hours). Older age also influenced the benefit, particularly for subjects >80 years of age (OR, 4.03; p=0.013).

Figure 1. mRS 0–2 Outcomes (As-Treated Population).

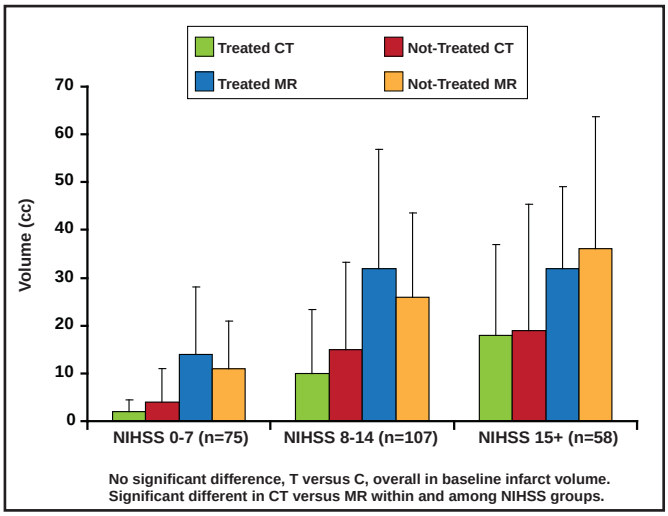


Reproduced with permission from W. Dillon, MD.

In addition to the baseline and 24-hour required imaging, centers were encouraged to perform baseline and post-treatment perfusion imaging (MR or CT) and angiograms. For the imaging analysis, 280 baseline CT or MR perfusion studies and 196 follow-up CT or MR perfusion studies were available for analysis. From these two groups, 148 with paired pre- and posttherapy CT or MRI perfusion sets were available for review. A significant perfusion change was defined as: volume change >10 cc and percentage change >20% for relative mean transit time (rMTT)/mismatch, or volume change >5 cc and percentage change >20% for core infarct.

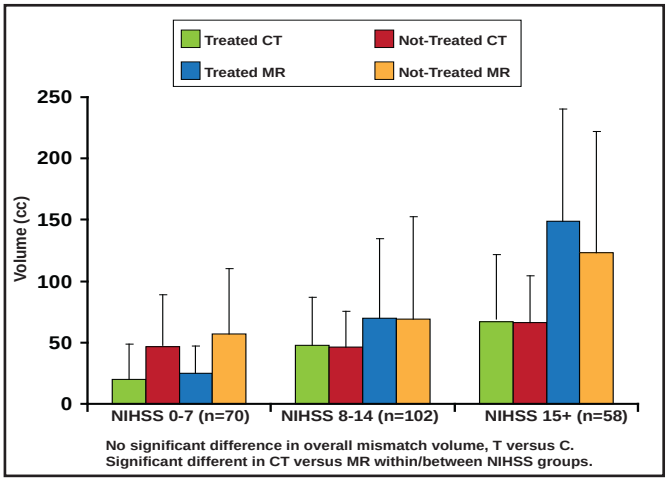
At baseline, there was no overall difference between treated and control groups with respect to core and mismatch volumes, but there was high variability in the mean. The core infarct and mismatch volumes were significantly larger on MRI versus CT across all NIHSS groups (Figures 2A and 2B). More proximal occlusions at baseline correlated with larger core infarcts and higher NIHSS scores. There were no significant differences between groups in the mean/median baseline CT or MR parameters (CBV, CBF, rMTT), measured on perfusion imaging. In terms of outcomes, however, those with MR mismatches at baseline showed improved responses to treatment, based on a 90-day dichotomized mRS 0–2 measure (OR, 15.75; 95% CI, 1.11 to 222.6; p=0.041); however, there was a large confidence interval.

Figure 2A. Baseline Imaging Characteristics: Core Infarct Volume.



Reproduced with permission from W. Dillon, MD.

Figure 2B. Baseline Perfusion Characteristics: Mismatch Volume.



Reproduced with permission from W. Dillon, MD.