No symptomatic intracerebral hemorrhages (sICHs) occurred in either Cohort 1 or controls; 3 (27%, with 2 fatal) sICHs occurred in Cohort 2. Patients with sICH had significantly ($p<0.04$) higher blood pressures during and after treatment.

Sustained complete, partial, and no recanalization was seen in 67%, 17%, and 17% of Cohort 1; 46%, 0%, and 55% of Cohort 2; and 33%, 25%, and 42% of control patients, respectively. Three-month mortality was 0% (Cohort 1), 30% (Cohort 2), and 0% (control). The median time to any recanalization tended to be shorter in Cohort 1 (30 min) and Cohort 2 (30 min) compared with controls (60 min; $p=0.054$). At 3 months, 75% of patients in Cohort 1, 50% in Cohort 2, and 36% in controls ($p=0.167$) achieved mRS scores of 0-1 (Table 1).

Table 1. TUCSON Primary Endpoints.

End-Point	Activity Endpoints (%)			
	Cohort 1 (1.4 mL infusion)	Cohort 2 (2.8 mL infusion)	Control	p
Sustained compete recanalization	67	46	33	0.221
Recanalization				0.177
Complete	67	46	33	
Partial	17	0	25	
Persisting occlusion	17	55	42	
Re-occlusion	8	27	8	0.331
Median minutes to any recanalization	30 min	30 min	60 min	0.054
Dramatic early clinical recovery	42	27	17	0.396
3-month mortality	0	30	0	0.022
mRS 0-1	75	50	36	0.167
mRS 0-2	83	60	55	0.297

Dr. Molina listed several limitations of the study, including a relatively small sample size, the inability to extend enrollment, and the use of an operator-dependent technology, such as TCD. Although the results were encouraging, the study was terminated by the sponsor due to administrative reasons. The rate of sICH that was observed in Cohort 2 may have been related to excessive blood pressure. Alternatively, bleeding with the higher μS dose could have been related to greater mechanical stress to the endothelium and tissues. Further studies will be needed to assess this issue.

The Field Administration of Stroke Therapy—Magnesium (FAST-MAG) Phase III Clinical Trial

A novel and innovative neuroprotective stroke treatment trial is underway in Los Angeles County that could impact 50% of the 600,000 patients diagnosed with ischemic stroke each year in the United States. The aim of the study is to demonstrate that paramedic initiation of intravenous magnesium sulfate ($MgSO_4$) within 2 hours of symptom onset improves the long-term functional outcome of hyperacute stroke patients. Jeffrey L. Saver, MD, David Geffen School of Medicine, Los Angeles, CA, presented the initial findings of the Field Administration of Stroke Therapy-Magnesium (FAST-MAG; NCT00059332) Phase III Trial. The results that were discussed in this poster involved 719 (55.3%) of the 1,298 planned patient enrollment into the multicenter, randomized, double-blind, placebo-controlled trial.

If given early enough, $MgSO_4$ reduces infarct volume, inhibits neuronal death, and attenuates motor impairment in animal models of cerebral ischemia [Enomoto T et al. *Clin Calcium* 2004]. A previous proof-of-concept study that involved 20 patients showed that field initiation of $MgSO_4$ to ischemic or hemorrhagic stroke patients is feasible and safe. Good functional outcome at 3 months (Rankin Scale Score ≤2) occurred in 60% of the treated patients [Saver JL et al. *Stroke* 2004]. However, early initiation of neuroprotective agents after stroke onset is crucial to success.

In the present study, suspected strokes were identified by the Los Angeles Prehospital Stroke Screen (LAPSS) method. Stroke severity was measured using the Los Angeles Motor Scale (LAMS), a 5-point prehospital deficit scale that characterizes pretreatment stroke severity. Patients were included in the study if they were aged 40 to 95 years, symptom onset occurred within 2 hours of treatment initiation, and a deficit was present at ≥15 minutes. Patients who were in a coma or who had rapidly improving neurologic deficits, pre-existing neurologic conditions and/or psychiatric or advanced systemic disease were excluded from the study. All patients were ambulance-transported. Prehospital explicit informed consent was obtained by cell phone. Paramedics administered an intravenous loading dose of $MgSO_4$ or matched placebo in the field at 4 grams over 15 minutes. In the emergency department, a maintenance infusion of

16 grams $MgSO_4$ or matched placebo was given over 24 hours. Patient demographics and baseline characteristics are shown in Table 1.

Table 1. Demographics and Baseline Characteristics of FAST-MAG Patients.

Age; mean years (range)	70 (40-95)
Gender (%)	
Male	58
Ethnicity (%)	
Hispanic	22
Race (%)	
White	80
Black	11
Asian	6
Pacific Islander	2
Stroke Severity (range)	
LAMS[1]	4.0 (1-5)
NIHSS[2]	9.0 (0-40)
Stroke Subtype (%)	
Cerebral Ischemia	72
Ischemic Stroke	62
TIA	10
Intracerebral hemorrhage	23
Stroke Mimic	4
Concomitant Therapy (%)	
IV TPA[3]	28

[1]Prehospital; [2]At hospital arrival and after treatment starts; [3]Among all cerebral ischemia patients.

The median time to study drug initiation from stroke onset was 46 minutes, the mean time of paramedic arrival to drug initiation was 30 minutes, and mean time from paramedic arrival and the patient's arrival in the emergency department was 35 minutes. Treatment was initiated within 1 hour of stroke onset in 73% and between 1 to 2 hours in 25% of patients. The primary study endpoint is the modified Rankin Scale (mRS) score, assessed 3 months poststroke. The Cochran-Mantel-Haenszel test will be used to compare outcomes between the $MgSO_4$ and placebo treatment groups. These results will be presented in a future report.

Dr. Saver concluded that prehospital administration of neuroprotective agents substantially reduces on-scene-to-needle time. He listed a number of innovative firsts for the FAST-MAG trial: first "golden" hour (<1 hour) stroke treatment trial; first acute (<3 hr) neuroprotective stroke treatment trial; first trial of neuroprotective drugs before recanalization therapies; first prehospital stroke RCT; and first prehospital RCT for any condition that employed physician-elicited informed consent.

Dramatic Early Improvement in the NINDS Trial: Better 90 Day Outcomes and No Increased Rates of Intracranial Hemorrhage

NIHSS baseline score and time to treatment <90 minutes are independent predictors of dramatic early response to rt-PA therapy. The occurrence of intracerebral hemorrhage (ICH) is similar between dramatic and nondramatic responders.

Clinical experience demonstrates that a certain percentage of patients with acute ischemic stroke improve rapidly after the administration of IV-rtPA [Felberg RA et al. *Stroke* 2002]. Although research in a small number of patients has pointed to the development of subtypes of mild hemorrhage as a marker for early recanalization and good clinical outcomes at 90 days (OR, 10.9) [Molina CA et al. *Stroke* 2002], anecdotal clinical experience has suggested a potential relationship between dramatic early improvement and posttreatment symptomatic ICH.

Jordan Bonomo, MD, University of Cincinnati, Cincinnati, OH, reported on the results of a retrospective study that used data from the rt-PA arm of the National Institute of Neurological Disorders (NINDS) trial [Kwiatkowski TG et al. *New Engl J Med* 1999] to evaluate dramatic early improvement after treatment with IV-rt-PA as a risk factor for the development of posttreatment ICH. A secondary objective was to characterize the subgroup of patients with dramatic early improvement.

Demographics, baseline clinical characteristics, rates of ICH, and outcomes were compared between subjects with and without dramatic improvement. Dramatic improvement was defined as either NIHSS ≤2 at 2 hours or a 10-point improvement from baseline at 2 hours after initiation of therapy [Alexandrov et al. *Stroke* 2000]. Logistic regression was used to predict posttreatment ICH, as well as good clinical outcome at 90 days (mRS 0-1).

Of the 312 patients who were treated with IV-rt-PA, 65 (20.8%) had dramatic early improvement and 246 (78.8%) did not. Early dramatic improvement was strongly associated with good clinical outcome at 90 days (78% dramatic responders vs 33% of nondramatic responders; p<0.0001). NIHSS baseline score and time to rt-PA therapy <90 minutes were the only independent predictors of early dramatic improvement. The occurrence of ICH by 36 hours